THESE DE DOCTORAT DE L'UNIVERSITE PIERRE ET MARIE CURIE ET DE L'ECOLE DES HAUTES ETUDES EN SANTE PUBLIQUE

Spécialité : Epidémiologie

ECOLE DOCTORALE PIERRE LOUIS DE SANTE PUBLIQUE
ED 393 Epidémiologie et Sciences de l'Information Biomédicale

---

Présentée par

YOUSSOUF Hassani

Pour obtenir le grade de
DOCTEUR

DE L'UNIVERSITE PIERRE ET MARIE CURIE ET
DE L'ECOLE DES HAUTES ETUDES EN SANTE PUBLIQUE

EFFETS RESPIRATOIRES DE LA POLLUTION ATMOSPHERIQUE : PRISE EN COMPTE DE PLUSIEURS NIVEAUX DE POLLUTION

Thèse soutenue le : 23 Décembre 2014

COMPOSITION DU JURY

Pr Isabella ANNESI-MESANO	Directrice de thèse
Pr Benjamin HANOUNE	Rapporteur
Pr Denis ZMIROU	Rapporteur
Pr Sébastien PAYAN	Examinateur
Pr Dominique VALEYRE	Examinateur
Pr Marc SCHENKER	Examinateur

REMERCIEMENTS

En tout premier lieu, je tiens à remercier très chaleureusement ma directrice de thèse, Isabella Annesi-Maesano, pour ces quatre années de travail sous sa responsabilité. Je la remercie pour les discussions enrichissantes que nous avons eues ensemble ainsi que pour sa disponibilité et sa confiance. Je la remercie infiniment pour m'avoir donné la chance d'atteindre cet objectif qui me tenait à cœur.

Je tiens également à exprimer ma gratitude à Benjamin HANOUNE, Sébastien Payan, Denis Zmirou, Dominique Valeyre, Marc Schenker d'avoir bien voulu me donner de leur temps pour faire partie de ce jury. Je suis particulièrement reconnaissant à l'égard de Benjamin Hanoune et Denis Zmirou, d'avoir accepté de juger mon travail de thèse en étant rapporteurs.

Mes sincères remerciements vont également à Marc Schenker non seulement pour sa présence en tant que membre de Jury mais aussi et surtout pour m'avoir accueilli au Center for Occupationnal and Environnemental Medecine, à l'Université de Californie à Davis, Etats-Unis, pendant 3 mois et pour les conseils avisés qu'il m'a donnés. Je remercie également ses collaborateurs pour l'accueil chaleureux qu'ils nous ont réservé, à moi et à ma femme, en particulier à Diane Mitchell avec qui je travaillais tous les jours, et à Sandra Freeland et Suzette Smiley-Jewell pour leurs immenses services.

Ce travail de thèse est basé sur plusieurs études épidémiologiques impliquant le travail et la participation de nombreuses personnes. Je tiens particulièrement à remercier Cathy Liousse, Laurent Roblou et Eric-Michel Assomoi pour leur travail qu'ils ont mené dans le cadre du projet PHASE et la mise à dispositions des données des émissions des incendies, Franck Vibert pour le dur travail qu'il a mémé sur le terrain dans le cadre de l'étude FERMA. Je remercie également Franke F. et Pascal L. du CIRE InVS - ARS Paca pour la mise à disposition des données sanitaires de l'Assistance Publique Hôpitaux de Marseille que nous avons utilisées dans l'étude de cas de Marseille.

Je remercie Guy Thomas, directeur de l'unité 707 (Epidémiologie, Système d'Information et Modélisation), pour m'avoir accueilli dans sa structure ainsi que

tous les membres de cette unité, et plus particulièrement Wideline Jacques et Liliane Narme pour m'avoir aidé à résoudre tout un tas de problèmes administratifs. Je remercie Dominique Costagliola, directrice de l'Ecole Doctorale ED393 et de l'Institut Pierre Louis de Santé Publique, pour les conseils qu'elle m'a donnés en sa qualité de ma tutrice et qui m'ont permis de mieux avancer sur ces travaux de recherches.

Merci en particulier à tous mes collègues qui font ou ont fait partie de l'équipe EPAR et avec qui j'ai passé de très bon moments, en particulier Cailang Zhou avec qui nous mangions souvent ensemble au restaurent universitaire et Soutrik Banerjee pour son aide technique sur le plan statistique et sa collaboration sur les projets.

Un grand merci à Amalia Tirsoreanu pour avoir bien voulu relire mon manuscrit et corriger les fautes d'orthographes sur un délai très court.

Ces remerciements seraient incomplets si je n'en adressais pas à ma famille et à mes amis sans qui ce travail n'aurait jamais abouti. Tout d'abord, je souhaite remercier mes parents qui dès mon jeune âge m'ont guidé et soutenu. En particuliers à mon oncle maternel Mohamed Kamaldine, qui s'est sacrifié pour me soutenir et me faire avancer, (ainsi que mes frères et sœurs) à un moment crucial de ma vie. Sans lui, je n'aurai probablement pas eu ce parcours et ne serais pas arrivé jusqu'à ce niveau d'études. Une mention spéciale pour ma grand-mère, je pense à elle et j'espère que j'aurai l'occasion de la revoir un jour.

Mes remerciements vont aussi à l'endroit de ma cousine et belle-sœur Hadidja Aliamini et son Mari Mr Youssouf Ben Ali, mon beau-frère, Youssouf Moumine, pour leur soutien indéfectible tout au long de ma scolarité et qui en sont les garants de la réussite de mes études en France. Qu'ils trouvent dans ces remerciements le témoignage de ma gratitude et ma reconnaissance. Je tiens également à remercier les autres membres de la familles pour leur soutien en premier lieu ma belle-sœur Hissani Aliamini , ma petite sœur Saniati Hassani sans oublier mes petits neveux, nièces, cousins, cousines, en premier lieu Moindjie Nassim, Moindjie Loubna, et la pétillante Moindjie Youmna, Housna Houssein, Fakri sans oublié le petit dernier DJae Camille Youssouf Moumine. J'ai eu la grande chance que vous soyez toujours là pour moi. Merci également à mon ami Saandi Hamza pour son soutien et son sens de service.

Enfin, en dernier lieu et elle est loin d'être la dernière sur ma liste, je tiens à remercier celle qui partage ma vie, ma femme, Antufa Aliamini, pour son soutien, sa compréhension et son sens de sacrifice dans ces moments où je devais consacrer plus de temps à atteindre cet objectif professionnel au détriment de notre vie de famille. Sans oublier bien sur notre petit bout de chou Mhoussine Youssouf, né durant cette dernière année de thèse, âgé de 2 mois au moment où je rédige ces remerciements, pour m'avoir donné un sens de responsabilité et les joies de la paternité. Je lui souhaite un parcours beaucoup plus meilleur que le mien et j'espère que j'aurai la possibilité et le temps de rendre ça possible, inchallah.

Et un grand merci aussi à tous ceux que j'ai pu oublier.

RESUME

Les objectifs de ces travaux de recherche sont d'étudier les effets respiratoires de la pollution atmosphérique en prenant en compte 3 niveaux d'exposition: le niveau macroscopique, le niveau semi-individuel et les biomarqueurs.

Pour la prise en compte du niveau macroscopique, nous avons étudié les effets sanitaires des émissions des feux de forêts incontrôlés dans une étude épidémiologique de type écologique. Au travers d'une revue de la littérature, nous avons observé que plusieurs études épidémiologiques avaient mis en évidence l'association entre l'exposition des émissions des feux de forêts et l'augmentation des symptômes et des maladies cardiopulmonaires pour les individus habitant à proximité. Quelques études ont également associé l'exposition aux particules fines et l'augmentation du taux de mortalité dont la mortalité respiratoire. La principale limite de ces études est donnée par l'évaluation de cette exposition, aucune mesure individuelle ou semi-individuelle n'étant entreprise pour l'estimer. Dans une étude de cas sur les incendies de Marseille de l'été 2009, en utilisant une approche de modélisation pour estimer les émissions et les concentrations anthropiques et liés à l'incendie, nous avons observé des effets à la limite de la signification 8 et 9 jours après l'exposition (lag8-lag9) entre les concentrations des particules fines ($PM_{2.5}$, les particules d'aerodiamètre inférieur à 2,5) issues des incendies et les effets respiratoires. Des effets significatifs ont été trouvés entre les concentrations en $PM_{2.5}$ d'origine anthropique et les consultations pour toutes causes entre 2 à 5 jours après l'exposition (lag2 à lag5).

Pour la prise en compte du niveau semi-individuel, nous avons étudié le lien entre la pollution domestique et professionnelle et les maladies respiratoires chez des agriculteurs auvergnats dans le cadre d'une étude de type transversale. En considérant une exposition globale à la ferme, nous avons observé que les dérivés halogénés et l'étyl-butoxyacetate étaient associés de façon significative aux maladies des petites voies aériennes définies par la spirométrie (DEM25-75 <80% et VEMS / CVF >70%). La concentration de benzène dans la pièce de vie principale (living) de la ferme était significativement associée à une augmentation du risque d'asthme, ce qui confirme les résultats d'autres études. Enfin, l'utilisation de l'acide mercapturique, métabolite du benzène, dans le cadre d'une étude de type cas témoin nichée nous a permis de mesurer la dose interne d'exposition à ce polluant parmi des enfants de l'école primaire et son lien avec l'asthme.

Les résultats mis en évidence dans le cadre de notre travail montrent la diversité des polluants susceptibles d'avoir des effets respiratoires, qu'il s'agit d'une exposition - en milieu professionnel ou au domicile - à court terme, avec des concentrations élevées, ou à long terme, avec de faibles concentrations. Une estimation pertinente de l'exposition doit demeurer un élément essentiel dans l'évaluation de l'impact sanitaire de la pollution atmosphérique.

Mots clés : épidémiologie, feux de forêts, effets sanitaires, pollution atmosphérique, asthme, Small airways diseases, COV, PM, exposition, milieu agricole.

ABSTRACT

The objectives of this research were to investigate the respiratory effects of air pollution by taking into account three levels of exposure: the macroscopic level, the semi-individual level and the individual level using biomarkers.

Regarding the macroscopic level, we studied the health effects of uncontrolled wildfire in an ecological study. Through a literature review, we found that several epidemiological studies have demonstrated the association between exposure to emissions from forest fires and increased cardiopulmonary symptoms and disease for individuals living nearby. Some studies have also linked exposure to fine particles and increased mortality rates. The main limitation of these studies was the exposure assessment. No individual or semi-individual measurements were undertaken in most studies.

Regarding the macroscopic level, we studied the health effects of uncontrolled wildfire in an ecological study. Through a literature review, we found that several epidemiological studies have demonstrated the association between exposure to emissions from forest fires and increased cardiopulmonary symptoms and disease for individuals living nearby. Some studies have also linked exposure to fine particles and increased mortality rates including respiratory mortality. The main limitation of these studies was the exposure assessment. No individual or semi-individual measurements were undertaken in most studies.

In a case study on fires Marseille in the summer of 2009, using a modeling approach to estimate the anthropogenic emissions and concentrations related to the wildfire, we observed effects to the limit of significance in 8 and 9 days after exposure (lag8 and lag 9) between the concentrations of fine particulate matter (PM2.5, particulate matter less than 2.5µm) from fires and respiratory effects. Significant effects were found between the concentrations of anthropogenic PM2.5 and consultations for all causes between 2-5 days after exposure (lag2 to lag 5).

Regarding the semi-individual level, we investigated the link between occupational and home air pollution exposure and respiratory diseases among farmers from Auvergne region. When we consider exposure in the overall exposure in the farm, we found that exposure to halogenated hydrocarbons and exposure to Ethyl butoxyacetate was significantly associated with disease of the small airways defined by spirometry (FEF 25-75 <80% and FEV / FVC> 70 %). the benzene concentration in the main living room of the farm was significantly associated with an increased risk of asthma, which confirms the results of other studies.

Finally, the use of the mercapturic acid, metabolite of benzene, in the context of a nested case-controls study, allowed us to measure the internal dose of exposure to this pollutant among children of primary school and its relationship with the asthma.

The results highlighted in the context of our work showed the diversity of pollutants likely to have respiratory effects, whether exposure - in the workplace or at home - in the short term, with high concentrations or long-term, with low concentrations. Relevant exposure estimate must remain a key element in assessing the health impact of air pollution

Keywords: epidemiology, forest fires, health effects, air pollution, asthma, Small airways diseases, VOC, PM, exhibition, agriculture.

PUBLICATIONS ET COMMUNICATIONS

Articles publiés :

1. **Youssouf, H.,** Liousse C., Roblou L., Assamoi E.M., Salonen RO., Maesano C., Banerjee S., Annesi-Maesano I. on behalf of the PHASE Study. Quantifying wildfires exposure for investigating health-related effects. Atmospheric Environment, 2014. 97(0): p. 239-251.
2. **Youssouf, H.,** Liousse, C., Roblou, L., Assamoi, E.M., Salonen, R.O., Maesano, C., Banerjee, S., Annesi-Maesano, I., on behalf the PHASE Study 2014. Non-accidental Health impacts of wildfire, International Journal of Environmental Research and Public 2014, *11*, 11772-11804.
3. Rive S, Hulin M, Baiz N, **Hassani Y,** Kigninlman H, Toloba Y, Caillaud D, Annesi-Maesano I. Urinary S-PMA related to indoor benzene and asthma in children. Inhalation toxicology. 2013;25:373-382.
4. Gennaro D'Amato, Isabella Annesi-Maesano, Lorenzo Cecchi, Mona Al-Ahmad, Fatma Al-Enezi, Saleh Al-Muhsen, Ignacio Ansotegui, Carlos E. Baena-Cagnani, David Baker, Karl Christian Bergmann, Louis Philippe Boulet, Hasan Bayram, Jeroen T.M. Buters, Maria D'Amato, Jeroen Douwes, Sarah Elise Finlay, Donata Garrasi, Maximiliano Gómez, Tari Haahtela, Rabih Halwani, **Youssouf Hassani**, Dennis Ledford, Basam Mahboub, Guy Marks, Paola Michelozzi, Marcello Montagni, Carlos Nunes, Jay Jae-Won Oh, Todor Popov, Portnoy, Erminia Ridolo, Nelson Rosário, Menachem Rottem, Mario Sánchez-Borges, Elopy Sibanda, Juan José Sienra-Monge, Carolina Vitale, Ruby Pawankar, Stephen T. Holgate. Meteorological Conditions, Climate Change, New Emerging Factors and Bronchial Asthma. A Statement of the World Allergy Organization, WAO Journal (*in press)*.

Articles soumis et insérés dans le manuscript

1. **Youssouf H.,** Caillaud D., Baïz N., Banerjee S., Ramousse O. Bertholon JF., Annesi-Maesano I. 2014. Exposure to particulate matter and volatile organic compounds in dwellings and stables and respiratory health in French farmers. *Indoor air (soumis)*

2. **Youssouf H.,** Mitchell D. Schenker MB. Caillaud D., Banerjee S., Baïz N., Ramousse O. Bertholon JF., Annesi-Maesano I. 2014. Risk factors for respiratory symptoms in French and California farmers. *International Archives of Occupational and Environmental Health (soumis)*
3. **Youssouf H,** Banerjee S, Liousse C, L. Roblou, Franke F, Pascal L, Annesi-Maesano I1, on behalf the PHASE study. The temporal lag structure of short term-term associations of fine particulate matter (PM2.5) and emergency visits in during the 2009 wildfire season in Marseille. *Environ Health Perspect (soumis).*

Communications scientifiques

1. **Youssouf H.** Banerjee, S., Liousse, C., Roblou, L., Assamoi, E.M., Salonen, R.O., Maesano, C., Annesi-Maesano, I., Forest fires case study Marseilles public health strategies. Reunion du projet PHASE (Public Health Adaptation Strategies to Extreme Weather Events in Europe), Rome, Italie 04-06 Juin 2014 (*communication orale*)
2. **Youssouf H.,** Liousse, C., Roblou, L., Assamoi, E.M., Salonen, R.O., Maesano, C., Banerjee, S., Annesi-Maesano, I., Inventory of wildfire emissions in Europe. Réunion du projet PHASE (Public Health Adaptation Strategies to Extreme Weather Events in Europe), Paris, France 13-15 Mai 2012 (*communication orale*)
3. **Youssouf, H.,** Liousse, C., Roblou, L., Assamoi, E.M., Salonen, R.O., Maesano, C., Banerjee, S., Annesi-Maesano, I., On behaf the PHASE study. wildfire, exposure assessement and related health impact. International smoke symposium, Université de Maryland à College Park MD, Etats-Unis, 21-24 Oct 2013 (*communication affichée*)

Publication didactique en dehors de la thèse

Youssouf H. Le risque sanitaire de la fumée issue des ménages comoriens. La gazette des Comores, édition 2165 du 18 avril 2014, disponible sur : http://www.lagazettedescomores.com/spip.php?article3224

ABREVIATIONS

ADMS	Atmospheric Dispersion Modelling System
AOD	Aerosol Optical Depth
AMMA	Analyses Multidisciplinaires de la Mousson Africaine
APHM	Assistance Publique Hôpitaux de Marseille
ARS	Agence Régionale de Santé
BaP	Benzo(a)pyrène
BPCO	broncho-pneumopathie chronique obstructive
CIRC	Centre international de recherche sur le cance
COV	Composés Organique Volatiles
CVF	Capacité Vitale Forcé
DARES	Direction de l'animation de la recherche, des études et des statistiques
DDT	Dichlorodiphényltrichloroéthane
ECE	Evènements Climatiques Extrêmes
eNO	exhaled Nitric Oxide (*Oxyde Nitrique exhalé)*
FERMA	Facteurs Environnementaux en milieu Rural et Maladies Allergiques et respiratoires
HAP	Hydrocarbure Aromatique Polycyclique
INVS	Institut Nationale de Veille Sanitaire
MIMO	Multiple Inputs Multiple Outputs
MODIS	MODerate Resolution Imaging Spectroradiometer
NASA	National Aeronautics and Space Administration
NIOSH	National Institute for Occupational Safety and Health
OMS	Organisation Mondiale de la Santé
OSPM	Operational street pollution model
PACA	Provence Alpes et Cote d'Azur
PCB	Polychlorobiphényles
PHASE	Public Health Adaptation Strategies to Extreme weather events
PDF	maladie du poumon de fermier
PM	Particulate Matter (Particules en suspension)
PM_{10}	Particules dont le diamètre est inférieur à 10 micromètres
$PM_{2.5}$	Particules dont le diamètre est inférieur à 2.5 micromètres
PPM	Partie Par Million
UE	Union Européenne
WP	Work Package
VGAI	Valeurs Guides de qualité d'Air Intérieur

VME	Valeur moyenne d’exposition
VMES	Volume Expiratoire Maximal par Seconde

TABLE DES MATIERES

REMERCIEMENTS **1**
RESUME **4**
ABSTRACT **5**
PUBLICATIONS ET COMMUNICATIONS **6**
ABREVIATIONS **8**
LISTES DES TABLEAUX ET DES FIGURES **13**
INTRODUCTION **14**
OBJECTIFS **21**
CHAPITRE I: EXPOSITION DE LA POLLUTION ATMOSPHERIQUE **22**
I. Introduction à la pollution atmosphérique 22
I.1. Définition 22
I.2. Sources de pollution atmosphérique 23
I.2.1. Sources des polluants de l''extérieur des locaux 23
I.2.2. Sources des polluants de l'intérieur des locaux 23
I.2.2.1. Les sources de pollution liées aux activités dans les habitations 24
I.2.2.2. Les sources liées aux produits de construction et d'aménagement 24
I.3 Niveaux d'exposition des populations 30
II. Niveaux de mesure de l'exposition à la pollution atmosphérique 31
CHAPITRE II: IMPACT SANITAIRE DES FEUX DE FORETS **34**
I. Présentation de la problématique 34
II. Exposition aux émissions issues des incendies 35
II.1. Définition des feux de forets 35
II.2. Composition de la fumée issue des feux de forets 35
II.3. Facteurs d'influence de l'émissions des polluants 38
II.4. Impact sanitaire des polluants issus des incendies 40
III. Présentation du projet PHASE visant à établir les risques sanitaires associés aux feux de bois 45
III.1. Présentation générale 45
III.2. Présentation du WP6: prévention des effets sanitaires des feux de forêt 47
IV. Effets sanitaires des émissions de feux de forêts : présentation des résultats 48
IV.1. Presentation de article 1: Quantifying wildfires exposure for investigating related-health effects 48
IV.2. Présentation de l'article 2 : Non-accidental health impact of wildfire 61

IV.2.1. Au-delà des effets non accidentels 95
IV.3. Presentation de l'article 3: The temporal lag structure of short term-term associations of fine particulate matter ($PM_{2.5}$) and emergency visits in during the 2009 wildfire season in Marseille. 96
V. Conclusions 111
CHAPITRE III : EXPOSITION EN MILIEU RURAL 113
I. Présentation de la problématique 113
II. Pollution en milieu agricole rural.....114
II.1. Les sources d'exposition liées à l'activité agricole 114
II.2. Caractéristiques des principaux polluants agricoles 115
II.3. Exposition à l'intérieur des habitations 117
II.3.1. Les sources liées à l'intérieur des habitations 118
II.3.2. Les sources liées aux produits de construction et d'aménagement 118
II.4. Les effets sanitaires des polluants en milieu agricole rural 118
III. Présentation des études 121
III.1. Etude des facteurs environnementaux du milieu Rural et Maladies Allergiques et respiratoires (FERMA).....121
III.2. UC Davis Farmer Health Study (FHS) : Etude de la santé des agriculteurs de l'Université de Californie à Davis 123
IV. Résultats issus de nos études épidémiologiques 124
IV.1. Presentation de article 4: Exposure to particulate matters and volatile organic compounds in dwellings and stables and respiratory health in French farmers.....124
IV.2. Presentation de l'article 5: Risk factors for respiratory symptoms in French and California farmers.....156
V. Conclusions 182
VI. Utilisation d'un biomarqueur pour évaluer l'exposition individuelle d'un polluant : cas du benzène 183
CHAPITRE IV : SYNTHESE ET REFLEXIONS 184
I. Principaux résultats 184
II. Discussion générale 187
II.1. Impact sanitaires des incendies.....187
II.2. Mieux évaluer l'exposition lors des incendies de forets 188
II.3.Inventaires des émissions de feux de forêts.....189
II.4. Résultats du de l'étude de cas à Marseille.....191
II.5. Evaluation des polluants agricoles et leurs effets sur la santé : Mieux évaluer l'exposition individuelle 192
II.6. Implication de la pollution intérieure dans la santé respiratoire des enfants à la ferme: volet « enfant » de l'étude FERMA.....193

II.7. La variabilité régionale en termes d'exposition aux polluants agricoles et les effets sanitaires.....195
II.8. Les points forts et les limites 196
II.8.1. Points forts 196
II.8.2. Limites.....198
CONCLUSIONS..... 200
ANNEXES..... 203
BIBLIOGRAPHIE..... 214
BIBLOGRAPHIE DU MANUSCRIT 214
BIBLOGRAPHIE DES ARTICLES PUBLIES.....221

LISTES DES TABLEAUX ET DES FIGURES

➢ Liste des Figures

Figure 1: Risque relatifs entre la mortalité due aux maladies respiratoires ou cardiopulmonaires et une augmentation de l'exposition à 10µg/m3 de NO_2 ou NO_x. Source : ERS White Book, 2014. 16
Figure 2: Sources de pollution à l'intérieur des habitations [23].....25
Figure 3: Les approches communes concernant la définition des actions de santé publique pour chaque évènement climatique extrême 46
Figure 4: Localisation des participants de l'étude phase I de l'étude FERMA adultes 122
Figure 5**:** Localisation des participants de la phase II de l'étude FERMA adultes 123
Figure 6: Trajectoire des particules en suspension de la fumée vers le système respiratoire 187

➢ Liste des tableaux

Tableau 1: Classification et caractéristiques des polluants à l'intérieur des habitations ..26
Tableau 2: Principaux polluants atmosphériques issus des émissions des feux de forets 37
Tableau 3: Les effets sanitaires des principaux polluants rencontrés dans les émissions des feux de forets.....41
Tableau 4: Pathologies respiratoires en milieu agricole et polluants associés 120

INTRODUCTION

La croissance urbaine nécessite le développement et l'accessibilité à plusieurs facilités comme le transport, l'énergie, l'éducation, l'eau… etc. Cette croissance entraine cependant l'augmentation du parc automobile et des industries pour subvenir aux besoins d'une population de plus en plus croissante. Les gaz et les substances chimiques produits par ces activités anthropogéniques, combinés à des conditions météorologiques défavorables, provoquent, de manière récurrente, des excès de pollution atmosphérique, partout dans le monde. Cette pollution de l'air s'accompagne d'une augmentation de la mortalité prématurée et des effets néfastes pour la santé humaine. Les quelques exemples les plus connus dans le passé sont celui de Donora[1], survenu en octobre 1948, et celui du brouillard de Londres en 1952[2] [1]. Mais des exemples plus récents existent aussi. Dès lors que les chercheurs ont commencé à s'inquiéter sur les impacts sanitaires de la pollution atmosphérique, plusieurs études épidémiologiques ont en fait mis en évidence l'association entre certains polluants atmosphériques et la santé humaine, en particulier les maladies respiratoires et cardiovasculaires. Cela même à de faibles concentrations, en dessous des valeurs standards de la qualité de l'air [2-7]. La liste des polluants mis en cause inclue les oxydes d'azote, le dioxyde de souffre, le monoxyde de carbone, les composés organiques volatiles (VOCs), les hydrocarbures aromatiques polycycliques (HAP) et les particules ou poussières en suspension (PM, particulate matter en anglais). Ces dernières peuvent être inhalées dans les voies aériennes et celles de diamètre inférieur à 2,5 µm, que l'on appelle les particules fines ($PM_{2.5}$), peuvent atteindre les alvéoles, où peuvent franchir la barrière et entrer dans la circulation sanguine et atteindre d'autres organes.

Lors des dernières estimations, publiées en mars 2014, l'Organisation Mondiale de la Santé (L'OMS) a indiqué que plus de 7 millions de décès prématurés en 2012 pouvaient être attribués à l'exposition à la pollution atmosphérique, dont environ 2 millions 6 cent mille à la pollution de l'extérieur des locaux. Soit 1 décès sur 8 dans le monde. La grande majorité des décès dus à la pollution

[1] Il s'agit d'un épisode de pollution atmosphérique formé par un épais smog qui était à l'origine de 20 morts et plus de 7000 personnes tombées malades à Donora en Pennsylvanie en 1948.
[2] Le grand smog de Londres de 1952 est le smog particulièrement dense qui recouvrit Londres durant la période allant du vendredi 5 au mardi 9 décembre 1952, considéré comme la pire pollution atmosphérique de toute l'histoire du Royaume-Uni

atmosphérique (51%) étaient essentiellement liés aux maladies cardiovasculaires et respiratoires [8]. Ces chiffres représentent le double des estimations précédentes et confirment que la pollution de l'air est désormais le premier risque environnemental pour la santé mondiale.

A ce jour, plusieurs études sur la pollution de l'air en milieu urbain ont été recensées [9-12]. On associe d'importants risques sanitaires à l'exposition aux PM en particulier les particules fines, et un lien étroit et quantitatif entre l'exposition à des concentrations élevées en particules (PM_{10} et $PM_{2,5}$) et un accroissement des taux de mortalité et de morbidité, au quotidien aussi bien qu'à plus long terme, ont été mis en évidence par plusieurs études épidémiologiques [13-15]. En effet, une exposition à long terme de PM_{10} est associée à une augmentation de 0.2 à 0.6% du taux de mortalité non accidentelle toutes causes confondues [16, 17] et d'une augmentation de 1.14% des hospitalisations dues aux maladies respiratoires pour chaque augmentation de 10µg/m^3 de PM_{10}. De même, une augmentation du taux de mortalité de 5% a été observée pour une augmentation de 10µg/m^3 de $PM_{2.5}$ pour une exposition à court terme [18], alors qu'à long terme, l'augmentation de 10µg/m^3 de $PM_{2.5}$ était associée à une augmentation de 6% du taux de mortalité chez les plus de 30 ans [19]. De même, la mortalité liée à une telle exposition baisse à mesure que les concentrations en petites et fines particules sont réduites, en supposant que les autres facteurs restent inchangés. De plus, l'ozone (O_3), le dioxyde d'azote (NO_2) et le dioxyde de soufre (SO_2) ont été associés à d'importants risques sanitaires, dont la mortalité (Figure 1).

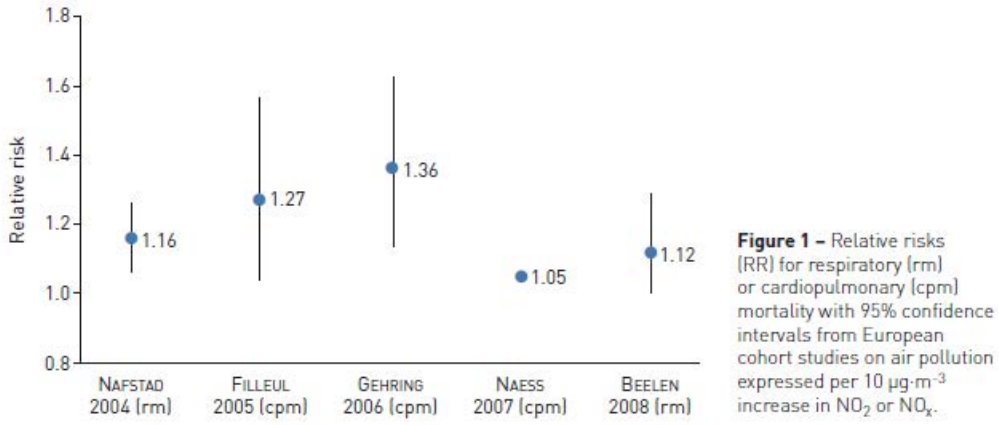


Figure 1 – Relative risks (RR) for respiratory (rm) or cardiopulmonary (cpm) mortality with 95% confidence intervals from European cohort studies on air pollution expressed per 10 $\mu g \cdot m^{-3}$ increase in NO_2 or NO_x.

Figure 1: Risque relatifs entre la mortalité due aux maladies respiratoires ou cardiopulmonaires et une augmentation de l'exposition à 10µg/m3 de NO_2 ou NO_x. Source : ERS White Book, 2014.

Comme c'est le cas pour les particules, les concentrations de ces gaz sont généralement plus importantes dans les zones urbaines, davantage lorsqu'il s'agit des zones urbaines des pays à revenu faible ou intermédiaire. Le dioxyde d'azote, un polluant majeur de l'atmosphère terrestre produit par les moteurs à combustion interne et les centrales thermiques est un gaz irritant pour les bronches et augmente la fréquence et la gravité des crises chez les asthmatiques et favorises les infections pulmonaires infantiles [20, 21] . L'ozone est l'un des principaux facteurs de risque de morbidité et de mortalité liées à l'asthme, le dioxyde d'azote et le dioxyde de soufre ayant, quant à eux, une incidence sur l'asthme, les affections bronchiques, les inflammations pulmonaires et l'altération des fonctions pulmonaires[22]. L'ozone est un gaz irritant de l'appareil respiratoire et des yeux. Il est associé à des problèmes respiratoires, le déclenchement de crises d'asthme, une diminution de la fonction pulmonaire et l'apparition de maladies respiratoires. Par ailleurs, plusieurs études européennes ont signalé un accroissement de la mortalité quotidienne de 0,3% et des maladies cardiaques de 0,4% pour chaque augmentation de 10 $\mu g/m^3$ de la concentration en ozone [22]. Quant au dioxyde de souffre, il affecte le système respiratoire, le fonctionnement des poumons et provoque des irritations oculaires. L'inflammation de l'appareil respiratoire entraîne de la toux, une production de mucus, une exacerbation de l'asthme, des bronchites chroniques et une sensibilisation aux infections respiratoires. Le nombre des admissions à

l'hôpital pour des cardiopathies et la mortalité augmentent les jours de fortes concentrations en SO_2 [22].

D'autres effets récemment identifiés incluent une dégradation des défenses de l'organisme aux infections microbiennes (particules fines) ainsi qu'une incidence sur la mortalité à long terme par effets mutagènes et cancérigènes (particules fines, benzène)…etc.

En milieu urbain, alors que les effets sanitaires de la pollution de l'air extérieur commencent à être bien documentés, on s'interroge toujours sur l'impact sanitaire des polluants présents dans l'air à l'intérieur des locaux. Ici, par rapport à l'extérieur, l'exposition à la pollution est plus diversifiée. Cette interrogation se justifie par le fait que dans les pays industrialisés, les hommes passent plus de 80% de leur temps dans le milieu intérieur, que ce soit à la maison ou au travail, à l' école, dans leurs véhicules [23, 24]. Parmi les polluants à l'intérieur des locaux, on retrouve le radon, gaz radioactif d'origine naturelle, ainsi que certains sous-produits issus des matériaux de construction, les polluants biologiques tels que les moisissures, les champignons, les bactéries, les virus, les acariens et la poussière, le monoxyde de carbone provenant des équipements de chauffage, la fumée du tabac, le dioxyde d'azote, le dioxyde de souffre, les particules respirables en suspension, les composés organiques volatiles, l'amiante qui provient de la détérioration des matériaux ayant servi à la construction des bâtiments, le formaldéhyde. Les effets sanitaires de tous ces polluants commencent à être documentés et des études épidémiologiques récentes ont indiqué que les polluants de l'air intérieur pourraient accroître le risque des phénomènes d'irritation, de sensibilisation allergique, des symptômes et des maladies respiratoires aigus ou chroniques et d'atteinte fonctionnelle pulmonaire [25, 26].

En milieu rural, très peu d'études ont été réalisées pour investiguer les effets sanitaire de la pollution atmosphérique. Pourtant, malgré les progrès des moyens de production, l'agriculture moderne est toujours associée à de nombreuses expositions dangereuses [27]. A l'extérieur des locaux, plusieurs sont les produits chimiques retrouvés dans les exploitations agricoles pouvant être inhalés : les pesticides (eux aussi des particules), les gaz d'échappement, les engrais et les oxydes d'azote [28-30]. Les maladies dues aux pesticides ont bien été identifiées, l'exposition professionnelle aux pesticides ayant entrainé une augmentation significative de la morbidité (asthme, broncho-pneumopathie

chronique obstructive (BPCO) ….) et de la mortalité (leucémie, cancers, ….) parmi les agriculteurs [28, 31]. Dans les pays industrialisés, le tracteur est couramment utilisé dans l'agriculture. Ainsi, la conduite sans une cabine fermée peut exposer le pilote à une grande quantité de poussière, lors de la préparation du sol ou de la récolte [32]. D'autres substances susceptibles d'être inhalées, comprennent divers gaz provenant du processus d'alimentation des animaux enfermés [33]. A l'intérieur des locaux et dans les lieux de travail. Parmi ces expositions, on trouve les poussières, comprenant des particules inorganiques telles que la silice, ainsi que des particules organiques - les moisissures, les bactéries, les endotoxines, les mycotoxines, les pollens, les céréales et les aliments pour animaux.

A côté des formes de pollution décrites ci-dessus, il y a d'autres sources occasionnelles de pollution, que ce soit dans les milieux ruraux ou dans ceux suburbains. La particularité de cette pollution occasionnelle est son intensité élevée sur une courte période d'exposition. C'est le cas de la pollution atmosphérique occasionnée par les feux des forêts. Ces incendies, même sur une courte période, génèrent, à travers la fumée dégagée, une pollution intense dont la composition est estimée à plusieurs milliers de composés chimiques, avec des concentrations généralement beaucoup plus élevées par rapport à la norme [34-36]. En effet, plusieurs études ont montré que la concentration de certains polluants contenus dans les émissions issues des incendies des forêts dépassait largement le seuil standard fixé par les institutions sanitaires [37-40]. Sur le continent nord-américain, l'augmentation des polluants est saisonnière, entre 3 à 8 mois suivant le climat, et variable en fonction des conditions météorologiques. Des concentrations de PM_{10} allant jusqu'à 800 µg/m^3 ont déjà été mesurées dans ces territoires [41], alors que le seuil de PM_{10} est fixé à 150 µg/m^3. Des concentrations moyennes, mesurées en 24 h de 200 à 400 µg/m^3 de $PM_{10,}$ sont souvent retrouvées.

Durant les incendies de 2003 en Colombie Britannique, les régions Kelowna et Kamloops avaient connu, pendant cinq semaines, des moyennes journalières, des particules fines très élevées, comparées au niveau de seuil standard fixés par l'agence de protection de l'environnement des Etats-Unis [39].

Plusieurs études épidémiologiques évaluant l'impact sanitaire des incendies ont été réalisées dans les continents nord-américains et en Australasie, deux zones

géographiques très touchées par les feux des forêts. Plusieurs études épidémiologiques ont évalué les effets à court terme des particules fines émises par les feux par des séries temporelles [41]. En Europe, très peu d'études ont été réalisées dans ce domaine, et pourtant le bassin méditerranéen est l'un des endroits les plus exposés aux feux des forêts en Europe avec 500 000 hectares brulés tous les ans [42]. Les études épidémiologiques réalisées à la fin précitée avaient mis en évidence un lien entre l'exposition aux émissions des feux des forêts, notamment aux particules fines, et l'augmentation des maladies respiratoires et cardiovasculaires, les visites dans les services d'urgence et les consultations [43-47]. Parmi les événements de santé mis en relation avec l'exposition aux incendies, on compte l'irritation des yeux et des voies aériennes, l'asthme, la BPCO, les infections des voies respiratoires supérieures, les symptômes respiratoires des voies aériennes inférieures et l'inhalation de la fumée. L'exposition aux $PM_{2.5}$, un des composants majeurs de la fumée, a été liée aussi à des effets cardio-vasculaires, y compris à l'augmentation de la morbidité et mortalité cardio-vasculaire, en particulier au risque d'infarctus du myocarde [48]. L'augmentation des visites dans les services médicaux d'urgence pour les symptômes cardio-pulmonaires et pour l'insuffisance cardiaque, ont également été associées, en grande partie, aux émissions des feux de forêts [49].

Les effets sanitaires de la pollution atmosphérique peuvent varier en fonction de plusieurs paramètres, et notamment la nature et la concentration des polluants émis dans l'atmosphère, la durée, le lieu et le niveau d'exposition à ces polluants. Dans les travaux présents, nous nous intéressons aux liens potentiels entre les maladies respiratoires et la pollution atmosphérique, en prenant en compte différents niveaux d'exposition : macroscopique, par la prise en compte de la pollution troposphérique (s'étendant du niveau du sol aux 3 premiers km), engendrée par les feux de forêts incontrôlés, mise en relation avec les données des statistiques de morbidité des habitants des zones autour des incendies, le niveau semi-individuel, par la mise en relation de la pollution domestique et professionnelle avec des données individuelles de santé respiratoire et la dose interne reçue par un individu par le biais d'un biomarqueur.

Ce manuscrit est organisé en 4 parties. La première partie décrit différents niveaux d'exposition à la pollution atmosphérique, du macroscopique aux

biomarqueurs, et les façons de l'appréhender. La deuxième partie présente une application de la prise en compte de la pollution macroscopique par l'estimation de l'impact sanitaire des émissions provoquées par les incendies des forêts, qui à ce jour a été peu investigué. La troisième partie décrit l'impact de la pollution de l'intérieur des locaux en milieux rural sur les maladies allergiques et respiratoires par une approche de type semi-individuelle. Dans cette partie, sera mentionnée aussi l'importance de disposer de biomarqueurs d'exposition aux polluants. Le récit se termine par une suite de réflexions sur la mesure de l'exposition à la pollution atmosphérique à partir des observations réalisées dans le cadre de ce travail de thèse ainsi que des données de la littérature.

OBJECTIFS

L'objectif général de cette thèse est d'étudier **l'impact respiratoire de la pollution atmosphérique, en prenant en compte différents niveaux d'exposition: celui macroscopique, par la prise en compte de l'exposition à court terme de la pollution engendrée par les incendies incontrôlés, celui semi-individuel, par l'étude de l'exposition de longue durée en milieu rural, dans un cadre à la fois domiciliaire et professionnel, et celui individuel par le biais de la prise en compte d'un biomarqueur**. Sa réalisation a été rendue possible par la réalisation de 3 études différentes : la première de type écologique, concernant l'impact sanitaire des émissions des feux des forêts dont celles aux particules fines, la deuxième de type transversale, sur l'exposition aux particules fines et ultrafines et les COVs en milieu rural et les maladies allergiques et respiratoires parmi des adultes et enfin une étude de type cas-témoin nichée parmi des enfants asthmatiques et des témoins.

Les objectifs spécifiques de cette thèse sont les suivants :

- Réaliser une analyse de la bibliographie de spécialité sur l'impact sanitaire de type respiratoire des émissions des feux et les mesures d'exposition utilisées par le biais de revues systématiques. Pour cela nous avons mis un accent particulier sur des sous-groupes d'individus vulnérables comme les pompiers, les personnes âgées, en se limitant aux effets non accidentels.
- Appliquer une méthode qui permette de séparer les émissions des feux de forêts de celles anthropogéniques, afin de mieux évaluer l'impact sanitaire des émissions dégagées par les incendies de 2009 à Marseille et les concentrations associées en utilisant des séries temporelles.
- Déterminer les effets sur la santé respiratoire de l'exposition aux COVs et aux particules (PM) mesurés objectivement dans les habitations et les lieux de travail, des agriculteurs de l'étude transversale FERMA.
- Mieux comprendre les différences régionales des caractéristiques agricoles et l'impact de la différence dans les symptômes respiratoires chez les agriculteurs de différentes régions géographiques.
- Etudier les interrelations relations entre exposition au benzène au domicile, exposition interne au benzène et asthme infantile.

CHAPITRE I: EXPOSITION DE LA POLLUTION ATMOSPHERIQUE

I. Introduction à la pollution atmosphérique

I.1. Définition

Selon l'article L220-2 du code de l'environnement, la pollution atmosphérique est définie comme «l'introduction par l'homme, directement ou indirectement, dans l'atmosphère et dans les espaces clos, des substances ayant des conséquences préjudiciables, de nature à mettre en danger la santé humaine, à nuire aux ressources biologiques et aux écosystèmes, à influer sur les changements climatiques, à détériorer les biens matériels, à provoquer des nuisances olfactives excessives». Cette définition ne considère pas comme polluants, les contaminants issus des processus naturels comme les émissions issues des éruptions volcaniques, les émissions des végétaux… etc pourtant pouvant menacer les êtres humains et les écosystèmes.

Une autre définition, beaucoup plus globale, a été donnée par le Conseil de l'Europe, dans sa déclaration de mars 1968, qui avait défini qu' « il y avait pollution atmosphérique lorsque la présence d'une substance étrangère ou une variation importante dans la proportion de ses composants était susceptible de provoquer un effet nocif, compte tenu des connaissances scientifiques du moment, ou de créer ou une nuisance ou une gêne ».

En raison de son caractère inévitable, l'exposition à ces pollutions atmosphériques concerne l'ensemble de la population. Les groupes les plus sensibles à la pollution de l'air sont les enfants, les personnes atteintes de pathologies particulières respiratoires et/ou cardiovasculaires, ainsi que les personnes âgées. La qualité de l'air est étroitement liée aux concentrations des substances naturellement présentes dans l'air ou introduites artificiellement par les activités humaines. Au cours de 15 dernières années, bien que les concentrations dans l'air ambiant pour de nombreux polluants aient diminué, de multiples études épidémiologiques et toxicologiques montrent que la pollution atmosphérique urbaine constitue toujours un enjeu majeur de santé publique.

Toutefois, l'évaluation de l'impact de la pollution atmosphérique sur la santé humaine reste difficile à appréhender car la pollution de l'air est un phénomène complexe, résultant de l'association d'un grand nombre de substances qui agissent sous des formes diverses. L'exposition individuelle à la pollution atmosphérique est très hétérogène.

I.2. Sources de pollution atmosphérique

La pollution atmosphérique peut être issue des émissions d'origine naturelle où anthropique, c'est à dire liées à l'activité humaine (foyers fixes ou mobiles de combustion, émissions industrielles, bricolage, constructions...). On distingue également les polluants primaires, directement émis, des polluants secondaires, issus de transformations chimiques au sein de l'atmosphère, parmi ces derniers l'ozone et les particules secondaires. Enfin, on retrouve à l'intérieur des locaux, la pollution de l'extérieur qui rentre dans ceux-ci par transfert.

I.2.1. Sources des polluants de l''extérieur des locaux

Parmi les principaux polluants rencontrés dans l'atmosphère à l'extérieur des locaux, on y trouve les particules ou poussières en suspension (PM) dont les particules fines, les composés organiques volatiles, les Hydrocarbures aromatiques polycycliques (HAP), les oxydes d'azote, le dioxyde de souffre, le monoxyde de carbone, les métaux lourds mais aussi les pollens et les odeurs. Ces polluants sont principalement émis par le trafic routier (camions et voitures diesels…), les installations de chauffage des secteurs résidentiel, tertiaire (charbon, fioul, bois…), industriel et agricole. Mais certains phénomènes naturels sont à l'origine de PM et gaz tels que les incendies, les éruptions volcaniques, la désertification [50-52]. Les polluants issus des incendies qui font l'objet de ce travail de thèse seront détaillés dans le chapitre II.

I.2.2. Sources des polluants de l'intérieur des locaux

Le comité scientifique de la Commission Européenne spécialisé dans les risques sanitaires liés à l'environnement identifie plus de 900 polluants pouvant être trouvés à l'intérieur des locaux [24]. Ils peuvent être classés en :

- Polluants biologiques : les allergènes, les bactéries, les moisissures, et les

virus

- Polluants physico-chimiques : les particules, le dioxyde d'azote, le formaldéhyde et les Composés Organiques Volatils (COVs).

On y retrouve également les radiations ionisantes (rayonnement gamma), le plomb et l'amiante. Les caractéristiques et les sources spécifiques de ces principaux polluants de l'air intérieur sont reprises dans le Tableau 1. La Figure 2 présente aussi les différentes sources de pollutions à l'intérieur des habitations.

I.2.2.1. Les sources de pollution liées aux activités dans les habitations

Une des premières sources de pollution intérieure anthropogénique est la fumée de tabac. En effet, elle contient plus de 4000 substances, sous forme de gaz ou de particules, dont certains sont reconnus ou soupçonnés d'être des irritants ou bien cancérogènes pour l'homme [26, 53]. L'utilisation d'appareils fonctionnant par des procédés de combustion, qu'ils soient à gaz, à mazout, à pétrole, au charbon ou au bois, génère également de nombreux polluants [54], principalement du dioxyde d'azote et des particules fines [55-57]. Il s'agit d'appareils utilisés pour la production d'eau chaude, de chauffage, ou pour la cuisson des aliments. L'utilisation de combustibles solides (le charbon et la biomasse) constitue également une des sources majoritaires de pollution [22].

D'autres activités humaines peuvent conduire à l'émission des polluants dans l'air intérieur, telles que l'utilisation des produits d'entretien [31] ou de nettoyage [55], d'encens et des bougies [13], ou bien les activités de bricolage [58]. La simple présence de l'être humain, des animaux domestiques et des plantes, est également source de divers contaminants biologiques , -les bactéries [15] ou les virus-, les gouttelettes salivaires et nasales expirées par l'homme [14], les allergènes, le pollen, surtout ceux provenant de l'extérieur des locaux. Les surfaces humides ou les réservoirs d'eau liés à l'utilisation de douches, d'humidificateurs, de nébuliseurs, ou encore les dégâts des eaux, peuvent conduire à la prolifération de nombreux micro-organismes, dont les moisissures [14].

I.2.2.2. Les sources liées aux produits de construction et d'aménagement

Les matériaux de construction, de revêtement (des sols et des murs), d'isolement, d'ameublement, de décoration, mais aussi les produits de mise en

œuvre et de finition utilisés dans ces différents matériaux, représentent une autre source importante de pollution [23, 58].

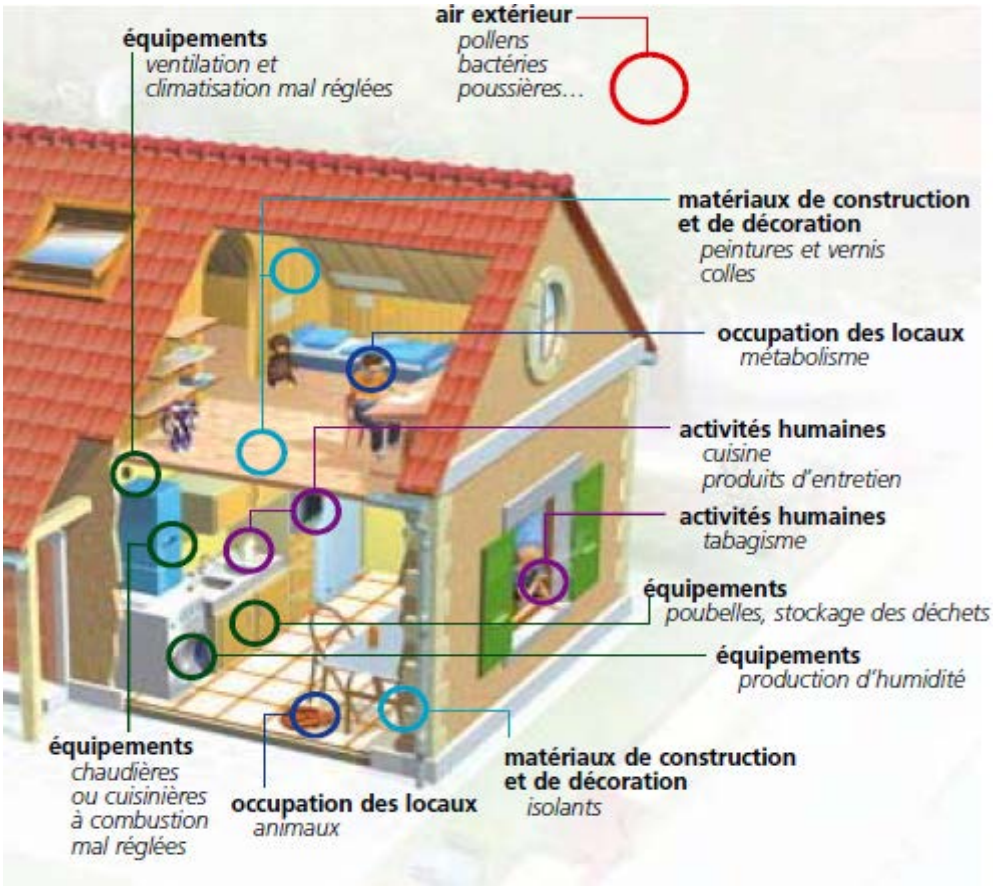


Figure 2: Sources de pollution à l'intérieur des habitations [23]

Les polluants du milieu intérieur agricole qui font partie de mon travail de thèse seront décrits dans le chapitre III.

Tableau 1: Classification et caractéristiques des polluants à l'intérieur des habitations

Polluants	**Caractéristiques**	**Sources principales**
Allergènes	- Principaux allergènes retrouves : • allergènes produits par les acariens, essentiellement les déjections et les débris des carapaces. Les espèces les plus fréquemment retrouvées sont *Dermatophagoides pteronyssinus* (*Derp1*) et *Dermatophagoides farinae* (*Derf1*). Leur prolifération est favorisée par un taux hygrométrique élevé. • allergènes présents dans la salive, la peau et les glandes anales des animaux domestiques (*Fel d1* pour le chat) ou nuisibles (*Mus m1* pour la souris) • spores issues des moisissures, notamment *Alternaria alternata* • allergènes de blattes (*Bla 1*), présents essentiellement dans leur carapace • et dans une moindre mesure les allergènes polliniques (*Bet v1* pour le bouleau ou *Amb a1* pour l'ambroisie)	- Sources extérieures : pollens, dégâts et infiltration d'eaux (moisissures, blattes, acariens) - Sources intérieures : • **Activités :** Présence d'eau/humidité et d'éléments nutritifs (moisissures, blattes, acariens, nuisibles), présence d'animaux domestiques • **Aménagement** : literies (matelas, sommiers, tapissiers, couettes, oreillers,…), canapés et fauteuils en tissus, tissus d'ameublement, tapis et moquettes (acariens), plantes vertes
Moisissures	- Nombreuses espèces retrouvées dans l'habitat, principalement Aspergillus et Penicillium [97]. - Peuvent émettre diverses substances dans l'atmosphère incluant les allergènes, les mycotoxines, les glucanes et certains composés organiques volatiles.	- Sources extérieures : Dégâts des eaux et infiltration, spores importes par l'air extérieur ; - Sources intérieures : • Activités **:** Présence d'eau/humidité et d'éléments nutritifs (matière organique) ; • **Aménagement :** Pièces humides, bas des murs mal isolés ou avec des défauts d'étanchéité ainsi qu'au niveau des ponts thermiques.

Tableau 1 : suite

Polluants	Caractéristiques	Sources principales
Bactéries (endotoxines, …)	- Bactéries et virus. - Endotoxines : lipopolysaccharides (LPS) issus de la couche externe des membranes des bactéries à Gram négatif	- Sources extérieures : Présence d'animaux d'élevage - Sources intérieures : • **Activités :** Humidité, manque d'hygiène, présence d'animaux domestiques
Particules	Mélange de différentes substances organiques et minérales (fumée de tabac, fibres, spores de moisissures, allergènes, particules diesel, …) en suspension dans l'air ; - Taille des particules : entre 0.005 et 100 µm, pouvant pénétrer plus ou moins profondément dans l'arbre respiratoire selon leur taille ; - Classification des particules principalement étudiées : PM_{10}, $PM_{2.5}$, $PM_{0.1}$ (nanoparticules de diamètre inférieur à 100 nm).	Sources extérieures : poussières naturelles, pollens, moisissures, fumées, particules fines des gaz d'échappement automobiles - Sources intérieures : • **Activités :** Tabagisme, cuisson des aliments, utilisation des appareils de chauffage et de combustion, utilisation d'aérosols, ménage (remise en suspension de la poussière), bricolage, repassage… • **Aménagement :** certains matériaux de construction
Oxydes d'azote (NO_x)	- Production de monoxyde d'azote (NO) à partir de phénomènes de combustion à haute température par oxydation de l'azote de l'air.	Production de NO_2 (polluant secondaire), le plus important en quantité émise, à partir de l'oxydation de NO dans l'air, notamment par l'ozone ; - Sources extérieures : foyers pour l'industrie et le chauffage, trafic automobile - Sources intérieures : • **Activités :** Utilisation d'appareils au gaz (cuisinières, chaudières, chauffe-eau, poêles à pétrole) et dans une moindre mesure, les poêles à bois ou à essence et la fumée de cigarette

Tableau 1 : suite

Polluants	Caractéristiques	Sources principales
Monoxyde de carbone (CO)	- Gaz qui se forme lors de la combustion incomplète de matières carbonées : charbon, pétrole, essence, fioul, gaz, bois.	- Sources extérieures : Gaz d'échappement de moteurs de voiture ; - Sources intérieures. **Activités :** • Utilisation d'appareils de combustion non ou mal raccordés à un conduit d'évacuation, fonctionnant dans de mauvaises conditions d'aération, mal entretenus ou mal utilisés ; • Fuites de conduits d'évacuation de gaz ; • Fumée de cigarette.
Composés organiques volatils (COVs) et semi-volatils	- Plus de 500 COVs décelés dans l'environnement intérieur - Comprennent notamment le benzène, le tetrachloroethylene, le toluène, les xylènes et aussi la famille des aldéhydes. - Parmi les substances semi-volatiles : pesticides, biphényles polychlores (PCB) et certains hydrocarbures aromatiques polycycliques (HAP)	- Sources extérieures : trafic routier, industries ; - Sources intérieures : • **Activités :** Utilisation d'aérosols et notamment de produits d'entretien, désodorisants, parfum d'intérieur, produits de bricolage (white-spirit), insecticides, vapeurs d'essence, photocopieurs, livres et magazines neufs
Formaldéhyde	- Compose organique de la famille des aldéhydes, de formule chimique, HCHO ; - Gaz incolore présentant une odeur caractéristique ; - Grande solubilité dans l'eau, facilitant son absorption par les voies respiratoires.	Sources intérieures : • **Activités :** Tabagisme, utilisation de bougies, bâtonnets d'encens, cheminés à foyer ouvert, cuisinière à gaz, poêles à pétrole ; • **Aménagement :** Produits de mise en œuvre et de finition (liants ou certaines colles), produits d'ameublement (meubles en contreplaque, certains meubles en bois).

Tableau 1 : suite

Polluants	Caractéristiques	Sources principales
Ozone	- Forte réactivité avec les surfaces de l'intérieur des locaux	- Production d'ozone (polluant secondaire) à partir de la transformation de polluants (NO2, CO, COVs) sous les effets du rayonnement solaire - Sources extérieures : production à partir des polluants émis par le trafic routier - Sources intérieures : • **Activités :** Présence de photocopieuses anciennes, imprimantes laser, humidificateurs d'air
Amiante	- Minéral d'origine naturelle se trouvant sous la forme de fibres extrêmement fines - Propriétés de résistance thermique, mécanique et chimique	- Sources intérieures : • **Aménagement :** Isolation endommagée, produits ignifuges, matériaux acoustiques
Plomb	- Métal employé depuis très longtemps en raison de sa grande malléabilité et ductilité et de son bas point de fusion, notamment pour la réalisation de conduites d'eau potable	- Sources intérieures : • **Aménagement :** Peinture écaillée dans les bâtiments anciens, canalisation ancienne
Radon	Gaz radioactif naturel, inodore, incolore issu de la désintégration de l'uranium et du radium présents dans la croute terrestre, en particulier dans les roches granitiques et volcaniques.	- Sources extérieures : sol - Sources intérieures : • **Aménagement :** certains matériaux de construction

I.3 Niveaux d'exposition des populations

La pollution est définie par une échelle de niveaux :

- **La pollution urbaine de fond**

La pollution de fond correspond à des niveaux de polluants minimaux auxquels la population est habituellement au moins exposée, par exemple dans une zone géographique. Ces niveaux correspondent aux concentrations en polluants mesurées à l'écart de toute source de pollution (industrielle ou automobile), et résultant à la fois de la pollution naturelle, des transferts de pollution à longue distance et de la dispersion des polluants émis localement (industries, chauffage, trafic routier…). Ils déterminent ainsi la qualité générale de l'atmosphère d'une zone donnée, et représentent le niveau d'exposition minimale, ressentie par l'ensemble de la population de la zone concernée [59].

- **La pollution urbaine de proximité**

La pollution de proximité est celle qui est mesurée à proximité des sources, du trafic automobile, en général. C'est la pollution maximale à laquelle les individus sont habituellement exposés. Cependant, récemment on a développé le mappage d'entières villes à des résolutions variables (jusqu'au kilomètre) afin de mieux estimer les niveaux des polluants auxquels les citadins sont exposés.

- **Les pics de pollution et les excès de pollution à court terme**

La pollution « de pointe » (« pic ») correspond à un instant donné à une forte hausse de la pollution ambiante, auxquels la population est ponctuellement exposée. Cela peut être due à des facteurs naturels comme les rayonnements solaires sans nuages, qui se passent en même temps qu'un évènement polluant (départ massif de véhicules). L'exposition à la pollution atmosphérique engendrée par les feux de forêts, par les volcans ou le désert est une exposition à court terme avec des niveaux voire des pics de polluants élevés, dépassant largement les valeurs seuils fixées par les institutions sanitaires [34, 35, 37, 58, 60, 61].

- **L'exposition de l'intérieur des locaux**

La pollution atmosphérique de l'intérieur constitue une pollution de proximité à laquelle les individus sont exposés de façon rapprochée pendant de longue

période. En l'absence de ventilation et d'évitement des sources, les niveaux des polluants restent constants voire augmentent lorsque les activités continuent à l'intérieur des locaux. La pollution de l'intérieur ne doit pas être négligée dans l'évaluation des risques associés à l'exposition à la pollution atmosphérique car les individus passent la majorité de leur temps à l'intérieur des locaux (domicile, travail, écoles….).

II. Niveaux de mesure de l'exposition à la pollution atmosphérique

Au niveau de la ville, la pollution de fond est mesurée par les stations de surveillance de la qualité de l'air avec des stations fixes alors que celle de proximité à une adresse donnée par des stations ou des appareils *in situ* ou des modèles de dispersion des polluants (Atmospheric Dispersion Modeling System-ADMS- [62], Operational Street Pollution Model-OSPM- [63], CALINE4 [64], Multiple Inputs Multiple Outputs-MIMO- [65]… etc. parmi d'autres). La pollution de l'air peut être surveillée aussi de façon macroscopique par satellite. C'est le cas de la pollution engendrée par les émissions de feux, les volcans et les poussières du désert dont on surveille par satellite les émanations qui sont dégagées dans la troposphère[3] jusqu'à une altitude de 3 km. La difficulté est alors de déterminer l'exposition réelle des individus à ces nuisances en les séparant de celles anthropogéniques. Par ailleurs, les mesures satellitaires, l'épaisseur optique des aérosols en particulier, utilisée pour extrapoler les émissions des polluants, souffrent des conditions météorologiques, notamment dans les zones nuageuses, ou avec une forte lueur de soleil, dans les zones enneigés ou désertiques vives parce qu'il est difficile de distinguer les aérosols des surfaces rafraichissantes [66].

A l'intérieur des locaux, des mesures *in situ* en continu ou passives pendant une période donnée par pompes aspirant l'air sur des filtres (pour les particules) ou capteurs passifs (pour les gaz), recueil sur support (pour les moisissures, les allergènes, les endotoxines) ou encore dans l'air par aspiration (moisissures, allergènes)…. sont généralement réalisées. Quelques rares études ont réalisé des mesures par capteur personnel. Une des difficultés lors de la mesure de la pollution de l'intérieur est représentée par le choix des polluants à mesurer de

[3] La troposphère est la partie inférieure de l'atmosphère terrestre, qui s'étend du sol jusqu'à une altitude variant d'environ 8 km à 15 kilomètres, selon la latitude et la saison.

façon prioritaire. Une autre difficulté est celle de disposer de mesures représentatives de la pollution habituelle de l'environnement choisi. Les mesures *in situ* ainsi que les mesures par des capteurs de courte durée peuvent ne pas être représentatives des expositions habituelles. C'est pour cela qu'on essaye de les réaliser dans des conditions habituelles. Des méthodes indirectes (questionnaires, check list …) ont été également utilisées. Notamment, des questionnaires ont été établis afin d'évaluer la présence ou non de certaines sources de polluants (la cuisinière à gaz pour le NO_2).

Dans tous les cas, une difficulté majeure dans l'estimation de l'exposition des individus est constituée par le fait que les individus se déplacent au cours du temps, de leur domicile aux lieux de travail et éventuellement de loisirs, dans les transports, à l'intérieur des locaux… et de ce fait sont exposés à des niveaux différents de pollution et à des polluants différents. Ceci peut être pris en compte par le biais de questionnaires de type budget espace-temps. Récemment, l'utilisation d'une approche de modélisation a été préconisée pour tenir compte des expositions aux polluants lors de plusieurs déplacements des individus dans différents environnements. Tout d'abord, un modèle a permis de tenir compte des expositions à la pollution de l'extérieur autours du domicile et des déplacements dans l'étude des effets à court terme de la pollution atmosphérique parisienne entre 2001 et 2004 sur la mortalité nnon-accidentelle [67]. Dans une étude plus récente réalisée par AirParif, l'utilisation d'un questionnaire caractérisant la mobilité spatio-temporelle de l'individu a été préconisée afin de réussir à modéliser correctement l'exposition individuelle [68]. Plus objective a été l'estimation de la pollution cumulative au niveau de la ville, de l'école et de l'habitation faite parmi des enfants portugais suivis pendant 2 ans, car basée sur des mesurages objectifs des principaux polluants dans ces endroits [69]. Un lien significatif entre l'exposition cumulée ainsi calculée et l'inflammation des voies aériennes a été observée.

Une autre approche est celle d'utiliser des biomarqueurs d'exposition à la pollution atmosphérique. Malheureusement, peu de tels marqueurs existent à ce jour. En plus des marqueurs d'exposition, il peut être intéressant de considérer les marqueurs d'effet du polluant sur l'organisme. Un marquer d'exposition reflète la concentration d'un polluant qui a traversé les barrières entre le milieu extérieur et l'organisme alors qu'un marqueur de l'effet du polluant est

généralement un indicateur d'une anomalie diagnostiqué médicalement à la suite de l'exposition au polluant (tel que le monoxyde d'azote (eNO) en tant que marqueur de l'inflammation des voies aériennes). L'avantage de l'utilisation de ces indicateurs biologiques est qu'ils reflètent l'exposition intégrée de l'individu bien qu'il s'avère difficile d'établir des relations entre les niveaux de pollutions ambiants et la dose interne mesurée dans le cas des premiers ou l'effet de celle-ci dans le cas des deuxièmes. Des modèles sont en cours de développement afin d'établir la relation entre les concentrations de l'air ambiant et celles issues du dosage de biomarqueurs [68].

Parmi les biomarqueurs d'exposition utilisés il y a les méthoxyphénols [70, 71] et la levoglucosane [72], biomarqueurs de l'exposition de la fumée de bois. Pour l'estimation de l'exposition lors des incendies de forêts, la lévoglucosane (1,6-anhydro-β-D-glucopyranose) est un marqueur de choix puisqu'il est assez spécifique pour la combustion de la biomasse [72, 73]. En fait, ce composé est un produit de la pyrolyse de la cellulose contenue dans la biomasse. Il est fréquemment utilisé comme traceur pour la combustion de la biomasse, car il est produit à des niveaux relativement élevés et est stable dans l'atmosphère [74, 75]. Lorsque la levoglucosane est utilisée comme biomarqueur pour l'inhalation de fumée de bois il est mesuré dans l'urine [72, 73]. Cependant, d'autres recherches sont nécessaires pour évaluer la relation quantitative entre les niveaux de lévoglucosane et la concentration des PM. D'autres biomarqueurs sont utilisés pour mesurer l'exposition des polluants. Parmi eux, l'acide S-phénylmercapturique urinaire est un biomarqueur spécifique pour le benzène et une bonne corrélation existe entre les concentrations atmosphériques de benzène, celles de benzène sanguin et urinaire et celles de S-PMA urinaire [76], L'hydroxyprene(1-OHP) est un biomarqueur de dose interne , éliminé principalement dans l'urine ou il est retrouvé en grandes quantités. Il est utilisé comme biomarqueur pour l'exposition au diesel, il a été utilisé pour évaluer l'exposition au diesel des adolescents de Harlem [77]. Les adduits de l'ADN du B[a]P qui sont spécifiques pour les HAP cancérigènes [78, 79].

CHAPITRE II: IMPACT SANITAIRE DES FEUX DE FORETS

I. Présentation de la problématique

Les feux de forêts incontrôlés constituent une préoccupation mondiale et toutes les régions du monde sont confrontées à des incendies même à diverses échelles. En raison des différents polluants contenus dans la fumée issue de ces incendies qui, même à court terme, dépassent largement les limites standards [34, 35, 39], les chercheurs commencent à s'intéresser sur l'impact sanitaire des émissions des feux de forêts. La plupart des études réalisées à ce sujet sont nord-américaines ou australiennes, deux continents se confrontant à de grands incendies chaque année. En Europe, très peu d'études en ont été réalisées. Pourtant, plusieurs régions européennes, en particulier les pays du bassin méditerranéen, doivent affronter chaque année de grands incendies, dont l'impact sanitaire des émissions dégagées n'est toutefois que très peu étudié. Le projet PHASE (Public Health Adaptation Strategies to Extreme Weather Events), financé par la Commission Européenne, se propose de combler les lacunes dans ce domaine.

Dans cette partie, après un bilan des connaissances épidémiologiques sur les associations entre les émissions de feux de forêts incontrôlées et la santé, nous nous intéressons à la méthodologie utilisée dans la littérature de spécialité, afin d'évaluer l'exposition liée aux émissions des feux. Dans un environnement extérieur connaissant beaucoup de sources de pollution liées au trafic routier, aux installations industrielles…etc., une meilleure estimation de l'exposition des émissions des feux de forêts et sa différenciation des autres sources, sont inhérentes à l'évaluation de l'impact sanitaire réel de ces émissions de feux de forêts. Une étude de cas sur les incendies de 2009 à Marseille, nous permettra de mettre en application la méthodologie que nous avons utilisée pour différencier les émissions de feux de forêts des émissions anthropogéniques. Cela dans le but de mieux évaluer l'impact sanitaire des émissions des feux de forêts.

II. Exposition aux émissions issues des incendies

II.1. Définition des feux de forets

Les feux de forêts sont un phénomène naturel très fréquent dans toutes les régions du monde, jouant un rôle clé dans la distribution et dans la composition de l'écosystème terrestre [80]. Cependant, l'homme a largement modifié les régimes des feux [81] et les activités humaines sont à l'origine d'un grand nombre de feux des forêts. Selon les rapports de la Commission Européenne sur les incendies, publiés en 2010 et en 2012, dans plusieurs pays européens, plus de 90% des incendies des forêts sur le continent étaient d'origine humaine [82, 83]. Les feux de forêts incontrôlés peuvent être d'origine criminelle, ou causés par la négligence humaine, comme les fumeurs qui jettent les mégots des cigarettes sans les éteindre, ou la perte du contrôle du feu à l'issue des activités agricoles. Seule une petite fraction des incendies des forêts sont causés par des phénomènes naturels, tels que la foudre [17], ayant pour origine la combustion spontanée, comme celle de la sciure de bois et des feuilles mortes. L'importance de la proportion de feux de forêts d'origine anthropogénique fait qu'à grande échelle, les incendies sont considérés comme un artefact relativement récent de l'intervention humaine en écologie forestière, en particulier par la réduction des herbivores [84]. En raison de leur fréquence et de leur durée au cours du dernier siècle, les feux de forêts anthropogéniques sont une préoccupation mondiale, étant considérés comme des causes de destruction des forêts et de la dégradation des sols [85]. Le changement climatique va très probablement augmenter la durée et la sévérité de la saison des incendies, ainsi que l'extension de la zone à risque et les sécheresses récurrentes. La réduction des quantités des précipitations est, par ailleurs, susceptible de mettre en péril la régénération des écosystèmes après l'incendie [84].

II.2. Composition de la fumée issue des feux de forets

La fumée issue des feux est un mélange complexe de dioxyde de carbone, de vapeur d'eau, de monoxyde de carbone, de particules, d'hydrocarbures et d'autres substances chimiques organiques, des oxydes d'azote et des oligo-éléments. Les composés individuels présents dans la fumée sont estimés à plusieurs milliers de composés chimiques [34]. Il y a différents types de bois et

de végétations. D'une manière générale, le bois est composé en majorité de cellulose (environ 50%), de lignine (20 à 30%), d'hémicellulose (15 à 25 %) et d'un faible pourcentage d'éléments minéraux (1 à 1.5%) [86]. D'autres composés, comme les tanins, et les autres polyphénols, les huiles, les graisses, les résines, les cires, et les amidons, en font également partie. Tous ces produits génèrent des composés différents lorsqu'ils sont brûlés [34].

Si l'incendie est dans l'interface d'une zone urbaine, il est possible que la flamme brûle également d'autres matériaux que les végétaux, en particuliers les déchets. Dans ce cas, à côté des émissions habituelles issues de la végétation, d'autres composés dangereux, tels que les dioxines (dibenzo-pdioxines polychlorés/dibenzo-furanes), peuvent être présents dans la fumée [87, 88].

Lorsque les feux éclatent dans une zone agricole ou à proximité des constructions en zone rurale ou urbaine, le bois, les plastiques, ou les engrais peuvent aussi être brûlés, et des matériaux tels que le verre pulvérisé, le ciment, la poussière, l'amiante, le plâtre, ou les autres composés chimiques peuvent être présents dans la fumée dégagée. Il est important de savoir que des particules radioactives peuvent parfois être trouvées dans la fumée. Leur origine peut être la végétation contaminée par la radioactivité [87, 88]. Les principaux polluants rencontrés lors des incendies de biomasse sont présentés dans le Tableau 2.

Tableau 2: Principaux polluants atmosphériques issus des émissions des feux de forêts

Composés	Exemples	Sources	Observations
Gaz inorganiques	Monoxide de carbone (CO)	Combustion incomplète de la matière organique	Transportés sur des longues distances
	Ozone (O3)	Produits secondaires des oxydes d'azotes et des hydrocarbures	Seulement présent sur la trajectoire du feu, transporté sur des longues distances
	Dioxyde d'azote (NO2)	Oxydation à haute température de l'azote présent dans l'air	Réactif : la concentration diminue à mesure que l'on s'éloigne du feu
Hydrocarbures	Benzène	Combustion incomplète de la matière organique	Transport, réagit avec les aérosols organiques
Aldéhydes	Acroléine	Combustion incomplète de la matière organique	L'acroléine et le formaldéhyde sont les principaux aldéhydes libérés lors des feux de foret
	Formaldéhyde (HCHO)	Combustion incomplète de la matière organique	
Particules	Particules inhalables (PM_{10})	Condensation des gaz de combustion; combustion incomplète de la matière organique; entraînement de fragments de végétaux et de cendres	Grosses particules et particules fines. Les grosses particules ne sont pas transportées et contiennent principalement de la terre et de cendres
	Particules respirables	Condensation de la combustion Gaz, combustion incomplète de la matière organique	Pour la fumée de biomasse, approximativement égal aux particules fines
	Fines particules ($PM_{2.5}$)	Condensation de la combustion Gaz, combustion incomplète de la matière organique	Transportés sur des longues distances, production primaire et secondaires
Hydrocarbures Aromatiques Polycycliques (PAHs)	Benzo[a]pyrene (BaP)	Condensation de la, combustion Gaz, Combustion incomplète de la matière organique	Les espèces spécifiques varient selon la composition de la biomasse

II.3. Facteurs d'influence de l'émissions des polluants

La composition de la fumée issue des feux de forêts est fonction de multiples facteurs : le type de végétation servant de carburant, la teneur en humidité, la température du feu et de l'oxygénation, les conditions du vent et d'autres facteurs météorologiques [34, 89], le type de feu, ainsi que la surface brûlée. La formule suivante a été utilisée par Liousse et al. [90] dans le cadre du projet « Analyses Multidisciplinaires de la Mousson Africaine » (AMMA), pour estimer les émissions journalières issues des feux de forêts pour les gaz (CO_2 CO, NO_X, SO_2, COV), pour le carbone noir (black carbone), ainsi que pour le carbone organique :

- **EM=**$\sum v(BA * GLCv * BDv * BEv * EFv)$
- EM : émissions estimées
- BA : Surface brûlée
- GLCv : pourcentage pour chaque classe de végétation
- BDv : densité de la biomasse (biomasse par unité de surface occupée par un type de végétation en kg/m²)
- BEv : efficacité de combustion (fraction de biomasse exposée au feu et effectivement consommée dans le feu)
- EF : est le facteur d'émissions (g/kg de matière sèche)

Le type de végétation

La végétation constitue un combustible et permet au feu de se développer. Son état de sècheresse et sa densité augmentent, respectivement, l'inflammabilité et la puissance du feu [59]. Plus le temps sera chaud, sec et venteux, plus la végétation sera sèche, plus le risque d'incendie sera élevé. La structure du peuplement de la zone concernée est aussi importante, même davantage que le type de végétation [91]. Les émissions dégagées sont fonction de la densité de biomasse et de la diversité de la végétation. Cette grande diversité explique, en partie, les difficultés rencontrées pour estimer la concentration des polluants dans la fumée. En effet, selon l'essence brûlée, les polluants et leur quantité sont différents.

Les différents types de feux des forêts

Nous pouvons en distinguer trois types, selon les caractéristiques de la végétation composante [92] :

Les feux de sol : ils brûlent la matière organique que l'on retrouve dans la dans la litière, l'humus ou les tourbières. Leur vitesse de propagation est faible. Bien que peu virulents, ils peuvent être très destructeurs, en s'attaquant aux systèmes souterrains des végétaux.

Les feux de surface : Ils brûlent les basses strates de végétation, c'est-à-dire la partie supérieure de la litière, la strate herbacée et les ligneux bas. Leur propagation peut être rapide lorsqu'ils se développent librement et que les conditions de vent ou de relief y sont favorables.

Les feux de cîmes : ils brûlent la partie supérieure des arbres, formant ainsi une couronne de feu. Ils libèrent en général de grandes quantités d'énergie et leur vitesse de propagation est très élevée. Leur intensité et leur contrôle sont fonction de la puissance du vent et du degré de sécheresse de la végétation.

Les conditions météorologiques

Les conditions climatiques, la température et l'humidité de l'air, la vitesse et la direction du vent, l'ensoleillement, l'historique des précipitations, la teneur en eau des sols, ont un effet particulièrement important sur les feux de forêts. La dynamique du développement et l'évolution du feu en sont dépendantes. Ainsi, une température élevée, un vent violent et un déficit hydrique de la végétation sont très favorables à l'éclosion et à la propagation de l'incendie. Tous ces facteurs climatiques affectent la quantité des polluants rejetés par les flammes [92]. Le vent attise les flammes en augmentant le flux d'oxygène, oriente la propagation et transporte des particules incandescentes au-delà des bords de la flamme. C'est ainsi que de la fumée peut être dégagé à des milliers de km de la source du feu, comme ce fût le cas des incendies ayant eu lieu en Indonésie en 1997. Dans cet exemple, la fumée avait été transportée à des milliers de kms, vers de nombreux pays du sud-est asiatique [38]. Quant à la température, elle conditionne cyclicité des feux de forêts. En Europe, la période propice pour les départs des feux est l'été, de juin à septembre, où les températures sont très élevées [82].

II.4. Impact sanitaire des polluants issus des incendies

Les effets sanitaires des feux de forêts incontrôlés sont divers : on en distingue les effets accidentels et non accidentels. Dans la thèse présente, nous portons un intérêt particulier aux effets non-accidentels, essentiellement liés à l'exposition de la population aux émissions dégagées par la fumée. Le Tableau 3 présente les effets sanitaires des principales émissions rencontrées dans la fumée issue des feux de forêts.

Tableau 3: Les effets sanitaires des principaux polluants rencontrés dans les émissions des feux de forêts

Polluants	**Effets sur la santé humaine**	**Observations**
Les particules en suspension	- Même à des concentrations faibles les PM provoquent des effets au niveau de la fonction respiratoire, entraine une augmentation de la morbidité et de la mortalité liées aux maladies respiratoires et cardiovasculaires - Les $PM_{2.5}$ pénètrent dans les alvéoles pulmonaires. Peuvent pénétrer dans le système sanguin ou rester dans les poumons et provoquer une maladie chronique des poumons telle que l'emphysème	**Valeurs limites des PM :** **$PM_{2.5}$:** - Moyenne annuelle : 10 µg/m3 - Moyenne sur 24 heures : 25 µg/m^3 **PM_{10}:** - Moyenne annuelle : 20 µg/m^3 Moyenne sur 24 heures : 150 µg/m^3
Les composés organiques volatiles	- Effets respiratoires (irritation des muqueuses et du système pulmonaire) - Nausées, maux de tête, vomissements, difficulté de concentration - Cancer (leucémie, poumon, foie, …) - Effets neurotoxiques et tératogènes	- Dans la fumée, les COVs ont des pressions de vapeur significatives à température ambiante - Le méthane et le CO produit proportionnellement aux COV, peuvent servir d'indicateurs de l'abondance des COVs dans la fumée
L'Ozone	- Effets respiratoires (toux, essoufflement, irritation du nez et de la gorge, - inflammation des voies respiratoires, altération de la fonction respiratoire, le volume et le débit pulmonaire)	- L'ozone est formé photo-chimiquement dans la partie supérieure des panaches de fumée - Dans les vallées ou la fumée est piégée et soumises à ces rections photochimiques dans la basse atmosphère

Tableau 3 : suite

Polluants	Effets sur la santé humaine	Observations
Monoxyde de carbone	- Maux de tête, nausées, vomissements, vertige, pertes de connaissance, coma - Effets neurologiques et cardiovasculaires - Mort en cas d'intoxication aigue	Valeurs Guides de qualité d'Air Intérieur (VGAI) court terme : - 10 mg/m3 pour une exposition de 8 h30 mg/m3 pour une exposition d'1 h - 60 mg/m3 pour une exposition de 30 min 100 mg/m3 pour une exposition de 15 min
Le formaldéhyde	Effets respiratoires (irritation des yeux, du nez et de la gorge, amplification de la réponse allergique, …) - Cancer du nasopharynx et des fosses nasales (CIRC : groupe 1)	- VGAI court terme : 50 µg/m^3 pour une exposition de 2h, pour les effets aigus - VGAI long terme : 10 µg/m^3 pour une exposition supérieure a un an, pour les effets chroniques
Radicaux libres	- Stress oxydatif et réponses inflammatoires, augmentation du risque de cancérisation de l'organisme - Autres effets possibles : troubles articulaires (arthrite), trouble de la vision (cataracte) - Les maladies cardiaques - Les maladies dégénératives (sclérose en plaques, la maladie d'Alzheimer, athérosclérose…)	Bien que la plupart des groupes de radicaux libres subissent une condensation à la sortie des flammes, ce qui réduit leur toxicité, certains peuvent persister jusqu' à 20 minutes après leur formation et présent donc un risque réel pour les personnes exposées à de la fumée fraichement formée à proximité du feu
Les acides organiques	- Irritation de la muqueuse membranaire	- Produits par oxydation des aldéhydes lors des incendies

Tableau 3 : suite

Polluants	Effets sur la santé humaine	Observations
Benzène	Maux de tête, vertige, anorexie, fatigue, pâleur, dyspnée, trouble de la vision Effets cancérigènes : effets hémotoxiques (anémie aplasique, leucémie, pancytopenie, moelle osseuse) Classé groupe 1 par le centre international de recherche sur le cancer (CIRC)	- VGAI court terme : 30 µg/m^3 pour une exposition d'une journée à 14 jours, pour les effets hématologiques non cancérogènes - VGAI intermédiaire : 20 µg/m^3 pour une exposition de plus de deux semaines à un an, pour les effets hématologiques non cancérogènes - VGAI long terme : 10 µg/m^3 pour une exposition supérieure à un an, pour les effets hématologiques non cancérogènes - Hygiène professionnelle - Valeur moyenne d'exposition (VME) : 3,25 mg/m3 pour 8 heures
Dioxyde de souffre	Inflammation des voies respiratoires, augmentation de l'asthme, bronchite chronique, infections respiratoires	- Gaz incolore d'odeur piquante, produit par la combustion d'énergies fossiles ou de minerais contenant du souffre - Le SO2 est l'un des précurseurs des PM2.5
Les HAP	Parmi les HAP, le benzo[a]pyrène est le plus dangereux : cancers des poumons, des tumeurs de la peau et du scrotum,	Les limites de l''Institut national américain pour la sécurité et la santé au travail (NIOSH) :35 ppm pour 8 d'exposition et 200 ppm pour un temps indéfini.
Dioxyde d'azote	Troubles respiratoires, infections pulmonaires, œdème pulmonaire, favorise les emphysèmes	Formé par la combustion de l'oxygène et de l'azote et provient essentiellement de la combustion des fossiles

Tableau 3 : suite

Polluants	Effets sur la santé humaine	Observations
Les radionucléides	conséquences sanitaires immédiate ou à long terme : -**Cesium-137**: cancérigène, cataracte et problèmes oculaires, reprotoxique, Hépatites, Atteinte du système cardio-vasculaire, Atteinte du système nerveux central, Diminution de la densité osseuse. - **Iodine-129** : Atteinte de la thyroïde, altération de la fonction pulmonaire, Maladies cardiovasculaires, cancers (thyroïdes, poumons)	- Les radionucléides tels que le césium-137, l'iodine-129 **et le** chlorine-36 peuvent être libéré dans l'atmosphère, le sol et l'eau lors des incendies de forêts - Environ 80-90% de l'Iodine et 40-70% du césium sont libérés dans l'atmosphère et leur concentration augmente en fonction de l'augmentation de la température du feu
Polychlorodibenzo-p-dioxines(PCDD)	modification du nombre de lymphocytes, diminution des réactions à certains allergènes. Excès de cancer sans localisation spécifique.	- Extrêmement persistant, - Largement répandu dans l'environnement
Fractions inorganiques des particules	- Les effets toxicologiques des fractions inorganiques émis lors des incendies ne sont pas encore quantifiés - Les effets sanitaires dépendent des substances en question telles que le plomb, l'amiante et le souffre	Généralement présent sous forme de trace dans la fumée, sa concentration dépend de la composition chimique de la biomasse brulée et de l'intensité du feu

III. Présentation du projet PHASE[4] visant à établir les risques sanitaires associés aux feux de bois

III.1. Présentation générale

Le Projet PHASE dirigé par le Dr Paola Michelozzi du département d'épidémiologie, ASL, Rome, visait à développer des stratégies d'adaptation de la santé publique en cas d'évènements climatiques extrêmes (ECE). C'est un projet de collaboration internationale, financé par l'Agence Exécutive pour la Santé et les Consommateurs[5], directement lié au programme de santé de l'Union Européenne de 2008-2013. Ce projet avait pour objet de fournir un cadre d'outils pour la préparation et la réponse aux évènements climatiques extrêmes (les vagues de chaleur, les vagues de froid, les inondations) et leurs conséquences environnementales (les feux de forêts, la pollution atmosphérique). Ceci dans le but de réduire l'impact sur la santé publique. La grande ambition du projet sus – mentionné était d'appliquer de nouvelles méthodes destinées à améliorer les connaissances des effets sur la santé de chaque ECE et d'identifier les facteurs de risque individuels. Un des éléments clés du projet PHASE était de mettre l'accent sur la santé publique. Ainsi, des outils ont été élaborés afin d'améliorer les efforts de prévention, et des sous-groupes vulnérables pour chaque ECE devaient être identifiés pour un meilleur ciblage des activités de prévention et d'optimisation des ressources.

Les objectifs généraux du Projet PHASE étaient les suivants:

- Renforcer la sensibilisation, parmi les populations et les institutions, sur les risques pour la santé, associés à chaque ECE;
- Accroître l'efficience et l'efficacité des systèmes d'alerte et les mesures de prévention pour chaque ECE, par une évaluation pertinente ;
- Fournir à l'UE et aux gouvernements nationaux un cadre d'outils pour améliorer la préparation et aider à atténuer les impacts sur la santé des ECE ;
- Cibler les activités de prévention pour les sous-groupes spécifiques qui sont à risque.

[4] http://www.hpa.org.uk/webc/HPAwebFile/HPAweb_C/1317140885697

[5] L'Agence Exécutive pour la Santé et les Consommateurs assiste la Commission Européenne dans la gestion des programmes et des mesures communautaires dans les domaines de la santé, de la politique des consommateurs et de la formation en matière de sécurité alimentaire.

Le projet PHASE était composé de 8 lots de travail (Work Package (WP)) :

- WP1 : La coordination du projet ;
- WP 2: La diffusion du projet ;
- WP 3: L'évaluation du projet ;
- WP 4: Les outils d'adaptation pour prévenir les impacts des vagues de chaleur et des vagues de froid;
- WP 5: Les outils d'adaptation pour prévenir les impacts sanitaires des inondations ;
- WP 6: La prévention des impacts sanitaires des feux de forêt ;
- WP 7: Les synergies entre la pollution atmosphérique, les ECE extrêmes et les feux de forêt ;
- WP 8: L'identification des sous-groupes vulnérables.

Les approches communes à chacune des WP concernant la définition des actions de santé publique, spécifiques à chaque ECE, sont présentées dans la Figure 3.

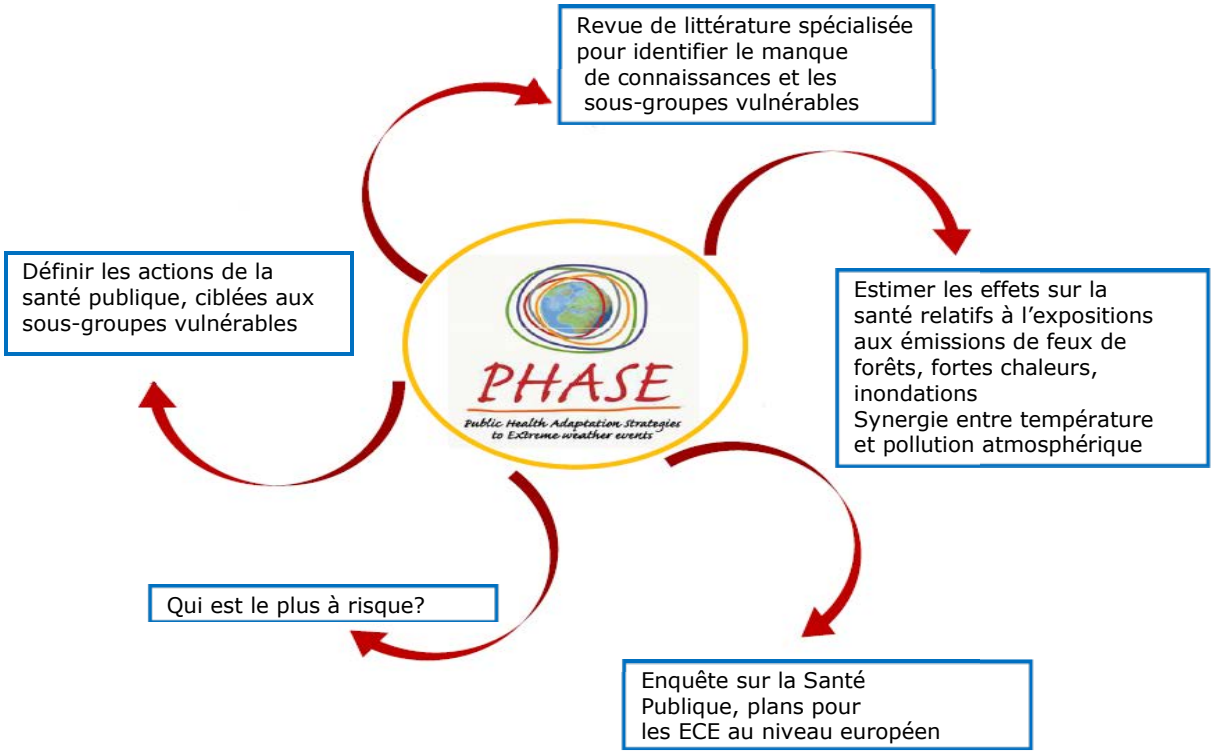


Figure 3: Les approches communes concernant la définition des actions de santé publique pour chaque évènement climatique extrême

III.2. Présentation du WP6: prévention des effets sanitaires des feux de forêt

Ce lot de travail dirigé par le Dr Isabella Annesi-Maesano visait à développer des stratégies d'adaptation de la santé publique, afin de prévenir les impacts sanitaires des feux de forêts. **Les objectifs de ce lot dans le cadre du Projet PHASE ont été les suivants :**

- Produire une revue systématique de littérature afin d'établir l'état des connaissances sur l'impact sanitaire des émissions des feux de forêts ;
- Effectuer un inventaire sur les feux de forêts en Europe : la surface brulée, le nombre de départ de feux, les émissions incluant le carbone noire et le carbone organique, les gaz dans les 10 dernières années ;
- Établir le lien entre l'exposition aux émissions et les données sanitaires pour les populations vivant à proximité dans les régions urbaines ;
- Identifier les sous-groupes vulnérables qui sont les plus susceptibles de subir les impacts sanitaires des feux de forêts ;
- Réaliser des études des cas pour certaines villes européennes dont les données sanitaires sont disponibles ;
- Développer des outils et des recommandations visant à soutenir la préparation et la réponse aux incendies de forêts.

IV. Effets sanitaires des émissions de feux de forêts : présentation des résultats

Pour étudier les effets sanitaires des émissions issues des incendies nous avons dans un premier temps fait des recherches bibliographiques pour identifier les méthodes utilisées dans les études épidémiologiques les ayant ciblées (Article 1). Nous avons également réalisé en parallèle une revue de la littérature de spécialité sur l'état des connaissances sur les effets sanitaires des émissions de feux de forêts (article 2). Enfin, nous avons adapté et appliqué une méthodologie qui nous a permis de différencier les émissions des feux de forêts des émissions anthropiques pour étudier les effets sanitaires des incendies qui ont eu lieu à Marseille en 2009 (article 3).

IV.1. Presentation de article 1: Quantifying wildfires exposure for investigating related-health effects

Plusieurs méthodes ont été utilisées par les études épidémiologiques pour évaluer l'exposition aux émissions des feux de forêts, dans le but d'en déterminer l'impact sanitaire. Ces méthodes vont du questionnaire personnel aux données de routine, des données issues des stations de surveillance de la qualité de l'air permettant de mesurer les concentrations des PM, jusqu'à l'utilisation récente des méthodes sophistiquées, impliquant les satellites et la modélisation.

Dans l'article 1 nous nous intéressons à ces différentes méthodes utilisées par les études sus – mentionnées, afin d'évaluer l'exposition aux feux de forêts. Cet article propose également un inventaire des émissions et des concentrations des polluants issus des feux de forêts en Europe pendant la période 2006 à 2010, après l'utilisation des données satellitaires et de la modélisation. Ceci dans le but d'évaluer les émissions de feux de forêts au niveau local, à l'aide des coordonnées spatiales.

Atmospheric Environment 97 (2014) 239–251

Contents lists available at ScienceDirect

Atmospheric Environment

journal homepage: www.elsevier.com/locate/atmosenv

Review

Quantifying wildfires exposure for investigating health-related effects

H. Youssouf [a, b], C. Liousse [c], L. Roblou [c], E.M. Assamoi [c], R.O. Salonen [d], C. Maesano [a, b], S. Banerjee [a, b], I. Annesi-Maesano [a, b, *], on behalf of the PHASE Study

[a] Epidemiology of Respiratory and Allergic Disease Department, UMR-S 1136, Institute Pierre Louis of Epidemiology and Public Health, INSERM, Paris, France
[b] Epidemiology of Respiratory and Allergic Disease Department, UMR-S 1136, Institute Pierre Louis of Epidemiology and Public Health, UPMC Sorbonne Universités, Paris, France
[c] Laboratory for Aerology Toulouse, France
[d] National Institute for Health and Welfare, Department of Environmental Health, Kuopio, Finland

HIGHLIGHTS

- Review of methods used to assess wildfire exposure and related health impact.
- Discussion of uncertainties of exposure assessment in the literature.
- Application of methods which allowed to have emissions at local area.
- Inventory of wildfire emissions in Europe from 2006 to 2010.

ARTICLE INFO

Article history:
Received 19 March 2014
Received in revised form
21 July 2014
Accepted 23 July 2014
Available online 23 July 2014

Keywords:
Wildfires
Exposure
Assessment
Inventory
Wildfire emissions
Health effects

ABSTRACT

A wildfire is an uncontrolled fire in an area of combustible vegetation that occurs in the countryside or a wilderness area. The United Nation International Strategy for Disaster Reduction estimates that between 3 and 4 million km^2 are affected by wildfire annually, with 18 000 km^2 occurring in Europe. The Mediterranean region is one of the most affected regions by wildfires in Europe. Nearly 500 000 ha, on average, are burned annually by 50 000 wildfires in the countries of southern Europe bordering the Mediterranean Sea. Wildfires or biomass burning seriously damage ecosystems and affect public health. A major difficulty related to the assessment of health impact of wildfire emissions derives from the complexity of wildfire exposure assessments. Based on the literature, several methods, including satellite data, chemical transport models and, less often, personal exposure monitoring are available. However, few investigations have used methods allowing separating wildfires emissions from air pollutants emissions from urban sources having the same components. An inventory of wildfires occurred in Europe between 2006 and 2010 was obtained in terms of burnt areas, duration and related emissions of major air pollutants (black carbon, particulate matter), as obtained using a hybrid model that allows excluding anthropic sources of air pollution.

© 2014 Elsevier Ltd. All rights reserved.

1. Introduction

Wildfires, also called biomass burning or vegetation fires include forest fires, brushfires, savanna fires and bushfires. Due to climate change, wildfires have become more problematic for public health and ecosystems in the past decades. A major difficulty related to understanding the impact of wildfires derives from the complexity of assessing wildfire exposure.

Fire, in general, is essential for some ecosystems. In many regions, controlled fire contributes to maintaining the structure and productivity of ecosystems and is integral to land management. In many countries, prescribed burns are practiced to avoid uncontrolled wildfire, and agricultural burning is used to facilitate harvesting. Fire is also caused by vandalism and tradition. Non-controlled wildfire, however, is a very significant disturbance to vegetation cover worldwide. Currently, satellite observations are used to monitor wildfires globally (Al-Saadi et al., 2005), but it is still difficult to provide an accurate assessment of the total global area affected by different fires (Goldammer et al., 2011). The United

* Corresponding author. Epidemiology of Allergic and Respiratory Diseases (EPAR), UMR-S 1136, Institute Pierre Louis of Epidemiology and Public Health, Medical School St Antoine, 27 rue Chaligny, 75571 Paris Cedex 12, France.
E-mail address: isabella.annesi-maesano@inserm.fr (I. Annesi-Maesano).

http://dx.doi.org/10.1016/j.atmosenv.2014.07.041
1352-2310/© 2014 Elsevier Ltd. All rights reserved.

Nations Office for Disaster Risk Reduction (ISDR) estimates that between 3 and 4 million km^2 of land are annually affected by fire. Mouillot and Field (2005) estimate a bigger area – 6 million km^2 – is burnt annually. On a percent basis, more than 30% of the global land surface is believed to have a significant fire frequency (Chuvieco et al., 2008). The African savanna is very fire-prone (Giglio et al., 2010; Liousse et al., 2004, 2010, 1996), and in Europe, 18,000 km^2 are burnt annually (van der Werf et al., 2010). More precisely, approximately 500 000 ha on average are burned annually by approximately 50 000 fires in southern European countries bordering the Mediterranean Sea (Goldammer et al., 2011). In 2009, 323 896 ha were burned in France, Portugal, Spain, Greece and Italy (European commission, 2010). Even if Mediterranean fires are small compared to fires in other areas of the world, they often cause significant damage to homes and businesses and threaten human beings and animals, because they occur so close to urban areas and are fueled by hot temperatures and high wind speeds. Wildfire incidents have increased in recent years in many parts of the world due to an upsurge in risk factors (climate change, extreme weather events, desertification), raising both public and political awareness of a growing and dangerous trend.

So far, despite the fact that wildfires take a heavy toll on human health worldwide, few studies reported health effects of wildfires (Youssouf et al., 2014). In particular health effects of trace gases and aerosols emitted by wildfires remain poorly quantified due to uncertainties on wildfire emissions assessment, and the taking into account of their transport and chemical evolution during the long range transport (ozone production, interactions between ozone and aerosols) (Fig. 1).

The aim of the present work was to identify the accuracy of the different methods that have been used in the literature to assess human exposure to wildfire in order to evaluate health effects of wildfire. In this regard, we suggest a method able to quantify wildfire emissions and concentrations appropriately. This method was applied to provide for the first time a detailed inventory of European wildfires between 2006 and 2010 in terms of burnt areas, and related air pollution emissions (Black carbon, particulate matter, etc.).

2. Methods

They included 2 steps.

1) Assessment of wildfire air pollutants emissions

In order to understand how wildfire exposure has been assessed in studies investigating health effects of wildfires, a literature search was performed in PubMed with the following Medical Subject Headings (MeSH) terms: “wildfires”, “bushfires”, “biomass burning”, “forest fires”, “wildfire emissions”, “wildfire smoke”, “vegetation smoke”, “health impact of wildfire”. Publications that fulfilled the following inclusion criteria were selected for further analysis: published during or before July 2013 with previously described MeSH terms, concerned with the health impacts of air pollution from wildfire, conducted as an epidemiological study (population based data), and published in English. In addition, some suitable published articles cited in the selected articles, but not selected by MeSH terms, were included because they concerned methodology. This procedure allowed identifying methods used in the literature to assess human exposure to wildfire and define their accuracy as defined by the degree of closeness of measurements of a quantity to that quantity's actual (true) value.

2) Performance in wildfire emissions assessment and wildfire inventory in Europe during the years 2006–2010

As the result of the literature search, wildfire inventory was obtained using the methodology introduced by Liousse et al. (2010). To resume this methodology: an integrated chain was constructed from visual localization of the wildfire, to emission estimates and exposure modeling using a RegCM4 model (Giorgi and Anyah, 2012; Solmon et al., 2006; Tummon et al., 2010). Burnt biomass regional distributions at 1 km spatial resolution and

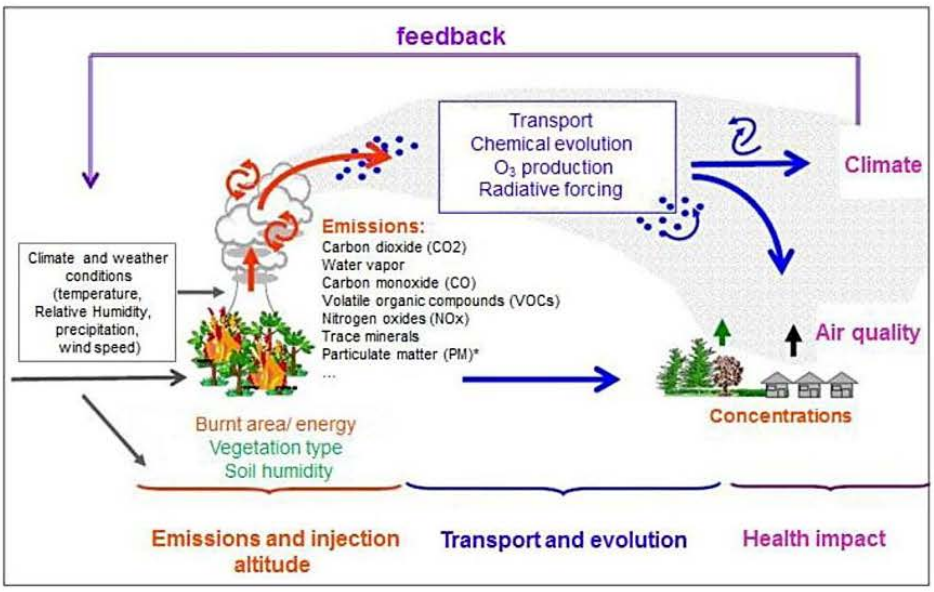


Fig. 1. Wildfire emissions, transport and related health impact « modified from (http://www.lmd.polytechnique.fr/~sturquet/research.htm) » *PM include mainly black carbon and organic carbon. Smoke particles are composed of about 60% of organic carbon (OC) and 5–10% of black carbon (BC) (Koppmann et al., 2005).

daily coverage from 2006 to 2010 were obtained from MODIS satellite burnt area data (delivered by EFFIS program, http://effis.jrc.it) with spatial coordinates (Latitude and longitude), which allow to have wildfire emissions at local area. Global Land Cover (GLC) vegetation maps and associated parameters for biomass density and combustion efficiency. Emission inventories were derived from burnt biomass regional distributions and emission factors for the different species of interest (Liousse et al., 2010).

3. Results

We present here how wildfire emissions and exposure have been quantified in the literature. Furthermore, a hybrid model that allows excluding anthropic sources of air pollution was used to have an inventory of wildfire in Europe for the period between 2006 and 2010. Burnt areas, related emissions and concentrations of major wildfire-related air pollutants (black carbon, particulate matter) were obtained.

3.1. Wildfire emissions quantification

Emissions from biomass burning include a wide range of gaseous compounds and particles contributing to the troposphere on local, regional, and even global scales (Fig. 1). Smoke composition depends on multiple factors, such as fuel type, moisture content, fire temperature and oxygenation, wind conditions and other weather-related influences (U.S. Environmental Protection Agency, 2008). Over 150 chemical species have been detected in the smoke of forest fuel combustion and pyrolysis experiments, including permanent gases such as CO, CO_2, NO_x, SO_x, Volatile Organic Compounds (VOCs) such as hydrocarbons, aldehydes, substituted furans, carboxylic acids, Benzene, Toluene, Xylene (BTX), Semi Volatile Organic Compounds (Polyaromatic Hydrocarbons, as well as Trace Elements such as Na, Mg, Ni, Cu, Pb, Fe, Mn) (Statheropoulos and Karma, October 2004). Besides emissions from combustion of forest fuel, other materials that are usually burnt during a vegetation fire can be found in vegetation smoke, meaning that wildfire smoke mixture depends on the flame-front pathway. If a vegetation fire is in the interface of an urban area, it is possible that the flame-front will co-burn fuels other than vegetation, such as wastes (Goldammer et al., 2009; Statheropoulos and Karma, 2007). In this case, synthesis of wildfire smoke can be the additive or synergistic result of all the possible emission products due to the pyrolysis and combustion of the vegetation and the wastes; significant quantities of hazardous components, such as dioxines (polychlorinated dibenzo-p-dioxines/polychlorinated dibenzofurans PCDDs/PCDFs), can also be contained in the resultant of smoke. However, when vegetation fires pass over rural fields or rural/urban constructions, then wood, plastics, or fertilizers can also be burned and materials, such as pulverized glass, cement, dust, asbestos, plaster, or other chemical compounds can be contained in the smoke produced. It has to be noted that radioactive species can, occasionally be found in wildfire smoke. Their origin can be from vegetation fuel radioactively contaminated (Goldammer et al., 2009; Statheropoulos and Karma, 2007).

Specific wildfire emissions have been rarely assessed. Data have shown that the relative contribution of biomass burning in open vegetation fires to the global annual emissions is approximately 41% of Carbon monoxide (CO), 15% of Nitrogen oxides (NOx), 32% of Black carbon (BC), and 64% primary organic carbon (POC). Assessing emissions from savannah, forest and agricultural fires requires knowledge of the appropriate emission factors as well as the spatial and temporal distribution of burnt biomass. This is a challenge due to remaining uncertainties. Many international experiments [DECAFE (Cachier et al., 1995; Lacaux et al., 1995), EXPRESSO (Delmas et al., 1999), SAFARI 2000 (Swap et al., 2002), SCAR (Hobbs et al., 1997)] under the International Geosphere Biosphere Program (IGBP), International Global Atmospheric Chemistry (IGAC), and Biomass Burning Experiment (BIBEX) umbrella have produced well characterized emission factors for tropical savannah and forest ecosystems. Little data exists for Mediterranean and boreal ecosystems. The particular ecosystem and vegetation types being burned determine the amount and composition of emissions. The first attempt to quantify burnt biomass on a global scale was based on land use statistics of the Food and Agriculture Organization of the United Nations (FAO) and general assumptions about percentages of surfaces burnt per year (Hao and Liu, 1994; Hao et al., 1990; Liousse et al., 1996). These estimates have been improved by satellite data: first, from active fire products (Cooke et al., 1996; Stroppiana et al., 2010), and then from satellite-derived burnt area products (AVHRR SPOT MODIS) (Liousse et al., 2004, 2010; Michel et al., 2005), and finally from the combination of both burnt areas and active fire satellite information (Hoelzemann et al., 2004; Ito and Penner, 2004; van der Werf et al., 2006). Vegetation types were considered differently by the following authors: constant ones with fixed representative ecosystems (Chin et al., 2002; Liousse et al., 2010; Mieville et al., 2010) or dynamic ones (vegetation models such as in GFED2 (van der Werf et al., 2006)) or in APIFLAMME (Turquety et al., 2010). Fire radiative energy (FRE), emitted radiant energy released during biomass combustion episodes, has been adopted as a new tool for determining variations in biomass combustion rates and production of atmospheric pollutants. Ichoku and Kaufman (2005) provided the first example by using a Moderate Resolution Imaging Spectroradiometer (MODIS), and another example was provided by Wooster et al. (2005). Now real-time emissions are given with the GFAS product in the Monitoring Atmospheric Composition and Change (MACC) and Global Monitoring for Environment and Security (GMES) program using MODIS FRE (Kaiser et al., 2012). While individual research groups have progressed in their ability to characterize emissions from biomass burning, there are substantial differences in the results obtained and methods used among the groups. In addition, differences exist between the assumptions made by the various groups concerning biomass density and emission factors (EF) and the link between FRE/emissions. Global intercomparisons have begun with collaborative programs between different research groups occurring, such as the GOFC-GOLD program, IGAC/iLEAPS/WMO Biomass Burning Initiative and the Fuel Consumption Intercomparison following the ACCENT/BBSO initiative (Stroppiana et al., 2010).

3.2. Wildfire exposure measurements and health impact in firemen

Many of wildfire emissions can have acute or long term health implications on the exposed populations, according to exposure limits given by official Organizations for health protection (U.S. Environmental Protection Agency, January 15, 2013; WHO, 1999). Among them, fines particles are the most harmful (WHO, 1999). Fine particles have been observed to causes changes in lung functions, leading to increases in respiratory and cardiovascular mortality and morbidity including asthma. Fine particles may reach the alveoli, and if not sufficiently cleared in the lungs and greats concentration, may enter the bloodstream or remain in the lung, resulting in chronic lung disease such as emphysema. Some VOCs may cause skin and eye irritation, drowsiness, coughing and wheezing, while other like benzene may be carcinogenic. Exposure to *Polycyclic Aromatic Hydrocarbons (PAHs)* has been linked to lung cancer in railway workers exposed to diesel exhaust fumes and occupational in coke oven and coal gas workers. Aldehydes are primarily mucus membrane irritant. Some such as formaldehyde may be carcinogenic and combination with other irritants (PAHs)

may lead to increase of carcinogenicity. Formaldehyde, the most abundantly produced in this class, causes eye, nose and throat irritation during smoke exposure. Free radicals are abundantly produced during the combustion of forest fuels. They may react with human tissues. Organic acids produced by oxidation of formaldehyde produced during the combustion of biomass fuels can cause a wide range of health impact including irritation of mucous membranes. Free radical abundantly produced during combustion of biomass fuels may react with human tissues. They have been observed to persist up to 20 min following formation and pose a problem for firefighters exposed to a fresh aerosol (Malilay, 1999).

Studies conducted in firemen provide an appropriate model for understanding health impact of wildfire emissions. Wildland (forest) firefighters comprise an occupational group with high exposure to biomass Smoke (Brauer, 1998). Reinhardt and Ottmar (2004) summarized measurements of smoke exposure among wildland firefighters and showed that firefighters can be exposed to significant levels of carbon monoxide (CO) and respiratory irritants, including formaldehyde, acrolein, and respirable particulate matter. Extensive research conducted during forest firefighting in the United States and Australia identified carbon monoxide and respiratory irritants as the major wildfire pollutants of concern to firefighters (Aisbett et al., 2012). In order to analyze the carbon monoxide poisoning among firefighters, Brotherhood et al. (1990) assessed the carboxyhemoglobin saturation (COHb%) levels from alveolar CO levels in 24 firefighters working with hand tools and in 12 accompanying scientific observers, before and after firefighting (duration 37–187 min) on 15 experimental bushfires. Carboxyhemoglobin levels increased on average by 0.7% per hour in the firefighters and by 0.3% per hour in the observers that indicate that firefighters are generally unlikely to experience hazardous levels of CO exposure. A risk assessment of firefighter exposure during prescribed burns and wildfires was conducted in Australia (Reisen et al., 2011). This study monitored air toxins within the breathing zone of the firefighters and showed that 30% of firefighters were exposed to high levels of a hazardous substance (i.e., CO, respirable particles, formaldehyde) that exceeded the occupational exposure standard (OES) for 5%–20% of time. Six percent of the firefighters were observed to have very high exposures (exceeding OES for more than 20% of time). However, the majority of firefighters (60%) had low or moderate exposures. Firefighters patrolling on top of ridges of steep burn areas or in downwind sectors tended to have high (44–62%) or very high (31–44%) exposures, with a large percentage of very high exposures experienced by supervisors (17%). This study was limited by the fact that monitoring was performed at only a small fraction of the burns conducted each year across Australia and may not be representative of the extensive program of fuel reduction burns carried out each year. Monitoring was restricted to tanker-based crews and to the later stages of campaign fire and did not include the initial more intense stage of the fires or hand crews. Lastly, neither firefighter work experience was taken into account, assuming that less experienced firefighters may endure higher smoke conditions, nor climatic factors influencing the smoke plume.

3.3. Wildfires human exposure assessment

Many studies document the impact of wildfire emissions at the population level, but to assign health effects from smoke emissions during a wildfire period involves a large uncertainty because many pollutants emitted by a wildfire can also be emitted by other pollution sources. Several methods, such as ground-based air quality monitoring (Chen et al., 2006; Morgan et al., 2010), remote sensing through satellite imagery (Rappold et al., 2011; van Donkelaar et al., 2010) and chemical transport models (Hodzic et al., 2007; Liousse et al., 2010), are used to quantify the impact of wildfire emissions on pollutant concentrations. The World Health Organization (WHO) recommends taking into account many parameters, such as monitoring of aerosol mass, visibility, meteorological parameters, optical depth and solar radiation, in order to decrease the uncertainty of measures and to accurately assess the impact of wildfire emissions on human health (WHO, 1999). In order to better estimate the relationship between wildfire exposure and corresponding health outcomes, both personal exposure and confounding factors (tobacco smoking, body mass index, comorbidities, and social economic status) should be taken into account. Methods should also allow distinction of wildfire emissions and air pollution from other sources. Epidemiological study methods have included collecting data from routine monitoring surveillance, counting the number of forest fires, employing self-administered questionnaires, and analyzing satellite data with or without the combination of modeling approaches. Commonly used exposure assessment methods are presented in Fig. 2, with their advantages and disadvantages presented in Table 1.

Exposure measured by the number of wildfires or questionnaires: Routine data or questionnaires can provide data on wildfire surface area, duration and number of events. To determine the respiratory and mental health effects of wildfires in the Galician municipalities of Spain in August 2006, Caamano-Isorna et al. (2011) ranked municipalities based on the number of wildfires observed in the study period: "no exposure" was defined as exposure to 0–3 wildfires, "medium exposure" as 4–10 wildfires and "high exposure" if >10 wildfires. Wildfire numbers were obtained from the Ministry of Health. Caamano-Isorna et al. found there was a high consumption of drugs for obstructed airway disease among pensioners, who are entitled to receive medication free of charge, during the months following wildfires in municipalities affected versus those unaffected by the wildfires. While the authors concluded that the wildfires had a significant effect on population health, the study was limited by not taking account personal exposure or including additional parameters, such as wildfire emissions, proximity to urban area, smoke transport, etc. Self-questionnaires were also used to assess the impact of wildfire on mental health during the October 2003 California firestorm that occurred at the wildland–urban interface (Marshall et al., 2007). The questionnaire was sent to the last known address of the 357 persons who were seeking assistance from adjacent American Red Cross and government relief centers who were recruited for the study. An additional questionnaire on fire exposure was included, which asked questions that included whether there was house damage or destruction by the fire, the respondents were able to see flames of the fire from their home or neighborhood, the respondents had difficulty breathing because of smoke or ashes, or the respondents were physically injured because of the fire. This questionnaire presented the same bias of interrelated reporting as discussed above. Künzli et al. (2006) used a web mail questionnaire to assess smoke exposure and occurrence of symptoms among children exposed to Southern California wildfires for a two-week period of the October 2003 fire season in the United States. Two cohorts of children participating in the University of Southern California Children's Health Study (CHS) were included in the study: CHS high school students (n = 873, 17–18 years) and elementary school children (n = 5 551, age 6–7 years). Wildfire exposure duration was quantified by the number of days of exposure during the two week period: not at all, 1–2 days, 3–5 days, 6–10 days and all of the days. While this study had the benefit of a well-characterized large study population, the design included some bias because many parents and students completed the fire questionnaire several months after the fire and both exposure and

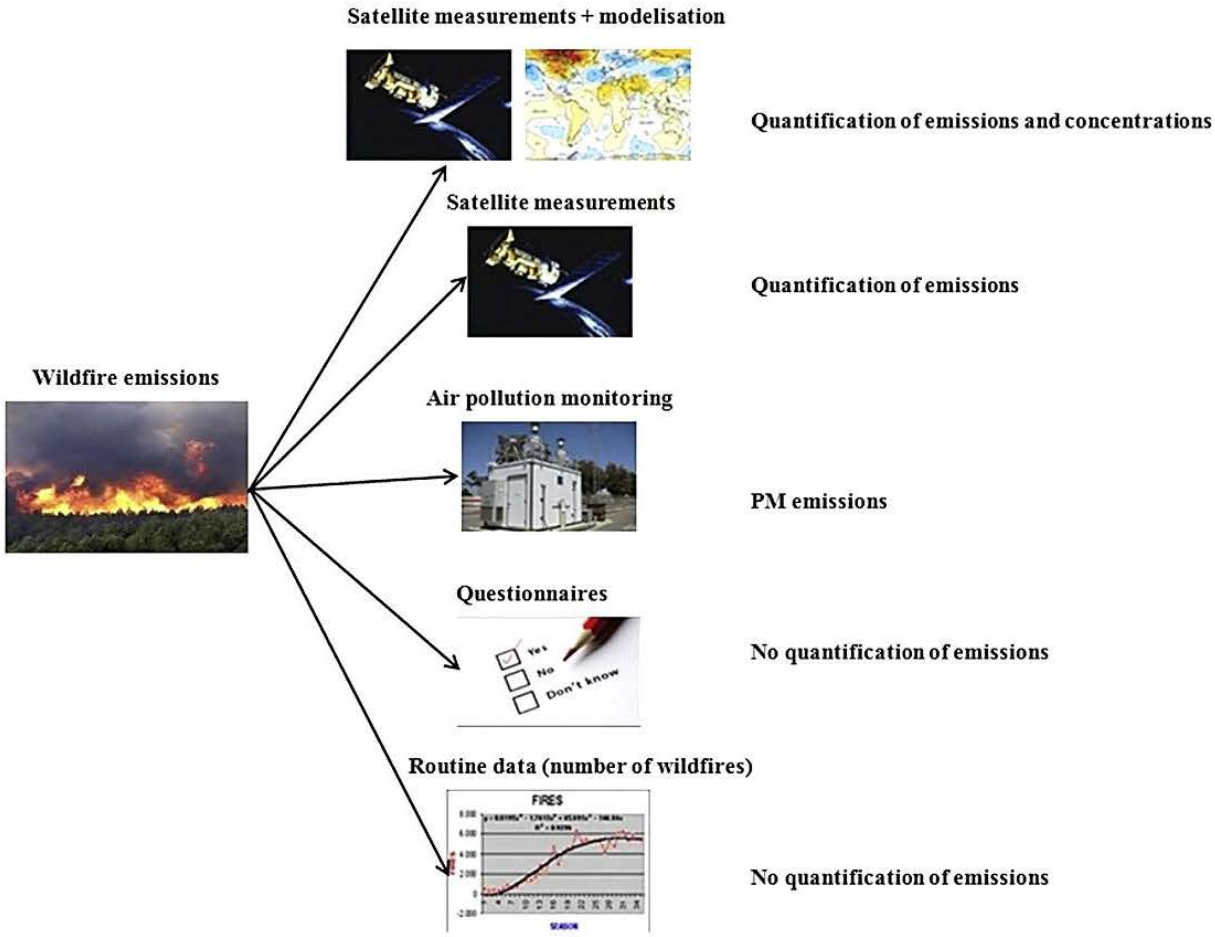


Fig. 2. Exposure assessment methods.

outcome were self-reported by the participants. In addition, because participants lived in the same area and knew each other, this could have led to interrelated reporting. Regardless, Künzli et al. found that exposure to wildfire was associated with an increase in eye and respiratory symptoms, medication use and physician visits. Questionnaire data (Künzli et al., 2006) from the first CHS high school student cohort was used by Mirabelli et al. (2009) to assess respiratory symptoms following wildfire smoke exposure; airway size was used as a susceptibility factor among the 465 non-asthmatic 16–19 year old participants. Web-based questionnaires were also used by Greven et al. (2011) to assess respiratory symptoms among firefighters in the Netherlands. This questionnaire corresponded to a version of the European Community Respiratory Health Survey questionnaire, with added

Table 1
Advantages and disadvantages of wildfire exposure assessments.

	Self-questionnaire	Routine data (firemen…)	Air pollution monitoring	Satellite measurement	Satellite data + chemical transport model
- Investigation of exposure ("exposed or not to wildfire")	+	+	++	+++	+++
	+	+++			
- Wildfire surface	+	+++		+++	
- Wildfire period				+++	
- Quantification of wildfire emissions	–	–	++	+++	
- Probability of:					
— Selection bias	+++	++	++	+	+
— Recall bias	+++	–	–	–	–
— Confounding	++	–	+++	+	+
- Time required	+	+	++	+ (++ for obtaining data)	+ (++ for obtaining data)
- Cost	+	+	++	+++	++++
- Accuracy	+	++	++	+++	++++
- Large scale	–	++	+	++	++
- Small scale	++	++	++	+++	+++
- Investigation of health effect	++	–	–	–	–

+++ very advantageous to + few advantageous and – no advantageous.

questions to identify the number of incidents, type, onset, and duration of symptoms and also possible exposure during the incident. Health outcomes and exposure assessment were based on self-reporting of the firefighters.

Exposure measured by monitoring stations: Many epidemiological studies use data from air pollution networks to assess the health impact of a wildfire. Network data is often recorded on a daily basis in many cases, which provides an advantage for analyzing outcomes with time. In order to determine the effects of wildfire smoke on daily mortality and hospital admissions in Sidney, Australia, Morgan et al. retrospectively studied PM_{10} concentrations from 1994 to 2002 (Morgan et al., 2010). PM_{10} exposure was measured by a tapered element oscillating microbalance (TEOM) at eight monitoring stations. The authors checked for days with bushfire or prescribed burns in newspaper archives and other sources. Bushfire days were defined as a city-wide 24 h average PM_{10} concentration that was higher than the 99th percentile for the study period. The contribution of bushfire PM_{10} to total PM_{10} was obtained by subtracting the background PM_{10}, as estimated from non-bushfire days. This study was limited by the potential for exposure misclassification; because the determination of bushfire days was limited to newspaper archives and other communication sources, it is possible that some bushfire days were missed/unreported and, thus the power of analysis was reduced. A recent Canadian study conducted in British Columbia (Elliott et al., 2013) established a link between fine PM and asthma dispensations in populations affected by forest fires. Ambient concentrations of PM were continuously measured for $PM_{2.5}$ and/or PM_{10} using TEOM. The province was divided into 89 local health areas (LHA), ranging in size from 40 to 130 000 km^2 whereas the population ranged from 542 to 352 783 in 2006. Any LHA with one or more TEOM was included. If an LHA had multiple stations, the one closet to the LHA population center was used. For LHA's with some measurements of $PM_{2.5}$ and PM_{10}, adjustment was realized using coefficients from linear models applied to all fire seasons. In 1997 in Singapore, haze pollution due to uncontrolled forest occurred from the end of August to the first week of November. Fifteen air monitoring stations located throughout the island were linked via public telephone network to a central control station. Twelve of the air monitoring stations were ambient stations and the other three were on the roadside. Air quality measurements were based on a reference method from the United States Environmental Protection Agency (US EPA), which uses the Pollutant Standards Index (PSI) developed for the reporting of daily air pollution concentrations (Emmanuel, 2000). The PSI converts daily pollutant concentrations measured at air monitoring stations to a simple number on a scale of 0–500. Intervals on the PSI scale are related to the potential health effects of the daily measured concentrations of the main air pollutants: SO_2, PM_{10}, NO_2, ozone and CO. The PSI intervals and the terms describing the air quality are as follows: good (0–50); moderate (51–100); unhealthy (101–200); very unhealthy (201–300); and hazardous (>300) (EPA, 1998). Many other epidemiological studies have used monitoring sites to assess wildfire emissions (Jalaludin et al., 2000; Kolbe and Gilchrist, 2009; Sillanpää et al., 2005). For example, Chen et al. (2006) used data from monitoring stations to assess the impact of air pollution due to wildfire and respiratory hospital admission in Brisbane Australia. For this study, PM_{10} measurements were made at five monitoring sites with TEOM instruments. However, only data from the monitoring site with the most complete records on PM_{10} (4.5% missing value) were used, which poses a problem of representativeness for the site selected.

Exposure measured using satellite data: As mentioned earlier, satellites have been used to take pictures of geographical areas burnt or active fire numbers by wildfire as a function of time. Moreover, satellite remote sensing has been used to directly detect aerosol since the 1970s (King et al., 1999). This technology has matured rapidly over the past few years, and current instruments aboard the United States National and Aeronautic Space Administration (NASA) and European Space Agency satellites can now provide derived measurements of trace gases and aerosols relating directly to most US EPA criteria air pollutants (Al-Saadi et al., 2005; Burrows et al., 1999; Fishman et al., 2003; King et al., 1999). For example, the MODIS instrument provides imagery for derived aerosol measurements such as aerosol optical depth (AOD) (Al-Saadi et al., 2005), which is defined as the dimensionless measure of light extinction integrated over the atmospheric column (Engel-Cox et al., 2004). Many studies have validated MODIS for the quantification of aerosols at ground level. MODIS aerosol data have been compared with measurements made at the Earth's surface and have been shown to be suitable for monitoring air quality events over local regional and global scales (Chu et al., 2003; Engel-Cox et al., 2004; Hutchison, 2003; Wang and Christopher, 2003). The relation between AOD and ground $PM_{2.5}$ concentrations can vary, however, because of changes in the mixing boundary layer, humidity and aerosol composition, meaning that different relationships may hold for different regions and seasons (Al-Saadi et al., 2005; Boyouk et al., 2010). Engel-Cox et al. (2004) used two kinds of monitoring stations, the Specification Trends and $PM_{2.5}$ Mass network (STN-M) from the US EPA, at ground based sites and data from the Interagency Monitoring of Protected Visual Environmental (IMPROVE) Colorado State University network to validate the link between MODIS AOD and $PM_{2.5}$. Quantitative analysis was performed in order to determine the association between satellite readings and ground-based measurements by calculating the correlation coefficient r of the two following linear regressions presenting $PM_{2.5}$ estimates from AOD values.

$$PM_{2.5}\ (\text{daily}) = 7.54 + 18.66 \times \text{AOD}$$

$$PM_{2.5}\ (\text{hourly}) = 6.35 + 22.5 \times \text{AOD}$$

As described above, Engel-Cox et al. (2004) confirmed that the correlation of MODIS AOD with ground based $PM_{2.5}$ varies by region. For example, the correlation was found higher in Eastern and Midwestern US, but the data were patchy and had lower correlations in the Western US. Of note, AOD values useful for $PM_{2.5}$ estimates and exposure measurements are also given for many worldwide stations by the ground-based NASA Aerosol Robotic Network (AERONET) network (Holben et al., 1998). Many epidemiological studies have also used satellite data to estimate personal exposure to wildfire emissions. Rappold et al. (2011) used an AOD measured by a geostationary operational environmental satellite (GEOS) to evaluate the exposure of 42 North Carolina counties to a dense plume produced by a peat bog wildfire over a 3 day window of time. The satellite provided AOD data every half-hour at 4 km resolution. AOD was scaled from 0 to 2, with the maximum value corresponding to a heavy haze. A threshold of AOD > 1.25 was chosen as an indicator of a high density plume. Counties with a minimum of 25% of geographic area exceeding this threshold were defined as being exposed to the smoke plume for each day in the high-exposure window. To improve the estimation of personal exposure to smoke emissions from Californian wildfires in 2003, Delfino et al. estimated $PM_{2.5}$ levels at the ZIP code level using spatial interpolation from measured $PM_{2.5}$, light extinction, meteorological conditions and smoke information from MODIS satellite images at 250 m resolution (Delfino et al., 2009). Analyses were performed during three wildfire periods: before (1–20 October 2003), during (21–30 Oct 2003) and after (31 October–15 November 2003). Available air pollution data from governmental

network sites was used to build prediction models. Spatial interpolations of $PM_{2.5}$ concentrations were determined using inverse distance weighting, kriging or cokriging methods for non-fire periods. Polygons based on satellite images were created to represent each smoke covered area under different smoke densities, and each polygon was assigned a $PM_{2.5}$ concentration value using measured or estimated concentrations from predictive models (Delfino et al., 2009). Holstius et al. (2012) analyzed the potential impact of exposure to wildfire emissions during pregnancy and birth weight during the California wildfire of October 2003. The potential wildfire exposure window, as defined by using MODIS satellite imagery, was from 21 October to 10 November 2003. Infants delivered before 21 October 2003 were assumed not exposed in utero. Infants delivered later than 10 November 2003, were also classified as unexposed. All remaining births were classified as exposed on the basis of temporal overlap between the wildfire exposure window and gestational intervals. High or low exposures were defined by the threshold of 40 $\mu g/m^3$: census tracts closer to monitors with average PM_{10} measures during the fires of <40 $\mu g/m^3$ were classified as low exposure, and tracts with average daily levels >40 $\mu g/m^3$ were classified as high exposure. This cut point split the PM_{10} monitors in the Southern California Air Basin in half, with 36% of births that gestated during the fires occurring in high exposure census tracts. This method of exposure measurement depended on satellite imagery to define the exposure window and the delay of exposition and PM monitor surveillance to define the cut point. An assumption was that if PM_{10} levels were >40 $\mu g/m^3$, then emissions from the wildfire were considered high even though baseline level emissions were not distinguished. In addition, no personal exposure or the interval between exposure target and home were taken into account. In the recent Canadian study reported above, MODIS was used to classify Local Health Areas (LHA) as fire affected and non-fire affected and to identify extreme fire days (Elliott et al., 2013). Recent studies (Cooper et al., 2012) have determined global exposure estimates from satellite data (MODIS, MSIR, OMI) linked to ground networks such as AERONET.

Exposure measured using satellite data, emissions and chemical transport models: Modeling approaches allow combination of multi-emissions, transport and satellite data to reach estimates of exposure. Both AOD and $PM_{2.5}$ concentrations may be calculated. Up to now, regional models [such as CHIMERE (Bessagnet et al., 2008)] could display PM concentrations whereas global models focused on AOD and aerosol composition. Now, both parameters may be retrieved from regional and global models. For both model types, satellite data assimilation would improve the accuracy of model concentration fields if a precise description of both model and observation uncertainties could be given. Modeling approaches do allow distinction between the role of the different sources of PM concentrations and exposure estimates. Here are a few examples. At the global scale, MODIS and Multiangle Imaging Spectroradiometer (MISR) AOD were combined into a single improved estimate of AOD. The AOD–$PM_{2.5}$ conversion factor was calculated using the global Chemical Transport Model (CTM) GEOS-Chem, and this factor was applied to the AOD so that $PM_{2.5}$ levels could be deduced (van Donkelaar et al., 2010). Johnston et al. (2012), used monthly resolved emissions estimates from Global Fire Emissions Database version 2 (GFED2) combined with satellite observations from the GEOS-Chem global 3D chemical transport model to estimate the average annual mortality associated with exposure to global landscape fire smoke-specific PM. Two sets of GEOS-Chem simulations spanning a ten year period (1997–2006) were performed. The first set included all aerosol emission sources (fossil fuel, biofuel, landscape fires, natural dust and sea salt), and the second set excluded landscape fire emissions to separate the contribution from this source. PM was estimated using MODIS AOD (Remer et al., 2005) and MISR AOD. The PM estimates were evaluated using ground based AOD from AERONET (Holben et al., 1998) due to the lack of $PM_{2.5}$ surface measurement in that study. At a regional scale, a meso-scale chemistry transport model, CHIMERE, was used with ground based and satellite aerosol optical measurements to investigate the effects of wildfire emissions in Europe during the intense fire season in the summer of 2003. The MODIS-derived daily smoke inventory and the injection altitude of smoke particles were taken into account. The same results have been obtained for other periods and areas with RegCM (Malavelle et al., 2011; Solmon et al., 2006; Tummon et al., 2010) and WRF models (Mahmud et al., 2012).

Personal exposure: To our knowledge, there are no published studies with measurements of personal PM exposures during episodes of smoke from wildfires with exception of data from firemen. However, in a still unpublished panel study conducted in Kotka, Finland, personal $PM_{2.5}$ measurements were conducted during an air pollution episode lasting 11 days. The episode was linked to wildfires in Western Russia based on ionic composition of the samples, backward trajectories, and satellite maps on fire areas. For 41 study subjects, one measurement day coincided with the episode, 1–11 measurements being conducted during the rest of the study period. Average personal $PM_{2.5}$ exposure during the episode was 22.1 $\mu g/m^3$, and during the rest of the study period, 6.6 $\mu g/m^3$. The respective outdoor concentrations were 25.3 and 4.9 $\mu g/m^3$. In this area, with typically low air pollution levels, daily personal exposures were thus increased 3-fold and outdoor concentrations 5-fold because of the episode. Instead of measuring personal exposure, Barn et al. measured indoor $PM_{2.5}$ concentrations in 12 homes in Canadian communities impacted by wildfire smoke (Barn et al., 2008). The indoor impact seemed modest as the average outdoor $PM_{2.5}$ concentration during the fire season was only 10.6 $\mu g/m^3$, i.e. even lower than during the heating season (16.2 $\mu g/m^3$). Based on the measurements, it was calculated that the infiltration factor was 0.61 (i.e., 61% of outdoor particles entered indoors and remained suspended in air) during fire season (indoor concentration 8.2 $\mu g/m^3$). Wu et al. conducted a study in Wu et al. (2006) which the infiltration factor for particles from agricultural burning in the state of Washington, U.S., was 0.62. The values reported in the two studies are within the range of infiltration factors reported for four European cities in the EXPOLIS study (0.59–0.70) (Hänninen et al., 2004), which implies that particles from wildfires penetrate as efficiently indoors, where people spend 80–90% of their time, as urban particles in general. Because of efficient penetration, staying indoors during smoke episodes may provide only moderate protection against exposure to particulate pollutants. During wildfires and prescribed burnings in Colorado, U.S., the average indoor/outdoor (I/O) ratio for $PM_{2.5}$ was as high as 0.8 even when all study participants kept their windows closed during the episode (Henderson et al., 2005). Indoor concentrations (14.7 $\mu g/m^3$) during the episode days were 3.2-fold compared to the non-episode period (4.6 $\mu g/m^3$). Highest I/O ratios were observed for the homes with the highest air exchange rates; this demonstrates how additional protection during episodes could be gained by limiting the flow rate of ventilation systems. Staying indoors and keeping doors and windows closed is the protective measure most often recommended in public service announcements for susceptible persons. Other recommendations include using air cleaners, wearing a protective mask, and finally leaving the affected area. The effectiveness of portable air cleaners on reducing indoor PM during fire episodes has been evaluated in two studies (Barn et al., 2008; Henderson et al., 2005). This was done using either high-efficiency particulate absorption (HEPA) filters or electrostatic air cleaners, and a considerable 63–88% reduction in indoor

concentration/infiltration was achieved for $PM_{2.5}$. However, the effectiveness of filtering systems against ultrafine particles (less than 0.1 μm (Seinfeld and Pandis, 1998)) or gaseous pollutants is unclear.

3.4. Inventory of wildfires in Europe during the years 2006–2010

Table 2 displays the distribution of the number of burnt areas, total burnt areas, total emissions over the period of BC, POC, CO, and NO_2 by country from 2006 to 2010 obtained using Liousse et al. model (Liousse et al., 2010). Countries with the highest number of fires during this period were Portugal (22.4%), Italy (22.6%) and Spain (13.5%), which together contributed to 58.5% of the total number of fires. However, in the same period, Greece, with only 6.8% of the fires, had the largest burnt land area (Fig. 3a). Fig. 3b presents the number of fires/total burnt area for each country. As defined, this ratio is high for countries with a large number of fires but small burnt area and low for countries with a small number of fires but large burnt area. As observed in Fig. 3b, Greece and Israel had the smallest ratio (0.07), followed by Turkey with a ratio equal to 0.1. Ratios are confirmed in Fig. 3a and Table 2 and indicate that even countries with a small number of fires had a large burnt area. For example, Turkey had 53 fires (1.3%) that corresponded to a total of 513.6 km^2, which represents 3.1% of the total burnt European area (Table 2). Countries with highest ratio (Kossovo with a ratio = 0.87, Romania with a ratio = 0.59) had a burnt area that was small compared to the number of fires. As presented in Table 2, 10 burnt areas represented 11.5 km^2 in Kossovo, and 2 burnt areas corresponded to 3.4 km^2 in Romania. As a comparison, in Israel, 2 burnt areas corresponded to 30.7 km^2. Wildfire emissions were important in Portugal, Greece and Spain for the pollutants considered, with emissions consisting of 26.4% of BC and 27.8% of CO, 18.9% BC and 18.1% of CO, 21.3% BC and 22.3% CO, respectively. Emissions of POC and NO_2 were also important in these countries (Fig. 4a and b). High emissions of all pollutants (BC, CO, NO_2 and POC) were also observed in Albany, Algeria, Italy and Turkey, although at lower levels than in Portugal, Greece and Spain. Compared to other Mediterranean countries, France had a smaller percent of number of burnt areas (1.4%) and proportion of wildfire emissions (1.2% for each pollutant considered) (Table 2). Total emissions of BC and CO obtained with the new inventory are of the order of 0.031 Tg and 5.3 Tg, respectively, over the whole period. Such values are in agreement with GFASv1 inventory (Kaiser et al., 2012) over Europe for the same period (0.03 and 4.92, respectively). Note that the GFED3 (van der Werf et al., 2010) inventory results in lower budgets of BC and CO emissions (0.02 and 3.2, respectively). Uncertainties linked to MODIS missing data for the 2006–2008 years or to the choice of Liousse et al. (2010) methodology will be discussed in a further paper.

4. Discussion

The main challenge to epidemiological studies that evaluate wildfire emissions during a given event is the estimation of personal exposure. So far, most of the used methods have not distinguished air pollution from wildfires from other source-oriented pollution. To address this problem, we applied a hybrid model allowing to characterize wildfire emissions from the others.

As discussed above, studies have used self-reported questionnaires, routine data (number of wildfires), air quality monitoring stations, chemical transport models, and satellite data with visibility or AOD, etc., to assess exposure to wildfire emissions. These methods have been sometimes combined to enhance the estimation of personal exposure to wildfire emissions (Henderson et al., 2011). Different degrees of uncertainty are associated with these methods (Table 1). Exposure assessments based on a self-administered questionnaire which estimates the exposure to fire based on the declaration of the individuals threatened by flames (Greven et al., 2011; Künzli et al., 2006), are poor and underestimate real exposure. For example, fire emissions may not be quantified but based on fire smell (Künzli et al., 2006), which is not sufficient to determine an exact exposure (Künzli et al., 2006). Several studies have also used air quality monitors to estimate the concentration of air pollutants emitted by a fire, especially PM.

Table 2
Wildfires in Europe between 2006 and 2010.

Country	Number of burnt areas		Burnt area (km^2)		BC (Tons of C)		CO (Tons of C)		NO_2		Primary OC (Tons of C)	
	Sum	(%)	Sum	(%)	Sum	(%)	Sum	(%)	Sum	(%)	Sum	(%)
Albania	310	(7.6)	1630.8	(9.7)	2175.4	(6.2)	362756.5	(6.2)	1664.3	(6.1)	19684.9	(6.0)
Algeria	482	(11.8)	NA		3236	(9.2)	509401.6	(8.7)	2479.9	(9.0)	28791.3	(8.8)
Bosnia and Herzego	96	(2.4)	533.0	(3.2)	408.7	(1.2)	60524.5	(1.0)	323.0	(1.2)	3206.4	(1.0)
Bulgaria	94	(2.3)	755.5	(4.5)	351	(1.0)	52972.1	(0.9)	248.8	(0.9)	2478.9	(0.8)
Croatia	53	(1.3)	378	(2.3)	282.8	(0.8)	39549.1	(0.7)	231.4	(0.8)	2123.8	(0.7)
Cyprus	20	(0.5)	50.2	(0.3)	108.5	(0.3)	17461.3	(0.3)	87.9	(0.3)	989.3	(0.3)
France	57	(1.4)	186.8	(1.1)	409.4	(1.2)	70031.2	(1.2)	316.6	(1.2)	3888.5	(1.2)
Greece	276	(6.8)	3614.79	(21.5)	6655.2	(18.9)	1055994.2	(18.1)	5413.7	(19.7)	59774.6	(18.3)
Hungary	2	(0.05)	8.0	(0.05)	10.9	(0.03)	1879.1	(0.03)	8.1	(0.03)	100.3	(0.03)
Israel	2	(0.05)	30.7	(0.2)	22.5	(0.1)	2366.2	(0.04)	21.6	(0.1)	144.5	(0.04)
Italy	920	(22.6)	2757.5	(16.4)	1960.8	(5.6)	279343.6	(4.8)	1588.2	(5.8)	14969.3	(4.6)
Kosovo	10	(0.2)	11.5	(0.1)	21.4	(0.1)	3774.1	(0.1)	16.2	(0.1)	208.4	(0.1)
Macedonia	108	(2.7)	576.5	(3.4)	472.3	(1.3)	70190.1	(1.2)	377.4	(1.4)	3775.9	(1.2)
Montenegro	67	(1.6)	284.6	(1.7)	226.2	(0.6)	37298.7	(0.6)	165.5	(0.6)	1922.1	(0.6)
Morocco	11	(0.3)	NA		80.8	(0.2)	13907.9	(0.2)	57.9	(0.2)	769.1	(0.2)
Portugal	911	(22.4)	2740.4	(16.3)	9267.4	(26.4)	1626479.4	(27.8)	7151.6	(26.1)	91233.5	(28.0)
Romania	2	(0.0)	3.4	(0.02)	5.1	(0.01)	891.1	(0.02)	3.8	(0.01)	48.5	(0.01)
Serbia	44	(1.1)	185.7	(1.1)	306.1	(0.9)	53441.7	(0.9)	231.6	(0.8)	2929.9	(0.9)
Slovenia	1	(0.02)	5.6	(0.03)	14.6	(0.04)	2596.0	(0.04)	11.2	(0.04)	145.7	(0.0)
Spain	548	(13.5)	2529.6	(15.1)	7471.8	(21.3)	1307138.4	(22.3)	5754.0	(21.0)	73064.2	(22.4)
Tunisia	5	(0.1)	NA		90.8	(0.3)	15794.9	(0.3)	70.6	(0.3)	887.0	(0.3)
Turkey	53	(1.3)	513.6	(3.1)	1561.6	(4.4)	265973.8	(4.5)	1225.8	(4.5)	14949.0	(4.6)
Total[a]	4072	(100.0)	16796.2	(100.0)	35139.3	(100.0)	5849765.4	(100.0)	27449.0	(100.0)	326085.0	(100.0)

BC: Black carbon; CO: Carbon Monoxide; NO_2: Nitrogen dioxide; OC: organic carbon; C: carbon.
[a] Total emissions of countries listed above, NA: not available; %: percentage.

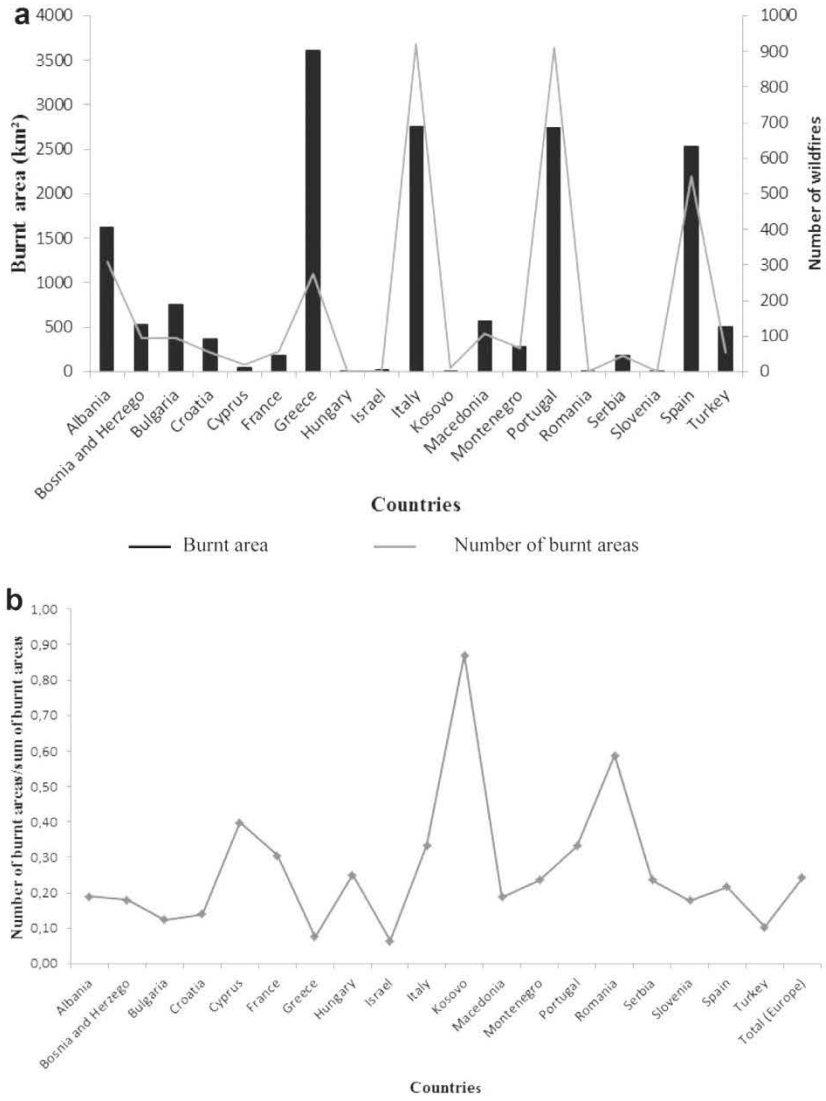


Fig. 3. a: Burnt area versus number of fire from 2006 to 2010. b: Ratio number of burnt areas/burnt areas versus countries.

Limitations of monitoring stations include not being able to monitor an entire wildfire area and being damaged by the fire (Delfino et al., 2009). The veritable problem, however, is to distinguish wildfire emissions from those caused by other sources. This problem arises frequently for all quantitative methods. Spatially-resolved particle mass data provided by satellites is superior to using data provided only by the nearest available monitoring station data because it better represents personal exposure (Delfino et al., 2009). However, it is important to recognize that errors in satellite resolution at the ground level may occur. Second, as discussed by Al-Saadi et al. (2005), MODIS AOD cannot be retrieved (or has more uncertainty) if a region is cloudy or has strong reflection of the sun from bodies of water and over snow (ice and bright desert areas). In some regions, correspondence between MODIS AOD and $PM_{2.5}$ has not been found, as may occur when aerosols are entirely aloft above the boundary layer and, therefore, do not influences surface air quality. In a study conducted in British Columbia, Canada, during the 2003 fire season, Henderson and colleagues (Henderson et al., 2011) used three different methods to assess smoke exposure and its association to respiratory and cardiovascular health outcomes: regulatory TEOM air quality monitors, smoke-related PM_{10} from a California puff dispersion model (CALPUFF) and a SMOKE exposure metric for plumes visible in satellite images. The findings differed depending on the assessment method used, and statistically significant outcomes were observed only with the TEOM air quality monitors. Overall, these results indicate a degree of uncertainty among methods. Notably, all of the described approaches may be combined within a modeling system, which is currently the only tool to allow separation of wildfires and other pollution source impacts through different simulations.

Another challenge in the determination of wildfire impact is population mobility, as people change their location by traveling from home to the office, shops, etc. In addition, it is difficult to evaluate personal exposure during wildfire events because people close to wildfires are often evacuated. All of these parameters add much bias and uncertainty to the exposure assessment of wildfire on human health. Satellite data have been used over the past decade and are found to better represent personal exposure (Delfino et al., 2009). Satellite data are often combined with

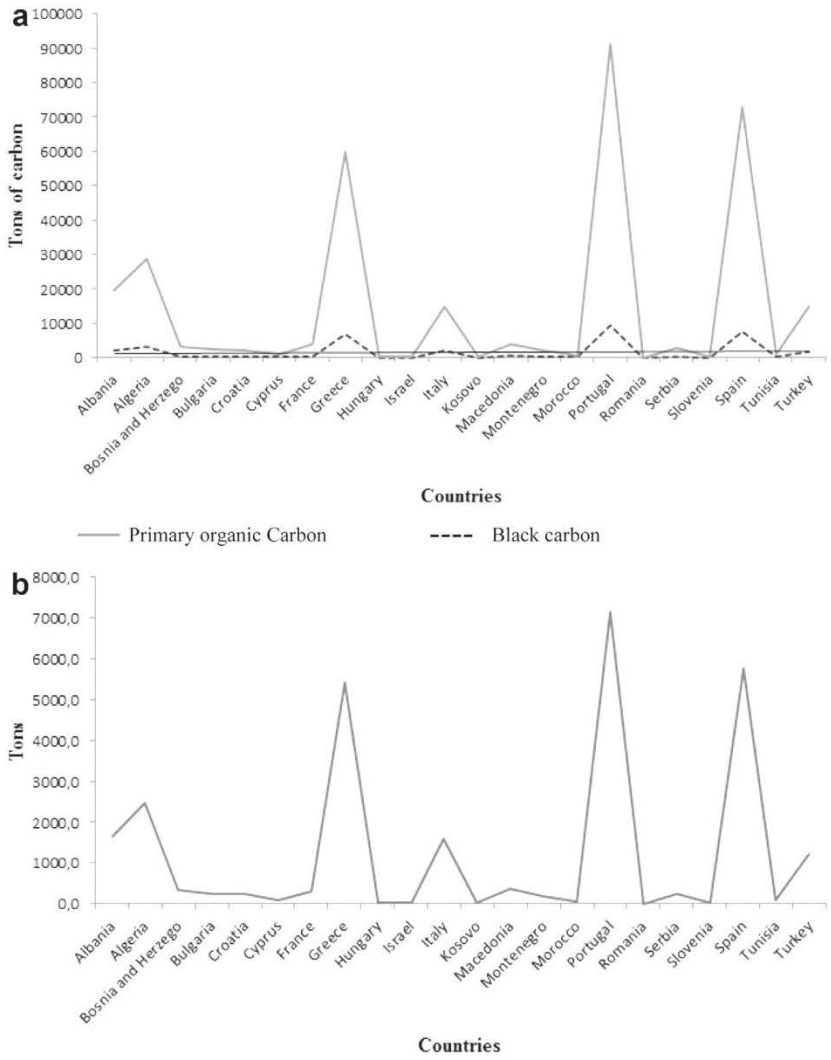


Fig. 4. a: Distribution of black carbon and primary organic carbon from 2006 to 2010. b: NO_2 distribution from 2006 to 2010.

chemical transport model or air quality monitoring station data in order to reduce uncertainty in the data. The type of burning biomass and the prevailing meteorological conditions are likely to affect the amount and quality of gaseous and particulate emissions in vegetation fires. Fire maps are produced by complex satellite techniques, but satellites alone cannot reliably assess the intensity of the burning and the emissions. Better assessment would improve the modeling of air mass transport and PM concentrations in air quality forecasts. Satellite based modeling techniques and early warning systems for susceptible populations should be developed in the near future. Improving wildfire exposure assessment methods will reduce the uncertainty of health outcomes and the association between pollution sources. Some studies have compared exposed and non-exposed regions; however, this comparison is most effective if the compared regions have the same climate characteristics (wind speed, temperature, etc.) and population exposed. Rappold et al. (2011) assessed the impact of a peat bog wildfire in North Carolina by comparing exposed counties ($n = 42$) to non-exposed reference counties ($n = 23$). The population of the exposed and reference counties were similar in terms of age, ethnicity, population density and socio-economic status. Health outcomes were significantly higher in exposed counties than in reference counties. Delfino et al. (2009) created an index of pre-wildfire period (1–20 October), wildfire period (21–30 October) and post-wildfire period (31 October–15 November) and tested $PM_{2.5}$ to this indicator to separate the effects of wildfire PM from other source-oriented PM. Aditama (2000) studied the health impact of haze from the Indonesian forest fire of 1997 by comparing data during September 1997 and June 1998 to data for two years earlier between 1995 and 1996. This study showed a significant increase of respiratory outcomes during the forest fire period. Most study data are collected retrospectively; therefore, the use of satellite data provides an opportunity to have real time datasets including hourly surface measurements and half-hour wildfire locations (Al-Saadi et al., 2005). The use of satellite data has improved the knowledge of the continental scale distribution and transport of PM across North America (Al-Saadi et al., 2005), and now satellite coverage and data are available for all regions of the world. Statistical analyses in several studies use time series analyses to determine fire related increase in health outcomes (Mott et al., 2005; Tham et al., 2009) and follow the impact of health effects at successive time intervals. Statistical analysis should be adjusted with all parameters that might have an impact in health outcomes. Climatic conditions like wind speed; temperature and relative

humidity should be taken into account in the analysis. To determine the impact of wildfire at the ZIP code level, Delfino et al. (2009) adjusted analyses to include weather, fungal spores (associated with asthma), day of week, ZIP code level and sociodemographic status.

The adoption of a standardized methodology using satellite data, emissions and chemical transport models will improve exposure assessment of wildfire emissions and, thus, personal wildfire exposure assessment.

For the first time, we applied a hybrid model to quantify the emissions and concentrations resulting from wildfires in Europe to be used to evaluate their health impact.

The inventory of wildfire emissions in Europe allowed us to quantify the number of burnt area, total burnt area and wildfire emissions (BC, CO, OCP NO_2) during five years from 2006 to 2010. Wildfire emissions in the Mediterranean countries have been previously studied. However, in our study we quantified BC, CO, OCP and NO_2 while in other studies (Narayan et al., 2007; Vilen and Fernandes, 2011), CO_2 emissions were quantified and comparison between these studies to our inventory could not be established. Indeed, Narayan et al. (2007) assessed the potential for CO_2 emissions mitigation in Europe through prescribed burning. In this study average burnt area in Europe were calculated during a period of five year (1999–2003). The comparison between this period of 1999–2003 to the period of 2006–2010 with our inventory in Europe shows a big difference in terms of burnt area and number of wildfire. In Greece, the burnt area increased in from 36214.6 ha in the period of 1999–2003 according Narayan et al. to 361 479 ha for our study. Burnt area increased 10 times over a period of less than 5 years.

Funding statement

This publication arises from the project PHASE (contract number EAHC 20101103) which has received funding from the European Union, in the framework of the Health Programme.

Acknowledgment

Data were provided by the European Forest Fire Information System – EFFIS (http://effis.jrc.ec.europa.eu) of the European Commission Joint Research Centre. ECCAD database (eccad.sedoo.fr) used to compare emission inventory budgets is also acknowledged. This manuscript was reviewed by Julian Gerson and edited by Suzette Smiley-Jewell.

References

Aditama, T.Y., 2000. Impact of haze from forest fire to respiratory health: Indonesian experience. Respirology 5, 169–174.
Aisbett, B., Wolkow, A., Sprajcer, M., Ferguson, S.A., 2012. "Awake, smoky, and hot": providing an evidence-base for managing the risks associated with occupational stressors encountered by wildland firefighters. Appl. Ergon. 43, 916–925.
Al-Saadi, J., Szykman, J., Pierce, R.B., Kittaka, C., Neil, D., Chu, D.A., Remer, L., Gumley, L., Prins, E., Weinstock, L., MacDonald, C., Wayland, R., Dimmick, F., Fishman, J., 2005. Improving National Air Quality forecasts with Satellite Aerosol Observations. Bull. Am. Meteorol. Soc. 86, 1249–1261.
Barn, P., Larson, T., Noullett, M., Kennedy, S., Copes, R., Brauer, M., 2008. Infiltration of forest fire and residential wood smoke: an evaluation of air cleaner effectiveness. J. Expo. Sci. Environ. Epidemiol. 18, 503–511.
Bessagnet, B., Menut, L., Curci, G., Hodzic, A., Guillaume, B., Liousse, C., Moukhtar, S., Pun, B., Seigneur, C., Schulz, M., 2008. Regional modeling of carbonaceous aerosols over Europe—focus on secondary organic aerosols. J. Atmos. Chem. 61, 175–202.
Boyouk, N., Léon, J.-F., Delbarre, H., Podvin, T., Deroo, C., 2010. Impact of the mixing boundary layer on the relationship between PM2.5 and aerosol optical thickness. Atmos. Environ. 44, 271–277.
Brauer, M., 1998. Health Impacts of Biomass Air Pollution (Kuala Lumpur, Malaysia).
Brotherhood, J.R., Budd, G.M., Jeffery, S.E., Hendrie, A.L., Beasley, F.A., Costin, B.P., Wu, Z.E., 1990. Fire fighters' exposure to carbon monoxide during Australian bushfires. Am. Ind. Hyg. Assoc. J. 51, 234–240.
Burrows, J.P., Weber, M., Buchwitz, M., Rozanov, V., Ladstätter-Weißenmayer, A., Richter, A., DeBeek, R., Hoogen, R., Bramstedt, K., Eichmann, K.-U., Eisinger, M., Perner, D., 1999. The Global Ozone Monitoring Experiment (GOME): mission concept and first scientific results. J. Atmos. Sci. 56, 151–175.
Caamano-Isorna, F., Figueiras, A., Sastre, I., Montes-Martínez, A., Margarita, T., Piñeiro-Lamas, M., 2011. Respiratory and mental health effects of wildfires: an ecological study in Galician municipalities (north-west Spain). Environ. Health 10.
Cachier, H., Liousse, C., Buat-Menard, P., Gaudichet, A., 1995. Particulate content of savanna fire emissions. J. Atmos. Chem. 22, 123–148.
Chen, L., Verrall, K., Tong, S., 2006. Air particulate pollution due to bushfires and respiratory hospital admissions in Brisbane, Australia. Int. J. Environ. Health Res. 16, 181–191.
Chin, M., Ginoux, P., Kinne, S., Torres, O., Holben, B.N., Duncan, B.N., Martin, R.V., Logan, J.A., Higurashi, A., Nakajima, T., 2002. Tropospheric aerosol optical thickness from the GOCART model and comparisons with satellite and sun photometer measurements. J. Atmos. Sci. 59, 461–483.
Chu, D.A., Kaufman, Y.J., Zibordi, G., Chern, J.D., Mao, J., Li, C., Holben, B.N., 2003. Global monitoring of air pollution over land from the Earth Observing System-Terra Moderate Resolution Imaging Spectroradiometer (MODIS). J. Geophys. Res. Atmos. 108 (D21), 4661. http://dx.doi.org/10.1029/2002JD003179.
Chuvieco, E., Giglio, L., Justice, C., 2008. Global characterization of fire activity: toward defining fire regimes from Earth observation data. Glob. Change Biol. 14, 1488–1502.
Cooke, W.F., Koffi, B., Grégoire, J.M., 1996. Seasonality of vegetation fires in Africa from remote sensing data and application to a global chemistry model. J. Geophys. Res. Atmos. 101, 21051–21065.
Cooper, M.J., Martin, R.V., van Donkelaar, A., Lamsal, L., Brauer, M., Brook, J.R., 2012. A satellite-based multi-pollutant index of global air quality. Environ. Sci. Technol. 46, 8523–8524.
Delfino, R.J., Brummel, S., Wu, J., Stern, H., Ostro, B., Lipsett, M., Winer, A., Street, D.H., Zhang, L., Tjoa, T., Gillen, D.L., 2009. The relationship of respiratory and cardiovascular hospital admissions to the southern California wildfires of 2003. Occup. Environ. Med. 66, 189–197.
Delmas, R.A., Druilhet, A., Cros, B., Durand, P., Delon, C., Lacaux, J.P., Brustet, J.M., Serça, D., Affre, C., Guenther, A., Greenberg, J., Baugh, W., Harley, P., Klinger, L., Ginoux, P., Brasseur, G., Zimmerman, P.R., Grégoire, J.M., Janodet, E., Tournier, A., Perros, P., Marion, T., Gaudichet, A., Cachier, H., Ruellan, S., Masclet, P., Cautenet, S., Poulet, D., Biona, C.B., Nganga, D., Tathy, J.P., Minga, A., Loemba-Ndembi, J., Ceccato, P., 1999. Experiment for Regional Sources and Sinks of Oxidants (EXPRESSO): an overview. J. Geophys. Res. Atmos. 104, 30609–30624.
Elliott, C.T., Henderson, S.B., Wan, V., 2013. Time series analysis of fine particulate matter and asthma reliever dispensations in populations affected by forest fires. Environ. Health 12.
Emmanuel, S.C., 2000. Impact to lung health of haze from forest fires: the Singapore experience. Respirology 5, 175–182.
Engel-Cox, J.A., Holloman, C.H., Coutant, B.W., Hoff, R.M., 2004. Qualitative and quantitative evaluation of MODIS satellite sensor data for regional and urban scale air quality. Atmos. Environ. 38, 2495–2509.
EPA, U., 1998. Report on US EPA Air Monitoring from Haze from S.E Asia Biomass Fires.
European Commission, 2010. Forest Fires in Europe 2010.
Fishman, J., Wozniak, A.E., Creilson, J.K., 2003. Global distribution of tropospheric ozone from satellite measurements using the empirically corrected tropospheric ozone residual technique: Identification of the regional aspects of air pollution. Atmos. Chem. Phys. 3, 893–907.
Giglio, L., Randerson, J.T., van der Werf, G.R., Kasibhatla, P.S., Collatz, G.J., Morton, D.C., DeFries, R.S., 2010. Assessing variability and long-term trends in burned area by merging multiple satellite fire products. Biogeosciences 7, 1171–1186.
Giorgi, F., Anyah, R.O., 2012. Introduction: the road towards RegCM4. Clim. Res. 52, 3–6.
Goldammer, J.G., Statheropoulos, M., Andreae, M.O., 2009. Impacts of vegetation fire emissions on the environment, human health, and security: a global perspective (Chapter 1). In: Bytnerowicz, A., A., M., Riebau, A., Andersen, C. (Eds.), Developments in Environmental Science.
Goldammer, J.G., Stocks, B.J., On behalf the Team of Authors of 'White paper on Vegetation, F., Global, C., 2011. Migration and Global Environmental Change (UK Government's Foresight Project). SR10: Specification for a State of Science Review – Wildland Fires, Government Office for Science, http://www.fire.uni-freiburg.de/GlobalNetworks/UK-Foresight-Project-Climate-Change-Migration-2011-SR-10-Wildland-Fire.pdf.
Greven, F.E., Rooyackers, J.M., Kerstjens, H.A.M., Heederik, D.J., 2011. Respiratory symptoms in firefighters. Am. J. Ind. Med. 54, 350–355.
Hänninen, O.O., Alm, S., Katsouyanni, K., Künzli, N., Maroni, M., Nieuwenhuijsen, M.J., Saarela, K., Srám, R.J., Zmirou, D., Jantunen, M.J., 2004. The EXPOLIS study: implications for exposure research and environmental policy in Europe. J. Expo. Anal. Environ. Epidemiol. 14, 440–456.
Hao, W.M., Liu, M.-H., 1994. Spatial and temporal distribution of tropical biomass burning. Glob. Biogeochem. Cycles 8, 495–503.
Hao, W.M., Liu, M.-H., Crutzen, P.J., 1990. Estimates of annual and regional releases of CO_2 and other trace gases to the atmosphere from fires in the tropics, based

on the FAO statistics for the period 1975–1980. In: Goldammer, D.J.G. (Ed.), Fire in the Tropical Biota. Springer Berlin Heidelberg, pp. 440–462.
Henderson, D.E., Milford, J.B., Miller, S.L., 2005. Prescribed burns and wildfires in Colorado: impacts of mitigation measures on indoor air particulate matter. J. Air Waste Manag. Assoc. 55, 1516–1526.
Henderson, S.B., Brauer, M., Macnab, Y.C., Kennedy, S.M., 2011. Three measures of forest fire smoke exposure and their associations with respiratory and cardiovascular health outcomes in a population-based cohort. Environ. Health Perspect. 119, 1266–1271.
Hobbs, P.V., Reid, J.S., Kotchenruther, R.A., Ferek, R.J., Weiss, R., 1997. Direct radiative forcing by smoke from biomass burning. Science 275, 1777–1778.
Hodzic, A., Madronich, S., Bohn, B., Massie, S., Menut, L., Wiedinmyer, C., 2007. Wildfire particulate matter in Europe during summer 2003: meso-scale modeling of smoke emissions, transport and radiative effects. Atmos. Chem. Phys. 7, 4043–4064.
Hoelzemann, J.J., Schultz, M.G., Brasseur, G.P., Granier, C., Simon, M., 2004. Global Wildland Fire Emission Model (GWEM): evaluating the use of global area burnt satellite data. J. Geophys. Res. Atmos. 109, D14504.
Holben, B.N., Eck, T.F., Slutsker, I., Tanré, D., Buis, J.P., Setzer, A., Vermote, E., Reagan, J.A., Kaufman, Y.J., Nakajima, T., Lavenu, F., Jankowiak, I., Smirnov, A., 1998. AERONET—a federated instrument network and data archive for aerosol characterization. Remote Sens. Environ. 66, 1–16.
Holstius, D.M., Reid, C.E., Jesdale, B.M., Morello-Frosch, R., 2012. Birth weight following pregnancy during the 2003 Southern California wildfires. Environ. Health Perspect. 120, 1340–1345.
Hutchison, K.D., 2003. Applications of MODIS satellite data and products for monitoring air quality in the state of Texas. Atmos. Environ. 37, 2403–2412.
Ichoku, C., Kaufman, Y.J., 2005. A method to derive smoke emission rates from MODIS fire radiative energy measurements. IEEE Trans. Geosci. Remote Sens. 43, 2636–2649.
Ito, A., Penner, J.E., 2004. Global estimates of biomass burning emissions based on satellite imagery for the year 2000. J. Geophys. Res. Atmos. 109, D14S05.
Jalaludin, B., Smith, M., O'Toole, B., Leeder, S., 2000. Acute effects of bushfires on peak expiratory flow rates in children with wheeze: a time series analysis. Aust. N. Z. J. Public Health 24, 174–177.
Johnston, F.H., Henderson, S.B., Chen, Y., Randerson, J.T., Marlier, M., Defries, R.S., Kinney, P., Bowman, D.M.J.S., Brauer, M., 2012. Estimated global mortality attributable to smoke from landscape fires. Environ. Health Perspect. 120, 695–701.
Kaiser, J.W., Heil, A., Andreae, M.O., Benedetti, A., Chubarova, N., Jones, L., Morcrette, J.J., Razinger, M., Schultz, M.G., Suttie, M., van der Werf, G.R., 2012. Biomass burning emissions estimated with a global fire assimilation system based on observed fire radiative power. Biogeosciences 9, 527–554.
King, M.D., Kaufman, Y.J., Tanré, D., Nakajima, T., 1999. Remote sensing of tropospheric aerosols from space: past, present, and future. Bull. Am. Meteorol. Soc. 80, 2229–2259.
Kolbe, A., Gilchrist, K.L., 2009. An extreme bushfire smoke pollution event: health impacts and public health challenges. N. S. W. Public Health Bull. 20, 19–23.
Koppmann, R., von Czapiewski, K., Reid, J.S., 2005. A review of biomass burning emissions, part I: gaseous emissions of carbon monoxide, methane, volatile organic compounds, and nitrogen containing compounds. Atmos. Chem. Phys. Discuss. 5, 10455–10516.
Künzli, N., Avol, E., Wu, J., Gauderman, W.J., Rappaport, E., Millstein, J., Bennion, J., McConnell, R., Gilliland, F.D., Berhane, K., Lurmann, F., Winer, A., Peters, J.M., 2006. Health effects of the 2003 Southern California wildfires on children. Am. J. Respir. Crit. Care Med. 174, 1221–1228.
Lacaux, J.P., Brustet, J.M., Delmas, R., Menaut, J.C., Abbadie, L., Bonsang, B., Cachier, H., Baudet, J., Andreae, M.O., Helas, G., 1995. Biomass burning in the tropical savannas of Ivory Coast: an overview of the field experiment Fire of Savannas (FOS/DECAFE 91). J. Atmos. Chem. 22, 195–216.
Liousse, C., Andreae, M.O., Artaxo, P., Barbosa, P., Cachier, H., Grégoire, J.M., Hobbs, P., Lavoué, D., Mouillot, F., Penner, J., Scholes, M., Schultz, M.G., 2004. Deriving global quantitative estimates for spatial and temporal distributions of biomass burning emissions. In: Granier, C., Artaxo, P., Reeves, C.E. (Eds.), Emissions of Atmospheric Trace Compounds. Springer, Netherlands, pp. 71–113.
Liousse, C., Guillaume, B., Grégoire, J.M., Mallet, M., Galy, C., Pont, V., Akpo, A., Bedou, M., Castéra, P., Dungall, L., Gardrat, E., Granier, C., Konaré, A., Malavelle, F., Mariscal, A., Mieville, A., Rosset, R., Serça, D., Solmon, F., Tummon, F., Assamoi, E., Yoboué, V., Van Velthoven, P., 2010. Updated African biomass burning emission inventories in the framework of the AMMA-IDAF program, with an evaluation of combustion aerosols. Atmos. Chem. Phys. 10, 9631–9646.
Liousse, C., Penner, J.E., Walton, J.J., Eddleman, H., Chuang, C., Cachier, H., 1996. Modelling biomass burning aerosols. In: Biomass Burning and Global Change, pp. 492–508.
Mahmud, A., Hixson, M., Kleeman, M.J., 2012. Quantifying population exposure to airborne particulate matter during extreme events in California due to climate change. Atmos. Chem. Phys. 12, 7453–7463.
Malavelle, F., Pont, V., Mallet, M., Solmon, F., Johnson, B., Leon, J.-F., Liousse, C., 2011. Simulation of aerosol radiative effects over West Africa during DABEX and AMMA SOP-0. J. Geophys. Res. Atmos. 116, D08205.
Malilay, J., 1999. A Review of Factors Affecting the Human Health Impacts of Air Pollutants from Forest Fires. WHO/UNEP/WMO, pp. 255–270.
Marshall, G.N., Schell, T.L., Elliott, M.N., Rayburn, N.R., Jaycox, L.H., 2007. Psychiatric Disorders Among Adults Seeking Emergency Disaster Assistance after a Wildland-urban Interface Fire, vol. 58. Psychiatric Services, Washington, D.C, pp. 509–514.
Michel, C., Liousse, C., Grégoire, J.M., Tansey, K., Carmichael, G.R., Woo, J.H., 2005. Biomass burning emission inventory from burnt area data given by the SPOT-VEGETATION system in the frame of TRACE-P and ACE-Asia campaigns. J. Geophys. Res. Atmos. 110, D09304.
Mieville, A., Granier, C., Liousse, C., Guillaume, B., Mouillot, F., Lamarque, J.F., Grégoire, J.M., Pétron, G., 2010. Emissions of gases and particles from biomass burning during the 20th century using satellite data and an historical reconstruction. Atmos. Environ. 44, 1469–1477.
Mirabelli, M.C., Künzli, N., Avol, E., Gilliland, F.D., Gauderman, W.J., McConnell, R., Peters, J.M., 2009. Respiratory symptoms following wildfire smoke exposure: airway size as a susceptibility factor. Epidemiology 20, 451–459.
Morgan, G., Sheppeard, V., Khalaj, B., Ayyar, A., Lincoln, D., Jalaludin, B., Beard, J., Corbett, S., Lumley, T., 2010. Effects of bushfire smoke on daily mortality and hospital admissions in Sydney, Australia. Epidemiology (Cambridge, Mass.) 21, 47–55.
Mott, J.A., Mannino, D.M., Alverson, C.J., Kiyu, A., Hashim, J., Lee, T., Falter, K., Redd, S.C., 2005. Cardiorespiratory hospitalizations associated with smoke exposure during the 1997, Southeast Asian forest fires. Int. J. Hyg. Environ. Health 208, 75–85.
Mouillot, F., Field, C.B., 2005. Fire history and the global carbon budget: a $1^\circ \times 1^\circ$ fire history reconstruction for the 20th century. Glob. Change Biol. 11, 398–420.
Narayan, C., Fernandes, P.M., van Brusselen, J., Schuck, A., 2007. Potential for CO_2 emissions mitigation in Europe through prescribed burning in the context of the Kyoto Protocol. For. Ecol. Manag. 251, 164–173.
Rappold, A.G., Stone, S.L., Cascio, W.E., Neas, L.M., Kilaru, V.J., Carraway, M.S., Szykman, J.J., Ising, A., Cleve, W.E., Meredith, J.T., Vaughan-Batten, H., Deyneka, L., Devlin, R.B., 2011. Peat bog wildfire smoke exposure in rural North Carolina is associated with cardiopulmonary emergency department visits assessed through syndromic surveillance. Environ. Health Perspect. 119, 1415–1420.
Reinhardt, T.E., Ottmar, R.D., 2004. Baseline measurements of smoke exposure among wildland firefighters. J. Occup. Environ. Hyg. 1, 593–606.
Reisen, F., Hansen, D., Meyer, C.P., 2011. Exposure to bushfire smoke during prescribed burns and wildfires: firefighters' exposure risks and options. Environ. Int. 37, 314–321.
Remer, L.A., Kaufman, Y.J., Tanré, D., Mattoo, S., Chu, D.A., Martins, J.V., Li, R.R., Ichoku, C., Levy, R.C., Kleidman, R.G., Eck, T.F., Vermote, E., Holben, B.N., 2005. The MODIS aerosol algorithm, products, and validation. J. Atmos. Sci. 62, 947–973.
Seinfeld, J., Pandis, S., 1998. Atmospheric Chemistry and Physics. Wiley Ed, New York.
Sillanpää, M., Saarikoski, S., Hillamo, R., Pennanen, A., Makkonen, U., Spolnik, Z., Van Grieken, R., Koskentalo, T., Salonen, R.O., 2005. Chemical composition, mass size distribution and source analysis of long-range transported wildfire smokes in Helsinki. Sci. Total Environ. 350, 119–135.
Solmon, F., Giorgi, F., Liousse, C., 2006. Aerosol modelling for regional climate studies: application to anthropogenic particles and evaluation over a European/African domain. Tellus B 58, 51–72.
Statheropoulos, M., Karma, S., 2007. Complexity and origin of the smoke components as measured near the flame-front of a real forest fire incident: a case study. J. Anal. Appl. Pyrolysis 78, 430–437.
Statheropoulos, M., Karma, S., October 2004. Health impacts of forest fires smoke on fire-fighters and populations. Associate European Center for Forest Fires (ECFF) 2.
Stroppiana, D., Brivio, P.A., Grégoire, J.M., Liousse, C., Guillaume, B., Granier, C., Mieville, A., Chin, M., Pétron, G., 2010. Comparison of global inventories of CO emissions from biomass burning derived from remotely sensed data. Atmos. Chem. Phys. 10, 12173–12189.
Swap, R., Annegarn, H.J., Suttles, J.T., Haywood, J., Helmlinger, M.C., Hely, C., Hobbs, P.V., Holben, B.N., Ji, J., King, M.D., Landmann, T., Maenhaut, W., Otter, L., Pak, B., Piketh, S.J., Platnick, S., Privette, J., Roy, D., Thompson, A.M., Yokelson, D.W.R., 2002. The Southern African Regional Science Initiative (SAFARI 2000): overview of the dry season field campaign. S. Afr. J. Sci. 98, 125–130.
Tham, R., Erbas, B., Akram, M., Dennekamp, M., Abramson, M.J., 2009. The impact of smoke on respiratory hospital outcomes during the 2002–2003 bushfire season, Victoria, Australia. Respirology 14, 69–75.
Tummon, F., Solmon, F., Liousse, C., Tadross, M., 2010. Simulation of the direct and semidirect aerosol effects on the southern Africa regional climate during the biomass burning season. J. Geophys. Res. Atmos. 115, D19206.
Turquety, et al., 2010. Analysis and Prediction of the Impact of Fires on Air Quality in the Mediterranean and Europe (Apiflame).
U.S. Environmental Protection Agency, January 15, 2013. National Ambient Air Quality Standards for Particulate Matter, pp. 3086–3287.
U.S. Environmental Protection Agency, C.O.o.E.H.H.A., Missoula County Health Department, California Air Resources Board, 2008. Wildfire Smoke – a Guide for Public Health Officials. California Department of Public Health.
van der Werf, G.R., Randerson, J.T., Giglio, L., Collatz, G.J., Kasibhatla, P.S., Arellano Jr., A.F., 2006. Interannual variability in global biomass burning emissions from 1997 to 2004. Atmos. Chem. Phys. 6, 3423–3441.
van der Werf, G.R., Randerson, J.T., Giglio, L., Collatz, G.J., Mu, M., Kasibhatla, P.S., Morton, D.C., DeFries, R.S., Jin, Y., van Leeuwen, T.T., 2010. Global fire emissions and the contribution of deforestation, savanna, forest, agricultural, and peat fires (1997–2009). Atmos. Chem. Phys. 10, 11707–11735.

IV.2. Présentation de l'article 2 : Non-accidental health impact of wildfire

Tous les ans, à travers le monde, des incendies se déclenchent sur plusieurs centaines de millions d'hectares de forêts et des formations végétales. Dans les années à venir, leur fréquence pourrait être augmentée, en raison du phénomène de réchauffement climatique.

Ces incendies entraînent la libération, à travers la fumée, de nombreux polluants sur la troposphère. En fonction de l'intensité des feux et d'autres paramètres métrologiques tels que la température, l'humidité relative…etc., la concentration de certains polluants émis est très élevée, dépassant largement le seuil fixé par les institutions sanitaires. Parmi les polluants émis, nombreux sont ceux connus pour leurs effets sanitaires. Les particules en suspension font partie des polluants émis. Celles-ci sont bien connues pour leurs effets néfastes sur la santé respiratoire. En effet, les particules ayant un diamètre inferieurs à 2.5 µm, représentant entre 80-90% des particules émises [86], ont la capacité de pénétrer dans les alvéoles pulmonaires et de provoquer ainsi des maladies chroniques des poumons.

Durant les dernières décennies, quelques études épidémiologiques se sont intéressées sur l'impact sanitaire des émissions des feux de forêts. Ces études ont essayé d'établir un lien entre l'exposition aux particules émises par la fumée issue des feux de forêts et les indicateurs de santé. Elles ont, par ailleurs, montré que l'exposition aux particules fines était associée à l'augmentation des admissions à l'hôpital pour des maladies respiratoires et cardiovasculaires [43-47, 49].

L'article 2 consiste en une revue systématique décrivant les études épidémiologiques sur les impacts sanitaires des feux de forêts. Cependant, cette revue reste cantonnée aux effets respiratoires non-accidentels de l'exposition aux émissions issues des incendies, ne traitant ni les effets accidentels, ni psychologiques, des incendies de forêts.

Int. J. Environ. Res. Public Health **2014**, *11*, 11772-11804; doi: 10.3390/ijerph111111772

OPEN ACCESS

International Journal of
Environmental Research and Public Health
ISSN 1660-4601
www.mdpi.com/journal/ijerph

Review

Non-Accidental Health Impacts of Wildfire Smoke

Hassani Youssouf [1,2], Catherine Liousse [3], Laurent Roblou [3], Eric-Michel Assamoi [3], Raimo O. Salonen [4], Cara Maesano [1,2], Soutrik Banerjee [1,2] and Isabella Annesi-Maesano [1,2,*]

1 Department of Epidemiology of Respiratory and Allergic Disease (EPAR), UMR-S 1136, Institute Pierre Louis of Epidemiology and Public Health, National Institute for Health and Medical Research (INSERM), 27 Rue Chaligny, 75012 Paris, France; E-Mails: hassani.youssouf@upmc.fr (H.Y.); carahenson@gmail.com (C.M.); soutrik.banerjee@upmc.fr (S.B.)

2 Department of Epidemiology of Respiratory and Allergic Disease (EPAR), UMR-S 1136, Institute Pierre Louis of Epidemiology and Public Health, University Pierre and Marie Curie (UPMC)—Sorbonne University, 27 Rue Chaligny, 75012 Paris, France

3 Laboratory of Aerology, National Center for Scientific Research (CNRS), University of Toulouse, 14 Avenue Edouard Belin, 31400 Toulouse, France; E-Mails: catherine.liousse@aero.obs-mip.fr (C.L.); laurent.roblou@aero.obs-mip.fr (L.R.); eric-michel.assamoi@aero.obs-mip.fr (E.-M.A.)

4 Environmental Epidemiology Unit, National Institute for Health and Welfare, P.O. Box 95, FI-70701 Kuopio, Finland; E-Mail: raimo.salonen@thl.fi

* Author to whom correspondence should be addressed; E-Mail: isabella.annesi-maesano@inserm.fr; Tel.: +33-1-4473-8449; Fax: + 33-1-4473-8454.

External Editor: Paul B. Tchounwou

Received: 25 July 2014; in revised form: 23 October 2014 / Accepted: 29 October 2014 / Published: 14 November 2014

Abstract: Wildfires take a heavy toll on human health worldwide. Climate change may increase the risk of wildfire frequency. Therefore, in view of adapted preventive actions, there is an urgent need to further understand the health effects and public awareness of wildfires. We conducted a systematic review of non-accidental health impacts of wildfire and incorporated lessons learned from recent experiences. Based on the literature, various studies have established the relationship between one of the major components of wildfire, particulate matter (particles with diameter less than 10 μm (PM_{10}) and less than 2.5 μm ($PM_{2.5}$)) and cardiorespiratory symptoms in terms of Emergency Rooms visits and hospital

admissions. Associations between wildfire emissions and various subclinical effects have also been established. However, few relationships between wildfire emissions and mortality have been observed. Certain segments of the population may be particularly vulnerable to smoke-related health risks. Among them, people with pre-existing cardiopulmonary conditions, the elderly, smokers and, for professional reasons, firefighters. Potential action mechanisms have been highlighted. Overall, more research is needed to better understand health impact of wildfire exposure.

Keywords: wildfires emissions; wildfire exposure; health impact; cardiorespiratory disease; particulate matter

1. Introduction

A wildfire is an uncontrolled fire of combustible vegetation that spreads quickly over woodland or brush. Wildfire smoke composition depends on multiple factors, such as fuel type, moisture content, fire temperature and oxygenation, wind conditions and other weather-related influences [1]. A large percentage of wildfires are caused directly or indirectly by human actions [2]. According to a 2010 European Commission report on forest fires, more than 95% of forest fires in many countries in Europe were of human origin and 53% were caused by smoking and fire making in Estonia [2]. However, wildfire spreads is influenced by environmental factors such as high temperatures, drought and temporary dry spells. In northern countries of the boreal hemisphere, fire danger conditions are generally observed in the summer when rain precipitation usually decreases. In tropical areas, fires occur during the dry season, from December to February in boreal hemisphere and from June to September in austral hemisphere. Due to climate change, wildfires have become more problematic for public health and ecosystems in the past decades [2].

It is estimated that wildfire smoke is composed by more than thousands individual chemical compounds and its composition depends on the fuel type, the temperature of the fire, and the wind conditions [1]. Primarily, wildfire smoke is composed of carbon dioxide and water vapor. Other common components of smoke present in lower concentrations are carbon monoxide (CO), formaldehyde, acrolein, polyaromatic hydrocarbons, benzene and particle Matter (PM), namely small particulates suspended in air, which include particles with diameters less than 2.5 micrometers ($PM_{2.5}$) and 10 micrometers (PM_{10}). However, about 80%–90% of mass particulate matter produced by wild land is within the fine particles ($PM_{2.5}$) range with high black carbon, organic carbon [3] and brown carbon contents [4].

Many of wildfire emissions can have acute or long term health implications on the exposed populations, according to the official Organizations for health protection [1,5,6]. Among the major components of wildfire smoke, fine particles ($PM_{2.5}$) affects ambient air quality and has various effects on human health [7]. These effects are expected to further increase during wildfire smoke episodes where $PM_{2.5}$ and PM_{10} concentrations above air quality standards can occur [8]. Standard values according to the United States Environmental Protection Agency (USEPA) are fixed in 24 h exposure, to 35 $\mu g/m^3$ for $PM_{2.5}$ and 150 $\mu g/m^3$ for PM_{10} [9]. Mean annual standard values according to the

World Health Organization (WHO) are 12 μg/m^3 for $PM_{2.5}$ and 35 μg/m^3 for PM_{10} respectively. In our observational data, we have found values 75 times higher than the WHO standard for $PM_{2.5}$ during a wildfire in Spain. Fine particles have been observed to causes changes in lung functions, leading to increases in respiratory and cardiovascular mortality and morbidity including asthma. Fine particles may reach the alveoli, and if not sufficiently cleared in the lungs and greats concentration may enter the bloodstream or remain in the lung, resulting in chronic lung disease such as emphysema. Other wildfire emissions like volatile organic compounds (VOCs) may cause skin and eye irritation, drowsiness, coughing and wheezing, while other like benzene may be carcinogenic [10,11].

The health effects of wildfires are less widely known [12]. So far, despite the fact that wildfires take a heavy toll on human health worldwide, few studies reported health effects of wildfires, in particular health effects of trace gases and aerosols emitted by wildfires remain poorly quantified due to uncertainties on wildfire emissions assessment, and the taking into account of their transport and chemical evolution during the long range transport (ozone production, interactions between ozone and aerosols) [11].

Some epidemiological studies have established the relationship between exposure to PM from wildfire smoke and increased visits to hospital emergency rooms and hospital admissions for cardiorespiratory diseases [13–18]. Exposure to wood smoke $PM_{2.5}$ from wild land fires and agricultural burning has been linked with cardiovascular effects, including increased cardiovascular mortality, risk of developing cardiovascular disease and risk of myocardial infarction [19]. However, with the exception of two literature reviews [8,11], limited to papers published until January 2012 [8,11,14], data on wildfire related health effects are sparse and many questions remain unanswered.

The aim of the present article was to contribute to the knowledge on health impacts of wildfires by providing a systematic review of non-accidental health outcomes related to wildfire exposure according to the literature, including subclinical effects and health effect in firefighters in order to understand mechanisms. In the present review, non-accidental has been defined any outcome where there is no identifiable incident, trauma, stress or other mental conditions resulting directly from the fire.

2. Methods

2.1. Search Strategy

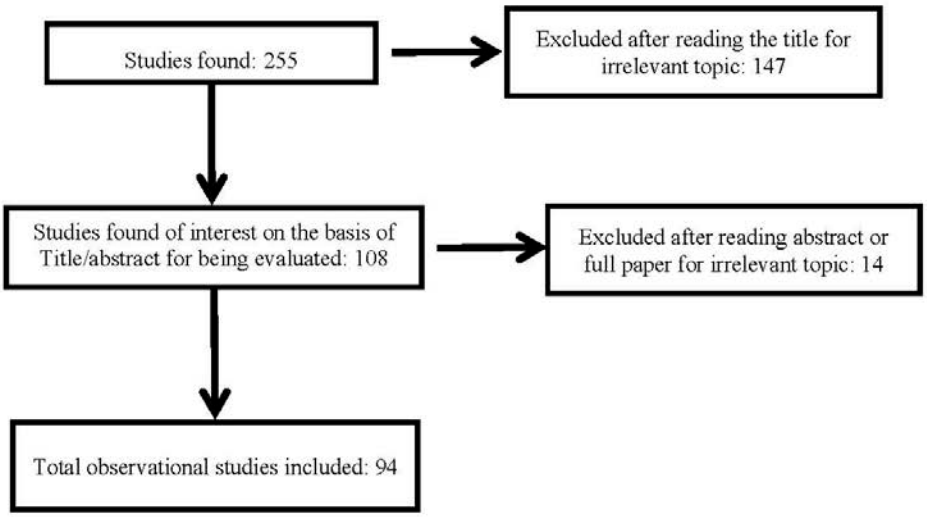
A literature search of online databases (PubMed, ISI, and Google Scholar) up to April 2014 without specifying the start date was performed using the terms, "wildfire smoke exposure", "bushfire smoke exposure", "forest fire smoke exposure", "wildfire emissions", "bushfire emissions", "forest fire emissions", "health effects of wildfire", "health effects of bushfire", "health effects of forest fire". In addition, references of the retrieved articles were examined to identify further relevant articles. A sifting process identified (from study titles, abstracts and the full paper) those studies suitable for inclusion in the review.

2.2. Eligibility Criteria

Published studies were included in this review if they met the following criteria: peer-reviewed original article, review article, population study (cohort, case-crossover, time-series, case–control or

cross-sectional study, meta-analysis (none)), written in English and reporting on non-accidental health impacts of wildfire. Figure 1 shows a flow diagram describing the study selection process.

Figure 1. Flow diagram of study selection process.



2.3. Data Abstraction

All but the studies meeting the above mentioned criteria were discarded. Data on health impact of wildfires were then systematically summarized in tables where the following characteristics were recorded for each study included: location, publication reference (first author's last name, year of publication), study population, health outcomes (hospital admissions, mortality), statistical methods, exposure assessment and findings. The percentage increase of health outcomes after exposure to particulate matter was extracted if available.

3. Results

3.1. Study Selection

The initial search by key words yielded 255 papers, 94 of which were considered as relevant to the original research question (Figure 1).

3.2. Wildfire Exposure Assessment

Several methods have been used to quantify exposure to wildfire emissions in epidemiologic studies investigating health impact of wildfires [11,14]. Self-administrated questionnaires which estimated the exposure to wildfire based on the declaration of the individuals threatened by flames miscalculated real exposure [16] due to report bias in the absence of a quantitative measure [16,20]. Usual objective methods included the number of known wildfires as a proxy for smoke episodes [11,21], the daily burned area as a proxy for daily smoke exposure [14] or more rarely PM measurements to identify single smoke episodes caused by known fires [22]. Air quality monitoring stations estimated the PM

concentration from all sources including those emitted by a fire. However in some cases, monitoring stations were not able to monitor an entire wildfire area [13]. Furthermore, the stations are sometimes far from wildfire sources and may be not representative of the burnt area. Recently, wildfire smoke exposure assessment has been estimated through multiple sources of information [14] as ground-based air quality monitoring [23,24], remote sensing through satellite imagery [18,25] and chemical transport models [26,27]. In particular satellite data were used to evaluate wildfire exposure because spatially-resolved particle mass data provided by satellites is superior to using data provided only by the nearest available monitoring station data [13]. In addition, satellites allow detections of plume *etc.* in which case daily variation in urban pollution is not be confounded with smoke exposure.

3.3. Study Design and Statistical Approaches to Evaluate Wildfire Health Effects

There has been considerable variability in study design and statistical approaches used to evaluate the health effects from wildfire smoke exposure. This can challenge the comparison of results, especially in regards to urban background PM and acute toxicity from wildfire. Concerning the study design, different approaches were taken in order to better distinguish the health impacts of air pollution from wildfire smoke to those from other sources of pollution and to better evaluate health outcomes before, during and after the wildfire exposure [13] and in exposed and non-exposed area [13,21]. A lot of statistical approaches were applied, among them paired *t*-tests and multiple regression [28], time-series analysis [29], logistic regression with repeated measures was used to estimate associations with each outcome [13], generalized linear model with negative binomial distribution and Poisson distribution [13], time-series analysis combined with generalized linear Poisson regression models [30]. Poisson distribution was used in several studies to take wildfire smoke exposure and daily health outcomes into account. Other studies use Case-crossover analysis [31] and ecological studies [21,32]. For all statistical methods, potential confounding factors were taken into account in the multivariate models [33].

3.4. Non-Accidental Health Effects Related to Wildfire

Based on the literature, non-accidental health outcomes that have been found related to wildfire emissions include: (1) all-causes and cardiorespiratory mortality (Table 1), (2) cardiorespiratory morbidity (Table 2), and (3) birth weight. In addition, it is well documented that certain segments of the population are particularly vulnerable to wildfire smoke-related health risks [34]. Among them people with pre-existing cardiopulmonary conditions [35], the elderly [32], smokers and firefighters [20].

3.4.1. Non-Accidental Health Effects at the Population Level

Table 1 and Table 2 present data showing links between wildfire and non-accidental morbidity and mortality.

Table 1. Exposure to wildfire and non-accidental mortality.

Location	Authors	Study Period	Population	Health Outcomes	Exposure Assessment/ Analytical Methodology	Findings
Sydney	Morgan *et al.* 2010 [24]	1994–2002		All causes mortality, Respiratory mortality and cardiovascular mortality, respiratory diseases admissions	Monitoring stations using TEOM instruments in 8 monitoring sites Wildfire PM_{10} is calculated by subtracting total PM_{10} by background PM_{10} (due to others sources) calculated as the 30-days moving average of PM_{10} without wildfire	PM_{10} was associated with small increase in all causes mortality at lag0 (0.80% CI : −0.24% to 1.86%) but not associated with respiratory mortality or cardiovascular mortality
Denver	Vedal and Duton [36]	2 days fire in Denver 9 June and 18 June 2002	Denver population area (2 millions)	All-cause mortality data for 2001 and 2002	PM was obtained from daily air pollution from network of monitoring sites for Colorado	9 June 2002: PM_{10} and $PM_{2.5}$ peak of 1 h concentration: 372 and 200 mg/m^3, respectively 18 June 2002: PM_{10} and $PM_{2.5}$ peak of 1 h concentration: 316 and 200 mg/m^3, respectively No perceptible increases in daily mortality could be attributed to the increase PM concentrations from wildfire
Kuala Lampur	Sastry *et al.* 2002 [37]	April and November 1997	Population of Kuala Lumpur (2.5 millions)	All-cause mortality data from 1994–1997	Daily measurement from Malaysian Meteorological Bureau	$PM_{10} > 210$ µg/m^3 is associated with increase of total non-trauma mortality (relative risk = 1.72 for 65–74)
Sydney	Johnston *et al.* 2011 [31]	1997–2004	Population of Sydney	All-cause mortality data from the Australian Bureau of Statistics	Events were defined as days for which the 24 h city-wide concentration of PM_{10} exceeded the 99th percentile	A recent study conducted by Johnston and colleagues in Sydney looked at the effects of bushfires between 1994 and 2007 and mortality. This study revealed that a 5% increase in non-accidental mortality at lag of 1 day (OR 1.05 (95% CI: 1.00–1.10)) was observed on days of high air pollution from bushfire smoke

Table 2. Exposure to wildfire and cardiorespiratory diseases.

Location	StudyAuthors	Study Period	Population	Health Outcomes	Exposure Assessment/ Analytical Methodology	Findings
North Carolina	Rappold *et al.* 2011 [18]	June 2008	Population of 42 North Carolina counties	Respiratory diseases	Use Aerosol Optical Depth (AOD) measured by satellite GEOS	In the counties exposed significant increase in cumulative RR for asthma (RR = 1.65 (95% CI: 1.25–2.1)), COPD (RR = 1.73 (95% CI: 1.06–2.83)) and pneumonia and acute bronchitis (RR = 1.59 (95% CI: 1.07–2.34))
				Emergency departments visits	AOD scale from 0–2, high density of plume if AOD > 1.25	ED visits of all respiratory diagnosis were elevated in the exposed counties (RR = 1.66 (95% CI: 1.38–1.91))
					Counties with 25% of areas with AOD > 1.25 were defined as exposed to the smoke plume for each day in high-expose window	Significant increase for Emergency department visits for cardiopulmonary symptoms (RR = 1.23 (95% CI: 1.06–1.43)) and heart failure (RR = 1.37 (95% CI: 1.01–1.85))
Southern California	Kunzli *et al.* 2006 [16]	October 2003	873 high school students and 551 elementary-school children from 16 communities in California	Respiratory diseases	Webmail questionnaire to assess smoke exposure and occurrence of symptoms	Prevalence rates of reported outcomes were much higher among individuals with asthma
				Medication usage	Exposure duration were quantified by the number of days of exposure during the two weeks (not at all, 1–2 d, 3–5 d, 6–10 d, all days)	Dry cough, medication and physician visits were more frequently reported by parents of elementary school children. High school students report eye symptoms
						Six or more days of fire smell was significantly associated with all outcomes
				Physician visits		Six days or more of fire smell is associated with more than four-fold higher rates of eyes symptoms, 3 fold dry cough and sneezing 2 for cold, sore throat, wet cough, medication use, physician visits and missed school due symptoms

Table 2. *Cont.*

Location	StudyAuthors	Study Period	Population	Health Outcomes	Exposure Assessment/ Analytical Methodology	Findings
Southern California	Mirabelli *et al.* 2009 [17]	October 2003	465 high school students from 12 communities	Respiratory diseases	Webmail questionnaire assess smoke exposure and the occurrence of symptoms	Forty percent (186 of 465) of population reported the odor of wildfire smoke at home
					Log-binomial regression to evaluate associations between smoke exposure and fire-related health symptoms	Increase respiratory and eye symptoms with increasing frequency of wildfire smoke exposure
					Ratio of maximum midexpiratory flow to forced vital capacity as marker of airway size	
Three Provinces of Netherlands (Groningen, Friesland and Drenthe)	Greven *et al.* 2011 [20]	12 months	1330 firefighters	General respiratory symptoms	Questionnaire web-based version of European community Respiratory Health Survey questionnaire, added question to identify the number of incidents, the type, the onset, and the duration of symptoms and possible exposure during the incident	OR of general respiratory symptoms were estimated between 1.2 (95% CI: 1.0–1.4) and 1.4 (95% CI: 1.2–1.7) per 25 fires An inhalation incident is strongly associated with the presents respiratory symptoms OR between 1.7 (95% CI: 1.1–2.7) and 3.0 (95% CI: 1.9–4.7).
				Atopy and bronchial hyper-responsiveness		
Brazilian Amazon Region	Ignotti *et al.* 2010 [32]	2004–2005	Population of Brazilian amazon region	Rates of respiratory hospitalization among children, elderly and intermediate age group and due to childbirth	Annual hours (AH%) of $PM_{2.5} > 80\ \mu g/m^3$ AH = (sum of hours with $PM_{2.5} > 80\ \mu g/m^3$/sum hours $PM_{2.5}$ is measured in the year) × 100 Use of a coupled aerosol and gas transport model to estimate atmospheric emission Use of satellite observations of fires to obtain several gas and aerosols particles from biomass burnings	1% of increase of the exposure indicator was associated to an increase of 8% of child hospitalization (children < 5 years), 10% increase in hospitalization of elderly, 5% increase of the intermediate age group

Table 2. *Cont.*

Location	StudyAuthors	Study Period	Population	Health Outcomes	Exposure Assessment/ Analytical Methodology	Findings
Singapore	Emmanuel *et al.* 2000 [38]	1997		Respiratory diseases	PM_{10}, $PM_{2.5}$, and other compounds(nitrogen dioxide, ozone, CO) were measured by 15 stations located through the Island linked via public telephone network to a central control station	Air quality was into the unhealthy range (PSI > 100) on 12 days, the highest PSI was 138.94% of particles observed were $PM_{2.5}$ Haze from the Indonesian forest fire was responsible of 30% increase in outpatient attendances
				Outpatient attendances, accident and emergencies, inpatient care, mortality data		Increase in PM_{10} levels from 50 $\mu g/m^3$ to 150 $\mu g/m^3$ was significantly associated with increase of 12% of upper respiratory tract illness, 19% asthma and 26% rhinitis No significant increase in hospitalization or mortality due to the smoke haze
Victoria, Australia	Tham *et al.* 2009 [39]	2002–2003		Hospital admissions, emergency attendances, air quality and meteorological data	Air pollution from the Aplington air quality monitoring station which had the most complete data and was located away from the coast freeways and industrial settings	Daily levels PM_{10} were strongly associated with respiratory emergency department attendances ($p < 0.001$) No association with hospital admissions ($p = 0.06$) After adjusting for confounding effects of maximum temperature and relative humidity, the strongest associations were observed between PM_{10} and daily respiratory emergency department attendances in Melbourne (RR = 1.018, 95% CI: 1.004–1.033, $p = 0.01$)
Vilnius	Ovadnevaite *et al.* 2006 [40]	August–September 2002	The population of Vilnius	Respiratory diseases, bronchial asthma	Air pollution data from Vilnius monitoring network	Significant increase of average hourly values of PM_{10}, NO_2, CO and SO_2 during several episodes in 2002 The number of respiratory diseases and bronchial asthma in September (after longer exposure) was up to 20 times higher (by comparison in July) in some regions about 3 times higher all over the city

Table 2. *Cont.*

Location	StudyAuthors	Study Period	Population	Health Outcomes	Exposure Assessment/ Analytical Methodology	Findings
Australia	Reisen *et al.* 2011 [41]	2005–2008	130 firefighters	Air toxics within the breathing zone of firefighters	One-way analyses of variance, Student *t*-tests	30% of firefighters had a high exposure risk *i.e.*, exposure to hazardous substance, CO, RP, and formaldehyde exceeds the occupational exposure standard (OES) to 5% to 20% of time, 6% had a very high exposure risk *i.e.*, exposure to hazardous substance exceeds OES for more than 20% of time
					CO values were Log-transformed in all tests to meet the assumption of normal distribution of variables	The majority of firefighters (60%) were exposed in low to moderate levels
Galice, Spain	Caamano-Isorna *et al.* 2011 [21]	2006	156 municipalities	Consumption drugs for anxiolytics-hypnotics and drugs for obstructive airway disease (DOADs) for respiratory health	Additive model for time series analysis	Higher consumption of DOADs among pensioners during the months after the wildfires The defined DDDs increased by 17 69 DDDs (95%CI: 0.86–34.51) for male pensioners (10.29% increase) $p < 0.05$ in comparison to male pensioners in municipality unaffected. For the female pensioners of the municipality affected, the increase was 12.9% of DDDs ($p < 0.05$) For anxiolytics-hypnotics consumption, there was a significant increase in the DDDs among men (pensioners and no pensioners) in affected municipality (15.88% $p < 0.05$ *vs.* 12.2% $p < 0.05$)

Table 2. *Cont.*

Location	StudyAuthors	Study Period	Population	Health Outcomes	Exposure Assessment/ Analytical Methodology	Findings
Sydney	Jalaludin *et al.* 2000 [15]	January 1994	Children with a reported history of wheezing in the previous 12 months (32 children recruited)	Peak expiratory flow rates (PEFR)	Generalized estimating equation models	After adjusting for the wildfire period and potential confounders, there was no significant association between mean PM_{10} and PEFR Children without bronchial hyperactivity had a significant negative association between PEFR and PM_{10}
Southern California	Delfino *et al.* 2009 [13]	October 2003	n = 40,856 (hospital admissions)	Respiratroy admissions, cardiovascular admissions	Generalised estimating equation models for Poisson data	Average increases of 70 μg/m^3 $PM_{2.5}$ during heavy smoke conditions was associated with 34% increase asthma admissions The strongest association between wildfire $PM_{2.5}$ and asthma admissions was observed among elderly aged 65–99 (10.1% increase per 10 μg/m^3 $PM_{2.5}$, 95%CI: 3%–17.8%) and children aged 0–4 (8.3% increase, 95% CI: 2.2%–14.9%) followed by adults aged 20–64 (4.1% 95% CI: 0.5% to 9%), no association for age 5–18 No evident association between wildfire related $PM_{2.5}$ on cardiovascular admissions
Sao Paulo State Brazil	Abrex *et al.* 2007 [30]	23 March 2003–27 July 2004	Population admitted for asthma in main hospital of Araraquara	Asthma hospital admissions	Time series analysis Generalized linear Poisson regression models	Asthma hospital admission during burning period were 50% higher than those observed during the non-burning period (p < 0.001) After stratification to non-burning and burning periods, it was observed that for the same variation of 10 μg/m^3 in TSP concentration, asthma hospital admissions increased by 9.7% (95% CI: 2.6–17.2) and 12.7% (95% CI: 2.2–24.3) respectively

Table 2. *Cont.*

Location	StudyAuthors	Study Period	Population	Health Outcomes	Exposure Assessment/ Analytical Methodology	Findings
Brisbane	Chen *et al.* 2006 [23]	1 July 1997– 31 December 2000	Patients admitted in Brisbane	Respiratory hospital admissions	generalized linear model with negative binomial distribution	An increase of PM_{10} from low (<15 μg/m^3) to high level (>20 μg/m) level, is accompanied by an increase of 19% in respiratory hospital admissions for wildfire days *vs.* 13% for background days
Indonesia	Kunii *et al.* 2002 [42]	29 September– 7 October 1997	n = 543	Respiratory diseases	8 monitoring sites between Jakarta (Java) and Jambi (Sumatra) were used to air quality measurements, Health effects measured by a face to face structured interview	Concentration of CO and PM_{10}: very unhealthy and hazardous levels Concentration of PAH were 6–14 times higher in the unaffected area, 91.3% of responders had respiratory symptoms due to the haze Elderly had a serious deterioration of overall health
Kuching, Malaisia	Mott *et al.* 2005 [35]	1 January 1995– 31 December 1998, fire period 1 Augst– 31 October 1997	Population of Kuching region in Malaysia (7 hospitals)	Hospitalizations, all causes, respiratory admissions, cardiovasuclar admissions	Comparison of health outcomes in the wildfire period or post-fire period basing on forecasting estimates established from a historical baseline period of 1 January 1995 through 31 July 1997	Increase respiratory hospitalizations specifically for patients with COPD and asthma patients Persons over aged 65 year with previous hospital admissions for any cause any cardiorespiratory disease, any respiratory disease or COPD were significantly more likely to be re-hospitalized during the follow-up period in 1997 than in the follow-up period in the pre-fire years of 1995 or 1996.

Table 2. *Cont.*

Location	StudyAuthors	Study Period	Population	Health Outcomes	Exposure Assessment/ Analytical Methodology	Findings
Australia	Morgan *et al.* 2010 [24]	1994–2002		Respiratory diseases, respiratory mortality and cardiovascular mortality, respiratory diseases admissions	Monitoring stations using TEOM instruments in 8 monitoring sites Wildfire PM_{10} is calculated by subtracting total PM_{10} by background PM_{10} (due to others sources) calculated as the 30-days moving average of PM_{10} without wildfire	A 10 $\mu g/m^3$ increase in wildfire PM_{10} is associated with: 1.24% (95% CI 0.22% to 2.27%) increase in all respiratory diseases admissions (at lag 0) 3.8% (1.4 to 6.26) increase in COPD admissions at lag 25.02 (1.77 to 8.37) increase in adult asthma at lag (0)
Darwin, Australia	Hanigan *et al.* 2008 [43]	April–November 1995–2005		Respiratory diseases admissions	Daily PM_{10} exposure level is determined using the visibility data to build a predictive model	An increase of 10 $\mu g/m^3$ in same-day estimated PM_{10} was associated with 4.81% (95% CI: −1.04%–11.1%) increase in total respiratory admissions
					Data from 2005 and 1995 were used to assess the performance of the model Predictive peaks of PM_{10} during 2000 and 2001 were mapped against wildfire activity records for this period	A strong association of wildfire PM_{10} and respiratory admission among indigenous people than non-indigenous people (15.02%, 95% CI: 3.73%–27.54% *vs.* 0.67%, 95% CI: 7.55%–9.6%)
Central Florida	Sorenson *et al.* 1999 [44]	June–July 1998	All ages	Emergency room visits, hospital admissions	descriptive statistics	Increased emergency-room visits and hospital admissions for asthma and bronchitis during fire period relative to same period in previous year
Malaysia	Brauer, 1998 [45]		All ages	Outpatient visits	Not specified	Increased visits for asthma, upper r espiratory tract symptoms, and rhinitis during vegetation fire episode periods of elevated, PM_{10} in Malaysia

Table 2. *Cont.*

Location	StudyAuthors	Study Period	Population	Health Outcomes	Exposure Assessment/ Analytical Methodology	Findings
Singapore	Chew *et al.* 1995 [46]		Children less than 12 years old	Emergency room visits	Multiple regression analysis	Increased asthma visits with PM_{10} during episode of exposure to biomass burning emissions in Singapore
Denver	Sutherland *et al.* 2005 [47]	June–July 2002	Adult with COPD	Symptoms	Standard descriptive statistics, repeated measurements ANOVA	Significant increase in symptom index (dyspnea, cough, chest tightness, wheezing, sputum production) on two days of elevated PM2.5 (65 $\mu g/m^3$) relative to control days (14 $\mu g/m^3$). Days of elevated PM attributed to fire smoke by satellite imaging
Kelowna and Kamloops Regions British Columbia	Moore *et al.* 2006 [48]	2003	All ages	Physician visits for respiratory, cardiovascular, and mental illness	Particulate matter obtained from monitoring network of the BC Ministry of Water	A 46% to 78% increase in physician visits for respiratory illness during a 3-week forest fire period in Kelowna, British Columbia
Malaysia	Hisham-Hashim *et al.* 1998 [49]	1997	Children	Lung function	Not specified	Decreased lung function in children during vegetation fire episode compared to preepisode measurements
Malaysia	Tan *et al.* 2000 [50]	1997	Adult military recruits	Blood markers of inflammation	Not specified	Bone marrow stimulated to release immature polymorphonuclear leukocytes into blood during period of exposure to forest fire smoke relative to period following smoke exposure
Isfahan rural areas, Iran	Golshan *et al.* 2002 [51]	1–80 years olds	Adults	Asthma medication, lung function, asthmatic and other respiratory symptoms	physician-administered health questionnaire, physical examinations and spirometry in symptomatic cases	Increased prevalence of respiratory symptoms and various asthma indicators, decreased lung function post-rice stubble burning period relative to period prior to burning in three communities in Iran
Darwin, Australia)	Johnston *et al.* 2002 [52]	April–31 October 2000	All Ages	Emergency room visits	Mean atmospheric concentration PM_{10} per cubic metre per 24-h period	Increased asthma visits associated with PM_{10}, especially for concentrations exceeding 40 $\mu g/m^3$
California	Duclos *et al.* 1990 [53]	August 1987	All ages	Emergency room visits	descriptive statistics	Increased respiratory visits in communities exposed to fire smoke

3.4.1.1. All-Cause and Cardiorespiratory Mortality

Few studies have evaluated the effects of wildfire emissions on mortality (Table 1). In a study conducted by Vedal and Duton [36], no effect was observed. However, small sample size probably led to the null result. Haenninen [54] showed that Vedal and Duton were not able to detect mortality effects from the observed data because their study could not in any realistic case produce a positive finding, and the expected negative finding should therefore not by any means be considered as evidence of lack of mortality risk from smoke particles.

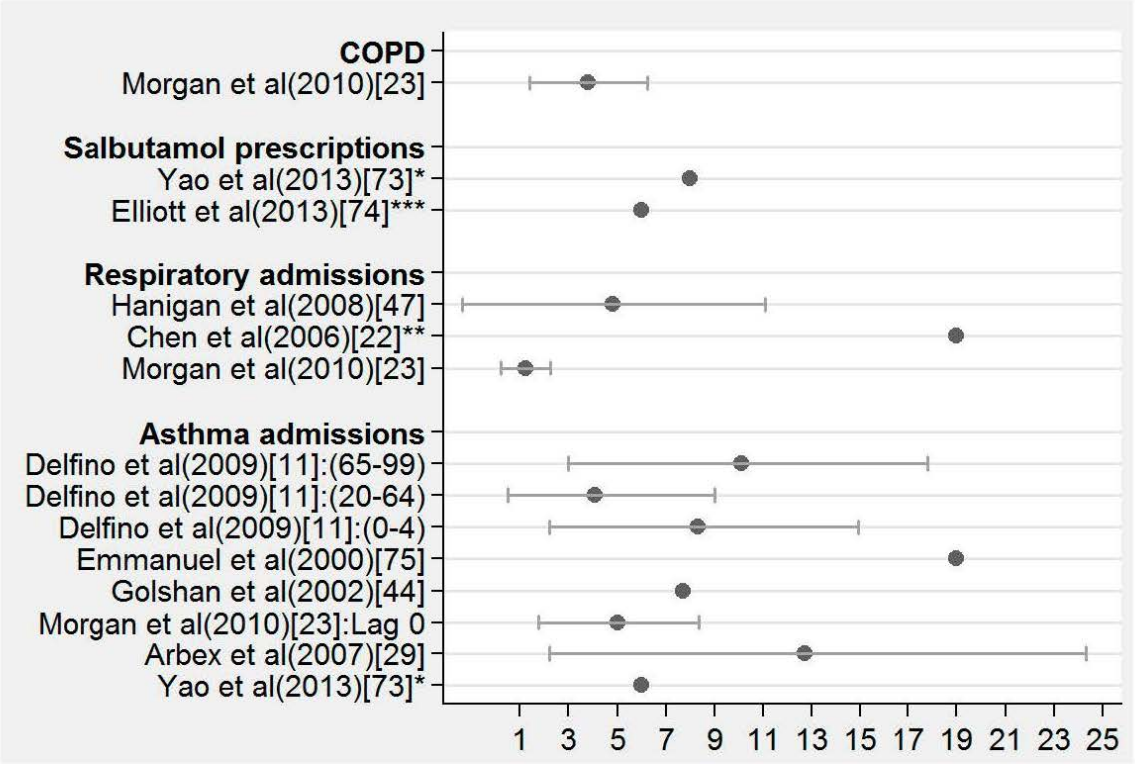
In 11 Southern Finnish provinces exposed to an additional population-weighted average $PM_{2.5}$ level of 15.7 $\mu g/m^3$ from wildfire smoke between 26 August and 8 September 2002, an increase of 10 $\mu g/m^3$ of urban $PM_{2.5}$ was associated with a 0.5% to 2% increase in mortality [55]. A larger study conducted after a widespread series of fires in Indonesia between April and November of 1997 showed high PM_{10} levels (>210 $\mu g/m^3$) associated with total non-trauma mortality [37]. When the authors extended the study period from 1994 to 1996 by using visibility instead of PM_{10} as the model predictor, severely impaired visibility (about 0.9 km, corresponding with the chosen PM_{10} limit value) was associated not only with increased total mortality, but also with increased cardiovascular and infant mortality. Another study conducted by Morgan and colleagues assessed the effects of bushfire smoke on daily mortality and hospital admissions in Sydney, Australia. This study distinguished the effect of bushfire PM_{10} from urban PM_{10}. Bushfire PM_{10} was associated with a small increase in all-cause mortality (0.80%) (95% CI 0.24%–61.86%) but not with respiratory or cardiovascular mortality at lag 0. A recent study conducted by Johnston and colleagues in Sydney investigated the effects of bushfires between 1994 and 2007 and mortality. This study revealed that a 5% increase in non-accidental mortality at lag 1 day (OR 1.05, 95% CI: 1.00–1.10) was observed on days with high air pollution from bushfire smoke [31]. Another recent study conducted by Johnston and colleagues estimated the global mortality attributable to smoke from wildfires and daily and annual exposure to $PM_{2.5}$ from fire emissions between 1997 and 2006. The authors combined outputs from a chemical transport model with satellite based-observations of aerosol optical depth (AOD). Study data indicated that the estimated average annual mortality associated with exposure to wild fire smoke was 339,000 deaths worldwide. Regions most affected were sub-Saharan Africa, with 157,000 wildfire related deaths, and South East Asia, with 110,000 wildfire related deaths [56]. This study did have some regional uncertainty in exposure measurements.

3.4.1.2. Cardiorespiratory Morbidity

Figure 2 presents the percent increase in adverse health outcomes except mortality as discussed in the literature per various increases in PM. According to the study, this ranged from 1 to 19. Increased respiratory symptoms were reported in connection with the 1997 Southeast Asian haze episode [42]. Ninety-one percent of the interviewed persons reported respiratory symptoms. The evidence of increased cardiovascular symptoms, e.g., palpitations (23% of respondents), is noteworthy. In both the USA and the Asian study, wearing masks was associated with decreased occurrence of symptoms. Aditama *et al.* [57] who studied in another analyze the health impact of this same episode of haze in the Southeast Asian by comparing data during September 1997 and June 1998 to data for 2 years

earlier between 1995 and 1996 found a significant increase of respiratory outcomes during the forest fire period. This 1997 Southeast Asian haze episode was also investigated by Frankenberg *et al.* [58] who combined data from a population-based longitudinal survey with satellite measures of aerosol levels to assess the impact of smoke on adult health. To account for unobserved differences between haze and nonhaze areas, they compared changes in the health of individual respondents. They found that between 1993 and 1997, individuals who were exposed to haze experienced greater increases in difficulty with activities of daily living than did their counterparts in nonhaze areas. The results for respiratory and general health, although more complicated to interpret, suggest that haze had a negative impact on these dimensions of health.

Figure 2. % increase [1] of respiratory morbidity outcomes as discussed in the literature per various increases in particle matter (PM) (Mean rate and 95% CI).



Notes: [1] Increase in PM is 10 μg/m^3, if it's not precised; * increase of 30 μg/m^3 of $PM_{2.5}$ in Yao *et al.* (2013) [59]; ** increase > 20 μg/m^3 of PM_{10} in Chen *et al.* (2006) [23]; *** Elliott *et al.* (2013) [60].

In the Children's Health study conducted in California, USA on the effect of smoke from a 2003 wildfire on respiratory symptoms, questionnaires were given to exposed children (age 6–7 years) and teenagers (age 16–19 years). Both respiratory and eye symptoms were observed to increase in children, and those children with the smallest airways had a 2-fold risk of experiencing respiratory symptoms (morning or nighttime dry cough, wet cough, wheezing) compared to other children [17]. Among teenagers, all symptoms (nose, eyes, throat irritation, cough, bronchitis, cold, wheezing,

and asthma attack) were increased in relation to smoke episodes [16]. Risk increased monotonically with the number of reported smoky days. There was also increased use of medication and physician's visits. Since both exposure assessment and evaluation of the health effects were based on questionnaires in the study, it should be noted that participant recall of symptoms might be biased, as they link exposure with worsening health. In the same year, a study of 465 non-asthmatic teenagers affected by 2003 wildfires in Spain revealed that individuals with smaller airways and poorer pre- existing lung function were more vulnerable to smoke effects [10].

Increased emergency department visits for cardiopulmonary symptoms were associated with exposure to smoke from a peat bog wildfire in North Carolina, USA, when smoke covered 42 rural counties. Daily counts of emergency department visits for all respiratory diagnoses were assessed and were found to be elevated in the exposed counties with a relative risk (RR) equal to 1.66 (95% CI: 1.38–1.91). Significant increase in cumulative RR for asthma (RR = 1.65, 95% CI: 1.25–2.1), COPD (RR = 1.73, 95% CI: 1.06–2.83) and pneumonia and acute bronchitis (RR = 1.59, 95% CI 1.07–2.34) was observed in exposed counties. There also was a significant increase in emergency department visits for cardiopulmonary symptoms (RR = 1.23, 95% CI: 1.06–1.43) and heart failure (RR = 1.37, 95% CI: 1.01–1.85) [18]. Morgan *et al.* [24] found that a 10 $\mu g/m^3$ increase in bushfire PM_{10} was associated with the following: a 1.24% increase (95% CI: 0.22%–2.27%) in all respiratory disease admissions and a 5.02% (95% CI: 1.77%–8.37%) increase in adult asthma admissions at lag0; and a 3.8% (95% CI: 1.4%–6.26%) increase in COPD admissions at lag 2.

A considerable impact of wildfire smoke on respiratory and cardiovascular health outcomes was established in British Columbia, Canada, when numerous fires burned in 2003. The association over a 92-day study period were examined between respiratory and cardiovascular physician visits and hospital admissions and three measures of smoke exposure: (1) tapered element oscillating microbalance (TEOM) based air quality PM monitoring, (2) smoke-related PM_{10} from a California puff (CALPUFF) dispersion model, and (3) smoke exposure metric for plumes visible in satellite images [61]. Respiratory physician visits were positively associated with all exposure metrics. A 30 $\mu g/m^3$ increase in total PM_{10} based on TEOM was found associated with increased respiratory physician visits (OR = 1.05, 95% CI: 1.03–1.06), asthma specific visits (OR = 1.16, 95% CI: 1.09–1.23) and respiratory related hospital admissions (OR = 1.15, 95% CI: 1.0–1.29) [61]. Limitations of the study included the TEOM air quality monitors measuring PM_{10} from all sources. While PM_{10} related to smoke was obtained with the help of the CALPUFF model, this method performs poorly under low wind conditions, when fires are typically smoldering and PM_{10} levels are high [61].

Elevated respiratory symptoms have also been associated with the burning of agricultural waste. In Winnipeg, Canada, a group of people with mild to moderate airway obstruction received a symptom questionnaire three weeks after a smoke episode caused by burning of straw and stubble. Forty-two percent of subjects reported having new or exacerbated symptoms (cough, wheezing, chest tightness, shortness of breath) during the smoke episode, and 20% reported having breathing trouble [62]. In Iran [51], burning of residues from rice farming was associated with the increased prevalence of respiratory symptoms, e.g., asthma attacks, use of asthma medication, and cough. Symptomatic subjects underwent spirometric testing. Both FEV1 (forced expiratory volume in 1 sec) and PEFR (peak expiratory flow rate) were decreased in association with the rice burning episode.

In Brazil, wildfires have been associated with increased rates of respiratory hospital admissions and emergency room visits (Table 2). Asthmatics in particular, but also those with COPD, are especially susceptible. Because levels of particulate air pollution are clearly more elevated during smoke episodes than the levels of gaseous pollutants, it is reasonable to assume that observed health effects are primarily due to PM. Unfortunately, very little information is available on any link between wildfire PM and cardiovascular hospital admissions. In some studies, effects have been observed [53,63], while in others the effects were stronger for respiratory admissions [13,43].

Using the incidence of daily counts of hospital admissions for respiratory and cardiovascular diagnoses Crabbe *et al.* [64] calculated the risk of hospitalization from wildfire exposure with respect to PM_{10}, in Darwin, Australia. The results suggest that respiratory admissions were associated with exposure to PM_{10} with a lag of 1 day when adjusted for flu and other confounders (RR = 1.025, 95 % CI: 1.000–1.051, $p < 0.05$). This effect is strongest for exposure to fine particulate matter concentrations (RR = 1.091, 95 % CI: 1.023–1.163, $p < 0.01$) when adjusted for flu. Respiratory admissions were also associated with black carbon concentrations recorded the previous day (RR = 1.0004, 95 % CI: 1.000–1.0008, $p < 0.05$), which did not change strength when adjusted for flu. Cardiovascular admissions had the strongest association with exposure to same-day PM and highest RR for exposure to fine particulate matter when adjusted for confounders (RR = 1.044, 95 % CI: 0.989–1.102).

Martin *et al.* [65] examined the association between validated bushfire smoke pollution events and hospital admissions in three eastern Australian cities from 1994 to 2007. Smoke events were defined as days on which bushfire smoke caused the 24-h citywide average concentration of airborne particles to exceed the 99th percentile of the daily distribution for the study period. They used a time-stratified case-crossover design to assess the association between smoke events and hospital admissions and compared health outcomes on event days with non-event days. This study showed that in Sydney, events were associated with a 6% (OR = 1.06, 95% CI: 1.02–1.09) same day increase in respiratory hospital admissions. Same day chronic obstructive pulmonary disease admissions increased 13% (OR = 1.13, 95% CI: 1.05–1.22) and asthma admissions by 12% (OR = 1.12, 95% CI: 1.05–1.19). Events were also associated with increased admissions for respiratory conditions in Newcastle and Wollongong.

Delfino *et al.* [13] analyzed the relationship between respiratory and cardiovascular hospital admissions and exposure to the southern California wildfires of 2003. Analyses were performed in terms of PM exposure and wildfire period. They found that several respiratory symptoms increased in relation with $PM_{2.5}$ during the wildfire period. For example, asthma admissions across all ages increased by 4.8% (95% CI: 2.1%–7.6%) in relation to $PM_{2.5}$ during the wildfire period. The strongest wildfire-related $PM_{2.5}$ associations with asthma admissions were for the elderly, ages 65–99 years (10.1% increase), and children ages 0–4 years (8.3%), followed by adults ages 20–64 years (4.1%). A small relative increase in admission rates for total cardiovascular outcomes in people aged 45–99 years in relation to $PM_{2.5}$ during the fires was observed. Considering the wildfire period, there were significantly increased risks for all respiratory hospital admissions after the fires compared with the pre-fire period. Admissions increased for all ages by 17% ($p < 0.001$), and in age groups 5–19 years by 37% ($p < 0.008$) and 65–99 years by 15% ($p < 0.004$). Respiratory admissions concerned were for asthma, acute bronchitis and bronchiolitis and pneumonia. There was a 6.1% increased

risk of combined cardiovascular admissions ($p < 0.05$), and an 11.3% increased risk of congestive heart failure admissions after the fires ($p < 0.06$). However, risk of cardiovascular admissions was lower during the fires by 4.4%. A recent reviews through 2010 [8] and 2012 [12] provides a background for respiratory symptoms from wildfire smoke in different regions in the world. As discussed in this review, although using different methods, all studies looking at Emergency Department presentations in relation to a wildfire smoke event have found associations and most studies have also found an association with hospital admissions. However, only a few studies have distinguished between the effects of wildfire PM_{10} and background PM_{10}. These studies suggest that PM_{10} from wildfire smoke is at least as toxic as urban PM_{10}, but more research is needed.

Some studies used modeling to develop quantitative assessment and prediction of respiratory health outcomes as hist relates to the location and timing of wildland fire emissions relevant for application to future wildfire scenarios. This approach were used by Thelen *et al.* [66] to study of the impacts on respiratory health of the 2007 wildland fires in and around San Diego County. Using coupled empirical and deterministic models describing PM emissions and atmospheric dispersion linked to spatially explicit syndromic surveillance health data records collected through the San Diego Aberration Detection and Incident Characterization system and a Generalized Additive Modeling (GAM) statistical approach, they found that the model captured the variability in emergency department visits due to several factors by including nine ancillary variables in addition to wildfire PM concentration. The model coefficients and nonlinear function plots indicate that at peak fire PM concentrations the odds of a person seeking emergency care is increased by approximately 50% compared to non-fire conditions (40% for the regional case, 70% for a geographically specific case). The sub-regional analyses show that demographic variables also influence respiratory health outcomes from smoke. Other studies addressed the impact of fire smoke but they considered only indoor settings and some of them experimented health impact of exposure wood smoke under controlled environmental conditions. In these studies significant health effects were reported [67–70].

3.4.1.3. Wildfire Exposure during Pregnancy and Birth Weight

Few studies analyzed the impact of wildfire exposure during pregnancy. One of them conducted by Holstius *et al.* [71] analyzed the potential impact of maternal exposure to wildfire emissions from the October 2003 California wildfire on birth weight. Potential wildfire exposure windows were defined using MODIS satellite imagery from 21 October to 10 November 2003. Holstius *et al.* used records for singleton term births delivered to mothers residing in California's South Coast Air Basin (SoCAB) during 2001–2005 ($n = 886,034$) and compared birth weights from pregnancies that took place entirely before or after the wildfire event with those pregnancies that occurred during the wildfire. Census tracts located close to air pollution monitors that measured an average daily PM_{10} level of <40 $\mu g/m^3$ during the fire were classified as low exposure, and census tracts with average daily PM_{10} level >40 $\mu g/m^3$ were classified as high exposure. Of the 886,034 births analyzed, 84.4% (n = 747,590) were unexposed in utero. Of the 138,444 babies that received in utero exposure, 43.5% were exposed in the first trimester, 28.5% were exposed in the second trimester, and 28% were exposed in the third trimester. Adjusted models revealed that mean birth weight was 6.1 g lower (95% CI: −8.7–−3.5) among infants exposed in utero during any trimester compared with unexposed

infants. Among those exposed in the third trimester, there was a reduction of 7 g (95%CI −11.8–−2.2). The largest estimated effect was observed in the second trimester, with a reduction of 9.7 g (95% CI: −14.5–−4.8). Kessler performed separate analyzes on the same birth records of babies delivered between 2001 and 2005 in the South Coast Air Basin in the same period and found the same results [72].

3.4.1.4. Subclinical Effects

In contrast to what has been observed for urban air pollution, there is only limited information on the subclinical effects of particles from wildfires. It has generally been assumed that health effect mechanisms are the same for biomass burning PM as for urban PM (e.g., combustion of fossil fuels). However, during wildfires PM concentrations are higher than those usually observed in urban settings so that a greater effect of PM is expected. Indeed we estimated a $PM_{2.5}$ concentration 75 higher than the WHO annual mean standard in Mangualde in Spain in 2002 (data not shown). The literature reports that biomass particles are at the origin of acute inflammation, oxidative stress and in analogy with biomass burning for domestic cooking, diminished response to infections.

3.4.1.4.1. Animal Models

In a recent study conducted in a mouse lung exposed to PM from wildfire, a very rapid cytotoxicity occurred in pulmonary macrophages and oxidative stress responses are seen after wildfire coarse PM instillation. Indeed, at 1 h after PM instillation, authors observed cytotoxicity because both decreased numbers of viable macrophages and increased dead macrophage percentages as compared to controls were observed. An increase in free isoprostanes, an indicator of oxidative stress, from control values of 28.1 ± 3.2 pg/mL to 83.9 ± 12.2 pg/mL was observed a half-hour after PM instillation [73].

Another study conducted during the 2008 wildfire season in California on mouse bioassay analyzed the Toxicity of $PM_{10-2.5}$ (PM with mass median aerodynamic diameter>2.5 μm and <10μm) and $PM_{2.5}$ obtained during the time of peak concentrations of smoke in the air and compared with PM samples collected under normal conditions from the region during the month of June 2007. Results showed that concentrations of PM were higher during the wildfire episodes and much more toxic to the lung on an equal weight basis than was PM collected from normal ambient air in the region. Toxicity was manifested as increased neutrophils and protein in lung lavage and by histologic indicators of increased cell influx and edema in the lung [74].

3.4.1.4.2. Human Beings and Firefighters

One study having evaluated the effect of air pollution from wildfires on systemic inflammation [50], proposed main pathway from exposure to cardiovascular health effects. Among U.S. servicemen, the 1997 Southeast Asian smoke-haze was associated with an increased neutrophil count in the blood, indicative of a bone marrow response to PM_{10}. In a Finnish study, conducted among patients, a 10-day forest fire smoke transport episode from Russia increased median values of IL-12 in ischemic heart disease patients' plasma by 227% but had no effect on other inflammatory markers such as IL-8, C-reactive protein, fibrinogen, white blood cell count and myeloperoxidase in blood circulation [75].

There are no studies on the possible effects of biomass PM on autonomous nervous function, another health effect mechanism proposed for PM.

3.4.1.4.3. Exposure Trials

Other investigations in a controlled human wood smoke exposure assessed the impact of exposure to wood smoke on systemic inflammation, oxidative stress. Wood smoke exposure was controlled by air filters [67,69,70] and climate controlled chamber [68], under different controlled environmental conditions. Indeed, portable air filters were used in a randomized crossover intervention study of 45 healthy adults exposed to consecutive 7-day periods of filtered and nonfiltered air to investigate the impact of wood smoke exposure and the endothelial function and the underlying role of oxidative stress and inflammation in relation to exposure reductions among healthy adults in a wood smoke impacted community. Air filters reduced indoor fine particle concentrations by 60%. Filtration was associated with a 9.4% (95% CI: 0.9%–18%) increase in reactive hyperemia index and a 32.6% (4.4%–60.9%) decrease in C-reactive protein. Decreases in particulate matter and the wood smoke tracer levoglucosan were associated with reduced band cell counts. There was limited evidence of more pronounced effects on endothelial function and level of systemic inflammation among males, overweight participants, younger participants, and residents of wood-burning homes. However, no associations were noted for oxidative stress markers [67].

In order to test the postulate that healthy volunteers exposed to wood smoke particles would demonstrate evidence of both pulmonary and systemic inflammation, ten healthy volunteers were exposed to filtered air and, 3 weeks or more later, to wood smoke particles. Each exposure included alternating 15 min of exercise and 15 min of rest for a total duration of 2 h. Wood smoke was generated by heating an oak log on an electric element and then delivered to the exposure chamber. Endpoints measured in the volunteers included symptoms, pulmonary function tests, measures of heart rate variability and repolarization, blood indices and analysis of cells and fluid obtained during broncho-alveolar lavage. The results showed that at 20 h after wood smoke exposure, blood tests demonstrated an increased percentage of neutrophils, and bronchial and broncho-alveolar lavage revealed a neutrophilic influx. This study conclude that exposure of healthy volunteers to wood smoke particles may be associated with evidence of both systemic and pulmonary inflammation [69].

Another study assessed the effect of systemic inflammation, oxidative stress and microvascular function after controlled wood smoke exposure, was assessed in a randomized, double-blinded, cross-over study among 20 non-smoking atopic subjects were exposed at rest to 14,220, or 354 $\mu g/m^3$ of particles from a well-burning modern wood stove for 3 h in a climate controlled chamber with 2 week intervals. The investigations have focused on the level of oxidatively damaged DNA, inflammatory markers and adhesion molecules before and 0, 6 and 20 h after exposure. Six hours after exposure, measured microvascular function non-invasively by digital peripheral artery tonometry following arm ischemia was measured. The microvascular function score was unaltered after inhalation of clean air (1.58 ± 0.07; mean ± SEM), low (1.51 ± 0.07) or high (1.61 ± 0.09) concentrations of wood smoke particles in atopic subjects, whereas unexposed non-atopic subjects had higher score (1.91 ± 0.09). The level of oxidatively damaged DNA, mRNA of ITGAL, CCL2, TNF, IL6, IL8, HMOX1, and OGG1 and surface marker molecules ICAM1, ITGAL and L-selectin in

peripheral blood mononuclear cells were not affected by inhalation of wood smoke particles. Exposure to wood smoke had no effect on markers of oxidative stress, DNA damage, cell adhesion, cytokines or MVF in atopic subjects [68].

3.4.2. Wildfire Health Effects in Firefighters and Mechanisms

Studies conducted among forest firefighters shed light on the physiological responses to wildfire smoke. Typically, health status right after the work-shift is compared to other time periods, but there is little information on exposure. Reinhardt *et al.* [76] summarized measurements of smoke exposure among wildland firefighters and showed that firefighters can be exposed to significant levels of CO and respiratory irritants, including formaldehyde, acrolein, and respirable particulate matter. Extensive research conducted during forest firefighting in the United States and Australia identified CO and respiratory irritants as the major wildfire pollutants of concern to firefighters [77].

To characterize the acute pulmonary and systemic inflammatory effects of exposure to forest fire smoke, Swiston *et al.* [78], analyzed 52 seasonal forest firefighters recruited before and/or after a day of firefighting. Exposure was assessed by questionnaires and measurement of CO levels. The pulmonary response was assessed by questionnaires, spirometry, and sputum induction. Peripheral blood cell counts and inflammatory cytokines were measured to define the systemic response. The authors found that estimate respirable particulate matter exposure was high (peak levels > 2 mg/m^3) during firefighting activities. Respiratory symptoms were reported by 65% of firefighters. The percentage sputum granulocytes increased from 6.5% to 10.9% ($p < 0.02$) following firefighting shifts with concurrent increases in circulating white blood cells (5.55×10^9 to 7.06×10^9 cells/L, $p < 0.0001$) and band cells (0.11×10^9 to 0.16×10^9 cells/L, $p < 0.01$). Serum IL-6, IL-8 and MCP-1 levels increased following firefighting ($p < 0.05$). There were no changes in band cells, IL-6, and IL-8 following strenuous physical exertion without firefighting. There was an association between changes in sputum macrophages containing phagocytized particles and circulating band cells ($p < 0.05$). These results showed that acute exposure to air pollution from forest fire smoke elicits inflammation within the lungs as well as a systemic inflammatory response.

In a study conducted to investigate the effect of occupational woodsmoke exposure on inflammatory biomarkers in firefighters, Twelve U.S. Forest Service wildland firefighters at the Savannah River Site, South Carolina, volunteered to give blood samples during four prescribed burns between February and March 2011. Concurrent personal $PM_{2.5}$ and CO monitoring of firefighters was conducted. IL-8 showed a significant cross-work shift difference as indicated by a post/pre-work shift ratio of 1.70 (95% CI: 1.35–2.13; $p = 0.0012$). Concentrations of IL-8, CRP, and ICAM-1 increased in >50% of samples across work shift. Firefighters who lighted fires as opposed to other work tasks had the largest cross-work shift increase in IL-8. A significant cross-work shift increase in IL-8 in blood samples was observed in healthy wildland firefighters working at prescribed burns [79].

In order to analyze the CO poisoning among firefighters, Brotherhood *et al.* [80] assessed the carboxyhemoglobin saturation (COHb%) levels from alveolar CO levels in 24 firefighters working with hand tools and in 12 accompanying scientific observers, before and after firefighting (duration 37–187 min) on 15 experimental bushfires. Carboxyhemoglobin levels increased on average

by 0.7% per hour in the firefighters and by 0.3% per hour in the observers that indicate that firefighters are generally unlikely to experience hazardous levels of CO exposure.

Benzene was also measured and found to be well below permissible exposure limits, with the highest concentrations occurring among firefighters working with engines and torches burning petroleum-based fuel. Most of these compounds had a health effects so that smoke inhalation is one of the greatest concerns for firefighter health [81].

Firefighting has been associated with decreased lung function, increased systemic and pulmonary inflammation, and respiratory symptoms [28,78,82]. By measuring pulmonary functions on 24 non-smoking United States Forest Service (USFS) firefighters and 2 current smokers recruited during the dormant winter burn seasons of 2003 and 2004, Adetona *et al.* [83] showed that for a given point in time during the season, each additional day of exposure was estimated to be associated with declines of 24 mL in pre-shift FVC and 24 mL in pre-shift FEV1 ($p < 0.01$). Furthermore, cardiovascular disease is the leading cause of on-duty death among firefighters and a major cause of morbidity [84,85]. According to the 2010 firefighter fatality report of the US Fire Administration, sudden cardiac death accounts for 49% of total firefighter fatalities at work [86]. Generalizability of the results to the general population is limited, however, because firefighters are exposed to fresh combustion particles and gaseous pollutants in the proximity of the fire, whereas populations located further away from fires are exposed to more aged particles and considerably lower levels of pollutants.

A risk assessment of firefighter exposure during prescribed burns and wildfires was conducted in Australia [41]. This study monitored air toxins within the breathing zone of the firefighters and showed that 30% of firefighters were exposed to high levels of a hazardous substance (*i.e.*, CO, respirable particles, formaldehyde) that exceeded the occupational exposure standard (OES) for 5% to 20% of time. Six percent of the firefighters were observed to have very high exposures (exceeding OES for more than 20% of time). However, the majority of firefighters (60%) had low or moderate exposures. Firefighters patrolling on top of ridges of steep burn areas or in downwind sectors tended to have high (44%–62%) or very high (31%–44%) exposures, with a large percentage of very high exposures experienced by supervisors (17%). This study was limited by the fact that monitoring was performed at only a small fraction of the burns conducted each year across Australia and may not be representative of the extensive program of fuel reduction burns carried out each year. Monitoring was restricted to tanker-based crews and to the later stages of campaign fire and did not include the initial more intense stage of the fires or hand crews. Lastly, neither firefighter work experience was taken into account, assuming that less experienced firefighters may endure higher smoke conditions, nor climatic factors influencing the smoke plume.

In another study, 64 career firefighters from the Fire Emergency Service Authority of Western Australia were allocated one of three filter types (particulate, organic vapor or organic vapor/formaldehyde). Data on spirometer, audiometry, self-reported symptoms and personal air sampling were collected before, during and after exposure to bushfire smoke from prescribed burns. Declines in lung function (Forced Expiratory Volume in One Second (FEV1) and oxygen saturation (SaO_2)) were demonstrated with exposure. Firefighters in the particulate filter group reported significantly more respiratory symptoms compared to the other filter groups after 60 and 120 min of exposure, respectively (67% and 64%, particle group; 22% and 18%, organic vapor group; 11% and 18%, organic vapor/formaldehyde group) [87].

A screening health risk assessment was performed to assess the upper-bound risks of cancer and noncancer adverse health effects among wildland firefighters performing wildfire suppression and prescribed burn management. Of the 15 substances in smoke that were evaluated, only benzene and formaldehyde posed a cancer risk greater than 1 per million, while only acrolein and respirable particulate matter exposures resulted in hazard indices greater than 1.0. The estimated upper-bound cancer risks ranged from 1.4 to 220 excess cancers per million, and noncancer hazard indices ranged from 9 to 360, depending on the exposure group. These values only indicate the likelihood of adverse health effects, not whether they will or will not occur [88].

Concerning the heart attack among firefighters, it's was reported by Aisebett *et al.*, in a study on wildfire suppression and its impact on firefighters' health in Australia, that fire agency may not completely illustrate the cardiovascular strains of firefighting. Fire agencies do not collect data on cardiac events that occur after the firefighter has completed their assigned shift. Furthermore, early warning signs such as chest pain/angina, increased fatigue, sensation of indigestion/heartburn, and excessive breathlessness that often precede fatal cardiac events are frequently ignored and not reported. The risk of a cardiac event during physical exertion is increased for individuals who possess two or more cardiovascular risk factors [89].

In order to protect firefighters against high particulate exposures which have been demonstrated to decrease lung function among firefighters, Edwards *et al.* [90] demonstrated the feasibility of using small real-time particle sensors to inform wildland firefighters so they may make informed decisions on the use of personal respiratory protection. Using 1 mg/m^3 as an indicator point for use of appropriately designed respiratory protection; such sensors could help prevent 16% to 74% of particulate exposure during prescribed burns when firefighters assess exposure as low or medium. Adherence to such a guideline for the use of respiratory protection would involve its deployment during 3% to 22% of individual 8-hour shifts. In addition, data-logging sensors would provide a valuable tool for tracking exposure to particulates among wildland firefighters for occupational health monitoring [90].

4. Public Awareness

Even when technical solutions exist to reduce exposure to wildfire smoke, the effectiveness of an intervention largely depends on public awareness and compliance with air pollution advisories. A recent USA study demonstrated that only 10-15% of those aware of public alerts for hot weather and urban air pollution episodes actually changed their behavior [91]. It was the personal perception of poor air quality or high temperature, rather than public advisories that typically led to the change in behavior.

It is unclear how effective public air pollution warning systems are in the case of wildfire smoke. Deterioration of air quality is usually easy to recognize, and a possible link between irritant symptoms with simultaneous high smoke concentrations can be identified. At the same time, there is probably a tendency to consider smoke from wildfires as something "natural" and thus, less harmful than, for example, vehicle exhaust. In a study conducted during a wildfire smoke episode among residents of Hoopa Valley National Indian Reservation in California [35], 66% of those residents who recalled a public service announcement took some action to reduce exposure. Most residents (83%) stayed indoors, while 16% left the area, and only 1% used an air filter, likely because air filters are not

common in homes. During the episode, ambient PM_{10} concentrations exceeded the US EPA's 24-h air quality standard (150 $\mu g/m^3$) for 15 days.

5. Discussion

Wildfires can cause significant health effects both in the population in the immediate vicinity as well as in those far from the fire [12] and several studies have sought to establish the link between exposure to wildfire and health outcomes. Among wildfire emissions, PM_{10} and $PM_{2.5}$ are the most studied as those having various effects on human health [7]. Furthermore, local daily and hourly $PM_{2.5}$ and PM_{10} concentrations can increase dramatically from a wildfire even if it is located hundreds of kilometers away because of long-transportation of the aerosol [38,92]. Different methods have been used to measure wildfire exposure but only the most recent enable us to avoid exposure miss-classification. In terms of health, several studies have found a significant association between PM and respiratory symptoms [16,18,35], increased respiratory hospital admissions [32] and increased emergency department visits. Studies have also found an association between daily mortality from wildfires for all-causes of death, including cardiovascular disease [37]. The effects of exposure to wildfire on cardiovascular disease and mortality, however, have not been sufficiently studied to support general conclusions [19].

Not everyone who is exposed to thick smoke will have health problems. The level and duration of exposure, age, individual susceptibility, including the presence or absence of pre-existing lung or heart disease, and other factors play significant roles in determining whether someone will experience smoke-related health problems [1]. Indeed, the elderly, people with pre-existing cardiopulmonary conditions, smokers and, for professional reasons, firefighters, may experience more severe short-term and chronic symptoms [13,41,47]. In addition, individuals with smaller airways may be more susceptible to the respiratory health effects of wildfire smoke [10]. Some epidemiological studies have observed various health effects among these specific groups [13,19,41,47]. More research is needed to evaluate long term health effects from exposure to wildfires.

Two previous reviews had dealt with health impact of wildfires [10,12]. In contrast with these reviews, our review covered more largely the literature on non-accidental health impact and included firefighters, a vulnerable subgroup exposed to fires for professional reasons. Existing data show that in addition to potential injuries, firefights may be concerned by various non-accidental health effects.

A limitation in all studies is exposure assessment. Even for conclusive studies, there is a large uncertainty on the evaluation of personal exposure because there is difficulty in distinguishing wildfire emissions from emissions due to other sources of pollution [8,11,14]. In addition, although available information suggests that wildfire smoke penetrates readily into indoor environments during air pollution episodes caused by wildfires, this has not been measured objectively. Lastly, there are no published studies on personal exposures to PM from wildfires in community settings.

Another limitation results from the paucity of statistical methods that have been used to relate wildfire exposure to health conditions. Other methods that could be applied include semi-parametric regressions for estimating associations between day-to-day variations in air pollution and mortality after controlling for confounding [93,94]. Such methods using Generalized Additive Model (GAM) to time-series health outcomes like mortality, morbidity, or hospitalization and studying the impact of PM

is well established in the last decade with numerous studies cited in the literature [93–96]. Hierarchical Models for estimating: National-average relative rates, national-average exposure-response relationship exploring heterogeneity of air pollution effects across the country are also possible [97]. Longitudinal methods have to be implemented to evaluate long term health effects from exposure to wildfires. However these methods which generally imply following individuals over time could be limited by the period and the variation of wildfire exposure area. In summary, various studies have established the relationship between one of the major components of wildfire, PM_{10} and $PM_{2.5}$, and cardiorespiratory in terms of hospital emergency rooms visits and hospital admissions. Associations between wildfire emissions and mortality or other diseases have been less investigated. Prevention against fires has to be implemented to protect the population, in particular the segments of the population vulnerable to smoke-related health risks, such as the elderly, people with pre-existing cardiopulmonary conditions, smokers and firefighters.

6. Conclusions

This review has demonstrated the impact of wildfire emissions on public health in terms of non-accidental effects at population level and among vulnerable subgroups. The main challenge for epidemiological studies that evaluate the impact of wildfire emissions during a given event is the estimation of personal exposure. So far, most of the used methods have not distinguished air pollution from wildfires from other source-oriented pollution. Various statistical approaches can be used in the epidemiological studies to take into account this uncertainty. However, so few have been applied. Main health effects of wildfire smoke are cardiorespiratory and associations between exposure to wildfire emissions and increasing of hospital admissions and emergency room visits for respiratory and cardiovascular diseases has been observed in the most studies. Few studies reported on cardiorespiratory mortality. Only a small number of studies found other non-accidental effects like the reduction of birth weight. However, various subclinical effects have been associated to wildfire exposure. Some these effects were tested healthy volunteers using a controlled human exposure, animal exposure or *in vitro* studies.

Acknowledgments

This publication arises from the project PHASE (contract number EAHC 20101103) which has received funding from the European Union, in the framework of the Health Programme.

Author Contributions

Isabella Annesi-Maesano conceptualized the study. Youssouf Hassani and Isabella Annesi-Maesano searched the articles, collected the data and drafted the manuscript. Soutrik Banerjee implemented the discussion on statistical methods. All co-authors read, edited and commented the paper.

Conflicts of Interest

The authors declare no conflict of interest.

References

1. Lipsett, M.; Materna, B.; Lyon Stone, S.; Therriault, S.; Blaisdell, R.; Cook, J. *Wildfire Smoke—A Guide for Public Health Officials*; California Department of Public Health: Sacramento, CA, USA; U.S. Environmental Protection Agency: Washington, DC, USA; California Office of Environmental Health Hazard Assessment: Sacramento, CA, USA; Missoula County Health Department: Missoula, MT, USA; California Air Resources Board: Sacramento, CA, USA, 2008.
2. European Commission. *Forest Fires in Europe 2010*; Institute for Environment and Sustainability: Ispra, Italy, 2010.
3. Ottmar, R.D. Smoke source characteristics. In *Smoke Management Guide for Prescribed and Wildland Fire*, 2001 ed.; Hardy, C.C., Ottmar, R.D., Peterson, J.L., Core, J.E., Seamon, P., Eds.; National Wildfire Coordinating Group, Fire Use Working Team: Boise, ID, USA, 2001; pp. 89–105.
4. Gyawali, M.; Arnott, W.P.; Lewis, K.; Moosmüller, H. *In situ* aerosol optics in Reno, NV, 5 USA during and after the summer 2008 California wildfires and the influence of absorbing and non-absorbing organic coatings on spectral light absorption. *Atmos. Chem. Phys.* **2009**, *9*, 8007–8015.
5. WHO Regional Office for Europe. *Health Risks of Particulate Matter from Long-Range Transboundary Air Pollution*; European Centre for Environment and Health: Bonn, Germany, 2006.
6. WHO Regional Office for Europe. *Health Effects of Particulate Matter*; WHO: Copenhagen, Denmark, 2013.
7. World Health Organization. *Health Guidelines for Vegetation Fire Events*; United Nations Environment Programme, WHO: Geneva, Swizerland, 1999.
8. Dennekamp, M.; Abramson, M.J. The effects of bushfire smoke on respiratory health. *Respirology* **2011**, *16*, 198–209.
9. U.S. Environmental Protection Agency. National ambient air quality standards for particulate matter. *Fed. Register* **2013**, *78*, 3086–3287.
10. Malilay, J. *A Review of Factors Affecting the Human Health Impacts of Air Pollutants from Forest Fires*; WHO: Geneva, Switzerland; UNEP: Nairobi, Kenya; WMO: Geneva, Switzerland, 1999; pp. 255–270.
11. Youssouf, H.; Lioussec, C.; Roblouc, L.; Assamoic, E.M.; Salonend, R.O.; Maesanoa, C.; Banerjeea, S.; Annesi-Maesano, I. Quantifying wildfires exposure for investigating health-related effects. *Atmos. Environ.* **2014**, *97*, 239–251.
12. Finlay, S.E.; Moffat, A.; Gazzard, R.; Baker, D.; Murray, V. Health impacts of wildfires. *PLoS Curr.* **2012**, *4*, doi:10.1371/4f959951cce2c.
13. Delfino, R.J.; Brummel, S.; Wu, J.; Stern, H.; Ostro, B.; Lipsett, M.; Winer, A.; Street, D.H.; Zhang, L.; Tjoa, T.; *et al.* The relationship of respiratory and cardiovascular hospital admissions to the Southern California wildfires of 2003. *Occup. Environ. Med.* **2009**, *66*, 189–197.
14. Henderson, S.B.; Johnston, F.H. Measures of forest fire smoke exposure and their associations with respiratory health outcomes. *Curr. Opin. Allergy Clin. Immunol.* **2012**, *12*, 221–227.

15. Jalaludin, B.; Smith, M.; O'Toole, B.; Leeder, S. Acute effects of bushfires on peak expiratory flow rates in children with wheeze: A time series analysis. *Aust. N. Z. J. Public Health* **2000**, *24*, 174–177.
16. Künzli, N.; Avol, E.; Wu, J.; Gauderman, W.J.; Rappaport, E.; Millstein, J.; Bennion, J.; McConnell, R.; Gilliland, F.D.; Berhane, K.; *et al*. Health effects of the 2003 Southern California wildfires on children. *Amer. J. Respir. Crit. Care Med.* **2006**, *174*, 1221–1228.
17. Mirabelli, M.C.; ünzli, N.; Avol, E.; Gilliland, F.D.; Gauderman, W.J.; McConnell, R.; Peters, J.M. Respiratory symptoms following wildfire smoke exposure: Airway size as a susceptibility factor. *Epidemiology* **2009**, *20*, 451–459.
18. Rappold, A.G.; Stone, S.L.; Cascio, W.E.; Neas, L.M.; Kilaru, V.J.; Carraway, M.S.; Szykman, J.J.; Ising, A.; Cleve, W.E.; Meredith, J.T.; *et al*. Peat bog wildfire smoke exposure in rural North Carolina is associated with cardiopulmonary emergency department visits assessed through syndromic surveillance. *Environ. Health Perspect.* **2011**, *119*, 1415–1420.
19. Naeher, L.P.; Brauer, M.; Lipsett, M.; Zelikoff, J.T.; Simpson, C.D.; Koenig, J.Q.; Smith, K.R. Woodsmoke health effects: A review. *Inhal. Toxicol.* **2007**, *19*, 67–106.
20. Greven, F.E.; Rooyackers, J.M.; Kerstjens, H.A.; Heederik, D.J. Respiratory symptoms in firefighters. *Amer. J. Ind. Med.* **2011**, *54*, 350–355.
21. Caamano-Isorna, F.; Figueiras, A.; Sastre, I.; Montes-Martínez, A.; Taracido, M.; Piñeiro-Lamas, M. Respiratory and mental health effects of wildfires: An ecological study in Galician municipalities (north-west Spain). *Environ. Health* **2011**, *10*, doi:10.1186/1476-069X-10-48.
22. Kolbe, A.; Gilchrist, K.L. An extreme bushfire smoke pollution event: health impacts and public health challenges. *N. S. W. Public Health Bull.* **2009**, *20*, 19–23.
23. Chen, L.; Verrall, K.; Tong, S. Air particulate pollution due to bushfires and respiratory hospital admissions in Brisbane, Australia. *Int. J. Environ. Health Res.* **2006**, *16*, 181–191.
24. Morgan, G.; Sheppeard, V.; Khalaj, B.; Ayyar, A.; Lincoln, D.; Jalaludin, B.; Beard, J.; Corbett, S.; Lumley, T. Effects of bushfire smoke on daily mortality and hospital admissions in Sydney, Australia. *Epidemiology* **2010**, *21*, 47–55.
25. Van Donkelaar, A.; Martin, R.V.; Brauer, M.; Kahn, R.; Levy, R.; Verduzco, C.; Villeneuve, P.J. Global estimates of ambient fine particulate matter concentrations from satellite-based aerosol optical depth: Development and application. *Environ. Health Perspect.* **2010**, *118*, 847–855.
26. Hodzic, A.; Madronich, S.; Bohn, B.; Massie, S.; Menut, L.; Wiedinmyer, C. Wildfire particulate matter in Europe during summer 2003: Meso-scale modeling of smoke emissions, transport and radiative effects. *Atmos. Chem. Phys.* **2007**, *7*, 4043–4064.
27. Liousse, C.; Guillaume, B.; Grégoire, J.M.; Mallet, M.; Galy, C.; Pont, V.; Akpo, A.; Bedou, M.; Castéra, P.; Dungall, L.; *et al*. Updated African biomass burning emission inventories in the framework of the AMMA-IDAF program, with an evaluation of combustion aerosols. *Atmos. Chem. Phys.* **2010**, *10*, 9631–9646.
28. Betchley, C.; Koenig, J.Q.; van Belle, G.; Checkoway, H.; Reinhardt, T. Pulmonary function and respiratory symptoms in forest firefighters. *Amer. J. Ind. Med.* **1997**, *31*, 503–509.
29. Analitis, A.; Georgiadis, I.; Katsouyanni, K. Forest fires are associated with elevated mortality in a dense urban setting. *Occup. Environ. Med.* **2012**, *69*, 158–162.

30. Arbex, M.A.; Martins, L.C.; de Oliveira, R.C.; Pereira, L.A.; Arbex, F.F.; Cançado, J.E.; Saldiva, P.H.; Braga, A.L. Air pollution from biomass burning and asthma hospital admissions in a sugar cane plantation area in Brazil. *J. Epidemiol. Community Health* **2007**, *61*, 395–400.
31. Johnston, F.; Hanigan, I.; Henderson, S.; Morgan, G.; Bowman, D. Extreme air pollution events from bushfires and dust storms and their association with mortality in Sydney, Australia 1994–2007. *Environ. Res.* **2011**, *111*, 811–816.
32. Ignotti, E.; Valente, J.G.; Longo, K.M.; Freitas, S.R.; de Souza Hacon, S.; Netto, P.A. Impact on human health of particulate matter emitted from burnings in the Brazilian Amazon region. *Rev. Saúde Públ.* **2010**, *44*, 121–130.
33. Gasparrini, A. Distributed lag linear and non-linear models in R: The package dlnm. *J Stat. Softw* **2011**, *43*, 1–20.
34. Fowler, C.T. Human health impacts of forest fires in the southern United States: A literature review. *J. Ecol. Anthropol.* **2003**. *7*, 39–63.
35. Mott, J.A.; Mannino, D.M.; Alverson, C.J.; Kiyu, A.; Hashim, J.; Lee, T.; Falter, K.; Redd, S.C. Cardiorespiratory hospitalizations associated with smoke exposure during the 1997, southeast Asian forest fires. *Int. J. Hyg. Environ. Health* **2005**, *208*, 75–85.
36. Vedal, S.; Dutton, S.J. Wildfire air pollution and daily mortality in a large urban area. *Environ. Res.* **2006**, *102*, 29–35.
37. Sastry, N. Forest fires, air pollution, and mortality in southeast Asia. *Demography* **2002**, *39*, 1–23.
38. Emmanuel, S.C. Impact to lung health of haze from forest fires: The Singapore experience. *Respirology* **2000**, *5*, 175–182.
39. Tham, R.; Erbas, B.; Akram, M.; Dennekamp, M.; Abramson, M.J. The impact of smoke on respiratory hospital outcomes during the 2002–2003 bushfire season, Victoria, Australia. *Respirology* **2009**, *14*, 69–75.
40. Ovadnevaitė, J.; Kvietkus, K.; Maršalka, A. 2002 summer fires in Lithuania: Impact on the Vilnius city air quality and the inhabitants health. *Sci. Total Environ.* **2006**, *356*, 11–21.
41. Reisen, F.; Hansen, D.; Meyer, C.P.M. Exposure to bushfire smoke during prescribed burns and wildfires: Firefighters' exposure risks and options. *Environ. Int.* **2011**, *37*, 314–321.
42. Kunii, O.; Kanagawa, S.; Yajima, I.; Hisamatsu, Y.; Yamamura, S.; Amagai, T.; Ismail, I.T. The 1997 haze disaster in Indonesia: Its air quality and health effects. *Arch. Environ. Health.* **2002**, *57*, 16–22.
43. Hanigan, I.C.; Johnston, F.H.; Morgan, G.G. Vegetation fire smoke, indigenous status and cardio-respiratory hospital admissions in Darwin, Australia, 1996–2005: A time-series study. *Environ. Health* **2008**, *7*, doi:10.1186/1476-069X-7-42.
44. Sorensen, B.; Fuss, M.; Mulla, Z.; Bigler, W.; Wiersma, S.; Hopkins, R. Surveillance of morbidity during wildfires—Central florida, 1998. *MMWR* **1999**, *48*, 78–79.
45. Brauer, M. *Health Impacts of Biomass Air Pollution*; Regional Offices for Southeast Asia and the Western Pacific, World Health Organization: Kuala Lumpour, Malesia, 1998.
46. Chew, F.T.; Ooi, B.C.; Hui, J.K.; Saharom, R.; Goh, D.Y.; Lee, B.W. Singapore's haze and acute asthma in children. *Lancet* **1995**, *346*, doi:10.1016/S0140-6736(95)92443-4.

47. Sutherland, E.R.; Make, B.J.; Vedal, S.; Zhang, L.; Dutton, S.J.; Murphy, J.R.; Silkoff, P.E. Wildfire smoke and respiratory symptoms in patients with chronic obstructive pulmonary disease. *J. Allergy Clin. Immunol.* **2005**, *115*, 420–422.
48. Moore, D.; Copes, R.; Fisk, R.; Joy, R.; Chan, K.; Brauer, M. Population health effects of air quality changes due to forest fires in British Columbia in 2003: Estimates from physician-visit billing data. *Can. J. Public Health* **2006**, *97*, 105–108.
49. Hisham-Hashim, J.; Hashim, Z.; Jalaludin, J.; Lubis, S.H.; Hashim, R. Respiratory function of elementary school children exposed to the 1997 Kuala Lumpur haze. *Epidemiology* **1998**, *9*, doi:10.1097/00001648-199807001-00330.
50. Tan, W.C.; Qiu, D.; Liam, B.L.; Ng, T.P.; Lee, S.H.; van Eeden, S.F.; D'Yachkova, Y.; Hogg, J.C. The human bone marrow response to acute air pollution caused by forest fires. *Amer. J. Respir. Crit. Care Med.* **2000**, *161*, 1213–1217.
51. Golshan, M.; Faghihi, M.; Roushan-Zamir, T.; Masood Marandi, M.; Esteki, B.; Dadvand, P.; Farahmand-Far, H.; Rahmati, S.; Islami, F. Early effects of burning rice farm residues on respiratory symptoms of villagers in suburbs of Isfahan, Iran. *Int. J. Environ. Health Res.* **2002**, *12*, 125–131.
52. Johnston, F.H.; Kavanagh, A.M.; Bowman, D.M.; Scott, R.K. Exposure to bushfire smoke and asthma: an ecological study. *Med. J. Aust.* **2002**, *176*, 535–538.
53. Duclos, P.; Sanderson, L.M.; Lipsett, M. The 1987 forest fire disaster in California: Assessment of emergency room visits. *Arch. Environ. Health* **1990**, *45*, 53–58.
54. Haenninen, O. Challenges in estimating the health effects of biomass smoke—Response to Sverre Vedal and Steven J. Dutton: Wildfire air pollution and daily mortality in a large urban area—Commentary. *Environ. Res.* **2008**, *106*, 423–424.
55. Hanninen, O.O.; Salonen, R.O.; Koistinen, K.; Lanki, T.; Barregard, L.; Jantunen, M. Population exposure to fine particles and estimated excess mortality in Finland from an east European wildfire episode. *J. Expo. Sci. Environ. Epidemiol.* **2009**, *19*, 414–422.
56. Johnston, F.H.; Henderson, S.B.; Chen, Y.; Randerson, J.T.; Marlier, M.; Defries, R.S.; Kinney, P.; Bowman, D.M.; Brauer, M. Estimated global mortality attributable to smoke from landscape fires. *Environ. Health Perspect.* **2012**, *120*, 695–701.
57. Aditama, T.Y. Impact of haze from forest fire to respiratory health: Indonesian experience. *Respirology* **2000**, *5*, 169–174.
58. Frankenberg, E.; McKee, D.; Thomas, D. Health consequences of forest fires in Indonesia. *Demography* **2005**, *42*, 109–129.
59. Yao, J.; Brauer, M.; Henderson, S.B. Evaluation of a wildfire smoke forecasting system as a tool for public health protection. *Environ. Health Perspect.* **2013**, *121*, 1142–1147.
60. Elliott, C.T.; Henderson, S.B.; Wan, V. Time series analysis of fine particulate matter and asthma reliever dispensations in populations affected by forest fires. *Environ. Health* **2013**, *12*, doi:10.1186/1476-069X-12-11.
61. Henderson, S.B.; Brauer, M.; Macnab, Y.C.; Kennedy, S.M. Three measures of forest fire smoke exposure and their associations with respiratory and cardiovascular health outcomes in a population-based cohort. *Environ. Health Perspect.* **2011**, *119*, 1266–1271.

62. Long, W.; Tate, R.B.; Neuman, M.; Manfreda, J.; Becker, A.B.; Anthonisen, N.R. Respiratory symptoms in a susceptible population due to burning of agricultural residue. *Chest* **1998**, *113*, 351–357.
63. Johnston, F.H.; Bailie, R.S.; Pilotto, L.S.; Hanigan, I.C. Ambient biomass smoke and cardio-respiratory hospital admissions in Darwin, Australia. *BMC Public Health* **2007**, *7*, doi:10.1186/1471-2458-7-240.
64. Crabbe, H. Risk of respiratory and cardiovascular hospitalisation with exposure to bushfire particulates: New evidence from Darwin, Australia. *Environ. Geochem. Health* **2012**, *34*, 697–709.
65. Martin, K.L.; Hanigan, I.C.; Morgan, G.G.; Henderson, S.B.; Johnston, F.H. Air pollution from bushfires and their association with hospital admissions in Sydney, Newcastle and Wollongong, Australia 1994–2007. *Aust. N. Z. J. Public Health* **2013**, *37*, 238–243.
66. Thelen, B.; French, N.F.N.; Koziol, B.W.; Billmire, M.; Owen, R.C.; Johnson, J.; Ginsberg, M.; Loboda, T.; Wu, S. Modeling acute respiratory illness during the 2007 San Diego wildland fires using a coupled emissions-transport system and generalized additive modeling. *Environ. Health* **2013**, *12*, doi:10.1186/1476-069X-12-94.
67. Allen, R.W.; Carlsten, C.; Karlen, B.; Leckie, S.; van Eeden, S.; Vedal, S.; Wong, I.; Brauer, M. An air filter intervention study of endothelial function among healthy adults in a woodsmoke-impacted community. *Amer. J. Respir. Crit. Care Med.* **2011**, *183*, 1222–1230.
68. Forchhammer, L.; Møller, P.; Riddervold, I.S.; Bønløkke, J.; Massling, A.; Sigsgaard, T.; Loft, S. Controlled human wood smoke exposure: Oxidative stress, inflammation and microvascular function. *Part Fibre Toxicol.* **2012**, *9*, doi:10.1186/1743-8977-9-7.
69. Ghio, A.J.; Soukup, J.M.; Case, M.; Dailey, L.A.; Richards, J.; Berntsen, J.; Devlin, R.B.; Stone, S.; Rappold, A. Exposure to wood smoke particles produces inflammation in healthy volunteers. *Occup. Environ. Med.* **2012**, *69*, 170–175.
70. Riddervold, I.S.; Bønløkke, J.H.; Mølhave, L.; Massling, A.; Jensen, B.; Grønborg, T.K.; Bossi, R.; Forchhammer, L.; Kjærgaard, S.K.; Sigsgaard, T.; *et al.* Wood smoke in a controlled exposure experiment with human volunteers. *Inhal. Toxicol.* **2011**, *23*, 277–288.
71. Holstius, D.M.; Reid, C.E.; Jesdale, B.M.; Morello-Frosch, R. Birth weight following pregnancy during the 2003 Southern California wildfires. *Environ. Health Perspect.* **2012**, *120*, 1340–1345.
72. Kessler, R. Followup in Southern California: Decreased birth weight following prenatal wildfire smoke exposure. *Environ. Health Perspect.* **2012**, *120*, doi:10.2307/41601744.
73. Williams, K.M.; Franzi, L.M.; Last, J.A. Cell-specific oxidative stress and cytotoxicity after wildfire coarse particulate matter instillation into mouse lung. *Toxicol. Appl. Pharmacol.* **2013**, *266*, 48–55.
74. Wegesser, T.C.; Pinkerton, K.E.; Last, J.A. California wildfires of 2008: Coarse and fine particulate matter toxicity. *Environ. Health Perspect.* **2009**, *117*, 893–897.
75. Huttunen, K.; Siponen, T.; Salonen, I.; Yli-Tuomi, T.; Aurela, M.; Dufva, H.; Hillamo, R.; Linkola, E.; Pekkanen, J.; Pennanen, A.; *et al.* Low-level exposure to ambient particulate matter is associated with systemic inflammation in ischemic heart disease patients. *Environ. Res.* **2012**, *116*, 44–51.
76. Reinhardt, T.E.; Ottmar, R.D. Baseline measurements of smoke exposure among wildland firefighters. *J. Occup. Environ. Hyg.* **2004**, *1*, 593–606.

77. Aisbett, B.; Wolkow, A.; Sprajcer, M.; Ferguson, S.A. "Awake, smoky, and hot": Providing an evidence-base for managing the risks associated with occupational stressors encountered by wildland firefighters. *Appl. Ergon.* **2012**, *43*, 916–925.
78. Swiston, J.R.; Davidson, W.; Attridge, S.; Li, G.T.; Brauer, M.; van Eeden, S.F. Wood smoke exposure induces a pulmonary and systemic inflammatory response in firefighters. *Eur. Respir. J.* **2008**, *32*, 129–138.
79. Hejl, A.M.; Adetona, O.; Diaz-Sanchez, D.; Carter, J.D.; Commodore, A.A.; Rathbun, S.L.; Naeher, L.P. Inflammatory effects of woodsmoke exposure among wildland firefighters working at prescribed burns at the Savannah River Site, SC. *J. Occup. Environ. Hyg.* **2013**, *10*, 173–180.
80. Brotherhood, J.R.; Budd, G.M.; Jeffery, S.E.; Hendrie, A.L.; Beasley, F.A.; Costin, B.P.; Wu, Z.E. Fire fighters' exposure to carbon monoxide during Australian bushfires. *Amer. Ind. Hyg. Assoc. J.* **1990**, *51*, 234–240.
81. Leonard, S.S.; Castranova, V.; Chen, B.T.; Schwegler-Berry, D.; Hoover, M.; Piacitelli, C.; Gaughan, D.M. Particle size-dependent radical generation from wildland fire smoke. *Toxicology* **2007**, *236*, 103–113.
82. Van Eeden, S.F.; Tan, W.C.; Suwa, T.; Mukae, H.; Terashima, T.; Fujii, T.; Qui, D.; Vincent, R.; Hogg, J.C. Cytokines involved in the systemic inflammatory response induced by exposure to particulate matter air pollutants (PM_{10}). *Amer. J. Respir. Crit. Care Med.* **2001**, *164*, 826–830.
83. Adetona, O.; Hall, D.B.; Naeher, L.P. Lung function changes in wildland firefighters working at prescribed burns. *Inhal. Toxicol.* **2011**, *23*, 835–841.
84. Soteriades, E.S.; Smith, D.L.; Tsismenakis, A.J.; Baur, D.M.; Kales, S.N. Cardiovascular disease in U.S. firefighters: A systematic review. *Cardiol Rev.* **2011**, *19*, 202–215.
85. Yang, J.; Teehan, D.; Farioli, A.; Baur, D.M.; Smith, D.; Kales, S.N. Sudden cardiac death among firefighters ≤45 years of age in the United States. *Amer. J. Cardiol.* **2013**, *112*, 1962–1967.
86. Choi, B.; Schnall, P.L.; Dobson, M.; Garcia-Rivas, J.; Kim, H.; Zaldivar, F.; Israel, L.; Baker, D. Very long (>48 h) shifts and cardiovascular strain in firefighters: A theoretical framework. *Ann. Occup. Environ. Med.* **2014**, *26*, doi:10.1186/2052-4374-26-5.
87. De Vos, A.J.; Cook, A.; Devine, B.; Thompson, P.J.; Weinstein, P. Effect of protective filters on fire fighter respiratory health during simulated bushfire smoke exposure. *Amer. J. Ind. Med.* **2006**, *49*, 740–750.
88. Booze, T.F.; Reinhardt, T.E.; Quiring, S.J.; Ottmar, R.D. A screening-level assessment of the health risks of chronic smoke exposure for wildland firefighters. *J. Occup. Environ. Hyg.* **2004**, *1*, 296–305.
89. Aisbett, B.; Phillips, M.; Sargeant, M.; Gilbert, B.; Nichols, D. Fighting with fire—How bushfire suppression can impact on fire fighters' health. *Aust. Fam. Physician* **2007**, *36*, 994–997.
90. Edwards, R.; Johnson, M.; Dunn, K.H.; Naeher, L.P. Application of real-time particle sensors to help mitigate exposures of wildland firefighters. *Arch. Environ. Occup. Health* **2005**, *60*, 40–43.
91. Semenza, J.C.; Wilson, D.J.; Parra, J.; Bontempo, B.D.; Hart, M.; Sailor, D.J.; George, L.A. Public perception and behavior change in relationship to hot weather and air pollution. *Environ. Res.* **2008**, *107*, 401–411.

92. Sillanpää, M.; Saarikoski, S.; Hillamo, R.; Pennanen, A.; Makkonen, U.; Spolnik, Z.; van Grieken, R.; Koskentalo, T.; Salonen, R.O. Chemical composition, mass size distribution and source analysis of long-range transported wildfire smokes in Helsinki. *Sci. Total Environ.* **2005**, *350*, 119–135.
93. Dominici, F.; McDermott, A.; Zeger, S.L.; Samet, J.M. On the use of generalized additive models in time-series studies of air pollution and health. *Amer. J. Epidemiol.* **2002**, *156*, 193–203.
94. Kim, S.-Y.; Peel, J.L.; Hannigan, M.P.; Dutton, S.J.; Sheppard, L.; Clark, M.L.; Vedal, S. The temporal lag structure of short-term associations of fine particulate matter chemical constituents and cardiovascular and respiratory hospitalizations. *Environ. Health Perspect.* **2012**, *120*, 1094–1099.
95. Dominici, F.; Peng, R.D.; Bell, M.L.; Pham, L.; McDermott, A.; Zeger, S.L.; Samet, J.M. Fine particulate air pollution and hospital admission for cardiovascular and respiratory diseases. *JAMA* **2006**, *295*, 1127–1134.
96. Fraga, J.; Botelho, A.; Sá, A.; Costa, M.; Quaresma, M. The lag structure and the general effect of ozone exposure on pediatric respiratory morbidity. *Int. J. Environ. Res. Public Health* **2011**, *8*, 4013–4024.
97. Peng, R.D.; Dominici, F. *Statistical Methods for Environmental Epidemiology with R: A Case Study in Air Pollution and Health Series*; Springer: New York, NY, USA, 2008.

© 2014 by the authors; licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution license (http://creativecommons.org/licenses/by/4.0/).

IV.2.1. Au-delà des effets non accidentels

Bien qu'ils ne soient pas présentés dans cette thèse, beaucoup d'effets accidentels et psychologiques sont également recensés lors des incendies de forêts [93, 94]. En fonction des paramètres météorologiques et de l'intensité des flammes, les incendies peuvent gagner rapidement le milieu suburbain et entrainer la destruction des habitations mais aussi des décès accidentels soit par intoxication ou par la prise au piège des flammes.

Les effets sanitaires accidentels des incendies concernent essentiellement les pompiers qui sont en première ligne pour lutter contre le feu et protéger la population. Entre 2000-2013, près de 300 pompiers sont décédés aux Etats-Unis dans l'exercice de leur fonction. Les dangers communs auxquels font face les pompiers sur la ligne de feu peuvent inclure la brulure, la chaleur, les blessures, l'inhalation de la fumée, les blessures liées aux véhicules (y compris les aéronefs), les glissades, les trébuchements, les chutes entre autres. De plus, l'effort physique intense et prolongé expose aux pompiers qui sont dans le front au risque des maladies liées à la chaleur et à la rhabdomyolyse[6] [95]. Lors du samedi noir[7] dans la région de victoria en Australie, les incendies ont tué 173 personnes et blessé 414 autres [96, 97]. Avant ce samedi, les incendies de forêts avaient causé la mort de 642 personnes [98].

La population peut aussi être touchée par les effets sanitaires accidentels liés aux incendies. Cependant, d'autres effets non accidentels comme les syndromes psychologiques ont été rapportés plusieurs mois après la fin des incendies. Parmi les plus décrits, il y a le syndrome posttraumatique. Beaucoup d'études ont montré que certaines personnes fragiles comme les jeunes enfants peuvent être victimes à des syndromes posttraumatiques après des évènements catastrophiques majeurs comme les grandes incendies [99-102]. En effet, lors de ces évènements, en plus des personnes ayant perdu la vie ou qui sont blessées, il y a celles qui perdent leurs habitations ou celles qui sont contraintes de les quitter. Ce sont des évènements très médiatisés qui marquent les esprits. Dans le cas du samedi noir en Australie les incendies avaient détruit plus de 3500 habitations et ont fait plus de 7562 personnes déplacées.

[6] En médecine, la rhabdomyolyse (du grec : rhabdo- : « rayé » myo- : « muscle » et –lysis : « destruction ») désigne une situation dans laquelle des cellules des muscles squelettiques, se dégradant rapidement, libèrent leur contenu dans la circulation sanguine.

[7] Le samedi noir désigne le Samedi 7 février 2009. En ce jour plus de 400 feux de forêts ont été allumés. Ces incendies ont causé plus de 173 décès, 414 blessés et plus de 7562 déplacés.

IV.3. Presentation de l'article 3: The temporal lag structure of short term-term associations of fine particulate matter ($PM_{2.5}$) and emergency visits in during the 2009 wildfire season in Marseille.

Les effets sanitaires des particules fines sont bien décrits dans la littérature. Cependant, le décalage entre l'exposition aux $PM_{2.5}$ et l'effet sanitaire n'est que peu étudié en raison du manque de données journalières disponibles [103]. A notre connaissance aucune étude ne s'est intéressée au décalage entre l'exposition aux $PM_{2.5}$ issues des émissions de feux de forêts et les effets sanitaires.

L'article 3 présente une étude de cas sur les incendies qui ont eu lieu à Marseille à l'été 2009. Pour étudier la persistance temporelle pouvant exister entre l'exposition aux $PM_{2.5}$ issues de différents sources de pollutions (feux de forêts, anthropiques et toutes les sources d'émissions) et ses effets sanitaires un modèle à retards échelonnés [103-105] a été employé. Un décalage de 10 jours a été utilisé, la recherche de relations sur des périodes plus longues posant des problèmes en termes de paramètres estimés dans le modèle et de convergence des algorithmes.

Les données sanitaires journalières ont été fournies par la division de l'Institut Nationale de Veille Sanitaire (INVS) de la région PACA et les concentrations journalières des particules fines ont été fournies par le laboratoire d'aérologie de Toulouse qui a surveillé les incendies par satellite. Un modèle a été ensuite appliqué pour estimer les émissions ainsi que les concentrations.

The temporal lag structure of short term-term associations of fine particulate matter ($PM_{2.5}$) and emergency visits in during the 2009 wildfire season in Marseille.

Youssouf H[1, 2], Banerjee S[1, 2], Liousse C[3], L. Roblou[3], Franke F[4], Pascal L[5], Annesi-Maesano I[1, 2], on behalf the PHASE study

[1]: Epidemiology of Respiratory and Allergic Disease Department, UMR-S 1136, Pierre Louis Institute of Epidemiology and Public Health, INSERM, Paris, France
[2]: Epidemiology of Respiratory and Allergic Disease Department, UMR-S 1136, Pierre Louis Institute of Epidemiology and Public Health, UPMC-Sorbonne Universités, Paris, France
[3]: Laboratory for Aerology Toulouse, France
[4]: InVS – PACA and Corsica, Marseille France
[5]: ARS-PACA, Marseille France

Abstract:

Background: The association between fine particulate matter (PM) and health outcomes has been consistently observed in the literature. Fewer studies have investigated the lag pattern of short-term associations between $PM_{2.5}$ and cardiovascular and respiratory diseases. However, the temporal lag pattern of $PM_{2.5}$ from wildfires has not yet been investigated.

Objectives: We explored the relative risks (RR) lag structure for all-cause, respiratory cause , cardiovascular cause and psychiatric consultations, and emergency room visits or hospitalizations and related them to the daily $PM_{2.5}$ concentrations from all types of emissions, anthropogenic emissions and wildfire emissions inventories, respectively.

Methods: $PM_{2.5}$ concentrations from all sources of pollution, anthropogenic emissions and wildfire emissions (total, anthropogenic and wildfire $PM_{2.5}$, respectively) was obtained using regional climatic model ($RegCM_4$) between June 1 and August 31, 2009 (92 days). The daily exposure data were linked to the daily health outcomes data in Marseille. We assessed the RRs lag structure for different health outcomes in relation to $PM_{2.5}$ concentrations starting from the same day until the 10th lag days (lag 0 – lag 10) in a distributed lag model framework and using quasi Poisson regression methods. We adjusted for temperature, relative humidity (RH) and day of the week using generalized additive model equation.

Results: For total and anthropogenic $PM_{2.5}$ concentrations, the RRs were generally larger at relatively shorter lags for cardiovascular cause and all-cause consultations (RR = 1.075 (95% CI=0.990-1.169) and RR = 1.016 (95% CI: 0.999-1.033), respectively at lag 2 for total $PM_{2.5}$ concentrations), for wildfire $PM_{2.5}$ concentrations, a longer lag duration was observed in the case of respiratory consultations (RR=1.018, 95% CI: 0.994-1.043 at lag 8, RR=1.017, 95% CI: 0.993-1.041 at lag 9).

Conclusion: Total and anthropogenic $PM_{2.5}$ were found to have immediate effect on cardiovascular cause and all-cause consultations, while $PM_{2.5}$ from wildfire showed a delayed pattern on respiratory cause consultations.

Key words: fine particulate matter, respiratory cause consultations, psychiatric consultations, cardiovascular cause consultations, distributed lag model, time series analyses.

Introduction

The health effects of air pollution have been subject to intense study in recent years. Exposure to pollutants such as airborne particulate matter and ozone has been associated with increases in mortality and hospital admissions due to respiratory and cardiovascular disease [35]. Over the past decade, time-series analysis studies conducted in many cities have provided information about the association between daily changes in levels of particulate matter (PM) and daily morbidity and mortality [106].

Short-term increases in ambient air pollutants are associated with an acute rise in mortality [4], hospital admissions [3], and emergency hospital visits [5]. In a short term exposure of particulate maters, many studies found an association between $PM_{2.5}$ and cardiovascular and respiratory diseases [103]. However temporal pattern differed for cardiovascular and respiratory diseases specifically, hospital admissions and emergency department visits. Indeed hospital admissions for cardiovascular diseases, such as heart failure, cerebrovascular disease, and abnormal heart rhythm, and emergency department visits and hospital admissions for ischemic stroke and transient ischemic attack have tended to show greater $PM_{2.5}$ health effect estimates on the same day or the previous exposure day [2, 3, 6, 107]. In contrast, emergency department visits for asthma and hospital admissions for respiratory tract infection showed larger health effect estimates for lags of 2–6 days [3, 11]. Kim et al [103]found after using the temporal lag structure to assess a short-term association of fine particulate matter chemical constituents and cardiovascular and respiratory hospitalizations that RRs were generally larger at shorter lags for total cardiovascular admissions, but at longer lags for total respiratory admissions. The delayed lag pattern was particularly prominent for asthma. Elemental and organic carbon generally showed more immediate patterns, whereas sulphate and nitrate showed delayed patterns.

Particulate matters are one of the major components of wildfire smoke. Several studies have established the relationship between particulate matters [particles with diameter less than 10 µm (PM_{10}) and less than 2.5 µm ($PM_{2.5}$)] from wildfire smoke and respiratory diseases, visits to hospital emergency rooms and hospital admissions. Until now, no study investigated the lag structure of cardiorespiratory morbidity due to wildfire emissions.

In the present study, we used a novel modeling approach to estimate daily $PM_{2.5}$ from all sources of pollution, wildfire and anthropogenic emissions [90] in order to

explore the lag structure of the association between $PM_{2.5}$ from different sources of emissions upon all-cause, cardiovascular cause, respiratory cause and psychiatric consultations, and emergency room visits or hospitalizations , in Marseilles during the summer 2009 (June 1 through August 31), using times series analysis.

Methods

- **Data collection**

The study period ran from June 1 until August 31, 2009. Health data, $PM_{2.5}$ data and environmental data were collected daily in this period.

Health data

Health data were provided by the PACA and Corsica's regional unit of the National Institute for Public Health Surveillance (InVS) in collaboration with the regional health agency of the PACA region (ARS-PACA). Health data collection included daily counts of emergency room visits and hospitalizations in AP-HM hospitals (La conception, La Timone hospital adults and children department and North University Hospital, adults and children department) and daily counts of emergency calls of SOS doctors, Marseilles. Daily counts in AP-HM hospitals included all-cause consultations, cardiovascular consultations corresponding to the codes of International Classification of Diseases and Related Health Problems, 10th Revision (ICD-10) of the chapter IX: I00-I99 corresponding to the entire list of diseases of the circulatory system, the codes ICD-10 of the chapter X: J00-J99 corresponding to the entire list of diseases of the respiratory system, and the codes ICD-10 of the chapter V: F00-F99 corresponding to the entire list of mental and behavioral disorders.

Environmental data

Daily maximum temperature and RH were extracted online in the Marseilles 'archives of the meteorological website' (http://www.meteorologic.net).

PM2.5 data

PM data were provided by the Laboratory of aerology of Toulouse and were obtained from modeling. Details about the methods of modelingare published elsewhere [90]. In brief, wildfire emission inventories are entered in the regional RegCM4 climatic model [108-110] to generate concentrations and then exposures linked to wildfires emission only. Other emissions (anthropogenic and natural emissions) are then also entered to test relative importance of wildfire emissions on resulting concentrations. RegCM4 simulations are performed with a spatial resolution of 15 km by 18 km vertical levels, from June 1 to September 15, 2009 with 15 days spin up, using ERA INTERIM meteorological fields. The

simplified aerosol module of RegCM4, including hydrophobic and hydrophilic organic carbon (OC) and black carbon (BC), sulphate (SO4), dust and sea salt particles has been selected for this simulation. BC, OC and SO4 schemes are detailed in Solmon et al. [109], dust scheme in Kok et al. [111] and Laurent et al. [112], and sea salt schemes in Gong et al. [113] and Monahan et al. [114]. PM2.5 concentrations were obtained from these modeled concentrations following the relationship:

Total $PM_{2.5}$ = $PM_{2.5}$ (BC) + $PM_{2.5}$ (OM) + $PM_{2.5}$ (Water Soluble) + $PM_{2.5}$ dust + $PM_{2.5}$ Seasalt

$PM_{2.5}$ (OM) = 0.75*1.7*1.3*POC

$PM_{2.5}$ (Water soluble) = 0.9*2.33*SO4

BC, POC, SO4, $PM_{2.5}$ (dust) and $PM_{2.5}$ (sea-salt) are given by the model. $PM_{2.5}$ dusts are obtained from the first two dust bins of the model, against $PM_{2.5}$ (sea-salt) from the first sea- salt bin of the model.

Note that 100% of total BC, 75% of total OC and 90% of total sulphates respectively, are considered to be in the $PM_{2.5}$ size range [115]. Total OC is obtained by multiplying Primary Organic Carbon(POC) by 1.3 [109], total organic matter (OM) by multiplying total OC by 1.7 [115]. The water soluble fraction is obtained by multiplying SO_4 by 2.33 [115].

First group of simulations only includes wildfire emissions. GFAS v1 inventory [116], (ECCAD) was selected for the run displayed here.

Second group of simulations only includes anthropogenic emissions (traffic, industries, power plant and residential heating). MACCity inventory (ECCAD) was selected for the run here. Third group of simulations includes wildfire emissions (GFAS v1), anthropogenic emissions (MACCity), but also dust and sea salt emissions.

Raw data were estimated every 6 hours from June 1 to August 31, 2009. Daily concentration of $PM_{2.5}$ was obtained by the mean concentration for 24 hours.

Statistical methods

Descriptive analyses were used to estimate means, standard deviation (SD), interquartile range and frequencies (percentages). Correlations between the different sources of $PM_{2.5}$ and between health outcomes were checked with Spearman rank correlation coefficient. The relationships between $PM_{2.5}$ and health outcomes were analyzed using the Generalized Additive Model (GAM), using distributed lag model framework and quasi Poisson regression model in which we controlled for the confounding factors such as meteorological factors (temperature, RH, wind speed) and day of the week

(weekday, Saturday and Sunday or a holiday). The quasi-Poisson model was used to take into account the overdispersion in the data (variance larger than the mean) as this method consists in estimating an additional dispersion parameter from the data and using it to adjust inference for overdispersion [117, 118]. The use of GAMs allow us to include smooth functions of natural (cubic) (or penalized) regression splines in the analysis [117]. The mgcv R-package's (by Simon Wood) glm() function was used to fit the models. Natural splines were used to smooth time using ns() function [119] within the glm() function. Penalized splines were also fitted for sensitivity analysis using s() function.

The natural cubic spline, with 3 degree of freedom (d.f.) for the time variable to account for any monthly variation and to take care of the temporal autocorrelations [120-123]. Distributed lag model framework considering lag0 to lag10 for PM was considered.

RESULTS

Table 1 presents descriptive statistics of daily emergency visits in AP-HM for all-cause consultations, cardiovascular cause consultations, respiratory cause consultations and psychiatric consultations, and the weather variables from June 1 to August 31, 2009 in Marseilles. The daily mean (±SD) of total consultations was 494.8 (±37.4) and the daily maximum consultations during this period were estimated to 606 consultations. On average (±SD), there were 30.3 (±8.8) respiratory cause consultations, 24.1 (±5.5) psychiatric consultations and 9.9(+/-3.1) cardiovascular cause consultations daily during the period of observation. The proportion of visits in cardiology, psychiatry and respiratory services represented, respectively, 2%, 6% and 5% of the all-cause consultations in this period. Finally, the daily average emergency consultations for "*SOS doctors*" were 153.8 (±45.4). Time series plots corresponding to the distribution of health outcomes are presented in Figure 1.

Table 1: Daily parameters of PM emissions, consultations, "SOS doctors" visits and environmental factors from June 1 to August 31, 2009

	Mean	SD	Minimum	3rd quartile	Maximum
AP-HM consultations					
All-cause	494.8	37.4	432.0	517.5	606.0
Cardiovascular	9.9	3.1	3.0	12.0	18.0
Respiratory	30.3	8.2	11.0	35.5	55.0
Psychiatric	24.1	5.5	6.0	27.0	39.0
"SOS doctors" visits	153.8	45.4	92.0	194.0	283.0
Environmental factors					
Maximum Temperature	30.4	2.8	22.6	32.4	34.8
Mean Temperature	24.5	2.2	19.0	26.0	29.0
Maximum Wind speed	46.3	15.3	25.9	53.7	103.7
Relative humidity	0.6	0.1	0.3	0.6	0.8
Day of the week	N	Weekday		Saturday	Sunday/Holiday
	92(100%)	64(69.6%)		12(13%)	16(17.4%)

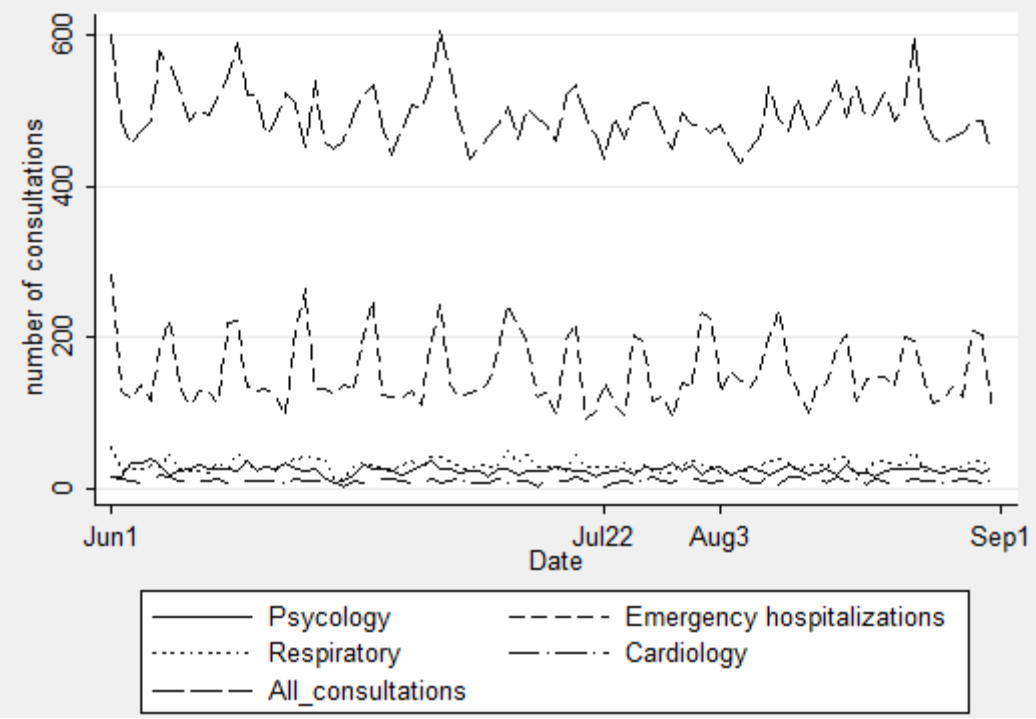


Figure 1: Time series plots of health outcomes

Figure 2 presents the modeling $PM_{2.5}$ concentrations obtained for Marseilles for the two groups of simulations ($PM_{2.5}$ from wildfire and anthropogenic) and for the whole period of simulation, from June 1 to August 31, 2009. During the study period, average daily mean concentrations of total $PM_{2.5}$, wildfire $PM_{2.5}$, and anthropogenic $PM_{2.5}$ were 44.0, 3.7, and 26.0 $\mu g/m^3$, respectively. We note in the Figure 2 that wildfire activity was observed in the whole period. According to the Bouches-du-Rhône county Directorate of Forestry and Agriculture, there were from June 15 to August 31 the 2009, 391 fires in the Bouche-du Rhone region, which burned 1,183 *ha* of surface area. However, intense wildfires occurred on July 22-23, 2009 in Marseilles and in August 3, 2009 in the cities of Muy and Roquebrune-sur-Argens in the Var near Marseilles on the. Most of the time during the simulation period, we observed that anthropogenic emissions were uniformly distributed with total $PM_{2.5}$ emissions except the days with peak wildfire activities. We observed that the concentration of $PM_{2.5}$ from wildfire emissions reached up to the European reference value for $PM_{2.5}$ ($25\mu g/m^3$), in the 22-23 July (55.6 $\mu g/m^3$ and 63.4 $\mu g/m^3$, respectively) and in 3 August (70.6 $\mu g/m^3$) as shown in Figure 2. Table 2 presents the correlation between health outcomes during the study period. We notice that all consultations were positively and significantly associated with daily emergency visits to the cardiology and respiratory services. Emergency room visits and hospitalizations with "*SOS doctors*" were positively and significantly associated with respiratory cause consultations and all-cause consultations. As presented in Table 3, $PM_{2.5}$ from all sources was significantly associated with $PM_{2.5}$ from anthropogenic emissions, $PM_{2.5}$ from wildfire emissions and with temperature. $PM_{2.5}$ from wild fire emissions was positively associated with temperature and negatively associated with RH. The highest correlation was observed between total $PM_{2.5}$ and wildfire $PM_{2.5}$ (ρ = 0.58).

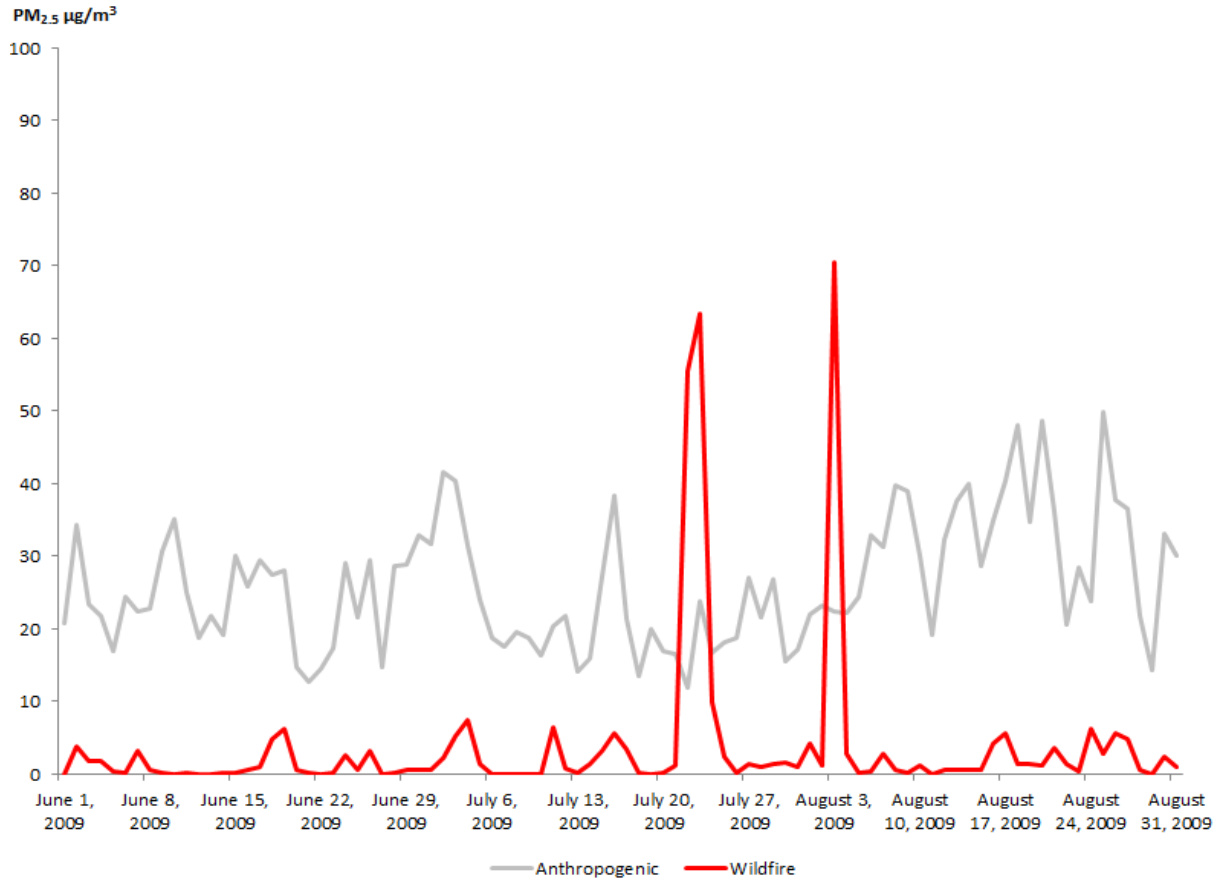


Figure 2: Modeled $PM_{2.5}$ concentration at Marseilles from June 1 to August 31 2009

Table 2: Pearson correlation coefficient between health outcomes from June 1 to September 1, 2009.

	All-cause consultations	Cardiovascular consultations	Emergency room visits and hospitalizations	Psychiatry consultations
Cardiovascular	0.29*			
Emergency room visits and hospitalizations	0.47*	0.06		
Psychiatry	0.11	0.05	-0.11	
Respiratory	0.51*	0.15	0.59*	0.06

Table 3: Pearson correlation coefficient between $PM_{2.5}$ concentrations and temperature and humidity from June 1 to September 1, 2009.

	Total $PM_{2.5}$	Anthropogenic $PM_{2.5}$	Wildfire $PM_{2.5}$	Relative humidity
Antopogenic $PM_{2.5}$	0.27*			
Wildfire $PM_{2.5}$	0.58*	-0.08		
Relative humidity	0.15	0.43*	-0.22*	
Temperature	0.28*	0.24*	0.23*	-0.04

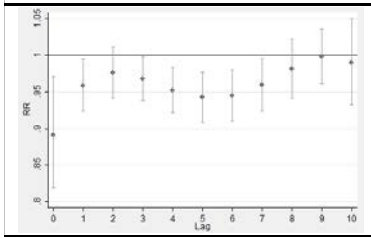
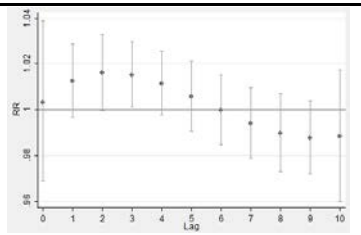
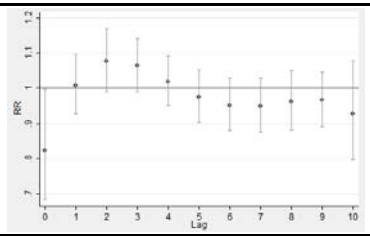
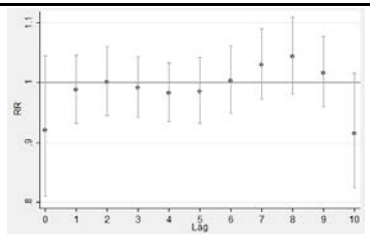
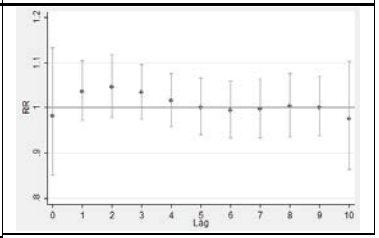
Figure 3 shows the health effect estimates from the distributed lag models for $PM_{2.5}$ mass from all emissions, from anthropogenic emissions and from wildfire emissions.

For $PM_{2.5}$ from all emissions, the largest effects on cardiovascular cause consultations and all-cause consultations were generally estimated at shorter pollutant lags and highest RR was observed at lag 2 for both (RR = 1.075 (95% CI=0.990-1.169) and RR = 1.016 (95% CI:0.999-1.033), respectively), whereas, the largest effects estimates for respiratory cause consultations tended to occur at longer lags (RR = 1.04 (95% CI=0.981-1.109) at lag 8). However no significant effect was observed between PM from total emissions and respiratory or cardiovascular cause consultations. The significant effect of PM2.5 from all emissions was observed on the increase of total consultations at lag 3 (RR = 1.015; 95% CI = 1.00-1.03).

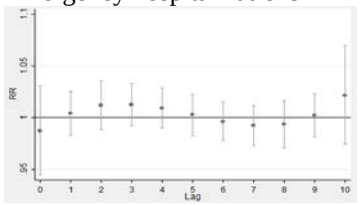
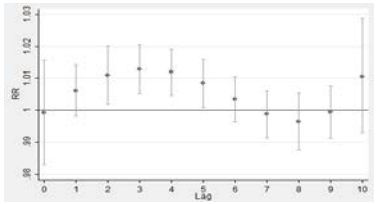
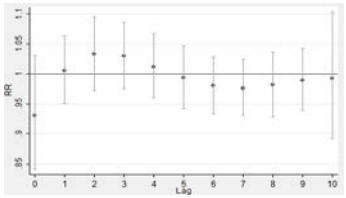
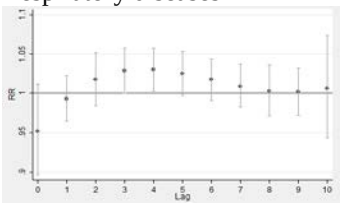
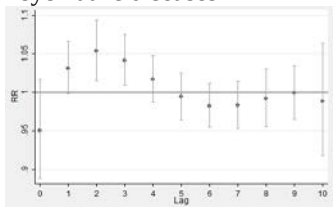
For PM2.5 from anthropogenic emissions, significant effect was observed for total consultations from lag 2 – lag 5 (RR = 1.011; 95% CI = 1.002-1.020, RR = 1.013; 95% CI = 1.005-1.021, RR = 1.012; 95% CI = 1.005-1.019, RR = 1.008; 95% CI = 1.001-1.016, respectively). The largest effect was observed at lag 2 for psychiatric disease RR = 1.053, which was significant with the increased risk at lag 3 (RR = 1.053; 95% CI = 1.015-1.094 and RR = 1.041; 95% CI = 1.009-1.074, respectively). No significant increase risk was observed for respiratory and cardiovascular disease emergency consultations.

Regarding $PM_{2.5}$ from wildfire emissions, the largest effect was observed at longer lags for respiratory disease at lag 8 – lag 9 and for psychiatric disease at lag 8. The relationships were borderline significant (RR=1.018, 95% CI: 0.994-1.043 at lag 8, RR=1.017, 95% CI: 0.993-1.041 at lag 9). However, no significant effect was observed between $PM_{2.5}$ from wildfire and the other health outcomes.

A: $PM_{2.5}$ from all emissions

Emergency hospitalizations	Total consultations	Cardiovascular diseases	Respiratory diseases	Psychiatric diseases
				

B: $PM_{2.5}$ from anthropogenic emissions

Emergency hospitalizations	Total consultations	Cardiovascular diseases	Respiratory diseases	Psychiatric diseases
				

C: $PM_{2.5}$ from wildfire emissions

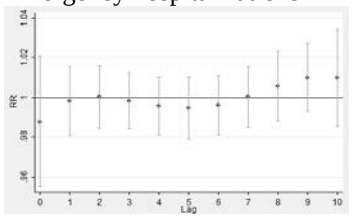
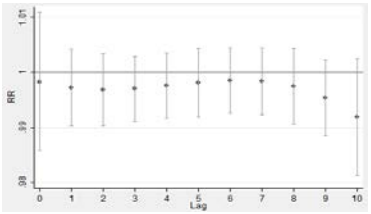
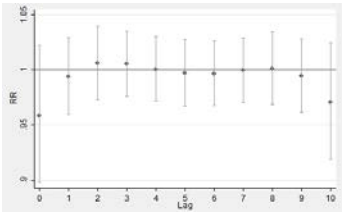
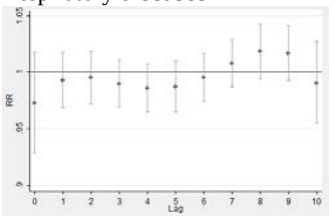
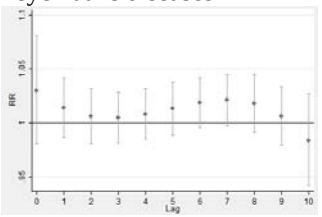
Emergency hospitalizations	Total consultations	Cardiovascular diseases	Respiratory diseases	Psychiatric diseases
				

Figure 3: the pattern of RRs from lag 0 to lag 10 from distributed lag model of all-cause, cardiovascular cause, respiratory cause and psychiatric consultations, and emergency room visits and hospitalizations for an increased risk of total $PM_{2.5}$, anthropogenic $PM_{2.5}$ and wildfire $PM_{2.}$

Discussion

We explored in this study, the temporal lag patterns on the effects of $PM_{2.5}$ from different source of pollution (all, anthropogenic and wildfire emissions) during the summer 2009 in Marseille. In Mediterranean region, the summer period is known to be the period of wildfire season in this area, theoretically the most dangerous time of year [42]. We found that during the period of the study, the European reference value for $PM_{2.5}$ was reached in the 3 days of major wildfire events. We found significant association between $PM_{2.5}$ from all emissions and the increase of total consultations at lag 3 and significant association between $PM_{2.5}$ from anthropogenic emissions and total hospital admissions and psychiatric admissions at shorter lag. RRs were generally larger at shorter lags for cardiovascular and total hospital admissions when considering $PM_{2.5}$ from all emissions but at longer lag for respiratory admissions when considering $PM_{2.5}$ from wildfire emissions.

Very few time series studies have been interested to explore the lag structure on short term exposure of $PM_{2.5}$ using daily measurement [103], However, to our knowledge, this study is the first to explore the temporal lag structure of short term-term associations of fine particulate matter ($PM_{2.5}$) from wildfire event and health outcomes.

Kim et al[103] found that $PM_{2.5}$ chemical constituents had more immediate estimated effect on cardiovascular disease and more delayed estimated effect on respiratory disease, this finding is consistent with that we found because in our study $PM_{2.5}$ from all emissions had the same tendency on cardiovascular disease and respiratory hospital admissions. In addition $PM_{2.5}$ wildfire emissions, which were strongly correlated with $PM_{2.5}$ from total emissions, had a delayed pattern on respiratory admissions. However, this effect was not significant.

Our modeling approach thus reveals convincing to analyze the each source influence on $PM_{2.5}$ concentrations, which is important to determine real health impact of wildfire fires.

In this study, no significant result observed considering $PM_{2.5}$ from wildfire emissions and all-causes and cardiovascular diseases. , However, a trend was observed for lag 8 and 9 for respiratory disease, which is compatible with the fact that many studies document the impact of wildfire emissions on respiratory health at short term exposure [3, 5, 103]. This trend could explain potential long-term effect of $PM_{2.5}$ from wildfire emissions in the respiratory pathways, even at low concentrations. However, the lack of power did not allow

us to observe the significant effects. A possible explanation of not finding an association could be the short period of exposure period when the concentration of $PM_{2.5}$ from wildfire exceeded the European threshold [124]. Also it could be explained that during July and August months, more subjects (i.e., at-risk population or denominator) could be on holidays compared to that during June. This could thus reduce the number of subjects at-risk when the incident occurred. Two possible events could happen actually: first, a net increase in the population at-risk due to more people from other areas coming to Marseille during the holiday season or second, a net decrease in the population at-risk due to more people who leaving the city during the holiday season. Therefore, the difference in number between the incoming and outgoing population at-risk could influence the outcome. Furthermore, most air pollution studies have used measures of ambient air pollution instead of personal exposure because estimating relevant exposures for each person can be daunting. According to this approximation; "misclassification of exposure is a well-recognized limitation of these studies" [104].

Modeling using RegCM4 allowed us to characterize distinguish $PM_{2.5}$ from all sources of emissions (all, anthropogenic and wildfire emissions) while most epidemiological studies concerned by the study of the impact of wildfire event did not distinguish wildfire emissions from the others sources. However, our study has a limit. Despite this advantage that our model provides by having emissions from each sources alone, we could better estimates personal exposure. In addition health data provided by APHM covers a large area around Marseilles. This fact did not allowed us to better estimate the real impact of wildfire emissions. One possible solution for assessment of personal exposure from wildfire, is the use of biomarkers as tested firefighters for the investigation of occupational wood smoke exposure [125].

Conclusion

Total and Anthropogenic $PM_{2.5}$ were found to have immediate effect on cardiovascular and total admissions, with a significant effect on total hospital admissions, while $PM_{2.5}$ from wildfire showed delayed pattern on respiratory admissions. The association between $PM_{2.5}$ from wildfire and health outcomes was not significant.

Acknowledgments

This publication arises from the project PHASE (contract number EAHC 20101103) which has received funding

from the European Union, in the framework of the Health Programme

V. Conclusions

A travers une revue de la littérature, nous avons pu mettre en évidence les études épidémiologiques qui ont pu établir des associations entre l'exposition aux émissions de feux de forêts et les effets sur la santé humaine.

Nous avons revu les méthodes utilisées dans la littérature pour évaluer l'exposition des émissions en vue de déterminer l'impact sanitaire des incendies au niveau de la population vivant à proximité. En effets plusieurs sources tels que le trafic routier, les installations industrielles… etc sont susceptibles de dégager dans l'atmosphère les mêmes polluants que ceux émis par les feux. D'où l'importance d'une meilleure évaluation de l'exposition. Celle-ci doit prendre en considération les émissions de feux de forêts ainsi que celles des autres sources de pollution. Certaines études ont essayé de différencier cette pollution de base à la pollution engendrée par les feux de forêts soit en développant une méthode qui permet de soustraire la pollution de base à celles émises par les émissions de feux de forêts [126] ou en créant un indicateur d'avant, pendant et après les feux de forêts puis comparaison des effets sanitaires dans ces différentes périodes [43].

A travers l'étude de cas que nous avons réalisé à Marseille pour évaluer les effets sanitaires des incendies qui ont eu dans la proche banlieue de cette ville à l'été 2009, nous avons appliqué une méthode qui nous a permis de différentier les émissions des feux de forêts des émissions anthropiques, ce qui a permis de limiter fortement le biais d'exposition. Néanmoins, seulement une association à la limite de la signification statistique a été observée entre l'exposition aux $PM_{2.5}$ issues des émissions de feux de forêts et les données sanitaires, dans le cas de la morbidité respiratoire. Une possible explication que nous pouvons avancer est la faible concentration des $PM_{2.5}$ issue des incendies et la très courte durée d'exposition, pour des incendies qui n'ont duré que 2 jours. De plus, malgré le fait que nous ayons pu différencier les émissions de feux de forêts des émissions anthropiques et que ces émissions soient obtenues au niveau local avec les coordonnées spatiales, nous n'avions pas eu des données sanitaires de proximités. Celles que nous avions eues étaient des données globales des consultations des hôpitaux de l'Assistance Publique Hôpitaux de Marseille (APHM). Une association significative entre l'exposition aux particules fines

provenant des émissions anthropiques et l'augmentation du nombre de consultations totales a été observée dans la période de l'étude. La distinction entre les $PM_{2.5}$ issues des feux de forêts des émissions anthropiques, nous a évité de conclure à tort sur un possible impact des émissions des feux de forêts.

Le niveau d'exposition dont il était question dans la plupart des études épidémiologiques évaluant l'impact sanitaire des émissions de feux de forêt est du type macroscopique puisque dans ces études, les émissions sont dégagées dans la troposphère et aucune exposition individuelle n'est évaluée. Dans certaines études avec les pompiers, des biomarqueurs ou des capteurs mobiles sont utilisées pour mesurer la concentration des polluants dans la zone de respiration. Toutefois, les pompiers constituent un sous-groupe particulier très exposé puisque ils sont en première ligne dans la lutte contre les incendies et donc ont un risque d'exposition beaucoup important que celui de la population générale mais en même temps les pompiers constituent un groupe de sujets bien portants, ce qui ne peut pas exclure le phénomène du travailleur sain (« Healthy workers effect »). En effet, dans la plupart des études en milieu professionnel, la population étudiée est une population de personnes au travail, donc sélectionnées pour être indemnes de maladie grave et incapacitante, ce qui peut entrainer une sous-estimation des effets sanitaires sur le moyen terme.

Un dispositif similaire utilisé au niveau de la population générale devrait permettre de mieux évaluer l'exposition au niveau individuelle dans de la population générale afin de mieux évaluer l'impact réel des émissions de feux de forêts sur la santé humaine.

CHAPITRE III : EXPOSITION EN MILIEU RURAL

I. Présentation de la problématique

En milieu agricole rural, la pollution de l'air à intérieur des habitations ou la pollution dans les lieux de travail, peuvent être considérées comme une pollution chronique, de par la fréquence de l'exposition. Dans ce cas, les mesures des polluants par des capteurs installés au domicile et dans les lieux de travail pour étudier l'impact sanitaire, sont considérées semi-individuelles. En effet, dans ce genre d'études, on utilise des données individuelles pour la santé respiratoire et les caractéristiques sociodémographiques, mais des données agrégées d'exposition provenant des capteurs fixes installés à domicile ou dans les lieux de travail, pour mesurer la qualité de l'air ambiant à l'intérieur. Peu d'études sur les liens entre la pollution atmosphérique et la santé respiratoires ont été réalisées en milieu agricole rural. Or dans les pays industrialisés, malgré les progrès en matière de production, l'agriculture moderne est associée à l'exposition à des nombreux polluants dont la plupart d'entre eux peuvent provoquer de nombreuses maladies respiratoires. En France, les fermes constituent à la fois le lieu de résidence et de travail des agriculteurs et la pollution observée dans les lieux de travail (étables, granges…etc.) peut également s'infiltrer dans les habitations et s'ajouter à la pollution intérieur engendrée par les différentes sources de pollution intérieur. Les principales sources de pollution intérieure sont constituées de la fumée du tabac, des équipements domestiques (chaudières, cuisinières…), matériaux de construction, de décoration, des animaux domestiques…etc. Parmi les polluants recensés on y trouve les PM et les COVs. L'impact sanitaire de ces 2 polluants est bien documenté.

En outre, lorsque les agriculteurs ont été comparés à la population générale de de la même région, une augmentation de la prévalence de symptômes respiratoires a été fréquemment observée chez les premiers mais des études sur la prévalence de symptômes respiratoires chez les différentes régions agricoles ont révélé une grande variabilité géographique [127].

Ce troisième chapitre nous permet à la fois d'évaluer l'exposition des COV et des PM et leurs effets sanitaires auprès des exploitants agricoles puis de comparer les effets sanitaires de l'exposition des polluants agricoles dans différentes régions.

II. Pollution en milieu agricole rural

Les travailleurs agricoles sont régulièrement exposés à des quantités élevées de polluants chimiques ou biologiques. Ces polluants soit sont générés par l'activité agricole qu'ils exercent, soit sont répandus volontairement pour lutter contre les animaux ou les plantes jugés nuisibles aux plantations, comme les pesticides. L'inhalation régulière de ces polluants explique la survenue des pathologies professionnelles pulmonaires en milieu agricole [128].

II.1. Les sources d'exposition liées à l'activité agricole

Les agriculteurs et les travailleurs agricoles ont un potentiel d'exposition à une multitude d'agents inhalables. Ces agents sont de nature chimique ou biologique: la poussière inorganique provenant du sol, la poussière organique contenant des micro-organismes (bactéries, champignons, acariens et virus transmis par les animaux), les parasites et les tiques (zoonoses), les mycotoxines, les allergènes, les gaz, les pesticides…etc [28]. Par ailleurs, ils sont également à risque pour les problèmes respiratoires dus aux micro-organismes et aux acariens dans les poussières organiques de céréales, du lait en poudre, de la farine, des épices, et aux maladies allergiques spécifiques comme le poumon du fermier et comme celui de l'éleveur d'oiseaux.

L'exposition à ces agents se produit quand les agriculteurs et les salariés agricoles sont en contact avec les animaux, participent à la récolte, à la transformation, au stockage des graines ou des autres matières végétales ou lorsque le sol, les plantes, les étables et les granges sont traités avec des produits chimiques tels que les pesticides, les désinfectants ou les engrais [28]. Les poussières végétales sont générées, par exemple, lors de l'entreposage de foin insuffisamment séché pouvant être à l'origine de pathologies pulmonaires, par mécanisme allergique.

L'enquête de 2010 de la Direction de l'Animation de la Recherche, des Etudes et des Statistiques (DARES), a montré que dans le secteur agricole, 37 % des salariés étaient exposés à des agents biologiques, principalement au contact d'animaux[129]. Contrairement au cas du contact humain, l'animal n'est pas forcément au centre de l'activité du salarié concerné. Il peut être un élément du contexte de travail. Concernant les animaux d'élevage, les expositions sont

prolongées, une fois sur deux, et ce, plus de 20 heures par semaine. Cela concerne surtout des hommes, des ouvriers et des techniciens agricoles mais aussi des conducteurs de tracteurs.

Dans l'agriculture, il existe des normes standards permettant de mesurer l'exposition des agents chimiques, alors que pour les agents biologiques, de telles normes n'existent pas et les limites d'exposition tolérées n'en sont pas disponibles. Néanmoins, les agriculteurs sont souvent exposés à des niveaux élevés des produits chimiques et les agents biologiques sont souvent au-dessus des limites recommandées [28].

II.2. Caractéristiques des principaux polluants agricoles

La poussière

Les agriculteurs travaillent souvent dans d'épais nuages de poussière lorsqu'ils cultivent le sol et lors de la récolte. Cette poussière peut être organique ou inorganique. La composition de la poussière organique est très hétérogène [130]. C'est un mélange de matière végétale, de pollen, de déjections d'animaux, d'insectes, de résidus de rongeurs et d'oiseaux, de plumes, de micro-organismes (virus, bactéries, nématodes, spores), de dérivés bactériens et pneumallergènes, de toxines bactériennes et fongiques, de pesticides et d'antibiotiques [70]. L'exposition aux poussières organiques peut varier aussi bien qualitativement que quantitativement, d'une filière agricole à une autre.

La fraction inorganique de la poussière provient essentiellement de la terre. La fraction minérale de la plupart des sols est dominée par les silicates, à l'exception des sols des territoires où le climat est très aride. Ici, la fraction inorganique peut être dominée par le carbonate de calcium et par les sels plus solubles (évaporites). Dans les sols des climats très chauds et humides, ce sont les oxydes, les hydroxydes de fer (goethite et hématite) et l'aluminium (gibbsite) qui prédominent exceptionnellement [131].

Les endotoxines

Les endotoxines, lipopolysaccharides (LPS) extracellulaires des bactéries à Gram négatif, sont les contaminants biologiques les plus étudiés de ces dernières décennies. Les endotoxines sont souvent rencontrées en milieu agricole et les fortes concentrations sont mesurées dans les élevages ainsi que dans les sites utilisant des grains /végétaux. Cependant, il n'existe aucune norme d'exposition

professionnelle commune déterminée au niveau international, ce qui fait qu'il existe une grande variété de normes d'exposition, en fonction des pays. Par exemple, au Pays-Bas, la valeur - limite reconnue est de 5 ng/m^3 pour une exposition durant huit heures. Les endotoxines induisent des syndromes respiratoires graves qui reposent principalement sur des mécanismes inflammatoires, toxiques et immunologiques. L'exposition aux endotoxines est associée au développement d'atteintes respiratoires, que ce soit en milieu professionnel [98] ou domestique [72, 94].

Les moisissures (expositions fongiques)

Les champignons de l'environnement sont de plus en plus mis en cause dans de nombreuses affections pulmonaires telles que l'asthme, les pneumopathies d'hypersensibilité comme la maladie du poumon du fermier (PDF), la broncho-pneumopathie chronique obstructive (BPCO), le syndrome toxique des poussières organiques [71, 128]. Les effets sur la santé sont dus soit à des réactions immunologiques, soit à des toxines. Celles liées aux moisissures sont présentes, parfois très temporairement, dans l'alimentation du bétail ou dans les fruits et les légumes, ayant un impact probablement sous-estimé en santé publique [73], malgré leur potentielle mise en cause dans le développement des cancers ou des néphropathies graves. La répartition spatiale de ces espèces fongiques et leurs concentrations varient de façon extrême, d'une activité à une autre, souvent au sein d'une même région. Cette variabilité spatiale est doublée par celle temporelle, avec l'évolution des procédures de production [71].

Les pesticides

Les pesticides (insecticides, raticides, fongicides, et herbicides) sont des composés chimiques dotés des propriétés toxicologiques, utilisés par les agriculteurs pour lutter contre les animaux (insectes, rongeurs) ou les plantes (champignons, mauvaises herbes) jugés nuisibles pour les plantations. Le premier usage intensif d'un pesticide, le DDT, remonte à l'époque de la Seconde Guerre Mondiale. Les principaux pesticides utilisés actuellement appartiennent à quelques grandes familles chimiques : les organochlorés (hydrocarbures chlorés), les organophosphorés, les pyréthroïdes, les carbamates, les phytosanitaires.

Une grande partie des pesticides est dispersée dans l'atmosphère, que ce soit lors de leur application, ou bien par évaporation ou par envol, à partir des plantes ou des sols sur lesquels ils ont été répandus. Disséminés par le vent et parfois loin de leur lieu d'épandage, ils retombent avec les pluies directement sur les plans d'eau et sur les sols d'où ils sont ensuite drainés jusque dans les milieux aquatiques, par les eaux de pluie (ruissellement et infiltration).

Si les pesticides ont été considérés, à un premier abord, bénéfiques, leurs effets secondaires nocifs ont rapidement été mis en évidence. Leur toxicité, liée à leur structure moléculaire, ne se limite pas en effet aux seules espèces que l'on souhaite éliminer. Ils sont notamment toxiques pour l'homme [74, 75, 127, 132-134].

Les autres polluants

Les agriculteurs risquent également d'être exposés à des substances sensibilisantes. Parmi ces dernières, il y a des sensibilisants cutanés tels que les protéines animales dans l'urine et les squames; la farine et certains légumes, les plantes, les épices et les sensibilisants respiratoires tels que :

- L'épithélium des animaux et l'urine
- Les plantes décoratives;
- Certains produits alimentaires, les plantes et les légumes (par exemple la poussière de grain de café, les protéines d'œuf, la farine et le grain de poussière, les fruits, les légumes, les poissons, les fruits de mer, la poussière de soja, les épices);
- les acariens de stockage;
- La poussière du bois, les panneaux composites;
- Les fibres textiles (la soie, par exemple, lors de la sériciculture).

II.3. Exposition à l'intérieur des habitations

En milieu agricole rural tout comme en ville, l'air intérieur des habitations et autres lieux de vie est contaminé non seulement par les polluants de l'air extérieur, mais aussi par des polluants provenant du bâtiment lui-même et des habitudes de vie des occupants.

II.3.1. Les sources liées à l'intérieur des habitations

L'activité agricole génère deux types de pollution: les pollutions ponctuelles qui peuvent être la conséquence soit de manipulations "accidentelles" de produits phytosanitaires soit de pollutions dues aux bâtiments d'élevage et les pollutions diffuses proviennent quant à elles de mauvaises pratiques de fertilisation ou de traitements phytosanitaires. Les pollutions diffuses sont notamment rencontrées dans les eaux souterraines. Ces pollutions sont susceptibles de pénétrer dans les habitations. En plus de sources de pollution rencontrées dans les habitations décrites précédemment, d'autres polluants spécifiques à l'activité agricole peuvent être rencontrés notamment les pesticides, les fertilisants, les polluants issus de la biomasse tels que les déchets des animaux, poussières organiques…etc. Tous ces polluants peuvent s'infiltrer dans les habitations de par la proximité du lieu de travail et des lieux de vie. De plus, la biomasse agricole peut être utilisée comme source d'énergie, dont la combustion génère beaucoup de polluants notamment les particules en suspensions en particulier les $PM_{2.5}$ [135].

II.3.2. Les sources liées aux produits de construction et d'aménagement

En milieu agricole, le bois est très utilisé dans la construction du bâtiment résidentiel mais aussi dans les bâtiments de travail comme les étables et granges. Depuis 1999, la région Auvergne accorde une aide aux exploitants et aux coopératives d'utilisation de matériels agricoles (CUMA) qui choisissent le bois pour un bâtiment d'élevage, de stockage ou de fourrage [136]. Comme les murs, le peut bois être source de nombreux polluants. De plus, il peut facilement être attaqué par les moisissures, les insectes, les acariens, qui sont des polluants domestiques très répandus en milieux agricoles.

II.4. Les effets sanitaires des polluants en milieu agricole rural

Les maladies respiratoires sont les maux les plus communément rencontrés chez les agriculteurs. Celles-ci sont causées par la pluralité de facteurs auxquels les agriculteurs sont exposés, parmi lesquels l'inhalation de gaz toxiques, de vapeurs de solvants, de fumées, l'exposition à des agents infectieux et les poussières organiques et inorganiques. Les recherches ont communément mis l'accent sur

les Pathologies Professionnelles Pulmonaires en milieu Agricole (PAPPA), composées des pneumopathies d'hypersensibilité, dont la plus fréquente et la plus connue est la maladie du poumon de fermier(PDF), la bronchite chronique agricole, les asthmes allergiques ou non allergiques, la rhinite et les bronchopneumopathies toxiques [27, 128]. Ces dernières regroupent plusieurs syndromes ou maladies, de fréquence et de gravité variables : le syndrome toxique des poussières organiques (ou la fièvre des poussières), la maladie des silos, exceptionnellement des atteintes pulmonaires accidentelles graves liées à certains pesticides [128].

Ces maladies respiratoires, sont complexes et intriqués dont le diagnostic, la prise en charge et le traitement sont difficiles et dont les conséquences sociales et financières peuvent être douloureuses [128]. Le Tableau 4 présente les pathologies respiratoires en milieu agricole et les polluants qui y sont associés, ainsi que la source de ces polluants.

Tableau 4: Pathologies respiratoires en milieu agricole et polluants associés [53-55]

Catégories	Sources	Environnement	Pathologies
Poussières organique	Grain, foin, l'endotoxine, L'ensilage, le coton, les aliments pour animaux, des sous-produits animaux, les micro-organismes, Acariens et insectes, Protéines et squames animales	Confinement animal, granges, silos, Moissons/récoltes	Asthme, rhinite, le syndrome toxique des poussières organiques, bronchite chronique, alvéolites allergiques extrinsèques, Obstruction bronchique
Poussières inorganiques	silicates	Récoltes/labours	fibrose pulmonaire, bronchite chronique
Gaz toxiques	NH4, CO, CO2 Méthane, H2S, SO2	Confinement animal, silos, fertilisants	Asthme, maladie des silos Irritation bronchique Œdème pulmonaire
pesticides	Paraquat, Organophosphorés Carbamates	Applications ou intoxication	Bronchospasme Œdème pulmonaire Fibrose pulmonaire
Fertilisants	ammoniaque anhydre	Applications, conteneur de stockage	Irritation des muqueuses
Desinfectants			irritants respiratoires, Bronchospasme
solvants	Diesel, solution de pesticides	conteneur de stockage	Irritation des muqueuses
Zootechnique (infections)	Microorganismes	Elevage, services vétérinaires	Fièvre Q, psittacose Mycobactérium bovis

III. Présentation des études

III.1. Etude des facteurs environnementaux du milieu Rural et Maladies Allergiques et respiratoires (FERMA)

Afin de mieux comprendre le rôle de la pollution atmosphérique et plus en général des facteurs environnementaux du milieu rural sur les maladies allergiques et respiratoires, une étude épidémiologique a été mise en place dans cet environnement à la fin des années 2000. Cette étude, ayant pour acronyme **FERMA** (Facteurs Environnementaux du milieu Rural et Maladies Allergiques et respiratoires) visait à :

- estimer la prévalence des maladies allergiques et respiratoires en milieu rural ;
- étudier les facteurs de cet environnement en lien avec ces pathologies.

Un des objectifs secondaires était de mieux cerner le rôle des polluants aériens biologiques et chimiques dans le risque de ces maladies. Cette étude s'est déroulée en Auvergne, dont 60% du territoire est occupé par l'agriculture et dont l'orientation majoritaire est la production animale (90.6% de la surface agricole utile dans cette région [96]. Ce choix a permis de pouvoir cibler une population issue du milieu agricole et/ou fréquemment en contact avec les animaux d'élevage.

L'étude FERMA est composée de 2 volets : un volet chez l'enfant, mis en place et réalisé en 2005, et un volet chez l'adulte réalisé entre 2009-2012 dont il est question dans ce document. Le volet adulte de l'étude FERMA est composé de 2 phases : la phase 1 et la phase 2.

La phase 1 de l'étude FERMA adultes est organisée par le service de pneumologie de Clermont Ferrand et l'Equipe Épidémiologie des maladies Allergiques Et Respiratoires (EPAR) de l'UMR-S 1136, Institut Pierre Louis d'épidémiologie et de Santé Publique, INSERM, UPMC, en partenariat avec la mutuelle de santé agricole. Au total 488 agriculteurs (337 exploitants et 151 ouvriers avec des données complètes) adhérant à la MSA ont été inclus dans l'étude lorsqu'ils ont eu leurs visites médicales de travail annuel.

La première phase de FERMA a permis de mesurer à l'aide d'un questionnaire standardisé et d'un bilan médical (pression artérielle, pouls, exploration fonctionnelle respiratoire, test de réversibilité, eCO, eNO, saturométrie…) réalisé par la médecine du travail la prévalence de plusieurs phénotypes de santé respiratoire parmi les 488 agriculteurs, leurs facteurs de risque ainsi que leur prise en charge. Deux volets spécifiques du questionnaire ont porté sur les caractéristiques du domicile et de l'exploitation agricole afin d'évaluer l'exposition à la pollution dans ces 2 environnements. La Figure 4 présente la localisation des participants de la phase 1 de l'étude FERMA pour les adultes.

La deuxième phase de l'étude FERMA adulte a été effectué sur un panel de 109 exploitants agricoles ayant accepté de mesurer la qualité de l'air dans leur domicile et dans leur lieu de travail (Annexe 1). Les mesures de pollution ont été réalisées à l'aide des capteurs spécifiques pendant une semaine. Cette seconde phase a permis de mesurer les particules (PM) de plusieurs tailles (nombre et masse) et 58 COVs (Composants Organiques Volatiles) *in situ* dans 66 fermes et dans les locaux professionnels associés et évaluer l'exposition à la pollution atmosphérique de 109 exploitants agricoles qui y résidaient (détails dans l'article 4). La Figure 5 présente la localisation des participants de la phase 2 de l'étude FERMA pour les adultes.

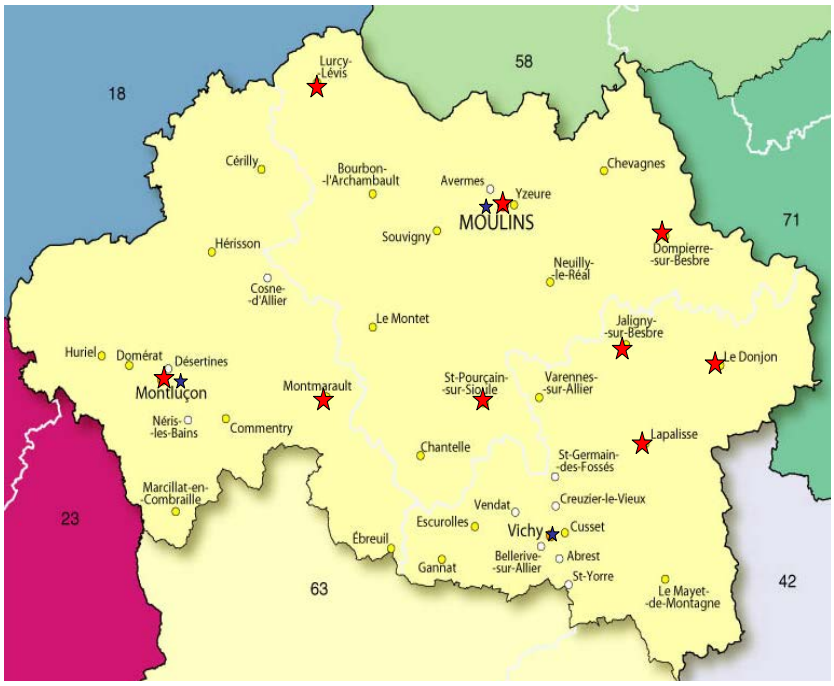


Figure 4: Localisation des participants de l'étude phase I de l'étude FERMA adultes

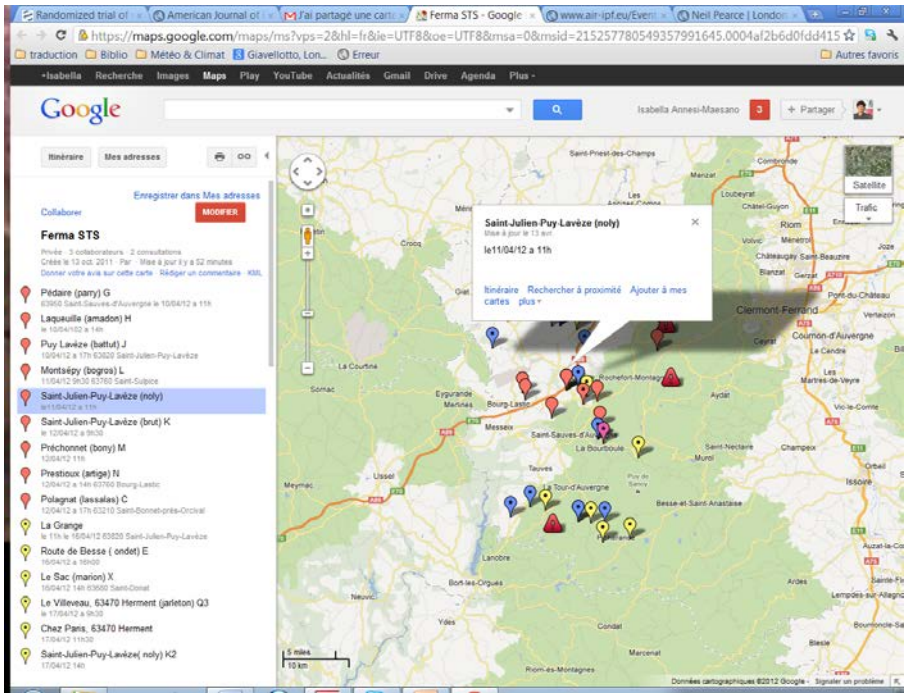


Figure 5**:** Localisation des participants de la phase II de l'étude FERMA adultes

III.2. UC Davis Farmer Health Study (FHS) : Etude de la santé des agriculteurs de l'Université de Californie à Davis

La Farmer Health Study (étude de la santé des agriculteurs) de l''Université de Californie, Davis est une étude épidémiologique sur l'impact des facteurs environnementaux sur la santé des agriculteurs californiens. La population d'étude a été choisie en 1992 sur une liste de 58 000 agriculteurs californiens enregistrés sur le service statistiques agricoles de la Californie (CASS). Parmi les 4500 agriculteurs sélectionnés aléatoirement pour participer à l'étude, 3773 ont pu être contacté par téléphone pour participer l'étude, et 2422 étaient admissibles à l'étude. Au final 1 947 agriculteurs (80,4%) ont répondu au questionnaire de l'étude [137].

Le premier volet des enquêtes réalisées dans le cadre de cette étude a eu lieu en 1993 et l'enquête finale a été réalisée en 2004, lorsque près de 900 des agriculteurs initialement inclus au début de l'étude en 1993, ont été contactés. L'objectif de l'étude était d'identifier la prévalence et les facteurs de risque de maladies aiguës et chroniques dans cette population qui est représentative des agriculteurs de Californie. Le but final de l'étude étant de prendre en compte les informations recueillies lors de l'étude afin de trouver des solutions pour

empêcher ou diminuer l'impact des maladies engendrées par ces facteurs environnementaux. La première principale cohorte de suivi a été menée en 1998 avec tous les agriculteurs de l'étude originale qui ont pu être contactés (67%). Une troisième enquête, achevée en 2004, est composée de tous les agriculteurs restants, qui ont pu être contactés (45%) [138]. Nous avons travaillé avec l'échantillon d'origine inclus en 1993 (détails dans l'article 5).

IV. Résultats issus de nos études épidémiologiques

IV.1. Presentation de article 4: Exposure to particulate matters and volatile organic compounds in dwellings and stables and respiratory health in French farmers

Les composés organiques volatiles et les PM font partie des polluants rencontrés dans les milieux agricoles. Les composés organiques volatils (COV) constituent une famille de produits très large comme le benzène, l'acétone, le perchloroéthylène… etc., qui se trouvent à l'état de gaz ou s'évaporent facilement dans les conditions normales de température et de pression. Leur volatilité leur confère l'aptitude de se propager plus ou moins loin de leur lieu d'émission, entraînant ainsi des impacts directs et indirects sur les animaux et la nature.

Tout comme les PM dont les effets sanitaires ont été bien discutés dans le chapitre II de ce document, les COV ont un impact direct sur la santé. Plusieurs normes de la qualité de l'air ont été établies afin de protéger les humains face aux différents polluants atmosphériques pouvant nuire à la santé. L'exposition à des vapeurs de benzène fut associée directement à la leucémie. Les effets cancérigènes du 1,3-Butadiène ont aussi été prouvés.

Les émissions de COV sont essentiellement dues à la combustion et à l'utilisation de solvants, dégraissants, conservateurs ... et proviennent donc de sources très nombreuses. Selon les données du CITEPA (centre interprofessionnel technique d'études de la pollution atmosphérique), En 2008, le secteur de l'agriculture représentait 14,5 % des émissions totales des COVs.

La phase 2 de l'étude FERMA nous as permis de mesurer les COVs et les PM dans les lieux du travail (étables et granges) et aux domiciles des agriculteurs. Les agriculteurs ainsi que tous les membres de la famille âgés de plus de 15 ans ont

répondu à un questionnaire sur la santé respiratoire et les habitudes de vie. L'article 4 présente les résultats des associations entre l'exposition aux COVs et PM et les symptômes respiratoires des agriculteurs de la région d'Auvergne.



Exposure to particulate matter and volatile organic compounds in dwellings and workplaces (stables and granaries) and respiratory health in French farmers

Journal:	*Indoor Air*
Manuscript ID:	Draft
Manuscript Type:	Original Article
Date Submitted by the Author:	n/a
Complete List of Authors:	Hassani, Youssouf; UMR-S 1136, Institute Pierre Louis of Epidemiology and Public Health, INSERM, UPMC, Paris France, Epidemiology of Respiratory and Allergic Disease Caillaud, Denis; University Hospital, University of Auvergne, Pulmonary Department BAIZ, Nour; UMR-S 1136, Institute Pierre Louis of Epidemiology and Public Health, INSERM, UPMC, Epidemiology of Respiratory and Allergic Disease Banerjee, Soutrick; UMR-S 1136, Institute Pierre Louis of Epidemiology and Public Health, INSERM, UPMC,, Epidemiology of Respiratory and Allergic Disease Ramousse, Ollivier; University Hospital, University of Auvergne, Pulmonary Department Bertholon, Jean-francois; UMR-S 1136, Institute Pierre Louis of Epidemiology and Public Health, INSERM, UPMC, Epidemiology of Respiratory and Allergic Disease Annesi-Maesano, Isabella; UMR-S 1136, Institute Pierre Louis of Epidemiology and Public Health, INSERM, UPMC, Epidemiology of Respiratory and Allergic Disease
Keywords:	asthma, farmers, VOCs, PM, glycol ethers, small airways disease

SCHOLARONE™
Manuscripts

Indoor Air - PROOF

Exposure to particulate matter and volatile organic compounds in dwellings and workplaces (stables and granaries) and respiratory health in French farmers

Youssouf H[1,2], Caillaud D[3], Baïz N[1,2], Banerjee S[1,2], Ramousse O[4], Bertholon JF[1,2], Annesi-Maesano I[1,2]

[1]Epidemiology of Respiratory and Allergic Disease Department, UMR-S 1136, Institute Pierre Louis of Epidemiology and Public Health, INSERM, Paris, France

[2]Epidemiology of Respiratory and Allergic Disease Department, UMR-S 1136, Institute Pierre Louis of Epidemiology and Public Health, UPMC Sorbonne Universités, Paris, France

[4] Mutuelle Salariés Agricoles, Clermont-Ferrand, France

Corresponding Author:
Isabella Annesi-Maesano
Epidemiology of Allergic and Respiratory Diseases (EPAR),
UMR-S 1136, Institute Pierre Louis of Epidemiology and Public Health, Medical School St Antoine, 27 rue Chaligny, 75571 Paris CEDEX 12
Phone: + 33 1 44738449
Fax: + 33 1 44738454
Email: isabella.annesi-maesano@inserm.fr

Abstract

We investigated respiratory health effect of elevated (> 3rd quartile value of the concentration distribution) exposure to PM (from ultrafine to Total Suspended Particles) and 19 VOCs (from 5 VOCs families) objectively assessed in dwellings and workplaces among 109 French farmers. Small Airways Disease was defined using spirometry and concerned 48 farmers. Elevated exposure to each VOCs and PM, a global score representing the number of VOCs with an elevated concentration and specific VOCs families scores were considered respectively.

In mean, VOCs concentrations were higher inside the dwelling than in workplaces. The reverse was observed for PM concentrations. After adjustment on confounders, asthma (9.3%) was positively associated with indoor elevated exposure to benzene (adjusted odds-ratio (ORa)=6.64, 95%CI: 1.56–28.27) and trichloroethylene (ORa=4.80 95% CI: 1.00-23.30) and the specific score for halogenated hydrocarbons (ORa=2.9; 95% CI: 1.3–6.8) and Small airway disease (SAD) (29.8%) with indoor elevated exposure to 2-butoxyetylacetate (ORa = 11.49, 95% CI: 1.55-85.37), the specific score for glycol ethers (ORa=2.0; 95% CI: 1.0–4.1) and elevated exposure to $PM_{2.5}$ (ORa=5.26, 95% CI: 1.09-25.28) in the granary/stable. COPD (4.26%) was not related to air quality. More epidemiological investigation with detailed exposure assessments and clinical measures of respiratory effects are needed in rural settings to validate these findings.

Key words*: asthma, farmers,* glycol ethers, *VOCs, PM, small airways disease, COPD*

Practical implications

Volatile organic compounds (VOCs) and particulate matters (PM) are associated with respiratory effects in urban settings. However few studies on the impact of exposure of VOCs and PM performed in rural area. This research represents a contribution for improving the knowledge on the impact of indoor air exposure in rural area as explorations were conducted in the dwellings and workplaces in the farms. This study provides evidence of an association between some VOCs and PM and respiratory symptoms, namely asthma and SAD in farms. Using multipollution approaches allowed establishing that asthma was positively associated with the halogenated hydrocarbons and SAD with glycol ethers. This study lays the foundation for further cohort or toxicological studies in order to confirm these associations and test for causality.

Introduction

In rural areas of industrialized countries allergic diseases, including asthma, are scarce but non-allergic asthma is common in adulthood. Chronic obstructive pulmonary disease (COPD) is more common among farmers than the general population, despite farmers having a lower prevalence of active smoking [139, 140]. Small airways diseases (SAD), pneumoconiosis (macules and nodules) and pathologic changes consistent with chronic bronchitis, emphysema and interstitial fibrosis predominate in farmworkers compared with non-farmworkers [141].

Respiratory disease in farm workers could be due to lifestyle-related and occupational characteristics of rural environments compared to urban ones. The rural work environment involves exposure to the physical hazards of weather, terrain, fires and machinery [142] as well as to various dust particles, including inorganic particles, such as silica, and various organic particles, such as molds, bacteria, endotoxins, mycotoxins, pollens, grains, and animal feed, found in different concentrations depending on the type of agriculture occupation [29, 30, 143]. In addition, farm workers may also be exposed to various gases during operations in confined animal feeding and to numerous chemicals used or generated on farms, such as pesticides, exhaust fumes, fertilizers, and nitrogen oxides [29, 30]. Animal agriculture is a source of very complex mixtures of volatile organic compounds (VOCs) [144]. New data have shown that due to the complexity of VOCs, multi-pollution is an important issue to take into account when assessing the health effects of these air pollutants [145, 146]. The health effects of exposure to indoor and outdoor air pollution in farms needs better assessment [147].

The purpose of this study was to determine the effects on respiratory health of exposure to particulate matter (PM) and 19 VOCs (from 5 VOCs families) objectively measured in dwellings and workplaces (stable and granary) and their combined effects among farmers drawn from the Environmental Factors of Allergic and Respiratory Diseases study (FERMA) conducted in the Auvergne region of France.

Materials and Methods

Study population

Four hundred-ninety four (494) farmers from several cities in the Auvergne region were recruited between 2009 and 2010 during the compulsory occupational medicine visit conducted by the "Mutuelle des Salariés Agricoles" (MSA) in subscribers (FERMA PHASE I). Among them, 109 living in 50 farms agreed to a follow-up occurring within 2 years and to an air pollution assessment of their home and workplace (FERMA PHASE II).

The data used in the present analysis are drawn from the FERMA PHASE II study. The survey was conducted from February to April 2012. A farmer is defined as the owner of the farmed land or any family member aged over 15 years living in the farm. According to French rural code, a farm is defined as a workplace where agricultural activity is practiced, with a minimal area of installation defined according to the type of agricultural activity and managed by a farm operator.

Air pollution measurements

Air quality was assessed in both the dwellings (living rooms and bedrooms) and workplaces (stables and granary). Fifty-nine VOCs and different PM mass size ranges were measured in the living room, stable and granary of the farms during the three month time period. However in each farm, measurements were done in one continuous week.

Two Radiello samplers (145 and 165) collected VOCs. Sensors were placed at a height far from obvious sources of pollution, such as a fireplace, stove, or newly purchased or cleaned furniture. The farmer was instructed to uninstall the samplers and pack them in the envelope provided to send them for analysis. Radiello VOCs measurement was performed by radial diffusive sampling on to 2,4-dinitrophenylhydrazine (2,4-DNPH) coated Florisil for aldehydes. Aldehyde-hydrazones formed in the cartridge were eluted by acetonitrile solvent and analyzed by liquid chromatography associated with a UV detector. Other VOCs were collected onto Carbograph 4 adsorbents (Radiello, Fondazione Salvatore Maugeri (FSM)). Adsorbed VOCs were extracted through thermodesorption and analyzed by gas phase chromatography equipped with flame ionization detector and/or mass spectrometry [146, 148].

PM ranging from 0.1 to 10 µm and Total Suspended Particulates (TSP) were assessed in the living room,

bedroom and granary/stable of the farms. A TSI P-track sensor (http://www.tsi.com/p-trak-ultrafine-particle-counter-8525/) was used in survey mode to display real-time particle number concentration (the number of particles present in a given volume) (pt/cm^3) of ultrafine particle matter (UFPM) having a diameter less than 0.1 µm (100 nm). An AEROCET 530 device (http://www.metone.com/particulate-aero531.php) was used in mass mode in two minutes of sample time to assess the mass concentration of PM_1, $PM_{2.5}$, PM_7, PM_{10} and the TSP (µg/m^3) respectively.

Nineteen VOCs among the fifty-nine measured and five PM mass size ranges were selected to study the potential impact of pollutants on respiratory diseases. The VOCs were selected on the basis of their potential impact on air quality or comfort and their known toxicity, according to a hierarchical classification designed by a panel of experts (www.air-interieur.org). These pollutants included three aldehydes (Acetaldehyde, acrolein and formaldehyde), twelve hydrocarbons (Benzene, 1,4-Dichlorobenzene, Etylbenzene, Styrene, Toluene, 1, 2,4-Trimethylbenzene, m/p-Xylene, o-Xylene , Tetrachloroethylene, Trichloroethylene, n-Decane and n-Undecane), and four glycols ethers (2-Butoxyethanol, 2-Butoxyetylacetate, 1-Metoxy-2-Propanol and 1-Metoxy-2-propylacetate). The different size ranges of PM were selected because of their potential health impact, especially in urban areas [35, 36].

Respiratory health outcomes

A medical doctor assessed the weight, height, blood pressure, pulse rate and oxygen saturation of the farmers. In addition, pulmonary function tests were performed, including spirometry using a MIR-Spirobank G spirometer system attached to a laptop computer. Measurements of the Fractional exhaled Nitric Oxide (FeNO) were performed using a standardized technique (guideline ERS / ATS) with the device Hyp'air FeNO (Medisoft). Measurements of the exhaled Carbon monoxide (eCO) were performed using the device PiCO+ (Respur). During the visit, the individuals were interviewed with a standardized questionnaire.

Asthma was defined on the base of the following question: "Have you been diagnosed with asthma by a physician?" COPD and SAD were

defined using spirometry. COPD, was defined according to the GOLD criteria, as FEV / FVC <70% after bronchodilation and SAD by a FEF25-75 <80% of the predicted level and FEV / FVC >70%, after bronchodilation during the reversibility test (with Salbutamol), with or without taking into account a reduced lung volume as assessed by one of the authors after analysis of the spirometric curve.

The standardized questionnaire allowed assessing factors considered potential confounders, such as age, sex, tobacco smoking habit (classed as: never, ex or current smoking), educational level, presence of pets and molds at home, growing up on a farm, and wood heating.

Statistical analyses

Descriptive analyses were performed using proportions in the case of qualitative variables and means with standard deviation (SD), minimum, maximum and interquartile ranges in the case of quantitative variables, such as the concentrations of air pollutants as well as the number in the case of UFPM. Correlations between quantitative variables were checked with Spearman's rank correlation coefficient.

Air pollutant distributions were provided in living room, the bedroom and the granary/stable for PM and living room, stable and granary for VOCs. For the purpose of the present analysis, the distributions of PM concentrations and number and VOCs concentrations were estimated in the whole farm (living room, stable, granary), and in stable/granary and dwelling (living room and bedroom) separately and the corresponding descriptive statistics (mean, median tertiles…) evaluated. The concentration in the whole farm was estimated by the mean of VOC or PM in the living room, stable and Granary. As all data from the living room were available, if missing values are observed in the Stable or Granary, the mean was calculated using available data from the living room and the workplace where data were available. Exposure in the stable and Granary was evaluated using the average mean of each pollutant in the two workplaces. Missing values were not taken into account for the analyses.

For investigating respiratory health effects of air pollutants, to indicate elevated exposure a binary exposure variable was introduced allowing avoiding the lack of linearity in the relation between the air pollutant

and the health outcome. In each setting (the whole farm, the stable/granary and inside the dwelling respectively), exposure was considered as elevated if the concentration of pollutant was higher than the 3rd quartile value. In contrast, if the concentration of pollutant was lower than the 3rd quartile value, the exposure was considered as low.

Relationships between each pollutants (elevated exposure vs. low exposure) and health outcomes were analyzed using the generalized estimating equation approach (GEE) with exchangeable covariance matrix to adjust for correlations within people belonging to the same dwelling through the GENMOD SAS procedure, while taking into account potential confounding factors. The GEE model characterizes the marginal expectation (average response for observations sharing the same covariates) as a function of covariates. This approach was needed because individuals within the same farm tend to be more alike in terms of attitudes and behaviors, their environment and, for some of them, genetics than individuals from different farms. For consistency, all models were adjusted for the same confounders. This decision was also justified by the fact that health outcomes (asthma and SAD) share many risk factors. Bivariate marginal analysis between potential confounders and both outcomes were performed. All variables associated with asthma or SAD with a $p < 0.30$ were considered as potential confounders. Selected covariates that were collinear to others were omitted. Age, sex and smoking status were included in all models regardless of whether they changed the effect estimates significantly because they have been included as potential confounders in comparable studies [145, 146, 149].

To take into account multi-exposure to pollutants and correlations among VOCs, a global VOCs score variable and specific VOCs scores variables according to the VOCs familiy were created as previously described [146] for each setting: each individual VOC concentration was categorized as 0 if less than the 3rd quartile value and 1 if greater. The global VOC score was then defined as the sum of the categorized VOCs concentrations. As a result, the global VOCs score represents the number of VOCs in the farm for which elevated (>3rd quartile value) concentrations were found. In the models, the global VOCs score,

ranging potentially from 0–19, was fitted as a continuous variable. Successively 5 specific VOCs scores, one for each VOCs family, were built using a similar approach, by summing categorized VOCs concentrations by family: 1) aromatic hydrocarbons (benzene, toluene, m/p-xylene, O-xylene, 1,2,4-trimethylbenzene, ethylbenzene and styrene), 2) aliphatic hydrocarbons (n-decane, n-undecane), 3) halogenated hydrocarbons (trichloroethylene, tetrachloroethylene, 1,4-dichlorobenzene), 4) glycol ethers (1-methoxy-2-propanol, 2-butoxyethanol, 1-methoxy-2-propylacetate and 2-butoxyethylacetate) and 5) aldehydes (formaldehyde, acrolein and acetaldehyde). The relationships between respiratory outcomes and global and specific VOCs scores were also investigated using the generalized estimating equation approach (GEE) as previously described.

Epidemiological analysis

We present the distributions of air pollutants and the relationships between respiratory outcomes and elevated exposure to air pollutants in the whole farm (living room, granary and stables), stable/granary and inside the dwellings (living room and bedroom) respectively.

Results

Description of population and respiratory symptoms

Measurements of air pollution were conducted on 50 farms located in three cities of the Auvergne region: Riom-ès-montagnes (19 farms), Saint-Sauve (19 farms) and Saugues (12 farms). One-hundred and nine eligible farmers completed the health questionnaire. Fifty nine percent (59.3%) of respondents were male and 40.7% female. Farmers' origin was distributed as following: 33% from Riom-ès-montagnes, 40.4% from Saint-Sauve and 26.6% from Saugues. As presented in Table 1, 38.0% of farmers were between 15 and 45 years old, 53.7% were between 45 and 65 years and only 8.3% were older than 65 years. Seven percent (7.3%) of farmers were current smokers, and 29.4% were former smokers. Thirty-two percent (32.1%) had completed high school, 62.0% had grown up in farm and 89.8% had worked in agricultural area before. Concerning the farm characteristics, 77.1% of farmers declared having pets, 5.5% declared having mold and fungi in

the house while water infiltration and humidity in the dwelling was declared by 14.1% and 29.4% of farmers, respectively. Demographic and farming characteristics of farmers participating in this study (FERMA PHASE II) and those who do not among those who participated in the FERMA PHASE I were similar (data not shown).

Table 2 presents the distribution of respiratory symptoms as declared by the farmers. In the past 12 months, sixteen percent (16.5 %) of the farmers stated that they had morning cough, 13% for phlegm, 16.8% short breath, and 18.4% shortness of breath after intense effort. Nine percent (9.3%) of farmers declared having asthma diagnosed by physician, and 44% declared having respiratory symptoms, such as sneezing, coughing, wheezing, shortness of breath, or dyspnea when handling reaped plants. Forty-eight farmers (44%) among those who completed the health questionnaire had a pulmonary function test. Among this sub-population of farmers, there were 29.8% of farmers suffering from SAD and 4.3% from COPD.

Table 1: Socio-demographical characteristics among farmer participants

	n	(%)
Population characteristics (n=109)		
Gender (male)	64	(59.3)
Age (years)		
[15-45]	41	(38.0)
]45-65]	58	(53.7)
>=65	9	(8.3)
Smoking status		
Curent smokers	8	(7.3)
Former smokers	32	(29.4)
Non-smokers	69	(63.3)
Education level		
<=*High school*	74	(67.9)
>*High school*	35	(32.1)
Lived on a farm as a child	44	(62.0)
Worked in agricultural area before	97	(89.8)
Farm characteristics		
Presence of pets	84	(77.1)
Presence of mold, fungi	6	(5.5)
Water infiltration in the dwelling last 12 months	13	(14.1)
Humidity in the dwelling in the last 12 months	27	(29.4)
Persistent condensation	21	(19.6)
Farm near a heavy traffic area	23	(25.6)
Month of visit		
February	32	(29.4)
March	35	(32.1)
April	42	(38.5)

Table 2: Frequency of respiratory symptoms among farmer participants

	Total		Male		Female	
Symptoms	**N**	**(%)**	**N**	**(%)**	**N**	**(%)**
Morning cough in the past 12 months	18	(16.5)	15	13.9	3	2.8
Phlegm in the past 12 months	14	(13.0)	11	10.3	3	2.8
Short of breath in the past 12 months	18	(16.8)	11	10.4	7	6.6
Difficulty of walking for another reason than heart or lung problems	14	(13.0)	10	9.4	4	3.7
Wheezing in the past 12 monthsin the past 12 months	12	(11)	9	8.3	3	2.8
Short of breath at rest last 12 months	6	(5.6)	4	3.7	2	1.9
Short of breath after intense effort last 12 months	20	(18.4)	13	12.0	7	6.5
Woken by an attack of shortness of breath in the past 12 months	3	(2.8)	3	2.8	0	0.0
Asthma	10	(9.3)	6	5.6	4	3.7
Nasal allergy	9	(8.3)	7	6.5	2	1.9
Respiratory distress when handling plants reaped	48	(44.0)	29	28.9	19	17.6
Severe respiratory problems interfered with usual daily activities	7	(6.4)	5	4.6	2	1.9
Chronic illness *	19	(39.6)	14	29.2	5	10.4
SAD*	14	(29.8)	9	19.1	5	10.6

*n=48; SAD: Small Airways Disease(FEF25-75 <80% of the predicted level and FEV / FVC <12%, after bronchodilation during the reversibility test)

Description of air quality in the farms (indoor, stable and granary)

VOCs distribution

Table 3 shows the proportion of farms with a VOC concentration below the limit of detection (LD) and between the LD and the limit of quantification (LQ) in the living room, stable and granary respectively. Five VOCs were found under the LD in more than 50% of the living rooms, and four VOCs had 100% of the value of the upper LQ. In more than 50% of the stables, 10 VOCs were present below the LD and 3 VOCs had 100% of the value of the upper LQ. In more than 50% of the granaries, 7 VOCs were detected under the LD, and 4 VOCs had 100% of the value of the upper LQ.

All farms had VOCs measured in the living room. However, only 33 farms had VOCs measurements done in the stable, and 19 farms had measurements done in the granary. The distribution of VOCs in the living room, stable and granaries is presented in the Table 4. Most VOCs had a higher mean in the living room, followed by the granary. The stables generally had the lowest VOCs means. The global VOCs score ranged between 0 and 13 (median: 5 and 3rd quartile: 7). Correlation coefficients between VOCs ranged between 0.01 (between acetaldehyde and 1,4-Dichlorobenzene) and 0.99 (between o-Xylene and xx and m/p-Xylene) (results not shown).

Table 3: Proportion of farms (POF) with Volatile Organic Compounds (VOCs) concentrations below the limit of detection (LD) or between the LD and the limit of quantification (LQ) in the farms (living room, stable and granary respectively)

	LD	LQ	POF <LD (%)	POF [LD, LQ] (%)	POF <LD (%)	POF [LD, LQ] (%)	POF <LD (%)	POF [LD, LQ] (%)
VOCs(µg/m^3)			Living Room		Stable		Granary	
Acetaldehyde	0.3	0.4	0.0	0.0	0.0	3.0	0.0	0.0
Acrolein	0.1	0.3	33.3	0.0	93.9	0.0	95.5	0.0
Formaldehyde	0.6	1.1	0.0	3.9	24.2	42.4	18.2	31.8
Benzene	0.4	1.1	0.0	42.0	0.0	39.4	0.0	36.8
1,4-Dichlorobenzene	0.07	0.2	27.3	22.0	90.9	6.1	79.0	15.8
Etylbenzene	0.3	0.9	9.1	23.6	51.5	33.3	15.8	47.4
n-Decane	0.07	0.2	0.0	0.0	0.0	0.0	0.0	0.0
n-Undecane	0.5	1.4	0.0	0.0	0.0	0.0	0.0	0.0
Styrene	0.1	0.3	0.0	7.3	0.0	51.5	0.0	31.6
Tetrachloroethylene	0.4	1.2	98.2	1.8	100	0.0	100	0.0
Toluene	0.4	1.3	0.0	7.3	0.0	48.5	0.0	21.5
Trichloroethylene	0.4	1.0	94.6	1.8	97.0	3.0	94.7	0.0
1, 2,4-Trimethylbenzene	0.03	0.1	0.0	0.0	0.0	0.0	0.0	0.0
m/p-Xylene	0.5	1.5	10.9	14.6	54.6	24.2	15.8	31.6
o-Xylene	0.2	0.6	6.0	20.0	33.3	48.5	15.8	31.6
2-Butoxyethanol	0.4	1.5	43.6	38.2	87.9	6.1	84.2	15.8
2-Butoxyetylacetate	0.3	1.0	80.0	18.2	84.9	15.1	100	0.0
1-Metoxy-2-Propanol	0.5	1.8	52.7	34.6	97.0	3.0	84.2	5.3
1-Metoxy-2-propylacetate	0.7	2.2	90.9	9.1	100	0.0	89.5	10.5

Table 4: Distribution of Volatile Organic Compounds (VOC) in the farms*

VOCs	Place	**Mean**(µg/m^3)	**Min**(µg/m^3)	**Median**(µg/m^3)	**3rd quartile** (µg/m^3)	**Max**(µg/m^3)
Acetaldehyde	L	18.60	1.53	16.64	23.76	66.70
	S	10.83	0.33	5.86	14.47	62.85
	G	14.95	1.26	8.97	18.97	74.28
Acrolein	L	0.66	0.00	0.51	0.77	3.80
	S	0.07	0.00	0.00	0.00	1.63
	G	0.08	0.00	0.00	0.00	1.26
Formaldehyde	L	15.01	0.39	13.04	19.32	59.52
	S	2.53	0.25	0.83	1.24	22.16
	G	3.04	0.26	1.18	2.27	24.15
Benzene	L	1.54	0.52	1.17	1.92	4.86
	S	1.29	0.62	1.12	1.52	2.66
	G	1.72	0.77	1.17	1.62	10.56
1,4-Dichlorobenzene	L	2.80	0.00	0.19	3.16	43.94
	S	0.09	0.00	0.03	0.06	1.26
	G	0.13	0.00	0.06	0.13	1.64
Etylbenzene	L	3.76	0.14	1.55	5.12	25.11
	S	0.77	0.14	0.25	0.43	6.47
	G	1.34	0.14	0.74	1.82	5.66
n-Decane	L	35.39	2.26	14.66	38.26	252.89
	S	10.59	2.20	5.03	6.84	96.93
	G	10.34	2.95	8.99	12.41	30.73
n-Undecane	L	42.35	3.51	24.34	47.03	248.53
	S	14.58	1.66	8.02	10.80	132.33
	G	12.47	1.89	9.88	16.59	33.60
Styrene	L	0.90	0.14	0.70	1.11	3.93
	S	0.39	0.14	0.29	0.39	1.32
	G	0.72	0.14	0.55	0.91	2.29
Tetrachloroethylene	L	0.08	0.00	0.05	0.05	0.55
	S	0.07	0.05	0.05	0.05	0.16
	G	0.09	0.05	0.05	0.11	0.22

L: Living room, S: stable, G: Granary.*: For each VOC, 79 measurements were in the Living room for 50 farms, 48 measurements in stables of 33 farms and 23 measurements in the granary of 19 farms

Table 4 continued: Distribution of Volatile Organic Compounds (VOC) in the farms

Air Pollutant	Place	Mean	Min	Median	3rd quartile	Max
Toluene	L	12.09	0.45	6.10	13.41	105.82
	S	2.13	0.45	1.30	2.16	11.19
	G	5.89	0.54	3.23	5.26	28.64
Trichloroethylene	L	0.10	0.00	0.00	0.00	2.05
	S	0.03	0.00	0.00	0.00	0.72
	G	0.28	0.00	0.00	0.00	3.23
1, 2,4-Trimethylbenzene	L	25.16	0.89	8.43	20.04	172.69
	S	4.78	0.57	1.24	2.25	58.73
	G	6.88	0.76	4.19	9.07	24.10
m/p-Xylene	L	11.24	0.26	3.76	13.94	81.82
	S	2.24	0.16	0.47	0.89	29.19
	G	3.69	0.16	1.83	4.96	17.34
o-Xylene	L	4.82	0.17	1.69	5.31	30.77
	S	1.12	0.11	0.28	0.40	15.47
	G	1.53	0.11	0.79	2.09	6.44
2-Butoxyethanol	L	2.00	0.00	0.43	1.07	87.20
	S	0.27	0.00	0.00	0.07	3.94
	G	0.18	0.00	0.00	0.50	0.72
2-Butoxyetylacetate	L	0.14	0.00	0.00	0.27	1.08
	S	0.09	0.00	0.00	0.18	0.72
	G	0.00	0.00	0.00	0.00	0.00
1-Metoxy-2-Propanol	L	1.33	0.00	0.42	0.84	13.68
	S	0.05	0.00	0.00	0.00	0.68
	G	0.54	0.00	0.10	1.36	2.04
1-Metoxy-2-propylacetate	L	0.19	0.00	0.00	0.00	2.02
	S	0.02	0.00	0.00	0.00	0.59
	G	0.15	0.00	0.00	0.00	0.98
Global VOCs score			1	5	7	13

L: Living room, S: stable, G : Granary.*: For each VOC, 79 measurements were in the Living room for 50 farms 48 measurements in stables of 33 farms and 23 measurements in the granary of 19 farms

Particulate matter distribution

Table 5 shows the distribution of PM in the farms. The living room presented the highest mean UFPM number concentration (19298.0/cm^3), with the highest median and the highest 3rd quartile (10478.0/cm^3 and 19390/cm^3, respectively). However, the maximum value of particle number concentration was observed in the bedroom (229300/cm^3). In terms of mass concentration, the granary had the highest mean, median and quartile of $PM_{2.5}$ (13.3 µg/m^3, 2.5 µg/m^3, 8 µg/m^3, respectively), PM_{10} (259.6 µg/m^3, 69.5 µg/m^3, 167 µg/m^3, respectively) and TSP (361.8 µg/m^3, 156.5 µg/m^3, 334 µg/m^3, respectively). The living room and the bedroom had similar PM values.

Table 5: Distribution of particulate matter (PM) in the farms

Air Pollutants	Place	Mean	Min	Median	3rd quartile	Max
UFPM (pt/cm^3)	L	19298.0	631	10478.0	19390	148466
	BR	17534.1	262	4928.0	18300	229300
	G/S	7066.8	725	3529.0	7385	41920
PM_1 (µg/m^3)	L	0.9	0	0.0	0	17
	BR	1.0	0	0.0	0	8
	G	0.8	0	0.0	1	12
$PM_{2.5}$ (µg/m^3)	L	4.0	1	2.0	4	40
	BR	4.5	0	1.0	3	46
	G/S	13.3	0	2.5	8	327
PM_{10} (µg/m^3)	L	30.7	10	25.0	32	159
	BR	26.4	0	16.0	28	159
	G	259.6	1	69.5	167	5733
TSP (µg/m^3)	L	48.4	13	37.0	55	208
	BR	46.3	0	26.0	42	452
	G/S	361.8	1	156.5	334	5561

UFPM: Ultrafine particulate matter; PM: Particulate Matter; TSP: Total Suspended Particles;
L: Living room, BR: Bed Room, G/S: Granary/Stable

Relationships of air pollution to respiratory health

Air pollution in the whole farm (living room, stable and granary)

When global exposure to air pollution in the whole farm (living room, stable and granary) was considered, there was a trend, although not significant, for an increased risk of asthma in case of elevated exposure to benzene dichlorobenzene and the halogenated hydrocarbons score. After adjustment for confounders, only the halogenated hydrocarbons score was significantly related to an increased risk of asthma (adjusted odds-ratio (ORa) = 2.02, 95% CI: 1.00-4.10) (Table 6). A trend was observed between SAD and the glycol ether score in the univariate analysis. After adjusting for confounders, the risk of SAD was significantly increased in the case of elevated exposure to 2-butoxyetylacetate (ORa = 11.49, 95% CI: 1.55-85.37) (Table 6). The risk of COPD was found significantly larger with elevated exposure to aldehydes (OR = 3.95, 95% CI: 1.09-14.26). After adjusting for confounders, the risk was still raised, but it was no more significant. No significant relationship was found between respiratory outcomes and the total VOCs score.

Table 6: Unadjusted and adjusted odds ratios (OR) between elevated exposure to global average VOCs in the farm* and asthma and Small Airways Disease (SAD) in the farmers

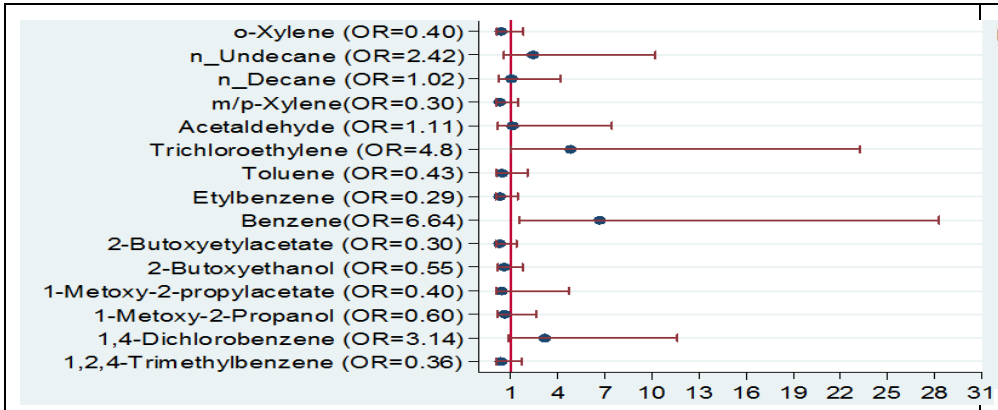
VOCs	Asthma				Small Airways Disease (SAD)			
	Crude OR (95% CI)		Adjusted OR (95% CI)		Crude OR (95% CI)**		Adjusted OR (95% CI)**	
Acetaldehyde	0.34	0.04-2.71	-	-	1.59	0.37-6.83	2.68	0.33-22.00
Acrolein	0.37	0.05-3.04	0.14	0.03-0.75	1.48	0.23-9.47	1.99	0.19-21.11
Formaldehyde	0.31	0.04-2.51	0.31	0.04-2.51	2.48	0.49-12.65	1.88	0.28-12.50
Benzene	2.45	0.67-8.96	4.11	0.91-18.5	2.08	0.41-10.60	1.37	0.19-9.72
1,4-Dichlorobenzene	3.00	0.91-9.93	5.62	0.83-37.91	0.68	0.12-3.86	0.98	0.15-6.45
Etylbenzene	0.75	0.15-3.72	0.40	0.08-1.90	0.85	0.15-4.95	1.01	0.14-7.19
n-Decane	1.06	0.27-4.17	1.03	0.25-4.17	0.63	0.11-3.58	1.87	0.18-19.40
n-Undecane	1.28	0.35-4.65	2.43	0.56-10.19	0.28	0.03-2.58	0.41	0.02-9.10
Styrene	0.33	0.041-2.69	-	-	3.56	0.81-15.66	8.86	0.65-119.99
Tetrachloroethylene	1.56	0.42-5.89	1.40	0.38-5.08	1.49	0.30-7.33	7.78	0.59-102.53
Toluene	0.57	0.12-2.86	0.37	0.07-1.97	1.40	0.29-6.85	2.43	0.42-14.14
Trichloroethylene	1.60	0.35-7.46	3.20	0.59-17.21	-	-	-	-
1, 2,4-Trimethylbenzene	0.34	0.04-2.78	0.41	0.09-1.91	0.82	0.14-4.81	1.08	0.09-12.36
m/p-Xylene	0.75	0.15-3.72	0.36	0.08-1.72	0.85	0.15-4.95	1.01	0.14-7.19
o-Xylene	0.75	0.15-3.72	-	-	0.85	0.15-4.95	1.01	0.14-7.19
2-Butoxyethanol	1.27	0.33-4.81	0.75	0.19-2.92	3.62	0.81-16.12	6.48	0.59-71.33
2-Butoxyetylacetate	0.53	0.11-2.48	0.26	0.06-1.26	**10.2**	**2.14-48.84**	**11.49**	**1.55-85.37**
1-Metoxy-2-Propanol	0.28	0.03-2.45	0.44	0.05-4.28	0.76	0.17-3.45	1.44	0.22-9.41
1-Metoxy-2-propylacetate	0.26	0.03-2.20	0.28	0.03-2.92	1.50	0.35-6.46	2.17	0.41-11.47
Halogenated hydrocarbons score	1.63	0.83-3.2	**2.02**	**1.00-4.10**	0.68	0.29-1.63	0.92	0.38-2.25
Glycolether score	0.69	0.39-1.22	0.60	0.33-1.12	1.58	0.94-2.66	1.86	0.93-3.69
Aromatic hydrocarbons	0.92	0.65-1.30	0.86	0.63-1.18	1.07	0.79-1.46	1.15	0.82-1.62
Aliphatic hydrocarbons	1.09	0.55-2.16	1.31	0.64-2.69	0.63	0.23-1.70	0.95	0.25-3.56
Aldehydes	0.45	0.11-1.37	0.23	0.06-0.78	1.63	0.73-3.68	1.69	0.59-4.80

SAD: Small Airways Disease (EF25-75 <80% of the predicted level and FEV / FVC <12%, after bronchodilation during the reversibility test), OR: odds ratios; (95% CI): 95% confidence interval;
Adjusted OR: odds ratio adjusted for gender, age, smoking habit, relative humidity, presence of pets and presence of mold,*: **: n=48 farmers

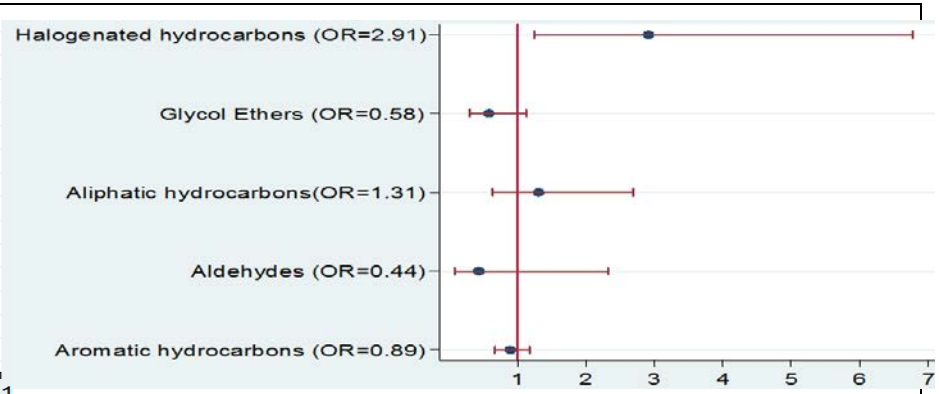
Air pollution in the dwellings

Benzene and trichloroethylene assessed in the living room were significantly associated with asthma (ORa= 6.64 (95% CI: 1.56–28.27) for benzene and =4.8 (95% CI: 1.0-23.3) for trichloroethylene) (Figure 1A). No other significant relationships were found (Fig. 1A). Marginal models did not converge for tetrachloroethylene, which had concentrations below the LD in most dwellings, or acrolein and formaldehyde, which had many missing values. A trend was observed between acetaldehyde and styrene in the living room and SAD after adjusting for confounder variables (Fig. 1C). No association was found between PM or single VOC and COPD. The global VOCs score was not related to asthma, COPD or SAD after adjusting for confounder variables. However, the halogenated hydrocarbons score was significantly associated with an increasing occurrence of asthma (ORa=2.9; 95% CI: 1.3–6.8) (Fig. 1B) and the glycol ethers score with an increasing occurrence of SAD (OR=2.0; 95% CI: 1.0–4.1) (Fig. 1D). Exposure to PM in the dwellings (living room or bedroom) was not related to respiratory outcomes (data not shown).

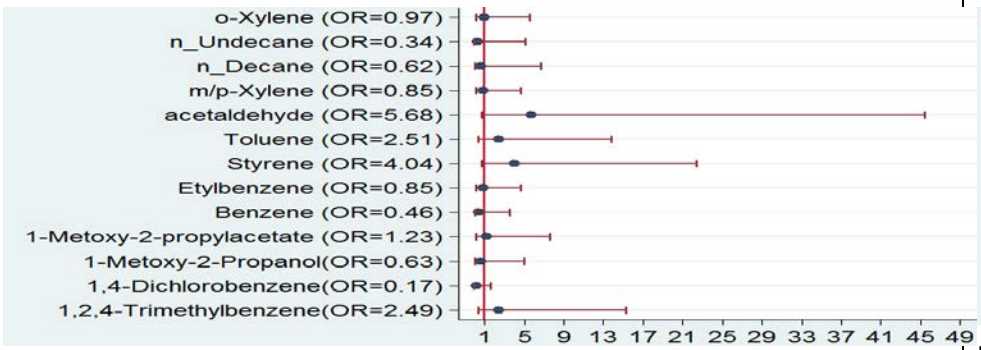
Figure 1: Adjusted ddds ratios (OR) of the relationship between asthma and exposure to Volatile Organic Compounds (VOCs) in living room



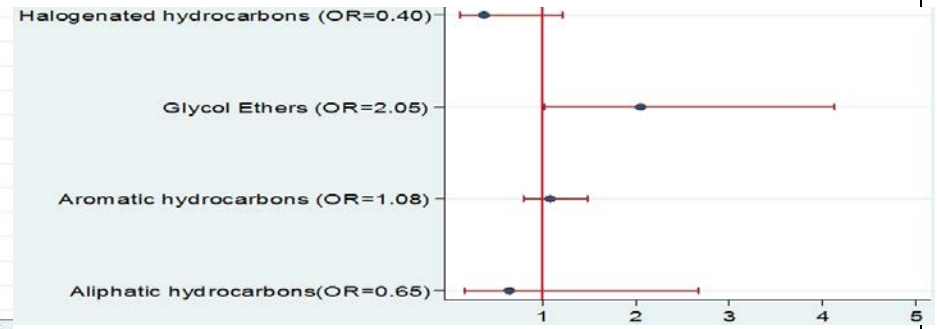
A: Odds ratios of the relationship between asthma and exposure to VOCs in living room (low/high) Odds ratios are adjusted for gender, age, smoking habit, relative humidity, presence of pets and presence of mold,



B: Odds ratios of the relationship between asthma and exposure to VOCs families (specific VOCs score) in living room (low/high) Odds ratios are adjusted for gender, age, smoking habit, relative humidity, presence of pets and presence of mold,



C: Odds ratios of the relationship between Small Airways Diseases (SAD) and exposure to VOCs in living room (low/high) Description: odds ratios are adjusted for gender, age, smoking habit, and presence of pets



D: Odds ratios of the relationship between SAD and exposure to VOCs families (specific VOCs score) in living room (low/high).Description: odds ratios are adjusted for gender, age, smoking habit, relative humidity, presence of pets and presence of mold,

Exposure was considered as high if the concentration of air pollutant was higher than the 3rd quartile value of the distribution and low if the concentration of air pollutant was lower than the 3rd quartile value of the distribution.

Air pollution in the workplaces (stable and granary):

Exposure to VOCs in stables or granary was not related to respiratory outcomes. No association was found between the global and specific VOCs scores and the health outcomes. Being exposed to elevated fine particles <2.5 µm (µg/m^3) in the stable and granary was significantly related to SAD after adjusting for confounders (ORa=5.26, 95% CI: 1.09-25.28) (Table 7).

Table 7: Unadjusted and adjusted odds ratios (OR) between elevated exposure to particulate matter (PM) in the stable and granary and asthma and small airways disease in the Stable/Granary

PM	Asthma				Small Airways Disease (SAD)			
	Crude OR (95% CI)		Adjusted OR (95% CI)		Crude OR* (95% CI)		Adjusted OR* (95% CI)	
Average Particles number (pt/cm^3)	2.48	0.68-8.97	2.43	0.50-11.80	1.65	(0.33-8.39)	1.85	(0.32-10.59)
PM_1 ($\mu g/m^3$)	0.63	0.14-2.91	1.07	0.19-5.84	0.56	(0.13-2.52)	0.50	(0.08-3.04)
$PM_{2.5}$ ($\mu g/m^3$)	0.29	0.04-2.42	0.30	0.05-1.69	**5.31**	**(1.25-22.65)**	**5.26**	**(1.09-25.28)**
PM_{10} ($\mu g/m^3$)	1.28	0.34-4.79	2.20	0.38-12.55	1.32	(0.31-5.58)	1.10	(0.22-5.42)
TSP ($\mu g/m^3$)	0.88	0.22-3.54	1.59	0.27-9.21	1.67	(0.39-7.13)	0.97	(0.15-6.44)

SAD: small airways disease, UFPM: Ultrafine particulate matter; PM: Particulate Matter; TSP: Total Suspended Particles; OR: odds ratios; (95% CI): 95% confidence interval; Adjusted OR: odds ratio adjusted for gender, age, smoking habit, relative humidity, presence of pets and presence of mold, *: n=48 farmers

Discussion

Main findings

This study explored the relationship between respiratory health and exposure to VOCs and PM in French farmers in the Auvergne region. Both benzene and trichloroethylene were found significantly associated with asthma, whereas $PM_{2.5}$ were significantly associated with SAD. When taking the specific VOCs family into account, asthma was positively associated with the halogenated hydrocarbons and SAD with glycol ethers (ORa=2.0; 95% CI: 1.0–4.1).

Literature

In urban areas, benzene exposure has been found associated with respiratory difficulty in children, including bronchitis, asthma and wheezing. Delfino et al. [150] found that ambient benzene was significantly and strongly associated with asthma symptom episodes (OR 5.93, P<0.01) among children with asthma in Los Angeles. The increased prevalence of asthma (exercise-induced, past year and lifetime) was significantly and positively associated with benzene among 4,907 children who had lived at their current address for the past three years. Among the 2,213 children living at their current address since birth, the associations persisted for lifetime asthma with benzene exposure (adjusted OR per interquartile range (95% CI) 1.3 (1.0–1.9) [151]. Our results are consistent with previous findings. Few studies have assessed the impact of VOCs in a rural area. One such study was conducted by Rive et al. [76] found that indoor benzene concentration was significantly associated with asthma in children, as indicated by urinary S-phenylmercapturic acid (SPMA). The odds-ratio for asthma was eight times higher in highly exposed children compared with weakly exposed children (exposure superior to the median, OR = 8.11; CI 95 %: 1.41–46.34). However, the association between benzene and asthma was significant only among non-atopic children (OR = 8.58; 95% CI: 1.4–51.59 vs. OR = 7.54; 95% CI: 0.55–103.21). These findings are important as infants and young children are particularly susceptible to developing respiratory diseases [152], and the prevalence of asthma is still increasing among them [153-155].

Association between exposure to trichloroethylene and asthma is consistent with that observed in the literature. Trichloroethylene, in addition to being carcinogen, has

been found to induce respiratory symptoms such as rhinitis [146] and asthma [156]. Blair et al. [157] found that men exposed to trichloroethylene from maintenance work on aircraft for at least one year between 1952 and 1956 in the U.S. state of Utah died more often from asthma than men in the general Utah population. Using a specific score for halogenated hydrocarbons (trichloroethylene, 1,4-dichlorobenzene and tetrachloroetylene), we also found a significant increase in asthma prevalence. Among the three compounds in this group, only trichloroethylene had a significant link with asthma. When considering the outdoor exposure in the farm, 2-butoxyetylacetate was found positively associated with SAD. To our knowledge, these are novel findings. In addition, the analysis of the specific VOCs score indicated that glycol ethers were significantly associated with SAD, which suggests that either a combined action of pollutants contributes to SAD or they are proxy of exposure to other pollutants. The mechanisms by which VOCs act on respiratory health are based on irritation [158]. ~~.~~ These findings are consistent with previous studies having focused on the effect of multi-pollution, including several [145, 146]. In the adult population, exposure to aromatic compounds has been found significantly associated with physician-diagnosed asthma (adjusted OR = 1.63, 95% CI: 1.17–2.27) [145]. In addition, total VOCs has been found associated with an increasing risk of shortness of breath in adults [159] and asthma in children [149].

The association between $PM_{2.5}$ and SAD is consistent with the results observed by Chrug et al. [160] that by examined samples taken from the lungs of 20 women from Mexico City, high PM zone, and control samples from 20 never-smoking, non-dust-exposed subjects from Vancouver, British Columbia, Canada, a low PM region. Women from Mexico City had abnormal small airways associated with fibrotic walls and excess muscle, of which many contained visible dust. The conclusion was that PM was retained in the walls of small airways and that, even in non-smokers, long-term exposure to high levels of ambient particulate pollutants was associated with SAD.

We used the 3rd quartile value in this investigation in order to categorize VOCs on the farms, and we defined a high exposure for dwellings with a concentration higher than this cut-off

point. This quartile was used to create a global score of exposure to VOCs in a previous study where significant associations between global score VOCs and asthma and rhinitis (odds ratio (OR) of 1.40 and 1.22, respectively) were found [146]. In our study, the association between the global VOCs score and asthma was not significant. This result could be explained by the high level of exposure observed by Billionnet et al. [146] as compared to our measures in a rural area. For example, the median and maximum values of benzene in the study by Billionnet et al. [146] were 13 µg/m^3 and 368.5 µg/m^3, respectively; whereas in our case, the median and maximum values of benzene in the living room were 1.2 µg/m^3 and 4.9 µg/m^3, respectively. The maximum value of benzene we found in the farm living room was even lower than the limit value of benzene in the atmosphere, according to the 2010 regulations of the European Commission (5 µg/m^3). Therefore, the exposure levels of VOCs that we measured on the rural farms are lower than in urban areas. This finding is consistent with the observation by Hulin et al. [158] that urban dwellings are more polluted than rural ones, with concentrations up to two times higher.

Study strengths and limitations

While there have been studies employing a multi-pollutant approach to assess exposure to several VOCs in urban dwellings [145, 146, 149], this study contributes to the literature by bringing a multi-pollutant analysis to a rural area where potential sources of VOCS, both indoor and outdoor, are numerous.

This study presents certain limitations. Apart from SAD and COPD that were assessed through spirometry, health outcomes of our study were obtained using a standardized self-administered questionnaire. This kind of data collection may have inherent bias for all the declarative data [161]. In addition, the number of farms participating in the study was limited, and the investigation was conducted only in the Auvergne region, which is not representative of other farming regions of France. Due to the low frequency of COPD using data from pulmonary function and gold criteria, marginal models did not converge for most VOCs and there were missing values. Thus, we were unable to perform analyses using COPD data. Due to the cross-

sectional design of the study, temporal relationships between VOCs and PM exposure and asthma cannot be established with certainty. Measurements were conducted for three months, and they may be a poor surrogate for past year exposure. Even if indoor and outdoor exposures were measured, we cannot rule out the possibility that respiratory symptoms were due to past indoor or outdoor exposures.

In conclusion, our findings drawn from a population-based sample suggest that VOCs and PM are linked with respiratory health, namely asthma and small airway diseases, in farmers. This cross-sectional study lays the foundation for further cohort or toxicological studies in order to confirm these associations and test for causality.

Acknowledgement: This manuscript was reviewed by Suzette Smiley-Jewell, Center for Occupational and Environmental Health (COEH), University of California, Davis. This publication arises from the project FERMA supported by The French National Research Program for Environmental and Occupational Health of ANSES (EST-07-71)

IV.2. Presentation de l'article 5: Risk factors for respiratory symptoms in French and California farmers

Malgré une faible prévalence de fumeurs chez les agriculteurs [28], plusieurs études ont montré que la proportion des exploitants agricoles souffrant de symptômes respiratoires était élevée par rapport à la population générale. De plus, les agriculteurs avaient des valeurs faibles de capacité vitale forcée (CVF) et de volume expiratoire maximal en une seconde (VEMS) par rapport à la population. Cependant, une grande variabilité sur la prévalence des symptômes respiratoires a été observée lorsqu'il s'agit de comparer des agriculteurs de deux régions différentes.

L'article 5 nous permet de mieux comprendre le rôle du tabagisme ainsi que cette variabilité géographique en comparant les agriculteurs de la région d'Auvergne participant à l'Etude FERMA et les agriculteurs californiens participant à l'étude FHS, en termes de caractéristiques agricoles, exposition et l'occurrence de symptômes respiratoires, en particulier l'asthme, le bronchite chronique, la toux et la rhinite allergique.

International Archives of Occupational and Environmental Health

Risk factors for respiratory symptoms in French and California farmers

--Manuscript Draft--

Manuscript Number:	IAOE-D-14-00267
Full Title:	Risk factors for respiratory symptoms in French and California farmers
Article Type:	Original Article
Keywords:	Farming, occupationnal exposure, respiratory symptoms, regional characteristics, agriculture
Corresponding Author:	Youssouf Hassani Institute Pierre Louis of Epidemiology and Public Health, INSERM, Paris, FRANCE
Corresponding Author Secondary Information:	
Corresponding Author's Institution:	Institute Pierre Louis of Epidemiology and Public Health, INSERM,
Corresponding Author's Secondary Institution:	
First Author:	Youssouf Hassani
First Author Secondary Information:	
Order of Authors:	Youssouf Hassani
	Diane Mitchell, Dr
	Marc B Schenker, Dr, MPH
	Soutrik Banerjee, Dr, MPH
	Nour Baiz, Dr
	Ollivier Ramousse, Dr
	Jean-François Bertholon, Dr
	Denis Caillaud, Dr
	Isabella Annesi-Maesano, Dr, MPH
Order of Authors Secondary Information:	
Abstract:	Objectives: The aim of this study was to determine risk factors for respiratory symptoms in French and Californian farmers. Methods: Farmers participating in the 2009-2010 FERMA study in Auvergne, France, (n=481) and the Farmer Health study in California, USA, (n=1947) were included. Respiratory symptoms and farming characteristics were assessed by questionnaire and risk factors associated with symptoms by logistic regression. Results: Asthma, chronic bronchitis and usual cough were less common in California (7.9%, 4.1% and 6%, respectively) than in French farmers (15.2%, 6.1% and 36.8%, respectively), but hay fever or allergic nasal symptoms were more prevalent in California (23.0%) than in France (20.5%). Respiratory symptoms were related to pesticide use in both countries. They were more associated with livestock production than with crops. Asthma symptoms among farmer smokers were more than six times higher in France compared to California, after adjustment for farming characteristics (OR=6.70, 95% CI=1.16-38.59). Tobacco use was associated with cough in both countries, but the strength of the relationship was higher in California (OR=5.57, 95% CI=3.24-9.57) than in France, where the association was not significant after adjustment for farming characteristics (OR=1.37, 95% CI=0.68-2.75). Conclusion: These results suggest that occupational exposure to agricultural contaminants combined with tobacco use has a great impact in the pathogenesis of respiratory diseases in farmers. These findings should be integrated into preventative efforts targeted at farmers in France and California in order to reduce smoking and

Powered by Editorial Manager® and ProduXion Manager® from Aries Systems Corporation

	potentially harmful agricultural exposures.

Powered by Editorial Manager® and ProduXion Manager® from Aries Systems Corporation

Risk factors for respiratory symptoms in French and California farmers

Youssouf H[1, 2], Mitchell D[3], Schenker MB[3], Banerjee S[1, 2], Baïz N[1, 2], Ramousse O[5], Bertholon JF[1, 2], Caillaud D[4], Annesi-Maesano I[1, 2]

[1]Epidemiology of Respiratory and Allergic Disease Department, UMR-S 1136, Institute Pierre Louis of Epidemiology and Public Health, INSERM, Paris France
[2]Epidemiology of Respiratory and Allergic Disease Department, UMR-S 1136, Institute Pierre Louis of Epidemiology and Public Health, UPMC Sorbonne Universités, Paris France
[3]Center for Occupational and Environmental Health, University of California, Davis, CA, USA
[4]Pulmonary Department, University Hospital, University of Auvergne, Clermont-Ferrand, France;
[5]Mutuelle Salariés Agricoles, Clermont-Ferrand, France;

ABSTRACT

Objectives: The aim of this study was to determine risk factors for respiratory symptoms in French and Californian farmers.

Methods: Farmers participating in the 2009–2010 FERMA study in Auvergne, France, (n=481) and the Farmer Health study in California, USA, (n=1947) were included. Respiratory symptoms and farming characteristics were assessed by questionnaire and risk factors associated with symptoms by logistic regression.

Results: Asthma, chronic bronchitis and usual cough were less common in California (7.9%, 4.1% and 6%, respectively) than in French farmers (15.2%, 6.1% and 36.8%, respectively), but hay fever or allergic nasal symptoms were more prevalent in California (23.0%) than in France (20.5%). Respiratory symptoms were related to pesticide use in both countries. They were more associated with livestock production than with crops. Asthma symptoms among farmer smokers were more than six times higher in France compared to California, after adjustment for farming characteristics (OR=6.70, 95% CI=1.16-38.59). Tobacco use was associated with cough in both countries, but the strength of the relationship was higher in California (OR=5.57, 95% CI=3.24-9.57) than in France, where the association was not significant after adjustment for farming characteristics (OR=1.37, 95% CI=0.68-2.75).

Conclusion: These results suggest that occupational exposure to agricultural contaminants combined with tobacco use has a great impact in the pathogenesis of respiratory diseases in farmers. These findings should be integrated into preventative efforts targeted at farmers in France and California in order to reduce smoking and potentially harmful agricultural exposures.

Keywords: farming, occupational exposure, respiratory symptoms, regional characteristics, agriculture

Introduction

Agriculture is an extremely hazardous industry associated with a large number of occupational injuries and chronic illnesses (Brackbill et al. 1994; Schenker 1996). Farmers are subject to respiratory diseases due to environmental exposures at work (Myers 1998; Sullivan et al. 1992; Zejda et al. 1994; Zejda and Dosman 1993). Respiratory exposures vary by the type of agricultural occupation and dust particles, including inorganic particles, such as silica, and organic particles, such as molds, bacteria, endotoxins, mycotoxins, pollens, grains, and animal feed. Numerous chemicals used or generated in farms may be inhaled (e.g., pesticides, exhaust fumes, fertilizers, and nitrogen oxides) (Donham and A. 2006; Schenker 1998; Von Essen and Donham 1997). Pesticide-induced illnesses are well documented and can result in both morbidity and mortality among agricultural populations (Schenker 1998). In industrialized countries, the tractor is commonly used in agriculture, and driving without an enclosed cab can expose the driver to much dust when preparing the ground or harvesting (Nieuwenhuijsen et al. 1998). Farmers can also be exposed to various gases generated from confined animal feeding operations (Langley 2011).

It has been reported that farmers have a higher prevalence of respiratory symptoms (Dalphin et al. 1998; Donham et al. 1984; Dosman et al. 1987; Toren and Horte 1997) and significantly lower values of forced vital capacity (FVC), forced expired volume in one second (FEV1) and maximum mid-expiratory flow rate (FEF25-75) than non-farming control populations from the same region (Dosman et al. 1987). In addition, agricultural workers tend to have higher risk factors for impaired pulmonary function than the general population (Davis-Lameloise et al. 2013; Fragar 2001), despite the fact that farmers have lower smoking prevalence than the general population (Schenker 1998).

A comparative study of region-related risk factors for respiratory symptoms in four European Countries (Denmark, Germany, Switzerland and Spain) and Californian farmers revealed great geographical variability of the prevalence of respiratory symptoms (Monso et al. 2003). Other studies have reached the same conclusion for other different farming regions (Cuthbert et al. 1984; Heinonen et al. 1987; Malmberg et al. 1988). The variability has been assumed related to regional characteristics, type of farming and socio-demographical factors from self-selection (Monso et al. 2003; Omland et al. 1999; Vogelzang et al. 1999).

The aim of this analysis is to better understand the regional differences in

farming characteristics and the impact of differences in tasks on respiratory symptoms among farmers from different regions. The present analysis of respiratory symptoms compared farmers from the French region of Auvergne and California in the United States to determine the distribution of asthma, chronic bronchitis, usual cough, hay fever or allergic nasal symptoms between the two regions. An assessment of the relationship between types of farming and respiratory symptoms was also done.

Methods

Design

A cross-sectional study of the distribution of respiratory symptoms and occupational exposure of French and California animal and/or crop farmers was performed. The French sample consisted of all farmers who participated in the first phase of the "Environmental factors for allergic and respiratory diseases [Facteurs Environnementaux et maladies allergiques et Respiratoires en Milieu rural en Auvergne (FERMA)]" study conducted in rural areas of the Auvergne region between 2009-2010. The Californian sample included all participants in the University of California, Davis, Farmer Health Study (FHS), recruited in 1993 and followed until 2004 to further investigate respiratory disease and symptoms.

Population

FERMA participants: Four hundred-ninety four (494) farmers from several cities in the Auvergne region were recruited between 2009 and 2010 during a compulsory occupational medicine visit conducted by the "Mutuelle des Salariés Agricoles" (MSA) in subscribers. A sample of 481 farmers who had completed data was selected to be included in this comparative study.

FHS participants: A Sample of 4,500 farmers were systematically selected from a list frame of 58,000 farms in California. Among the contacted farmers who were eligible for the study, 1,947 (80.4%) completed an interviewer-conducted questionnaire in 1993. Details about enrollment in the FHS are published elsewhere (Schenker et al. 2002).

Data collection

Standardized questionnaires were used in both studies. In the FERMA study, farmers were presented with an e-questionnaire that consisted of an enriched version of the Burden of Obstructive Lung Diseases (BOLD) questionnaire (Buist et al. 2005) completed by a technician on their socio-demographic characteristics, health, lifestyle, farm characteristics, occupational activities, food behaviors and potential risk

factors, including occupational exposures. Respiratory symptoms investigated included asthma, chronic bronchitis, cough, and hay fever or allergic nasal symptoms. Farmers were asked if a physician had diagnosed them with asthma or chronic bronchitis. Along with assessing smoking, alcohol and diet, the questionnaire assessed exposures at home and work. Occupational exposures included livestock (how many times they were in contact with livestock and what kind of contact they had with livestock), plants produced, use of fertilizer, pesticides, and / or tractor. The use of protective equipments (massk) during occupational activities was recorded.

All interviews of the California farmers were done using a Computer-Assisted Telephone Interview (CATI) system. Many items concerned demographics, farm characteristics, occupational exposures and specific health outcomes. Standardized questions were included from the National Health Interview Survey (NHIS) and the National Health and Nutrition Epidemiological Survey (NHANES III) (Schenker et al. 2002). Respiratory questions were adapted from the American Thoracic Society-Division of Lung Diseases 1978 questionnaire. Other items concerned protective equipment use and exposures that pose potential occupational hazards for farmers, such as pesticides, fertilizers and powered farming equipment (driving a tractor).

The same respiratory symptoms were defined in both studies. Only items using the same wording in both questionnaires were included in the present study. However, two variables needed to be transformed before their inclusion in the present analysis: 1) *Fertilizer use:* In the FHS questionnaire, the variable "loading or spreading of manure" was merged with "mixing, loading or application of chemical fertilizers" to correspond with the FERMA variable; and 2) *Farming Characteristics:* The French and California questionnaires differed in the characterization of the farm by the commodities. A "type of activity" (animal production, crop production, or both animal and crop production) existed in the French study and was created as follows for the California study:

- *Crop production:*

Did you grow any root crops?

Did you grow any field crops that were dry harvested?

Did you grow any vegetable, vine or shrub crops that were mechanically or hand harvested?

Did you grow any vegetable, vine or shrub crops that were mechanically harvested?

Did you grow any special crops, such as bedding plants, Christmas trees, cut flower,

herbs nursery products, ornamentals, potted plants timber or mushrooms?

- *Animal production:*

Did you raise any livestock, poultry, fish, bees or other animals?

Did you raise any animals for milk production, such as cows or goats?

Did you raise in open range any beef cattle, horses, mules, sheep and lambs, goats or pigs?

Did you raise inside buildings, feedlots or corrals any beef cattle, veal, lambs, sheep or pigs?

Did you raise any other animals, such as fish, bees, rabbits or other birds?

Statistical analyses

Basic descriptive analyses were performed after stratification by region and given as proportions, means with standard deviation (SD) or medians when appropriate. The Chi-squared distribution was used to compare the frequency of respiratory symptoms in the two regions and an unpaired t-test was used to compare continuous variables.

The associations between health outcomes and farming characteristics, by region were analyzed using univariate and multivariate logistic regression models. All variables that showed an association ($p<0.25$) with the outcome variable in the univariate model were entered in the multivariate model, and the most parsimonious model that still explained the data was accepted as the final model (W. and S. 1989).

First, to assess type of farming as a risk factor for respiratory symptoms, an occupational model was created for every respiratory symptom as the dependent variable, without regional stratification. This model was adjusted for farming characteristics, the type of activity [animal exposure, crop exposure, both animal and crop exposure], and for potential sociodemographical confounders (age, sex, current smoker and age they started smoking).

Second, to analyze the potential association between farming region and respiratory symptoms, univariate and multivariate models were created for every respiratory symptom with “region” introduced in the model as an independent variable. The multivariate model was adjusted for sociodemographical confounders (age, sex, smoking status) in a first step and for sociodemographical confounders and farming characteristics (the same as in the occupational model) in a second step. Smoking was assessed as an interaction variable in the models to check for an effect modification. Then, analyzes were stratified among smokers and non-smokers.

Lastly, to assess regional association of cough and asthma, and of cough and smoking, two multivariate models were created with "usually has a cough" as the dependent variable and asthma and current smoker (yes/not) respectively as the independents variables. Models were stratified by region. The first multivariate model included asthma and was adjusted for age, sex and current smoking in a first step and for age, sex, current smoking and farming characteristics associated with each respiratory symptom (the same as in the occupational model previously described) in a second step. The second model included smoking status and was adjusted with age and sex in the first step and age and sex and farming characteristics (the same as in the occupational model) in a second step.

Results were given as odds ratios (OR) with 95% confidence intervals (95% CI). All statistical tests were two sided, and a p-value <0.05 was reported as statistically significant.

Results

In total, 481 farmers from the FERMA study and 1,947 farmers from the FHS study were analyzed. Auvergne farmers worked full time, corresponding to the legal working time in France, which is fixed at 35 hours a week (Prunier-Poulmaire and Gadbois 2001). However, in California, there were 737 farmers (37.9%) with less than 20 hours farming a week. Only the 1,210 Californian farmers (62.1%) who had more than 20 hours of farming a week were included in the comparative analysis with French farmers. Comparison between Californian farmers who spent more than 20 hours and those who spent less than 20 hours of farming during a week is presented in the supplemental materials.

Region-related risk factors and symptoms and occupational exposure

Table 1 shows the comparison of socio-demographic characteristics, risk factors for exposure and respiratory symptoms between Auvergne and California. Farmers from the French cohort were younger (46.8 vs 52.9 years, p<0.0001) and had a higher proportion of women (28.3 vs 7.7 percent, p<0.0001) than in the Californian cohort. Californian farmers had a higher educational level than French farmers (31.9 vs 15.6 percent university degree, p<0.0001), and 84.6 percent of California farmers lived with partners, while only 63 percent of French farmers lived with partners. Although both French and US farmers began smoking at similar ages, the prevalence of smokers in France was almost twice that in California (21.1 vs 11.5 percent, respectively). Compared to Auvergne farmers, more Californian farmers handled pesticides (50.8 vs 18.1 percent,

p<0.0001) and fertilizers (53.3 vs 39.1 percent, p<0.0001). Furthermore, Auvergne agriculture was dominated by livestock production, with 56% of farmers involved in at least one animal production, or at least one livestock and vegetable crop (42.9%), while in California most farmers produced vegetable crops with 89.8% of farmers involved in at least one type of crop production.

In addition to differences in exposure between farms in Auvergne and California, regional differences in the distribution of respiratory symptoms were observed; Auvergne farmers had a higher frequency of asthma (15.2 vs 7.9 percent, p<0.0001) and usual cough (36.8 vs 6.0 percent, p<0.0001). An increased proportion of chronic bronchitis was observed in Auvergne farmers compared to Californian farmers (6.1 vs 4.1 percent), but this difference was not statistically significant. However, in California there were more farmers that reported hay fever or allergic nasal symptoms (23 vs 20.5 percent), although this difference was not statistically significant.

Table 1: Regional risk factors and farming characteristics in French and California farmers

	France n=481 (%)	California n=1210 (%)	p-value
Sociodemographic characteristics			
Age, mean+/-SD	46.8+/-11.8	52.9+/-13.2	<.0001
Sex (females)	129 (28.3)	93 (7.7)	<.0001
Education level (university degree)	72 (15.6)	383 (31.9)	<.0001
Live with partner	264 (63.0)	1026 (84.9)	<.0001
Tobacco smoking			
Age start smoking cigarettes regularly, mean+/-SD	18.1+/-4.4	18.8+/-5.2	0.0808
Cigarettes/day entire time smoke, mean+/-SD	6.5+/-10.3	22.6+/-12.7	<.0001
Cigarettes smoke per day now, mean+/-SD	13.9+/-9.1	5.5+/-10.5	<.0001
Ever smoked cigarettes regularly	208 (45.3)	510 (42.2)	0.2486
Current smoker	96 (21.1)	139 (11.5)	<.0001
Former smoker	112 (24.6)	367 (30.5)	<.0001
Respiratory symptoms or diseases			
Asthma	62 (15.2)	96 (7.9)	<.0001
Chronic bronchitis	25 (6.1)	49 (4.1)	0.0842
Usually have a cough	173 (36.8)	72 (6.0)	<.0001
Hay fever or allergic nasal symptoms	96 (20.5)	278 (23.0)	0.2771
Farming characteristics			
Live on farm	481 (100.0)	884 (73.1)	<.0001
Use fertilizers	125 (39.1)	641 (53.3)	<.0001
Pesticides use	58 (18.1)	614 (50.8)	<.0001
Production of at least one animal	218 (56.0)	473 (39.1)	<.0001
Production of at least one animal and one crop	167 (42.9)	404 (33.4)	0.0006
Production of at least one crop	4 (1.0)	1086 (89.8)	<.0001
Tractor use	234 77.7)	980 (81.0)	0.2041

Type of farming as a risk factor for respiratory symptoms

A specific occupational model for every respiratory symptom was constructed without regional stratification. Farming type was assessed as a risk factor for asthma, chronic bronchitis, usual cough and hay fever or allergic nasal symptoms. Adjustment for potential sociodemographical confounders and covariates were made (Table 2). We found that compared to vegetable exposure, exposure due to livestock or mixed production (crop and livestock production) was significantly related to the risk of developing asthma (OR=4.1, 95% CI=1.9-8.9 and OR=2.6, 95% CI=1.3-5.2, respectively). Farmers using pesticides also had a risk of developing asthma significantly larger than those who were not exposed to pesticides (OR=2.2, 95% CI=1.2-3.9). Exposure to livestock was also significantly related to usual cough among farmers compared to farmers producing crops only (OR=3.9, 95% CI=1.9-7.5). No significant results were observed for chronic bronchitis or hay fever or allergic nasal symptoms.

Table 2: Type of farming as a risk factor for respiratory symptoms or diseases (occupation model) in French and California farmers

Variables	Asthma	Chronic bronchitis	Hay fever or allergic nasal symptoms	Usually have a cough
Animal exposure vs crop	**4.12(1.90-8.94)**	1.13(0.40-3.17)	0.98(0.53-1.80)	**3.86(1.9-7.54)**
Animal and crop exposure vs crop	**2.60(1.31-5.15)**	1.05(0.46-2.38)	0.69(0.42-1.15)	1.05(0.56-1.97)
Pesticide use	**2.17(1.20-3.94)**	1.30(0.62-2.71)	1.43(0.93-2.21)	0.77(0.43-1.38)
Fertilizer use				1.18(0.64-1.94)
Live on farm		1.29(0.53-3.14)	0.86(0.53-1.41)	1.78(0.85-3.74)

*Data are presented as odds ratio (95% confidence interval) adjusted for age, sex, current smoker and age started smoking. Exposures were introduced in the model when p<0.25. Crop corresponds to the reference category.

Region-related risk factors for respiratory symptoms among smokers and non-smokers

Multivariable analyses were performed after stratification for smoking to determine the impact of regional farming characteristics on the prevalence of respiratory symptoms (high prevalence of asthma, chronic bronchitis and usual cough in Auvergne farmers and hay fever or allergic nasal symptoms in Californian farmers respectively) (Table 3).

For nonsmokers, working in Auvergne emerged as a relevant risk factor for asthma, chronic bronchitis and usual cough in both the univariate and the adjusted (sociodemographic characteristics) analysis. However working in Auvergne corresponded to a lower risk for hay fever or allergic nasal symptoms after adjusting for other confounders (OR=0.67, 95% CI=0.49-0.93). After adjustment for sociodemographical confounders and types of farming in the defined occupational model, only the risk of usual cough continued to be significantly higher in the Auvergne farmers compared to California farmers, but the adjustment of the models for types of farming decreased the strength of the association (OR=9.22, 95% CI=5.23-16.10).

For smokers, working in Auvergne increased the risk factor for asthma and usual cough in the univariate analysis and in the multivariate analysis after adjustment for sociodemographical confounders and farming characteristics. No significant association was found with region for the models containing chronic bronchitis or hay fever/allergic nasal symptoms. After adjustment for sociodemographical confounders and type of farming, the risk of asthma was more than 6-fold in Auvergne versus California (OR=6.70, 95% CI=1.16-38.59) while no significant association was observed among non-smokers (OR=1.14, 95% CI=0.67-1.96). In smokers, the risk of usual cough was lower than in nonsmoker in univariate analyses, OR=4.6(2.56-8.34). Yet, after adjustment for sociodemographical confounders, the association was stronger, although still lower than in non-smokers, OR=8.63 (4.01-18.56). After adjustment for sociodemographics and type of farming, the risk of usual cough among smokers was higher than in non-smokers (OR=11.69, 95% CI=2.75-49.67; OR=9.22, 95% CI=5.23-16.10, respectively).

Table 3: Region-related risk factors for respiratory symptoms among smokers and non-smokers in French and California farmers

	Non smoker					Smoker				
				Adjusted OR (95% CI)					Adjusted OR (95% CI)	
Symptoms or diseases	France	California	Crude OR	Sociodemographic variables	Sociodemographic variables + exposure	France	California	Crude OR	Sociodemographic variables	Sociodemographic variables + exposure
Asthma	45(14.4)	87(8.2)	**1.89 (1.29-2.78)**	**1.76 (1.15-2.68)**	1.14 (0.67-1.96)	14(18.4)	9(6.5)	**3.26 (1.34-7.95)**	**5.12 (1.70-15.39)**	**6.70 (1.16-38.59)**
Chronic bronchitis	20(6.4)	35(3.3)	**2.00 (1.14-3.52)**	**2.08 (1.10-3.90)**	1.73 (0.76-3.95)	5(6.5)	13(9.4)	0.67 (0.23-1.97)	0.53 (0.14-2.00)	1.50 (0.21-10.63)
Usually have a cough	117(33.0)	45(4.2)	**11.15 (7.69-16.17)**	**11.70 (7.82-17.49)**	**9.22 (5.23-16.10)**	48(50.5)	25(18.1)	**4.6 (2.56-8.34)**	**8.63 (4.01-18.56)**	**11.69 (2.75-49.67)**
Hay fever or allergic nasal symptoms	70(19.8)	253(23.7)	0.79 (0.59-1.07)	**0.67 (0.49-0.93)**	0.77 (0.49-1.21)	22(23.4)	25(18.0)	1.39 (0.73-2.64)	1.16 (0.54-2.50)	1.47 (0.36-6.0)

*Data are presented as n (%) unless otherwise stated. OR: odds-ratio. Exposure refers to farming characteristics (occupational model). Nonsmokers include those who have never smoked and former smokers. The univariate model contained each respiratory symptom and farming region only ($p < 0.25$). Adjustments included sociodemographic variables in the models of nonsmokers (age, sex and for former smokers), farming region and farming characteristics. For the second model (smokers), adjustments included the sociodemographic variables with age, sex and current number of cigarettes per day. Exposure variables were the same as in the first model. OR: odds ratio (95% confidence interval).

Association of cough with asthma and smoking

To understand the link between asthma and smoking in relation to chronic cough among farmers, we analyzed farmers suffering from cough separately for each region. Cough was introduced in the model as the dependent variable as a function of smoking or asthma (Table 4). The models were adjusted for sociodemographic factors and farming characteristics in the two agricultural areas. We noticed that among the Auvergne farmers suffering from cough, 21.9% reported having asthma compared to 12.5% for California farmers. In the Auvergne region, after adjustment with sociodemographic characteristics, the risk of asthma was significantly higher among farmers suffering from cough than in those who did not suffer from cough (OR=2.22, 95% CI=1.28-3.91). The association was slightly higher after adjustment for sociodemographic factors and farming type simultaneously (OR=2.44, 95% CI=1.24-4.80). No significant association was found between asthma and cough among California farmers. Regarding tobacco use, the proportion of Auvergne farmers who were smokers among those who suffered from cough was 29.1% versus 35.7% in California farmers. A significant association was found between cough and tobacco use among Californian farmers. The risk of cough with tobacco use was elevated after adjustment with sociodemographic factors (OR=5.51 (3.22-9.41)) and farming characteristics (Table 4). In the French farmers, the adjusted association between tobacco use and cough was lower (OR=1.97 (1.28-3.20)). Furthermore, no significant association was observed between cough and tobacco use after adjustment for sociodemographic factors and farming characteristics (OR=1.37 (0.68-2.75)).

Table 4: Regional association between cough and asthma and smoking in French and California farmers

Symptoms or diseases	France (n=481)	California (n=1210)
1) Asthma		
-Reported	32(21.9)	9(12.5)
-Crude OR	**2.16(1.25-3.73)**	1.72(0.83-3.58)
-Adjusted for sociodemographic and current smoker, OR	**2.22(1.28-3.91)**	1.96(0.90-4.11)
-Adjusted for sociodemographic, current smoker and farming, OR	**2.44(1.24-4.80)**	1.92(0.83-2.87)
2) Current smoker		
-Reported	48(29.1)	25(35.7)
-Crude OR	**2.08(1.31-3.29)**	**5.02(2.97-8.50)**
-Adjusted for sociodemographic current smoker OR	**1.97(1.28-3.20)**	**5.51(3.22-9.41)**
-Adjusted for sociodemographic, current smoker and farming OR	1.37(0.68-2.75)	**5.57(3.24-9.57)**

* Data are presented as n (%) unless otherwise stated. OR: Odds-ratio. Models are by region. The first model was usually having a cough as a function of asthma. Adjustment was on sociodemographic variables (age, sex), current smoker and the type of farming associated with each respiratory symptoms in the occupational model ($p<0.25$). The second model was usually having a cough as a function of current smoker. Adjustment was on sociodemographic variables (age and sex) and the type of farming associated with each respiratory symptoms in occupational model ($p<0.25$). OR: odds ratio (95% confidence interval).

Discussion

This study analyzed the prevalence of respiratory symptoms in a sample of French and California farmers and analyzed the impact of regional agricultural factors on these symptoms. In California, we used a subsample of a representative statewide cohort of farmers, those who spent more than 20 hours a week farming, for comparison with the French farmers. The group of farmers who spent less than 20 hours farming a week was likely to be older than the group who spent more than 20 hours farming a week and not involved in farms tasks requiring a lot of physical effort (see supplement). The less than 20 hours farming a week group includes those who had another occupation. These findings agree with those observed by Voaklander et al. (Voaklander et al. 2012), who assessed machinery exposure among older farmers. They found that for all categories except the operation and maintenance of combines, there was a significant negative linear trend linking the number of days worked to increasing age ($P < 0.05$ across all categories), with a large drop in days worked for those aged greater than 75 years. However, when they assessed each activity as a proportion of the total activity, they found that there were significant positive relationships between age and the proportion of time devoted to tractor operation ($P < 0.05$). This finding means that older farmers spent more time operating a tractor. However, we found that California farmers who spent less than 20 hours farming a week had a proportion of tractor use lower than those who spent more than 20 hours farming. The significant negative relationships between the age and the proportion of time devoted to all-terrain vehicles operation ($P < 0.05$), large animal tasks ($P < 0.05$), and small animal tasks ($P < 0.05$), is in agreement with our observation. Farmers who spent more than 20 hours farming per week were younger and were more involved in tasks that require more physical effort, such as the above mentioned tasks.

No significant difference in respiratory symptoms was observed among those who spent more than 20 hours farming a week and those who spent less than 20 hours farming a week. This lack of difference may be explained by the fact that those who spend less than 20 hours farming a week could be exposed in occupational tasks other than farming. Furthermore, the prevalence of asthma and chronic bronchitis among farmers who spent more than 20 hours a week (7.9% and 4.1%) were similar to those obtained by Schenker et al. (Schenker et al. 2005) when they assessed the agricultural dust exposure and respiratory symptoms among the 1,947 California farmers participating in the FHS study (7.8% and 3.8%). For these reasons,

comparative analyses with the French cohort were performed using the subsample of California farmers who spent more than 20 hours farming a week.

Using an occupational model without regional stratification, we found an association between asthma and pesticide use. Exposure to pesticide use was linked to an increase in asthma prevalence (OR=2.17, 95% CI=1.20-3.94). This finding is in agreement with that observed by Baldi et al. (Baldi et al. 2013), who found that pesticide use and history of pesticide poisoning were significantly associated with allergic asthma on vineyards (OR=1.35, 1.02–1.80), fruit-growing (OR=1.56, 1.01–2.40) and grasslands (OR=1.35, 1.03–1.76). Other research has demonstrated a doubling of both allergic and non-allergic asthma with high pesticide exposure events (Hoppin et al. 2009).

Working in the rural Auvergne was found to involve a significantly higher risk of asthma and cough than farming in California. In a previous study, Monso et al. (Monso et al. 2003) compared the FHS farmers to European farmers from four countries (Denmark, Germany, Switzerland and Spain) and found that the prevalence of asthma was higher in California than in Europe. Monso et al. (Monso et al. 2003) also found nasal allergy to be higher in California than in France (23 vs 20.5 percent), but our study did not have similar results. Considering chronic bronchitis among non-smokers, Monso et al. found its prevalence was higher in Europe than in California (9.6% vs 3.3%, respectively). This finding was confirmed in our study because the prevalence of chronic bronchitis in non-smoking farmers in Auvergne and California was equal to 6.4% vs 3.3%, respectively. However, French farmers were not included in the comparative analyses conducted by Monso et al. Furthermore, data from the FERMA study were gathered in the Auvergne region only and may not be representative of all French farmers.

When both Auvergne and California were considered without stratification, livestock exposure only or crop and livestock exposure had greater association with increased asthma than crop exposure only. This result is in agreement with previous analyses performed by Schenker et al. (Schenker et al. 2005) and Monso et al. (Monso et al. 2003) in the FHS cohort. Monso et al. found that asthma was mainly due to exposure to gold poultry.

Among farmers suffering from cough, we noticed that the prevalence of asthma was very high compared to the rest of the population. This may be due to the close relation between asthma and coughing; coughing is considered one the symptoms of asthma. We also found more current

smokers among farmers suffering from cough in both regions compared to farmers who did not suffer cough. A significant association between cough and asthma was observed in France. In California, the relationship was not statistically significant. Perhaps there was a lower number of asthmatics with cough in California. Both regions demonstrated a relationship between current tobacco use and cough. This result was in agreement with Smit et al., who found that cough symptoms were associated with exposure to irritants such as cigarette smoke and occupational exposures ($p < 0.05$) (Smit et al. 2012).

The association between cough and tobacco use was stronger in California than in France, where it was no longer significant after adjusting for farming characteristics (OR=1.37 (0.68-2.75)) despite the fact that many studies have shown that current smoking increases the likelihood of chronic cough after adjusting for agricultural exposures (Donham et al. 1989; Holness et al. 1987; Manfreda et al. 1989; Wilkins et al. 1999). Wilkins et al. found that tobacco use was significantly associated with chronic cough with an adjusted prevalence odds ratio equal to 7.72 (95% CI=3.14–18.99) (Wilkins et al. 1999). This difference with observed results allowed us to investigate whether smoking had been adequately controlled for in the analyses, especially in the FERMA study. Monso et al. (Monso et al. 2003) found that 22.3% of European farmers were current smokers. This finding is consistent with what we found among French farmers participating in the FERMA study, with a 21.1% prevalence of current smokers. Further analyses are needed to better understand why no significant association was observed between cough and tobacco use after adjusting for sociodemographic factors and farming characteristics in the Auvergne region. Possible causes could be the type of smoking habit, including the number of cigarettes, or the type of farming.

The French data did not allow us to explore details of the type of animal or crop exposures, which is a limitation of the study. In addition, the French and California studies were performed at two different periods: from 2009 to 2010 for the FERMA study, while farmers were recruited in 1993 in the California study. Many significant evolutions in farming techniques, protection, and exposure awareness occurred and were implemented during that almost 20 years of time difference. Despite the time gap between the two studies and the fact that the French study concerned only farmers from the Auvergne region, our findings are in agreement to what has been observed in other comparatives studies. However, data interpretation must be done with caution because of the limits.

In conclusion, similarities and differences in the distribution of respiratory symptoms and diseases in French and California farmers were found that were partly explained by regional differences. We discovered that smoking increased the risk of asthma and usual cough, and this effect had a regional variability. We observed that farmers suffering from cough were at greater risk of asthma, and this risk was increased by tobacco use and agricultural exposure. This phenomenon was significant in France, where the number of farmers who smoke was double that in California. Taken into account smoking status and usual cough, our findings shows that smoking increased the risk of cough, and this effect is increased by agricultural exposure, especially in California. It is well established that smoking increases the risk of lung diseases (Mio et al. 1997), as do agriculture exposures (Schenker 1998). Furthermore, cigarette smoke and mineral dusts affect the same anatomic locations in the small airways (Wright et al. 1992). These results suggest that occupational exposure to agricultural contaminants combined with tobacco use has a greater impact in the pathogenesis of respiratory diseases in farmers than smoking only. These findings should be integrated into preventative efforts targeted at farmers in France and California in order to reduce smoking and potentially harmful agricultural exposures.

Acknowledgement: This manuscript was reviewed by Suzette Smiley-Jewell, Center for Occupational and Environmental Health (COEH), University of California, Davis. FERMA study was supported by The French National Research Program for Environmental and Occupational Health of ANSES (EST-07-71)

References

Baldi I, et al. (2013) Agricultural exposure and asthma risk in the AGRICAN French cohort. Int J Hyg Environ Health doi:10.1016/j.ijheh.2013.08.006

Brackbill RM, Cameron LL, Behrens V (1994) Prevalence of chronic diseases and impairments among US farmers, 1986-1990. Am J Epidemiol 139(11):1055-65

Buist AS, et al. (2005) The Burden of Obstructive Lung Disease Initiative (BOLD): rationale and design. COPD 2(2):277-83

Cuthbert OD, Jeffrey IG, McNeill HB, Wood J, Topping MD (1984) Barn allergy among Scottish farmers. Clin Allergy 14(2):197-206

Dalphin JC, et al. (1998) Prevalence of asthma and respiratory symptoms in dairy farmers in the French province of the Doubs. American journal of respiratory and critical care medicine 158(5 Pt 1):1493-8 doi:10.1164/ajrccm.158.5.9709108

Davis-Lameloise N, et al. (2013) Occupational differences, cardiovascular risk factors and lifestyle habits in South Eastern rural Australia. BMC Public Health 13:1090 doi:10.1186/1471-2458-13-1090

Donham K, A. T (2006) Agricultural respiratory diseases Agricultural Medicine Occupational and Environmental Health for the Health Professions. Blackwell Publishing, Victoria, Australia, p 65-144

Donham K, Haglind P, Peterson Y, Rylander R, Belin L (1989) Environmental and health studies of farm workers in Swedish swine confinement buildings. Br J Ind Med 46(1):31-7

Donham KJ, Zavala DC, Merchant JA (1984) Respiratory symptoms and lung function among workers in swine confinement buildings: a cross-sectional epidemiological study. Arch Environ Health 39(2):96-101

Dosman JA, Graham BL, Hall D, Van Loon P, Bhasin P, Froh F (1987) Respiratory symptoms and pulmonary function in farmers. J Occup Med 29(1):38-43

Fragar L (2001) The health of the people in agriculture and its interdependence with the health of rural communities. N S W Public Health Bull 12(6):155-159

Heinonen OP, Horsmanheimo M, Vohlonen I, Terho EO (1987) Prevalence of allergic symptoms in rural and urban populations. Eur J Respir Dis Suppl 152:64-9

Holness DL, O'Blenis EL, Sass-Kortsak A, Pilger C, Nethercott JR (1987) Respiratory effects and dust exposures in hog confinement farming. Am J Ind Med 11(5):571-80

Hoppin JA, et al. (2009) Pesticide use and adult-onset asthma among male farmers in the Agricultural Health Study. The European respiratory journal 34(6):1296-303 doi:10.1183/09031936.00005509

Langley RL (2011) Consequences of respiratory exposures in the farm environment. N C Med J 72(6):477-80

Malmberg P, Rask-Andersen A, Hoglund S, Kolmodin-Hedman B, Read Guernsey J (1988) Incidence of organic dust toxic syndrome and allergic alveolitis in Swedish farmers. Int Arch Allergy Appl Immunol 87(1):47-54

Manfreda J, Cheang M, Warren CP (1989) Chronic respiratory disorders related to farming and exposure to grain dust in a rural adult community. Am J Ind Med 15(1):7-19

Mio T, Romberger DJ, Thompson AB, Robbins RA, Heires A, Rennard SI (1997) Cigarette smoke induces interleukin-8 release from human bronchial epithelial cells. Am J Respir Crit Care Med 155(5):1770-6 doi:10.1164/ajrccm.155.5.9154890

Monso E, et al. (2003) Region-related risk factors for respiratory symptoms in European and Californian farmers. Eur Respir J 21(2):323-31

Myers M (1998) Health problems and disease patterns in agriculture. ILO

Encyclopedia of Occupational Health and Safety 3(64):60-65
Nieuwenhuijsen MJ, Kruize H, Schenker MB (1998) Exposure to dust and its particle size distribution in California agriculture. Am Ind Hyg Assoc J 59(1):34-8 doi:10.1080/15428119891010316
Omland O, Sigsgaard T, Hjort C, Pedersen OF, Miller MR (1999) Lung status in young Danish rurals: the effect of farming exposure on asthma-like symptoms and lung function. The European respiratory journal 13(1):31-7
Prunier-Poulmaire S, Gadbois C (2001) The French 35-hour workweek: a wide-ranging social change. J Hum Ergol (Tokyo) 30(1-2):41-6
Schenker M (1998) Respiratory Health Hazards in Agriculture. Respiratory and Critical Care Medicine 158(5):S1-S76
Schenker MB (1996) Preventive medicine and health promotion are overdue in the agricultural workplace. J Public Health Policy 17(3):275-305
Schenker MB, et al. (2005) Agricultural dust exposure and respiratory symptoms among California farm operators. J Occup Environ Med 47(11):1157-66
Schenker MB, Orenstein MR, Samuels SJ (2002) Use of protective equipment among California farmers. Am J Ind Med 42(5):455-64 doi:10.1002/ajim.10134
Smit LA, et al. (2012) Transient receptor potential genes, smoking, occupational exposures and cough in adults. Respir Res 13:26 doi:10.1186/1465-9921-13-26
Sullivan JB, Gonzales G, Krieger GR, Runge CF (1992) Health-related hazards of agriculture. in Hazardous Materials Toxicology: Health Chemical Principles of Environmental
Toren K, Horte LG (1997) Asthma mortality and occupation in Sweden 1981-1992. Am J Ind Med 31(6):678-81
Voaklander D, Day L, Dosman J, Hagel L, Pickett W (2012) Older farmers and machinery exposure-cause for concern? Am J Ind Med 55(11):1044-50 doi:10.1002/ajim.22111
Vogelzang PF, van der Gulden JW, Tielen MJ, Folgering H, van Schayck CP (1999) Health-based selection for asthma, but not for chronic bronchitis, in pig farmers: an evidence-based hypothesis. The European respiratory journal 13(1):187-9
Von Essen S, Donham K (1997) Respiratory disease related to work in agriculture. In: Langley RL MR, Meggs WJ, Roberson GT, (ed) Safety and Health in Agriculture, Forestry & Fisheries. Government Institutes Inc, Rockville, MD p353-384
W. HD, S. L (1989) Applied logistic regression, New York
Wilkins JR, 3rd, Engelhardt HL, Rublaitus SM, Crawford JM, Fisher JL, Bean TL (1999) Prevalence of chronic respiratory symptoms among Ohio cash grain farmers. Am J Ind Med 35(2):150-63
Wright JL, Cagle P, Churg A, Colby TV, Myers J (1992) Diseases of the small airways. Am Rev Respir Dis 146(1):240-62 doi:10.1164/ajrccm/146.1.240
Zejda JE, et al. (1994) Respiratory health status in swine producers relates to endotoxin exposure in the presence of low dust levels. J Occup Med 36(1):49-56
Zejda JE, Dosman JA (1993) Respiratory disorders in agriculture. Tuber Lung Dis 74(2):74-86 doi:10.1016/0962-8479(93)90031-r

Supplement

Californian farmers who spend more than 20 hours farming a week versus those who spend less.

Comparison of sociodemographic characteristics, farming exposure and respiratory symptoms between California farmers who spent more than 20 hours farming a week and those who spent less than 20 hours is presented in Table 5. Average working time for Californian farmers who spent more than 20 hours a week differed significantly with average working time of those who spent less than 20 hours (47.5h +/-18.9 vs 8.8 +/-5.5). Farmers who spent less than 20 hours farming a week were older (56.9+/-13.2 vs 52.9+/-13.2, $p<0.0001$) and consisted of more females (13.5 vs 7.7 percent). There were no significant difference between the two groups in the age started smoking and the number of cigarettes smoked per day. However, a significant difference was observed between the two groups in smoking status ($p=0.0489$). Concerning respiratory symptoms, the prevalence of asthma and chronic bronchitis was higher among farmers who spent more than 20 hours farming a week than those who spent less, while the latter had a higher prevalence of usual cough and fever or other nasal symptoms than farmers who spent more than 20 hours farming a week. However, these differences were not statistically significant. Concerning exposure on farms, farmers who spent more than 20 hours farming a week had more exposure to environmental characteristics than those who spent less than 20 hours farming a week. Indeed, farmers who spent more than 20 hours farming a week were more exposed to fertilizers (53.3% vs 47.4%), pesticides (50.8% vs 39.2%), livestock (39.1% vs 27.9%), and tractor use (81.0% vs 70.0%) than those with fewer hours. However, farmers who spent less than 20 hours farming a week were more exposed to crops (95.4% vs 89.8%).

Table 5: Sociodemographic characteristic and respiratory symptoms among California farmers according the average hours farming per week

	Work less than 20h a week	Work more than 20h a week	p-value
Sociodemographical status			
Number of subjects	737	1210	
Hour farming a week, mean +/-SD	8.8+/-5.5	47.5+/-18.9	<.0001
Age, mean+/-SD	56.9+/-13.2	52.9+/-13.2	<.0001
Sex (females)	93 (13.5)	93 (7.7)	<.0001
Education level (university degree)	244 (35.5)	383 (31.9)	0.1167
Live with partner	591 (86.0)	1026 (84.9)	0.5182
Smoking status			
Age start smoking cigarettes regularly, mean+/-SD	18.2+/-4.3	18.8+/-5.2	0.1009
Cigarettes/day entire time smoke, mean+/-SD	22.5+/-12.0	22.6+/-12.7	0.8839
Cigarettes smoke per day now, mean+/-SD	5.9+/-12.2	5.5+/-10.5	0.5501
Current smoker	86 (12.5)	139 (11.5)	0.0489
Former smoker	242 (35.2)	367 (30.5)	
Never smoker	359 (52.3)	699 (58.0)	
Exposure			
Live on farm	487 (70.7)	884 (73.1)	0.2666
Fertilization use	326 (47.4)	641 (53.3)	0.0129
Pesticide use	270 (39.2)	614 (50.8)	<.0001
Animal production	192 (27.9)	473 (39.1)	<.0001
Animal and crop production	165 (24.0)	404 (33.4)	<.0001
Crop production	657 (95.4)	1086 (89.8)	<.0001
Tractor use	483 (70.0)	980 (81.0)	<.0001
Respiratory symptoms			
Ever had asthma	53 (7.7)	96 (7.9)	0.8438
Chronic bronchitis	26 (3.8)	49 (4.1)	0.7619
Usually have a cough	45 (6.5)	72 (6.0)	0.6159
Fever or other nasal symptoms	173 (25.1)	278 (23.0)	0.3015

V. Conclusions

Dans cette section, nous avons pu mesurer l'exposition aux COVs et PM dans le lieu de travail et le domicile des agriculteurs de la région d'Auvergne. Par ailleurs, nous avons également pu comparer la variabilité régionale en termes d'exposition et la distribution des symptômes, en particuliers les maladies respiratoires dans 2 régions différentes (en Auvergne et en Californie).

Les résultats de la première étude nous ont permis de constater qu'en Auvergne, la concentration des COVs était très élevée dans les habitations que dans les lieux de travail. De plus, l'asthme était significativement associé au benzène et au trichloréthylène. En considérant des sous-groupes de COVs, l'asthme était également associé aux composés halogénés. La maladie des petites voies aériennes était associée au 2-butoxyetylacetate et à la famille des glycols éthers. Il est à noter que ces associations ont été observées en considérant l'exposition à l'intérieur des habitations. Plus d'investigations épidémiologiques avec plus de détails sur l'exposition et les mesures d'effets respiratoires en milieu rural sont nécessaires pour valider ces résultats.

La comparaison entre les agriculteurs français de l'Auvergne et californiens nous a permis de constater la variabilité régionale en termes d'exposition et l'occurrence des symptômes respiratoires. En effet, travailler dans la région rural de l'Auvergne présentait un grand risque de l'asthme, de la toux et la bronchite chronique qu'en Californie alors que les agriculteurs californiens étaient plus à risque pour la rhinite allergique. En considérant les 2 régions ensemble, nous avons observé que l'usage des pesticides était significativement associé à l'augmentation du risque de l'asthme. Ces résultats doivent être intégrés dans les efforts de prévention auprès des agriculteurs en France et en Californie afin de réduire l'usage et les polluants dangereux dans l'agriculture.

VI. Utilisation d'un biomarqueur pour évaluer l'exposition individuelle d'un polluant : cas du benzène

Le benzène est un polluant ubiquitaire à l'intérieur des habitations qu'à l'extérieur. Cette présence se répercute sur la santé respiratoire de la population exposée. Dans le but de mieux évaluer l'exposition individuelle du benzène afin d'étudier son impact sur l'asthme, nous avons utilisé un biomarqueur spécifique de l'exposition du benzène, l'acide S-phénylmercapturique urinaire (S-PMA) chez un échantillon d'enfants à travers une étude cas-témoins [76].

L'exposition au benzène a été évaluée dans les logements de 63 enfants (32 asthmatiques et 31 témoins) à travers l'identification des sources de benzène et à l'évaluation *in situ* avec des échantillonneurs passifs. La détermination de l'acide S-phénylmercapturique urinaire a été obtenue par chromatographie liquide couplée à une spectrométrie de masse.

Nous avons observé qu'à domicile, les enfants asthmatiques ont été significativement plus exposés au benzène ambiant que les témoins ($p \leq 0,05$). L'exposition au benzène a aggravé de façon significative les symptômes d'asthme de manière générale chez les enfants non atopiques. L'acide S-phénylmercapturique urinaire était significativement associée à des concentrations de benzène dans l'ensemble de la population (coefficient de régression = 0,28, Intervalle de Confiance (IC) à 95%: de 0,07 à 0,49; $p < 0,05$) et l'asthme (OR = 7,69; IC 95%: 1,37 à 42,52 pour une augmentation de 1 µg / g de créatinine de l'acide S-phénylmercapturique urinaire). Toutefois, après ajustement à l'exposition au tabac, les allergies familiales, l'âge et le sexe, cette relation a persisté mais n'était plus significative (OR = 4,95; IC 95%: 0,91 à 27,4, $p < 0,10$). Les concentrations de benzène et d'acide S-phénylmercapturique urinaire étaient plus élevées chez les enfants vivant dans des logements construit après 1948 et et dans les appartements.

Notre étude met en évidence la relation entre l'asthme chez l'enfant et la concentration de benzène à domicile, même à de faibles niveaux de ce polluant. Ce résultat a été confirmé lors de l'examen de l'acide S-phénylmercapturique urinaire, qui a été lié à la fois aux concentrations de benzène et à l'asthme. Des études épidémiologiques et toxicologiques complémentaires sont nécessaires pour confirmer nos résultats.

.

CHAPITRE IV : SYNTHESE ET REFLEXIONS

I. Principaux résultats

Les résultats de ces travaux de thèse ont utilisés des données issues de 4 études épidémiologiques basées sur 2 thèmes de recherche : étude des effets sanitaires des émissions de feux de forêt et l'impact de l'exposition en milieu agricole et les maladies allergiques et respiratoires. Ces résultats ont permis d'obtenir de nouvelles informations sur la qualité de l'air et ses associations avec la santé respiratoire dans 2 contextes différents avec différentsniveaux d'exposition à la pollution atmosphérique : un niveau macroscopique et un niveau semi-individuel. Un résultat supplémentaire a permis de réaliser le biomonitoring dans les urines d'un polluant, le benzène, présent dans l'air et de les mettre en relation avec l'asthme infantile.

Impact Sanitaire des feux de foret

A travers une revue de la littérature, nous avons constaté que plusieurs études épidémiologiques se sont intéressées à l'impact sanitaire des émissions de feux de forêts. Lors d'un épisode de feux de forêts, les concentrations de certains polluants dépassent largement le seuil de tolérance fixé par les autorités sanitaires. Or beaucoup de ces polluants sont connus pour être nocif pour la santé. C'est le cas des particules fines qui ont la capacité de s'introduire dans les alvéoles pulmonaires et même dans le sang et provoquer des maladies chronique des poumons. Plusieurs études épidémiologiques ont trouvé des associations significatives entre l'exposition aux fumées issues des feux de forêts et l'occurrence des symptômes respiratoires et cardiovasculaires. Ces associations ont été observées en termes d'admissions à l'hôpital et d'hospitalisations. Très peu d'études ont analysé l'impact de l'exposition des émissions issues des incendies et la mortalité due aux maladies cardiorespiratoires mais les résultats sont disparates. Alors que Vedal et Duton [162] avaient estimé qu'il n'y avait aucune association entre l'exposition aux émissions issues des incendies et la mortalité, d'autres au contraire ont montré que l'exposition aux émissions de

feux de forêts était bien associée à l'augmentation du taux de mortalité [126, 163-166].

Plusieurs méthodes ont été utilisées pour évaluer l'exposition aux émissions issues des feux de forêts. C'est l'un des points clés pour mieux évaluer l'impact sanitaire de ces émissions. Ces méthodes vont des simples questionnaires individuels et la récolte des données de routine dans les différentes institutions spécialisées, aux méthodes sophistiquées utilisant de la modélisation et des données satellitaires. Chacune de ces méthodes présentait des avantages et des inconvénients. La méthode d'évaluation de l'exposition utilisant des questionnaires individuels présente l'inconvénient de ne pas pouvoir quantifier les émissions mais c'est la seule méthode permettant de récolter les données individuelles de santé. Les stations de surveillance de la qualité de l'air permettent de quantifier les émissions et en particulier les particules fines mais l'inconvénient est que ces stations enregistrent toutes les émissions y compris celles provenant des autres sources de pollution. Les méthodes d'évaluation utilisant les données satellitaires permettent une meilleure estimation de la surface brulée et peuvent être combinées avec la modélisation pour en déduire la concentration des émissions. Des émissions, on peut obtenir des concentrations. Dans certaines études, l'épaisseur optique mesurant la densité des aérosols (AOD) fournit par le spectrophotomètre imageur à résolution moyenne MODIS, à bord des satellites Terra et Aqua de la NASA [167], a été reliée aux $PM_{2.5}$ et permet d'en déduire sa concentration horaire ou journalière [167]. Cette méthode, validée en faisant des comparaisons avec les données des stations de surveillance de la qualité de l'air basées au sol, a été utilisée dans certaines études épidémiologiques pour faire des estimations de l'exposition lors des incendies de forêts [49, 66].

Le plus grand challenge de toutes ces méthodes d'évaluation de l'exposition aux émissions de feux de forêts est de différencier les émissions de la fumée issues des feux de forêts à celles des autres sources de pollutions. Dans certaines études, les auteurs ont essayé de faire cette distinction en soustrayant les concentrations des émissions de base à celles de toutes les émissions [126] ou en créant un indicateur d'avant pendant et après le feu puis en comparant les données sanitaires dans les différentes périodes [43]. D'autres études définies des régions exposées et des régions non exposées en utilisant un seuil de

l'épaisseur optique puis comparaison des données sanitaires de ces 2 régions [49].

A travers une étude de cas des incendies qui ont eu lieu à Marseille en 2009, nous avons utilisé des données satellitaires et de la modélisation pour calculer et différencier les émissions issues des incendies aux émissions anthropiques. Nous avons utilisé ces données avec un modèle de retard échelonnés pour calculer les effets à court termes des concentrations issues des incendies avec un décalage à 10 jours. Nous avons observé que les concentrations anthropiques avaient un effet significatif sur les consultations totales. Bien qu'aucun effet significatif n'a été observé entre les particules fines issues des incendies et les données sanitaires, une relation à la limite de la signification était observée dans le cas des consultations pour maladies respiratoires.

Exposition en milieu rural

De grandes variations de concentration des COVs et des PM selon les lieux considérés ont pu être mises en évidence. Les concentrations aux domiciles des agriculteurs étaient plus élevées que sur les lieux du travail. Néanmoins, les concentrations étaient globalement faibles avec beaucoup de COVs qui étaient en dessous de la limite de quantification.

Plusieurs résultats obtenus en termes d'effets potentiels de la pollution intérieure sur la santé respiratoire sont également à souligner. Les associations observées entre l'asthme et l'exposition aux contaminants physico-chimiques (articles 4 et 5) permettent non seulement de confirmer certaines des relations observées dans des études précédentes réalisées en milieu urbain mais aussi de mettre en avant d'autres polluants ayant fait l'objet de très peu de publications (le trichloréthylène et les composés halogénés). De même, une association entre la maladie des petites voies aériennes et le glycol éthers a été mise en évidence.

De plus, des différences régionales en termes d'exposition et d'occurrence des symptômes respiratoires ont pu être mises en évidence entre la région de l'Auvergne et la Californie (article 5). Ces résultats ont pu confirmer ceux d'autres études qui avaient mis en évidence une variabilité régionale entre les agriculteurs européens et californiens sur certaines maladies respiratoires comme l'asthme, la bronchite chronique et la rhinite allergique. Le tabac associé à

l'exposition des polluants agricoles, augmentait le risque des maladies respiratoires chez les agriculteurs.

II. Discussion générale

II.1. Impact sanitaires des incendies

Dans cette thèse, nous nous sommes focalisés sur les effets sanitaires issus des émissions de feux de forêts, cela en sachant que le bois est très utilisé comme source d'énergie pour se chauffer ou pour préparer le repas par environ 3 milliards de personnes dans le monde, soit presque la moitié de l'humanité. L'utilisation de cette source d'énergie n'est pas sans conséquence puisque l'OMS estime que plus de 4 millions de personnes meurent prématurément de maladies imputables à la pollution de l'air domestique due à la cuisine à base de combustibles solides à base du biomasse (bois, déjections animales, résidus agricoles) et du charbon [128]. La figure 6 présente la trajectoire des particules dans le système respiratoire en fonction de leurs tailles.

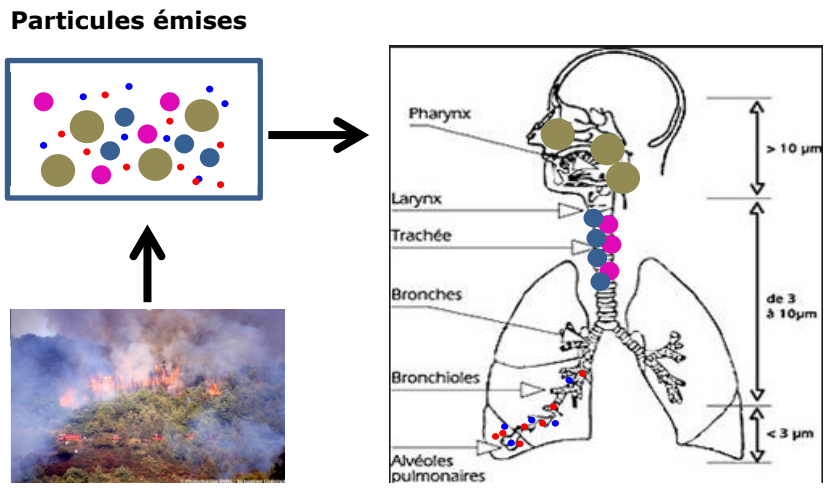


Figure 6: Trajectoire des particules en suspension de la fumée vers le système respiratoire

II.2. Mieux évaluer l'exposition lors des incendies de forets

Plusieurs méthodes ont été utilisées dans les études épidémiologiques pour évaluer l'exposition aux émissions des incendies. Ces méthodes avaient pour objectif de mieux évaluer les effets sanitaires de ces émissions. Parmi ces méthodes, citons les questionnaires individuels, les données de routine, les stations de surveillance de la qualité de l'air, les données satellitaires et la modélisation. Bien que des associations significatives entre l'exposition aux émissions issues des incendies et les données sanitaires aient été trouvées, l'estimation de l'exposition aux polluants pourrait être erronée en raison des incertitudes dans la mesure de l'exposition. En effet, la plupart de ces méthodes ne différencient pas les émissions des feux par rapport à celles des autres sources de pollution. Cette indifférenciation est susceptible de biaiser ces études, cela pouvant entrainer un jugement faussé sur le réel impact des émissions des feux.

Dans toutes ces méthodes aucune mesure individuelle en continu ou discontinue de l'exposition aux émissions n'a été évaluée. Or, pour mieux évaluer l'impact sanitaire des émissions, il y a besoin de se rapprocher de l'exposition individuelle. L'évaluation de l'exposition sur la base des auto-questionnaires entraine un biais de déclaration, alors que les stations de surveillance de la qualité de l'air spécifiques aux PM mesurent également toutes les émissions anthropiques [392].

En ce qui concerne les données satellitaires, il est important de reconnaître que des erreurs dans la résolution au niveau du sol peuvent se produire. Dans certains cas, les données satellitaires peuvent ne pas être récupérées (ou avec plus d'incertitude) si la région est nuageuse ou s'il y a une forte réflexion du soleil dans les cours d'eau et sur la neige. Dans certaines régions, la correspondance entre l'épaisseur optique fournit par les satellites et les $PM_{2.5}$ n'a pu être trouvée lorsque les aérosols sont entièrement en altitude au-dessus de la couche limite et qu'ils n'ont pas d'influence sur la qualité de l'air [393].

Toutes les approches décrites peuvent être combinées dans un système de modélisation, qui est actuellement le seul outil pour permettre la séparation des émissions issues des incendies à celles des autres sources de pollution à travers différentes simulations.

Pour pallier ces problèmes d'incertitudes, une des solutions possibles est l'usage des capteurs portatifs ou des biomarqueurs spécifiques de la combustion de biomasse. Les biomarqueurs bien que n'offrent que des estimations indirectes, peuvent être un bon moyen pour mieux évaluer l'exposition lors des incendies de forêts, en raison de leur spécificité. Le biomarqueur idéal serait un indicateur dépendant de la dose d'exposition, en plus d'un prédicteur d'effets physiologiques, et obtenues par des techniques non invasives [72]. Cependant, un objectif plus réaliste serait la combinaison d'un marqueur d'exposition et d'un autre marqueur d'effet séparé[72].

Les capteurs portatifs ont été utilisés dans certaines études sur la pollution atmosphérique en milieu urbain pour évaluer l'exposition individuelle sur des volontaires, tout en tenant compte de la durée d'exposition [129]. D'autres capteurs portatifs ont été utilisés par des pompiers pour mesurer l'exposition au niveau de la respiration. A partir d'une cohorte américaine avec mesure individuelle de l'exposition, un effet possible des hydrocarbures aromatiques polycycliques (HAP) sur le poids de naissance a aussi été décrit [79]. Cette technique utilise un biomarqueur spécifique des HAPs. Parmi eux, les adduits de l'ADN du B[a]P semblent particulièrement intéressants puisqu'ils représentent la dose efficace au plus près du site d'action toxique des HAP [78, 79]

Cette méthode pourrait être utilisée par un échantillon de population pour mieux évaluer l'exposition individuelle aux HAPs issues des incendies. Cependant, il existe de nombreux autres polluants tout aussi dangereux dans les incendies est nécessaire de mieux évaluer leur exposition.

II.3.Inventaires des émissions de feux de forêts

Nous avons utilisé la méthode développée par Liousse et al. [90], pour réaliser l'inventaire des émissions et de la surface brulée en Europe entre 2006-2010. Cette méthode nous a permis d'avoir les émissions ainsi que les concentrations au niveau local avec les coordonnées spatiales. Cette même méthode a permis également de déterminer et différencier les concentrations des $PM_{2.5}$ en Europe et plus précisément à Marseille à l'été 2009 et ces données ont été utilisées pour évaluer l'impact des incendies qui ont eu lieu en Juillet 2009 dans cette ville.

Cette méthode a été utilisée auparavant pour réaliser un inventaire quotidien des feux de forêt en Afrique sur la période de 2000-2007 à une résolution spatiale horizontale de 1 km x 1 km pour les particules en suspension et les gaz. L'inventaire obtenu a été comparé à d'autres inventaires obtenus avec d'autres méthodes. Un facteur de 2.4 de différence entre les inventaires de la version 2 de la base de données mondiale sur les émissions de feu (Globale Fire Emissions Database version 2 GFED2) et l'inventaire AMMABB (du projet Analyses Multidisciplinaires de la Mousson Africaine- AMMA) a été trouvé mais considéré comme raisonnable compte tenu de la grande incertitude inhérente à la détermination des émissions de feux de forêts [168].

Cette méthode a été également comparée au modèle global ORISAM-TM4 pour le black carbon. Les comparaisons ont été également réalisées entre la surface, la colonne intégrée et les observations satellitaires du projet AMMA. Les principales caractéristiques semblent être bien reproduites par le modèle global lorsque la mise à jour des émissions de feux de biomasse est incluse [90].

La variabilité saisonnière des concentrations du black carbon est bien simulée sur 3 sites du projet AMMA. Les principaux problèmes semblent être liés à une résolution grossière de la grille, ce qui ne permet pas une capture locale des gigantesques incendies et la modélisation de la poussière, qui il faudra encore travailler. Des sous-estimations similaires [169] sont également obtenues en utilisant le modèle régional RegCM3 mis en œuvre avec le même schéma que le modèle ORISAM-TM4 [90].

Un autre modèle développé dans le cadre du projet Analyse et prévision de l'impact des feux sur la qualité de l'air en Europe et Méditerranée (APIFLAME) permet de calculer de cadastres d'émissions à partir des feux détectés par satellite. Ce modèle est flexible en termes de domaine et de paramètres utilisés, et permet l'évaluation des émissions à haute résolution spatiale et temporelle, indispensables à la modélisation de leur impact sur la qualité de l'air. Ce modèle intègre les modèles de chimie de transport pour mieux représenter le transport des panaches.

L'intégration des émissions dans les modèles CHIMERE et Polyphemus pour deux cas d'étude (étés 2007 et 2010) a mis en évidence l'importance de cette source : les comparaisons aux observations de surface et satellitaires sont

significativement améliorées, ainsi que la capacité des modèles à reproduire les épisodes de pollution particulaire (dépassements de seuils). Cette source a été intégrée au système de prévision Prev'Air1 qui donne des prévisions de qualité de l'air diffusées quotidiennement [170].

II.4. Résultats du de l'étude de cas à Marseille

- ***Associations entre l'exposition aux émissions des feux de forêts et la santé***

Nous n'avons constaté qu'aucune association significative entre les données sanitaires et les émissions issues des incendies ($PM_{2.5}$) observée. Cependant, une association à la limite de la signification existait pour les consultations respiratoires aux lag 8 et lag 9. Une explication possible du manque de signification pourrait être de 2 ordres :

- Une concentration de $PM_{2.5}$ issue des incendies relativement faibles lors de la période de l'étude. Bien qu'il y ait eu des incendies sur toute la période de l'étude, seuls 2 pics importants de $PM_{2.5}$ issues des émissions de feux de forêts ont été observés (article 3). Ces 2 pics correspondaient à des concentrations autour de 70µg/m^3 sur une durée d'exposition très courte (moins de 2 jours d'exposition).

- La mobilité de la population: La période estivale est une période de vacances, la mobilité de la population (par exemple, la population à risque) pourrait donc réduire le nombre de sujets à risque lors de l'incident.

L'impact de la pollution atmosphérique dépend de plusieurs paramètres dont la durée d'exposition et la concentration des polluants [95]. Nous avons constaté que l'incendie de Marseille à l'été 2009 n'a duré que 2 jours et la concentration des $PM_{2.5}$ était à priori relativement faible pour causer des effets sanitaires. Ces résultats sont conformes à ceux obtenus par l'étude de l'INVS qui a été réalisée immédiatement après l'événement et qui n'avait pas obtenu de liens significatifs entre les incendies de Marseille de l'été 2009 et l'augmentation des effets sanitaires [171]. Toutefois, l'existence d'un lien potentiel entre les feux et la morbidité respiratoire sur un décalage de 8-9 jours (lag8 et lag9) va dans le sens d'un effet à plus long termes sur les voies aériennes.

- ***Le modèle utilisé pour l'estimation de l'impact sanitaire***

Pour étudier l'impact sanitaire des émissions de feux de forêts nous avons utilisé des méthodes d'analyse de séries temporelles et le modèle additif généralisé (GAM:Generalized Additif Model), développé par Hastie and Tibshirani [57] (article 3). L'événement sanitaire modélisé est un nombre de cas, qui se caractérise d'une part par un faible effectif journalier, et d'autre part par une sur-dispersion des valeurs observées. Nous avons utilisé ce modèle avec un modèle de retard échelonné pour tenir compte des décalages entre l'exposition et les effets sanitaires [172, 173]. Ce modèle a été utilisé dans plusieurs études épidémiologiques pour évaluer les associations à court terme entre l'exposition aux particules fines et les données sanitaires en particulier les hospitalisations pour cause de maladies respiratoires et cardiovasculaires [103, 120]. A notre connaissance, c'est la première fois que ce modèle a été utilisé pour évaluer les effets sanitaires de l'exposition aux particules fines issues des feux de forêts.

Dans notre analyse sur les données sanitaires recueillies à l'APHM, nous avons remarqué un manque d'une forte saisonnalité apparente visuellement dans l'analyse de séries chronologiques. L'analyse de sensibilité avec le modèle GAM et une spline de régression pénalisée a montré des différences avec les résultats obtenus avec la fonction natural spline mais a montré des tendances similaires. La fonction de réponse a été exprimé en risque relatif (RR), pour chaque augmentation de 10 unités dans tous les $PM_{2.5}$, et pour une augmentation d'une unité $PM_{2.5}$ [173].

II.5. Evaluation des polluants agricoles et leurs effets sur la santé : Mieux évaluer l'exposition individuelle

Dans cette étude, nous avons eu une estimation semi-individuelle de l'exposition aux COVs et PM au domicile des agriculteurs et dans leur lieu de travail. Pour les associations avec la santé, nous avons utilisé la concentration moyenne du domicile (salle de séjour), ainsi que la concentration moyenne à la ferme avec la salle de séjour, l'étable et la grange. L'utilisation d'une concentration moyenne nous paraissait appropriée car les mesures d'exposition ont été réalisées sur une courte période (une semaine), avec une faible variabilité sur les différentes

mesures. Cette approche n'aurait pu être valable si nous avions des fortes variabilités sur les mesures puisqu'il y aurait des moments ou l'exposition serait beaucoup plus forte et susceptible d'avoir un impact beaucoup plus fort que d'autres. De même, l'impact de l'exposition aurait été différent sur une longue période de mesure qui aurait prolongé la durée de l'exposition. Des associations significatives entre l'exposition dans la salle de séjour et les indicateurs de santé respiratoires ont été mises en évidence. Néanmoins, il est à signaler que les données des chambres à coucher n'étaient pas prises en compte car non exploitables et seules 19 et 33 fermes sur les 50 fermes étudiées, avaient des données disponibles respectivement sur les étables et la grange. De plus, même si la ferme constitue le domicile et le lieu de travail, le temps passé dans chaque activité et à domicile n'était pas pris en compte. Or l'exposition individuelle est une somme d'expositions caractérisées par la concentration en polluant et la durée passée par l'individu dans ce microenvironnement [95]. L'estimation de l'exposition individuelle nécessite donc de connaitre les activités de l'individu dans le temps et dans l'espace ainsi que les variations temporelles des concentrations en polluants dans les différents microenvironnements extérieurs et intérieurs [95]. Deux individus exposés à une même concentration de polluants dans leur logement mais passant un temps différent à l'intérieur de celui-ci pourraient donc subir un impact sanitaire différent [96].Des analyses supplémentaires sont donc nécessaires afin de prendre en compte cette dimension.

II.6. Implication de la pollution intérieure dans la santé respiratoire des enfants à la ferme: volet « enfant » de l'étude FERMA

Comme cela a été présenté précédemment, l'étude FERMA a été composée de 2 volets : un volet chez l'enfant réalisé en 2005 et un volet chez l'adulte dont nous avons présenté un partie des résultats dans la 3ème partie de ce manuscrit (article 4 et 5). Dans cette section, nous allons présenter un résumé des résultats de l'étude FERMA chez les enfants avec des comparaisons avec les enfants en ville. Deux études ont été réalisées pour comparer l'exposition des enfants en milieu rural par rapport à des enfants en ville : une étude transversale et une étude cas-témoins.

L'étude transversale [96] à l'école était constituée du questionnaire standardisé sur les maladies allergiques et respiratoires, du bilan médical effectué par un médecin et de mesures de pollution dans les classes et préaux. Au total, 357 enfants, correspondant aux critères d'inclusion (enfants d'agriculteurs et/ou en contact régulier avec les animaux d'élevage), ont été invités à participer à l'étude. 330 enfants (91%) ont répondu au questionnaire principal et 271 (76%) ont participé aux 2 phases du protocole (questionnaire principal et bilan médical). Ces 330 enfants issus du milieu rural de l'Auvergne ont été comparés à des enfants du milieu urbains. Des prévalences plus faibles de rhino-conjonctivite et de sensibilisation allergique ont pu être observées chez les enfants du milieu rural comparé à ceux du milieu urbain (8.0% vs. 11.6% et 15.4% vs. 28.1% respectivement). La qualité de l'air était meilleure à la campagne, avec des concentrations jusqu'à 6 fois plus faibles pour le dioxyde d'azote. Enfin, des prévalences plus fortes de ces pathologies ont pu être observées chez les enfants du milieu urbain exposés à de fortes concentrations de polluants en classes. Cette étude confirme les précédentes publications qui suggèrent un effet protecteur de l'environnement rural sur les maladies allergiques. De plus, elle met en évidence l'importance du transfert d'air de l'extérieur à l'intérieur des locaux en milieu urbain.

L'étude cas-témoin [158] nichée à domicile a été conduite selon les mêmes méthodes que celles menées en milieu urbain. Les mesures de pollution ont été réalisées pendant une semaine en ciblant les mêmes polluants : NO_2, $PM_{2.5}$, formaldéhyde composés organiques volatils ainsi qu'allergènes et endotoxines, par prélèvement de poussière. Les questionnaires sur les caractéristiques de l'habitat ont également été complétés par les habitants. Au final, la population d'étude était constituée de 51 enfants : 24 asthmatiques et 27 contrôles vivant dans les zones rurales avoisinantes de Clermont-Ferrand. Ces enfants ont été comparés à une autre population cas-témoins d'un milieu urbain constitué de 32 asthmatiques et 31 témoins. Les mêmes composés évalués à la campagne ont été évalués au domicile des enfants dans le milieu urbain dans les mêmes conditions pendant une semaine. Les résultats ont montré que les logements urbains ont été plus pollués que les zones rurales, avec des concentrations allant jusqu'à deux fois plus élevées. Dans l'ensemble de la population, l'exposition à l'acétaldéhyde et le toluène était significativement associée à un risque plus

élevé d'asthme. Dans la population urbaine, l'association avec du toluène était significative chez les enfants étudiés pendant l'hiver, et avec du toluène, xylène, éthylbenzène et lorsque les cas ont été limités aux seuls enfants asthmatiques. En milieu rural, une relation entre l'asthme et l'exposition au formaldéhyde a été observée (OR = 10,7, IC 95% 1,69 à 67,61). Ces résultats suggèrent que l'exposition quotidienne en continu aux polluants peut être impliquée dans l'asthme, même en cas de faible exposition, comme ce qui a été observé dans les zones rurales. Ces résultats pourraient également indiquer un effet spécifique de la pollution intérieure dans le milieu rural. En effet, dans l'Etude Ferma adulte, nous avons trouvé des résultats significatifs à l'intérieur avec d'autres COVs comme le benzène et le trichloréthylène, ce qui peut renforcer cette hypothèse. Cette étude a permis d'utiliser un biomarqueur spécifique pour le benzène, le l'acide S-phénylmercapturique urinaire (S-PMA), pour évaluer l'exposition individuelle de ce polluant chez les enfants.

II.7. La variabilité régionale en termes d'exposition aux polluants agricoles et les effets sanitaires

Nous avons comparé les agriculteurs français de l'Auvergne et californiens en termes d'exposition et l'occurrence des symptômes respiratoires pour analyser la variabilité régionale. Cette comparaison s'est basée sur 2 études qui ont été réalisées sur 2 périodes différentes. Nous avons observé que les agriculteurs français de l'Auvergne étaient plus à risque de développer de l'asthme, bronchite chronique et la toux par rapport à leurs homologues californiens qui eux étaient plus à risque à la rhinite allergique. Une précédente étude avait comparé les agriculteurs californiens à des agriculteurs Européens de 4 pays (Allemagne, Danemark, Espagne, Suisse) et des différences régionales ont été observées sur la prévalence de la rhinite allergique, l'asthme, la bronchite chronique et la pneumonie. L'asthme a été associé à l'élevage de la volaille et à la culture de fleurs tandis que la bronchite chronique semble être liée à élevage des porcs, des lapins, et la culture des graines qui produisent de l'huile et des fleurs. Cependant, la forte prévalence de l'asthme chez les agriculteurs californiens semble plus liée aux facteurs sociodémographiques qu'aux caractéristiques agricoles [127]. De même, cette étude avait montré qu'en Europe, la forte

prévalence de la bronchite chronique chez les agriculteurs était indépendante du tabac et semble plus lier aux facteurs agricoles en particuliers la production des animaux dans des espaces confinés ou des serres et l'exposition aux poussières d'intérieur. Ce qui met en lumière l'importance de l'exposition dans les lieux de travail à l'intérieur.

Dans cette étude, nous avons fait des comparaisons sur les pratiques agricoles, les facteurs environnementaux et les symptômes respiratoires sur deux périodes différentes dans deux régions de deux pays développés. Cette étude aurait pu nous donner une idée précise sur l'efficacité des méthodes mis en œuvre pour la protection des agriculteurs dans les pays développés Toutefois,, la variabilité géographique et la conception des deux études ne nous a pas permis de tester cette hypothèse.

II.8. Les points forts et les limites

II.8.1. Points forts

Revue de la littérature sur l'impact sanitaire des émissions de feux de forets

Dans la littérature, des études se sont intéressées à l'impact sanitaire des émissions de feux de forêts mais très peu de revues se sont exclusivement consacrées à ce sujet et à notre connaissance aucune n'était systématique. Dans la revue de la littérature que nous avons présentée, nous nous sommes intéressés exclusivement aux émissions des feux de forêts mais en se limitant aux effets non accidentels.

La revue des mesures d'exposition des émissions de feux de forets

Dans cette thèse, nous avons revu les méthodes utilisées dans la littérature pour évaluer l'impact sanitaire des émissions des feux de forêts ainsi que les incertitudes qui y sont associées. Les méthodes d'expositions utilisées sont de type macroscopique, certes puisque évaluent l'impact d'exposition dans la troposphère mais l'utilisation des coordonnées spatiales fournies par les données satellitaires permet d'avoir des émissions à proximité de la population et réduire les incertitudes au niveau de l'exposition. Nous avons utilisé cette technique pour réaliser l'inventaire des émissions de feux de forêts en Europe entre 2006-

2010 et pour la première pour étudier l'impact sanitaire d'un incendie dans le cadre d'une étude de type de cas.

Distinction entre émissions de feux de forêts et celles des autres sources de pollution

Pour l'étude de cas des incendies qui ont lieu à Marseille en 2009, nous avons utilisé de la modélisation pour différencier les émissions anthropiques des émissions issues des feux de forêt. Ce point est les principales sources d'incertitudes dans la plupart des études épidémiologiques puisque les émissions telles que les particules en suspension peuvent bien être émises par d'autres sources de pollution (industrielles, trafic routier. etc.). Cette distinction a permis de réduire l'incertitude au niveau de l'exposition. Dans notre étude, nous avons utilisé la distribution quasi-Poisson robuste pour estimer l'IC à 95% pour les PM, alors que dans d'autres études, ils ont utilisé la distribution de Poisson.

L'exposition en milieu agricole : la mesure à domicile et dans le lieu de travail

Alors que pour évaluer l'impact d'exposition aux émissions issues des feux de forêts nous avons utilisé une approche macroscopique, en milieu agricole rural nous avons utilisé des estimations semi-individuelles pour mesurer l'exposition aux polluants. L'usage des capteurs au domicile et dans les lieux de travail des agriculteurs nous a permis d'avoir la concentration des polluants auxquels les agriculteurs ont été exposés à un moment donné dans leur maison et dans leur lieu de travail. Même s'il s'a agi d'une estimation indirecte, la mise en relation de ces mesures d'exposition et les données sanitaires nous a permis d'évaluer l'impact de ces expositions dans la santé respiratoires des agriculteurs

L'utilisation d'un biomarqueur

L'utilisation de l'acide S-phénylmercapturique, un biomarqueur spécifique pour le benzène nous a permis de mieux évaluer l'exposition individuelle de ce polluant qui a été relié à la fois aux concentrations de benzène et à l'asthme. Ce biomarqueur nous a permis de confirmer l'effet du benzène sur l'asthme chez les enfants exposés. Nous avons aussi identifié au moins un biomarqueur qui pourrait être utilisé dans le cas de l'exposition à la combustion du bois.

II.8.2. Limites

Comme dans la plupart des études réalisées dans le cadre de la recherche scientifique, les travaux présentés dans cette thèse présentent des limites.

Dans la revue de la littérature que nous avons présentée, nous n'avons pris en compte que les effets non accidentels alors que les incendies de forêts sont connus aussi pour avoir des effets sanitaires accidentels et plus encore les effets psychologiques dont sont victimes les témoins de ces évènements tragiques en particuliers les enfants. Parmi les effets accidentels, il y a des effets aigus de type respiratoires, la fatalité due à l'intoxication ou à la prise au piège par les feux, les blessures ….etc parmi les pompiers, les habitants de proximité, les personnes fragiles telles que les personnes âgées, les enfants et les personnes ayant des problèmes respiratoires préexistantes (les asthmatiques…etc). Les travaux que nous avons présentés ici n'ont pas pris en compte les effets des feux de bois dans les pays en développement alors qu'on estime que plus de de 3 milliards d'individus (presque la moitié de l'humanité) utilise le bois comme source d'énergie. Les effets sanitaires d'une telle exposition chronique sont bien documentés.

Dans l'étude de l'impact entre les émissions de feux de forêts et la santé à Marseille, malgré le fait que nous ayons des données d'exposition au niveau local, nous n'avons pas réussi à avoir les données sanitaires de la population à proximité de l'évènement. Les données sanitaires de l'APHM couvrent une large population.

Dans la comparaison entre les agriculteurs français de la région d'Auvergne et californiens, les résultats ont été obtenu à partir d'une analyse transversale basée sur les résultats de 2 études épidémiologiques réalisées dans 2 période différentes. Le recrutement des agriculteurs Californiens a débuté en 1993 et l'étude s'est poursuivie jusqu'en 2004 alors que le recrutement de l'étude FERMA a eu lieu en 2009-2010. Les comparaisons ont porté sur la pratique agricole au moment de l'inclusion. La différence entre les 2 périodes d' inclusion est énorme et les pratiques agricoles pourraient être évoluées tout au long de cette période par la prise de conscience du danger de l'exposition en milieu agricole mais aussi par l'amélioration des techniques de production. Cependant, aucun changement majeur n'est intervenu dans la pratique de l'agriculture dans les décennies

considérées. Enfin, que ce soit dans l'étude FERMA ou FHS, les données sanitaires ont été recueillies à l'aide de questionnaires aux agriculteurs. Ce genre de questionnaires présente en général un biais de déclaration. Une autre limite à l'étude FERMA est que les agriculteurs français incus dans l'étude FERMA ne représente pas un échantillon représentatif de l'ensemble des agriculteurs français, alors que les agriculteurs du FHS ne représentent que ceux de la Californie et non l'ensemble des agriculteurs américains.

CONCLUSIONS

Ce travail de thèse nous a permis d'apporter de nouveaux éléments quant aux effets sanitaires associés à la pollution atmosphérique à l'intérieur qu'à l'extérieur dans des domaines dans lesquels les données faisaient défaut. L'analyse des différentes données épidémiologiques a permis de souligner la complexité de l'étude des effets de la pollution de l'air. Nous avions considéré trois niveaux d'expositions dans 2 contextes différents: une exposition aiguë à court terme et une évaluation macroscopique de l'exposition dans le cadre des émissions engendrées par les incendies de forêts, et une exposition chronique dans environnement professionnel et à domicile avec une mesure d'exposition semi-individuelle ou individuelle à l'aide d'un biomarqueur.

Tout d'abord nous avons cherché à s'imprégner sur l'état des connaissances sur l'étude de l'impact sanitaire des émissions de feux de forêts. Nous avons observé comme il a été décrit dans la littérature que lors des incendies de forêts, suivant les conditions métrologiques, le type de végétation et l'intensité des feux, certains polluants émis dépassaient largement le seuil de tolérance fixé par les autorités sanitaires [34-36, 61]. La plupart de ces polluants sont connus pour leurs effets sanitaires et leur rôle dans les maladies respiratoires et cardiovasculaires, à l'image des particules fines et des COVs [10]. Les études épidémiologiques ont établi des liens entre les émissions et les effets sanitaires et des associations ont été trouvées entre l'exposition aux émissions issues des incendies et les effets respiratoires, cardiovasculaires en termes d'augmentation des admissions à l'hôpital et dans les services d'urgence [43, 46, 49, 126], et même sur l'augmentation du taux de mortalité. Cependant, le plus grand défi à ces études est l'estimation de l'exposition. L'exposition étant macroscopique, l'estimation de l'exposition est indirecte et cela augmente l'incertitude sur l'évaluation de l'impact sanitaire de ces émissions d'autant plus que d'autres sources émissions contribuent à la pollution. Plusieurs études avec des séries temporelles ont permis d'analyser l'exposition à court terme comme c'est le cas lors des incendies avec les effets sanitaires en utilisant des modèles de retard échelonnés. Nous avons utilisé cette méthode pour évaluer l'impact sanitaire lors des incendies de Marseille. Dans notre étude aucun effet sanitaire n'a été observé entre les particules fines issues de feux et les données sanitaires. Cela

pourrait s'expliquer en partie par des concentrations de PM relativement faibles lors de la période de l'incendie. Même si le seuil de 25µg/m^3 des $PM_{2.5}$ a été dépassé lors des grands incendies de Marseille, l'absence d'effets significatifs sur la santé pourrait s'expliquer aussi par la courte période d'exposition. Néanmoins le fait de distinguer les PM des différentes sources d'émissions nous a permis de confirmé l'absence d'impact et éviter de conclure à tort les effets sanitaires des émissions de feux de forêts car sur cette période, les émissions anthropiques avaient un impact significatif sur l'augmentation du nombre de consultations dans les hôpitaux de l'APHM.

Nous avons également considéré une estimation semi-individuelle pour évaluer l'association entre l'exposition des polluants en milieu rural et l'occurrence des maladies respiratoires en particulier l'asthme et les maladies des petites voies aériennes. Nous avons travaillé particulièrement sur l'exposition avec les COV et les PM au domicile et dans les lieux de travail des agriculteurs de la région d'Auvergne. Cette étude nous a permis de constater que le benzène tout comme le trichloréthylène avaient des associations significatives avec l'asthme. En utilisant une approche d'analyse de multi pollution nous avons observé que les composés halogénés étaient associés significativement à l'asthme alors que les glycols éthers étaient associés aux maladies des petites voies aériennes. Il est à noter que les associations significatives avec les syndromes respiratoires étaient obtenues en considérant la pollution intérieure aux domiciles des agriculteurs. Alors que l'exposition dans les étables et les granges n'avaient donné de résultats significatifs contrairement à ce qui a été observé dans la littérature [174]. Ce résultat pourrait s'expliquer par un manque de puissance statistique car seuls 33 étables et 19 granges avaient des données disponibles.

Comme dans l'exposition macroscopique, l'exposition semi-individuelle ne permet qu'une estimation indirecte des polluants en milieu agricole. Pour confirmer ces résultats, il y a besoin d'avoir l'exposition individuelle. Plusieurs méthodes ont été développées pour mesurer l'exposition individuelle soit par des capteurs portatifs ou par mesure indirecte par des biomarqueurs. Dans le cadre d'une étude de type cas témoin nichée, l'utilisation d'un biomarqueur spécifique pour le benzène, l'acide S-phénylmercapturique, nous a permis de mieux évaluer l'exposition individuelle de ce polluant. D'autres études ont utilisé

l'hydroxypyrène un biomarqueur spécifique pour l'exposition au diesel [77] et les adduits de l'ADN du B[a]P, spécifique pour les HAP [78, 79].

En conclusion, la pollution atmosphérique constitue un problème majeur de sante publique qu'il ne faut plus négliger. Les résultats mis en évidence dans le cadre de notre travail montrent la diversité des polluants pouvant avoir des effets respiratoires, que l'exposition soit à court terme avec des concentrations élevées ou à long terme avec des concentrations faibles.

Les résultats obtenus dans l'étude des facteurs environnementaux en milieu agricole et l'apparition des maladies allergiques et respiratoires nous ont confirmé l'importance d'étudier la pollution intérieure même en milieu rural [158].

Une variabilité régionale en termes d'exposition, comme le montrent l'inventaire des feux établi en Europe ainsi que les mesures faites par nos soin dans des fermes en Auvergne, et d'apparition des symptômes a été observée. En revanche, la différence d'apparition des symptômes respiratoires chez des agriculteurs de 2 régions différentes ne peut être expliquée par les seules différences de pratique agricole, mais par le fait que d'autres facteurs, comme les données sociodémographiques ou l'usage de tabac, peuvent influencer l'augmentation de ces symptômes respiratoires d'une région à l'autre.

L'intérêt grandissant pour la pollution atmosphérique engendrée par les émissions de feux de forêts, que ce soit des chercheurs, des pouvoirs publics ou du grand public, est une opportunité à saisir afin de mettre en place des études de grande ampleur permettant de répondre aux nombreuses questions restant en suspens et de développer des outils pertinents permettant de mieux évaluer l'exposition à cette pollution et son impact sur la santé humaine. L'apport des nouvelles données issues des satellites sur la surveillance des incendies devrait permettre de cibler les actions à mener en termes de prévention et de règlementation et pouvoir ainsi limiter les expositions et protéger les populations. Les biomarqueurs et les remote sensors pourraient être une alternative crédible pour l'évaluation individuelle de l'exposition à certains polluants à l'intérieur des habitations afin de mieux évaluer les effets sanitaires. Une attention particulière doit être portée aux sous-groupes les plus vulnérables, afin de mieux les protéger des effets de cette pollution.

ANNEXES

Annexe 1 : Mesure de la qualité de l'air à la ferme

Annexe 3 : Fiche prélèvements environnementaux

Inserm
Institut national
de la santé et de la recherche médicale

MSA auvergne

FERMA

Facteurs Environnementaux du milieu Rural et Maladies Allergiques et respiratoires

Fiche Prélèvements environnementaux

Personne qui a pauser les cartouches :

☐ **Jean Claude Calard**

☐ **Franck Vibert**

☐ **Autre :**_____

Identifiant :_____

Date :___/____/____

Adresse : _____

_____

_____

Code postal :_____

Ville : _____

MAISON		
Cartouche 145 :		
Cartouche 165 :		
ETABLE		
Cartouche 145 :		
Cartouche 165 :		

20

Poussières		
Echantillons salon :		
Echantillon lit :		

COVs et aldéhydes

Cartouche 145 * (benzène, toluène, ethybenzène, m+p-xylènes, oxylène, styrène, 1,2,4 triméthylbenzène et autre hydrocarbures aromatiques C9, trichloréthylènes, tetrachloréthylène, 1,1,1-trichloroéthane, 1,4 dichlorobenzène, alphapinène, limonène, 2-méthylpentane, 3-méthylpentane, n-hexane et autre isomères, n-heptane et isomères, n-octane et isomères, n-nonane et isomères, n-décane et isomères, n-undécane et isomères, n-décane et isomères, n-undécane et isomère, n-dodecane et isomère, cyclohexane, 1- butanol, 2 éthyl-1- hexanol, 1 méthoxy-2-propanol, 2 éthoxy-éthanol, 2 éthoxyéthylacétate, 2 butoxy-éthanol, n-butyl, acétate, isopropylacétate, dimethydisulfure)
Cartouche 165** (formaldéhyde, acétaldéhyde, acroléine, propanal, butanal , benzaldéhyde ,isopentanal, pentenal, hexanal)

21

Tableau pour particules et poussières \ Aerocet 531

FERMA : Facteurs Environnementaux du milieu Rural et Maladies Allergiques et respiratoires. BPCO en milieu agricole.
Etude réalisée par le CHU de Clermond-Ferrand, l'INSERM et la MSA-Auvergne

Personne effectuant les mesures :

☐ **Jean Claude Calard**

☐ **Franck Vibert**

☐ **Autre :**_____

Date : _____

Heure : _____

Nom ou Code patient : _____

Adresse : _____

Rue : _____

Ville : _____

_____

Code postal :_____

MAISON

Lieux	Numéro de prise	heure	PM 1	PM 2.5	PM 7	PM 10	TSP
☐ Salon ☐ Cuisine ☐ Salle de bain ☐ Chambre parents ☐ Chambre enfant 1 ☐ Chambre enfant 2 ☐ Couloir		____h ___mn __s					
☐ Salon ☐ Cuisine ☐ Salle de bain ☐ Chambre parents ☐ Chambre enfant 1 ☐ Chambre enfant 2 ☐ Couloir		____h__ mn ___s					
☐ Salon ☐ Cuisine ☐ Salle de bain ☐ Chambre parents ☐ Chambre enfant 1 ☐ Chambre enfant 2 ☐ Couloir		___h ___ mn __s					

☐ Salon ☐ Cuisine ☐ Salle de bain ☐ Chambre parents ☐ Chambre enfant 1 ☐ Chambre enfant 2 ☐ Couloir							
Lieux							
☐ Salon ☐ Cuisine ☐ Salle de bain ☐ Chambre parents ☐ Chambre enfant 1 ☐ Chambre enfant 2 ☐ Couloir							
☐ Salon ☐ Cuisine ☐ Salle de bain ☐ Chambre parents ☐ Chambre enfant 1 ☐ Chambre enfant 2 ☐ Couloir		____h ___mn __s					
☐ Salon ☐ Cuisine ☐ Salle de bain ☐ Chambre parents ☐ Chambre enfant 1 ☐ Chambre enfant 2 ☐ Couloir							
☐ Salon ☐ Cuisine ☐ Salle de bain ☐ Chambre parents ☐ Chambre enfant 1 ☐ Chambre enfant 2 ☐ Couloir							
☐ Salon ☐ Cuisine ☐ Salle de bain ☐ Chambre parents ☐ Chambre enfant 1 ☐ Chambre enfant 2 ☐ Couloir							

☐ Salon ☐ Cuisine ☐ Salle de bain ☐ Chambre parents ☐ Chambre enfant 1 ☐ Chambre enfant 2 ☐ Couloir		___h ___ mn __s						
☐ Salon ☐ Cuisine ☐ Salle de bain ☐ Chambre parents ☐ Chambre enfant 1 ☐ Chambre enfant 2 ☐ Couloir		___h ___ mn __s						

MODE MASSE

☐ Salon ☐ Cuisine ☐ Salle de bain ☐ Chambre parents ☐ Chambre enfant 1 ☐ Chambre enfant 2 ☐ Couloir		____h ___mn __s					
☐ Salon ☐ Cuisine ☐ Salle de bain ☐ Chambre parents ☐ Chambre enfant 1 ☐ Chambre enfant 2 ☐ Couloir		____h ___mn __s					
☐ Salon ☐ Cuisine ☐ Salle de bain ☐ Chambre parents ☐ Chambre enfant 1 ☐ Chambre enfant 2 ☐ Couloir		____h ___mn __s					

MODE COMPTAGE

ETABLE

MODE MASSE

Lieux	Numéro de prise	heure	PM 1	PM 2.5	PM 7	PM 10	TSP
□ Etable		____h ___mn __s					

MODE COMPTAGE

Lieux	Numéro de prise	heure	PM 0,5 µ	PM 5,0 µ
□ Etable		____h ___mn __s		

Surface de l'étable
Hauteur (max) de l'étable
Décrire le lieu où les mesures sont faites (milieu étable, porte…)
Animaux sont dans l'étable
Si OUI ? COMBIEN

25

Tableau pour relève de particules / P-trak

FERMA : Facteurs Environnementaux du milieu Rural et Maladies Allergiques et respiratoires.
BPCO en milieu agricole.
Etude réalisée par le CHU de Clermont-Ferrand, l'INSERM et la MSA-Auvergne

Personne effectuant les mesures :

☐ **Jean Claude Calard**

☐ **Franck Vibert**

☐ **Autre :**_____

Date : _____

Heure : _____

Code patient :_____

Adresse :_____

Rue :_____

Ville :_____

Code postal :_____

MESURE CONCENTRATION PM

MAISON

Lieu	Num : test	Heure début	Heure de fin	H min / prv	H max/ prv	AVG
☐ Salon ☐ Cuisine ☐ Salle de bain ☐ Chambre parents ☐ Chambre enfant 1 ☐ Chambre enfant 2 ☐ Couloir		__h___ mn __s	__h__ mn__s	__h __mn __s Prélèvement …… pt/cc	__h__mn__s Prélèvement ……. pt/cc	Prélèvement …… pt/cc

☐ Salon ☐ Cuisine ☐ Salle de bain ☐ Chambre parents ☐ Chambre enfant 1 ☐ Chambre enfant 2 ☐ Couloir		__h ___mn __s	__h __mn __s	__h __mn __s Prélèvement …… pt/cc	_h __mn __s Prélèvement …… pt/cc	Prélèvement …… pt/cc
☐ Salon ☐ Cuisine ☐ Salle de bain ☐ Chambre parents ☐ Chambre enfant 1 ☐ Chambre enfant 2 ☐ Couloir		__h ___mn __s	_h __mn __s	___h__ mn __s Prélèvement …… pt/cc	__h ___mn __s Prélèvement …… pt/cc	Prélèvement …… pt/cc
☐ Salon ☐ Cuisine ☐ Salle de bain ☐ Chambre parents ☐ Chambre enfant 1 ☐ Chambre enfant 2 ☐ Couloir		__h ___mn __s	_h __mn __s	___h__ mn __s Prélèvement …… pt/cc	__h ___mn __s Prélèvement …… pt/cc	Prélèvement …… pt/cc
☐ Salon ☐ Cuisine ☐ Salle de bain ☐ Chambre parents ☐ Chambre enfant 1 ☐ Chambre enfant 2		__h___ mn __s	__h__ mn__s	__h __mn __s Prélèvement …… pt/cc	__h__mn__s Prélèvement …… pt/cc	Prélèvement …… pt/cc

☐ Couloir						
☐ Salon ☐ Cuisine ☐ Salle de bain ☐ Chambre parents ☐ Chambre enfant 1 ☐ Chambre enfant 2 ☐ Couloir		__h ___mn __s	__h __mn __s	__h __mn __s Prélèvement …….. pt/cc	_h __mn __s Prélèvement ……..pt/cc	Prélèvement …….. pt/cc

AVG : Average

☐ Salon ☐ Cuisine ☐ Salle de bain ☐ Chambre parents ☐ Chambre enfant 1 ☐ Chambre enfant 2 ☐ Couloir		__h ___mn __s	_h __mn __s	__h__ mn __s Prélèvement …….. pt/cc	_h __mn __s Prélèvement …….. pt/cc	Prélèvement …….. pt/cc

ETABLE

28

MODE MASSE

Lieux	Num : test	Heure début	Heure de fin	H min / prv	H max/ prv	AVG
☐ Etable	__h ___mn __s	_h __mn __s	__h__ mn __s Prélèvement ……. pt/cc	_h __mn __s Prélèvement ……. pt/cc	Prélèvement …… pt/cc	__h ___mn __s

29

BIBLIOGRAPHIE

BIBLOGRAPHIE DU MANUSCRIT

1. Lipfert, F.W., *A critical review of studies of the association between demands for hospital services and air pollution.* Environ Health Perspect, 1993. **101 Suppl 2**: p. 229-68.
2. Lisabeth, L.D., et al., *Ambient air pollution and risk for ischemic stroke and transient ischemic attack.* Ann Neurol, 2008. **64**(1): p. 53-9.
3. Dominici, F., et al., *Fine particulate air pollution and hospital admission for cardiovascular and respiratory diseases.* JAMA, 2006. **295**(10): p. 1127-34.
4. Touloumi, G., et al., *Short-term effects of air pollution on total and cardiovascular mortality: the confounding effect of influenza epidemics.* Epidemiology, 2005. **16**(1): p. 49-57.
5. Guo, Y.M., et al., *[Association between ambient temperature and hospital emergency room visits for cardiovascular diseases: a case-crossover study].* Zhonghua Liu Xing Bing Xue Za Zhi, 2009. **30**(8): p. 810-5.
6. Ito, K., et al., *Fine particulate matter constituents associated with cardiovascular hospitalizations and mortality in New York City.* Environ Health Perspect, 2011. **119**(4): p. 467-73.
7. *Les expositions aux agents biologiques dans le milieu de travail en 2003.* Première Synthèse Informations . Dares, 2006. **26.1**.
8. FLAMANT HULIN, M., *Pollution intérieure et santé respiratoire :Données issues des milieux urbain et rural*. 2010, Universite Pierre et Marie Curie.
9. Youssouf, H., et al., *Quantifying wildfires exposure for investigating health-related effects.* Atmospheric Environment, 2014. **97**(0): p. 239-251.
10. Malilay, J., *A Review of Factors Affecting the Human Health Impacts of Air Pollutants from Forest Fires*. 1999, World Health Orgnaization: Geneva, Switzerland/United Nations Environment Programme: Nairobi, Kenya/World Meteorological Organization:Geneva, Switzerland. p. 255-270.
11. Peel, J.L., et al., *Ambient air pollution and respiratory emergency department visits.* Epidemiology, 2005. **16**(2): p. 164-74.
12. Gyawali, M., et al., *In situ aerosol optics in Reno, NV, 5 USA during and after the summer 2008 California wildfires and the influence of absorbing and non-absorbing organic coatings on spectral light absorption.* Atmos. Chem. Phys., 2009. **9**: p. 8007–8015.
13. Li, P., et al., *Association between particulate matter and its chemical constituents of urban air pollution and daily mortality or morbidity in Beijing City.* Environ Sci Pollut Res Int, 2014.
14. Pope, C.A., et al., *Relationships Between Fine Particulate Air Pollution, Cardiometabolic Disorders and Cardiovascular Mortality.* Circ Res, 2014.
15. Xie, W., et al., *Relationship between fine particulate air pollution and ischaemic heart disease morbidity and mortality.* Heart, 2014.
16. Samoli, E., et al., *Acute effects of ambient particulate matter on mortality in Europe and North America: results from the APHENA study.* Environ Health Perspect, 2008. **116**(11): p. 1480-6.
17. World Health Organization, *Health effect of particulate matter. Policy implications for countries in eastern Europe, Caucasus and central Asia*. 2013.
18. Schwartz, J., F. Laden, and A. Zanobetti, *The concentration-response relation between PM(2.5) and daily deaths.* Environ Health Perspect, 2002. **110**(10): p. 1025-9.
19. Pope, C.A., 3rd, et al., *Lung cancer, cardiopulmonary mortality, and long-term exposure to fine particulate air pollution.* JAMA, 2002. **287**(9): p. 1132-41.
20. Gauderman, W.J., et al., *Childhood Asthma and Exposure to Traffic and Nitrogen Dioxide.* Epidemiology, 2005. **16**(6): p. 737-743 10.1097/01.ede.0000181308.51440.75.
21. Samet, J.M., et al., *Nitrogen dioxide and respiratory illnesses in infants.* Am Rev Respir Dis, 1993. **148**(5): p. 1258-65.
22. Organisation Mondiale de la Santé. *Qualité de l'air ambiant (extérieur) et santé*. 2014 Mars 2014 [cited 2014 13 novembre]; Available from: http://www.who.int/mediacentre/factsheets/fs313/fr/.
23. Holt, P.G., et al., *The role of allergy in the development of asthma.* Nature, 1999. **402**(6760 Suppl): p. B12-7.
24. Woodcock, A. and A. Custovic, *ABC of allergies. Avoiding exposure to indoor allergens.* BMJ, 1998. **316**(7137): p. 1075-8.

25. Annesi-Maesano, I. and W. Dab, *[Air pollution and the lung: epidemiological approach].* Med Sci (Paris), 2006. **22**(6-7): p. 589-94.
26. Granier, C., et al., *Evolution of anthropogenic and biomass burning emissions of air pollutants at global and regional scales during the 1980–2010 period.* Climatic Change, 2011. **109**(1-2): p. 163-190.
27. Schenker, M.B., et al., *Agricultural dust exposure and respiratory symptoms among California farm operators.* J Occup Environ Med, 2005. **47**(11): p. 1157-66.
28. Schenker, M., *Respiratory Health Hazards in Agriculture.* Respiratory and Critical Care Medicine, 1998. **158**(5): p. S1-S76.
29. Donham, K. and T. A., *Agricultural respiratory diseases*, in *Agricultural Medicine Occupational and Environmental Health for the Health Professions*. 2006, Blackwell Publishing: Victoria, Australia. p. 65-144.
30. Von Essen, S. and K. Donham, *Respiratory disease related to work in agriculture.*, in *Safety and Health in Agriculture, Forestry & Fisheries*, M.R. Langley RL, Meggs WJ, Roberson GT,, Editor. 1997, Government Institutes Inc: Rockville, MD
p. 353-384.
31. Tago, D., H. Andersson, and N. Treich, *Pesticides and health: a review of evidence on health effects, valuation of risks, and benefit-cost analysis.* Adv Health Econ Health Serv Res, 2014. **24**: p. 203-95.
32. Nieuwenhuijsen, M.J., H. Kruize, and M.B. Schenker, *Exposure to dust and its particle size distribution in California agriculture.* Am Ind Hyg Assoc J, 1998. **59**(1): p. 34-8.
33. Langley, R.L., *Consequences of respiratory exposures in the farm environment.* N C Med J, 2011. **72**(6): p. 477-80.
34. USEPA, *Wildfire Smoke: A Guide for Public Health Officials.* 2008.
35. WHO Regional Office for Europe, *Health risks of particulate matter from long-range transboundary air pollution*. 2006, European Centre for Environment and Health: Bonn, Germany.
36. WHO Regional Office for Europe, *Health effects of particulate matter*. 2013, WHO: Copenhagen, Denmark.
37. *Acute Effects of Bushfires on Respiratory Symptoms in Childr... : Epidemiology*. 2013/02/27/12:11:19; Available from: http://journals.lww.com/epidem/Fulltext/2003/09001/Acute_Effects_of_Bushfires_on_Respiratory_Symptoms.260.aspx
http://journals.lww.com/epidem/Abstract/2003/09001/Acute_Effects_of_Bushfires_on_Respiratory_Symptoms.260.aspx.
38. Emmanuel, S.C., *Impact to lung health of haze from forest fires: the Singapore experience.* Respirology (Carlton, Vic.), 2000. **5**(2): p. 175-182.
39. Moore, D., et al., *Population health effects of air quality changes due to forest fires in British Columbia in 2003: estimates from physician-visit billing data.* Canadian Journal of Public Health. Revue Canadienne De Santé Publique, 2006. **97**(2): p. 105-108.
40. Sillanpää, M., et al., *Chemical composition, mass size distribution and source analysis of long-range transported wildfire smokes in Helsinki.* The Science of the Total Environment, 2005. **350**(1-3): p. 119-135.
41. Brauer, M., *Health Impacts of Biomass Air pollution*. 1998: Kuala Lumpour, Malesia.
42. *Forest fire in Europe, Middle East and North Africa*. 2011, European Comission.
43. Delfino, R.J., et al., *The relationship of respiratory and cardiovascular hospital admissions to the southern California wildfires of 2003.* Occupational and Environmental Medicine, 2009. **66**(3): p. 189-197.
44. Henderson, S.B. and F.H. Johnston, *Measures of forest fire smoke exposure and their associations with respiratory health outcomes.* Curr Opin Allergy Clin Immunol, 2012. **12**(3): p. 221-7.
45. Jalaludin, B., et al., *Acute effects of bushfires on peak expiratory flow rates in children with wheeze: a time series analysis.* Australian and New Zealand Journal of Public Health, 2000. **24**(2): p. 174-177.
46. Künzli, N., et al., *Health effects of the 2003 Southern California wildfires on children.* American Journal of Respiratory and Critical Care Medicine, 2006. **174**(11): p. 1221-1228.
47. Mirabelli, M.C., et al., *Respiratory symptoms following wildfire smoke exposure: airway size as a susceptibility factor.* Epidemiology (Cambridge, Mass.), 2009. **20**(3): p. 451-459.
48. Naeher, L.P., et al., *Woodsmoke health effects: a review.* Inhalation Toxicology, 2007. **19**(1): p. 67-106.

49. Rappold, A.G., et al., *Peat bog wildfire smoke exposure in rural North Carolina is associated with cardiopulmonary emergency department visits assessed through syndromic surveillance.* Environmental Health Perspectives, 2011. **119**(10): p. 1415-1420.
50. Calabrese, S. and W. D'Alessandro, *Characterization of the Etna volcanic emissions through an active biomonitoring technique (moss-bags): Part 2 - Morphological and mineralogical features.* Chemosphere, 2014.
51. Garrison, V.H., et al., *Inhalable desert dust, urban emissions, and potentially biotoxic metals in urban Saharan-Sahelian air.* Sci Total Environ, 2014. **500-501C**: p. 383-394.
52. Johnston, F.H., et al., *Vegetation fires, particulate air pollution and asthma: A panel study in the Australian monsoon tropics.* International Journal of Environmental Health Research, 2006. **16**(6): p. 391-404.
53. Merchant, J.A., *Agricultural exposures to organic dusts.* Occup Med, 1987. **2**(2): p. 409-25.
54. Kirkhorn, S.R. and V.F. Garry, *Agricultural lung diseases.* Environ Health Perspect, 2000. **108 Suppl 4**: p. 705-12.
55. Dalphin, J.C., *[Respiratory pathology in the agricultural environment].* Rev Prat, 1998. **48**(12): p. 1313-8.
56. European Commission, *Forest Fires in Europe 2010*. Institute for Environment and Sustainability: Ispra (VA) Italy.
57. Hastie, T. and T. R., *Generalized Additive Models, no. 43 in Monographs on Statistics and Applied Probability*. 1990, London: Chapman&Hall.
58. Bubach, D., L. Dufou, and S.P. Catan, *Evaluation of dispersal volcanic products of recent events in lichens in environmental gradient, Nahuel Huapi National Park, Argentina.* Environ Monit Assess, 2014. **186**(8): p. 4997-5007.
59. Host, S., E. Chatignoux, and I. Grémy, *Pollution atmosphérique de proximité liée au trafic : expositions et effets sanitaires. Observatoire régional de santé d'Ile-de-France, Decembre 2009.*
60. Cuoco, E., et al., *Impact of volcanic plume emissions on rain water chemistry during the January 2010 Nyamuragira eruptive event: implications for essential potable water resources.* J Hazard Mater, 2013. **244-245**: p. 570-81.
61. U.S. Environmental Protection Agency, *National Ambient Air Quality Standards for Particulate Matter.* Federal Register, 2013. **78**(10): p. 3086-3287.
62. Connan, O., et al., *Comparison of RIMPUFF, HYSPLIT, ADMS atmospheric dispersion model outputs, using emergency response procedures, with (85)Kr measurements made in the vicinity of nuclear reprocessing plant.* J Environ Radioact, 2013. **124**: p. 266-77.
63. Hung, N.T., et al., *Air pollution modeling at road sides using the operational street pollution model--a case study in Hanoi, Vietnam.* J Air Waste Manag Assoc, 2010. **60**(11): p. 1315-26.
64. Wu, J., et al., *Comparing exposure assessment methods for traffic-related air pollution in an adverse pregnancy outcome study.* Environ Res, 2011. **111**(5): p. 685-92.
65. Wang, D. and S. Song, *Robust model-based sensor fault monitoring system for nonlinear systems in sensor networks.* Sensors (Basel), 2014. **14**(10): p. 19138-61.
66. Al-Saadi, J., et al., *Improving National Air Quality Forecasts with Satellite Aerosol Observations.* Bulletin of the American Meteorological Society, 2005. **86**(9): p. 1249-1261.
67. Valari, M., L. Menut, and E. Chatignoux, *Using a chemistry transport model to account for the spatial variability of exposure concentrations in epidemiologic air pollution studies.* J Air Waste Manag Assoc, 2011. **61**(2): p. 164-79.
68. AirParif, *Caractérisation de l'exposition personnelle d'un échantillon de franciliens*. 2008.
69. Martins, P.C., et al., *Airways changes related to air pollution exposure in wheezing children.* Eur Respir J, 2012. **39**(2): p. 246-53.
70. Clark, M., et al., *Urinary methoxyphenol biomarkers and woodsmoke exposure: comparisons in rural Guatemala with personal CO and kitchen CO, levoglucosan, and PM2.5.* Environ Sci Technol, 2007. **41**(10): p. 3481-7.
71. Dills, R.L., et al., *Evaluation of urinary methoxyphenols as biomarkers of woodsmoke exposure.* Environ Sci Technol, 2006. **40**(7): p. 2163-70.
72. Migliaccio, C.T., et al., *Urinary levoglucosan as a biomarker of wood smoke exposure: observations in a mouse model and in children.* Environ Health Perspect, 2009. **117**(1): p. 74-9.
73. Engling, G., et al., *Determination of levoglucosan in biomass combustion aerosol by high-performance anion-exchange chromatography with pulsed amperometric detection.* Atmospheric Environment, 2006. **40, Supplement 2**(0): p. 299-311.
74. Fraser MP and L. K., *Using levoglucosan as a molecular marker for the long-range transport of biomass combustion aerosols.* Environ Eng Sci 2000. **34**(21): p. 4560–4564.

75. Simoneit RRT, et al., *Levoglucosan, a tracer for cellulose in biomass burning and atmospheric particles.* Atmos Environ, 1999. **33**(2): p. 173-182.
76. Rive, S., et al., *Urinary S-PMA related to indoor benzene and asthma in children.* Inhal Toxicol, 2013. **25**(7): p. 373-82.
77. Northridge, M.E., et al., *Diesel exhaust exposure among adolescents in Harlem: a community-driven study.* Am J Public Health, 1999. **89**(7): p. 998-1002.
78. Marie, C., et al. *Cinétiques de formation et de réparation des adduits de l'ADN du benzo[a]pyrène*. Bulletin d'Information en Santé Environnementale 2008; Available from: http://www.inspq.qc.ca/bise/post/2008/11/01/Cinetiques-de-formation-et-de-reparation-des-adduits-de-le28099ADN-du-benzoapyrene.aspx.
79. Perera, F.P., et al., *A summary of recent findings on birth outcomes and developmental effects of prenatal ETS, PAH, and pesticide exposures.* Neurotoxicology, 2005. **26**(4): p. 573-87.
80. Thelen, B., et al., *Modeling acute respiratory illness during the 2007 San Diego wildland fires using a coupled emissions-transport system and generalized additive modeling.* Environ Health, 2013. **12**: p. 94.
81. Pausas, J.G. and J.E. Keeley, *A Burning Story: The Role of Fire in the History of Life.* BioScience, 2009. **59**(7): p. 593-601.
82. Soteriades, E.S., et al., *Cardiovascular disease in US firefighters: a systematic review.* Cardiol Rev, 2011. **19**(4): p. 202-15.
83. Yang, J., et al., *Sudden cardiac death among firefighters </=45 years of age in the United States.* Am J Cardiol, 2013. **112**(12): p. 1962-7.
84. Gomez-Rey, M.X. and S.J. Gonzalez-Prieto, *Short and medium-term effects of a wildfire and two emergency stabilization treatments on the availability of macronutrients and trace elements in topsoil.* Sci Total Environ, 2014. **493C**: p. 251-261.
85. Certini, G., *Effects of fire on properties of forest soils: a review.* Oecologia, 2005. **143**(1): p. 1-10.
86. Ottmar, R.D., *Smoke source characteristics*, in *Smoke Management Guide for Prescribed and Wildland Fire*, R.D.P. C.C.O. Hardy, Janice L.; Core, John E.; Seamon, Paula, Editor. 2001, National Wildfire Coordinating Group, Fire Use Working Team: Boise. p. 89-105.
87. Goldammer, J.G., M. Statheropoulos, and M.O. Andreae, *Chapter 1 Impacts of Vegetation Fire Emissions on the Environment, Human Health, and Security: A Global Perspective*, M.A. A. Bytnerowicz, A. Riebau and C. Andersen, Editor. 2009, Developments in Environmental Science.
88. Statheropoulos, M. and S. Karma, *Complexity and origin of the smoke components as measured near the flame-front of a real forest fire incident: A case study.* Journal of Analytical and Applied Pyrolysis, 2007. **78**(2): p. 430-437.
89. Ottmar, R.D., *Smoke source characteristics*, in *Smoke Management Guide for Prescribed and Wildland Fire: 2001 Edition*, C.C.O. Hardy, Roger D.; Peterson, Janice L.; Core, John E.; Seamon, Paula, Editor. 2001: National Wildfire Coordinating Group, Fire Use Working Team. Boise, ID. p. 89-105.
90. Liousse, C., et al., *Updated African biomass burning emission inventories in the framework of the AMMA-IDAF program, with an evaluation of combustion aerosols.* Atmos. Chem. Phys., 2010. **10**(19): p. 9631-9646.
91. Ndedy Dicka, H., H. Saint Obert, and J. Triquet, *Projet d'évaluation des risques sanitaires, feux de biomasse. Ingénieur du Genie Sanitaire, promotion 2010-2011 EHESP*.
92. *Réduction des émissions des composés organiques volatils (COV)*. 10 mars 2011 [cited 2014 10 Octobre]; Available from: http://www.developpement-durable.gouv.fr/Reduction-des-emissions-des.html.
93. Caamano-Isorna, F., et al., *Respiratory and mental health effects of wildfires: an ecological study in Galician municipalities (north-west Spain).* Environmental Health, 2011. **10, doi:10.1186/1476-069X-10-48**.
94. Fayard, G.M., *Fatal work injuries involving natural disasters, 1992-2006.* Disaster Med Public Health Prep, 2009. **3**(4): p. 201-9.
95. Zou, B., et al., *Air pollution exposure assessment methods utilized in epidemiological studies.* J Environ Monit, 2009. **11**(3): p. 475-90.
96. FLAMANT HULIN, M., *Pollution intérieure et santé respiratoire : Données issues des milieux urbain et rural*. 2010, UPMC.
97. Cameron, P.A., et al., *Black Saturday: the immediate impact of the February 2009 bushfires in Victoria, Australia.* The Medical journal of Australia, 2009. **191**(1): p. 11-16.
98. Cameron, P.A., et al., *Black Saturday: the immediate impact of the February 2009 bushfires in Victoria, Australia.* Med J Aust, 2009. **191**(1): p. 11-6.

99. McFarlane, A.C., *Relationship between psychiatric impairment and a natural disaster: the role of distress.* Psychological medicine, 1988. **18**(1): p. 129-139.
100. McFarlane, A.C., J.R. Clayer, and C.L. Bookless, *Psychiatric morbidity following a natural disaster: an Australian bushfire.* Social psychiatry and psychiatric epidemiology, 1997. **32**(5): p. 261-268.
101. McFarlane, A.C. and M. Van Hooff, *Impact of childhood exposure to a natural disaster on adult mental health: 20-year longitudinal follow-up study.* The British Journal of Psychiatry: The Journal of Mental Science, 2009. **195**(2): p. 142-148.
102. Yelland, C., et al., *Bushfire impact on youth.* Journal of Traumatic Stress, 2010. **23**(2): p. 274-277.
103. Kim, S.-Y., et al., *The temporal lag structure of short-term associations of fine particulate matter chemical constituents and cardiovascular and respiratory hospitalizations.* Environmental health perspectives, 2012. **120**(8): p. 1094-1099.
104. Dominici, F., et al., *On the use of generalized additive models in time-series studies of air pollution and health.* Am J Epidemiol, 2002. **156**(3): p. 193-203.
105. Zanobetti, A., et al., *Generalized additive distributed lag models: quantifying mortality displacement.* Biostatistics (Oxford, England), 2000. **1**(3): p. 279-292.
106. *Revised Analyses of Time-Series Studies of Air Pollution and Health*. 2003, HE A LTH EFFECTS INSTITUTE.
107. Metzger, K.B., et al., *Ambient air pollution and cardiovascular emergency department visits.* Epidemiology, 2004. **15**(1): p. 46-56.
108. Giorgi, F. and R.O. Anyah, *INTRODUCTIONThe road towards RegCM4.* Climate Research, 2012. **52**: p. 3-6.
109. Solmon, F., F. Giorgi, and C. Liousse, *Aerosol modelling for regional climate studies: application to anthropogenic particles and evaluation over a European/African domain.* Tellus B, 2006. **58**(1): p. 51-72.
110. Tummon, F., et al., *Simulation of the direct and semidirect aerosol effects on the southern Africa regional climate during the biomass burning season.* Journal of Geophysical Research: Atmospheres, 2010. **115**(D19): p. n/a-n/a.
111. Kok, J.F., *A scaling theory for the size distribution of emitted dust aerosols suggests climate models underestimate the size of the global dust cycle.* Proc Natl Acad Sci U S A, 2011. **108**(3): p. 1016-21.
112. Laurent, B., et al., *Modeling mineral dust emissions from the Sahara desert using new surface properties and soil database.* J. Geophys. Res., 2008. **113**: p. D14218.
113. Gong, S.L., L.A. Barrie, and J.-P. Blanchet, *Modeling sea-salt aerosols in the atmosphere 1. model development.* J. Geophys. Res., 1997. **102**(D3): p. 3805–3818.
114. Monahan, E.G., D.E. Spiel, and K.L. Davidson, *A model of marine aerosol generation via whitecaps and wave disruption, in Oceanic Whitecaps*, E.a.N. Monahan, G. M.,, Editor. 1986., D. Reidel: Norwell, MA, USA. p. 167–174.
115. Puxbaum, H., et al., *A dual site study of PM2.5 and PM10 aerosol chemistry in the larger region of Vienna, Austria.* Atmospheric Environment, 2004. **38**(24): p. 3949-3958.
116. Kaiser, J.W., et al., *Biomass burning emissions estimated with a global fire assimilation system based on observed fire radiative power.* Biogeosciences, 2012. **9**(1): p. 527-554.
117. Fraga, J., et al., *The lag structure and the general effect of ozone exposure on pediatric respiratory morbidity.* Int J Environ Res Public Health, 2011. **8**(10): p. 4013-24.
118. Hardin, J. and J. Hilbe, *Generalized Linear Models and Extensions; Stata Corporation*. 2011: College Station, TX, USA.
119. Wood, S. *Package 'mgcv'*. 2014 March, 31, 2014 [cited 2014 April, 01/2014].
120. Braga, A.L., A. Zanobetti, and J. Schwartz, *The lag structure between particulate air pollution and respiratory and cardiovascular deaths in 10 US cities.* Journal of occupational and environmental medicine / American College of Occupational and Environmental Medicine, 2001. **43**(11): p. 927-933.
121. Dominici, F., et al., *Does the effect of PM10 on mortality depend on PM nickel and vanadium content? A reanalysis of the NMMAPS data.* Environmental health perspectives, 2007. **115**(12): p. 1701-1703.
122. Hajat, S., et al., *Outdoor air pollution and infant mortality: analysis of daily time-series data in 10 English cities.* J Epidemiol Community Health, 2007. **61**(8): p. 719-22.
123. Zanobetti, A., et al., *The temporal pattern of mortality responses to air pollution: a multicity assessment of mortality displacement.* Epidemiology, 2002. **13**(1): p. 87-93.
124. USEPA, *National Ambient Air Quality Standards for Particulate Matter*. January 15, 2013. p. 3086-3287.

125. Hejl, A.M., et al., *Inflammatory effects of woodsmoke exposure among wildland firefighters working at prescribed burns at the Savannah River Site, SC.* J Occup Environ Hyg, 2013. **10**(4): p. 173-80.
126. Morgan, G., et al., *Effects of Bushfire Smoke on Daily Mortality and Hospital Admissions in Sydney, Australia.* Epidemiology, 2010. **21**(1): p. 47-55.
127. Monso, E., et al., *Region-related risk factors for respiratory symptoms in European and Californian farmers.* Eur Respir J, 2003. **21**(2): p. 323-31.
128. WHO. *Pollution de l'air à l'intérieur des habitations et la santé*. 2014 Mars 2014 [cited 2014 15 octobre]; Available from: http://www.who.int/mediacentre/factsheets/fs292/fr/.
129. ANSES. *Mesure de l´exposition individuelle à la pollution atmosphérique : premiers résultats sur un échantillon de Franciliens*. 2008 24 mars 2008 [cited 2014 15 Octobre]; Available from: http://www.afssa.fr/ET/PPN8A28.htm?pageid=452&newsid=315&MDLCODE=news.
130. Li, H., et al., *Chromatographic determination of 1, 4-beta-xylooligosaccharides of different chain lengths to follow xylan deconstruction in biomass conversion.* J Ind Microbiol Biotechnol, 2013. **40**(6): p. 551-9.
131. Sarigiannis, D., et al., *Total exposure to airborne particulate matter in cities: the effect of biomass combustion.* Sci Total Environ, 2014. **493**: p. 795-805.
132. Hoppin, J.A., et al., *Pesticide use and adult-onset asthma among male farmers in the Agricultural Health Study.* Eur Respir J, 2009. **34**(6): p. 1296-303.
133. Hoppin, J.A., et al., *Pesticides and adult respiratory outcomes in the agricultural health study.* Ann N Y Acad Sci, 2006. **1076**: p. 343-54.
134. VALARI, M., *Modélisation de la pollution atmosphérique urbaine et impact sur la santé*, in *Laboratoire de Météorologie Dynamique de l'Institut Pierre-Simon Laplace*. 2009, Ecole Polytechnique.
135. Kundu, S. and E.A. Stone, *Composition and sources of fine particulate matter across urban and rural sites in the Midwestern United States.* Environ Sci Process Impacts, 2014. **16**(6): p. 1360-70.
136. Ministère de l'agriculture, *Qualité architecturale des bâtiments agricoles*. 2003: Paris.
137. Schenker, M.B., M.R. Orenstein, and S.J. Samuels, *Use of protective equipment among California farmers.* Am J Ind Med, 2002. **42**(5): p. 455-64.
138. *University of California, Davis Farmer Health Study*. 2009 15 septembre 2009 [cited 2014 16 octobre]; Available from: http://agcenter.ucdavis.edu/research/FHS/home.php.
139. Eduard, W., N. Pearce, and J. Douwes, *Chronic bronchitis, COPD, and lung function in farmers: the role of biological agents.* Chest, 2009. **136**(3): p. 716-25.
140. Society, A.T., *Respiratory Health Hazards in Agriculture.* Am J Respir and Crit Care Med, 1998. **158(suppl)**: p. S1-S76.
141. Schenker, M.B., et al., *Pneumoconiosis from agricultural dust exposure among young California farmworkers.* Environ Health Perspect, 2009. **117**(6): p. 988-94.
142. Myers, M., *Health problems and disease patterns in agriculture.* ILO Encyclopedia of Occupational Health and Safety, 1998. **3**(64): p. 60-65.
143. Sullivan, J.B., et al., *Health-related hazards of agriculture. in Hazardous Materials Toxicology: Health Chemical Principles of Environmental* 1992.
144. Ni, J.Q., et al., *Volatile organic compounds at swine facilities: a critical review.* Chemosphere, 2012. **89**(7): p. 769-88.
145. Arif, A.A. and S.M. Shah, *Association between personal exposure to volatile organic compounds and asthma among US adult population.* Int Arch Occup Environ Health, 2007. **80**(8): p. 711-9.
146. Billionnet, C., et al., *Quantitative assessments of indoor air pollution and respiratory health in a population-based sample of French dwellings.* Environ Res, 2011. **111**(3): p. 425-34.
147. Ciganek, M. and J. Neca, *Chemical characterization of volatile organic compounds on animal farms.* Veterinarni Medicina, 2008. **53**: p. 641-651.
148. Bentayeb, M., et al., *Higher prevalence of breathlessness in elderly exposed to indoor aldehydes and VOCs in a representative sample of French dwellings.* Respir Med, 2013. **107**(10): p. 1598-607.
149. Rumchev, K., et al., *Association of domestic exposure to volatile organic compounds with asthma in young children.* Thorax, 2004. **59**(9): p. 746-51.
150. Delfino, R.J., et al., *Asthma symptoms in Hispanic children and daily ambient exposures to toxic and criteria air pollutants.* Environ Health Perspect, 2003. **111**(4): p. 647-56.
151. Penard-Morand, C., et al., *Long-term exposure to close-proximity air pollution and asthma and allergies in urban children.* Eur Respir J, 2010. **36**(1): p. 33-40.

152. Zar, H.J. and T.W. Ferkol, *The global burden of respiratory disease-Impact on child health.* Pediatr Pulmonol, 2014.
153. Annesi-Maesano, I., et al., *Time trends in prevalence and severity of childhood asthma and allergies from 1995 to 2002 in France.* Allergy, 2009. **64**(5): p. 798-800.
154. Mitha, N., et al., *[Indoor air quality and adult asthma].* Rev Mal Respir, 2013. **30**(5): p. 374-413.
155. Schernhammer, E.S., et al., *Time trends of the prevalence of asthma and allergic disease in Austrian children.* Pediatr Allergy Immunol, 2008. **19**(2): p. 125-31.
156. Chen, H.H., et al., *Effects of trichloroethylene and perchloroethylene on muscle contractile responses and epithelial prostaglandin release and acetylcholinesterase activity in swine trachea.* Toxicol Sci, 2005. **83**(1): p. 149-54.
157. Blair, A., et al., *Mortality and cancer incidence of aircraft maintenance workers exposed to trichloroethylene and other organic solvents and chemicals: extended follow up.* Occup Environ Med, 1998. **55**(3): p. 161-71.
158. Hulin, M., D. Caillaud, and I. Annesi-Maesano, *Indoor air pollution and childhood asthma: variations between urban and rural areas.* Indoor Air, 2010. **20**(6): p. 502-14.
159. Norback, D., et al., *Asthmatic symptoms and volatile organic compounds, formaldehyde, and carbon dioxide in dwellings.* Occup Environ Med, 1995. **52**(6): p. 388-95.
160. Churg, A., et al., *Chronic exposure to high levels of particulate air pollution and small airway remodeling.* Environ Health Perspect, 2003. **111**(5): p. 714-8.
161. McGauran, N., et al., *Reporting bias in medical research - a narrative review.* Trials, 2010. **11**: p. 37.
162. Vedal, S. and S.J. Dutton, *Wildfire air pollution and daily mortality in a large urban area.* Environmental Research, 2006. **102**(1): p. 29-35.
163. Hanninen, O., *Challenges in estimating the health effects of biomass smoke--response to Sverre Vedal and Steven J. Dutton: Wildfire air pollution and daily mortality in a large urban area.* Environ Res, 2008. **106**(3): p. 423-4; discussion 425.
164. Johnston, F., et al., *Extreme air pollution events from bushfires and dust storms and their association with mortality in Sydney, Australia 1994–2007.* Environmental Research, 2011. **111**(6): p. 811-816.
165. Johnston, F.H., et al., *Estimated global mortality attributable to smoke from landscape fires.* Environmental health perspectives, 2012. **120**(5): p. 695-701.
166. Sastry, N., *Forest fires, air pollution, and mortality in southeast Asia.* Demography, 2002. **39**(1): p. 1-23.
167. Engel-Cox, J.A., et al., *Qualitative and quantitative evaluation of MODIS satellite sensor data for regional and urban scale air quality.* Atmospheric Environment, 2004. **38**(16): p. 2495-2509.
168. Stroppiana, D., et al., *Comparison of global inventories of CO emissions from biomass burning derived from remotely sensed data.* Atmos. Chem. Phys., 2010. **10**(24): p. 12173-12189.
169. Malavelle, F., et al. *Regional radiative impacts of mixed dust and carbonaceous aerosols over West Africa during AMMA experiment*. in *3rd international AMMA conference,* . July 2009. Ouagadougou,.
170. Turquety, S., et al., *Analyse et prévision de l'impact des feux sur la qualité de l'air en Europe et Méditerranée (APIFLAME)* 2013.
171. INVS, *Feux de forêts: Marseille, Carpiagne.* Le point épidémio, 2009.
172. Gasparrini, A., *Distributed Lag Linear and Non-Linear Models in R: The Package dlnm.* J Stat Softw, 2011. **43**(8): p. 1-20.
173. Gasparrini, A. and B. Armstrong, *Distributed lag non-linear models: the R the package dlnm. London School of Hygiene and Tropical Medecine. UK. dnlm version 1.6.7; 2013-05-16.*
174. Guillam, M.T., et al., *Chronic respiratory symptoms of poultry farmers and model-based estimates of long-term dust exposure.* Ann Agric Environ Med, 2013. **20**(2): p. 307-11.

BIBLOGRAPHIE DES ARTICLES PUBLIES

- Adetona, O., et al., Personal PM (2.5) exposure among wildland firefighters working at prescribed forest burns in southeastern United States. Journal of Occupational and Environmental Hygiene, 2011. 8(8): p. 503-511.
- Aditama, T.Y., Impact of haze from forest fire to respiratory health: Indonesian experience. Respirology (Carlton, Vic.), 2000. 5(2): p. 169-174.
- Afifi, W.A., E.D. Felix, and T.D. Afifi, The impact of uncertainty and communal coping on mental health following natural disasters. Anxiety, Stress, and Coping, 2011.
- Aisbett, B., et al., Fighting with fire--how bushfire suppression can impact on fire fighters' health. Australian Family Physician, 2007. 36(12): p. 994-997.
- Aisbett, B., et al., "Awake, smoky, and hot": Providing an evidence-base for managing the risks associated with occupational stressors encountered by wildland firefighters. Applied Ergonomics, 2012.
- Aldersley, A., S.J. Murray, and S.E. Cornell, Global and regional analysis of climate and human drivers of wildfire. The Science of the Total Environment, 2011. 409(18): p. 3472-3481.
- Allen, R.W., et al., An air filter intervention study of endothelial function among healthy adults in a woodsmoke-impacted community. Am J Respir Crit Care Med, 2011. 183(9): p. 1222-30.
- Al-Saadi, J., et al., Improving National Air Quality Forecasts with Satellite Aerosol Observations. Bulletin of the American Meteorological Society, 2005. 86(9): p. 1249-1261.
- Alston, E.J., I.N. Sokolik, and B.G. Doddridge, Investigation into the use of satellite data in aiding characterization of particulate air quality in the Atlanta, Georgia metropolitan area. Journal of the Air & Waste Management Association (1995), 2011. 61(2): p. 211-225.
- Alves, C.A., et al., Emission of trace gases and organic components in smoke particles from a wildfire in a mixed-evergreen forest in Portugal. The Science of the Total Environment, 2011. 409(8): p. 1466-1475.
- Analitis, A., I. Georgiadis, and K. Katsouyanni, Forest fires are associated with elevated mortality in a dense urban setting. Occupational and Environmental Medicine, 2011.
- Annesi-Maesano, I., et al., Time trends in prevalence and severity of childhood asthma and allergies from 1995 to 2002 in France. Allergy, 2009. 64(5): p. 798-800.
- Arbex, M.A., et al., Air pollution from biomass burning and asthma hospital admissions in a sugar cane plantation area in Brazil. Journal of Epidemiology and Community Health, 2007. 61(5): p. 395-400.
- Arbex, M.A., et al., Impact of outdoor biomass air pollution on hypertension hospital admissions. Journal of epidemiology and community health, 2010. 64(7): p. 573-579.
- Arif, A.A. and S.M. Shah, Association between personal exposure to volatile organic compounds and asthma among US adult population. Int Arch Occup Environ Health, 2007. 80(8): p. 711-9.
- Baldi, I., et al., Agricultural exposure and asthma risk in the AGRICAN French cohort. Int J Hyg Environ Health, 2013.

- Bentayeb, M., et al., Higher prevalence of breathlessness in elderly exposed to indoor aldehydes and VOCs in a representative sample of French dwellings. Respir Med, 2013. 107(10): p. 1598-607.
- Bessagnet, B., et al., Regional modeling of carbonaceous aerosols over Europe—focus on secondary organic aerosols. Journal of Atmospheric Chemistry, 2008. 61(3): p. 175-202.
- Betchley, C., et al., Pulmonary function and respiratory symptoms in forest firefighters. American Journal of Industrial Medicine, 1997. 31(5): p. 503-509.
- Billionnet, C., et al., Quantitative assessments of indoor air pollution and respiratory health in a population-based sample of French dwellings. Environ Res, 2011. 111(3): p. 425-34.
- Blair, A., et al., Mortality and cancer incidence of aircraft maintenance workers exposed to trichloroethylene and other organic solvents and chemicals: extended follow up. Occup Environ Med, 1998. 55(3): p. 161-71.
- Boman, B.C., A.B. Forsberg, and B.G. Järvholm, Adverse health effects from ambient air pollution in relation to residential wood combustion in modern society. Scandinavian journal of work, environment & health, 2003. 29(4): p. 251-260.
- Booze, T.F., et al., A screening-level assessment of the health risks of chronic smoke exposure for wildland firefighters. Journal of Occupational and Environmental Hygiene, 2004. 1(5): p. 296-305.
- Boyouk, N., et al., Impact of the mixing boundary layer on the relationship between PM2.5 and aerosol optical thickness. Atmospheric Environment, 2010. 44(2): p. 271-277.
- Brackbill, R.M., L.L. Cameron, and V. Behrens, Prevalence of chronic diseases and impairments among US farmers, 1986-1990. Am J Epidemiol, 1994. 139(11): p. 1055-65.
- Braga, A.L., et al., Health effects of air pollution exposure on children and adolescents in Sao Paulo, Brazil. Pediatr Pulmonol, 2001. 31(2): p. 106-13.
- Brauer, M., Health Impacts of Biomass Air pollution. Kuala Lumpur: World Health Organization, Regional Offices for Southeast Asia and the Western Pacific. 1998.
- Brotherhood, J.R., et al., Fire fighters' exposure to carbon monoxide during Australian bushfires. Am Ind Hyg Assoc J, 1990. 51(4): p. 234-40.
- Buist, A.S., et al., The Burden of Obstructive Lung Disease Initiative (BOLD): rationale and design. COPD, 2005. 2(2): p. 277-83.
- Burrows, J.P., et al., The Global Ozone Monitoring Experiment (GOME): Mission Concept and First Scientific Results. Journal of the Atmospheric Sciences, 1999. 56(2): p. 151-175.
- Caamano-Isorna, F., et al., Respiratory and mental health effects of wildfires: an ecological study in Galician municipalities (north-west Spain). Environmental Health, 2011. 10.
- Cachier, H., et al., Particulate content of savanna fire emissions. Journal of Atmospheric Chemistry, 1995. 22(1-2): p. 123-148.
- Cançado, J.E.D., et al., The impact of sugar cane-burning emissions on the respiratory system of children and the elderly. Environmental health perspectives, 2006. 114(5): p. 725-729.
- Chen, H.H., et al., Effects of trichloroethylene and perchloroethylene on muscle contractile responses and epithelial prostaglandin release and acetylcholinesterase activity in swine trachea. Toxicol Sci, 2005. 83(1): p. 149-54.

- Chen, L., K. Verrall, and S. Tong, Air particulate pollution due to bushfires and respiratory hospital admissions in Brisbane, Australia. International Journal of Environmental Health Research, 2006. 16(3): p. 181-191.
- Chew, F.T., et al., Singapore's haze and acute asthma in children. Lancet, 1995. 346(8987): p. 1427.
- Chin, M., et al., Tropospheric Aerosol Optical Thickness from the GOCART Model and Comparisons with Satellite and Sun Photometer Measurements. Journal of the Atmospheric Sciences, 2002. 59(3): p. 461-483.
- Choi, B., et al., Very Long (> 48 hours) Shifts and Cardiovascular Strain in Firefighters: a Theoretical Framework. Ann Occup Environ Med, 2014. 26(1): p. 5.
- Chu, D.A., et al., Global monitoring of air pollution over land from the Earth Observing System-Terra Moderate Resolution Imaging Spectroradiometer (MODIS). Journal of Geophysical Research: Atmospheres, 2003. 108(D21).
- Churg, A., et al., Chronic exposure to high levels of particulate air pollution and small airway remodeling. Environ Health Perspect, 2003. 111(5): p. 714-8.
- Chuvieco, E., L. Giglio, and C. Justice, Global characterization of fire activity: toward defining fire regimes from Earth observation data. Global Change Biology, 2008. 14(7): p. 1488-1502.
- Ciganek, M. and J. Neca, Chemical characterization of volatile organic compounds on animal farms. Veterinarni Medicina, 2008. 53: p. 641-651.
- Cooke, W.F., B. Koffi, and J.M. Grégoire, Seasonality of vegetation fires in Africa from remote sensing data and application to a global chemistry model. Journal of Geophysical Research: Atmospheres, 1996. 101(D15): p. 21051-21065.
- Cooper, M.J., et al., A Satellite-Based Multi-Pollutant Index of Global Air Quality. Environmental Science & Technology, 2012. 46(16): p. 8523-8524.
- Crabbe, H., Risk of respiratory and cardiovascular hospitalisation with exposure to bushfire particulates: new evidence from Darwin, Australia. Environ Geochem Health, 2012. 34(6): p. 697-709.
- Cuthbert, O.D., et al., Barn allergy among Scottish farmers. Clin Allergy, 1984. 14(2): p. 197-206.
- Dalphin, J.C., et al., Prevalence of asthma and respiratory symptoms in dairy farmers in the French province of the Doubs. Am J Respir Crit Care Med, 1998. 158(5 Pt 1): p. 1493-8.
- Dassen, W., et al., Decline in children's pulmonary function during an air pollution episode. Journal of the Air Pollution Control Association, 1986. 36(11): p. 1223-1227.
- Davis-Lameloise, N., et al., Occupational differences, cardiovascular risk factors and lifestyle habits in South Eastern rural Australia. BMC Public Health, 2013. 13: p. 1090.
- De Vos, A.J.B.M., et al., Respiratory irritants in Australian bushfire smoke: air toxics sampling in a smoke chamber and during prescribed burns. Archives of Environmental Contamination and Toxicology, 2009. 56(3): p. 380-388.

- Delfino, R.J., et al., The relationship of respiratory and cardiovascular hospital admissions to the southern California wildfires of 2003. Occupational and Environmental Medicine, 2009. 66(3): p. 189-197.
- Delfino, R.J., et al., Asthma symptoms in Hispanic children and daily ambient exposures to toxic and criteria air pollutants. Environ Health Perspect, 2003. 111(4): p. 647-56.
- Delmas, R.A., et al., Experiment for Regional Sources and Sinks of Oxidants (EXPRESSO): An overview. Journal of Geophysical Research: Atmospheres, 1999. 104(D23): p. 30609-30624.
- Dennekamp, M. and M.J. Abramson, The effects of bushfire smoke on respiratory health. Respirology (Carlton, Vic.), 2011. 16(2): p. 198-209.
- Dominici, F., et al., On the use of generalized additive models in time-series studies of air pollution and health. Am J Epidemiol, 2002. 156(3): p. 193-203.
- Dominici, F., et al., Fine particulate air pollution and hospital admission for cardiovascular and respiratory diseases. JAMA, 2006. 295(10): p. 1127-34.
- Dominici, F., et al., Does the effect of PM10 on mortality depend on PM nickel and vanadium content? A reanalysis of the NMMAPS data. Environmental health perspectives, 2007. 115(12): p. 1701-1703.
- Donham, K. and T. A., Agricultural respiratory diseases, in Agricultural Medicine Occupational and Environmental Health for the Health Professions. 2006, Blackwell Publishing: Victoria, Australia. p. 65-144.
- Donham, K., et al., Environmental and health studies of farm workers in Swedish swine confinement buildings. Br J Ind Med, 1989. 46(1): p. 31-7.
- Donham, K.J. and A. Thelin, Agricultural respiratory diseases. In: Agricultural Medicine Occupational and Environmental Health for the Health Professions. Victoria, Australia: Blackwell Publishing. 2006: p. 65-144.
- Donham, K.J., D.C. Zavala, and J.A. Merchant, Respiratory symptoms and lung function among workers in swine confinement buildings: a cross-sectional epidemiological study. Arch Environ Health, 1984. 39(2): p. 96-101.
- Dosman, J.A., et al., Respiratory symptoms and pulmonary function in farmers. J Occup Med, 1987. 29(1): p. 38-43.
- Dost, F.N., Acute toxicology of components of vegetation smoke. Reviews of Environmental Contamination and Toxicology, 1991. 119: p. 1-46.
- Duclos, P., L.M. Sanderson, and M. Lipsett, The 1987 forest fire disaster in California: assessment of emergency room visits. Archives of Environmental Health, 1990. 45(1): p. 53-58.
- Eduard, W., N. Pearce, and J. Douwes, Chronic bronchitis, COPD, and lung function in farmers: the role of biological agents. Chest, 2009. 136(3): p. 716-25.
- Edwards, R., et al., Application of real-time particle sensors to help mitigate exposures of wildland firefighters. Archives of Environmental & Occupational Health, 2005. 60(1): p. 40-43.

- Elliott, C.T., S.B. Henderson, and V. Wan, Time series analysis of fine particulate matter and asthma reliever dispensations in populations affected by forest fires. Environmental health: a global access science source, 2013. 12.
- Emmanuel, S.C., Impact to lung health of haze from forest fires: the Singapore experience. Respirology (Carlton, Vic.), 2000. 5(2): p. 175-182.
- Engel-Cox, J.A., et al., Qualitative and quantitative evaluation of MODIS satellite sensor data for regional and urban scale air quality. Atmospheric Environment, 2004. 38(16): p. 2495-2509.
- Finlay, S.E., et al., Health impacts of wildfires. PLoS currents, 2012. 4.
- Fishman, J., A.E. Wozniak, and J.K. Creilson, Global distribution of tropospheric ozone from satellite measurements using the empirically corrected tropospheric ozone residual technique: Identification of the regional aspects of air pollution. Atmos. Chem. Phys., 2003. 3(4): p. 893-907.
- Forchhammer, L., et al., Controlled human wood smoke exposure: oxidative stress, inflammation and microvascular function. Part Fibre Toxicol, 2012. 9: p. 7.
- Fowler, C.T., Human Health Impacts of Forest Fires in the Southern United States: A Literature Review1. Journal of Ecological Anthropology, 2003. 7(1).
- Fraga, J., et al., The lag structure and the general effect of ozone exposure on pediatric respiratory morbidity. Int J Environ Res Public Health, 2011. 8(10): p. 4013-24.
- Fragar, L., The health of the people in agriculture and its interdependence with the health of rural communities. N S W Public Health Bull, 2001. 12(6): p. 155-159.
- Frankenberg, E., D. McKee, and D. Thomas, Health consequences of forest fires in Indonesia. Demography, 2005. 42(1): p. 109-129.
- Gasparrini, A., Distributed Lag Linear and Non-Linear Models in R: The Package dlnm. J Stat Softw, 2011. 43(8): p. 1-20.
- Gasparrini, A. and B. Armstrong, Distributed lag non-linear models: the R the package dlnm. London School of Hygiene and Tropical Medecine. UK. dnlm version 1.6.7; 2013-05-16.
- Ghio, A.J., et al., Exposure to wood smoke particles produces inflammation in healthy volunteers. Occupational and Environmental Medicine, 2011.
- Giglio, L., et al., Assessing variability and long-term trends in burned area by merging multiple satellite fire products. Biogeosciences, 2010. 7(3): p. 1171-1186.
- Giorgi, F. and R.O. Anyah, INTRODUCTIONThe road towards RegCM4. Climate Research, 2012. 52: p. 3-6.
- Goldammer, J.G., M. Statheropoulos, and M.O. Andreae, Chapter 1 Impacts of Vegetation Fire Emissions on the Environment, Human Health, and Security: A Global Perspective, M.A. A. Bytnerowicz, A. Riebau and C. Andersen, Editor. 2009, Developments in Environmental Science.
- Goldammer, J.G., et al., Migration and Global Environmental Change (UK Government's Foresight Project). SR10: specification for a state of science review-wildland fires, in Government Office for Science. 2011: http://www.fire.uni-freiburg.de/GlobalNetworks/UK-Foresight-Project-Climate-Change-Migration-2011-SR-10-Wildland-Fire.pdf.

- Golshan, M., et al., Early effects of burning rice farm residues on respiratory symptoms of villagers in suburbs of Isfahan, Iran. International journal of environmental health research, 2002. 12(2): p. 125-131.
- Gong, S.L., L.A. Barrie, and J.-P. Blanchet, Modeling sea-salt aerosols in the atmosphere 1. model development. J. Geophys. Res., 1997. 102(D3): p. 3805–3818.
- Greven, F.E., et al., Respiratory symptoms in firefighters. American journal of industrial medicine, 2011. 54(5): p. 350-355.
- Guillam, M.T., et al., Chronic respiratory symptoms of poultry farmers and model-based estimates of long-term dust exposure. Ann Agric Environ Med, 2013. 20(2): p. 307-11.
- Guo, Y.M., et al., [Association between ambient temperature and hospital emergency room visits for cardiovascular diseases: a case-crossover study]. Zhonghua Liu Xing Bing Xue Za Zhi, 2009. 30(8): p. 810-5.
- Gyawali, M., et al., In situ aerosol optics in Reno, NV, 5 USA during and after the summer 2008 California wildfires and the influence of absorbing and non-absorbing organic coatings on spectral light absorption. Atmos. Chem. Phys., 2009. 9: p. 8007–8015.
- Hajat, S., et al., Outdoor air pollution and infant mortality: analysis of daily time-series data in 10 English cities. J Epidemiol Community Health, 2007. 61(8): p. 719-22.
- Hanigan, I.C., F.H. Johnston, and G.G. Morgan, Vegetation fire smoke, indigenous status and cardio-respiratory hospital admissions in Darwin, Australia, 1996–2005: a time-series study. Environmental Health, 2008. 7(1).
- Hänninen, O., Challenges in estimating the health effects of biomass smoke--response to Sverre Vedal and Steven J. Dutton: Wildfire air pollution and daily mortality in a large urban area. Environmental Research, 2008. 106(3): p. 423-424; discussion 425.
- Hänninen, O.O., et al., The EXPOLIS study: implications for exposure research and environmental policy in Europe. Journal of exposure analysis and environmental epidemiology, 2004. 14(6): p. 440-456.
- Hanninen, O.O., et al., Population exposure to fine particles and estimated excess mortality in Finland from an East European wildfire episode. Journal of Exposure Science and Environmental Epidemiology, 2009. 19(4): p. 414-422.
- Hao, W.M. and M.-H. Liu, Spatial and temporal distribution of tropical biomass burning. Global Biogeochemical Cycles, 1994. 8(4): p. 495-503.
- Hao, W.M., M.-H. Liu, and P.J. Crutzen, Estimates of Annual and Regional Releases of CO2 and Other Trace Gases to the Atmosphere from Fires in the Tropics, Based on the FAO Statistics for the Period 1975–1980, in Fire in the Tropical Biota, D.J.G. Goldammer, Editor. 1990, Springer Berlin Heidelberg. p. 440-462.
- Hardin, J. and J. Hilbe, Generalized Linear Models and Extensions; Stata Corporation. 2011: College Station, TX, USA.
- Heinonen, O.P., et al., Prevalence of allergic symptoms in rural and urban populations. Eur J Respir Dis Suppl, 1987. 152: p. 64-9.
- Hejl, A.M., et al., Inflammatory effects of woodsmoke exposure among wildland firefighters working at prescribed burns at the Savannah River Site, SC. J Occup Environ Hyg, 2013. 10(4): p. 173-80.

- Henderson, D.E., J.B. Milford, and S.L. Miller, Prescribed burns and wildfires in Colorado: impacts of mitigation measures on indoor air particulate matter. Journal of the Air & Waste Management Association (1995), 2005. 55(10): p. 1516-1526.
- Henderson, S.B., et al., Application of land use regression to estimate long-term concentrations of traffic-related nitrogen oxides and fine particulate matter. Environmental Science & Technology, 2007. 41(7): p. 2422-2428.
- Henderson, S.B., et al., Three measures of forest fire smoke exposure and their associations with respiratory and cardiovascular health outcomes in a population-based cohort. Environmental Health Perspectives, 2011. 119(9): p. 1266-1271.
- Henderson, S.B. and F.H. Johnston, Measures of forest fire smoke exposure and their associations with respiratory health outcomes. Curr Opin Allergy Clin Immunol, 2012. 12(3): p. 221-7.
- Hisham-Hashim, J., et al., Respiratory function of elementary school children exposed to the 1997 Kuala Lumpur haze. Epidemiology 1998. 9(4): p. S1.
- Hobbs, P.V., et al., Direct Radiative Forcing by Smoke from Biomass Burning. Science, 1997. 275(5307): p. 1777-1778.
- Hodzic, A., et al., Wildfire particulate matter in Europe during summer 2003: meso-scale modeling of smoke emissions, transport and radiative effects. Atmos. Chem. Phys., 2007. 7(15): p. 4043-4064.
- Hoelzemann, J.J., et al., Global Wildland Fire Emission Model (GWEM): Evaluating the use of global area burnt satellite data. Journal of Geophysical Research: Atmospheres, 2004. 109(D14).
- Holben, B.N., et al., AERONET—A Federated Instrument Network and Data Archive for Aerosol Characterization. Remote Sensing of Environment, 1998. 66(1): p. 1-16.
- Holness, D.L., et al., Respiratory effects and dust exposures in hog confinement farming. Am J Ind Med, 1987. 11(5): p. 571-80.
- Holstius, D.M., et al., Birth weight following pregnancy during the 2003 Southern California wildfires. Environmental health perspectives, 2012. 120(9): p. 1340-1345.
- Hoppin, J.A., et al., Pesticide use and adult-onset asthma among male farmers in the Agricultural Health Study. Eur Respir J, 2009. 34(6): p. 1296-303.
- Hosmer, D.W. and S. Lemeshow, Applied logistic regression, ed. J.W.a. Sons. 1989, New York.
- Hossack, B.R., et al., Interactive effects of wildfire, forest management, and isolation on amphibian and parasite abundance. Ecological applications: a publication of the Ecological Society of America, 2013. 23(2): p. 479-492.
- Hulin, M., D. Caillaud, and I. Annesi-Maesano, Indoor air pollution and childhood asthma: variations between urban and rural areas. Indoor Air, 2010. 20(6): p. 502-14.
- Hutchison, K.D., Applications of MODIS satellite data and products for monitoring air quality in the state of Texas. Atmospheric Environment, 2003. 37(17): p. 2403-2412.
- Huttunen, K., et al., Low-level exposure to ambient particulate matter is associated with systemic inflammation in ischemic heart disease patients. Environ Res, 2012. 116: p. 44-51.

- Ichoku, C. and Y.J. Kaufman, A method to derive smoke emission rates from MODIS fire radiative energy measurements. IEEE Transactions on Geoscience and Remote Sensing, 2005. 43(11): p. 2636-2649.
- Ignotti, E., et al., Impact on human health of particulate matter emitted from burnings in the Brazilian Amazon region. Revista De Saúde Pública, 2010. 44(1): p. 121-130.
- Ito, A. and J.E. Penner, Global estimates of biomass burning emissions based on satellite imagery for the year 2000. Journal of Geophysical Research: Atmospheres, 2004. 109(D14).
- Ito, K., et al., Fine particulate matter constituents associated with cardiovascular hospitalizations and mortality in New York City. Environ Health Perspect, 2011. 119(4): p. 467-73.
- Jalaludin, B., et al., Acute effects of bushfires on peak expiratory flow rates in children with wheeze: a time series analysis. Australian and New Zealand Journal of Public Health, 2000. 24(2): p. 174-177.
- Johnston, F., et al., Extreme air pollution events from bushfires and dust storms and their association with mortality in Sydney, Australia 1994–2007. Environmental Research, 2011. 111(6): p. 811-816.
- Johnston, F.H., et al., Ambient biomass smoke and cardio-respiratory hospital admissions in Darwin, Australia. BMC Public Health, 2007. 7.
- Johnston, F.H., et al., Estimated global mortality attributable to smoke from landscape fires. Environmental health perspectives, 2012. 120(5): p. 695-701.
- Johnston, F.H., et al., Exposure to bushfire smoke and asthma: an ecological study. The Medical Journal of Australia, 2002. 176(11): p. 535-538.
- Johnston, F.H., et al., Vegetation fires, particulate air pollution and asthma: A panel study in the Australian monsoon tropics. International Journal of Environmental Health Research, 2006. 16(6): p. 391-404.
- Kaiser, J.W., et al., Biomass burning emissions estimated with a global fire assimilation system based on observed fire radiative power. Biogeosciences, 2012. 9(1): p. 527-554.
- Kessler, R., Followup in Southern California: decreased birth weight following prenatal wildfire smoke exposure. Environmental health perspectives, 2012. 120(9).
- Kim, S.-Y., et al., The temporal lag structure of short-term associations of fine particulate matter chemical constituents and cardiovascular and respiratory hospitalizations. Environmental health perspectives, 2012. 120(8): p. 1094-1099.
- King, M.D., et al., Remote Sensing of Tropospheric Aerosols from Space: Past, Present, and Future. Bulletin of the American Meteorological Society, 1999. 80(11): p. 2229-2259.
- Koenig, J.Q., Air pollution and asthma. The Journal of Allergy and Clinical Immunology, 1999. 104(4 Pt 1): p. 717-722.
- Kok, J.F., A scaling theory for the size distribution of emitted dust aerosols suggests climate models underestimate the size of the global dust cycle. Proc Natl Acad Sci U S A, 2011. 108(3): p. 1016-21.
- Kolbe, A. and K.L. Gilchrist, An extreme bushfire smoke pollution event: health impacts and public health challenges. New South Wales Public Health Bulletin, 2009. 20(1-2): p. 19-23.

- Koppmann, R., K. von Czapiewski, and J.S. Reid, A review of biomass burning emissions, part I: gaseous emissions of carbon monoxide, methane, volatile organic compounds, and nitrogen containing compounds. Atmospheric Chemistry and Physics Discussions, 2005. 5(5): p. 10455-10516.
- Kunii, O., et al., The 1997 haze disaster in Indonesia: its air quality and health effects. Archives of environmental health, 2002. 57(1): p. 16-22.
- Künzli, N., et al., Health effects of the 2003 Southern California wildfires on children. American Journal of Respiratory and Critical Care Medicine, 2006. 174(11): p. 1221-1228.
- Lacaux, J.P., et al., Biomass burning in the tropical savannas of Ivory Coast: An overview of the field experiment Fire of Savannas (FOS/DECAFE 91). Journal of Atmospheric Chemistry, 1995. 22(1-2): p. 195-216.
- Langley, R.L., Consequences of respiratory exposures in the farm environment. N C Med J, 2011. 72(6): p. 477-80.
- Laurent, B., et al., Modeling mineral dust emissions from the Sahara desert using new surface properties and soil database. J. Geophys. Res., 2008. 113: p. D14218.
- Leonard, S.S., et al., Particle size-dependent radical generation from wildland fire smoke. Toxicology, 2007. 236(1-2): p. 103-113.
- Liousse, C., et al., Deriving Global Quantitative Estimates for Spatial and Temporal Distributions of Biomass Burning Emissions, in Emissions of Atmospheric Trace Compounds, C. Granier, P. Artaxo, and C.E. Reeves, Editors. 2004, Springer Netherlands. p. 71-113.
- Liousse, C., et al., Updated African biomass burning emission inventories in the framework of the AMMA-IDAF program, with an evaluation of combustion aerosols. Atmos. Chem. Phys., 2010. 10(19): p. 9631-9646.
- Lipfert, F.W., J. Zhang, and R.E. Wyzga, Infant mortality and air pollution: a comprehensive analysis of U.S. data for 1990. Journal of the Air & Waste Management Association (1995), 2000. 50(8): p. 1350-1366.
- Lisabeth, L.D., et al., Ambient air pollution and risk for ischemic stroke and transient ischemic attack. Ann Neurol, 2008. 64(1): p. 53-9.
- Long, W., et al., Respiratory symptoms in a susceptible population due to burning of agricultural residue. Chest, 1998. 113(2): p. 351-357.
- Mahmud, A., M. Hixson, and M.J. Kleeman, Quantifying population exposure to airborne particulate matter during extreme events in California due to climate change. Atmos. Chem. Phys., 2012. 12(16): p. 7453-7463.
- Malavelle, F., et al., Simulation of aerosol radiative effects over West Africa during DABEX and AMMA SOP-0. Journal of Geophysical Research: Atmospheres, 2011. 116(D8).
- Malilay, J., A Review of Factors Affecting the Human Health Impacts of Air Pollutants from Forest Fires. WHO/UNEP/WMO, 1999: p. 255-270.
- Malmberg, P., et al., Incidence of organic dust toxic syndrome and allergic alveolitis in Swedish farmers. Int Arch Allergy Appl Immunol, 1988. 87(1): p. 47-54.
- Manfreda, J., M. Cheang, and C.P. Warren, Chronic respiratory disorders related to farming and exposure to grain dust in a rural adult community. Am J Ind Med, 1989. 15(1): p. 7-19.

- Marshall, G.N., et al., Psychiatric disorders among adults seeking emergency disaster assistance after a wildland-urban interface fire. Psychiatric services (Washington, D.C.), 2007. 58(4): p. 509-514.
- Martin, K.L., et al., Air pollution from bushfires and their association with hospital admissions in Sydney, Newcastle and Wollongong, Australia 1994-2007. Australian and New Zealand journal of public health, 2013. 37(3): p. 238-243.
- McGauran, N., et al., Reporting bias in medical research - a narrative review. Trials, 2010. 11: p. 37.
- Metzger, K.B., et al., Ambient air pollution and cardiovascular emergency department visits. Epidemiology, 2004. 15(1): p. 46-56.
- Michel, C., et al., Biomass burning emission inventory from burnt area data given by the SPOT-VEGETATION system in the frame of TRACE-P and ACE-Asia campaigns. Journal of Geophysical Research: Atmospheres, 2005. 110(D9).
- Mieville, A., et al., Emissions of gases and particles from biomass burning during the 20th century using satellite data and an historical reconstruction. Atmospheric Environment, 2010. 44(11): p. 1469-1477.
- Migliaccio, C.T., et al., Urinary levoglucosan as a biomarker of wood smoke exposure: observations in a mouse model and in children. Environ Health Perspect, 2009. 117(1): p. 74-9.
- Mio, T., et al., Cigarette smoke induces interleukin-8 release from human bronchial epithelial cells. Am J Respir Crit Care Med, 1997. 155(5): p. 1770-6.
- Mirabelli, M.C., et al., Respiratory symptoms following wildfire smoke exposure: airway size as a susceptibility factor. Epidemiology (Cambridge, Mass.), 2009. 20(3): p. 451-459.
- Mitha, N., et al., [Indoor air quality and adult asthma]. Rev Mal Respir, 2013. 30(5): p. 374-413.
- Monahan, E.G., D.E. Spiel, and K.L. Davidson, A model of marine aerosol generation via whitecaps and wave disruption, in Oceanic Whitecaps, E.a.N. Monahan, G. M.,, Editor. 1986., D. Reidel: Norwell, MA, USA. p. 167–174.
- Monso, E., et al., Region-related risk factors for respiratory symptoms in European and Californian farmers. Eur Respir J, 2003. 21(2): p. 323-31.
- Moore, D., et al., Population health effects of air quality changes due to forest fires in British Columbia in 2003: estimates from physician-visit billing data. Canadian Journal of Public Health. Revue Canadienne De Santé Publique, 2006. 97(2): p. 105-108.
- Morgan, G., et al., Effects of Bushfire Smoke on Daily Mortality and Hospital Admissions in Sydney, Australia. Epidemiology, 2010. 21(1): p. 47-55.
- Mott, J.A., et al., Cardiorespiratory hospitalizations associated with smoke exposure during the 1997, Southeast Asian forest fires. International Journal of Hygiene and Environmental Health, 2005. 208(1-2): p. 75-85.
- Mouillot, F. and C.B. Field, Fire history and the global carbon budget: a 1°× 1° fire history reconstruction for the 20th century. Global Change Biology, 2005. 11(3): p. 398-420.
- Myers, M., Health problems and disease patterns in agriculture. ILO Encyclopedia of Occupational Health and Safety, 1998. 3(64): p. 60-65.

- Naeher, L.P., et al., Woodsmoke health effects: a review. Inhalation Toxicology, 2007. 19(1): p. 67-106.
- Narayan, C., et al., Potential for CO2 emissions mitigation in Europe through prescribed burning in the context of the Kyoto Protocol. Forest Ecology and Management, 2007. 251(3): p. 164-173.
- Ni, J.Q., et al., Volatile organic compounds at swine facilities: a critical review. Chemosphere, 2012. 89(7): p. 769-88.
- Nieuwenhuijsen, M.J., H. Kruize, and M.B. Schenker, Exposure to dust and its particle size distribution in California agriculture. Am Ind Hyg Assoc J, 1998. 59(1): p. 34-8.
- Norback, D., et al., Asthmatic symptoms and volatile organic compounds, formaldehyde, and carbon dioxide in dwellings. Occup Environ Med, 1995. 52(6): p. 388-95.
- Omland, O., et al., Lung status in young Danish rurals: the effect of farming exposure on asthma-like symptoms and lung function. Eur Respir J, 1999. 13(1): p. 31-7.
- Ottmar, R.D., Smoke source characteristics, in Smoke Management Guide for Prescribed and Wildland Fire, R.D.P. C.C.O. Hardy, Janice L.; Core, John E.; Seamon, Paula, Editor. 2001, National Wildfire Coordinating Group, Fire Use Working Team: Boise. p. 89-105.
- Ovadnevaitė, J., K. Kvietkus, and A. Maršalka, 2002 summer fires in Lithuania: Impact on the Vilnius city air quality and the inhabitants health. Science of The Total Environment, 2006. 356(1–3): p. 11-21.
- Peel, J.L., et al., Ambient air pollution and respiratory emergency department visits. Epidemiology, 2005. 16(2): p. 164-74.
- Penard-Morand, C., et al., Long-term exposure to close-proximity air pollution and asthma and allergies in urban children. Eur Respir J, 2010. 36(1): p. 33-40.
- Peng, R.D. and F. Dominici, Statistical Methods for Environmental Epidemiology with R. A Case Study in Air Pollution and Health Series. 2008.
- Perrino, C. and M. Gherardi, Optimization of the coating layer for the measurement of ammonia by diffusion denuders. Atmospheric Environment, 1999. 33(28): p. 4579-4587.
- Prunier-Poulmaire, S. and C. Gadbois, The French 35-hour workweek: a wide-ranging social change. J Hum Ergol (Tokyo), 2001. 30(1-2): p. 41-6.
- Puxbaum, H., et al., A dual site study of PM2.5 and PM10 aerosol chemistry in the larger region of Vienna, Austria. Atmospheric Environment, 2004. 38(24): p. 3949-3958.
- Rappold, A.G., et al., Peat bog wildfire smoke exposure in rural North Carolina is associated with cardiopulmonary emergency department visits assessed through syndromic surveillance. Environmental Health Perspectives, 2011. 119(10): p. 1415-1420.
- Reinhardt, T.E. and R.D. Ottmar, Baseline measurements of smoke exposure among wildland firefighters. J Occup Environ Hyg, 2004. 1(9): p. 593-606.
- Reisen, F., D. Hansen, and C.P.M. Meyer, Exposure to bushfire smoke during prescribed burns and wildfires: firefighters' exposure risks and options. Environment International, 2011. 37(2): p. 314-321.
- Remer, L.A., et al., The MODIS Aerosol Algorithm, Products, and Validation. Journal of the Atmospheric Sciences, 2005. 62(4): p. 947-973.

- Riddervold, I.S., et al., Wood smoke in a controlled exposure experiment with human volunteers. Inhal Toxicol, 2011. 23(5): p. 277-88.
- Rive, S., et al., Urinary S-PMA related to indoor benzene and asthma in children. Inhal Toxicol, 2013. 25(7): p. 373-82.
- Rumchev, K., et al., Association of domestic exposure to volatile organic compounds with asthma in young children. Thorax, 2004. 59(9): p. 746-51.
- Sastry, N., Forest fires, air pollution, and mortality in southeast Asia. Demography, 2002. 39(1): p. 1-23.
- Schenker, M.B., Respiratory Health Hazards in Agriculture. Respiratory and Critical Care Medicine, 1998. 158(5): p. S1-S76.
- Schenker, M.B., Preventive medicine and health promotion are overdue in the agricultural workplace. J Public Health Policy, 1996. 17(3): p. 275-305.
- Schenker, M.B., et al., Agricultural dust exposure and respiratory symptoms among California farm operators. J Occup Environ Med, 2005. 47(11): p. 1157-66.
- Schenker, M.B., M.R. Orenstein, and S.J. Samuels, Use of protective equipment among California farmers. Am J Ind Med, 2002. 42(5): p. 455-64.
- Schenker, M.B., et al., Pneumoconiosis from agricultural dust exposure among young California farmworkers. Environ Health Perspect, 2009. 117(6): p. 988-94.
- Schernhammer, E.S., et al., Time trends of the prevalence of asthma and allergic disease in Austrian children. Pediatr Allergy Immunol, 2008. 19(2): p. 125-31.
- Seinfeld, J.H. and S.N. Pandis, Atmospheric chemistry and physics: from air pollution to climate change, first edition. 1998, Hoboken, N.J.: J. Wiley.
- Semenza, J.C., et al., Public perception and behavior change in relationship to hot weather and air pollution. Environmental research, 2008. 107(3): p. 401-411.
- Sillanpää, M., et al., Chemical composition, mass size distribution and source analysis of long-range transported wildfire smokes in Helsinki. The Science of the Total Environment, 2005. 350(1-3): p. 119-135.
- Smit, L.A., et al., Transient receptor potential genes, smoking, occupational exposures and cough in adults. Respir Res, 2012. 13: p. 26.
- Solmon, F., F. Giorgi, and C. Liousse, Aerosol modelling for regional climate studies: application to anthropogenic particles and evaluation over a European/African domain. Tellus B, 2006. 58(1): p. 51-72.
- Soteriades, E.S., et al., Cardiovascular disease in US firefighters: a systematic review. Cardiol Rev, 2011. 19(4): p. 202-15.
- Statheropoulos, M. and S. Karma, Complexity and origin of the smoke components as measured near the flame-front of a real forest fire incident: A case study. Journal of Analytical and Applied Pyrolysis, 2007. 78(2): p. 430-437.
- Statheropoulos, M. and S. Karma, Health impacts of forest fires smoke on fire-fighters and populations. Associate European Center for Forest Fires (ECFF), October 2004. 2.
- Stefanidou, M., S. Athanaselis, and C. Spiliopoulou, Health impacts of fire smoke inhalation. Inhalation Toxicology, 2008. 20(8): p. 761-766.

- Stroppiana, D., et al., Comparison of global inventories of CO emissions from biomass burning derived from remotely sensed data. Atmos. Chem. Phys., 2010. 10(24): p. 12173-12189.
- Sullivan, J.B., et al., Health-related hazards of agriculture. in Hazardous Materials Toxicology: Health Chemical Principles of Environmental 1992.
- Sutherland, E.R., et al., Wildfire smoke and respiratory symptoms in patients with chronic obstructive pulmonary disease. The Journal of Allergy and Clinical Immunology, 2005. 115(2): p. 420-422.
- Swap, R., et al., The Southern African Regional Science Initiative (SAFARI 2000): overview of the dry season field campaign. SOUTH AFRICAN JOURNAL OF SCIENCE, 2002. 98(3-4): p. 125-130.
- Swiston, J.R., et al., Wood smoke exposure induces a pulmonary and systemic inflammatory response in firefighters. The European Respiratory Journal: Official Journal of the European Society for Clinical Respiratory Physiology, 2008. 32(1): p. 129-138.
- Tan, W.C., et al., The human bone marrow response to acute air pollution caused by forest fires. American journal of respiratory and critical care medicine, 2000. 161(4 Pt 1): p. 1213-1217.
- Tham, R., et al., The impact of smoke on respiratory hospital outcomes during the 2002-2003 bushfire season, Victoria, Australia. Respirology (Carlton, Vic.), 2009. 14(1): p. 69-75.
- Thelen, B., et al., Modeling acute respiratory illness during the 2007 San Diego wildland fires using a coupled emissions-transport system and generalized additive modeling. Environ Health, 2013. 12: p. 94.
- Toren, K. and L.G. Horte, Asthma mortality and occupation in Sweden 1981-1992. Am J Ind Med, 1997. 31(6): p. 678-81.
- Touloumi, G., et al., Short-term effects of air pollution on total and cardiovascular mortality: the confounding effect of influenza epidemics. Epidemiology, 2005. 16(1): p. 49-57.
- Tummon, F., et al., Simulation of the direct and semidirect aerosol effects on the southern Africa regional climate during the biomass burning season. Journal of Geophysical Research: Atmospheres, 2010. 115(D19).
- Turquety, S., et al., Analysis and Prediction of the Impact of Fires on Air Quality in the Mediterranean and Europe (Apiflame). 2010.
- U.S. Environmental Protection Agency, National Ambient Air Quality Standards for Particulate Matter. January 15, 2013: p. 3086-3287.
- U.S. Environmental Protection Agency, Wildfire Smoke: A Guide for Public Health Officials. 2008.
- U.S. Environmental Protection Agency, National Ambient Air Quality Standards for Particulate Matter. January 15, 2013. p. 3086-3287.
- Van der Werf, G.R., et al., Interannual variability in global biomass burning emissions from 1997 to 2004. Atmos. Chem. Phys., 2006. 6(11): p. 3423-3441.

- Van der Werf, G.R., et al., Global fire emissions and the contribution of deforestation, savanna, forest, agricultural, and peat fires (1997–2009). Atmos. Chem. Phys., 2010. 10(23): p. 11707-11735.
- Van Donkelaar, A., et al., Global estimates of ambient fine particulate matter concentrations from satellite-based aerosol optical depth: development and application. Environmental Health Perspectives, 2010. 118(6): p. 847-855.
- Van Eeden, S.F., et al., Cytokines involved in the systemic inflammatory response induced by exposure to particulate matter air pollutants (PM(10)). American journal of respiratory and critical care medicine, 2001. 164(5): p. 826-830.
- Vedal, S. and S.J. Dutton, Wildfire air pollution and daily mortality in a large urban area. Environmental Research, 2006. 102(1): p. 29-35.
- Vilen, T. and P.M. Fernandes, Forest fires in Mediterranean countries: CO2 emissions and mitigation possibilities through prescribed burning. Environ Manage, 2011. 48(3): p. 558-67.
- Voaklander, D., et al., Older farmers and machinery exposure-cause for concern? Am J Ind Med, 2012. 55(11): p. 1044-50.
- Vogelzang, P.F., et al., Health-based selection for asthma, but not for chronic bronchitis, in pig farmers: an evidence-based hypothesis. Eur Respir J, 1999. 13(1): p. 187-9.
- Von Essen, S. and K. Donham, Respiratory disease related to work in agriculture., in Safety and Health in Agriculture, Forestry & Fisheries, M.R. Langley RL, Meggs WJ, Roberson GT,, Editor. 1997, Government Institutes Inc: Rockville, MD p. 353-384.
- Vora, C., et al., 2007 San Diego wildfires and asthmatics. The Journal of asthma: official journal of the Association for the Care of Asthma, 2011. 48(1): p. 75-78.
- Wan, V., et al., A comparison of classification algorithms for the identification of smoke plumes from satellite images. Statistical Methods in Medical Research, 2011. 20(2): p. 131-156.
- Wang, J. and S.A. Christopher, Intercomparison between satellite-derived aerosol optical thickness and PM2.5 mass: Implications for air quality studies. Geophysical Research Letters, 2003. 30(21).
- Wegesser, T.C., K.E. Pinkerton, and J.A. Last, California wildfires of 2008: coarse and fine particulate matter toxicity. Environmental Health Perspectives, 2009. 117(6): p. 893-897.
- WHO Regional Office for Europe, Health risks of particulate matter from long-range transboundary air pollution. 2006.
- WHO Regional Office for Europe, Health effects of particulate matter. 2013.
- Wilkins, J.R., 3rd, et al., Prevalence of ROPS--equipped tractors and farm/farmer characteristics. J Agric Saf Health, 2003. 9(2): p. 107-18.
- Wilkins, J.R., 3rd, et al., Prevalence of chronic respiratory symptoms among Ohio cash grain farmers. Am J Ind Med, 1999. 35(2): p. 150-63.
- Williams, K.M., L.M. Franzi, and J.A. Last, Cell-specific oxidative stress and cytotoxicity after wildfire coarse particulate matter instillation into mouse lung. Toxicol Appl Pharmacol, 2013. 266(1): p. 48-55.
- Wood, S., Package 'mgcv'. Version 1.8-3; August 29, 2014.

- Wood, S. Package 'mgcv'. 2014 March, 31, 2014 [cited 2014 April, 01/2014].
- Wooster, M.J., et al., Retrieval of biomass combustion rates and totals from fire radiative power observations: FRP derivation and calibration relationships between biomass consumption and fire radiative energy release. Journal of Geophysical Research: Atmospheres, 2005. 110(D24).
- World Health Organization, Health guidelines for vegetation fire events. 1998.
- World Health Organization. , Health guidelines for vegetation fire events. 1999.
- Wu, C.-F., et al., Agricultural burning smoke in Eastern Washington: Part II. Exposure assessment. Atmospheric Environment, 2006. 40(28): p. 5379-5392.
- Xanthopoulos, G., Wildland fires: Mediterranean, in Journal of Crisis Response. 2009. p. 50-51.
- Yang, J., et al., Sudden cardiac death among firefighters </=45 years of age in the United States. Am J Cardiol, 2013. 112(12): p. 1962-7.
- Yao, J., M. Brauer, and S.B. Henderson, Evaluation of a Wildfire Smoke Forecasting System as a Tool for Public Health Protection. Environmental health perspectives, 2013.
- Youssouf, H., et al., Quantifying wildfires exposure for investigating health-related effects. Atmospheric Environment, 2014. 97(0): p. 239-251.
- Youssouf , H., et al., Non-accidental Health impacts of wildfire, submitted on IJERPH, 2014.
- Zanobetti, A., et al., The temporal pattern of mortality responses to air pollution: a multicity assessment of mortality displacement. Epidemiology, 2002. 13(1): p. 87-93.
- Zejda, J.E., et al., Respiratory health status in swine producers relates to endotoxin exposure in the presence of low dust levels. J Occup Med, 1994. 36(1): p. 49-56.
- Zejda, J.E. and J.A. Dosman, Respiratory disorders in agriculture. Tuber Lung Dis, 1993. 74(2): p. 74-86.