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TOPICAL REVIEW

Combined impacts of climate and air pollution on human health and agricultural productivity

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Abstract

Climate change and air pollution can interact to amplify risks to human health and crop production. This has significant implications for our ability to reach the Sustainable Development Goals (e.g. SDGs 2, 3, 13, 15) and for the design of effective mitigation and adaptation policies and risk management. To be able to achieve the SDG targets, closer integration of climate change and air pollution both in terms of impact assessment for human health and agricultural productivity and respective policy development is needed. Currently, studies estimating the impacts of climate and air pollutants on human health and crops mostly treat these stressors separately, and the methods used by the health and agricultural science communities differ. Better insights into the methods applied in the different communities can help to improve existing and develop new methods to advance our knowledge about the combined impacts of climate change and air pollution on human health and crops. This topical review provides an overview of current methodologies applied in the two fields of human health and agricultural crop impact studies, ranging from empirical regression-based and experimental methods to more complex process-based models. The latter are reasonably well developed for estimating impacts on agricultural crops, but not for health impacts. We review available literature addressing the combined effects of climate and air pollution on human health or agricultural productivity to provide insights regarding state-of-the-art knowledge and currently available methods in the two fields. Challenges to assess the combined effect of climate and air pollution on human health and crops, and opportunities for both fields to learn from each other, are discussed.

1. Introduction

The 21st century poses fundamental challenges for mankind faced with unprecedented climate change, resource exploitation, environmental pollution, biodiversity loss and an increasing population to feed and to provide safe and sustainable living conditions for. This century is also shaped by great ambitions to tackle these challenges marked by major landmark agreements of the United Nations related to reducing global warming to below 1.5 °C as outlined in the Paris Agreement (UNFCCC 2015), the Sustainable Development Goals (SDGs) recognizing that climate change and sustainable development are closely linked (UNDP 2016), and the 'Sendai Framework for Disaster Risk Reduction' with a focus on understanding risks and investing in disaster risk reduction for resilience (UNISDR 2015). Climate change caused by anthropogenic fossil-fuel emissions is associated with a gradual rise in global mean temperature and sea level (IPCC 2013). It also manifests itself in changes in the frequency and intensity of weather and climate extremes, such as heatwaves and heavy precipitation (IPCC 2012, Sillmann *et al* 2013). The impacts of these extremes will be felt much earlier than gradual mean changes in climate and they are already occurring today leading to higher climate-related risk for many sectors, including aspects of agricultural productivity and human health (IPCC 2018).

Currently, climate-related hazards, such as heat, drought, and floods, are responsible for 90% of all disasters worldwide. While sustainable development can reduce exposure and vulnerability and thus the consequences of disasters, climate change can in turn increase the occurrence and frequency of climate-related hazards (Russo *et al* 2019) and also threaten the achievement of several SDGs, such as SDG2 (Zero hunger), SDG3 (Good health and well-being), and SDG15 (Life on land) (IPCC 2018, 2019, FAO, IFAD, UNICEF 2020). In addition, air pollution has become a key concern for global public health and global crop production. Particulate matter (i.e. $PM_{2.5}$, fine inhalable particles, $\leqslant 2.5\ \mu m$ in aerodynamic diameter) is currently the largest environmental cause of ill health and premature death worldwide and is projected to remain so towards 2050 (Lelieveld *et al* 2015). The effects of air pollutants on agriculture are less well known, but global scale assessments suggest yield losses could amount to between 3% and 16% for staple crops due to ozone (O_3) pollution, with losses set to worsen by 2030 primarily due to O_3 increases in Asia (Emberson 2020). While sustainable intensification and climate-smart agriculture seek to address the challenge of joint climate adaptation and mitigation (Lipper *et al* 2014), these approaches do not consider detailed effects of other aspects of environmental changes and, in particular, are not tested for extreme conditions of climate and instances of air pollution episodes, let alone their combined impacts.

The purpose of this topical review is to provide an overview of available literature on the combined effects of climate and air pollution on both human health and agricultural productivity in terms of the state-of-the-art knowledge and currently available methods in these different disciplines, and to suggest possible ways forward towards more comprehensive impact assessments.

1.1. Interactions between climate and air pollution and their role as stressors for human health and agricultural productivity

There is a complex interplay between anthropogenic emissions, interactions of greenhouse gases, air pollutants and climate variables in the atmosphere and their role as stressors impacting human health and agricultural productivity as illustrated in figure 1.

Climate or meteorological conditions can affect air quality in several ways, including through changes in natural and anthropogenic emission and impacts on atmospheric processes such as transport, mixing, deposition and chemical transformation, which are of importance both for background concentrations and pollution episodes (Jacob and Winner 2009). There is evidence that when extreme weather and air pollution episodes occur together, their impacts are non-linearly amplified beyond the sum of their individual effects (Willers *et al* 2016). A large number of studies have established links between meteorological factors and air pollution in terms of aerosols or particular matter (PM) at local and regional scales (e.g. Demuzere *et al* 2009, Tai *et al* 2012, Hou and Wu 2016, Otero *et al* 2016), showing that pollutants and their precursors have different meteorological dependencies that are further complicated by seasonal and regional variations (Jacob and Winner 2009, Shen *et al* 2017).

Air pollution episodes can result from a combination of elevated emissions and unfavorable weather conditions, such as extreme temperatures and stagnant air, as typical for heatwaves and cold spells, that allow the accumulation of pollutants in the near surface atmosphere (Jacob and Winner 2009, Otero *et al* 2016, Schnell and Prather 2017). These kinds of air pollution episodes along with heatwaves will worsen under future climate (Horton *et al* 2014, Russo *et al* 2015). Heatwaves are also often connected to elevated levels of harmful air pollutants released during wildfires or generated by photochemical reactions that exert further stress to humans and the environment. The 2003 European heatwave and co-occurring O_3 pollution episode has been recognized as a prototype of potential future climate events (Vautard *et al* 2005). According to Dear *et al* (2005), O_3 played an important role in enhancing the number of deaths during the 2003 heat wave, in addition to the high minimum temperatures during nighttime, with potentially over 50% of the excess deaths being attributable to O_3.

The impacts of climate change on air pollution concentrations have been termed a ‘climate penalty’, which can be defined as the deterioration of air quality due to a warming climate, in the absence of changes in anthropogenic polluting activities (Fu and Tian 2019). Different approaches have been presented to quantify the potential for climate warming to exacerbate O_3 and $PM_{2.5}$ pollution (Bloomer *et al* 2009, Rasmussen *et al* 2013, Colette *et al* 2015, Lemaire *et al* 2016, Lacressonnière *et al* 2017). The climate penalty on air pollution concentrations has also been estimated in terms of the associated health impacts. E.g. it has been estimated that expected increases in O_3 mortality may worsen due to climate change effects on air quality and, similarly, that expected reductions in $PM_{2.5}$ mortality may be counteracted (Von Schneidemesser *et al* 2020). Moreover, air pollutants have also been found to influence surface climate, such as regional temperature and precipitation patterns (Falloon and Betts 2010a). Particularly aerosols, such as sulphates and

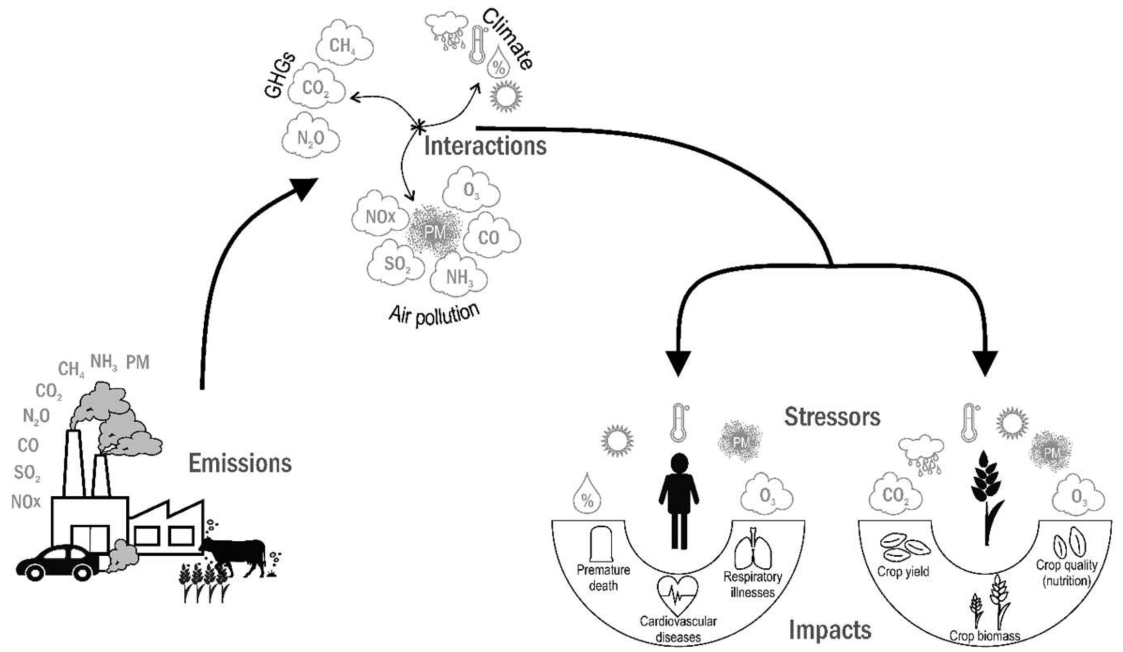

Figure 1. The complex interplay between anthropogenic emissions, interactions of greenhouse gases (GHGs), air pollutants and climate variables in the atmosphere and their role as stressors impacting human health and agricultural productivity. Greenhouse gases and air pollutants are emitted from multiple sources and can also form secondary pollutants (e.g. ozone). The combination of key stressors can cause a variety of impacts on human health and crops.

black carbon, have been found to alter precipitation (including monsoon patterns in some parts of the world) (Ramanathan *et al* 2005, Sillmann *et al* 2017).

Recent evidence suggests that the impacts of climate and air pollution on human health and agricultural crops can be amplified or modified when these stressors occur together, and in particular during extreme weather events (Dear *et al* 2005, Mills *et al* 2018b). This is important for a number of reasons. Emissions leading to impacts on human health and agriculture arise from common sources, therefore emission control efforts should be optimized, which can be done using an impact-focused approach that considers combined effects on both human health and agriculture. Furthermore, many air pollutant emissions that affect human health arise from the agriculture sector (e.g. ammonia, an important $PM_{2.5}$ precursor gas, and emissions from agricultural residue burning). Often agricultural regions are located close to highly polluted urban centers (e.g. the Indo-Gangetic plain in India), which highlights the benefits that could be gained from a coherent emission reduction policy at local to regional scales. In addition, human health and agricultural production are closely connected, for instance through food availability and quality (i.e. affecting nutrition) and worker productivity in the agricultural sector (Orlov *et al* 2020). The number of people affected by hunger globally has been slowly on the rise since 2014 and projections show that the world is not on track to achieve Zero Hunger by 2030 (SDG2) and, despite some progress, is also not on track to meet global nutrition targets (FAO, IFAD, UNICEF 2020).

Thus, air pollution and climate change represent a global concern that must be considered jointly to identify the co-benefits and possible trade-offs of reducing GHG and air pollution emissions (Hess *et al* 2020, Von Schneidemesser *et al* 2020). It is also important to get a more comprehensive understanding of their impacts in the context of global warming and achieving the SDGs, because climate change can affect the severity of impacts caused by air pollution and, vice versa, air pollution can alter the magnitude of impacts caused by climate change. Decision-making for these two stressors in conjunction and for the rather different fields of human health and agriculture is, however, very challenging. There exist a range of methods to estimate impacts of climate and air pollutants, which often treat these stressors separately, and are developed to a large extent by different communities.

Common to the impact assessments in both fields of human health and agriculture, is the inclusion of aspects of exposure and vulnerability of the affected system when estimating the impacts of hazards (i.e. air pollution and/or climate-related hazards). However, as discussed in more detail in section 3 of this topical review, methods used to estimate combined climate and air pollution impacts tend to favor different approaches for human health versus agriculture. There is also a need to consider the different time frames over which these stressors (and their control) play out, with air pollution and climate change working on near-term and long timeframes, respectively.

To estimate the future risk to human health and agriculture, further information on the changes in probability and magnitude of a specific hazard or the combination of different hazards are needed (IPCC 2012). The latter requires an increased understanding of the probability of compound events (e.g., when hazardous climate events co-occur with high air pollution episodes), which is an emerging field of research (Zscheischler *et al* 2018). Effective mitigation and adaptation measures to reduce the risk of adverse impacts on agricultural crops and human health requires going beyond current methodology. The sharing of best practice in both fields will support the development of improved impact and risk assessment methods that capture both the magnitude, extent as well as the likely frequency of impacts on both human health and agriculture to inform policymaking.

1.2. Structure of the topical review

In section 2 we will first give a non-exhaustive introduction of literature that addresses the impacts on human health or agriculture from either climate or air pollution separately. In section 3, we will discuss in more detail the methodologies that are currently applied to study the combined effect of climate and air pollution on health or agriculture. In section 4, we describe the main findings of a semi-structured literature review (see supplementary figure S1 (available online at stacks.iop.org/ERL/16/093004/mmedia)) on the combined effects of climate and air pollution on health and agricultural endpoints with reference to the effectiveness of the methodological approach in understanding interactions.

The scan for papers discussed in section 4 focused specifically on the combined effects of climatic and pollution variables, including review papers, meta-analyses, and original research papers using different models and/or experimental approaches. For human health, the bulk of literature we reviewed focuses on the air pollutants O_3 and particulate matter ($PM_{2.5}$), and aspects of non-optimal temperatures, including cold and hot extremes. The PubMed database was searched as it is a comprehensive source of biomedical and life sciences literature. To review the combined effects of air pollution and meteorological variables on human health, the following search syntax was applied to all fields: ((interact* OR synergist*) AND (air pollution OR ozone OR PM10 OR PM2.5)) AND temperature) AND (mortality OR death OR disease OR illness OR morbidity). The majority of the included studies used a time-series design, usually with daily mean temperature and air pollutant concentration as independent variables. Below, we also report findings from four longitudinal cohort studies, three studies using a case-crossover design and one prospective observational study, all being state-of-the-art epidemiological designs but not necessarily rendering comparable results. Population groups included in the studies varied, with several studies focusing on older adults, whereas in the studies including all people, sub-group analyses were often reported for age and gender strata. Data on a range of different weather variables and air pollutants from meteorological networks and monitoring stations were applied as proxies in the exposure assessment, which may have led to biases in the exposure assessment (no studies monitored individual exposure or attempted to take into consideration other factors than ambient conditions). Below, we report findings for other pollutants than those in the search term in the case such findings were given. The health endpoints in the studies varied substantially, but with the majority addressing different cardiovascular and respiratory outcomes. Considering the above parameters and, as illustrated in figure 5, the studies overall showed a high degree of heterogeneity. As the quantitative estimates across the studies in most cases are not comparable due to heterogeneity, we decided to report here only the *direction* of the interaction effects in the reviewed studies (indicated by arrows in tables 2 and 3), focusing on how temperature indices are reported to affect the air pollution impacts on health and, vice versa, how air pollutants are reported to affect the temperature impacts on health.

For agricultural crops, the bulk of the literature we reviewed focused on climatic changes in precipitation (and associated water availability) and temperature as well as O_3 and aerosol air pollutants since these play a significant role in determining agricultural productivity across broad geographical regions. The agricultural section of the review is based on systematic searches in ORIA which covers the major search engines including agricultural references, including Web of Science, MedLine, PubMed, SCOPUS, AGRIS, JSTOR. For the impacts on agriculture, the following syntax was applied to title searches: (climat* OR extreme OR temperature OR heat OR drought OR precip* OR humidit*) AND (*pollution OR ozone OR particulate*) AND (agri* OR agro* OR yield OR crop). Both the health and agricultural searches covered papers published from 1990 to 2020. The syntax-based search results were scanned on title for relevance, and then further filtered based on abstract scans, using a set of inclusion and exclusion criteria which are described in table S1 (supplementary material). Relevant papers were singled out and then complemented with any additional relevant papers referred to in the references (also known as snowballing). Regarding the search on health studies, several papers using the term modification instead of or in addition to terms for interaction were found through snowballing (see section 3.1.1 below regarding these terms). Adding the term modif* (for modification or modifying) would increase the number of hits to 496. Figure S1 (supplementary material) illustrates the methodology of the systematic review and the number of papers identified at each step of the review process. Regarding the search on agricultural crop studies, we focused the review on modelling studies (since reviews of the substantial body of empirical data have been conducted by others previously) and extracted information from a variety of observational assessment and process-based modelling methods, which included agricultural yield as an endpoint.

Finally, based on this review, we propose in section 5 how research in this area should be further developed to provide an improved understanding of the impacts associated with future combinations of air pollution and climate change.

2. Impacts of climate and air pollution on human health and agriculture

2.1. Human health

2.1.1. The impacts of non-optimal temperatures

During the last two decades, the number of epidemiological studies investigating the exposure-response (ER) relationship between indicators of thermal stress and health effects has been growing steadily. Studies of this relationship usually have a temperature index as the primary weather variable, but indices including other variables, most often humidity, are also applied (e.g. figure 1). The ER functions for the temperature effect typically show a U- (or V- or J-) shape[8], with a certain midrange temperature interval associated with no enhanced risk, while temperatures below and above the midrange are associated with increased risks (figure 2(a)). The change-point typically varies across regions. The temperature at which mortality is at its lowest may be denoted the optimal temperature (OT) (Honda *et al* 2014, Gasparrini *et al* 2015). Daily time-series regression analysis and case-crossover designs are the most commonly applied method for establishing the ER relationship for heat stress and mortality and morbidity (Bunker *et al* 2016, Vicedo-Cabrera *et al* 2019). The shape of the ER relationship as temperature increases is not clear and may vary across regions, with some studies indicating nonlinearities with significant increases at the extremes of the temperature distribution (Kolb *et al* 2007, Deschênes and Greenstone 2011). Understanding the determinants of regional variability in the health impacts of heat and the role of adaptive mechanisms in modifying these impacts is key to assess the potential public health consequences of global warming (Medina-Ramon and Schwartz 2007).

Estimates from the Global Burden of Disease Study (IHME 2020) are based on ER functions for temperature and mortality outcomes and show that about 2 million premature deaths per year are currently caused by non-optimal temperatures, of which about 85% are caused by low temperatures and 15% by high temperatures. For high income countries, the cold-related burden is 15 times greater than the heat-related burden, whereas this relationship is switched for other regions, such as south Asia where the heat-related burden is 1.7 times greater than the cold-related burden and sub-Saharan Africa where it is 3.6 times greater (Murray *et al* 2020). In a recent study by (Vicedo-Cabrera *et al* 2021), location-specific ER functions were applied in an estimation of the contribution of human-induced climate change to heat-related mortality over the period 1991–2018, found to be 37% on average for the 43 countries included in the study.

Regarding the major health endpoints affected by non-optimum temperatures, reviews and meta-analyses conclude that both high and low temperatures are linked to cardiovascular and respiratory mortality and morbidity (Basu 2009, Astrom *et al* 2011, Turner *et al* 2012, Ye *et al* 2012, Yu *et al* 2012, Cheng *et al* 2014, Benmarhnia *et al* 2015, Lian *et al* 2015, Li *et al* 2015b, Bunker *et al* 2016, Phung *et al* 2016, Xu *et al* 2016, Moghadamnia *et al* 2017, Wang *et al* 2017, Sun *et al* 2018). According to a review by Cheng *et al* (2019), the major focus of studies to date has been on heat and/or cold (using various temperature indices), whereas fewer studies analyzed heat waves and cold spells, and temperature variability received the least attention. Studies show that cold effects tend to be delayed and persist for a longer period (up to a few weeks), whereas the effects of hot temperatures are acute and last for a few days only. Xu *et al* (2016) reviewed studies of heat wave-related deaths and concluded that the heatwave intensity plays a relatively more important role than duration. This implies that it may not be appropriate to fit temperature-health relationships for both cold and heat in the same model, with same length of lags (Cheng *et al* 2019).

In addition to cardio-respiratory effects, studies have revealed an association between ambient temperature and a range of other endpoints, including diarrheal diseases (Carlton *et al* 2016), maternal health (Kuehn and McCormick 2017), infant mortality (Son *et al* 2017), and renal diseases (Hansen *et al* 2008). Moreover, exposure to non-optimum temperature may affect performance of various perceptual, cognitive, and psychomotor task types (Hancock *et al* 2007).

2.1.2. The impacts of air pollution

Inhalation of fine particulate matter ($PM_{2.5}$) poses health risks as it penetrates into sensitive regions of the body and can lead to serious health problems and premature mortality (WHO 2013). Tropospheric O_3 has also been shown to have considerable negative health effects that may lead to premature mortality (Brauer *et al* 2012, Silva *et al* 2013) and is linked

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[8] An N-formed shape is reported in some studies as well, which could be explained by a lower mortality on very cold days due to reduced general activity (Barreca 2012, Honda *et al* 2014).

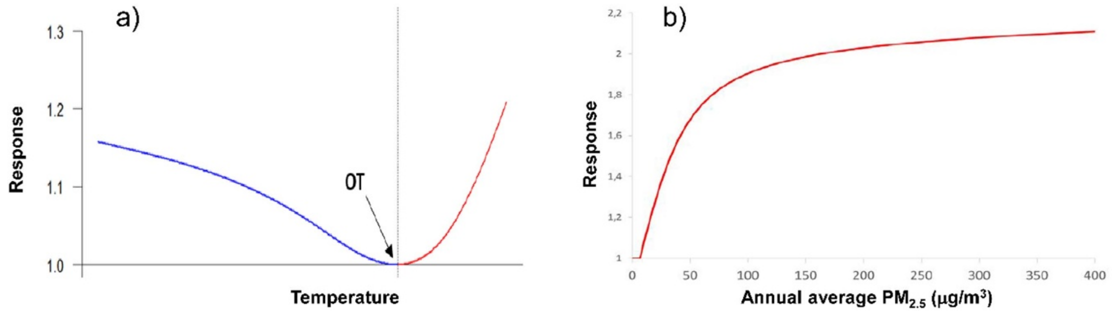

Figure 2. Exposure-response curves. (a) Illustrative U-curve for the relationship between exposure to ambient temperature and the response (here the relative risk of premature death). OT: optimum temperature. (Figure rendered with permission from Antonio Gasparrini). (b) Exposure-response relationship between long-term exposure to PM2.5 and the response (here the relative risk of dying from a stroke in people 65–70 years of age (based on lookup table in (Apte *et al* 2015)).

to asthma in children (Zheng *et al* 2015). According to the World Health Organization (WMO) and the Global Burden of Disease Study (IHME 2020), air pollution causes about seven million premature deaths per year, of which about 0.4 million deaths are caused by ambient O_3 pollution and the remaining burden is caused by ambient and household $PM_{2.5}$. Other pollutants, including NO_2 and SO_2 are also found to pose health risks (Johns and Linn 2011, Mills *et al* 2016).

Health effects of specific air pollutants have been established by means of different methods. These methods include laboratory studies *in vitro* and *in vivo*, for instance to explore the role of oxidative stress on pulmonary inflammatory response associated with air pollution exposure and the use of clinical studies where people are deliberately exposed to specific air pollutants under conditions simulating ambient exposures (Li *et al* 1996, Sehlstedt *et al* 2010). The main approach to modelling health impacts of air pollution exposure in applied studies, including for future projections, is the use of ER functions derived from epidemiological studies. A substantive amount of epidemiological studies using various designs to reveal either short-term or longer-term impacts have demonstrated association between air pollution and a range of health endpoints, including cardiopulmonary mortality and hospitalization rates, maternal health, neurodevelopment and cognitive impairment in children, and increased risk of hospitalizations for neurological disorders and diabetes among the elderly (Lanki *et al* 2006, Pope 3rd *et al* 2009, Calderon-Garciduenas *et al* 2014, Stafoggia *et al* 2014, Zanobetti *et al* 2014, Balakrishnan *et al* 2018). The quantitative relationships between air pollution exposure and health effects are thus well established and have been subject to extensive review (see e.g. US-EPA 2009, Hei 2010, Shah *et al* 2013, WHO 2013, Atkinson *et al* 2014). Figure 2(b) shows an example of the ER function for stroke mortality in elderly (65–70 years) and long-term exposure to PM2.5.

2.2. Agricultural crops

2.2.1. The impacts of climate and climate extremes

Climate has a strong influence on crop productivity, with changes in temperature and precipitation being the dominant factors affecting crop yields (Lobell and Field 2007). Temperature plays a critical role in plant developmental stage, leaf phenology, physiology and reproduction, and each crop has a temperature range for optimum performance. Even a brief period of extremes of seasonal or diurnal temperatures can cause severe yield reductions in many crops, with some plant stages being particularly sensitive (Wheeler *et al* 2000, Porter and Semenov 2005, Ugarte *et al* 2007). Increased yield variability and reduced yields (Troy *et al* 2015) are likely to result from projected increases in heat waves and droughts (Meehl and Tebaldi 2004, Schär *et al* 2004, Beniston *et al* 2007). Extremely high daytime temperatures are damaging and occasionally lethal to crops (Porter and Gawith 1999, Schlenker and Roberts 2009). Increased frequency of unusually hot nights may also be damaging (Peng *et al* 2004, Wassmann *et al* 2009, Welch *et al* 2010). Conversely, the reduction in frost occurrence events may reduce risk under climate change though if the length and timing of the growing season also changes, the risk related to this temperature hazard may remain largely the same as under current day conditions (Olesen *et al* 2011).

Rainfed cropping systems are likely to suffer from water stress in situations where rainfall is substantially reduced by climate change. Flowering, pollination and grain filling of most cereal crops are particularly sensitive to water stress (Rosenzweig *et al* 2001). Less information is available concerning the potential impacts of changes in extreme rainfall and flooding (Falloon and Betts 2010a), with impacts depending on the magnitude and duration of the event, type and growth stage of the crop, and the temperature during flooding. Crops are more easily damaged by flooding during reproductive stages, such as pollination, than during the vegetative and flowering stages. Most crops are largely intolerant to flooding (with rice being the obvious exception), with damage (or destruction) occurring via impacts on transpiration, leaf area expansion and productivity, and increasing pest and disease problems (Falloon and Betts 2010a). Irrigation plays an important role in avoiding yield losses due to climate change induced variability in rainfall, exemplified by the fact that even in regions with sufficient seasonal rainfall, irrigated yields can surpass rainfed yields; irrigation can also moderate the effects of temperature stress (Grassini *et al* 2009).

Two different methods are commonly used to assess the effect of changes in climate on agricultural yields. Firstly, process-based crop models used in conjunction with global circulation models to assess the effect of climate scenarios on yield and secondly, statistical regression modelling of historical yield and climate data to assess crop yield responses to climate variables. Meta-analyses of these various types of studies are useful to summarize outcomes and assess consensus of the magnitude and direction of altered yields with changing climate, such as in the 5th Assessment Report of the Intergovernmental Panel on Climate Change (IPCC AR5) (Challinor *et al* 2014). One such meta-analysis, described in the IPCC AR5, explored the effect of changes in mean climate and the IPCC AR5 concluded that there is *medium confidence* that across many global regions, climate trends have negatively affected wheat and maize production, with effects on rice and soybean being less obvious. These negative impacts of warming were further quantified using a general linear model applied to data from 1700 published studies for wheat, rice and maize and found an average yield loss of 4.9% per °C (Challinor *et al* 2014). However, it should be noted that there is also *high confidence* in the IPCC AR5 that warming has benefitted crop production in some high-latitude regions (e.g. northeast China, the UK) (Porter *et al* 2014).

However, it is increasingly recognized that the impacts of climate change on agriculture will be a function of the probability, frequency and severity of possible extreme events (Rosenzweig *et al* 2001), though studies exploring the impact of such extreme events using either historical data or model projections are extremely limited (Troy *et al* 2015). This is largely due to the challenges in aggregating data across different growing regions as well as selecting an appropriate assessment method and climate extreme metric (e.g. that can adequately relate extremes to changes in yield). Climate extreme studies have found that non-linear and threshold type relationships exist between yield and both precipitation and temperature climate indices (Porter and Semenov 2005, Schlenker and Roberts 2009, Troy *et al* 2015, Daloz *et al* 2021). Figure 3 provides a good example of such non-linearity. Various temperature extreme metrics (heat waves, no. of hot days, min-, mean-, max-temperatures) are plotted against average crop yields for wheat, soy, corn and rice across the US according to probability density functions. This allows the correlation between a yield value and a climate index to be described without prior assumptions of the type of relationship (e.g. linear or non-linear) (Troy *et al* 2015). The results show high variability in the correlations between different extreme climate metrics and changes in yield both within and between species (though it should be emphasized these results do not demonstrate causation and do not allow for confounding variables). This highlights the need for further research to understand which characteristics of climate extremes (e.g. number of hot days above a threshold, mean temperature, heatwaves) are the most important determinants of yield and whether combinations of multiple climate extremes (e.g. extreme indices of temperature and precipitation) would result in further compounding of yield losses. It is also important to address how these yield losses may vary between crops and in relation to other environmental variables.

2.2.2. The impacts of air pollution

A number of air pollutants (PM, O_3, SO_2, NO_x, NH_3, fluorides) have been found to impact on the growth and productivity of agricultural crops (Emberson *et al* 2003, CLRTAP 2017). O_3 and PM are considered the most important due to the size of the impact resulting from elevated ambient concentrations and the prevalence, especially over rural and agricultural regions, of damaging concentrations of these pollutants.

O_3 is a powerful and aggressive oxidant that has adverse effects on agricultural crops and productive grasslands. Effects include reduced growth and yield, visible injury, reductions in photosynthesis, alterations to carbon allocation, reductions in green leaf area including earlier leaf senescence and changes to the quality of harvestable products such as cereal grains (Fuhrer and Booker 2003, Ashmore 2005, Fiscus *et al* 2005, Heath 2008, Fuhrer 2009, Ainsworth *et al* 2012, Ainsworth 2017). Our understanding of these effects is based on extensive empirical investigation using a variety of methods (e.g. transect studies, chemical protectant studies, filtration and fumigation studies) to compare the effect of different levels of pollutant concentration on crop physiology, growth and yield, and to develop ER relationships (Emberson *et al* 2003). Flux-based metrics (which allow for the effects of climate-related parameters on O_3 uptake) show that the sensitivity to O_3 varies by species type and cultivar with some of the more sensitive crops being wheat, tomato, soybean and salad crops (Mills *et al* 2007). ER functions for wheat, potato and tomato have been developed for yield as shown in figure 4; ER functions also exist for temperate and Mediterranean grasslands. ER relationships have been developed with different endpoints to take into consideration the crop response of most importance (e.g. grain yield, 1000-grain weight, protein yield, fruit quality, etc.). These ER relationships can be used in

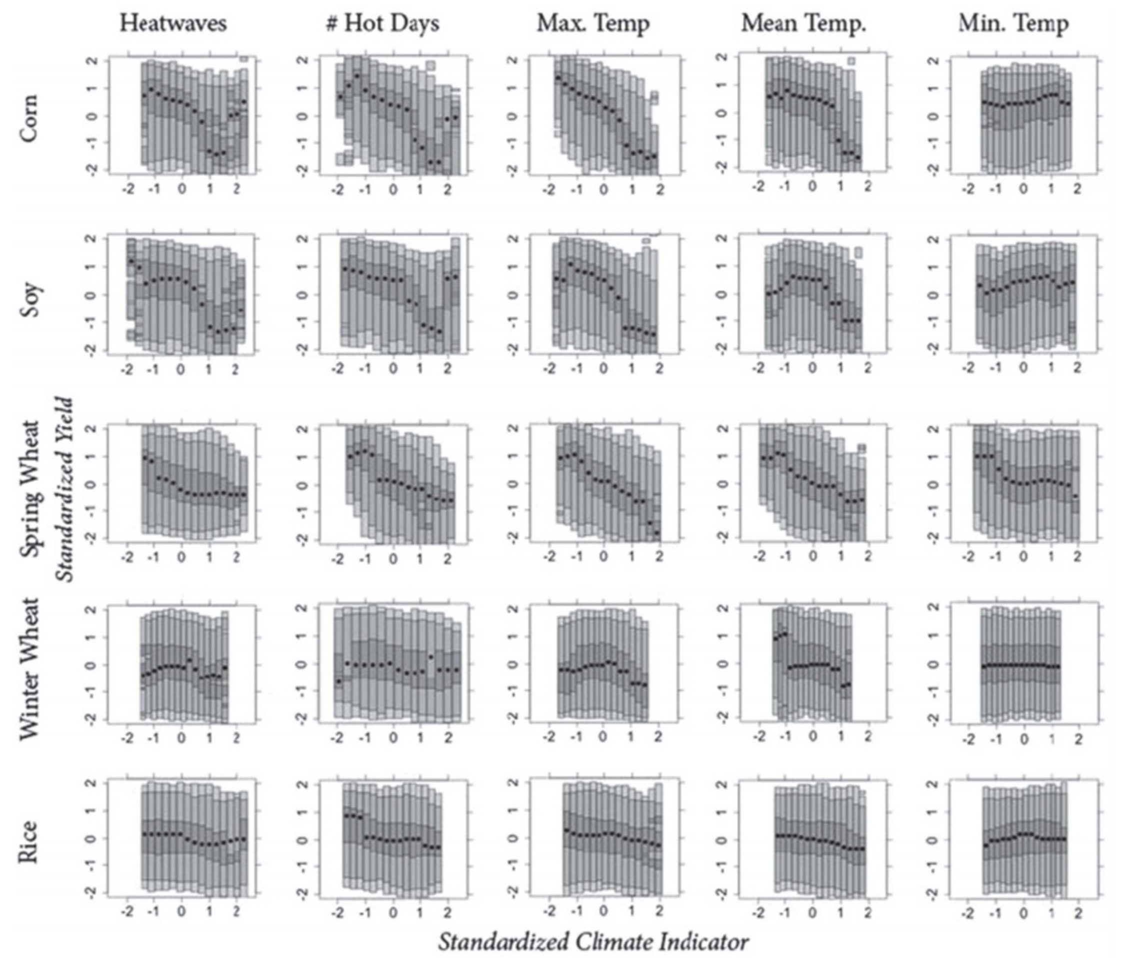

Figure 3. Conditional probabilistic relationships between five different temperature characteristics and crop yields across the growing season for five crops covering the period 1948–2010. These relationships are derived using the epidemiological type of approach described in section 3.1.2. The black dot in each panel is the mode of the conditional probability of yield for each slice of the climate index values; the darkest grey color contains the 50% highest density region, the medium grey the 95% density, and the light grey the 99% density. Reproduced from Troy *et al* (2015). © IOP Publishing Ltd. CC BY 3.0.

conjunction with atmospheric chemistry transport models and agricultural statistics on growing season and yield to estimate economic losses with a range of studies showing that between US$ 14 and 26 billion were lost in the year 2000 as a result of O_3 induced reductions in crop yield (Emberson 2020).

Particulate Matter (PM), commonly referred to as aerosol when considered in relation to vegetation, includes dust, sulphates, nitrates, secondary organics, organic carbon and black carbon. It will affect crop productivity predominantly via changes in radiation quantity and quality but also through aerosol deposition to the canopy which can limit penetration of radiation to the photosynthetic machinery, cause damage via particle toxicity (e.g. heavy metal and acidic particles) or where the particles can wedge open stomata causing the plant to lose control of gas exchange (Mina *et al* 2018). An increase in the diffuse component of radiation can benefit plant productivity up to a certain point. This may be due to a number of mechanisms including increased penetration of radiation into the crop canopy (promoting more efficient canopy level photosynthesis) or through alterations to crop microclimate that might limit the need for transpirational cooling (Mercado *et al* 2009). There are no ER functions that are capable of assessing these different types of damage caused by total aerosol load on agricultural crops. This is due to the non-linearities in the relationship between aerosol and yield which preclude the effectiveness of using simple ER functions based on changes to solar irradiance alone which would tend to overestimate yield losses due to aerosol pollution (Chameides *et al* 1999, Tie *et al* 2016). Semi process-based models (e.g. land ecosystem models) and process based models offer the opportunity to model the effect of aerosol on radiation quantity and quality and the consequences for crop productivity as discussed further in section 3.2.2 (Mercado *et al* 2009). Other approaches have explored the effect of aerosols (a large contributor to the Atmospheric Brown Cloud, ABC) on regional climate (precipitation and temperature), using regression models (Auffhammer *et al* 2006). Clearly, studies that assess changes in yield due

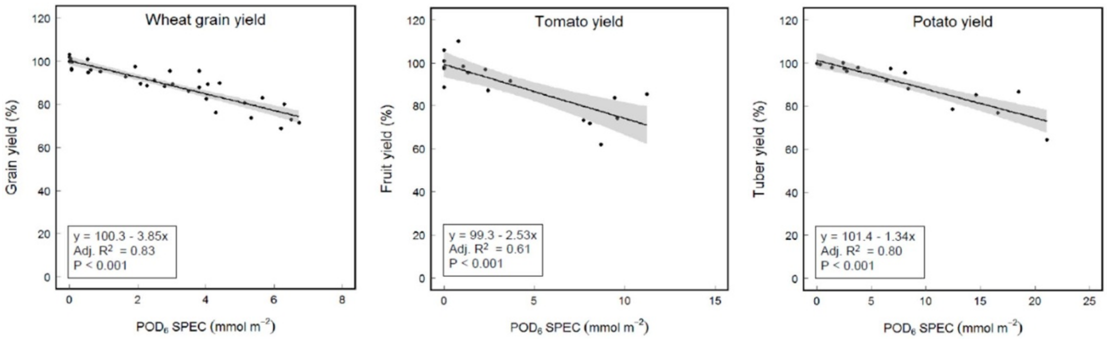

Figure 4. European flux based exposure response (ER) functions for wheat grain yield, tomato fruit yield and tuber yield of potato and POD_6SPEC (the accumulated stomatal O_3 flux above a threshold of 6 nmol m^{-2} s^{-1} estimated using a species-specific parameterization for stomatal conductance) for sunlit leaves. The grey areas show the 95% confidence interval. Reproduced with permission from CLRTAP (2017).

to the combined effect of aerosols on climate variables (radiation quantity and quality, temperature and precipitation) as well as direct effects of aerosol deposition on plant productivity are needed. However, our limited understanding of the processes by which aerosols will influence crop productivity, both indirectly (through changes in meteorology) and directly (through damage via deposition to the crop), have so far precluded studies that would comprehensively assess these effects of aerosols. Section 4 provides details of the progress in modelling approaches that has been made to assess these effects.

3. Methodological approaches studying the combined effects of air pollution and climate

The development of robust ER relationships has been crucial to our ability to assess the expected damage caused by air pollution and/or climate to crops or human health (see also figure 1). There are two main methodological approaches to developing ER relationships (and hence understanding the influence of air pollution and/or climate on human health and agriculture). These are: (a) empirical regression-based studies that explore response or damage of a receptor to prevailing pollutants or climatic conditions (used in both human health and crop impact assessments) and (b). Experimental studies that control exposure of a receptor to pollution or certain environmental (climatic) conditions (mostly used for crop impact assessment, but also include clinical trials for human health response to air pollution and heat stress). Important in the development of ER relationships are the metrics that are used to express the exposure (to climate variables or pollutants) over time and the response variable caused by such exposure, to ensure that key responses to each stressor are captured. The respective response of a human body or a plant to a pollutant or climate stressor is also a function of their vulnerability (i.e. the sensitivity or susceptibility to harm and lack of capacity to cope and adapt to one or more stressors). An exemplary list of the more commonly used metrics for pollution and climate along with the response parameters often associated with these metrics are provided in table S2 (supplementary material). Although this list is not comprehensive, it shows the wide range of 'exposures' and 'responses' that can be recorded, even when only considering pollutants and climate change acting as individual stressors.

There are fundamental differences in health and agricultural modeling for projection of future impacts or damages. In agricultural modelling the state-of-the-art methods are process-based models as described in section 3.3 below, that are based and calibrated on insights from experimental studies (section 3.2). Whereas for projections of future health impacts, process-based models do not exist, and state-of-the-art methods rely on statistical relationships based on epidemiological studies (section 3.1). Table 1 presents an overview of the methods applied in studies quantifying the impacts of air pollution and climate on human health and crops, which are further detailed below. The table provides an assessment of how commonly used these methods are in the respective fields of human health and agriculture based on the literature reviewed in this paper.

3.1. Empirical regression-based methods

3.1.1. Methods for human health

Epidemiologic evidence suggests that air pollutants, particularly $PM_{2.5}$ (or PM_{10}) and O_3 may confound the estimation of non-optimal temperature impacts on health (e.g. due to heatwaves) (Turner *et al* 2012). Vice versa, temperature may confound the estimation of air pollution impacts on health (Stafoggia *et al* 2008). Confounding may be difficult to avoid because meteorological variables and air pollution concentrations often vary in a similar way (multicollinearity). The confounding effect is believed to be relatively small, however, and as described above, there is

Table 1. Overview of the methods to quantify the combined impacts of air pollution and climate on human health and crops as described in detail in section 3. The number of '+' signs behind the symbol for human health and crops indicates how much this method is applied (i.e. how many studies were found in the literature review) in the respective discipline, with '+' indicating very limited number of studies and '+++' indicating many studies, respectively.

Approach	Human health	Arable crops	Robustness
Empirical regression-based studies	Daily time-series and case-crossover designs (mainly); mortality and morbidity endpoints. Controlling for confounding factors, and investigating interaction and modification.	Statistical multiple linear regression techniques that analyze time series of historical data to derive relationships between crop yields and climate variables and pollution	🧍 +++ Many studies establish combined effects, but these are not applied in future projections. Large heterogeneity across studies. 🌿 + Not many studies. Choice of metric and consideration of confounding factors important.
Experimental studies	No experimental evidence on combined effects of heat stress and air pollutants.	Fumigation &/or filtration studies conducted in field chambers &/or Free Air Concentration Enrichment (FACE) facilities allow for control of pollutant dose over crop growing season	🧍 n.a. 🌿 +++ Numerous studies. However, field chambers may cause artifacts in pollutant & climate variables; FACE only allows for addition of pollution and difficult to manipulate climate variables; limited by factorial design.
Modelling studies	No modelling studies accounting for combined effects of heat stress and air pollutants, apart from some studies that project changes in the air pollution health effects as a consequence of climate change (e.g. Von Schneidemesser *et al* 2020).	**Semi-process-based** use existing process-based land-ecosystem models that incorporate the effects of O_3 on ecosystem carbon and water dynamics through the direct effect of the pollutant on photosynthesis and damage. **Flux-based** use stomatal flux-based metrics and associated ERs to explore the influence of climate variables on the uptake (or dose) of air pollution and consequent damage. **Process-based** incorporate interaction between climate & pollution variables, crop characteristics and environment/management to assess damage.	🧍 + A few studies, but these cover only the atmospheric interactions of climate change and air pollution and resulting health effects. 🌿 ++ Growing number of studies. However, **semi-process-based studies are** dependent on use of an appropriate pollutant metric. Flux-based studies are dependent on representativeness (by species/cultivar and geographical location) of empirical ERs. **Process-based studies** require robust model formulation and parameterisation (by species/cultivar/management) which is reliant on interpretation of available empirical data.

abundant evidence of an independent effect of both temperature and air pollution on mortality (Bell *et al* 2008, Basu 2009). As reviewed in section 4 below, a growing body of literature is, however, reporting modifying and interacting effects on the association between air pollution, thermal stress, and health.

To model the combined effect of co-occurring exposure to air pollution and temperature, interaction between the stressors needs to be assessed. Several studies use nonparametric bivariate response surface models to visually explore the joint pattern or relationship of air pollutants and temperature (e.g.

(Stafoggia *et al* 2008, Burkart *et al* 2013, Li *et al* 2015a, Tian *et al* 2018a, Guo *et al* 2019)). By including interaction terms in the parametric regression models, or by means of multiple linear regression models, interaction can be assessed quantitatively (Katsouyanni *et al* 1993, Ren *et al* 2008, Burkart *et al* 2013, Chen *et al* 2018, Lee *et al* 2019). Hu *et al* (2008) used time-series classification and regression trees to assess interaction. If the joint effect is higher than the effect expected by the sum of the individual effect, there is a synergistic interaction. If it is lower, there is an antagonistic effect. Departures from additive joint effects can also be assessed using the relative excess risk due to interaction (Wang *et al* 2020). One should note that the terminology is ambiguous for what constitutes effect modification and interaction, and their assessment is very sensitive to confounding, lack of independency, and measurement error (VanderWeele 2009, Corraini *et al* 2017). In air pollution epidemiology, the terms modification and interaction are often used interchangeably. When the authors report how stratification affects an association, one may consider the output as estimates of effect modification. We found that most studies use one-way stratification, meaning they investigate how the association between temperature and health differs across air pollution strata or, vice versa, how the association between air pollutants differs across temperature strata, whereas some investigate the interaction both ways (Chen *et al* 2018).

Stratification of the sample population by, e.g. age, gender, and socio-economic status, enables an investigation of the modifying effect of these parameters. This can help identify sub-populations particularly vulnerable to co-exposure to air pollution and non-optimal temperatures and establish the ER relationship for vulnerable sub-populations. In a review of epidemiological studies of mortality and high temperatures, Basu (2009) concluded that whilst there are general trends regarding vulnerable sub-groups, such as the elderly, women, and people with low socio-economic status, the size and distribution of these groups varied by location and study population, implying a need for region-specific policies, especially in urban areas. This is likely to be the case when considering vulnerability to co-exposure to non-optimum temperatures and air pollution as well, since the nature and size of interaction effects vary across studies (Chen *et al* 2019).

3.1.2. Methods for agriculture

The situation for agriculture is a little different since the mechanisms by which climate variables (e.g. radiation, temperature, water availability) and atmospheric CO_2 concentrations influence crop physiology, development, growth and yield are well established. Since exposure and sensitivity to air pollution will depend upon some of these key physiological responses, we know that the effect of climate variables and air pollution are inextricably linked. Therefore, it follows that climate variables will have a confounding effect on air pollution. Since air pollution can also impact plant physiology (e.g. by altering fundamental mechanisms, such as photosynthesis and stomatal conductance), we also know that air pollution will influence responses to climate variables. What is less well known are the exact mechanisms by which pollution and climate variable stressors will interact, and more specifically, their combined thresholds for response and damage.

Empirical regression-based studies can help identify, and to some extent constrain, the scale and magnitude of the response to such interactions between climate and air pollution stressors by providing observational evidence of combined effects, but these studies are rare with respect to exploring impacts on crops (see table 1). Those that do exist use a variety of statistical multiple linear regression techniques (e.g. Burney and Ramanathan 2014, McGrath *et al* 2015, Liu *et al* 2016, Gupta *et al* 2017, Tai and Martin 2017) to analyze 5–30 year time series of historical data to explore the relationship between past crop yield outcomes and trends or inter-annual variations in weather variables (e.g. monthly temperature and precipitation; temperature extremes) and pollution.

An important consideration for such models is the selection of an appropriate index to quantify the level of pollution or change in climate variable to use in the regression modelling. Indices representing pollution vary from the use of metrics representing emissions (e.g. Burney and Ramanathan 2014) to pollutant concentrations (e.g. Tai and Martin 2017) and pollutant uptake. Climate metrics range from growing season means of temperature and precipitation (Burney and Ramanathan 2014) to those with a focus on a single climate extreme index such as killing degree days (KDD) (Tai and Martin 2017) (see also table S2). There are a number of key challenges with this type of empirical regression-based approach. Firstly, it is important to understand how confounding factors may influence yield response to the selected index (e.g. high temperatures and reduced soil water that tend to co-occur with O_3 and themselves cause yield losses are not captured by an index that simply relates O_3 exposure to yield). Secondly, it may be that the inadvertent selection of resistant crop cultivars may cause a change in the yield response to pollution and climate over time that the index is unable to account for, and thirdly, it is important to ensure that the pollution metrics accurately estimate damage.

3.2. Experimental studies

3.2.1. Studies for human health

While epidemiological analyses as described in section 3.1 provide an estimate of the statistical association between exposure and mortality and morbidity impacts on a population level, from which ER relationships are derived, toxicological studies (including animal studies), and clinical studies can improve understanding of the underlying physiological mechanisms that are responsible for the increased health risk, such as those linked to, e.g. inflammation, oxidative stress, heat cytotoxicity, and ischemia (Mora *et al* 2017, Longhin *et al* 2020). Regarding air pollution, clinical studies include controlled human exposure experiments where subjects (usually healthy young adults) are exposed to elevated air pollutant concentrations while transient and reversible biomarker or physiologic responses are evaluated. The World Health Organization uses results from such chamber studies in addition to large-scale epidemiologic studies when establishing Air Quality Guidelines, while also accounting for toxicological evidence from, e.g. animal studies and *in vitro* models, to strengthen plausibility of an effect (WHO 2005). In the US, the US-EPA conducts controlled human inhalation-exposure studies to support the establishment and review of the National Ambient Air Quality Standards (NAAQS) for criteria pollutants. According to an evaluation by NAS (2017), controlled human-inhalation exposure studies provide unique information that cannot be obtained from animal inhalation studies nor from epidemiological studies. Examples of the evaluated studies are Devlin *et al* (2014) and Madden *et al* (2014).

Controlled human exposure studies are also carried out to enhance the understanding of heat stress on humans. For instance, studies have investigated short-term responses in cardiac function (Hodges *et al* 2018), arterial function (Kaldur *et al* 2016), molecular mechanisms affecting stress-associated responses that can lead to organ damage (Bouchama *et al* 2017), and how various physiological responses to heat are affected by labor intensity (Yang *et al* 2017). In sports medicine, heat stress is often studied in context of heat adaptation (see, e.g. Tyler *et al* 2016).

We have not found any experimental or toxicological studies addressing the effects of co-exposure to hot temperatures and air pollution, and hence, we limit the review of combined effects in section 4 to epidemiological evidence.

3.2.2. Studies for agriculture

For agricultural crops, experimental studies have been far more widely used because they do not have the same constraints as experiments to investigate human health. This is likely the reason why these studies are far more prevalent in the literature than the empirical regression-based studies discussed previously.

A substantial and growing body of experimental evidence exists, demonstrating the combined impacts of air pollution (predominantly focusing on O_3), CO_2 and climate variables on crop physiology, development, growth and yield. The methods used for these experimental studies are usually open top chamber or free air concentration enrichment (FACE) experiments that allow controlled additions of pollution concentrations (including CO_2), sometimes under a particular climate (meteorological regime such as reduced precipitation or variable temperatures). The effect of pollution in combination with climate-related factors is then investigated by increasing the factorial design of experiments. FACE studies have the advantage of being conducted under field conditions (with the introduction of very little, if any, experimental artifact). However, only additions of pollution or CO_2 concentrations above ambient concentrations can be made, which, at very polluted sites, complicates efforts to develop ER relationships across the full range of exposures.

These experiments, especially FACE studies, are costly and limited in scope (e.g. number and range of interacting variables that can be explored, global geographical coverage). Nevertheless, reviews of these studies (Fuhrer 2003, 2009, Ainsworth *et al* 2012) have identified some common responses to key combinations of stressors. These are described below in relation to the leaf- and canopy-level processes with most studies focusing on how this combination of stressors influences either the pollutant dose or the plant response to an effective pollutant dose.

Data from multiple experiments, locations and years can be pooled from studies which use a common approach to defining pollutant exposures and plant response (such as change in biomass or yield), allowing the development of robust ER functions. This type of approach was used to explore air pollution effects on crops in North America and Europe, where research programs conducting standardized filtration and fumigation experiments at multiple locations were run during the 1980s and 1990s (Emberson 2020). This allowed the development of robust ER functions for these regions, but brought into question the transferability of these ER functions to other global regions where different climates and management practices may alter the sensitivity of the crop response to pollution (Emberson *et al* 2009). These empirical data also made clear that pollutants were unlikely to act individually. In most polluted environments there is a complex mix of pollutants sometimes referred to as a 'pollutant cocktail' to which plants are exposed and which can also modify the underlying soil through acidification and eutrophication (HTAP 2010). We also know that the conditions that often lead to high pollutant levels (especially in relation to the photochemical pollutant O_3) often co-occur with other meteorological or climatic conditions that are likely to cause stress (e.g. heat stress, drought stress, low atmospheric humidity, etc). This clearly demonstrated the importance of understanding how multiple pollutants might act together to alter physiology, growth and productivity, and how these effects may interact with other, climate-related, environmental stressors. To apply such knowledge to understand the scale of effects on a regional to a global basis will arguably require a modelling approach. Therefore, it is becoming increasingly important to improve our understanding of the mechanisms by which pollutants and climate variables interact to cause damage (Emberson *et al* 2018).

3.3. Towards process-based modelling studies

3.3.1. Studies for human health

Several studies have considered how climate change induced changes in air pollution may affect health outcomes in the future (e.g. Schneidemesser *et al* 2020). These studies take into consideration atmospheric interactions between climate and air pollution. To our knowledge, the quantitative estimates of potential joint effects of exposure to air pollution and non-optimal temperatures, as shown in epidemiological studies, have not been applied to project future health effects. Moreover, we do not know of any bottom-up modelling attempts taking into consideration the various drivers and mechanisms that may be involved in the combined effects of climate and air pollutants, such as atmospheric interactions as well as changes in exposure patterns and physiological mechanisms leading to adverse health outcomes.

3.3.2. Studies for agriculture

To fully account for the interactions between air pollution and climate variables on crop response, an understanding of the key processes that will influence pollutant concentrations, climate variability, pollutant deposition and subsequent impact is required (Emberson *et al* 2018). To date, three main modelling approaches, reflecting different levels of understanding of processes, have been applied. These can be classified as (a) semi-process-based modelling; (b) flux-based modelling and (c) process-based modelling and are described below.

3.3.2.1. Semi-process-based modelling

Semi-process-based modelling uses existing process-based land-ecosystem models that incorporate the effects of O_3 (predominantly using concentration-based O_3 indices) or aerosol on ecosystem carbon and water dynamics through the indirect (in the case of aerosols) or direct effect of the pollutant on photosynthesis or plant productivity (Emberson *et al* 2018). As such, these models are in theory able to address interactive effects of O_3, aerosol and other environmental drivers (e.g. climate variables, land use, management practices, [CO_2], nitrogen deposition, etc) on plant growth. A limitation of these models for O_3 is that the processes that will influence gas exchange and hence O_3 uptake that are inherent in process-based modelling are not actually used to estimate pollutant uptake (e.g. rather a concentration based O_3 index is often used to estimate O_3 damage) so there is an inconsistency within the model construct that is likely to be important in determining effects (see section 3.2.1). For aerosols, these models offer the opportunity to assess the effect of aerosol on radiation quantity and quality and the consequences for crop productivity (Mercado *et al* 2009, Schiferl and Heald 2018) by relating a change in diffuse radiation to a whole season effect on productivity (e.g. radiation use efficiency). However, these models are currently unable to capture the full canopy-climate interactions and processes that are necessary to fully describe the diurnal and seasonal interactions between aerosols, solar radiation (quantity and quality) and canopy architecture.

3.3.2.2. Physiological flux-based modelling

There are a growing number of studies that have used the stomatal flux-based metrics and associated ER relationships (see section 2.1) to explore the influence of climate variables on the uptake (or dose) of air pollution and consequent damage (Emberson *et al* 2020). These studies can both provide estimates of the magnitude of damage (both in terms of productivity, but also associated production and economic losses) as well as the geographical locations and biophysical (including climatic) conditions that are most likely to lead to damage.

3.3.2.3. Process-based modelling studies of combined climate and air pollution effects

The two hybrid approaches described above have elements of process-based modelling, but also rely on empirical relationships for substantial components of air pollution's impact on development, growth and productivity. All modelling relies to some extent on empirical relationships, but it is possible to define these by ever more discrete processes of pollution damage. Often these processes incorporate the influence of climate variables and characteristics of the crop (and variety) and environment (e.g. elevation, geographical location, soil textures, etc). This provides a far more integrated approach that, in theory, allows the influence of different factors (e.g. physiological traits, crop management practices and different ranges and combinations of environmental conditions) to be explored in relation to their role in determining damage from a combination of stresses (Emberson *et al* 2018). The benefit of this type of modelling approach is nicely illustrated for aerosols where both indirect (effects of aerosol on radiation, precipitation, temperature which will influence the resources available for crop productivity) and direct effects (via deposition and toxicity that will cause direct damage), and their diurnal and seasonal variability in causing effects to canopy and leaf scale processes, can be taken into account (Zhang *et al* 2018a). These types of modelling studies have become more common over the past 5 years or so though still tend to focus on single pollutants in relation to multi-climate variable stresses.

4. Combined effects of climate and air pollution for human health and agricultural crops

In the following section, we review the main findings regarding combined effects of air pollution and climate variables for human health and agricultural crops. For health, such findings are derived from epidemiological studies. For agricultural crops, findings on combined effects are derived from empirical regression-based, experimental, as well as the various types of modelling studies described in section 3.

4.1. Human health

Meteorological factors, including temperature, can modify the association between air pollution and health by affecting people's exposure to air pollution. This can happen, for instance, as temperature may affect the concentration of air pollutants in ambient air, as described in section 1. Meteorological factors can also affect people's exposure to air pollution by modifying their activity pattern, e.g. how much time they spend outdoors and to what extent windows are kept open (Katsouyanni 1995, Tian *et al* 2018b). Modification of the association between air pollution and health may also happen if thermal stress makes people more sensitive to air pollution (Ren *et al* 2006). Vice versa, air pollution can modify the association between health effects and meteorological factors. This implies that the health impacts of extreme temperatures can be enhanced during high pollution days, because air pollution can make people more sensitive to the effects of non-optimal temperatures. The indications that air pollutants and extreme temperatures may multiply their health effects by acting on the same pathophysiological pathways (Qin *et al* 2017) imply that any co-occurrence of non-optimal temperatures and air pollution, which itself would enhance the health risks from these stressors, could be further enhanced. Tables 2 and 3 renders the reviewed studies on combined effects. As we discuss below, the statistical approach does not provide evidence of what are the drivers and mechanisms behind the reported combined effects.

4.1.1. Temperature modifies the air pollution impacts on health

We found two systematic review and meta-analysis studies addressing how temperature modifies (interacts with) the association between air pollution and mortality (see table 2). In the study by Chen *et al* (2017a), 16 studies on the modifying effect of temperature on the association between PM_{10} and non-accidental, cardiovascular disease (CVD), and respiratory disease (RD) mortality were included in the meta-analysis. The authors concluded that there was moderate evidence that high temperatures enhance the effect of PM_{10} on mortality, and that the modifying effect was largest for respiratory deaths. In the study by Li *et al* (2017), epidemiological evidence on the modification of temperature on the effects of several air pollutants on non-accidental and CVD mortality was reviewed. Nine studies (all in China) were included in the meta-analysis. The authors concluded that hot temperatures increase the effects of PM_{10} and O_3 on non-accidental and CVD deaths. Cold temperatures enhanced the effect of O_3 on all non-accidental deaths, but diminished the effect of PM_{10} on CVD deaths.

As described in the following, newer studies not included in the two meta-analyses also report modifying effects of temperature on the association between PM and mortality and O_3 and mortality (cf table 2(a)). They also report modifying effects of temperature on the effects of SO_2 and NO_2. Several new studies have also investigated joint effects of temperature and air pollutants on morbidity endpoints (cf table 2(b)).

In a study in European urban areas, Chen *et al* (2018) investigated effects modification of air pollution and temperature on total natural and CVD mortality both ways, by analyzing both the temperature-stratified associations between air pollution and mortality and the air pollution-stratified association between temperature and mortality. Pollutants included ultrafine particles (diameter $\leqslant$100 nm), $PM_{2.5}$, PM_{10}, and O_3. The associations between air pollutants and mortality were generally stronger at high temperatures compared to low, with the strongest modifying effect of temperature found for $PM_{2.5}$. High levels of air pollution increased both heat- and cold-related mortality risks. A study in China found that high temperatures significantly enhanced the effects of O_3 on nonaccidental, CVD, and RD mortality, especially on older adults (Shi *et al* 2020). Tian *et al* (2018a) found that high temperatures increased the effect of PM_{10} on non-accidental, CVD and RD mortality in Beijing. Qin *et al* (2017) found that high temperatures enhanced the effect of PM_{10} and SO_2 on non-accidental and RD mortality, and the effect of NO_2 on RD mortality. Chen *et al* (2017b) found that the effects of SO_2 on mortality were larger on high temperature days than on days with low temperatures. On the other hand, by including data on age-specific deaths and applying an abridged life table approach to calculate the years of life lost (YLL), the authors found that the effects on YLL were larger on low temperature days than on

Table 2. Overview of studies covered by the review that reported temperature interaction with the air pollution effects on mortality and morbidity health endpoints. The arrows show the direction of the interaction effect. $T\uparrow$: the study reports the heat effect; $T\downarrow$: the study reports the cold effect. The air pollutants' effect arrows shows whether the health effect of the pollutant increases ($\uparrow$) or decreases ($\downarrow$). The air pollutants are particulate matter $\leqslant 2.5\ \mu$m or $\leqslant 10\ \mu$m in aerodynamic diameter (PM2.5 and PM10, respectively), ultrafine particles (UFP), ozone (O_3), nitrogen dioxide (NO_2), sulfur dioxide (SO_2), and carbon monoxide (CO).

Stressor effect	Reference	Direction of interaction effect	Health endpoint	Location
(a) Mortality				
	Chen *et al* 2017a (review and meta-analysis)	$T\uparrow \Rightarrow PM_{10}$ effect$\uparrow$	Non-accidental, CVD and RD	Worldwide
	Li *et al* 2017 (review and meta-analysis)	$T\uparrow \Rightarrow PM_{10}$ and O_3 effect$\uparrow$	CVD and non-accidental	Worldwide
	As above	$T\downarrow \Rightarrow O_3$ effect$\uparrow$	Non-accidental	
	As above	$T\downarrow \Rightarrow PM_{10}$ effect$\downarrow$	CVD	
	Chen *et al* 2018	$T\uparrow \Rightarrow PM_{2.5}$, PM_{10}, UFP, and O_3 effect$\uparrow$ *(both ways, see below)*	Non-accidental, CVD	Europe
	Shi *et al* 2020	$T\uparrow \Rightarrow O_3$ effect$\uparrow$	Non-accidental, CVD and RD (esp. in older adults)	
	Tian *et al* 2018a	$T\uparrow \Rightarrow PM_{10}$ effect$\uparrow$	Non-accidental, CVD and RD	China
	Qin *et al* 2017	$T\uparrow \Rightarrow PM_{10}$ and SO_2 effect$\uparrow$	Non-accidental, RD	
	As above	$T\uparrow \Rightarrow NO_2$ effect$\uparrow$	RD	China
	Chen *et al* 2017b	$T\uparrow \Rightarrow SO_2$ effect$\uparrow$	Non-accidental, CVD and RD	China
	As above	$T\downarrow \Rightarrow SO_2$ effect$\uparrow$	Years of life lost (YLL)	
	Duan *et al* 2019	$T\downarrow \Rightarrow NO_2$ effect$\uparrow$	CVD (esp. in older men)	China

(Continued.)

Table 2. (Continued.)

Stressor effect	Reference	Direction of interaction effect	Health endpoint	Location
(b) Morbidity				
	Hsu *et al* 2017	T↓ ⇒ $PM_{2.5}$ effect↑	CVD hospitalization	USA
	Morris and Naumova 1998	T↓ ⇒ CO effect↑	Congestive heart failure (CVD) hospitalization	USA
	Vanasse *et al* 2017	T↓ ⇒ $PM_{2.5}$ effect↑	Heart failure (CVD) hospitalization (in older adults)	Canada
	Huang *et al* 2017	T↓ ⇒ $PM_{2.5}$, PM_{10} and CO effect↑	Onset of acute coronary syndrome (CVD)	Taiwan
	Qiu *et al* 2018	T↓ ⇒ $PM_{2.5}$, PM_{10} and SO_2 effect↑	COPD (RD) hospitalization	China
	Qiu *et al* 2013b	T↓ ⇒ NO_2, O_3 and SO_2 effect↑	COPD (RD) hospitalization	China
	As above	T↓ ⇒ PM_{10}, NO_2, and O_3 effect↑	IHD (CVD) hospitalization	
	Chen *et al* 2017c	T↓ ⇒ $PM_{2.5}$ effect↑	Influenza transmission (RD)	China
	Wang *et al* 2019	T↓ ⇒ PM_{10} effect↑	Birth weight	China
	Ren and Tong 2006	T↑ ⇒ PM_{10} effect↑	RD and CVD hospitalization and emergency room visits	Australia
	Zhang *et al* 2018b	T↑ ⇒ $PM_{2.5}$, PM_{10} effect↑	All-cause, RD and CVD emergency room visits	China
	Tobaldini *et al* 2020	T↑ ⇒ PM_{10} effect↑	Out-of-hospital cardiac arrest (CVD)	Italy
	Zhang *et al* 2019	T↑ ⇒ $PM_{2.5}$ effect↑	Type 2 diabetes, cerebral stroke, and coronary heart disease hospitalization	China
	Stingone *et al* 2019	T↑ ⇒ $PM_{2.5}$ effect↑	Occurrence of congenital heart defects	USA
	Lee *et al* 2018	T↑ ⇒ $PM_{2.5}$, PM_{10}, NO_2, and O_3 effect↑	Emergency room visits for migraine	South Korea
	Guo *et al* 2019	T↑ ⇒ $PM_{2.5}$, PM_{10}, NO_2, and SO_2 effect↑	Hospital outpatient visits for atopic dermatitis	China
	Yitshak-Sade *et al* 2018	T↑ ⇒ $PM_{2.5}$ effect↑	RD hospitalization	USA
	As above	T↓ ⇒ $PM_{2.5}$ effect↑	Cardiac (CVD) hospitalization	
	Chen *et al* 2019	T↑ ⇒ SO_2 effect↑	RD and CVD emergency department visits	China
	As above	T↓ ⇒ NO_2 effect↑	Neurological disease emergency department visits	

Table 3. Overview of studies covered by the review that reported air pollution interaction with the temperature effects on mortality and morbidity endpoints. The arrows show the direction of the interaction effect. Air pollutant↑: the study reports whether the effect of an increasing concentration enhances the health effect of non-optimal temperatures (either heat or cold effect). (Air pollutants are described in table 2).

Stressor effect	Reference	Direction of interaction effect	Health endpoint	Location
(a) Mortality				
	Ren *et al* 2008	O_3↑ ⇒ heat effect↑	CVD	USA
	Breitner *et al* 2014	O_3↑ ⇒ heat & cold effect↑	Non-accidental, CVD and RD (esp. in older adults)	Germany
	Analitis *et al* 2014	O_3 and PM_{10}↑ ⇒ heat effect↑	Non-accidental, **CVD** and RD	Europe
	Scortichini *et al* 2018	PM_{10}↑ ⇒ heat effect↑	Non-accidental	Italy
	Analitis *et al* 2018	O_3 and PM_{10}↑ ⇒ heat effect↑	Non-accidental, CVD	Europe
	Chen *et al* 2018	$PM_{2.5}$, PM_{10}, O_3↑ ⇒ heat effect↑	Non-accidental	Europe
	As above	UFP↑ ⇒ cold effect↑	Non-accidental, CVD	
	Li *et al* 2015a	PM_{10}↑ ⇒ heat effect↑	Total, non-accidental, CVD, RD	China
	Lee *et al* 2018	PM_{10}, CO, O_3 and NO_2↑ ⇒ heat effect↑	Total, CVD, RD	Japan, Taiwan
(b) Morbidity				
	Ren *et al* 2006	PM10↑ ⇒ heat effect↑	CVD and RD (mortality and morbidity)	Australia
	Ren *et al* 2011	O_3↑ ⇒ heat effect↑	Heart rate variability	USA
	Xu *et al* 2013	PM_{10} and O_3↑ ⇒ cold effect↑	Paediatric influenza	Australia
	Parry *et al* 2019	PM_{10}↑ ⇒ heat effect↑	CVD hospitalization	Australia
	Lepeule *et al* 2018	Black carbon ($PM_{2.5}$)↑ ⇒ heat effect↑	Reduced lung function in older adults	USA
	Wang *et al* 2020	$PM_{2.5}$↑ ⇒ heat effect↑	Risk of preterm birth	China

high temperature days. This could imply that younger people are especially vulnerable to the combination of low temperature and SO_2 pollution, but the authors refrain from speculating what may be the reasons behind this. A study in South China found that NO_2 increased the risk of CDV mortality and that this effect was enhanced in cold weather and particularly for elderly men (Duan *et al* 2019).

Whereas the majority of studies that examined the interaction between temperature and air pollutants have focused on daily number of deaths, for which data are often easily available, an increasing number of studies find that temperatures can also modify air pollution effects on morbidity endpoints (cf table 2(b)). Several studies have looked at the modifying effect of season only, not by temperature level as such, and we did not include these in the review, but refer to the recent review and meta-analysis by Bergmann *et al* (2020). They found that the morbidity effects of CO and O_3 were stronger in the warm season, while the morbidity effects of SO_2 and NO_2 were lower in the warm season. Morbidity effects of $PM_{2.5}$ and PM_{10} were not significantly affected by season.

The studies examining how temperature modifies the morbidity effects of air pollutants vary as to whether they find an enhanced air pollution effect at higher or lower temperatures. Hsu *et al* (2017) found that low temperatures enhanced the effect of $PM_{2.5}$ on CVD hospitalization. Morris and Naumova (1998) found that the effect of carbon monoxide (CO) on hospital admissions for congestive heart failure (a CVD endpoint) was enhanced at low temperatures. In a cohort study among elderly, Vanasse *et al* (2017) found that the effect of $PM_{2.5}$ on heart failure hospitalization and death was enhanced at low temperatures. Huang *et al* (2017) found that air pollution, together with atmospheric pressure and relative humidity, had significant interaction effects with temperature on the occurrence of acute coronary syndrome (ACS). Combinations of higher $PM_{2.5,}$ PM_{10}, and CO concentrations with low temperatures were associated with enhanced risk of ACS occurrence in the study. Qiu *et al* (2018) found that low temperatures enhanced the effects of particulate pollution (PM_{10} and $PM_{2.5}$) and SO_2 on hospitalization for chronic obstructive pulmonary disease (COPD). Qiu *et al* (2013a) found that the effect of NO_2, O_3, and SO_2 on COPD emergency hospitalization was enhanced on cool and dry days. However, no consistent modifying effect of weather factors on the effects of particulate pollution was found. Using the same data set, but looking at emergency hospitalization for ischemic heart disease (IHD), Qiu *et al* (2013b) found a similar pattern, with an increase in the detrimental effects of air pollution on cool and dry days in the cool season. The effects of PM_{10}, NO_2, and O_3 on IHD hospitalization were found to decrease greatly in the warm and humid season. Chen *et al* (2017c) found that the effect of $PM_{2.5}$ on the risk of influenza transmission was higher on cold days than on hot days. While not a morbidity end-point as such, (Wang *et al* 2019) found evidence of an interactive effect of PM_{10} and ambient temperature for birth weight, showing that low temperatures exacerbated the negative effects of PM_{10}.

Other studies find that morbidity effects are enhanced at high temperatures. Ren and Tong (2006) found that the effect of PM_{10} on several morbidity endpoints was higher on warm days than on cold days. The morbidity end-points included were daily respiratory hospital admissions, cardiovascular hospital admissions, respiratory emergency visits, and cardiovascular emergency visits. Zhang *et al* (2018b) found that the effect of $PM_{2.5}$ and PM_{10} on hospital emergency room visits (all, respiratory, and cardiovascular) in Beijing was enhanced at high temperatures, with the modifying effect of temperature being more pronounced for $PM_{2.5}$. Tobaldini *et al* (2020) found that the effect of PM_{10} in triggering out-of-hospital cardiac arrest was enhanced by high temperatures. Zhang *et al* (2019) found that the effect of $PM_{2.5}$ on hospital admissions for several diseases (type 2 diabetes, cerebral stroke, and coronary heart disease) was enhanced on hot days. A study by Stingone *et al* (2019) provides limited evidence that extreme heat events during early phase of pregnancy (i.e. critical embryonic period for cardiac development) can enhance the association between $PM_{2.5}$ and occurrence of congenital heart defects (the most common category of birth defects). Lee *et al* (2018) found that the levels of the air pollutants $PM_{2.5}$, PM_{10}, NO_2, O_3, and CO were significantly associated with emergency room visits for migraine. The PM effect was significantly stronger on high-temperature days compared to low-temperature days. Guo *et al* (2019) found that the effect of various air pollutants ($PM_{2.5}$, PM_{10}, NO_2, and SO_2) on hospital outpatient visits for atopic dermatitis was enhanced on hot days. In a study of $PM_{2.5}$ and hospital admissions for various cardiopulmonary endpoints among older adults (>65 year), Yitshak-Sade *et al* (2018) found that the effect of $PM_{2.5}$ for cardiac admissions was larger on colder days, while the opposite was the case for respiratory admissions as the $PM_{2.5}$ effect was larger on warmer days. Chen *et al* (2019) also report effects in different directions and partly nonlinear interaction. The effect of SO_2 on emergency departments visits (EDV) for respiratory and circulatory diseases was higher on hotter days, whereas the effect of NO_2 on EDV for neurological diseases was higher on colder days.

4.1.2. Air pollution modifies the temperature impacts on health

Several studies have assessed whether air pollution modifies the association between temperature and health (see table 3), but to our knowledge no systematic review and meta-analysis has been published. O_3 and particulate matter ($PM_{2.5}$ and/or PM_{10}) are identified as the most important effect modifiers in the available studies.

A study in the U.S. by Ren *et al* (2008) found that the association between CVD mortality and daily maximum temperatures in summer was enhanced by O_3. In a time-series analysis of the association between temperature and mortality in Germany, Breitner *et al* (2014) suggested some effect modification of O_3 on the U- or J-shaped ER relationship between temperature and mortality, but no modifying effects of PM_{10} was found. Effect modification by PM is, however, found in the following studies. Using time-series mortality data from the Euro-HEAT database, Analitis *et al* (2014) found that the heat wave effect on mortality was enhanced both on days with high levels of PM_{10} and on days with high levels of O_3, particularly for cardiovascular mortality. Similar results were found in Italy, where Scortichini *et al* (2018) found much larger heat effect estimates for non-accidental mortality when the PM_{10} concentration was elevated. Effect modification by O_3 was also found, but only for the northern cities. Analitis *et al* (2018) found evidence that, in the warm season, O_3 and PM_{10} enhanced the effect of hot temperatures on all-cause and CVD mortality, respectively, with no evidence of interaction during the cold season. In the study in European urban areas mentioned above, investigating two-way interactions, Chen *et al* (2018) found that both heat- and cold-related mortality risks (non-accidental and cardiovascular) were enhanced at high levels of PM. For heat-related mortality, a significant effect modification was found for $PM_{2.5}$, PM_{10}, and O_3. For cold-related mortality, effects modification was found for ultrafine PM. Similarly, in a study in South China, (Li *et al* 2015a) found that both cold and hot effects on several mortality end-points (all-cause, non-accidental, CVD, and respiratory) increased with the quartiles of PM_{10}. (Lee *et al* 2019) used data for 16 cities in Northeast Asia and reported that heat mortality (total, cardiovascular, and respiratory) was enhanced by PM_{10}, CO, O_3, and NO_2. A study by Wang *et al* (2020) found that the risk of preterm birth, a leading cause of death in children <5 years of age, was enhanced by exposure to heatwaves during the final gestational week. For less extreme heatwaves, the combined effects of $PM_{2.5}$ exposure and heatwaves were found to be synergistic.

In a study in Australia, Ren *et al* (2006) found that PM_{10} significantly enhanced the temperature effect for several cardiovascular and respiratory mortality and morbidity outcomes. In a cohort study in the US of heart rate variability (HRV) among older men,

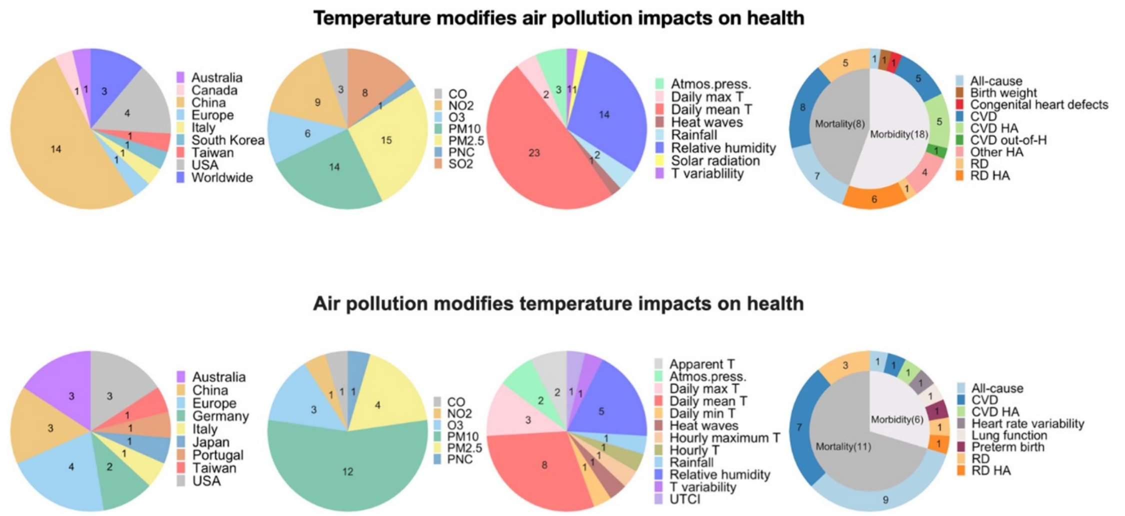

Figure 5. Illustration of the heterogeneity of the reviewed studies in terms of study region, air pollutants, meteorological indicators considered, and health endpoints addressed. HA: hospital admissions; O-HA: out-of hospital cardiac arrest; CVD: cardiovascular disease; RD: respiratory disease. The numbers in the colored pies indicate the number of studies investigating the respective variable. In the last column, the numbers in brackets show the total number of studies investigating either mortality or morbidity, which can include different health endpoints.

a risk factor for sudden death from CVD, Ren *et al* (2011) found that higher ambient temperature was associated with an adverse impact on HRV during the warm season, but not during the cold season, and that the temperature effect was significantly greater when ambient O_3 levels were high. No modifying effect of $PM_{2.5}$ was found.

In a study of influenza incidence among children during the cold season in Australia, Xu *et al* (2013) found that PM_{10} and O_3 played an important role in the relationship between low temperatures and the disease, i.e. increasing air pollution enhanced the cold effect on pediatric influenza. In a study during the warm season in Australia, Parry *et al* (2019) found some evidence that PM_{10} may enhance the effect of heatwaves on hospital admissions for main CVDs. A study of lung function among elderly by Lepeule *et al* (2018) found that two important metrics for lung function, i.e. forced vital capacity and forced expiratory volume in one second (FEV_1), showed a significant decrease with increasing temperature and increasing relative humidity. While no synergistic effect of temperature and humidity was found, the effect of temperature on lung function was greater when combined with high exposure to black carbon (a subcomponent of $PM_{2.5}$).

4.1.3. Conclusion for human health impacts

The reviewed studies show that there may be substantial interactions between air pollution and temperatures when it comes to the impact on mortality and morbidity, with most studies reporting joint effects for the variables particulate air pollution, O_3 and daily mean temperatures. Most of the studies reported an effect modification, whereas some estimated an interaction term to quantify the synergistic effect between temperature and air pollution on human health. There is, however, considerable variation and heterogeneity across studies, and the largest joint effects may be found both at high and low levels of the respective variables. As seen in figure 5 and tables 2 and 3, most of the reviewed studies investigate the impact of temperature on the association between air pollutants and health. Among these, the studies that investigated mortality (table 2(a)) mostly reported that hot temperatures enhanced the effect of air pollution. Overall, these studies support the findings in the two previous meta-analyses on this effect (Chen *et al* 2017a, Li *et al* 2017), even though a diminishing effect of cold temperatures on CVD deaths was not reported in any of the reviewed studies. Regarding the studies on morbidity (table 2(b)) mixed results were reported, with a similar number of studies reporting that either hot or cold temperatures enhanced the effect of air pollutants.

The majority of studies investigating the impact of air pollutants on the association between temperature and health (cf table 3) reported that increasing levels of air pollutants enhanced the heat effects on mortality and morbidity.

As evident from figure 5, the studies reviewed above have a high degree of heterogeneity in terms of, e.g. study region, weather indices, air pollutants, and health endpoints studied, and do not lend themselves for meta-analysis. The varied findings may be caused by characteristics in the study population (including age, housing standard, and socio-economic status), geographical features (including topography, urban design, green space), as well as the prevailing climate in the geographical setting. To model the future joint effects of climate change and air pollution, a comprehensive assessment of such factors is needed.

As pointed out by several authors, the meteorological parameters included in most studies (temperature indices and potentially adding relative humidity) may not be sufficient to explain health links, and it has been suggested that a 'synoptic air masses' approach or approaches using indices assumed to represent actual thermal comfort (such as Humidex, Heat Index, UTCI, and WBGT) should be pursued (Morabito *et al* 2006, Vanos *et al* 2014, Huang *et al* 2017). To what extent such approaches may better represent risks of death and disease is however not clear. Multi-parameter approaches are so far difficult to implement in climate change impact studies as few epidemiological studies have applied the approach and outcomes of climate models for these additional parameters are inherently more uncertain than temperature projections. However, as noted by Scortichini *et al* (2018), regarding the Mediterranean countries, the predicted increase in heat waves and stagnation events implies that it is time to include air pollution in public health heat prevention plans. In the different regions of the world, specific and different synoptic conditions may be of most concern when it comes to synergistic effects of air pollution and meteorological conditions, implying the need for regionally tailored policies.

Most epidemiological studies assessing the combined impact of temperature and air pollution have looked at short-term lag periods, which does not reveal whether there are impacts on mortality and morbidity beyond that period. In the early days of air pollution epidemiology, the focus was typically also on short-term impacts. When researchers started looking into longer-term impacts, effect estimates for some mortality end-points increased by up to one order of magnitude (Zanobetti *et al* 2003, Aunan and Pan 2004). It also became clear that the observed excess mortality linked to air pollution is not merely a result of fragile peoples' death advancing a few days forward (the so-called harvesting effect). The etiology involved in temperature effects can be quite different from the etiology involved in air pollution effects, and there is increasing interest and need for understanding whether there may be long term consequences for health and longevity linked to exposure to recurrent or chronic high levels of thermal stress, potentially in combination with air pollution (Zanobetti and Peters 2015, Zanobetti and O'Neill 2018). This would improve the modeling of future health effects of climate change.

Finally, an inherent limitation of current studies on combined effects of temperature indices and air pollution on health outcomes is the statistical approach. As described above, there may be different reasons why health effects of heat stress in combination with air pollution are amplified or attenuated, including atmospheric conditions, behavioral factors affecting the actual exposure, and physiological interactions. Current methods are poorly set up to explain and disentangle the various drivers and mechanisms behind reported interactions, and thus for application in scenario projections under a changing climate.

4.2. Agricultural crops

Over the past couple of decades there have been many empirical studies that have explored the combination of climate change effects (e.g. changes in temperature and soil water) and air pollution (primarily ozone, but increasingly aerosols) on crop physiology, development, growth and yield. These have been comprehensively reviewed in the literature and are not repeated here (see reviews by Fuhrer 2003, 2009, Emberson *et al* 2018). We find that these studies give good insight as to the key interacting variables and their effect (both positive and negative) on response variables such as yield, however, for practical reasons, they are limited in terms of the range of combinations of climate and pollution variables explored meaning that a comprehensive understanding of interactions is limited by data availability. We discuss these key interactions between climate variables and air pollution here; and elucidate further how these influence crop productivity and other important ecosystem services relevant to agriculture.

As illustrated in figure 6, climate variables will influence physiology in ways that can both increase and decrease pollution uptake (exposure) of plants via the stomates. For example, increased atmospheric concentration of CO_2 or increased levels of drought stress are generally considered to reduce leaf level stomatal conductance (gsto) (Ainsworth and Rogers 2007), which will decrease O_3 flux into the leaves and ultimately limit O_3 damage (Fuhrer 2003, Fiscus *et al* 2005, Bernacchi *et al* 2006). Elevated CO_2 concentration may simply benefit the plant by increasing delivery of CO_2 for photosynthesis which will enhance water use efficiency—this is commonly referred to as the CO_2 fertilization effect. Conversely, pollutants can also modify plant access to abiotic resources (e.g. solar radiation) by processes such as 'dimming' that limit the amount of solar radiation reaching the earth's surface or by affecting the quality of solar radiation via absorbance and reflectance enhancing the diffuse fraction of radiation. How plants respond to these changes is dependent upon whole canopy metabolism and potential feedbacks, which are important in determining the canopy level response to combinations of stresses. Here we describe some of the key interactions between pollution and climate variables that have been identified in the literature and explore what these will mean for productivity. It is also important to note that climate-related variables (notably CO_2) and O_3 pollution have also been found to interact and cause changes in nutritional quality (i.e. protein yield and concentration of grains). Yield vs. protein tradeoffs for wheat in response to CO_2 and O_3 were found to be constrained by close relationships between effects on grain biomass and less than proportional effects on grain protein (Pleijel and Uddling 2012). Understanding these processes will be crucial to assess the influence of climate and air pollution on nutritional quality as well as productivity, the latter being the focus here due to the relative maturity of our understanding of productivity related issues.

4.2.1. Climate variables modify the air pollution impacts on crops/vegetation

Climate variables (here we also include CO_2 as a climate-related variable) impact crop growth directly, but also indirectly through their influence on crop response to air pollution. For example, a decrease in precipitation may lead to below optimum water availability, which will reduce gsto and hence limit O_3 uptake. Drought and elevated (CO_2) significantly ameliorate the detrimental effects of elevated (O_3) on a number of physiology, growth, development and yield variables; with the benefit from elevated (CO_2) found to be slightly greater than that from drought (Feng *et al* 2008, Fuhrer 2009). Management practices (e.g. increased irrigation in response to climate induced water stress that may increase gas exchange) may also influence crop response to pollution (Teixeira *et al* 2011). With climate change, growing seasons will tend towards becoming warmer and drier, which may exacerbate the effects of O_3 (Ainsworth *et al* 2012, McGrath *et al* 2015). Elevated CO_2 has also been found to cause modest increases in leaf area index (LAI) (Ainsworth and Long 2005, Dermody *et al* 2008), which will affect, among other things, O_3 deposition, canopy microclimate and feedback to soil water stress (Fuhrer 2009), all of which will play a role in determining plant growth and productivity.

Temperature will also alter gsto (Urban *et al* 2017), and hence O_3 uptake and consequent damage. The effect of temperature change on O_3 sensitivity will, to some extent, depend on the direction and magnitude of the change in relation to the plant's temperature optimum for gsto. For example, if temperature exceeds optimum levels, this reduces gsto and consequently decreases O_3 uptake. However, if temperatures exceed critical thresholds, then heat stress may be induced (Hansen *et al* 2019). Temperature will also affect atmospheric water deficits (the dryness of the air), which will also influence gsto, transpiration and transpirational cooling (Fiscus *et al* 2012, VanLoocke *et al* 2012). Changes in temperature will have a number of consequences that will alter tolerance of crops to pollution (Osborne *et al* 2019). Changes in seasonal temperature will modify the growth period or phenology (with changes in crop growing season altering prevailing pollutant exposure). For example, warmer temperatures may mean that extended growing seasons coincide with higher O_3 concentration, providing that heat stress does not limit growth and productivity. Conversely, warmer temperatures may also accelerate plant development, which could mean that the period in which the crop is exposed to harmful O_3 will be reduced (Fuhrer 2009).

Warmer temperatures in winter, coupled with wetter springs, were also suggested as the reason for enhanced leaf visible injury damage to wheat in Northern Italy (Picchi *et al* 2010). Crop distribution will also be affected by climate change as crops are selected to cope with whatever the mix of warmer temperatures, heat stress and droughts might be at a particular location (Elsgaard *et al* 2012), and this will alter which crops are exposed to prevailing pollutant profiles at different geographical locations. Similarly, longer-term temperature changes may also influence cultivar selection (with crop varieties selected for tolerance to heat stress (with the potential for crop physiological traits to alter sensitivity to pollution). The strong O_3-temperature covariation also implies that field observations on temperature impacts may arise in part from O_3 exposure at high temperatures, and this confounding effect is typically not included in model based risk assessment studies (Tai *et al* 2014). For example, warming expressed as KDD was found to reduce global crop production by >10% by 2050 with O_3 trends either exacerbating or offsetting a substantial fraction of these climate impacts depending on which emissions scenario was used in the simulation (Tai *et al* 2014). On average, 53% (wheat), 22% (maize) and 47% (soybean) of the observed sensitivities of yields to heat (KDD) in fact arose from higher O_3 in association with KDD, instead of the inherent harm of excess heat, and the combined effects of O_3 and temperature differed significantly from the individual effects. The influence of such confounding effects challenges the interpretation of empirical results and would benefit from further study.

Water and heat stress along with the stress resulting from the amount of O_3 that is taken up will likely combine, perhaps in a synergistic or additional manner, to cause metabolic changes that will ultimately affect growth, development and yield. Our current lack of understanding of how these variables interact is evident in a study by McGrath *et al* (2015) exploring US maize and soybean yield responses to $[O_3]$ from 1980 to 2011. They found greater damage to crop yields from background $[O_3]$ during dry years, which is counter-intuitive to the notion that stomatal closure during times of drought would limit O_3 uptake and negative impacts of O_3 on productivity (Tingey and Hogsett 1985).

4.2.2. Air pollution modifies the climate impact on crops

Determining the agricultural impacts of climate variability and air pollution is further complicated by the

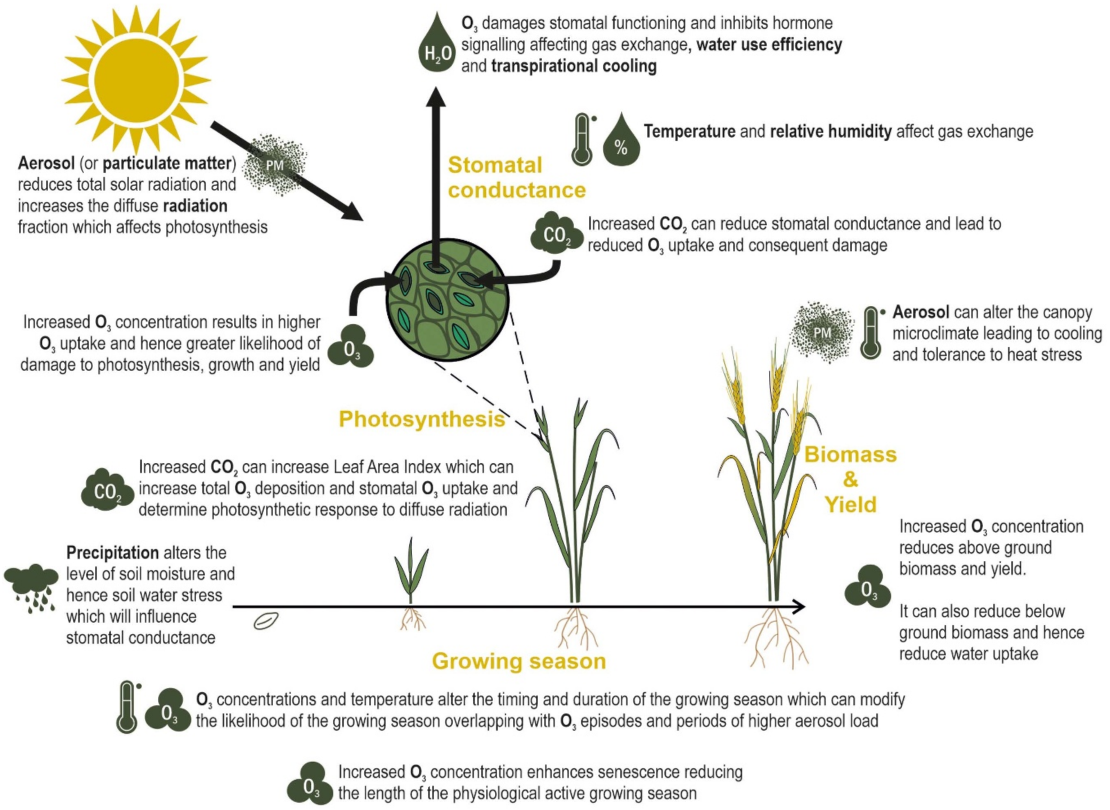

Figure 6. The different interacting effects of climate and air pollution on crops. Key climate variables and air pollutants primarily impact stomatal conductance, photosynthesis, growing seasons, biomass and subsequently crop yields. The effect of these stressors is variable and strongly influenced by the interaction between stressors.

effect of air pollution on crop responses that will in turn alter response to climate variability. For example, O_3 can impact water use efficiency through damage to the guard cells that regulate gsto (Maier-Maercker 1999, Fiscus *et al* 2005, Mills *et al* 2009, Wilkinson and Davies 2009, 2010). This may inhibit the plant's ability to respond to changes in temperature and precipitation and consequently reduce resilience to climate variability, particularly water stress. Studies have shown that elevated O_3 concentration may prevent stomatal closure in response to drought through changes in the perception of hormone signaling that allow plants to 'sense' a drying soil and close stomata to prevent undue water loss. Such changes would cause plants and canopies to use more water in times of drought (Wilkinson and Davies 2010, Hayes *et al* 2012, Wagg *et al* 2012). A better understanding of the mechanisms by which O_3 and drought-induced signaling pathways interact is clearly needed to fully understand this interaction. Unfortunately, understanding how combinations of increased temperature, drought, and O_3 might interact to influence plant transpiration and hence water balance, as well as growth and productivity, is complicated by our limited knowledge of the processes involved (Arneth *et al* 2010).

It should be noted that leaf level changes in physiology resulting from pollution and climate variable stress do not always result in expected effects at the canopy level complicating efforts to scale impacts from the leaf to canopy. Studies have shown that elevated CO_2 concentration may not always protect plants from changes in senescence and carbon allocation caused by elevated O_3 concentration (Fiscus *et al* 2005), and the influence of combined climate variable and O_3 stress on productivity is not clear (Lobell and Gourdji 2012). This may be because the benefits from reduced O_3 uptake at equivalent levels of photosynthesis may not translate into similar changes in yield due to other factors limiting whole canopy C assimilation (e.g. early resource depletion under elevated CO_2 (Fiscus *et al* 2005)). Elevated O_3 concentration can also induce a more substantial decrease in belowground (−27%) biomass than in aboveground (−18%) biomass (Feng *et al* 2008), (Tian *et al* 2016). With implications for plant tolerance of water stress. Such effects were considered a likely reason why the combined effects of O_3 and drought led to an annual mean reduction of crop yield by 10% during 1981–2010 in China (Tian *et al* 2016). Ozone can also cause early onset and completion of senescence that would have further implications for growing season duration, hence limiting C assimilation for yield and altering water use (Emberson *et al* 2018).

4.2.3. Integrating effects of combined climate variables and air pollution

The results of the few empirical regression-based studies that have been performed show that the effects of both air pollution and climate change on crop yields can be detected in agricultural productivity statistics, thus providing a ‘real world’ demonstration of the combined influence of these stressors. These crop productivity studies use a similar approach as epidemiological studies on the health impacts from thermal stress and air pollution (see section 3.1). These studies are also useful in determining the relative importance of air pollution vs. climate change. Statistical models that explain the influence of climate variables on yield can be applied to assess the benefits to yield of reductions in both GHGs as well as pollutants that influence climate. For example, a study conducted across nine Indian states found that the simultaneous reduction of Atmospheric Brown Clouds (ABCs) (consisting of aerosols, O_3, SO_2, NO_x etc) and GHGs could have caused an increase in annual mean rice harvest of ∼6% and ∼14% during the periods between 1966–1984 and 1985–1998, respectively. These changes in production were simulated via increases in June to September rainfall and decreases in October to November minimum temperature, the climate variables identified as most crucial for production that were substantially influenced by ABCs. However, the direct effects of air pollution on production were not specifically included although heavy rains may have reduced the aerosol concentration to which plants were exposed during the June to September period (Auffhammer *et al* 2006). Climate variables (temperature and precipitation), O_3 and aerosol precursor emissions were also found to impact on wheat yields in India with yields being 36% lower in 2010 than they would have been in the absence of climate change and air pollution (Burney and Ramanathan 2014). Air pollution was found to have caused greater yield reductions (around 90% of all losses) than climate change over the time period investigated, and it was also clear that adverse impacts of air pollution on yields have increased in recent times (Burney and Ramanathan 2014). Such studies help to emphasize the large differences in the length of time over which air pollution and climate effects will play out. Severe air pollution episodes will have immediate impacts on crops but can be episodic in nature with high concentrations lasting only a few days/weeks over particular regional ‘hot spot’ locations. By contrast, climate variables will tend to change more slowly over time with the continued buildup of GHGs in the atmosphere and associated effects gradually increasing over decades (such as surface air temperatures). A particular concern will be the co-occurrence of pollution episodes and extreme weather events which could have devastating impacts. Understanding the frequency with which such compound events will tend to occur in the future will be an important determinant of risk (Zscheischler *et al* 2018).

Other studies have focused on aerosols and climate variables. Gupta *et al* (2017) performed a regression analysis on the effects of aerosols on temperature and solar radiation and subsequent effects on wheat yields in India. They found that reducing aerosol pollution by one standard deviation over the period 1981–2009 would increase wheat yields in India by 4.8%. This was found to roughly compensate for the yield reduction of 5.2% caused by the increases in temperature alone over the same period. These studies are useful in demonstrating the magnitude and extent of the relative effects of air pollution and climate variables on yield. However, they are limited by the tendency to use emissions data as a proxy for pollutant concentrations, the inability to account for confounding variables, and the exclusion of the direct effects of pollutants on crop physiology and yield (focusing only on pollution as a modifier of climate variables). Efforts to account for the confounding effects of the correlation between temperature and O_3 in the interpretation of changes in crop yield statistics have employed new empirical models (e.g. partial derivative linear regression models) to estimate spatial variations in the sensitivity of wheat across the U.S. and Europe (Tai and Martin 2017). Application of these methods find that future warming and unmitigated O_3 pollution can combine to cause an average decline in U.S. wheat, maize and soybean production by 13%, 43% and 28%, respectively, and a smaller decline for European crops (Tai and Martin 2017). These types of studies demonstrate the advantage of modelling approaches being able to characterize and assess the influence of confounding variables.

To understand the combined effects of climate variables and air pollution on pollutant uptake (i.e. exposure), risk assessment modelling methods to estimate O_3 uptake based on modifying climate variables (i.e. flux response models) are helpful in identifying the bio-physical conditions that might lead to enhanced exposure. The warmer regions of India were identified in a study by Tang *et al* (2013) as having particularly high yield losses of between ∼8%–9% for China and ∼5%–8% for India for 2020 projections compared to 2000. Ozone impacts to wheat yield have also been found to be particularly large in humid rain-fed and irrigated areas of major wheat-producing countries (e.g. the United States, France, India, China and Russia) with estimates of O_3 reduced yields of ∼10% and ∼6% in the northern and southern hemispheres respectively (Mills *et al* 2018a). The greatest yield losses were found in the warm-temperate-moist, tropical-moist and tropical-wet climates of the northern hemisphere and the tropical-moist and -wet climates of the southern hemisphere. Enhanced yield losses in these regions were due to conditions that often maximize stomatal uptake of O_3

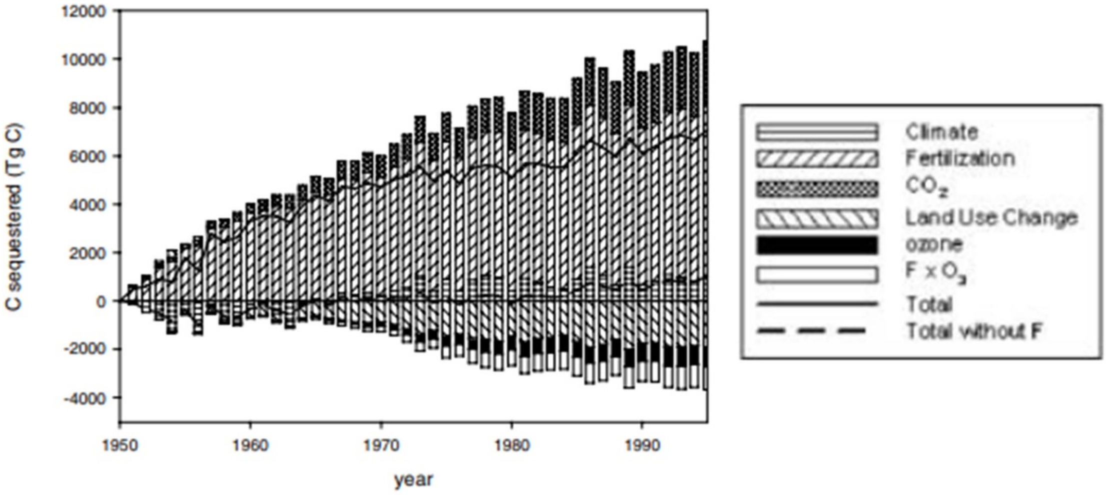

Figure 7. Transient net primary productivity and net carbon exchange (expressed as C sequestered (T g C)) responses from 1950 to 1995 across the US showing how O_3 compares with other disturbances (CO_2 concentration, climate variability, land use, agricultural management, ozone and cross terms between O_3 and N fertilization). This study uses the semi-process based modelling type of approach. Reproduced from Felzer *et al* (2004). CC BY 4.0.

with mean yield losses per climatic zone of 12%–17% and 9%–11% for northern and southern hemisphere, respectively. Most importantly, they found that O_3 could reduce the potential yield benefits of increased irrigation in response to climate change, because added irrigation increases the uptake and subsequent negative effects of the pollutant. They simulated fully irrigated conditions which resulted in additional O_3 related production losses which were highest in developing countries and upper-middle-income countries (totaling 1.8 and 1.2 Tg, respectively).

Semi-process-based modelling (see section 3.3.2.1) can also be applied to assess the integrated effects of climate variables and pollution at regional scales and for different ecosystems around the globe. Some general conclusions can be drawn from these model applications. First, the effect of O_3 pollution on productivity (often defined as gross primary productivity or net primary productivity (NPP)) is generally greater than that resulting from the increase in CO_2 when both are considered over time periods of a number of decades (Felzer *et al* 2004, Reilly *et al* 2007). Second, crop response to air pollution and climate variables will likely occur under a variety of crop management practices and in combination with regional scale land-use change. Therefore, it is useful to assess the relative importance of other factors that will influence productivity. O_3 and climate change effects were substantially less than the influence of agricultural management (+46.2%) and change in land use (−26.8%) on C sequestration across the US for 1950–1995 (see figure 7, Felzer *et al* 2004).

Similarly, a net increase in crop NPP (from 0.896 Pg C yr^{-1} in the 1980s to 0.978 Pg C yr^{-1} in the 1990s) and mean carbon storage in agricultural systems (from 4194.2 g C m^{-2} yr^{-1} in the 1980s to 5068.8 g C m^{-2} yr^{-1} between 2000 and 2005) was modelled in Chinese agriculture in response to a range of factors. The combined contributions of mean climate variability/change, O_3 and CO_2 concentration and nitrogen deposition to the total NPP and soil organic carbon were less than 20% between 1980 and 2005. Increases in NPP were mainly due to a change in land management practices (e.g. application of nitrogen fertilizers), nevertheless the study shows that NPP could have been higher without the combined effect of climate change and O_3 (Ren *et al* 2012).

However, consideration should also be given to the effect on productivity of multiple pollutants acting together (i.e. O_3 and aerosol). Semi-process-based modelling has been used to assess the contrasting effects of O_3 toxicity reducing yields, and aerosols (via enhanced diffuse radiation) increasing yields with aerosol offsetting much, if not all, of the O_3 yield effects on staple crops (with changes in yield estimated at +5.6%, −3.7%, and +4.5% for maize, wheat, and rice, respectively) across the globe in 2010 (Schiferl and Heald 2018). Potential future emission reductions by 2050 may result in a net negative effect on crop production in geographical locations dominated by aerosol (Schiferl and Heald 2018). However, this modelling uses a rather crude integrated whole season response of yield to changes in diffuse radiation and excludes aerosol effects that might be influenced by canopy characteristics such as LAI (Matsui *et al* 2008) and caused by deposition to canopy surfaces.

Process-based models allow a more complete analysis of the interactive effects of climate change, elevated CO_2 and pollution on crop growth and productivity, exploring effects related to uptake (exposure), resource availability (pollution modified climate variables) as well as impact (at least in terms of effects on fundamental plant physiological processes

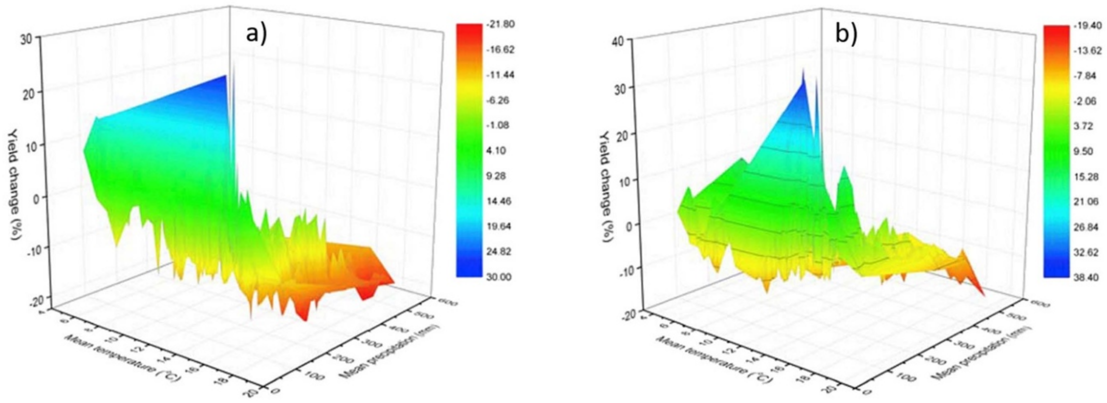

Figure 8. Combined effect of climate change, O_3 and CO_2 on wheat productivity (z-axis) in relation to mean temperature (x-axis) and precipitation (y-axis) from 1 March to 31 May during the 2020s for eastern China under the HadGEM2-ES (a) and MIROC-ESM-CHEM (b) climate scenarios. This study uses the process-based modelling type of approach. Reprinted from Tao *et al* (2017), Copyright (2017), with permission from Elsevier.

such as photosynthesis, development and yield). Effects on physiology can be estimated via reversible effects on photosynthesis and effects on both photosynthesis and development by non-reversible effects on green LAI simulating the O_3 influence on senescence (and thus indirectly on photosynthesis) (e.g. Ewert and Porter 2000, Tao *et al* 2017, Schauberger *et al* 2019). This allows the relative effects of interacting variables such as CO_2, O_3 and aerosol to be assessed. For example, elevated CO_2 was found to increase wheat productivity by 2.8%–9.0% whilst increasing O_3 concentrations was found to reduce productivity by 2.8%–11.7% for China in the 2020s, relative to the 2000s (Tao *et al* 2017). The combined effects of CO_2 and O_3 were less than O_3 only, on average by 4.6%–5.2%, however, with O_3 damage outweighing CO_2 benefits in most of the region. The effects of O_3 vary with temperature, availability of water and local O_3 concentrations, and are large in areas with high temperature, precipitation and local O_3 concentrations such as the southern parts of Chinese wheat production areas, mainly because the effect of O_3 on photosynthesis or biomass growth is less for stress than non-stress conditions (Tao *et al* 2017). Figure 8 shows modelling results that suggest that the combined effects of climate change, elevated CO_2 and rising O_3 concentrations on wheat productivity are dominated by climate change, but with substantial modifications from the effects of CO_2 and O_3.

Schauberger *et al* (2019) used a process-based model to estimate global historical O_3-induced yield losses between the years 2008 and 2010 for soybean and 'Western' and 'Asian' wheat. Results showed variation in yield losses between species and countries with estimates of between 2% and 10% of ozone-free yields for soybean, 0% and 27% for Western wheat and 4% and 39% for Asian wheat. For wheat, these estimates broadly agree with those of Mills *et al* (2018) using flux-based modelling approaches. The model simulated responses to different climate conditions and showed the antagonistic roles of O_3 and CO_2 on crop yield, and the reduction of yield in irrigated systems due to the increased gsto and hence O_3 uptake. The authors concluded that O_3 damage was dependent on co-factors (including temperature, CO_2 concentration and, in particular, water status).

Finally, the benefit of process-based models is also nicely exemplified by efforts to assess the combined effects of aerosols, mediated via changes in climate variables, on yield. (Zhang *et al* 2017) used a model capable of assessing the effects of aerosol modified canopy shading on photosynthesis of rice growing across China. This allowed the identification of a threshold of 250 W m^{-2} average growing season solar radiation below which, a reduction in aerosol load would be beneficial for yields (since direct radiation would be increased) and above which, the same reduction in aerosol load would be detrimental to yields (as diffuse radiation would be reduced). The net-effect on rice yields in China were estimated as increases of between 0.8%–2.6% with aerosol concentration reductions from 20% to 100%. Applying this type of modelling to assess the combined effect of O_3, aerosol, CO_2 and climate variables will be crucial to enhance our knowledge of the O_3-aerosol interaction effects on crop yield found by Schiferl and Heald (2018) using semi-process-based modelling approaches. Such work has already been performed to assess the effects of these multiple stress combinations on carbon uptake to terrestrial ecosystems in China (Yue *et al* 2017).

4.2.4. Conclusion for agriculture impacts

Climate variables and air pollution will influence physiology in ways that can both increase and decrease uptake (exposure), modify effective pollutant dose (i.e. the toxic effect of pollutants on plant metabolism and plant functioning) or influence access to resources (e.g. aerosol pollution modifying the quantity and quality of solar radiation received by a plant or influencing local precipitation patterns). Understanding these effects is complicated due to the non-linearities and multiple variables involved (e.g. elevated CO_2 concentrations may reduce pollutant uptake, but also enhance water use efficiency) so that identifying which of these factors has the greatest effect on yield requires an understanding of plant metabolism at the canopy level; see also figure 6. However, there are some key take-home messages from the studies that have been performed to date. The empirical approaches using statistical regression analyses are extremely useful in demonstrating the detrimental impact of climate and air pollution variables in long-term agricultural yield statistics, and suggest that air pollution has had a disproportionately greater impact than climate change on yield reductions over equivalent time periods in those regions where elevated air pollution concentrations persist year on year. Development of the flux-based risk assessment method for O_3 has also allowed identification of the bio-physical conditions that might result in the greatest risk from the combination of climate change and air pollution (e.g. warmer, wetter regions in the tropics). The use of hybrid process-based ecosystem models has also shown that air pollutants can have antagonistic effects on yield (O_3 reducing yields whilst aerosols can increase yields) and that improvements in agricultural management practices to enhance yields can be made less effective under conditions of climate change and pollution, with implications for the ecosystem services provided by agriculture such as carbon sequestration.

It also becomes important to understand feedbacks that exist between vegetation and the atmosphere. Two feedback processes have been identified as particularly important, the first is the effect of reduced biomass leading to a reduction in carbon sequestration leading to enhanced levels of atmospheric CO_2 (Sitch *et al* 2007), and the second is related to O_3 induced changes in stomatal control of transpiration that were found to affect stream flow and hydrology (Sun *et al* 2012). The latter may also affect energy balances and hence land surface temperatures. This requires a far better understanding of pollutants' influence on interactions and exchanges between terrestrial vegetation and the atmosphere.

Process-based models could help us better understand climate and pollution interactions and their regional and global scale influence on vegetation-atmosphere feedbacks as well as to better interpret empirical data. Ideally such models should be carefully used in combination with empirical data (e.g. to parameterize, develop and evaluate models) and with observational assessments of impacts, the latter has probably been underused in the crop effects work to date (due to the ease by which crops can be more directly investigated under harsh regimes of pollution and climate stress) (Fuhrer and Booker 2003, Holmes *et al* 2006, Ainsworth *et al* 2012).

5. Challenges and opportunities for future research

5.1. Challenges of combined climate and air pollution impact modelling

The literature presented in this review highlights considerable challenges in establishing the combined climate and air pollution effects on human health and agricultural crops that need to be addressed to improve modelling of future impacts linked to changes in air pollution and climate. The key challenges found are summarized in the following points:

(a) **Confounding and interactive effects**: difficulties exist in disentangling the impact of temperature and other meteorological factors and air pollutants due to their confounding and interactive effects besides the range of other modifying factors as introduced in section 3.1 and further discussed in 4.2. For crops, for instance, O_3 and high temperatures tend to co-occur, both of which can impact yields; O_3 and aerosols occurring at the same location can have antagonistic effects on yield, and O_3 and climate change effects can be substantially less important than the effects of agricultural management (e.g. irrigation, use of resilient crop varieties) and land use and finally, O_3 can negate the effects of changes in management practices intended to improve crop yields with consequences both for productivity and other ecosystem services such as carbon sequestration. Similarly, for health, factors such as, e.g. age and health status, and a range of factors affecting exposure, are vital for determining the magnitude of the response. Thus, the choice of methods and careful documentation of underlying assumptions for deriving relationships is important.

(b) **Data availability**: there is often little empirical data to develop the multivariate relationships between air pollutants, meteorological factors and their impacts on agricultural crops or human health (see sections 4.1 and 4.2). Often measurements are very localized (or limited to specific regions) (see e.g. figure 5), targeted to specific projects or purposes, rely on exposure proxies, and are not continuous over a longer time period.

(c) **Model complexity:** agricultural or human health impacts can be caused by many interrelated stressors, which are difficult to represent in one model. For instance, crop models need to be designed in a way that captures key processes (cf figure 6) whilst avoiding over-complexity so that they can be coupled with air quality and climate models. Regarding health effects, attribution of temperature effects and air pollution effects may likewise be difficult to establish in the currently applied epidemiological methods (cf sections 3.1.1 and 3.2.1.), particularly in the case of synergistic effects.

(d) **Dose-response relationships:** most dose-response relationships for crop effects obtained from empirical data provide linear responses (as described in section 2.2). These are unable to cope with the antagonistic impacts resulting from multiple pollutants (e.g. O_3 and aerosols) They are also unable to capture influences on sensitivity to crop damage from meteorology, soil nutrients, agricultural management and species/cultivar specific tolerance (Challinor *et al* 2014, Porter *et al* 2014). Regarding health effects, the exposure-response relationship for temperature is U-curved with a steepening curve at high temperatures whereas the relationship for air pollutants may be curvilinear, flattening off at high concentrations (see figure 2). This could complicate the modelling of combined effects, for instance if the air pollution exposure exceeds the levels captured in available ER functions.

(e) **Differences in system scale:** different methods and data are available for different system scales, in terms of impacts on individual or plant leaf level versus population or plant canopy level (see details about methods in section 3). For instance, climate variables and air pollution in combination can both increase and decrease uptake (exposure) of air pollutants in individual plants or humans. In plants this can modify effective dose or access to resources (e.g. solar radiation). In addition, effects at the leaf level may not play out to equivalent effects at the canopy level due to non-linear effects on canopy metabolism and the influence of agricultural management practices (see section 4.2.2). For example, most large area impact studies assume optimal agronomic management which bear little resemblance to the reality (Rosenzweig *et al* 2013). Similarly, for health impacts, climate variables and air pollution can influence physiology and health endpoints very differently on an individual versus a population level, or in country or global aggregated estimates, depending on, e.g. age and gender (demographic characteristics), health status, socio-economic conditions (including worker environments and labor conditions), adaptation policies, and the functioning of health systems.

(f) **Temporal and spatial scales:** pollutants, like O_3 and aerosols, affect agricultural crops and human health directly as well as indirectly via their impact on temperature and other meteorological variables, and their distribution is highly variable in space and time (cf. sections 1, 3.2, 4.2.3). Understanding trends over time (e.g. multiple years) is important to assess the relative contribution of air pollution and climate change to impacts, and time series of 10–20 years are ideally required for impact attribution (cf section 4.2.3). However, air pollution and climate events (particularly extreme events) can occur at certain locations over short periods of days to weeks, creating regional impact hotspots, which become less prominent when integrated as yield losses over the growing season or annual mean death counts (section 1).

5.2. Opportunities for future research

Overall, this literature review clearly showed that there are important interactions between climate variables, particularly temperature, and air pollution in terms of impacts on human health and crop productivity. In most cases this leads to enhancing damage, which has significant implications for our ability to reach the Sustainable Development Goals (i.e. SDG 2, 3, 13, 15) and for the design of effective mitigation and adaptation policies and risk management. Consequently, a closer integration of climate change and air pollution both in terms of impact assessment and respective policy development is urgently needed (Sanderson *et al* 2017, Von Schneidemesser *et al* 2020). To be able to accomplish this ambition, there is a need for further development of modelling approaches to account for a broader portfolio of factors that influence the relationships between exposure to environmental factors and outcomes for agricultural productivity and human health as outlined in this review. While the crop modeling community to some extent is applying process-based approaches already (cf table 1), this is a more difficult endeavor for health impact modeling. An important difference between health and agricultural impact studies in this respect is that experimental studies, mimicking possible future conditions in terms of climate change and air pollution conditions, can be conducted with agricultural crops, but not as such for human health.

Regarding human health, joint effects of meteorological variables and air pollutants are currently derived from epidemiological studies using empirical regression-based models. Thus, estimated interaction effects are mere statistical associations that may or may not be causal and whose root causes are difficult to disentangle. Further research is needed to understand whether reported interaction effects revealed statistically are caused by an effect on the exposure, which could be linked to, e.g. atmospheric interactions, geography, urban characteristics, housing standards, human behavior, or other factors leading to differential exposure, or whether there are actual pathophysiological interaction effects. To enable projection of health effects in a rapidly changing and warming world, process-based modelling approaches should be pursued, supported by knowledge based both on epidemiological, experimental, and clinical studies, and potentially exploiting bottom-up prognostic physiological models for human thermal stress (Petersson *et al* 2019, Buzan and Huber 2020). Moreover, robust health impact modelling needs to also account for the multitude of other factors that determine whether ambient environmental stressors actually lead to adverse physiological responses and eventually to health damage in a population, such as demography, health status, activity level, time spent indoors, occupational exposure, and a wide portfolio of adaptive measures and mechanisms (Vanos *et al* 2020). In order to be relevant for population-wide assessments, outputs would, however, need to be validated against current approaches based on population-based epidemiological studies.

Regarding agricultural crop productivity, empirical regression-based approaches to analyze impacts could be used more effectively in combination with process-based crop modelling studies to constrain or compare the scale and magnitude of impacts simulated by the latter. For example, regional scale, process-based modelling assessments could be compared with results from equivalent (in terms of spatial and temporal scale) observational regression-based assessments to see if the estimated impacts can be discerned in the agricultural statistics. This combined study approach would give far more credence to results of modelling studies, whilst the modelling studies could inform which of the interacting variables were most important in driving the results (Zhang *et al* 2017).

More large-scale and long-term studies for human health and agricultural crops, respectively, should be carried out in climatologically hot regions (Africa, India, South-Asia), where heat extremes are becoming a serious threat (Schwingshackl *et al* 2021, Ncongwane *et al* 2021). Currently, much of the ER evidence is derived from more temperate regions (e.g. Europe and North America) (Vicedo-Cabrera *et al* 2018, 2021). In this context, more knowledge is also needed from climate science with respect to the regional specific probability of exceedances for critical thresholds or tipping points in health and agricultural systems to enable science and policy to identify hotspot regions around the globe and provide information for effective emission and development policies for these regions.

In conclusion, we suggest that approaches to modelling future health impacts of the combined stressors climate change and air pollution may benefit from considering knowledge derived from clinical, experimental, and diagnostic approaches regarding the physiological mechanisms that may lead to synergistic effects from co-exposure to hot temperatures and air pollution. Vice versa, the field of crop modelling may benefit from the lessons derived from epidemiology or empirical regression-based studies in terms of the combined effect of climate and air pollution.

Data availability statement

No new data were created or analyzed in this study.

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