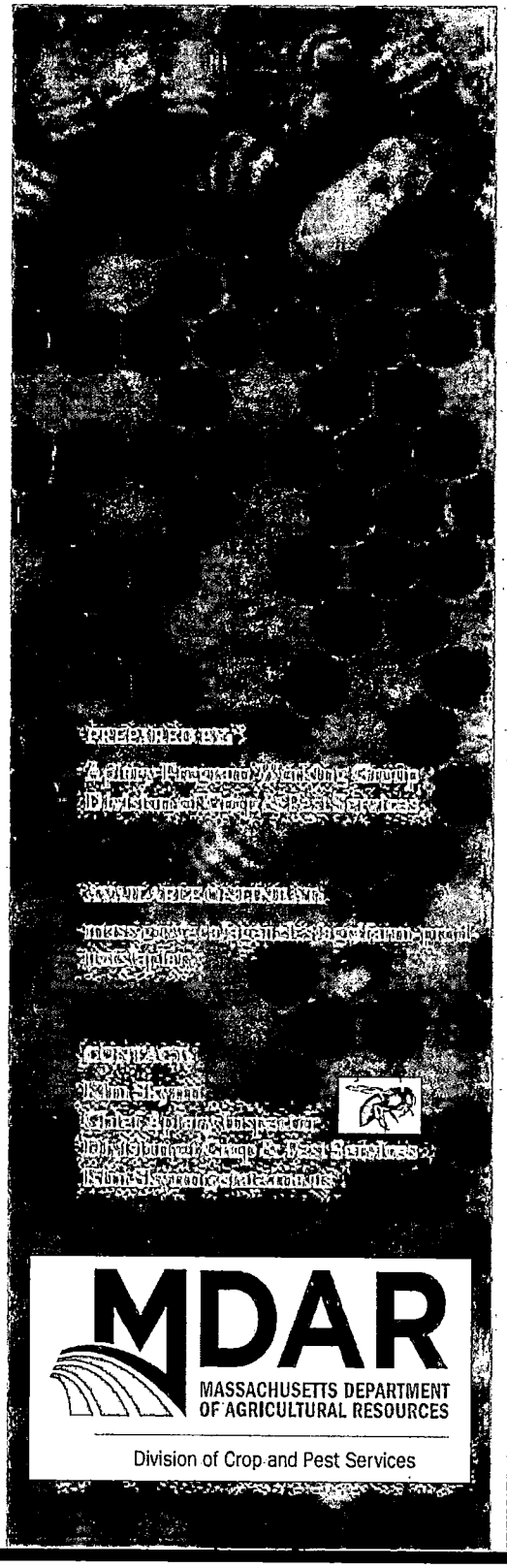
MASSACHUSETTS

Pollinator Protection Plan



MDAR

MASSACHUSETTS DEPARTMENT OF AGRICULTURAL RESOURCES

Division of Crop and Pest Services

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THE COMMONWEALTH OF MASSACHUSETTS
EXECUTIVE OFFICE OF ENERGY AND ENVIRONMENTAL AFFAIRS

Department of Agricultural Resources
101 University Drive, Suite C-4, Amherst, MA 01002
413-548-1905 fax: 413-548-1901 www.mass.gov/agr

MDAR

CHARLES D. BAKER, Governor | KARYN E. POLITO, Lt. Governor | MATTHEW A. BEATON, Secretary | JOHN LEBEAUX, Commissioner

Agriculture is a vital part of life in Massachusetts, providing our state with valuable commodities, land preservation, employment opportunities, and economic growth. Currently home to 7,755 farms consisting of 523,000 acres of operating farmland, Massachusetts is a key Northeastern U.S producer of crops, such as our native cranberry. Over 45% of agricultural commodities in our state rely on our rich diversity of pollinators for crop pollination. Over the past decade, populations of pollinators nationwide have been experiencing significant challenges in their ability to survive and flourish. Given the diversity of stressors affecting pollinators, there is a need to effectively evaluate, sustain and enhance their populations.

The Department has taken the direction to states contained in President Obama's 2014 Memorandum *Creating a Federal Strategy to Promote the Health of Honey Bees and Other Pollinators* seriously and developed this *Massachusetts Pollinator Protection Plan*. This plan is designed to improve the overall health of pollinator populations by providing stakeholders with a set of voluntary guidelines that facilitate communication, collaboration and recommendations of best management practices. As new scientific research becomes available, this adaptive, living document will be updated to reflect these advances.

I am confident that working with the many interested and involved stakeholders, and by educating the public at-large, we will be able to provide improved support for pollinators throughout the Commonwealth.

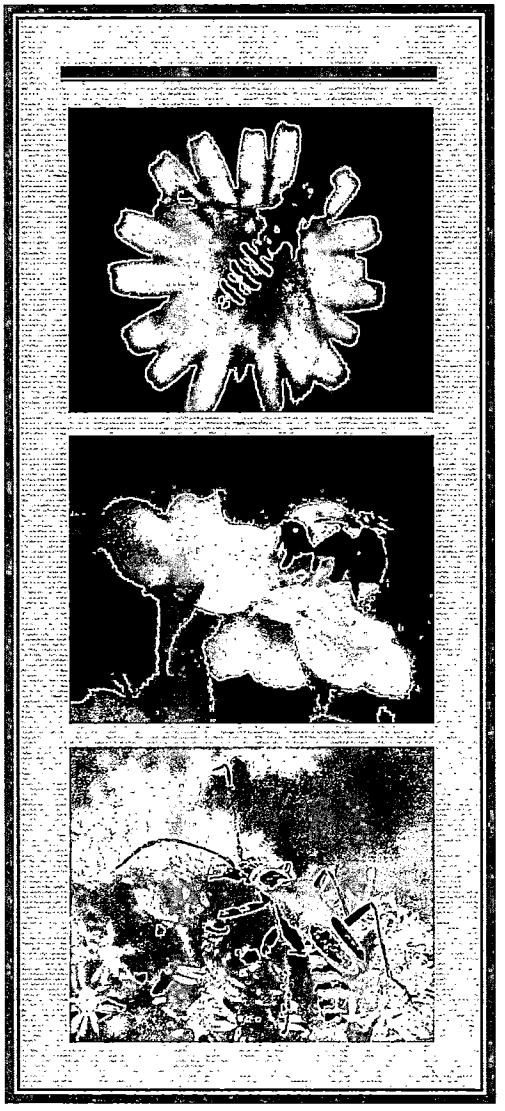
Sincerely,

John Lebeaux

Commissioner,
Department of Agricultural Resources

THE IMPORTANCE OF POLLINATORS

Pollinators provide critical services needed for agricultural and natural ecosystems in order to ensure the sustainability and biodiversity of our environment. This includes both managed pollinators, that have been domesticated for agricultural use and are directly managed by humans, and wild pollinators. In addition to being a part of the food chain, wild and managed pollinators are also directly responsible for the majority of pollination in plants. Without this transfer of pollen from flower to flower, there would be little opportunity for plant reproduction and subsequently for fruit and seed production.



Worldwide, it is estimated that 88% of flowering plants require a pollinator, typically an insect, for pollination[1]. These pollinators increase the fruit or seed set for 75% of crop plants, making them responsible for 35% of global food production[2]. The pollination services they provide also supply birds and mammals with approximately 25% of their diets. In the US alone, over 91 of the most prominent crops, ranging from tree nuts and fruits, berries, and many vegetables are dependent specifically on insect pollinators for reproduction[3]. In Massachusetts, over 45% of agricultural commodities rely on pollinators, mainly wild and managed bees, for pollination. While the economic value of both wild and managed bee pollinators in natural ecosystems is difficult to estimate, they contribute an average of $1,200 per acre in crops, given the increase in visitation rates and subsequently greater fruit set and overall yield[4]. The US Department of Agriculture National Agricultural Statistics Service (NASS) recently estimated that the value of crop pollination by managed bees was $355 million in 2015/2016 for 33 major crops[5]. It is also estimated that wild bees in US crops can provide $3 billion per year in pollination services[6].

Insect pollinators include a diverse group of organisms: bees, butterflies, moths, flies, beetles, and wasps. There are approximately 20,000 bee species worldwide and 4,000 in the US. Among these, the managed bee pollinator *Apis mellifera* (European honey bee) is the most utilized and universally available species[7]. Butterfly and moth populations are very diverse, with 167,500 species worldwide and 12,075 in the United States[8]. While butterflies and moths are easily identifiable in the landscape, with most members providing pollination services, they typically only transport pollen incidentally during the collection of nectar from plants. Only a small subset of the considerably larger insect orders, such as flies (120,000 species worldwide with 19,600 species in US), beetles (350,000 species

worldwide with 23,700 species in the US), and wasps (75,000 species worldwide), actively contribute to pollination, since the majority either do not visit flowers to collect resources or actually cause damage to plants through direct feeding[8]. However, flies are considered to be great pollinators of some plants given their attraction to putrid odors, pale colors and pollen-producing flowers[9]. Members of this group serve as unique pollinators for some plants including midges with cocoa flowers, mosquitoes with bog orchids, fungus gnats with Jack-in-the Pulpit flowers, and carrion flies with skunk cabbage[9]. Beetles are the first group of documented pollinators for angiosperm plants, and are still essential for these ancient plants such as Magnolia. They often eat petals and other floral parts when they visit flowers as well as defecate[10]. Beetles prefer to pollinate flowers that have a spicy, sweet or fermenting scent and moderate nectar/high pollen rewards[10]. Similar to bees, wasps are considered to be important pollinators of plants given their need to collect both pollen and nectar to sustain their high energy metabolic needs[11]. However, the majority of wasps are also carnivorous since they will capture other insects for food[11].

Though the presence and contributions from these other insects is important, bees are still considered to be the most abundant and efficient pollinators, given their need to collect both pollen and nectar to feed developing brood and hairy bodies designed to collect and carry pollen from flower to flower[7]. Massachusetts has a rich diversity of wild pollinators, including an estimated 380 species of bees and 120 species of butterflies. Managed pollinators are also found in abundance in our state, with four bee species used in crop pollination: honey bees (*Apis mellifera*), bumble bees (*Bombus impatiens*), leafcutting bees (*Megachile rotundata*), and orchard bees (*Osmia lignaria*).

HISTORICAL AND CURRENT STATUS OF POLLINATORS

A. Managed and Wild Bees

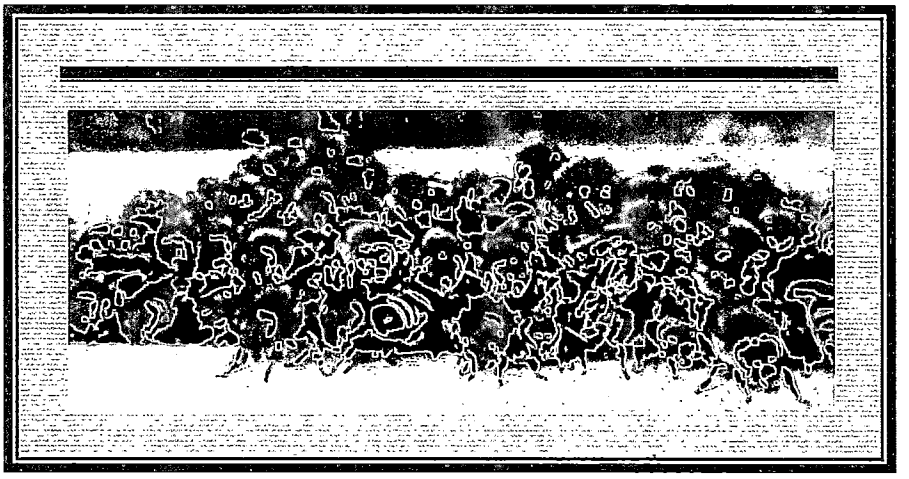
The European honey bee, *Apis mellifera*, was introduced into the Colony of Virginia from Europe in 1622. Subsequent honey bee shipments were documented to occur from 1630-1638 to Massachusetts and it is estimated that by 1650 all New England farms had a colony. However, honey bee colonies rapidly declined after 1670 presumably due to the occurrence and widespread virulence of the bacterial pathogens American Foulbrood (AFB) and European Foulbrood (EFB). It wasn't until the creation of apiary programs, establishment of laws and regulations requiring honey bee colony inspection, and invention of the removable frame in 1852 that foulbrood outbreaks started to become less frequent. Given this, little was known about the factors causing weak or dead colonies, prior to the availability of removable frames and as such if present, diseases were able to run their course undetected. Beekeepers also during this time period traditionally harvested honey from the weakest and heaviest hives in their apiary, thus indirectly mediating diseases[12]. In 1891, entomologists documented the first incident of non-target impacts of agricultural pesticides on honey bees[13].

From 1920-1940, honey bee populations presumably increased due to the availability of optimal forage, better climatic conditions and the Federal Honey Bee Act of 1922 that prevented the spread of tracheal mites into the US[12,14]. Tracheal mites were discovered in 1919

on the Isle of Wight in England and the occurrence and potential destruction from these mites were so devastating that the US responded by creating the legislation[14]. Unfortunately, this period of honey bee population increases are only based on hearsay since the USDA unsuccessfully attempted to collect honey bee production numbers every 10 years prior to 1943, but these data were inconsistent thus not allowing for correlations to be made in the fluctuations in colony numbers over time. However in 1944, the USDA National Agricultural Statistics Service (NASS), started recording the quantity of honey-producing colonies in the US and creating the historical data set that we compare to date. From 1945-1980, honey bee populations increased again which may have been due to the availability of antibiotics for EFB and AFB treatment[12]. However, in 1984 and 1987 US honey bee populations plummeted again given the introduction and detection of Tracheal and Varroa mites[14]. Prior to the introduction of these mites, overwintering losses of 10% were considered normal[12]. In 2006/2007, an alarming number of beekeepers experienced 30-90% of colony losses, much higher than historical levels, during the active bee season with symptoms that were inconsistent with any known cases of death[15,16]. The phenomenon became known as Colony Collapse Disorder (CCD), and is defined as a syndrome when a honey bee colony exhibits these specific criteria[15]:

- Little to no build-up of dead bees in the hive or at the hive entrance;
- Rapid loss of adult honey bee population despite the presence of queen, capped brood, and food reserves;
- Absence or delayed robbing of the food reserves;
- Loss not attributable to Varroa mite or Nosema loads.

Despite being considered to be a potential long term threat to honey bees, the reported cases of CCD have declined significantly from 60% of losses attributed in 2008 to not being mentioned in the latest colony loss reports[15]. Once CCD focused mass attention on honey bees, a closer look at the USDA NASS data showed that the number of honey-producing colonies in the US dropped 60% over 60 years, from a high of 5.9 million in 1947 to 4 million in 1970 to 3 million in 1990 and then 2.3 million in 2008[12]. In 2006, the Bee Informed Partnership (BIP) also started monitoring national levels of honey bee colonies from self-reported beekeeper surveys. While this data was initially set up to record winter losses in honey bee colonies, in 2010 the survey became more comprehensive by including year-round data collection. The latest survey data from BIP indicated an increased loss level of 44% for 2015/2016, compared to 41% for 2014/2015, significantly higher than the acceptable level of 18%. The most alarming trend in these data is the increasing number of summer colony losses when honey bee colonies are supposedly building healthy populations. Locally, Massachusetts beekeepers reported an annual loss of 55.75% of honey bee colonies



over the 2015/2016 season, which is in the top 10% of states with the highest levels of loss. Massachusetts also experienced the highest level of colony losses in New England during 2015/2016[17]. After hearing reports of unpredictable honey bee colony losses during late summer and early fall 2015, the Massachusetts Department of Agricultural Resources (MDAR) created a state wide survey for beekeepers to report colony loss data for the 2015/2016 season. The results of this survey indicated that on average, beekeepers lost 30% of their honey bee colonies, with some counties reporting up to 41% loss. This survey data aligned more closely with the national averages.

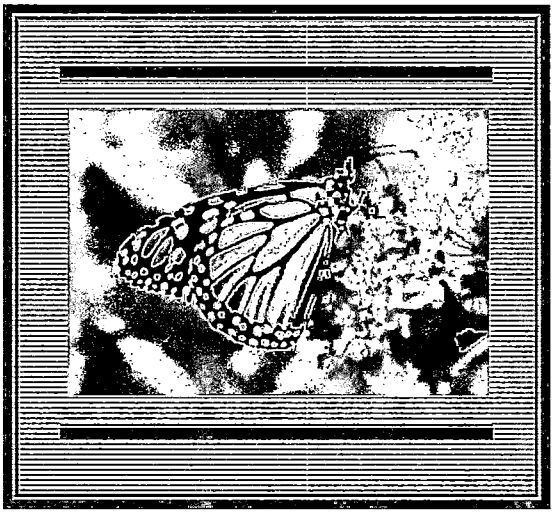
National assessments indicate there are several health stressors involved in the decline of pollinator populations including pests, parasites and pathogens, lack of genetic diversity, habitat loss and forage degradation, poor population genetics, competition, honey bee management strategies, pesticide use and climate change [15,16,17,20,21,22,23]. Locally, the Massachusetts Division of Fisheries and Wildlife and its Natural Heritage and Endangered Species Program (NHESP) list habitat loss, fire suppression, introduced parasitoids and pathogens, deer browsing, off-road vehicles, and pesticides as the major threats facing pollinators[18,19]. While pollinator populations may be able to overcome a single one of these stressors, when a suite of these pressures overlap, evolve and interact with one another, they can place an intense pressure on pollinators.

While little data is available on wild bee abundance, given the difficulty in monitoring populations, studies have shown population declines similar to those of honey bees for many species[20,23]. Similar to managed bees, wild pollinator decline is linked to the degradation, fragmentation, and loss of habitat, and also to pesticides, parasitoids and pathogens[20,23]. A recent assessment by the International Union for Conservation of Nature's Bumblebee Specialist Group found that more than one quarter of North American bumble bee species are at risk of extinction[24]. The Massachusetts Division of Fisheries and Wildlife and the Natural Heritage and Endangered Species Program (NHESP), lists seven (7) species of wild bees that are of concern[18,19].

While wild bees face many of the same risks as managed bees, their biology and behavior are different in that some of the universal protections put into place for managed bees often fail to address wild bee concerns. For instance, unlike honey bee colonies with thousands of workers, nearly 90% of wild bees are solitary ground nesters meaning they do not live in colonies with multiple workers[7]. As such, they do not have a buffer to protect future generations if the egg-laying female dies before the reproductive cycle is complete. Compared to managed bees, wild bees also have potentially different exposure routes of habitat disturbance and pesticides given their different life histories. For example, ground nesting wild bees would be subject to disturbance from tillage since it could damage their brood chambers and subsequently nest sites. Wild bees that gather mud or plant materials to construct brood cells may force immature bees to be exposed to higher quantities or levels of pesticides, given the close proximity to their developing chamber to the chemicals. These bees may also come into contact more frequently with pesticide residues from soil drenches, chemigation, and seed coatings.

B. Other Wild Pollinators

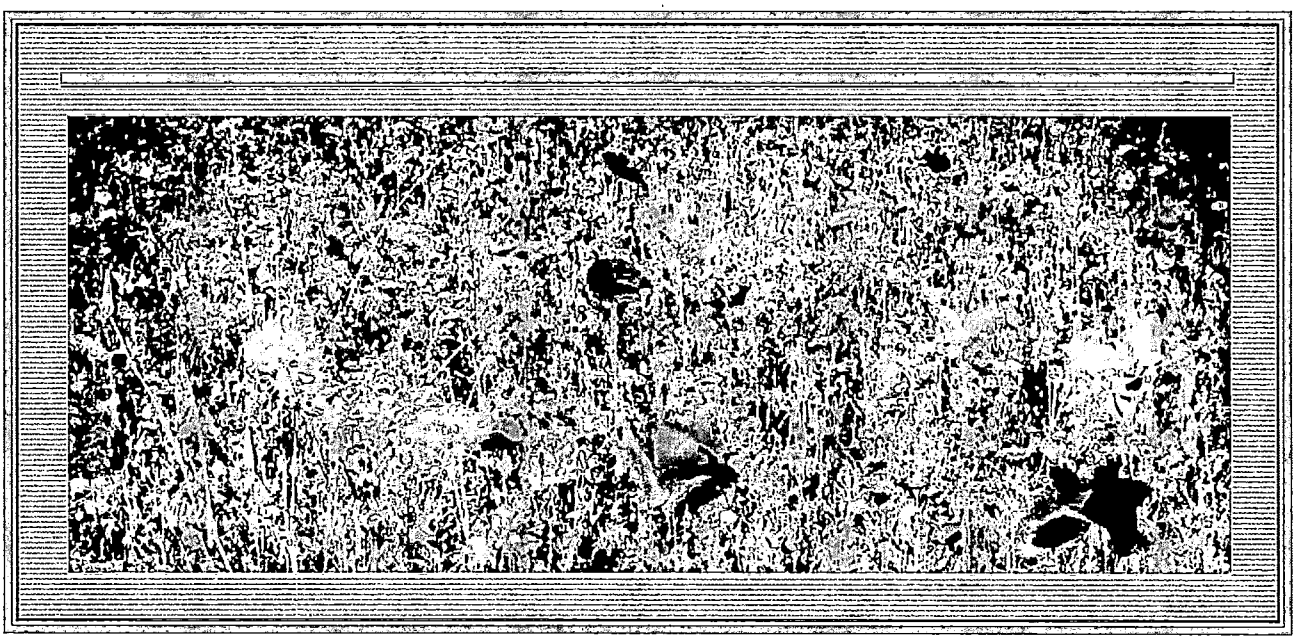
Among the wild non-bee pollinators, monarch butterflies (*Danaus plexippus plexippus*) are one of the most well-known and identifiable species, given their long-distance seasonal migration and massive winter gatherings in Mexico and California. Their annual migration flight is made each fall from the northern plains of the US and Canada to the forests north of Mexico City, while some of the population also overwinters in forests along the California Coast[25]. The monarch population breeding areas east of the Rocky Mountains include the Central and Eastern United States and as far north as southern Canada, with the most important being the Corn Belt in the Midwestern United States[26]. Unfortunately, monarch butterfly populations have been in decline over the past 20 years, as citizen science counting data indicates the population has been reduced to less than 300,000 in 2015 from 1.2 million butterflies in 1997[25]. These estimates reveal an 80% reduction in the population in Central Mexico and 74% in California[25]. The most important drivers of these population declines are habitat loss, climate change, and pesticide use[25,26]. Habitats are not only important as overwintering sites, but also important for food resources given that they require different plants based on their life cycle: milkweed for immature growth of caterpillars in spring and summer and a variety of late blooming flowers for adults in fall. Unfortunately, monarch butterflies are not the only pollinator species in peril, given that MA NHESP currently lists nineteen (19) species of butterflies and moths and nine (9) species of beetles as endangered, threatened, or of special concern[18,19].



THE POLLINATOR PROTECTION PLAN (PPP)

Given the diversity of factors involved in the decline of managed bees and monarch butterflies, combined with the need to effectively evaluate, sustain and enhance these populations, there was a national memorandum issued in 2014 by President Barrack Obama, followed by the release of the *National Strategy to Promote the Health of Honey Bees and Other Pollinators* calling on Federal Agencies to coordinate their efforts to improve managed bee pollinator health, increase monarch populations and increase pollinator habitat. The specific overarching goals of this memorandum included[27]:

- Honey bees: Reduce honey bee colony overwintering mortality to no more than 15% within 10 years.
- Monarch butterflies: Increase the Eastern population of the monarch butterfly to 225 million butterflies occupying an area of approximately 15 acres in the overwintering grounds in Mexico, through domestic/international actions and public-private partnerships, by 2020.
- Pollinator habitat acreage: Restore or enhance 7 million acres of land for pollinators over the next 5 years through Federal actions and public/private partnerships.



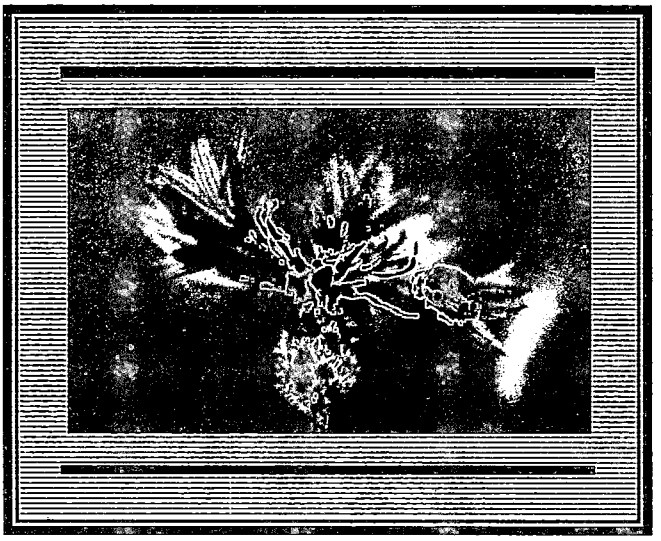
A key component of this strategy was the engagement of all states to develop independent state-level Managed Pollinator Protection Plans (MP3) that facilitate collaboration and provide a set of recommendations of practices for those key stakeholders involved in the protection of managed bee pollinators and monarch butterflies, including state agencies, beekeepers, pesticide applicators, land managers/farmers, the nursery/landscaping industry, and homeowners. However, the creation of these plans is on a state by state basis and as such flexible in content as represented by the current diversity of plan types and focus nationwide. Despite being initially centered on creating plans for managed pollinators, many states have adopted to include measures to conserve and protect non-managed, wild pollinators.

The process of drafting the Massachusetts Pollinator Protection Plan (PPP) began in November 2014, when the Massachusetts Farm Bureau established a Pollinator Stewardship Group with the purpose of constructing a draft plan for submission to MDAR. In a separate effort within the same timeframe, eight county level honey beekeeping associations also drafted their own pollinator protection plan. Both documents were then submitted to MDAR in October 2015 for consideration in crafting the state-wide pollinator plan. MDAR combined these documents, while also adhering to the State FIFRA (Federal Insecticide Fungicide Rodenticide Act) Issues Research and Evaluation Group (SFIREG) and Environmental Protection Agency (EPA) *MP3 Guidance*, to create the first draft of this plan. That first draft was developed to provide a set of voluntary guidelines to outline the roles of states, honey beekeepers, pesticide applicators, land managers/farmers, nurseries/landscapers, and the general public in protecting managed bee pollinator health.

The initial draft plan was released for public comment on February 26th, 2016 with all comments being due on April 30th, 2016. During this time period, a total of 7 listening sessions were held all over the state, with 93 attendees providing verbal comments. A total of 2,504 written comments (hard copy and electronic) were also received during this time period, from

the following stakeholder groups: academia, a country club director, a physician, a town council member, beekeepers (hobbyist, sideliner and commercial), Beyond Pesticides, Cape Cod Cranberry Growers Association, Environment Massachusetts, farmers, Golf Course Superintendents Association of New England, GreenCape, homeowners, Irrigation Association of New England, Massachusetts Association of Landscape Professionals, Massachusetts Association of Lawn Care Professionals, Massachusetts Arborists Association, Massachusetts Audubon Society, Massachusetts Beekeepers Association (representing 3,188 members from 9 county bee organizations), Massachusetts Farm Bureau, Mosquito Squad, New England Pest Management Association, Northeast Organic Farming Association, Responsible Industry for a Sound Environment, students, The Green Industry Alliance, Toxics Action Center, University of Massachusetts-Extension and the Xerces Society.

MDAR then compiled and created a document summary of all the comments, and released it to the public on September 14th, 2016. After these comments were released, MDAR began editing and re-writing the plan to not only consider these comments, but also re-focus the content to better suit the needs of pollinators in MA. Given this, the current version of the plan has expanded beyond the federal directive to not only address many of the comments that were submitted, but also to give the document a broader focus that includes wild pollinators. The purpose of the current draft of this plan is to provide a set of Best Management Practices (BMPs) guidelines for stakeholders to reference when performing actions that could involve either managed or wild pollinators. These guidelines are not regulatory in nature, but rather a set of practices that, if performed correctly, can preventatively mitigate unintended negative impacts on pollinators and/or proactively establish hospitable conditions under which populations can thrive and become sustainable. To accomplish these goals, the plan includes a list of future projects that MDAR is working on in an effort to provide and increase the sustainability of performing the actions outlined in this document. The effectiveness and impact of this plan will be reviewed by MDAR on an annual basis by assessing a variety of performance metrics and using the *SFIREG Joint Working Committee Performance Measures for Managed Pollinator Protection Plans (MP3)* as reference. For a detailed description of these metrics, see Appendix A.



Please note that while this plan focuses on wild bees, managed bees and Monarch butterflies, all strategies listed in this document would also provide direct benefit to all other pollinator populations. This plan is a living document, and will need to be updated and changed periodically as new scientific data becomes available, in order to keep the information relevant and applicable. The collective actions and considerations of all stakeholders will ultimately determine not only the relevance of this

plan and its suggestions, but the future of pollinator populations in the Commonwealth.

THE ROLE OF MASSACHUSETTS DEPARTMENT OF AGRICULTURAL RESOURCES (MDAR)

The Massachusetts Department of Agricultural Resources (MDAR) supports farms in its mission to ensure the long-term viability of agriculture in Massachusetts. Through its four divisions – Agricultural Conservation and Technical Assistance, Agricultural Markets, Animal Health, and Crop and Pest Services – MDAR strives to support, regulate and enhance the rich diversity of the Commonwealth's agricultural community to promote economically and environmentally sound food safety and animal health measures, and fulfill agriculture's role in energy conservation and production.

A. Apiary Program

Massachusetts is home to a large and diverse beekeeping industry, with current estimates indicating the presence of 4,000-4,500 beekeepers managing 40,000-45,000 hives. In addition to pollination services that managed bees provide, honey is also an important agricultural commodity produced in the Commonwealth. MDAR's Apiary Program was established to promote and sustain apiculture in the Commonwealth by providing support to honey beekeepers, pesticide applicators, farmers, land managers, educators, regulators and government officials. MDAR considers the Apiary Program to be an integral component of the department and will work to ensure adequate funding and staffing to provide support to honey beekeepers and other stakeholders.

The program staff consists of a full time Chief Apiary Inspector and a team of seasonal full time inspectors, with yearly contracts to service the state. Seasonal Apiary Inspectors support the Chief Apiary Inspector by performing annual health and regulatory inspections of apiaries, evaluating colonies for the presence of parasites, pathogens and pests, and providing education to stakeholders. While the program works to inspect as many colonies as possible given the staff and budget, the presence of these parameters combined with voluntary inspection requests and voluntary apiary registration processes, makes it impossible to visit every beekeeper each season. Inspection data is compiled and reported out on an annual basis. All inspectors work with county-level bee organizations, universities, other state agencies, regional inspectors and national organizations to stay updated on the needs of honey beekeepers and the health concerns facing pollinator populations.

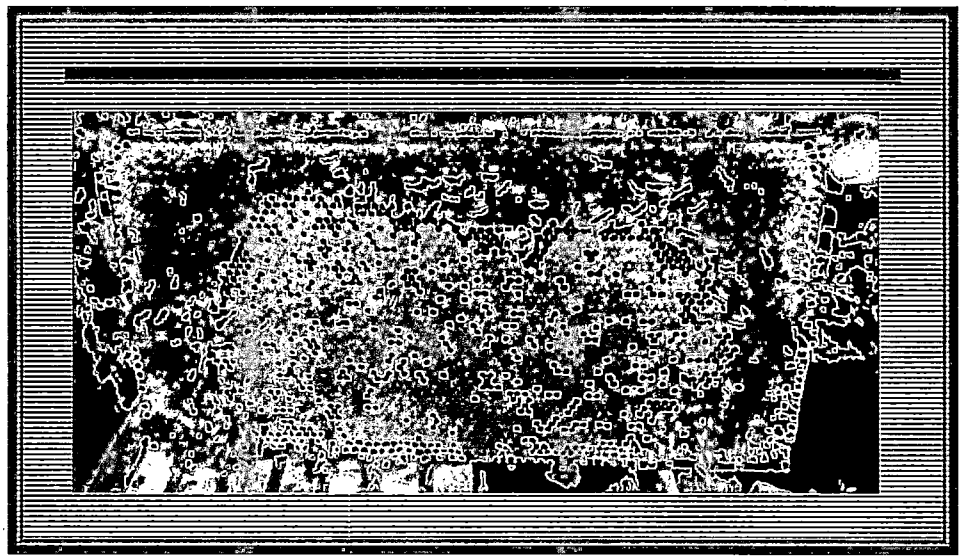
MDAR is currently evaluating and updating the Apiary Program to determine ways that it can provide better support while also ensuring the health and sustainability of honey bee populations in the Commonwealth. Traditionally, the Apiary Program has been heavily focused on providing outreach and extension type education to honey beekeepers through the following supportive services:

- Technical assistance, continuing education, and outreach to all audiences on topics related to honey bee biology, hive management, and pollination.
- Communication with beekeepers to determine their needs.
- Keeping up to date on the status of pollinators.

- ❖ Marketing of honey and other bee products as agricultural commodities.
- ❖ Collaboration with other government agencies.
- ❖ Creation and maintenance of a state apiary to provide a portal for educational demonstrations and projects related to honey bee health.

The re-structured program will not only continue this focus, but also exercise its regulatory role by ensuring compliance of the laws and regulations pertaining to honey bees: *Chapter 128, Massachusetts General Law, Sections 32-36B* and *330 CMR 8.00: Apiary Inspection Regulations*. This regulatory role involves performing the following actions:

- ❖ Providing routine health inspections of honey bee colonies for detection, suppression and elimination of infectious diseases.
- ❖ Issuing quarantines and destruction orders for incidences of American Foulbrood.
- ❖ Conducting health inspections of imported and designated honey bee colonies for export through the detection and suppression of infectious diseases.
- ❖ Checking permits to ensure compliance of requirements for interstate movement of colonies and equipment.



- ❖ Consulting with state and local agencies on to ensure compliance of state laws and regulations.
- ❖ Investigating bee kill incidences suspected to be due to pesticide misuse, through collaboration with the Pesticide Enforcement Program.
- ❖ Investigating other bee kill incidences to determine presence of infectious diseases.
- ❖ Providing notification of apicultural health concerns to the public in the event of an infectious disease outbreak.

B. Pesticide Enforcement Program

MDAR's Pesticide Enforcement Program is tasked with protecting the environment by providing licenses to individuals who apply pesticides, registering pesticide products used in the Commonwealth, and enforcing both federal and state pesticide laws and regulations. Pesticide Enforcement administers the provisions of the *Massachusetts Pesticide Control Act* and the regulations in *333 CMR 1-14*. MDAR is also designated as the lead state agency for the enforcement of the Federal Pesticide Statute (FIFRA) by the US Environmental Protection Agency (EPA). The Pesticide Inspection Team consists of a Chief Pesticide Inspector and a team of inspectors that investigate allegations of pesticide misuse and inspect dealer establishments, pest control businesses and pesticide producer establishments. The program also acts as

support staff for the Pesticide Board, Pesticide Board Subcommittee, MDAR department heads, and the Apiary Program.

The Pesticide Enforcement Program will continue its partnership with the Apiary Program to investigate reported bee kills, using guidelines created by the Environmental Protection Agency *EPA Guidance for Inspecting Alleged Cases of Pesticide-Related Bee Incidences* and *Guidance for Assessing Pesticide Risks to Bees*. All data collected on managed bee pollinator health in association with the reported bee kills will be analyzed, converted to an electronic format, and provided to the public in an annual report. This data will be reviewed to determine if there are any trends regarding pesticides and pollinator health. The program will work with the Chief Apiary Inspector to develop outreach materials and include pollinator safety information as part of any pesticide applicator training that the program participates in. MDAR will also encourage outside programs to include pollinator safety in any training provided to pesticide applicators.

BEST MANAGEMENT PRACTICES AND ACTIONS TO BENEFIT POLLINATORS

A. Beekeepers

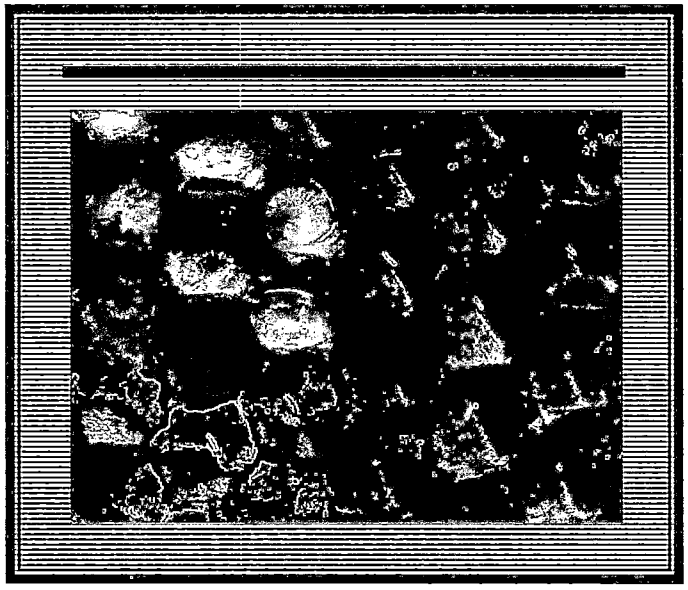
Beekeepers have a larger responsibility for the overall health and welfare of managed bee colonies. This includes taking steps to ensure good bee health, proper hive husbandry, continuing education of beekeepers, and communication with land managers, farmers, pesticide applicators, and the public to mitigate pesticide risk and enhance forage. The Massachusetts Beekeeper Association *Best Management Practices for Beekeepers* should be used as a guideline for good husbandry practices in beekeeping. If additional support is needed, beekeepers should consider attending a bee school and/or working with a mentor to learn about beekeeping practices. Currently, there are opportunities for classroom instruction, field training, and mentoring provided by knowledgeable beekeepers to members of county beekeeping associations. For a list of the county beekeeping associations in your area visit the *Massachusetts Beekeeping Association* website. In addition, beekeepers must comply with Massachusetts Apiary Laws and Regulations related to honey beekeeping: *Chapter 128, Massachusetts General Law, Sections 32-36B* and *330 CMR 8.00-8.07: Apiary Inspection Regulations*. Beekeepers should also check with the municipality in which the apiary is located, in case there are local ordinances that also apply.

In an effort to maximize pollinator health, beekeepers are also encouraged to consider the following practices:

- To ensure colony survival, establish your apiary in a location that provides adequate forage resources and water supply, proper environmental conditions (i.e. sun exposure, windbreak and using the proper density of colonies based on area. Refer to the BMPs listed above for density estimates, which are vital to ensuring the adequate forage resources as well as decreased conditions for disease and parasite spread. Establish and try to maintain a positive relationship with neighbors, land managers and farmers through direct communication when establishing and/or moving the apiary so that bees

are provided with the most beneficial habitat parameters and are not considered a nuisance or public safety issue.

- ❖ If supplying bees for pollination, setup a pollination contract in advance. That contract should outline at a minimum: the pollination fee, number of colonies per acre, payment schedule, bloom timeline/pollination schedule, and removal date. This ensures that both the farmer and beekeeper interests are protected. For additional information, review the *USDA Insect Pollination of Cultivated Crops* and sample contracts: *University of Florida Sample Pollination Contract*, *Michigan State University Sample Pollination Contract*
- ❖ Learn to recognize and understand the life history, biology and management of honey bees and their common pests, parasites, and pathogens. There are several guides available from USDA *Diagnosis of Honey Bee Diseases* and the Pennsylvania State University Extension that can assist in learning more about these organisms:
  - *A Field Guide to Honey Bees and Their Maladies*
  - *A Quick Reference Guide to Honey Bee Parasites, Pests, Predators and Diseases*
  - *Beekeeping Basics*



- ❖ Regularly inspect colonies to determine the incidence and level of common pests, parasites and pathogens. When present, incorporate Integrated Pest Management (IPM) practices for control, and evaluate pest pre/post population levels regarding treatment so that informed decisions can be made. "IPM is defined as a decision-making framework that utilizes least hazardous pest management options only when there is a demonstrated need, and takes special precautions to reduce the hazards of pest management activities to people, other living organisms, and the environment. It employs a four-phase strategy: (1) Reduce conditions that favor pest populations, (2) Establish an economic threshold of how much damage can be tolerated before pest control must occur, (3) Monitor pest populations, and (4) Control pests with the most specific pest control option when the pre-established damage threshold is reached"[27]. Along with their informative guide, the Honey Bee Health Coalition just released a series of instructional videos that demonstrates how to evaluate for Varroa mites and install treatments. Be sure to only use currently registered pesticide products for treatment, and use them according to label instructions (Remember: *The Label is the Law*!). Obtain a commercial pesticide applicator license if you are applying treatments to colonies not owned by you and in another beekeepers' apiary. If additional assistance is needed, considering contacting

the MDAR Apiary Program to request a routine annual health inspection and/or registering your apiary.

- ❖ Stay up to date on new developments in honey bee husbandry so that you can practice the most effective management techniques. For example, replacing a portion of old brood comb every year is a great way to not only practice good colony hygiene but also prevent pathogen buildup in colonies. There are a few national organizations that periodically provide updated information:
    - *American Association of Professional Apiculturists*
    - *American Bee Journal*
    - *American Beekeeping Federation*
    - *American Honey Producers Association*
    - *Bee Culture Magazine*
    - *Beesource Beekeeping*
    - *Honey Bee Health Coalition*
    - *Project Apis m.*
- ❖ Support colony health by providing, when needed, supplemental feeds of sugar (dry or syrup) and pollen (fresh or protein patty) as well as providing an additional water source.
- ❖ Support colony health by adequately preparing colonies for winter by ensuring an adequate workforce, healthy queen, food stores, low pest/pathogen levels, ventilation, insulation, windbreak and mouse guard/entrance reducer to prevent pest invasion prior to the start of winter.
- ❖ Work with the local beekeeping community to encourage queen rearing of northern adapted bees, in order to increase vitality and genetics.
- ❖ Incorporate swarm management strategies into the apiary to minimize the loss of potential swarms and encourage the re-homing behavior of swarming bees to prevent a public concern.
- ❖ Be aware of agricultural production practices in your area and communicate with land managers/farmers and nursery/landscaping professionals on strategies to mitigate potential negative impacts from pesticides prior to application.
- ❖ Communicate with local nurseries to alert them to the locations of any nearby apiaries and/or colonies, so that you are kept informed about any potential pesticide applications that could impact their colonies.
- ❖ Communicate with pesticide applicators to provide location information for the apiary, or provide visible markers such as flags to clearly mark locations. Contact your local Mosquito Control Project and submit information to be included on their "No Spray" list.
- ❖ In the case of "Bee Kills" where pesticide use or an infectious disease (i.e. American Foulbrood) is suspected, report to MDAR promptly for investigation.
- ❖ Participate in state and national surveys related to hive health, so that the status of Massachusetts honey bees can be documented and tracked over time.

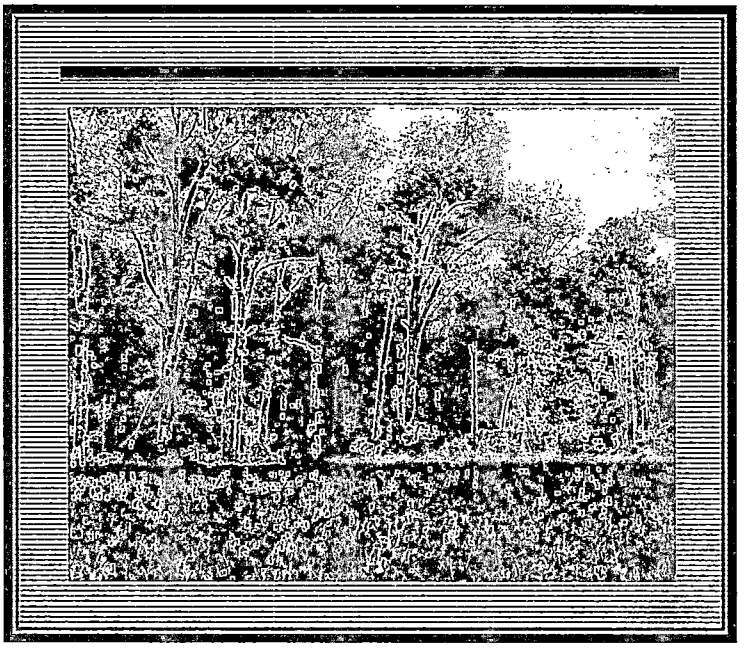
B. Pesticide Applicators

Pesticides have the ability to negatively impact pollinators based on the type, rate, timing, and proximity to the colony of the materials used. Communication, cooperation, and education among stakeholders are the best tools to use to avoid non-target impacts of pesticides on pollinators. Information about hive locations as well as locations of agricultural commodities grown near apiaries should be shared between stakeholders, as must anticipated pesticide products to be used and timing of applications. Stakeholders must also cooperate and educate one another about their individual needs so that the best decisions can be made for mitigating negative impacts on pollinators. Given this, pesticide applicators should follow BMP's for using pesticides in a way that minimizes the risk to pollinators, such as:

- Communicate with beekeepers in the area about pesticide applications.
- Follow Integrated Pest Management (IPM). See the IPM specific information above for additional explanation.
- Reduce non-target exposure to pesticides by considering bloom periods of crops and nearby weeds, and avoiding application at those times.
- Only treat target areas.
- Do not spray or drift onto flowers/plants/trees when they are in bloom and when pollinators would be visiting them.
- When possible, apply pesticides early in the morning or later in the evening during times when pollinators are less active and/or not foraging in or near the treatment area.
- Stay current on product label changes and product reviews from EPA.
- Choose pesticide products wisely. Look for products that are listed as non-toxic, that have a low toxicity, short residual toxicity, and/or repellent properties to bees. There are several guidelines available to determine bee toxicity of pesticides:
    - EPA: *Guidance for Assessing Pesticide Risks to Bees*, *Policy Mitigating Acute Risk to Bees from Pesticide Products*
    - Michigan State University (MSU): *Minimizing Pesticide Risk to Bees in Fruit Crops*
    - Oregon State University (OSU): *How to Reduce Bee Poisoning from Pesticides*
    - The University of California Statewide Agricultural and Natural Resources Integrated Pest Management Program (UC IPM): *Bee Precaution Pesticide Ratings*
- Read and be familiar with BMP's created by national pest control agencies:
    - National Pest Management Association (NPMA): *Pollinator Protection Best Management Practices*
- When possible, use larger droplet sizes and drift reduction products.
- Learn more about pollinators including, but not limited to specific information on their life histories, biology, and distribution and occurrence in the landscape.
- Attend training sessions that offer information about the following topics:
    - Pollinators and pesticides
    - IPM
    - Drift management
    - Laws and regulations

In addition, pesticide applicators must follow the existing pesticide laws (*M.G.L.c. 132B*) and regulations (*333 CMR*), including but not limited to:

- *All persons shall use a pesticide in such a manner that there be no unreasonable adverse effect on the non-target environment.* 333 *CMR 13.02(5)*
- *All persons shall;*
  - *Use only methods and equipment which insure proper application of materials;*
  - *Operate in a careful manner and only when conditions are proper for controlling pests in the locality. 333 CMR 13.06*
- *All persons are prohibited from applying pesticides, which bear a warning statement on the label concerning bees, to fruit trees, alfalfa, clover or trefoil grown as field-crops while in bloom without making reasonable inquiry as to the presence of apiaries on the premises or within a 2.5 mile radius of the application site. If apiaries are found to occur within 2.5 miles of the application site, the applicator shall provide 24 hours' pre-notification to owners of the apiaries. Reasonable inquiry shall consist of obtaining a current Apiary list from the Department and checking with known agricultural establishments within a 2.5 mile radius of the application site to determine if pollinator hives are on-site. 333 CMR 13.07(2)*
- *No person shall distribute, handle, dispose of, discard, or store any pesticide or pesticide container in such a manner as to cause injury to humans, vegetation, crops, livestock, wildlife, beneficial insects, to cause damage to the environment, or to pollute or contaminate any water supply, waterway, groundwater or water body. M.G.L.c. 132B Section 6*
- *No person shall distribute any pesticide that does not conform to any requirement of its registration or permit. M.G.L.c. 132B Section 6*
- *No person shall use a registered pesticide in a manner that is inconsistent with its labeling or other restrictions imposed by the department. No person shall use a pesticide which is the subject of an experimental use permit inconsistently with the terms and conditions of said permit. M.G.L.c. 132B Section 6A*



C. Land Managers and Farmers

Pollinators require flowering plants for food resources (pollen and nectar), water sources and habitat for nesting. A variety of agricultural crops are very attractive to pollinators[29]. Given this, land managers and farmers serve an important role in sustaining pollinators by providing these resources. Private and government agencies overseeing land also provide these resources and thus are encouraged to incorporate pollinator habitat as part of their management

regime. A variety of land types can be augmented to include suitable pollinator habitat, such as municipal and state-owned parcels, areas around public buildings, land along highways and within the highway median, land within power line right-of-ways, golf courses, cemeteries, forests, landfills, and parcels within existing agricultural landscapes such as hedge rows, field borders, waste and fallow areas. Land parcels are also important for commercial stationary and migratory beekeepers since these areas can serve as temporary or permanent apiary locations, staging yards for colony transport and forage resources for honey production. Land managers and farmers should work with beekeepers to offer land parcels for these uses and aid in selecting appropriate apiary locations. Incorporating pollinator habitat and pollinator-friendly land management practices also provides benefit to land managers and farmers, since research has shown that pollinator-dependent crops have higher visitation rates and increased yields when a diversity of pollinators are present in the landscape[30,31]. Crops grown for fodder also benefit from pollinators since adequate pollination is required for seed set[29].

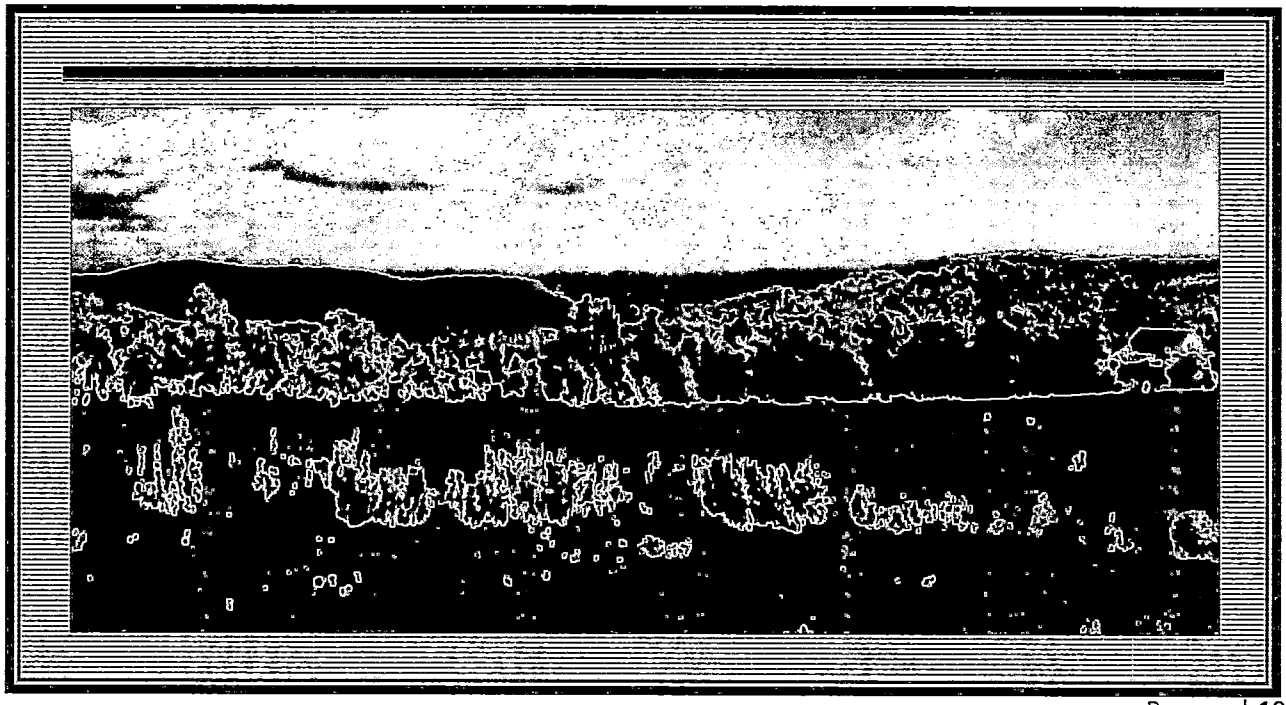
The first step in designating, designing, and/or restoring habitat for pollinators is to survey the area and determine if your goals of creating habitat can be met in the designated space. If additional funding is needed to accomplish the objectives, there are several national and state level programs available to provide financial assistance and/or incentives for incorporating, improving and/or expanding pollinator habitat:

- MA Department of Fish and Game: *MassWildlife Habitat Management Grant Program*
- MA Department of Conservation and Recreation: *Land and Recreation Grants and Loans*, *Forest Stewardship Program*
- Natural Resource Conservation Service (NRCS): *Conservation Stewardship Program (CSP)*, *Environmental Quality Incentives Program (EQIP)*, *Agricultural Conservation Easement Program (ACEP)*, *Using Farm Bill Programs for Pollinator Conservation*
- US Department of Agriculture (USDA): *Conservation Reserve Program (CRP)*, *Conservation Reserve Enhancement Program (CREP)*
- US Forest Service (USFS): *Pollinator-Friendly Best Management Practices for Federal Lands*

There may also be local assistance available in the form of grants, subsidies or scholarships from government or private agencies and organizations. The next step is to determine if and to what extent the landscape already has beneficial components, such as existing sources of water and natural areas. Natural areas like forests, woodlands, and wetland habitat provide not only a diversity of flowering plants, but also potential nest sites and water resources for pollinators. It is also important to either establish pollinator habitat in the vicinity of an existing water source, or to provide water (often even something simple, like a dish with rocks in the bottom, would suffice). Natural areas can also benefit agricultural land since farm fields adjacent to natural areas have higher pollinator abundance and subsequently higher crop fruit set compared to those surrounded only by farmland[31,32]. To provide nest sites for pollinators, it is important to leave a small area of fallow/bare soil, leaf piles, downed or dead wood, and grasses in the landscape.

After accounting for natural areas, nesting sites and water resources, incorporate pollinator-friendly plants suitable to the landscape (i.e. that grow well in that soil type, exposure to sunlight, moisture levels, etc.). Pollinators can benefit from a variety of plants, including both native and non-native species; select plant species that are appropriate for the habitat (i.e. use native species in or near conservation areas). Another important part of the process of building pollinator habitat is to select plants that provide a diversity of flower types, and a continuous supply of floral resources and bloom throughout the season. As part of any landscaping effort, it is best to consult planting lists and guidelines specific for the region, including:

- Canadian Pollination Initiative (NSERC-CANPOLIN): *Pollination in the Agricultural Landscape*
- NRCS: *Monarch Butterflies*, *How Farmers Can Help Pollinators*, *New England Pollinator Handbook*
- Pollinator Partnership and North American Pollinator Protection Campaign (NAPPC): *Selecting Plants for Pollinators: A Regional Guide For Farmers, Land Managers and Gardeners in the Eastern Broadleaf Forest Oceanic Providence*
- Sustainable Agriculture Research and Education (SARE): *Managing Alternative Pollinators*
- UMass: *Pollinators in the Landscape I* and *Pollinators in the Landscape II*
- USDA: *Improving Forage For Native Bee Crop Pollinators*, *Enhancing Nest Sites For Native Bee Crop Pollinators*, *Attractiveness of Agricultural Crops to Pollinating Bees*
- USFS: *Plant Milkweed for Monarchs*
- University of Maine (UM): *Landscaping for Butterflies in Maine*
- Xerces Society: *Monarch Conservation*, *Milkweeds: A Conservation Practitioners Guide*, *Monarch Butterflies and Butterfly Larvae/Host Plants for*



Eastern United States, *Farming for Pollinators*, *Farming with Pollinators*, *Establishing Pollinator Meadows from Seed*, *Conservation Cover for Pollinators: New England Installation Guide and Job Sheet*

In addition to incorporating plants into the landscape, land managers and farmers can also augment management practices to create, promote or enhance pollinator habitat. These practices include the following:

- Add strips of pollinator-friendly species to field margins, or between rows.
- Plant pollinator-friendly species as cover crops or as an intercrop.
- Manage the landscape to incorporate multiple types of crops that bloom at the same time offering an array of floral resources for pollinators.
- Reduce tillage intensity to allow for more nest sites for ground nesting pollinators.
- Reduce or eliminate mowing practices to increase blooming time of flowers or allow additional plant species to flower.
- Incorporate legumes as part of fodder field management, to increase nitrogen while also providing floral resources for pollinators.
- Suppress pesticide use when not necessary. Instead, use IPM and reduced risk chemicals, if necessary. Use the guidelines listed on pages 15-16 of this guide to determine the toxicity of pesticides to bee pollinators. There are also several other guides available with more information about how to incorporate these practices:
  - North American Pollinator Protection Campaign (NAPPC): *Protecting Pollinators: How and Why Pesticide Applicators Can Help Them*
  - SARE: *Manage Insects on Your Farm*
  - University of Florida (UF): *Minimizing Honey Bee Exposure to Pesticides*
  - US Department of Transportation Federal Highway Administration: *Literature Review: Pollinator Habitat Enhancement and Best Management Practices in Highway Rights-of-Way*, *Pollinators and Roadsides: Best Management Practices for Managers and Decision Makers*
  - USDA: *Preventing or Mitigating Potential Negative Impacts of Pesticides on Pollinators Using Integrated Pest Management and Other Conservation Practices*
  - Xerces Society: *Guidance to Protect Habitat From Pesticide Contamination*
- Work with state agencies to determine the BMPs needed for weedy, invasive plants by either timing management applications after bloom or providing replacement forage options using non-invasive plants.
- Participate in state and national surveys related to bee forage and land use, so that the status of MA landscapes as floral resources for pollinators can be documented and tracked.

D. Nurseries and Landscapers

Nurseries serve an important role in sustaining pollinator health by providing opportunities for property owners and landscapers to purchase plants that provide resources for pollinators to use for nectar and pollen foraging and as habitat. The landscaping industry has also made

strides in recent years in the development of pollinator-friendly landscaping options. Nursery owners/managers and landscapers not already doing so should consider the following:

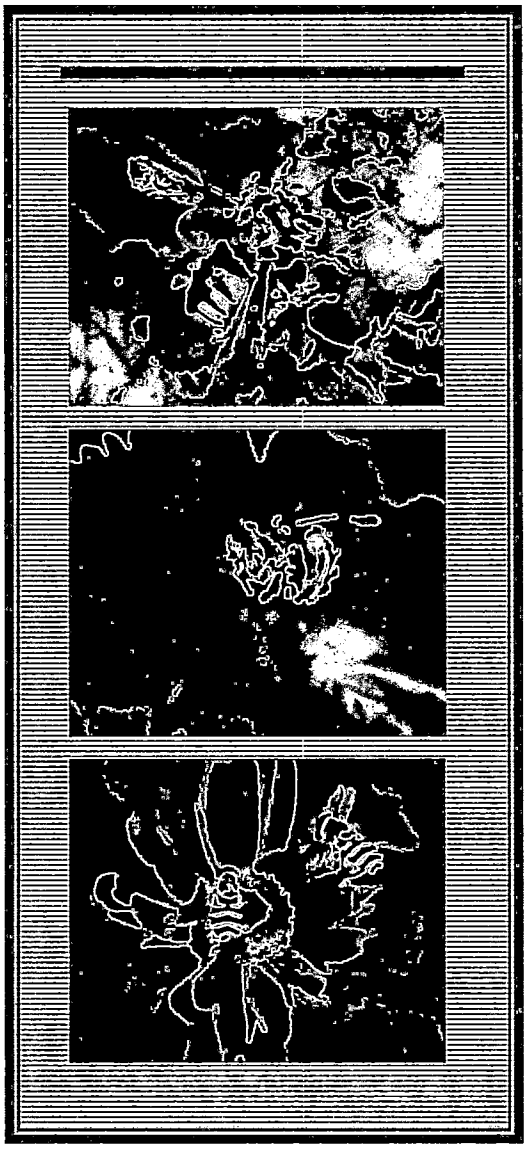
- Provide pollinator-friendly (and weed and invasive-free) planting options (annuals, perennials, shrubs and trees) and seed mixes to property owners, and encourage the creation and/or expansion of pollinator-friendly habitat wherever possible. See the pollinator plant lists above for more information.
- When possible, provide property owners with resources to assist in creation of pollinator-friendly habitats, where planting plans encourage the use of a variety of plant species in order to attract the greatest diversity of pollinators over the course of the entire growing season.
- Apply IPM practices in planting yards, greenhouses, and retail areas to minimize potential impact of pesticide application on pollinator insects. When pesticide application is deemed necessary, choose reduced risk chemicals whenever feasible.
- Reach out to University of Massachusetts Extension and other university researchers to keep informed about the latest developments in creating pollinator habitats.
- Stay up to date with industry Best Management Practices (BMPs) as they become available:
    - Horticultural Research Institute: *Grow Wise Bee Smart: Best Management Practices for Bee Health in the Horticultural Industry*
- Work with local beekeepers or beekeeping groups to ensure you are aware of the locations of any nearby apiary, and that beekeepers are kept informed about any potential pesticide applications that could impact their colonies.
- Also, keep beekeepers informed about updates to pollinator gardening options and work with beekeepers on issues related to finding the most optimal plants for honey production (i.e. new plant species, research into pollinator habitat design, etc.).

E. Homeowners and Gardeners

Homeowners and gardeners can play an important part in supporting pollinators by maintaining, enhancing, and/or increasing pollinator habitat on their property. The key to thinking about pollinator habitat is considering plants that provide food, water and shelter to meet the needs of all pollinators. These plants can include both native and non-native/ornamentals, although it has been shown that gardens with native plants tend to support more diverse pollinator groups while also being drought tolerant and requiring less management than those with non-native plantings[33,34,35,36]. Some steps to consider:

- Select plants that fit the area, taking into account the soil type, drainage, slope, and the amount and location of sunlight throughout the day.
- Select pollinator-friendly plant species. You can familiarize yourself with common pollinator insects with an identification guide such as the Xerces Society's *Streamlined Bee Monitoring Protocol*.
- Use the *NAPPC Pollinator Syndromes* and *USFS Pollinator Syndromes* charts to help you determine what criteria to look for in selecting plants.
- Do some research on the plants that would be best for your area. If you are interested in identifying the species of wildflowers that are already in your yard prior to making changes visit the New England Wildflower Society's Go Botany website for keys.

- Your local nursery or landscaper will often have guidance on creating the best pollinator habitat on your land. To find a source for native plants, check with your local nursery or use the directory provided by Plant Native: *Native Plant List for Connecticut, Massachusetts and Rhode Island*. If you are selecting non-native species, remember that some cultivars have been modified and do not provide pollen and nectar, such as tulips, daffodils, petunias, and ornamental roses. Some examples of resources that provide regional native and non-native plant lists suitable for Massachusetts are:



  - *BeeSmart Pollinator Gardener App*
  - Bringing Nature Home: *Plant List for Butterflies and Moths*
  - Massachusetts Butterfly Club: *Butterfly Gardening 101: Western Massachusetts*
  - MSU: *Protecting and Enhancing Pollinators in Urban Landscapes*
  - New England Wildflower Society: *State of New England's Native Plants*
  - NRCS: *How Gardeners Can Help Pollinators*, *Pollinator Friendly Plants for Northeast United States*
  - OSU: *Nurturing Mason Bees in Your Backyard in Western Oregon*
  - UMass: *Gardening to Support Pollinators*, *Planting For Pollinators*
  - USDA: *Massachusetts Plant Hardiness Zone Map*
  - USFWS: *Attracting Pollinators to Your Garden*, *Attracting Pollinators To Your Garden Using Native Plants*, *Pollinator Plant Lists*
  - Xerces Society: *Pollinator Plants for Northeast Region*, *Pollinator Friendly Parks: How to Enhance Parks, Gardens, and Other Greenspaces for Native Pollinator Insects*

- When designing a garden or landscape around your home, make sure the plants you choose are diverse not only in the number and types of each species, but also in the timing of flowering (throughout the growing season). Design the area so that there are large sections consisting of several species of plants that all flower at the same time, with an overall array of plants flowering throughout the season. Keep in mind that many pollinator species may feed on different plants as larvae versus when they are adults.
- Your landscape should include a variety of plant types such as wildflowers, grasses, herbs, fruits, vegetables, shrubs and trees.

- Avoid invasive, noxious and weedy plants that may be harmful to other plants through overcrowding that reduces the diversity of floral resource available. Though note that if local ordinances allow, weeds such as dandelions, clover and other flowering plants in lawns can be important early season food resources for pollinators at times when other flowers are unavailable.
- Provide a water source for pollinators either in the form of a bird bath or a shallow dish with stones in the bottom to prevent drowning. If you are targeting butterflies specifically, you could also provide a salted area for adults to use in obtaining sodium by simply adding some salt to a moist area of soil.

- The majority of pollinators are considered to be central place foragers meaning that they forage very close to their nest. Taking this into account, nesting materials need to be provided in close proximity to flowering plants. However, before thinking about nesting areas, take a tour of the existing habitat and determine if it already consists of any active nests. If so, avoid disturbing them and instead incorporate these into your habitat plans. When thinking about providing nesting material for pollinators, it is important to remember that pollinators can use a variety of above and below ground areas as nests. Providing nesting areas can be as simple as leaving some undisturbed space or as complex as installing pollinator specific boxes such as "bee hotels". A great guide to use when constructing bee boxes has been produced by the *Xerces Society*. If providing nest boxes, keep in mind that some types have low occupancy success rates such as those for bumble bees and others have to be very specific to meet pollinator needs, such as nest entry diameter for certain species of solitary bees. Nest boxes also have to be periodically cleaned to prevent the occurrence and spread of infectious disease. If local ordinances allow, some of the best nesting areas consist of leaving falling logs, leaf litter abandoned bird nests and mammal burrows as nesting sites for pollinators.
- If you are going to use pesticides be sure to incorporate the same IPM strategies described above. Read pesticide labels, follow label instructions carefully, and apply the materials in way that minimizes potential impact to pollinators. This includes considering the time of year and time of day for applications in order to minimize exposure to pollinators. It is also important to consider removing or mowing blooming plants that are flowering in the lawn prior to pesticide application, to mitigate the potential exposure to foraging pollinators.

After you have created the pollinator habitat on your property complete with food, water and nesting resources, consider telling others about your accomplishments, including posting signage and showing the area to your neighbors and others in the community to help spread the word on the importance of pollinator habitat. There are also several national organizations you can contribute to by collecting citizen science data on the pollinators attracted to your yard and/or getting recognition for the incorporation of pollinator habitat:

- *BeeSpotter*
- *Bumble Bee Watch*
- *eButterfly*
- *Monarch Watch*
- National Pollinator Garden Network: *Million Pollinator Garden Challenge*
- *Native Buzz Project*
- NRCS: *Pollinator Habitat Sign*
- *Red Admiral and Painted Lady Butterfly Research Site*
- *The Great Sunflower Project*
- Wild Ones: *Native Plant Butterfly Garden or Habitat Recognition Program*

FUTURE ACTIONS AND IMPROVEMENTS

This plan is voluntary, not regulatory, and meant to be for educational purposes. MDAR will periodically review and modify the plan as needed to ensure that it meets the needs of stakeholders in providing the most comprehensive protection strategies for pollinators. Efforts will be made to find additional funding through grants or budgetary allocations for pollinator outreach, protection and assistance.

To better meet the needs of honey beekeepers and provide support for all pollinator species, the MDAR Apiary Program is in the process of updating its services as well as evaluating future additional projects:

- ❖ Updated inspection request service providing options for webpage information submission in addition to the existing paper process.
- ❖ Updated webpage where stakeholders can access information related to beekeeping, bee health, apiary laws and regulations.

- Creating a State Apiary with the purpose of providing support to beekeepers through demonstrations of beekeeping practices, hive management strategies, public outreach, and data collection on parameters related to bee health. In 2016, the first MDAR State Apiary was established on the University of Massachusetts-Amherst Agricultural Learning Center farm. It consisted of a total of 12 colonies initiated from package bees purchased in New England. The apiary was setup to mimic a standard apiary in Western Massachusetts consisting of hive stands and a bear fence. An additional State Apiary is planned for Eastern Massachusetts, with the goal of providing similar services to local beekeepers.
- Provide outreach education for honey beekeepers on topics related to honey bee biology, hive management, and pest, parasite and pathogen detection and treatment options.
- Participate in the annual National USDA Honey Bee Survey.
- Collect and analyze data on local honey bee health to better assess the population. The State Apiary can also be used to collect data assessing honey bee health.
- Launch a Varroa Mite IPM program and disperse alcohol mite wash kits to beekeepers for population monitoring throughout the season.
- Provide outreach to pesticide applicators, including the creation of pollinator safety BMPs and training programs for both the Pesticide Application Continuing Education credit courses and prep courses as well as pest control company continuing education programs.
- Research the feasibility of creating internally or incorporating one of the commercially available voluntary hive mapping programs, such as *BeeCheck* or *The Honey Bee and Pesticide Mapping Program*, as a method of improving communication between beekeepers and pesticide applicators and mitigating the negative risks of pesticide exposure.
- Launch a *Bee Aware* program for honey beekeepers by using the model that the Mississippi Beekeepers Association implemented with success consisting of putting up distinctive black and yellow flags around honey bee colonies to note their location for alerting pesticide applicators.
- Create and distribute pollinator kits to K-12 classrooms for promoting and educating about the importance of pollinators.
- Partner with other state agencies to create a MA specific pollinator plant seed mix packet for distribution.
- Partner with other state agencies and academic institutions to determine the most optimal plants for honey production.
- Collaborate with UMass to create a Master Beekeeping educational program.
- Create a Monarch butterfly planting and release program focused on habitat and population enhancement.
- Partner with other state agencies to apply for grant funding to increase pollinator habitat and forage statewide as well as designate more existing acreage for pollinator habitat.

ACKNOWLEDGEMENTS

We wish to acknowledge and thank all the stakeholders, organizations and members of the general public that was involved in the process of creating this plan. We sincerely appreciate your willingness to participate, passion for the topic and feedback for without these contributions, this plan would not have been possible.

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- Swallowtail butterfly on pink flower; Jennifer Forman-Orth, MDAR
- Honey bees on comb; Kim Skyrm, MDAR

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Page 23: Pollinator habitat with sign; https://www.flickr.com/photos/usdagov/14211811813
Page 24: State Apiary at UMass; Kim Skyrm, MDAR

APPENDIX A: PERFORMANCE METRICS

MDAR will evaluate the effectiveness and impact the plan has had on the health of pollinators using the performance metrics listed below. Key areas of interest include the educational outreach and change in behavior of stakeholder groups, reduction in exposure of bees to pesticides, methods to improve bee health including the data from the MDAR Apiary Program, and compliance of regulations related to reducing risks to bee populations. When needed, baseline data will be collected related to the performance metrics listed below to enhance and compliment current collection strategies. This combination of qualitative and quantitative data will be analyzed on an annual basis to provide a detailed assessment of the plan.

A. Outreach
- Number of pollinator related inquiries via phone and email received by MDAR
- Number of pollinator specific trainings provided by MDAR
- Number of trainings that contained pollinator information provided by MDAR
- Outreach materials developed and provided by MDAR for stakeholder groups:
    - Beekeepers
    - Pesticide applicators
    - Farmers/Land managers
    - Nurseries/Landscapers
    - Homeowners/Gardeners
    - Other stakeholder groups

B. Behavioral Changes
- Number of individuals (pre vs. post plan):
    - Registering honey bee apiaries
    - Requesting honey bee colony inspections
    - Requesting pollinator specific trainings
    - Requesting to be on a "No Spray List" for mosquito control applications
- New laws and/or regulations that are created

C. Reducing Exposure to Pesticides
- Number of calls alleging pesticide suspected bee kills
- Number of bee kills investigated
- Number and types of pesticides found in samples

- Number of bee kills which resulted in pesticides found in samples, but inconclusive of involvement with colony death
- Number of bee kills determined to be due to pesticides

D. Improving Hive Health

- Apiary Inspection Program:
    - Summary of results from annual MA Hive Survey
    - Summary of results from annual USDA Honey Bee Survey
    - Beekeeper satisfaction with services provided by the Apiary Program
    - Number of inspectors
    - Amount of packages, nucleus colonies (nucs), and colonies imported into MA
    - Amount of imported nucs and colonies inspected from imported material
    - Amount of nucs and colonies exported from MA
    - Amount of exported nucs and colonies inspected from exported material
    - Number of counties and cities visited
    - Number of beekeepers visited and colonies inspected
    - Number of bee kills not related to pesticide use
    - Occurrence and amount of pests, parasites and pathogens detected:
        - Bacteria: American Foulbrood and European Foulbrood
        - Fungi: Nosema spp., Chalkbrood, Stonebrood
        - Parasites: Varroa mites, Tracheal mites
        - Pests: Wax moths, Small Hive Beetles (SHB), Mice, Bears
        - Viruses: Sacbrood Virus (SBV), Deformed Wing Virus (DWV), Chronic Bee Paralysis Virus (CBPV), Black Queen Cell Virus (BQCV), Kashmir Bee Virus (KBV), Israeli Acute Paralysis Virus (IAPV), Slow Bee Paralysis Virus (SBPV), Acute Bee Paralysis Virus (ABPV)
        - Other Issues: Colony Collapse Disorder (CCD), Idiopathic Brood Disease Syndrome (IBDS), Parasitic Mite Syndrome (PMS), Snot Brood, K-Wing
        - Invasive Species: Africanized Honey Bees
        - New pests, parasites and pathogens

E. Future Actions and Improvements

- Number of new projects implemented
- Number of participants in new projects
- Amount of new acreage designated and/or created for pollinator habitat statewide

https://sciencing.com/pollution-effects-birds-5317418.html

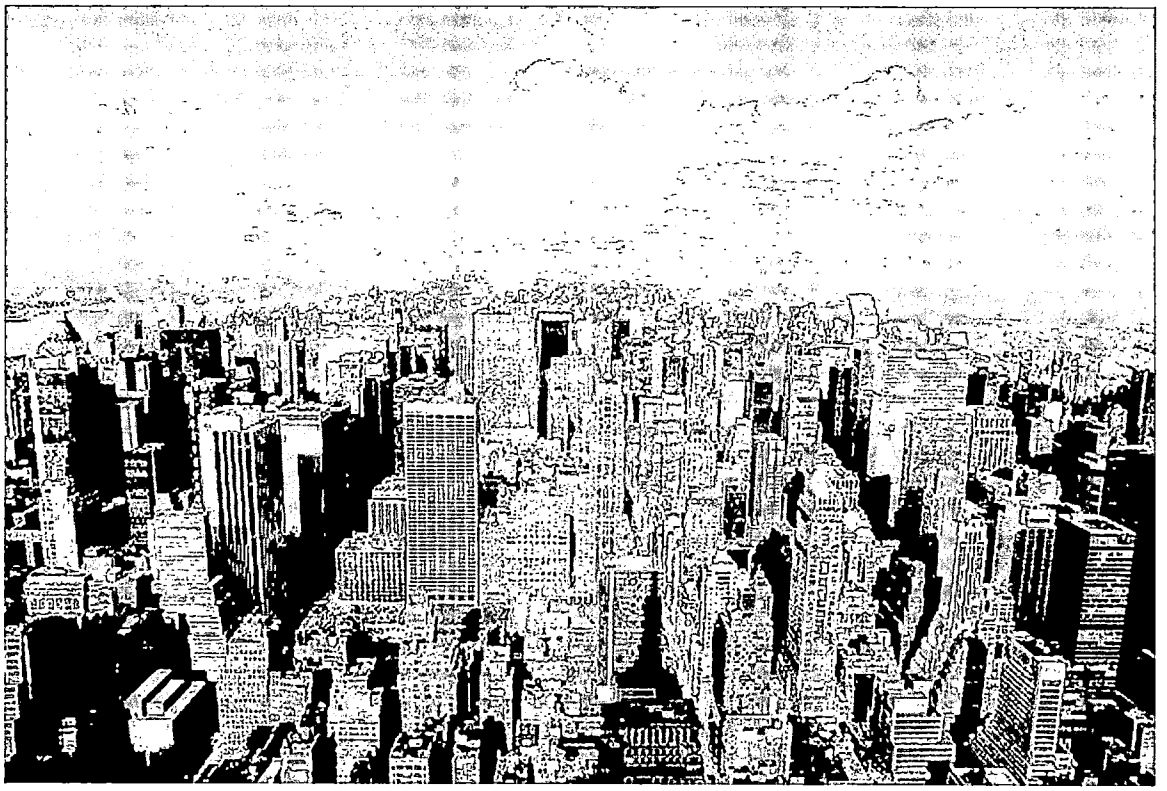
SCIENCE

Pollution Effects on Birds

Updated April 24, 2017
By Jonae Fredericks

Pollution is all around us. It is in the air that we breathe, the water we drink and the food that we eat. But humans are not the only ones combating the problems of poor air quality and chemically laced food and water. The animals of our planet are in crisis, as well, especially the birds.

Noise Pollution



Some people just want some peace and quiet, and apparently, so do the birds. The University of Colorado at Boulder has conducted a three-year study that proves that noise pollution affects birds and their habits. The biggest problem that birds face when there is too much noise is their ability to communicate. Birds that vocalize at lower frequencies are easily drowned out by noise pollution, affecting their ability to attract a mate and socialize with the other birds in their

community. But finches and other birds that vocalize at a higher frequency appear uninfluenced by the hustle and bustle of noise pollution--apparently ignoring the mass exodus of their fellow, winged friends.

Oil Pollution

Birds that are considered "water birds" are greatly affected by what is known as oil pollution. According to National Geographic, approximately 500,000 water birds are killed every year due to oil spills. When birds unexpectedly happen on an oil spill in their home water area, the oil coats their feathers and causes them to stick together. Feathers ordinarily provide a waterproof protection for birds, but when the feathers are covered in oil they lose this quality. This causes some of their skin to become exposed and at risk to the elements. Birds who attempt to clean their feathers will often ingest the oil and become ill or even die from poisoning.

Video of the Day

Light Pollution

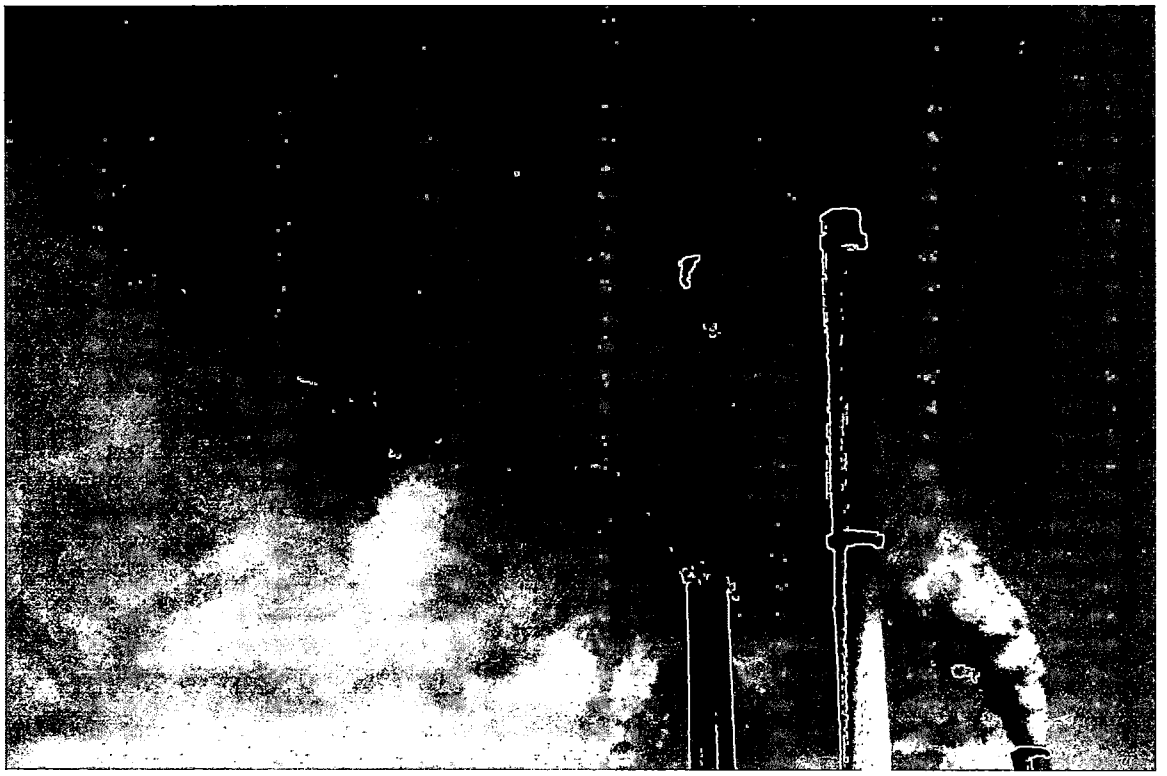
There is such a thing as too much light, at least, in the bird world. Bright city lights look beautiful at night when viewed from a distance, but that is no consolation for the bird that can't find the way home. Birds use the bright stars in the sky to determine the route for the next day, and when the city lights interfere with their view, birds can become confused and disoriented.

World Migratory Bird Day explains that light pollution can affect the flight patterns of birds, rendering their usual migration paths impossible to follow. City birds are also finding it very difficult to sleep with all of the bright lights, and some birds have become uncharacteristically active at night. Unfortunately, light pollution also causes some birds to succumb to deadly collisions with buildings and other objects in the sky that may be difficult to see when "blinded by the light".

Water Pollution

Think twice before you send that helium balloon up into the sky. Heavy winds commonly lead balloons to the ocean, and many a bird has been found with a balloon string hanging from his beak or wrapped around his neck. But balloons are just the beginning. The University of Michigan reports that municipal, agricultural and industrial waste account for the majority of water pollution throughout the world. Pesticides and heavy metals that are leaked into rivers, lakes and streams can cause illnesses and death in birds, threatening individual species. Water pollutants can also reduce the amount of oxygen in the water that eventually kills the fish. Birds that rely on fish as a source of food will often need to move to other areas to feed, causing an upset to the natural balance.

Air Pollution



Poor air quality due to smog and noxious gases can have a devastating effect on the bird population in dense areas. Not surprisingly, these pollutants have even drifted up into the polar regions, putting the lives of arctic birds at risk. According to PowerWorks Incorporated, birds have very high respiratory rates, which make them even more susceptible to pollutants in the air and to airborne impurities.

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SHORT COMMUNICATION

Stress decreases pollen foraging performance in honeybees

Célia Bordier[1], Simon Klein[2,3], Yves Le Conte[1], Andrew B. Barron[3,*] and Cédric Alaux[1,*,‡]

ABSTRACT

Foraging in honeybees is energetically demanding. Here, we examined whether stressors, which generally increase metabolic demands, can impair foraging performance. A controlled non-pathogenic stressor (immune challenge) resulted in a change in the foraging preferences of bees. It reduced pollen foraging and increased the duration of trips in pollen foragers. Stress also reduced the amount of octopamine in the brain of pollen foragers (a biogenic amine involved in the regulation of foraging and flight behaviour in insects). According to the literature, flight metabolic rate is higher during pollen foraging than during nectar foraging, and nectar gives a higher energetic return relative to the foraging effort when compared with pollen. We thus propose that stress might be particularly detrimental to the performance of pollen foragers, and stressed bees prefer the energy-rich resource of nectar. In conclusion, stress, even at low levels, could have consequences for bee foraging behaviour and thereby the nutritional balance of the colony.

KEY WORDS: Immune challenge, Flight, Biogenic amine, Radio-frequency identification device

INTRODUCTION

For honeybees, which are central-place foragers relying on pollen and nectar from flowers, foraging behaviour places demands on both cognitive capacity (Klein et al., 2017) and metabolic capacity: indeed, insect flight is known to be among the most intense and energy-demanding physiological processes in the animal kingdom (Dudley, 2000). The metabolic rates of flying insects, mainly fuelled by carbohydrates, can be up to 170 times higher than those of resting individuals (Bartholomew and Casey, 1978). As a consequence, it is expected that environmental stressors (e.g. parasites and temperature changes), which often impose increased metabolic demands (Bordier et al., 2017a; Johnson and White, 2009), could compromise foraging performance. Deciphering how stress impacts honeybee foraging performance might therefore help us better understand the mechanisms underlying colony decline and failure, which continues to be an issue of widespread concern (Goulson et al., 2015; Potts et al., 2010).

Stressors may directly limit bees' energetic reserves and thus reduce foraging performance. Indeed, there are several reports of a reduction of global flight activity in parasitized bees due to energy depletion (Kralj and Fuchs, 2010; Alaux et al., 2014; Naug, 2014; Wolf et al., 2014). Stressors may also affect forager decision-making processes as a consequence of the energetic challenges of the stressor, in which case bees may show a preference for carbohydrate-rich resources to supply their own energy needs. The finding that the gene coding for the pheromone biosynthesis-activating neuropeptide, a neuropeptide known to be present at higher levels in nectar foragers than in pollen foragers (Brockmann et al., 2009), is over-expressed in parasitized bees (McDonnell et al., 2013) provides some indirect support for this hypothesis. Stress can decrease sucrose responsiveness (Pankiw and Page, 2003), which is lower in nectar foragers than in pollen foragers (Pankiw and Page, 2000), suggesting that stress might cause a change in foraging preference. In addition, it has been shown that parasitized bees are less likely to forage for pollen (Lach et al., 2015). Together, these findings suggest that stressed bees may favour nectar over pollen foraging. This could have consequences for the nutritional balance and development of the colony, as the majority of larva protein intake indirectly comes from pollen supply (Brodschneider and Crailsheim, 2010; Pernal and Currie, 2000). Moreover, pollen nutrition promotes immunocompetence and parasitism tolerance of adult bees (Alaux et al., 2010; Di Pasquale et al., 2013).

To test the hypothesis that stress can induce a change in foraging performance, without any potential effects of parasite manipulation of host metabolism (Adamo, 2012; Biron and Loxdale, 2013), we exposed bees to a non-pathogenic immune challenge. Immune responses are energetically costly, and even simple responses, like encapsulation, can raise metabolic rate by up to 28% in insects (Ardia et al., 2012; Freitak et al., 2003). We then tracked their foraging behaviour throughout their life with a radio-frequency identification device (RFID), and a camera at the colony entrance to identify whether they carried pollen loads. Finally, we assessed the influence of stress on brain biogenic amine levels, which are known to be involved in the regulation of bee behaviour (Schulz and Robinson, 2001; Schulz et al., 2002).

MATERIALS AND METHODS

Experiments were performed from January to April 2016 with honeybees (*Apis mellifera* Linnaeus 1758) obtained from the research apiary at Macquarie University (Sydney, NSW, Australia). We tested the influence of stress on foraging behaviour (experiment 1) and brain biogenic amine signalling (experiment 2). Frames containing late-stage pupae were collected from three donor colonies and placed into an incubator overnight at 34°C. Newly emerged bees were marked on the thorax with either a RFID tag for experiment 1 or a paint mark for the experiment 2, and released into host colonies. They were then re-captured when 7 days old and placed in plastic cages with *ad libitum* sugar solution (50% w/v). Half of the bees were given an immune challenge, which consisted of piercing the cuticle between the third and the fourth tergites of the abdomen using a 0.15 mm needle. If a haemolymph drop was released after the pin prick, the bee was discarded. Previous studies have shown that the bee's immune system is activated by this

[1]INRA, UR 406 Abeilles et Environnement, 84914 Avignon, France. [2]Research Center on Animal Cognition, Center for Integrative Biology, National Center for Scientific Research (CNRS), University Paul Sabatier (UPS), 31062 Toulouse, France. [3]Department of Biological Sciences, Macquarie University, North Ryde, NSW 2109, Australia.
*Joint senior authors

‡Author for correspondence (cedric.alaux@inra.fr)

C.A., 0000-0002-3045-2599

Received 2 October 2017; Accepted 2 January 2018

wounding alone, without pathogen infection (Alaux et al., 2014; Evans et al., 2006; Siede et al., 2012). Control bees did not receive any pin prick. Handled bees (control and immune challenged) were given an additional paint mark on the abdomen to identify them by their treatment group before they were released back into their colony. This procedure was repeated three times with different bees.

Experiment 1: impact of immune challenge on foraging performance

Following the stress treatment at 7 days, 380 control and 370 stressed bees in total (n=3 trials) were released into a small nucleus hive equipped with a modified entrance. Bees had to use a specific path to exit the hive and another one to enter the hive. Each path was made of transparent 1 cm diameter plastic tubing (Bunnings, Gordon, NSW, Australia). To avoid bees using the wrong path, a plastic gate with plastic bristles, which bees could use in only one direction, was placed at the end of each path. The traffic of bees was also regulated using infrared-activated gates placed at the beginning of each path (Arduino Technology, Arduino, Adafruit and Little Bird Electronics, Hornsby, NSW, Australia). Each time a bee broke the infrared beam, the linked gates were closed behind the bee for 10 s, which was the time needed for bees to cross the path and RFID system. Each path was equipped with a RFID reader (Invengo, Guangzhou, China; Perry et al., 2015; Søvik et al., 2015) to monitor each of the entrance and exit channels. Each RFID tag (diameter 4 mm, mass 1 mg) had a unique digital identifier read by the antennae at the entrance and exit. The entrance path was also equipped with a digital video camera (Logitech, Lausanne, Switzerland) and a white LED light enclosed in a plastic box. Motion detection video recording software (ZoneTriger, Omega Unfold Inc., Montreal, QC, Canada) was used to visually identify whether bees carried pollen or not.

Experiments continued until the last recording of the last bee, i.e. 55 days. RFID data, i.e. bee ID, direction (entry into or exit from the hive) and time (day, hours, minutes and seconds), were recorded in .csv files. From these data, we were able to reconstruct trips outside the hive for each bee. RFID readings were time matched with readings from the camera, and videos taken from 10 s before RFID detection were inspected to identify the resource for the returning bees (pollen or not pollen). Only data for bees with an RFID tag and paint marks on their abdomen were analysed. Trips shorter than 30 s were not considered as foraging flights and were excluded from the study. As in Perry et al. (2015), trips longer than 8 h were also removed.

Of the 380 control and 370 immune-challenged bees, a completed foraging flight was recorded at least once from 96 and 74 bees, respectively. This loss of bees could be due to the loss of tag prior to leaving the hive, ejection from the colony by nestmates or death of the bee during its first flight. In total, 979 flights identified as pollen (n=154) or non-pollen (which can be nectar, water or an empty crop; n=825) foraging flights were recorded. The number of foraging flights appeared to be relatively low for a total of 170 bees, but was probably explained by the fact that the experimental device contained only one entry and one exit path (one bee at a time could use the path), and that many bees completed a very low number of flights (median, first and third quartiles: 4, 2, 8 foraging trips per bee, respectively). A maximum of 83 completed foraging trips per bee was recorded and 20 bees completed more than 20 trips.

Experiment 2: impact of immune challenge on brain biogenic amine levels

After the stress treatment on day 7, 637 control and 695 immune-challenged bees in total were introduced into a normal Langstroth colony (n=3 trials). Bees returning to the colony when they were between 24 and 28 days old were sampled and immediately flash-frozen in liquid nitrogen. Whether they carried pollen or not was also noted. Frozen heads were freeze-dried for 60 min at a pressure below 300 mTorr (~40 Pa; VirTis Benchtop™) and −35°C and then stored at −80°C until brain dissection and biogenic amine analysis. Brain dissections (including optic lobes, antennal lobes, the central brain and gnathal ganglion) were performed on dry ice.

Brain biogenic amine (octopamine, OA; dopamine, DA; tyramine, TYR; and serotonin, 5-HT) levels were measured using high-pressure liquid chromatography (HPLC) following the protocol described by Søvik et al. (2013) and also used later (Scheiner et al., 2014; Søvik et al., 2015). Briefly, the HPLC system was composed of a pump and an autosampler (Agilent 1200 Series, Agilent Technologies, Santa Clara, CA, USA), coupled to an electrochemical detector (ESA Coulochem III, Chelmsford, MA, USA) connected to an analytical cell (ESA 3011A). A 100 mm Hypersil BDS octadecylsilane column was used to separate samples (ThermoFisher Scientific, Waltham, MA, USA). Signals were integrated using ChemStation software (Agilent Technologies) with reference to a standard curve obtained from perchloric acid solutions containing 10 pg μl^{-1} of dihydroxybenzylamine and varying amounts of OA, DA, TYR and 5-HT (Sigma-Aldrich).

In total, we obtained information on brain levels of biogenic amines for 94 control bees (32 with pollen and 62 without pollen) and 50 immune-challenged bees (12 with pollen and 38 without pollen). TYR was detected in only 14% of brains, and thus was not analysed.

Statistical analysis

All statistics were performed using the statistical software R version 3.2.1 (http://www.R-project.org/). For experiment 1, the last day any individual bee was detected using RFID was assumed to mark the date of bee death. We then compared the probability of survival between stressed and control bees using the Kaplan–Meier test ('surfit' function of the survival package in R) (Therneau and Lumley, 2014).

Aspects of the foraging performance of bees were analysed using mixed models. The choice of best-fit model was based on the smaller sample size-corrected Akaike's information criterion (AICc) (Burnham and Anderson, 2004). Variation in total number of completed foraging flights per bee, the collected resource (pollen or not pollen) and foraging trip duration were each analysed using different mixed models and fitted with a Poisson, binomial and Gaussian distribution, respectively (based on the distributions of our experimental data). To analyse the number of trips and the collected resource, the treatment (immune challenged or control) and trial were set as fixed and random explanatory variables, respectively. To analyse foraging trip duration, collected resource and honeybee identification were added as fixed and random explanatory variables, respectively.

The normality and the homoscedasticity of brain biogenic amine levels were such that parametric analyses were appropriate for these data. Biogenic amine amounts were analysed using a repeated measures ANOVA followed by Tukey's *post hoc* comparison. Treatment and the resource collected (pollen or not pollen) were analysed as fixed factors, while trial was analysed as a random factor.

RESULTS AND DISCUSSION

Experiment 1: impact of immune challenge on survival and foraging performance

Survival probability did not differ between the control and immune-challenged groups (Kaplan–Meier test, P=0.42; Fig. 1A).

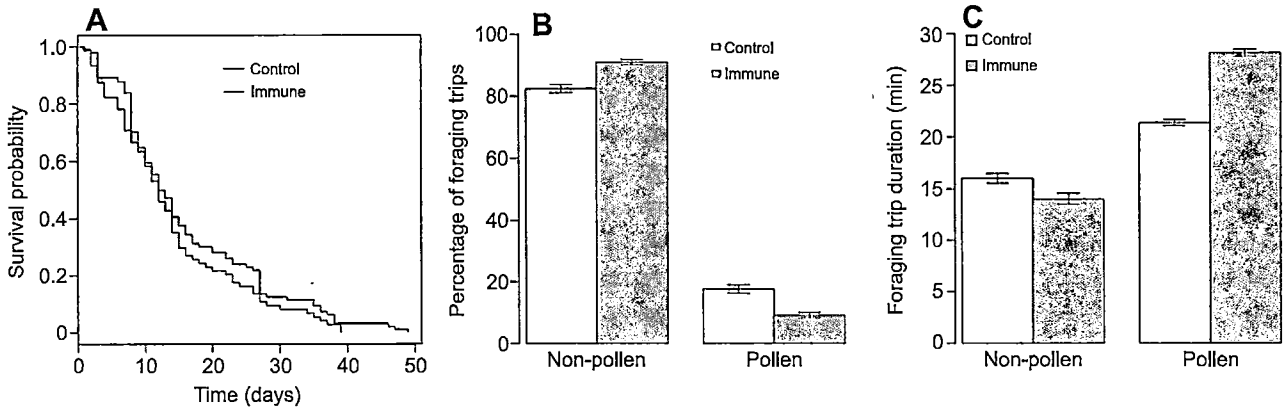

Fig. 1. Survival probability and foraging trip characteristics according to treatment. (A) Survival over 49 days for control bees and immune-challenged bees. Day 0 was the day of stress exposure. Bees from the two treatment groups did not differ in survival probability (Kaplan–Meier test, P=0.42). (B) Percentage of pollen and non-pollen foraging trips. (C) Foraging trip duration. For B and C, the mean and 95% confidence intervals predicted by the model (Table 1) are shown according to the collected resource and the treatment: control (n=100 pollen and 401 non-pollen foraging trips) and immune challenge (n=54 pollen and 424 non-pollen foraging trips). Immune-challenged bees performed fewer but longer pollen foraging trips than control bees.

The best-fit model explaining the variability in the number of trips per bee (lowest AICc) included a significant effect of treatment (Table 1). Immune-challenged bees completed slightly more flights than control bees [mean predicted values with 95% confidence interval: 6.46 (6.12–6.80) versus 5.22 (4.95–5.49), respectively].

A significant switch in foraging preference was detected, with immune-challenged bees performing 1.9 times fewer pollen foraging trips [9.14% (8.32%–9.96%)] than control bees [17.56% (16.20%–18.91%); Fig. 1B and Table 1].

Considering foraging trip duration, the best-fit model included a significant interaction between treatment (immune challenged or control) and the collected resource (pollen or not pollen) (Table 1). Pollen foraging trips were longer than non-pollen foraging trips (Fig. 1C), but trip duration for each collected resource also varied with treatment. Immune-challenged bees performed slightly shorter non-pollen foraging trips than control bees (Fig. 1C), but when foraging for pollen, immune-challenged bees performed 30% longer trips than control bees (Table 1).

Experiment 2: impact of immune challenge on brain biogenic amine levels

Brain DA and 5-HT levels did not differ significantly between treatment groups (ANOVA: P=0.67 and P=0.14, respectively) or the collected resource (ANOVA: P=0.75 and P=0.27, respectively; Fig. 2A,B). However, we found a significant treatment×resource interaction for brain OA levels (ANOVA: P=0.02; Fig. 2C). No difference in brain OA levels was found in non-pollen foraging bees (Tukey's *post hoc* tests: P=1); however, when sampled on return to the hive carrying pollen, immune-challenged bees had significantly less OA in the brain than control bees (~27% less, Tukey's *post hoc* tests: P=0.032; Fig. 2C).

Experimental findings

In this study, we have provided experimental evidence for a stress-induced decrease in pollen-foraging performance in honeybees. The non-pathogenic immune challenge stress applied did not affect bee survival, as has been found previously (Alaux et al., 2014), but did induce a shift in resource collection. An increase in non-pollen foragers (water foragers, nectar foragers and/or bees with empty crops) was observed at the expense of pollen foragers. As more than 90% of non-pollen foragers are nectar foragers and bees with empty crops (Bordier et al., 2017b) and these bees have lower sucrose responsiveness than pollen foragers (Pankiw and Page, 2003), we could reasonably assume that stress decreased bee sucrose responsiveness. Stressed bees may prefer to forage for resources that are rich in carbohydrates to overcome the energetic cost of the stress, as has been observed with parasitism of honeybees (Lach et al., 2015). Indeed, compared with pollen, nectar gives a higher energetic return relative to the foraging effort (8:1 gain with pollen versus 10:1 gain with nectar; Winston, 1987). Similarly,

Table 1. Summary of best-fit mixed models to analyse the impact of immune challenge on foraging behaviour

	Explanatory variables				
Dependent variable	Fixed	Random	No. of statistical units	d.f.	AICc
No. of foraging trips	**Treatment**	Trial	170 bees from 3 trials	**3**	**1594.7**
	Null			2	1606.1
Foraging trip duration	**Treatment×resource**	Trial/bee	979 observations of 170 bees from 3 trials	**6**	**9120.3**
	Treatment+resource			5	9129.0
	Treatment			4	9148.3
	Resource			4	9130.9
	Null			3	9150.2
Foraging preference	**Treatment**	Trial	170 bees from 3 trials	**3**	**379.2**
	Null			2	391.3

Three models were fitted to analyse the number of foraging trips, foraging trip duration and foraging preference (pollen or not pollen). Only summaries of the best-fit models are shown. For each model, fixed and random explanatory variables, the number of statistical units, degrees of freedom (d.f.) and corrected Akaike's information criterion (AICc) are detailed. For each dependent variable, the selected model, i.e. the one with the lowest AICc, is indicated in bold.

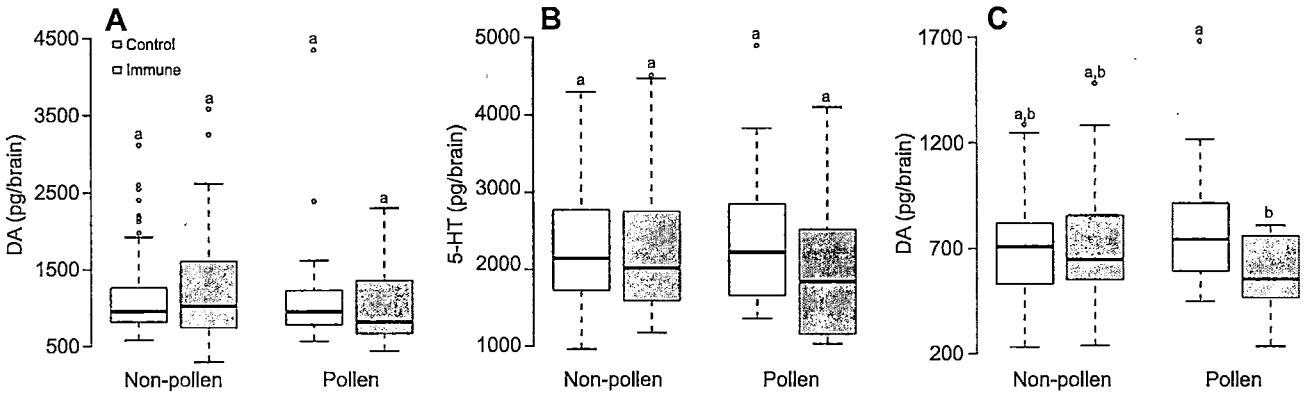

Fig. 2. Brain biogenic amine levels in response to immune challenge in different forager groups. Dopamine (DA, A), serotonin (5-HT, B) and octopamine (OA, C) levels are shown for control (n=32 pollen and 62 non-pollen foragers) and immune-challenged bees (n=12 pollen and 38 non-pollen foragers), according to the collected resource. Boxes show the first and third interquartile range with the line denoting the median. Whiskers encompass 90% of the individuals, beyond which each outlier is represented by a circle. Plots that do not share a common letter are statistically different (P<0.05, ANOVA followed by Tukey's *post hoc* comparisons).

bumblebees exposed to pesticides were found to exhibit lower pollen foraging performance (Feltham et al., 2014; Gill and Raine, 2014).

Such changes in foraging decision making could cause a nutritional imbalance with a pollen deficit at the colony level, and thereby affect colony development. Indeed, pollen shortage may have detrimental effects on brood care, resulting in undernourished larvae (Blaschon et al., 1999) and emerging adults with behavioural deficiencies (Scofield and Mattila, 2015). Moreover, pollen nutrition during the adult stage is essential for stress tolerance (DeGrandi-Hoffman et al., 2010; Di Pasquale et al., 2013; Wahl and Ulm, 1983). Finally, under extreme pollen shortage, nurse bees may reduce the number of larvae that need to be fed, and cannibalize eggs and young larvae (Schmickl and Crailsheim, 2001).

Pollen foraging trips were also 30% longer for immune-challenged bees, suggesting a significant effect of the stressor on foraging capacity. It has been found that the thorax temperature differs between different classes of foragers, in the order pollen>nectar>water foragers (Feuerbacher et al., 2003). These differences were linked to flight metabolic rate, with pollen foragers exhibiting a 10% higher hovering metabolic rate than nectar foragers, regardless of their loads (Feuerbacher et al., 2003). The authors suggested that pollen foragers require more power output to generate the same vertical lift as nectar foragers. We therefore propose that immune-challenged bees spend more time on pollen-collecting trips because it is the most energetically demanding resource to collect (Feuerbacher et al., 2003) and the stressor probably decreases the energy budget of the bees. The increase in foraging trip duration may simply reflect more time resting rather than any other changes in flight characteristics (e.g. distance, speed, etc.) (Wolf et al., 2014). It is also possible that a lower energy budget induced by the stressor caused cognitive impairment in pollen foragers and thus affected their navigation capacities (Jaumann et al., 2013), lengthening their trip times.

Finally, we found that brain OA level was depressed in immune-challenged pollen foragers. OA is known to increase sucrose responsiveness in bees (Scheiner et al., 2002) and stimulate flight activity (Fussnecker et al., 2006), and therefore the drop in OA level is in accordance with the behavioural changes observed in pollen foragers after stress exposure. A previous study reported a rapid decrease in OA and DA but not 5-HT levels in response to stress exposure (chilling anaesthesia and vertical spin; Chen et al., 2008). We did not find variation in DA levels after our stress exposure. However, to conclude on the nature of the causal role of biogenic amines in honeybee stress responses, functional studies involving manipulation of OA, DA and 5-HT signalling would be required.

Conclusion

Our study suggests that the highly energy-demanding foraging activity of pollen foragers makes them susceptible to stress, even at low levels, which could potentially affect the colony nutrient balance (pollen versus nectar). Therefore, future studies on whether stress narrows the colony foraging flexibility in response to environmental changes might help us to better understand colony decline.

Acknowledgements

We thank F. Kamhi and B. V. Entler for their help with laboratory work, A. Cabirol for her help with fieldwork, and H. Dechatre and A. Faure for their help in data analyses.

Competing interests

The authors declare no competing or financial interests.

Author contributions

Conceptualization: C.B., A.B.B., C.A.; Methodology: C.B., S.K.; Formal analysis: C.B., S.K.; Resources: A.B.B.; Writing - original draft: C.B., C.A.; Writing - review & editing: C.B., S.K., Y.L.C., A.B.B., C.A.; Supervision: A.B., C.A.

Funding

C.B. was supported by an ANR (Agence Nationale de la Recherche) project (ANR-13-ADAP-0002) and by a travelling fellowships grant of the Company of Biologists sponsored by Journal of Experimental Biology (JEBTF-150809).

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Environ. Sci. Technol. 2011, 45, 34–38

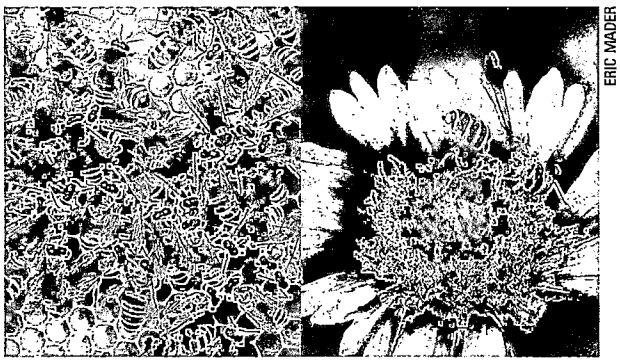
Environmental Science & Technology
Feature

The Plight of the Bees†

MARLA SPIVAK*
University of Minnesota, St. Paul, Minnesota

ERIC MADER
MACE VAUGHAN
Xerces Society for Invertebrate Conservation, Portland, Oregon

NED H. EULISS, JR.
U.S. Geological Survey, Jamestown, North Dakota



ERIC MADER

Some environmental issues polarize people, producing weary political stalemates of indecision and inaction. Others, however, grab hold of our most primeval instincts, causing us to reach deeply into our memories of childhood, and our first direct experiences with nature: the bumble bee nest we poked at with a stick; the man at the county fair with the bee beard. Those memories expand backward in time to our barefoot ancestors who climbed trees and robbed honey. They help define the human experience and provide context to our own place in the world.

And so the plight of the bees strikes a common chord. For a brief moment simple matters of politics, economics, and nationality seem irrelevant.

Colony collapse disorder, the name for the syndrome causing honey bees (*Apis mellifera*) to suddenly and mysteriously disappear from their hives—thousands of individual worker bees literally flying off to die—captured public consciousness when it was first named in 2007 (*1*). Since then, the story of vanishing honey bees has become ubiquitous in popular consciousness—driving everything from ice cream marketing campaigns to plots for *The Simpsons*. The untold story is that these hive losses are simply a capstone to more than a half-century of more prosaic day-to-day losses that beekeepers already faced from parasites, diseases, poor nutrition, and pesticide poisoning (*2*).

The larger story still is that while honey bees are charismatic and important to agriculture, other important bees are also suffering, and in some cases their fates are far worse (*3*). These other bees are a subset of the roughly 4000 species of wild bumble bees (*Bombus*), leafcutter bees (*Megachile*), and others that are native to North America. While the honey bee was originally imported from Europe by colonists in the early 17th century, it is these native bees that have evolved with our local ecosystems, and, along with honey bees, are valuable crop pollinators.

People want to know why bees are dying and how to help them. This concern provides a good opportunity to more closely examine pollinators and our dependence upon them. Bees are reaching their tipping point because they are expected to perform in an increasingly inhospitable world.

Pollination Economics. The service of animal mediated pollination is essential for the reproduction of nearly 70% of the world's flowering plants (*4*). Butterflies, some beetles, flies, hummingbirds, and even some bats provide some pollination services, inadvertently moving pollen (the plant's male gametes) from anther to stigma as they sip nectar or eat pollen from flowers.

Yet among pollinators, bees are unique. In addition to sipping nectar to fuel their own flight, they are one of the few animals to actively gather large amounts of pollen (and hence inadvertantly move some of it widely between flowers). Rich in protein, the pollen of many plant species serves as the principle food source for developing bee larvae. Wasps in contrast, while close relatives of bees, typically feed on meat, often in the form of other insects, during their larval stage.

More than one-third of the world's crop species such as alfalfa, sunflower, and numerous fruits and vegetables depend on bee pollination, an ecological service valued in North America at $20 billion a year (*5*–*7*). The cereal grains that make up the largest part of our diets, such as corn, rice, and wheat, are wind pollinated. Thus the prospect of human starvation in the absence of bees is remote, but crop declines in the most nutritious—and arguably, most interesting—parts of our diet like fruit, vegetables, and alfalfa hay for meat and dairy production, are possible.

Worldwide, over the past five decades, there has been a 45% increase in the number of managed honey bee hives. That trend, however, does not keep pace with a 300% increase in bee-pollinated crop production in the same time period (*8*). In North America the trends in honey bee numbers are decidedly downward, with the number of managed hives decreasing by 50% since the 1950s and the amount of crop acreage requiring bee pollination at an all time high (*4*). Pollination biologists doubt the prospect of a food security crisis, but suggest that in the future, as per-acre crop yields decline in the absence of enough pollinators, more acres of farmland may be needed to meet consumer demands (*9*).

Bees in a Mechanized World. Like people, honey bees have always suffered from disease. Records of mass bee die-offs in the U.S. extend as far back as 1869 (*10*). Those early losses were largely buffered by a prepesticide and prein-

† This manuscript is part of the Environmental Policy: Past, Present, and Future Special Issue.

* Corresponding author e-mail: spiva001@umn.edu.

10.1021/es101468w
Published on Web 09/14/2010

dustrial rural landscape. Our current issues affecting bees began after World War II as small farms, interspersed with woods, wetlands, and meadows were replaced with larger-scale homogeneous crops, particularly wind-pollinated cereal crops (*11*).

To support that increase in farm scale, new low-cost synthetic fertilizers supplanted crop rotations with nitrogen-fixing cover crops like clover and alfalfa, formerly reliable and ubiquitous sources of pollen and nectar. Along with synthetic fertilizers, newly available chemical pesticides were introduced to control the pests and diseases that spread quickly among large fields of genetically identical crops. In addition to their direct toxicity to bees, these chemicals further reduced other beneficial biodiversity from farm systems, including beneficial insects that prey upon crop pests (making insecticides even more essential) and flowering weeds on crop borders, roadsides, and other noncropped rural lands that provided supplemental sources of nectar and pollen.

Many of these changes were fostered by federal farm subsidies favoring corn, particularly as a feedstock for beef, pork, and poultry production. Where bee-pollinated crops do exist, they typically occur in larger acreages providing only a single pollen and nectar source for a few short weeks during the year. This feast or famine situation fails to support wild bees that need food throughout their adult lives. Although honey bees may store food (in the form of honey and packed pollen) for times of dearth, lack of diverse floral resources is now demonstrated to diminish their immune response (*12*).

Added Insult: New Parasites and Pathogens. In the 1980s, two obligate parasites of honey bees were introduced into the U.S., the tracheal mite (*Acarapis woodi*), first found in the UK, and the varroa mite (*Varroa destructor*). Varroa mites are native to Asia where the host bee species, *Apis cerana* [sp] has evolved a resistance to them. Over time, bees in the U.S. developed natural resistance to tracheal mites, but the effects of *Varroa destructor* have been particularly devastating and hard to overcome. This mite lives up to its name by reducing the lifespan of adult bees, suppressing their immune system, and transmitting viruses as it sucks blood from one bee and moves on to the next (*13*).

Untreated colonies infected with *V. destructor* die within 6 months to 2 years. Without treatment, 80–90% of hives in the U.S. would likely die within 2–3 years. If we did not depend on honey bees to pollinate our commercial monocultures of fruits, vegetables, nuts, and seed crops, we could possibly afford to withhold treatments and allow nature to take her course, letting only the fittest colonies survive. However, in the 10–20 years it would take for the national honey bee population to rebound, crop production would suffer.

Finding a way to control *V. destructor* has been an agonizing puzzle to beekeepers and researchers. How do you kill a bad "bug" on a beneficial "bug"? Mites (which are arachnids) have been quick to develop resistance to synthetic pesticides (*14*), making them exceedingly difficult to control. The effects of *Varroa* mites are compounded by the viruses they transmit from bee to bee (*15*) The mite can facilitate the horizontal transmission of at least five viruses between adult bees and larvae (*16*). Viruses also can be transmitted vertically through male semen and queen-laid eggs (*17*). Where the mites do not directly kill the bees, the viruses will.

Along with mites, an introduced fungal gut parasite (also from Asia), called *Nosema ceranae* could impart the final blow. It is unclear at this point if nosema kills colonies alone (*18*), or if it acts in combination with viruses, with pesticides, or with nutritional stress (*19, 20*).

Recipe for Disaster: Colony Collapse Disorder. Reports of massive bee die-offs in the winter of 2006/2007 (*10*), and every winter since, appeared against the backdrop of habitat loss and nutritional stress, escalating pesticide use, viruses, and other pathogens. The rising demand for pollination of large monoculture crops, and the necessary cross-country transportation of colonies to meet that demand, have further exacerbated all of those stress factors.

The specific symptoms of the massive die-offs seemed unusual: colonies lost their workers rapidly and unexpectedly, leaving the queen, food stores, and brood abandoned in the nest, and no dead bees were observed in the area. These specific symptoms were called colony collapse disorder (CCD) (*19*). The disappearance of so many bees from a hive caught the media's attention and the public's imagination. It is very natural for sick bees to leave the colony to die; but the scale of the die-offs is alarming.

Teasing apart the synergistic effects of multiple factors to determine the primary cause of CCD is exceedingly difficult (*21, 22*). Studies have been unable to pinpoint a single factor that distinguishes CCD from control colonies. The most likely answer is that the losses are due to multiple, interactive factors (*10, 23, 24*).

The Other Bees. Before the honey bee was introduced from Europe in 1622, over 4000 species of bees were native to North America (*25*). These include a vast and colorful diversity of bumble bees, mason and leafcutter bees, mining bees, sweat bees, and others.

Many of these bees are more efficient crop pollinators than the non-native honey bee, especially for New World fruits and vegetables such as pumpkin, tomato, cranberry, and blueberry (e.g., refs *26 and 27*). This specialization results in more efficient pollination and higher yields for certain crops valued at at least $3 billion USD annually (*6, 28, 29*). Recent research has demonstrated that native bees in some cases provide all necessary pollination when adequate foraging and nesting habitat is available, making them crucially important as honey bees continue to decline (*30, 31*).

Unfortunately while honey bees have been the focus of most media on disappearing bees, scientists are also documenting declining native bee numbers across the country (*3*), including the possible extinction of some species (*32*). Native bees are facing unprecedented habitat loss, pesticide threats, and introduced diseases.

Most of our native bees eke out a solitary existence, going about their business of pollinating flowers hidden from our daily view. Native bees in the temperate zone begin to emerge from winter hibernation in spring and early summer to feed, mate, and raise a new generation. Solitary female bees raise a new generation of bees in the soil, hollow twigs, rock crevices, and dead trees. Alone, she provisions each egg with a small mass of pollen and nectar that will provide all the protein required for the immature larval bee to develop into an adult. The entire process can take up to a full year for some species and will occur only if the nesting site is not tilled, poisoned, or otherwise disturbed. Such nesting sites are sparse in urban and agricultural landscapes.

In contrast to the majority solitary native bees, a few native bees, like bumble bees (*Bombus* spp.), are social, living in small annual colonies founded in the spring by an individual queen after she wakes from winter hibernation. Bumble bee nests are typically located within a dry cavity, such as an abandoned mouse nest, a cavity in a tree, or under a tussock of grass, and at their peak may contain more than a hundred workers.

Bumble bees are often the first bees active in spring and the last bees active in the fall. Thus, early blooming and late-blooming plants like wildflowers are especially important to their survival. A second feature that makes bumble bees important pollinators is their unique ability to buzz-pollinate flowers by disengaging their wings from their flight muscles, and using those muscles to shake their entire body at a frequency close to a middle C musical note (~262 Hz) (*33*).

This vibration significantly increases the release of pollen from some flowers, including tomatoes, peppers, blueberries, and cranberries. Few other bees have the ability to perform buzz-pollination.

These combined factors make bumble bees significantly more efficient pollinators of many crops than honey bees on a bee-for-bee basis. Ironically, this same efficiency may have become instrumental in the downfall of several bumble bee species. According to a leading theory, efforts by several multinational companies to rear and distribute bumble bees for managed pollination are thought to have introduced or amplified one or more bumble bee diseases (*4*). According to this hypothesis, the pathogens then spread to wild bumble bees in the late 1990s as bumble bees were transported throughout the U.S. for pollination of tomatoes and other crops (*34, 35*).

It now appears that several formerly very widespread species of bumble bees have declined across most of their ranges (*3*). In mid-1990s surveys, the yellow-banded bumble bee (*Bombus terricola*) was the most abundant bumble bee in Wisconsin. Ten years later it made up less than 1% of the state's bumble bees. Across the continent, a similar fate has befallen the western bumble bee (*B. occidentalis*). Once the most abundant bumble bee on the West Coast, its' numbers have also crashed and it is now rarely seen. Another species, Franklin's bumble bee (*B. franklini*), once native to Oregon–California, is now believed extinct (*3*).

Roughly 45 bumble bee species are native to North America, and while many species seem to be resistant to diseases, others are clearly not. Bumble bees frequently seen on crop flowers and in gardens give the appearance of stable populations, but the diversity of species is in rapid decline.

Turning it Around. Bee declines can be attributed to three factors:

1. Bees have their own diseases and parasites that weaken and kill them (*10, 19, 23*). Sick bees are more susceptible to the effects of poor nutrition and pesticide poisoning, and vice versa.
2. Many flowers, nest sites, and nesting materials are contaminated with pesticides (*24*). Bees pick up the insecticides, herbicides, and fungicides applied to home gardens and lawns, golf courses, roadsides, and crops. These pesticides, alone and in combination, can be toxic.
3. There are not enough blooming flowers over the length of the growing season in our agricultural and urban landscapes to support bees (*36, 37*).

Responses to the first factor are limited primarily to policy makers, the research community, and beekeepers themselves. The second two of these factors are scalable and can be addressed at the individual and national level. We now address responses to these factors beginning with measures to curb the effects of bee parasites and disease.

Emerging Responses to Declines in Bee Health. To study CCD and other pollinator health issues, the 2008 Farm Bill approved more than $17 million in funding annually for five years for the U.S. Department of Agriculture (USDA) and for university research grants. The Farm Bill also approved another annual $2.75 million for five years to increase honey bee health inspections. Since the Farm Bill became law this funding has never been fully appropriated.

The 2008 Farm Bill also dictated that current USDA competitive grant programs should include pollinators—honey bees and native bees—as research priorities. As a result, research programs funded by the USDA under the National Institute of Food and Agriculture (NIFA), such as the Specialty Crops Research Initiative (SCRI) and the Agriculture and Food Research Initiative (AFRI), made pollinators a research priority in 2010 (*38*).

Along with research funding, statutory measures have been proposed to address pollinator health under the authority of the Plant Protection Act, the Honey Bee Act, and the Animal Health Act, all of which designate regulatory authority to the USDA Animal and Plant Health Inspection Service (APHIS). To address declining bumble bees specifically, in 2010 a group of more than 60 scientists working in collaboration with the Xerces Society for Invertebrate Conservation submitted a petition to the agency to implement rules prohibiting the movement of bumble bees outside of their native range and to require disease-free certification of commercially produced bumble bees prior to shipment within their range. That petition is still under administrative review.

Protection from Pesticides. A factor that can be addressed at multiple levels is the use of pesticides. In particular, while extensive literature exists on the sublethal effects of insecticides on bees in the laboratory, little exists on sublethal effects to colonies under natural conditions (*24, 39*). Common insecticides such as neonicotinoids and pyrethroids have been shown to affect learning, foraging activities, and nest site orientation by honey bees at sublethal doses (*40, 41*).

To assess the effects of pesticides on bees, the U.S. Environmental Protection Agency (EPA) uses a multistep process. The first of these steps is an acute contact toxicity test on honey bees that provides a median lethal dose (LD_{50}) based upon a single exposure; i.e., a dose that causes death to 50% of the exposed subjects (*42*).

If sublethal effects are observed, the EPA can, on a case-by-case basis, require additional studies, such as assessment under field conditions. No formal agency guidelines exist however on when such additional tests must be conducted (*42*). Risk assessment data collected through this multistep process are used to determine suitability of the product for legal registration (use), and to provide label information to end users (e.g., potential harm to honey bees).

One major uncertainty behind this assessment approach is the extent to which honey bees can be considered an appropriate surrogate for other pollinators. Larval honey bees are fed glandular secretion from adult bees that contains a very small proportion of pollen and nectar, whereas larvae of native bees feed directly on pollen and nectar and thus potentially have more direct exposure to pesticides. In addition many native bees are significantly smaller than honey bees, and are likely impacted by correspondingly smaller doses. Current EPA assessment protocols do not address this issue.

Individual farmers and homeowners have the ability to mitigate harm to pollinators through simple changes in application methods such as avoiding treatments around blooming plants or to areas where bees are nesting. Evening spraying when bees are less active is another simple, underutilized way to reduce harm. The best course of action, and the one most accessible to gardeners, for whom insect damage is cosmetic rather than economic, is to eliminate the use of pesticides entirely.

An important but under-recognized consideration is that the same landscape features that support healthy pollinator numbers also support other beneficial insects, especially those that prey upon crop pests, further reducing the need for pesticides.

The Need for Habitat. The third major challenge facing bees is a lack of season-long food sources, especially in agricultural landscapes where, if bee-pollinated plants even exist, they typically consist of large monocultures like cranberries, canola, or almonds, which provide only a few weeks of abundant food followed by a season-long dearth. Roughly 360 million ha or more than one-third, of the lower 48 states are managed as private cropland, pasture, or rangeland (*43*). This makes agriculture the largest land use activity in the country and thus one with the most potential impact on bees.

The USDA agencies responsible for administering and providing technical oversight on private lands are the Farm Service Agency (FSA) and the Natural Resources Conservation Service (NRCS). These agencies have achieved monumental conservation gains by coupling direct farm management advice to farmers with cash incentives to establish permanent, noncrop vegetation on highly erodible lands (*44*). As of 2004, more than 13 million ha were enrolled in various USDA conservation programs providing varying levels of benefits to wildlife (*44*). Both FSA and NRCS implement conservation policy through the Farm Bill (an omnibus statute passed roughly every 5 years). Of special significance is the 1985 Farm Bill establishing the Conservation Reserve Program (CRP) which offered landowners incentive payments to establish permanent, noncrop vegetation on highly erodible lands. Subsequent Farm Bills added additional conservation programs, include the Wildlife Habitat Incentives Program (WHIP) and the Environmental Quality Incentives Program (EQIP) (*44*). In the 2008 Farm Bill, all conservation programs, especially EQIP, were designated as funding mechanisms for the enhancement of bee habitat on private farms and ranches (*45*).

The 2008 Farm Bill was the first one to directly prioritize pollinators in USDA administered programs. This development occurred in direct response to CCD and the less publicized declines of native bees. Implementation of this prioritization has largely been left to individual states. For example, the Michigan NRCS and FSA developed a pollinator initiative through the CRP program that authorizes funding for the creation of up to 1101 ha of wildflower plantings on fruit farms to support resident native bees. As of this writing, nearly 405 ha of bee habitat have been enrolled. In California the NRCS supported the establishment of more than 445 ha of new bee habitat through the EQIP and WHIP programs in 2009. In addition, over the past several years, California NRCS has supported the creation of approximately 80 km of hedgerows that consist of pollen- and nectar-producing native plants. Similar efforts are underway in states as diverse as Maine, Florida, Pennsylvania, Wisconsin, and Oregon.

While the bee health research provisions of the Farm Bill have been difficult to implement due to nonappropriation of funds, the conservation provisions addressing the deficiency of habitat through USDA programs is proving to be very successful. Ongoing research supported by NRCS Conservation Innovation Grants, the NRCS Agricultural Wildlife Conservation Center, and others is documenting changes in pollinator and beneficial insect communities around NRCS conservation plantings that target pollinators.

In nonfarm settings, educational efforts reaching homeowners and greenspace managers can encourage the greater incorporation of floral diversity in parks and urban landscapes. One particular opportunity is the potential for incorporating bee-friendly native wildflowers in roadside vegetation programs. Initial investigation indicates that roadside plantings may provide corridors for pollinator movement, refuge from pesticides in adjacent farm fields, erosion control, and lower vegetation management costs for transportation agencies (*46*). Initial research also indicates that pollinator mortality from traffic may actually be lower when native wildflowers are abundant, as it reduces the need for foraging over greater distances (*47*).

Specific habitat guidelines for all of these landscapes (rural, urban, roadside) vary across regions. Baseline habitat guidelines encourage the inclusion of at least 3 different plant species that bloom at any given time during the growing season (spring, summer, fall), with more being even better (*45*). Recommendations often include clumping single species in groups to increase foraging efficiency by bees, and placement of foraging habitat adjacent to nest sites. The majority of native bees nest in the ground, with a few species using woody snags, brush piles, and clump-forming grasses. Another important consideration is the protection of potential nest sites from disruptive management practices like widespread burning or tillage (*48*).

Concluding Remarks

Pollinators are receiving more conservation attention today than at any other time in history. Scientists, conservationists, and farmers are working harder than ever—in partnership—to understand how pesticides, diseases, and habitat loss impact pollinator populations. They are also working to understand the most successful strategies for creating landscapes that support the greatest abundance of these important insects.

At the same time, the public and policy-makers are increasingly aware of the problems afflicting bees and the critical role they play in food production and natural systems. This awareness by such diverse audiences has led to significant positive policy changes (e.g., the 2008 Farm Bill) due in large part to the bipartisan appeal of policies and habitat conservation efforts that support crop production, honey bee colony health, and wild native bees and wildlife. Pollinator conservation provides a venue for diverse audiences to collaborate to solve common problems.

But there is no reason to wait for research and policy to mitigate the plight of the bees. Individuals can modify their immediate landscapes to make them healthier for bees, whether that landscape is a public rangeland in Wyoming or a flower box in Brooklyn. It is also possible to reduce agricultural and urban pesticide use to mitigate bee poisonings. We can engage in the sustainable management of honey bees and native bees (*49*). Promoting the health of bee pollinators can begin as an individual or local endeavor, but collectively has the far-reaching potential to beautify and benefit our environment in vital and tangible ways.

Marla Spivak is Distinguished McKnight Professor at the University of Minnesota, Department of Entomology. Her research and extension efforts focus on protecting the health of bee pollinators and promoting sustainable beekeeping practices. Eric Mader is Assistant Pollinator Program Director at the Xerces Society for Invertebrate Conservation and Extension Professor of Entomology at the University of Minnesota. He works to promote native bee conservation practices among farmers and government agencies. Mace Vaughan, the Xerces Society's Pollinator Conservation Program Director, works nationwide to oversee habitat restoration and educational outreach for native pollinators nationwide. He holds a joint Pollinator Conservation Specialist position with the USDA's Natural Resources Conservation Service. Ned H. Euliss, Jr., is a Research Biologist with the U.S. Geological Survey's Northern Prairie Wildlife Research Center. His research focus is on how land use and climate futures affect the sustainability of contemporary landscapes, including their provisioning of pollination services.

Acknowledgments

Funding support to M.S. was provided by the USDA National Institute of Food and Agriculture (NIFA) Agriculture and Food Research Initiative (AFRI) Managed Pollinator Coordinated Agricultural Project 2009-85118-05718, and to M.S. and N.H.E., Jr. by a USDA NIFA AFRI Competitive Grant 2010-65615-20631. We also thank Scott Hoffman Black and Sarina Jepsen of the Xerces Society for their feedback.

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Cannabidiol oil has purported health benefits, including helping to relieve chronic pain.

DRUG REGULATION

From menace to medicine

Cannabidiol could offer an effective treatment for a variety of conditions. But the substance's uncertain legal status is stalling serious investigation.

BY MICHAEL EISENSTEIN

Cannabidiol (CBD) is an illegal drug with no redeeming value. It is also a useful prescription medicine for epilepsy, with considerable potential for treating numerous other conditions. And it is a natural dietary supplement or 'nutraceutical' with countless evangelists in the health and wellness community. Although contradictory, all three statements are true from different perspectives, and clinical researchers are frustrated.

"In New York City, you can go to a latte shop and get a CBD product, but if I want to do a clinical trial, I've got to get a 2,000-pound safe and go through six months of paperwork and licensing," says Orrin Devinsky, director of the NYU Langone Comprehensive Epilepsy Center in New York City. Like the cannabis plant from which it is derived, CBD, a type of cannabinoid, is classified by the US Drug Enforcement Administration in the same way as are heroin and lysergic acid diethylamide (LSD) — schedule 1 substances with "high potential for abuse" and "no currently accepted medical use".

This flies in the face of current evidence. Numerous studies have shown that CBD is a safe and non-habit-forming substance that does not produce the 'high' associated with tetrahydrocannabinol (THC), the main psychoactive component of cannabis[1]. In 2018, the US Food and Drug Administration (FDA) determined that Epidiolex — a purified CBD product developed by GW Pharmaceuticals in Histon, UK — effectively reduces the frequency of seizures in certain rare forms of paediatric epilepsy. This approval has heartened the cannabinoid research community, which has long recognized the medicinal potential of CBD but come up against scepticism and regulatory constraints on the road to the clinic.

But at the same time, the many manufacturers that promote CBD-laden oils, lotions and foods as a panacea for various health issues, often with minimal regard for local laws or medical evidence, are putting CBD's medical advocates in an uncomfortable position. "I get calls and e-mails all the time — not just from families, but from physicians who have no clue how to address the requests they get from patients," says Yasmin Hurd, director of the Addiction Institute of Mount Sinai in New York City. "It's a real problem."

STUCK IN THE WEEDS

The breakthrough approval of Epidiolex was driven by strong investment from GW Pharmaceuticals, as well as vigorous advocacy from families of children with epilepsy who had heard tantalizing anecdotes about CBD's effects from jurisdictions in which medical cannabis is legal. "About eight years ago, a patient's father said he was hearing stories about families in Colorado and California who use high-CBD strains for their kids' epilepsy," says Devinsky. "He asked me to do a trial." As a medical student, he had been taught the history of medicinal cannabis, including well-documented uses of the plant by nineteenth-century physicians to treat seizures. Indeed, cannabis has been part of the clinical armamentarium for epilepsy for more than 4,000 years.

Research on CBD in the 1970s and 1980s focused on its interplay with other cannabinoids, and particularly THC. "Whereas THC can induce psychotic symptoms, impair cognition and make people anxious, CBD appears to do the opposite," says Philip McGuire, a psychiatrist at King's College London.

The first clues that CBD might suppress epileptic episodes came from a small clinical trial[2] in 1980. It was led by Raphael Mechoulam, a chemist at the Hebrew University of Jerusalem, whose work on the synthesis and biochemical characterization of cannabinoids in the 1970s had led researchers to begin to explore the medicinal properties of CBD. A number of other trials that explored the compound's pharmaceutical properties followed, although scientists conducting early forays into CBD clinical research faced an uphill battle. F. Markus Leweke, a psychiatrist who specializes in mental illness at Sydney Medical School, Australia, recalls struggling for seven years to publish findings from a randomized controlled trial that demonstrated that CBD might offer an effective treatment for psychotic symptoms in schizophrenia[3]. "We got about 15 rejection letters," says Leweke. "And this is a paper that has since been cited almost 500 times."

Forty years on from Mechoulam's initial work, extensive randomized controlled trials have decisively shown that this purified cannabinoid can profoundly benefit children with certain epileptic disorders. "Over those

trials, we saw about a 26–28% reduction in frequency over placebo in all convulsive seizures for Dravet syndrome and drop seizures for Lennox–Gastaut syndrome," says Devinsky, who has led several such studies[4,5]. "Some of the patients became, and remain, seizure-free."

Preclinical data from rodent and cell-culture studies have hinted at the possible benefits of using CBD to help treat disorders that range from Parkinson's disease to chronic pain. The range of conditions in which CBD is being tested might seem diverse, but it is a compound with far-reaching, if poorly understood, physiological effects. Antonio Zuardi, a psychiatrist at the University of São Paulo in Brazil, notes that something on the order of 20 possible mechanisms of action have been described to date for CBD. "These multiple pharmacological effects may justify the wide range of possible therapeutic activities."

The mechanism of CBD's action on cannabinoid receptors, at least, is well understood. CBD can bind to the cannabinoid receptor CB_1, which is the same receptor that THC seeks out in the brain. Unlike THC, however, CBD restrains rather than activates CB_1 signalling, and therefore doesn't induce the psychoactive effects of its cannabinoid cousin.

But CBD wears many hats. It seems to mediate its antiepileptic effects by binding to a protein called GPR55, which can otherwise trigger the onset of seizures by promoting the hyperactivation of neurons[6]. In addition, CBD acts on receptors that mediate pain signalling and inflammation, as well as at least one receptor for the neurotransmitter serotonin, 5-HT_{1A}[7]. Gabriella Gobbi, a psychiatrist and neuroscientist at McGill University in Montreal, Canada, has found that CBD's physiological effect on the brain resembles that of selective serotonin reuptake inhibitor (SSRI) drugs[8], which are used to treat clinical depression. "After a few days, you get this sensitization of 5-HT_{1A}, like you would with an SSRI, and increased serotonin signalling," she says. Further experiments in rats failed to capture an antidepressant effect, but her team found that CBD-mediated modulation of 5-HT_{1A} could relieve neuropathic pain in the animals.

MULTITASKING MOLECULE

Beyond epilepsy, clinical data to support the medicinal benefits of CBD are more limited, mainly due to the small scale and inconsistent design of trials. "We have very few double-blind, randomized placebo-controlled trials," says Gobbi. But exciting progress is being made towards treating several conditions.

Psychosis — particularly in the context of schizophrenia — is one such area of promise. In 1995, Zuardi and Mechoulam reported the case of a person with schizophrenia who experienced meaningful relief from their symptoms when treated with high doses of CBD[9]. Several subsequent small-scale clinical studies detected similar hints of efficacy. In their groundbreaking trial[3], Leweke and his colleagues put the compound through a particularly rigorous test by comparing its effects with those of amisulpride, a potent medication for schizophrenia. "We saw a significant decrease in symptoms over time for both compounds, and CBD beat amisulpride in terms of side effects, by far," Leweke says. The team also found a clue to the mechanism by which CBD might exert its antipsychotic effects: treatment with CBD was associated with elevated levels of anandamide, a cannabinoid produced by the body that seems to offer protection from psychosis.

McGuire and his colleagues conducted a randomized controlled trial that showed that CBD can have an additive effect when used with conventional antipsychotic drugs[10]. Together, they were better able to control symptoms such as hallucinations and delusions than could conventional medication alone. His team has received funding for a large, international trial to test whether CBD can be developed as a licensed medicine for treating psychosis.

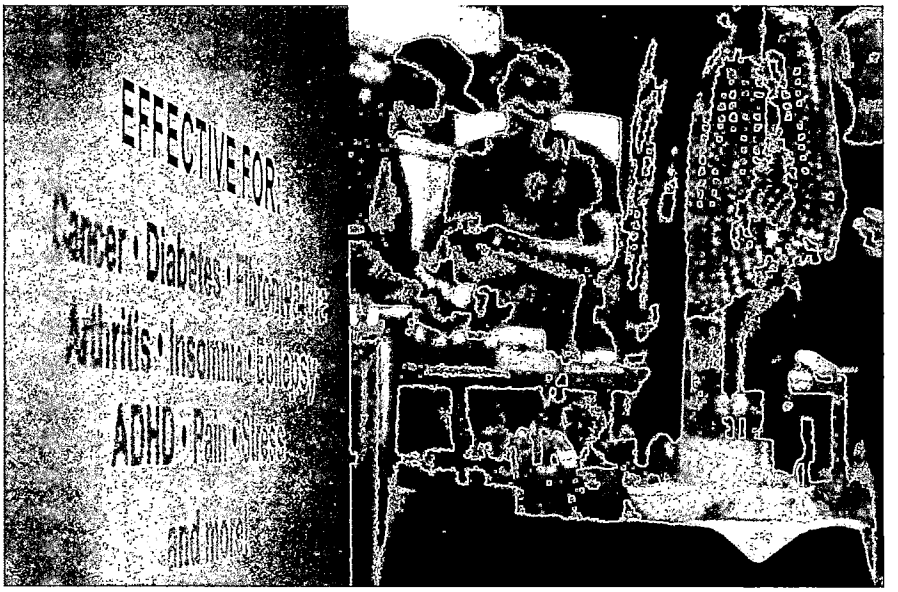
"We have very few double-blind, randomized placebo-controlled trials."

Anxiety disorders are another mental-health condition that CBD has been shown to help alleviate. Zuardi and his colleagues used a test that simulates speaking in public to show that pretreatment with a single dose of CBD can reduce the associated discomfort in people with social anxiety disorder[11]. A similar effect has been observed in healthy people in anxiety-inducing situations[12], and several researchers are exploring CBD as a means of soothing social stress in people with autism spectrum disorder. Devinsky notes that many of his patients with epilepsy have also been diagnosed with autism spectrum disorder, and he is involved in two clinical trials that aim to test whether CBD can meaningfully reduce the irritability and anxiety of those with autism. "Many parents wanted to keep their children on it even if the seizures didn't improve, because they're calmer and sleeping better," he says.

And although cannabis been demonized as a gateway to more dangerous substances, Hurd has found that it might actually contain an effective antidote for potentially deadly addictions. After observing that rats with a heroin addiction were less likely to seek out the opioid when treated with CBD, she began to investigate whether CBD might have the same effect on people with an opioid dependency. On the basis of an encouraging pilot study, Hurd and her team conducted a randomized controlled trial in 42 abstinent heroin users, who had avoided taking the drug for up to three months after years of routine or heavy use[13]. The researchers then exposed the participants to drug paraphernalia and videos that showed heroin use — cues that normally provoke strong cravings in people with a dependency — and then measured participant-reported responses and physiological indicators of stress and anxiety. "Cue-induced craving is associated with increased cortisol levels and increased heart-rate, and CBD reduced those," she says. Participants receiving CBD also reported lower levels of drug craving and anxiety relative to placebo group, and Hurd notes that the beneficial effects persisted for a week after the final administration of CBD.

A DIFFICULT DELIVERY

Despite its promise, CBD's impact as a drug has been mixed. Importantly, it is relatively safe. The side effects most commonly associated with a high dose of Epidiolex include digestive problems, rash and drowsiness, as well as the potential for liver damage in patients taking certain other medications. For example, Devinsky notes that patients who are receiving valproic acid to treat seizures or migraines might be at



RODGER BOSCH/AFP/GETTY

Claims about the health benefits of cannabis are often overstated and lack supporting evidence.

ERIK S. LESSER/EPA/SHUTTERSTOCK

Campaigners show support for legalizing cannabis for medical use in Atlanta, Georgia.

an elevated risk. But in many of the CBD trials conducted so far — particularly in the realm of antipsychotic drugs, which are known for their strong side effects — CBD has proved more tolerable than existing alternatives. "The side effects weren't significantly worse than with placebo," says McGuire of his 2018 study of CBD in people with schizophrenia[10].

This is important because people typically require large doses of the drug to experience a clinical benefit — in many studies, the doses used are as high as 1 gram or more. This is because CBD is poorly absorbed by the body, with most of every dose being excreted before it can take effect. "If you take it orally, the bioavailability is in the range of 4–6%, which is terrible," says Devinsky. "If you take it after a fatty meal, you can get that up to 16–20%." Zuardi notes that his group routinely observes a bell-shaped dose–response curve for CBD. For example, whereas 300 milligrams of CBD might reduce a person's anxiety, the same person might not get any relief from a dose of either 100 milligrams or 900 milligrams. To complicate matters further, this sweet spot for CBD dosing can differ not only between symptoms, but also between patients.

This is one of several reasons why researchers caution against self-medication with CBD products targeted at consumers. CBD is available in shops worldwide, but the legality of such sales varies widely. In Canada, selling cannabis and its derivatives is legal, whereas the European Union authorizes the sale of CBD derived from hemp (low-THC varieties of cannabis) but not from marijuana (high-THC cannabis). In the United States, the latest Farm Bill, which was enacted in 2018, potentially legalizes the production of CBD from hemp under certain conditions — although the sale of CBD products generally remains ostensibly illegal. Regardless of the legal situation at the federal level, CBD commercialization remains something of a free-for-all in the United States — individual states are making their own laws, and the FDA has taken only limited action to enforce federal laws on CBD. "They've sent some notices to companies that have made medical claims, but that's about it," says Marcel Bonn-Miller, a psychologist at the University of Pennsylvania, Philadelphia, and global scientific director at Canopy Growth Corporation, a cannabis company in Smiths Falls, Canada. (An FDA spokesperson responded that the agency "is working quickly to continue to clarify our regulatory authority over products containing cannabis and cannabis-derived compounds like CBD".)

Many such claims lie beyond the bounds of medical evidence — including that regarding CBD preparations that purport to prevent cancer or to treat Alzheimer's disease. However, even products that make more modest claims could be problematic. In 2017, Bonn-Miller and his colleagues performed chemical analyses on 84 products purchased online from 31 companies, and found that only 31% were accurately labelled with regard to CBD content[14]. What's more, many commercially available preparations have been found to be contaminated with intoxicating doses of THC, heavy metals and pesticides, as well as toxic solvents from the CBD extraction process. In a case reported by the US Centers for Disease Control and Prevention, up to 52 people in Utah became seriously ill or were hospitalized after using a CBD oil that contained an intoxicating synthetic cannabinoid drug. The possibility of such contamination is concerning to all potential users, and especially to people who are seeking relief from the effects of a health condition. "It's one thing if you've got too much THC in gummy bears you're using with friends, but something entirely different if it's a kid you're giving CBD for medical reasons," says Bonn-Miller. "I don't trust any CBD product until I've done the tests."

BETWEEN TWO WORLDS

The regulatory disconnect that surrounds CBD creates an odd situation in which the public can self-medicate using a potentially questionable product, while scientists face a struggle to perform high-quality clinical trials. "The fact that CBD remains schedule 1 in the United States is unconscionable," says Devinsky. That restrictive classification, he says, "is impairing research".

Obtaining sufficient quantities of pharmaceutical-grade CBD to conduct a well-powered clinical trial is already difficult. "It's extremely expensive," says Leweke. "You need about one gram a day, and the list price is about 60 euros [US$67] per gram." This is because the process of extracting CBD from the cannabis plant is complex and arduous — and when the goal is to obtain CBD for use in people, the substance must meet the high bar set for clinical-grade preparations, under which only minimal quantities of THC or other contaminants are permissible. Several companies have developed strategies for manufacturing fully synthetic CBD, an approach that essentially eliminates concerns about purity. But synthetic CBD still falls under the schedule 1 classification in the United States, which creates extra economic and bureaucratic hurdles for clinical trials. Even in Canada, where recreational cannabis has been legalized, Gobbi describes a complex application process and a more than six-month wait to obtain government authorization to conduct a CBD study in people or animals.

Unfortunately, if studies such as these are not done — or not done properly — then consumers will be left to fend for themselves in a poorly monitored marketplace. In that scenario, the signal of true clinical benefit would almost certainly be drowned out by the noise from personal anecdotes and the placebo effect, which could jeopardize the future of a potentially valuable medicine. "Humans are notoriously bad when they think they see patterns," says Devinsky. "When everyone is convinced that they're right with no data, I call that religion — and CBD is currently religion for the average person." ■

Michael Eisenstein *is a freelance writer in Philadelphia, Pennsylvania.*

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Structure of deformed wing virus, a major honey bee pathogen

Karel Škubník[a], Jiří Nováček[a], Tibor Füzik[a], Antonín Přidal[b], Robert J. Paxton[c], and Pavel Plevka[a,1]

[a]Structural Virology, Central European Institute of Technology, Masaryk University, 62500 Brno, Czech Republic; [b]Department of Zoology, Fishery, Hydrobiology, and Apidology, Faculty of Agronomy, Mendel University in Brno, 613 00 Brno, Czech Republic; and [c]Institute of Biology/Zoology, Martin Luther University Halle-Wittenberg, 06120 Halle, Germany

Edited by Wolfgang Baumeister, Max Planck Institute of Chemistry, Martinsried, Germany, and approved February 10, 2017 (received for review September 20, 2016)

The worldwide population of western honey bees (*Apis mellifera*) is under pressure from habitat loss, environmental stress, and pathogens, particularly viruses that cause lethal epidemics. Deformed wing virus (DWV) from the family *Iflaviridae*, together with its vector, the mite *Varroa destructor*, is likely the major threat to the world's honey bees. However, lack of knowledge of the atomic structures of iflaviruses has hindered the development of effective treatments against them. Here, we present the virion structures of DWV determined to a resolution of 3.1 Å using cryo-electron microscopy and 3.8 Å by X-ray crystallography. The C-terminal extension of capsid protein VP3 folds into a globular protruding (P) domain, exposed on the virion surface. The P domain contains an Asp-His-Ser catalytic triad that is, together with five residues that are spatially close, conserved among iflaviruses. These residues may participate in receptor binding or provide the protease, lipase, or esterase activity required for entry of the virus into a host cell. Furthermore, nucleotides of the DWV RNA genome interact with VP3 subunits. The capsid protein residues involved in the RNA binding are conserved among honey bee iflaviruses, suggesting a putative role of the genome in stabilizing the virion or facilitating capsid assembly. Identifying the RNA-binding and putative catalytic sites within the DWV virion structure enables future analyses of how DWV and other iflaviruses infect insect cells and also opens up possibilities for the development of antiviral treatments.

colony collapse disorder | virus | structure | *Apis mellifera* | honey bee

The western honey bee (*Apis mellifera*) plays a vital role in world agriculture by providing pollination services to diverse commercial crops, a service valued at US$ 215 billion annually (1). In addition, honey bees pollinate numerous wild flowering plants, thereby supporting biodiversity (2, 3). However, over the past two decades, honey bees have suffered from elevated mortality in North America and Europe (4, 5). Colony losses have been associated with the exotic ectoparasitic mite *Varroa destructor*, which feeds on honey bee hemolymph, thereby vectoring numerous honey bee viral pathogens, in particular the iflavirus deformed wing virus (DWV). In the absence of varroa, DWV levels are low, and the virus causes asymptomatic infections. Varroa-infested colonies show elevated levels of DWV (6, 7). Symptoms associated with acute DWV infections include the death of pupae, as well as deformed wings, shortened abdomen, and cuticle discoloration of adult bees that die soon after pupation, causing colony collapse (6, 8). Indeed, winter colony mortality is strongly correlated with the presence of DWV, irrespective of the levels of varroa infestation (8, 9). DWV-induced loss of honey bees, coupled with a long-term decline in beekeeping, has become a serious threat to adequate provision of pollination services, threatening food security and ecosystem stability (1).

Viruses from the order *Picornavirales*, including the family *Iflaviridae*, have nonenveloped icosahedral virions that are about 30 nm in diameter (10). Iflavirus capsids protect 10,000-nt-long ssRNA genomes, which are translated into polyproteins that are cotranslationally and posttranslationally cleaved by viral proteases to produce structural (capsid-forming) and nonstructural proteins (11). The major capsid proteins VP1, VP2, and VP3 originating from a single polyprotein form a protomer, the basic building block of the pseudo-T3 icosahedral capsid. The entire capsid consists of 60 such protomers, arranged in 12 pentamer units of 5 protomers each.

Previously, the structure of the iflavirus Chinese sacbrood virus was characterized to a resolution of 25 Å by cryo-electron microscopy. The structure confirmed the pseudo-T3 icosahedral symmetry of its capsid and a smooth outer surface of the virion (12). Recently, we determined the structure of the iflavirus slow bee paralysis virus (SBPV) to a resolution of 2.6 Å by X-ray crystallography (13). Despite its efficient transmission by *V. destructor*, SBPV infection is a rare disease of honey bees (14). The structure revealed that the C-terminal extension of capsid protein VP3 of SBPV forms a globular protruding (P) domain positioned at the virion surface. The P domain is anchored to the core of the VP3 subunit by a 23-residue-long flexible linker that allows the P domain to attach to different areas of the capsid (13). In addition, the P domain contains the putative active site Asp-His-Ser, which is conserved among several iflaviruses (13). Iflaviruses were also proposed to harbor short VP4 subunits consisting of only about 20 residues (11, 14); however, electron density

Significance

Honey bee populations in Europe and North America have been decreasing since the 1950s. Deformed wing virus (DWV), which is undergoing a worldwide epidemic, causes the deaths of individual honey bees and collapse of whole colonies. We determined three-dimensional structures of DWV at different conditions and show that the virus surface is decorated with protruding globular extensions of capsid proteins. The protruding domains contain a putative catalytic site that is probably required for the entry of the virus into the host cell. In addition, parts of the DWV RNA genome interact with the inside of the virus capsid. Identifying the RNA binding and catalytic sites within the DWV virion offers prospects for the development of antiviral treatments.

Author contributions: P.P. designed research; K.Š. and A.P. performed research; R.J.P. contributed new reagents/analytic tools; K.Š., J.N., T.F., and P.P. analyzed data; and K.Š., R.J.P., and P.P. wrote the paper.

The authors declare no conflict of interest.

This article is a PNAS Direct Submission.

Freely available online through the PNAS open access option.

Data deposition: Cryo-EM maps of the DWV virions from different conditions have been deposited in the Electron Microscopy Data Bank (EMDB) (accession nos. EMD-4014, EMD-3574, EMD-3570, and EMD-3575); the corresponding coordinates and structure factors have been deposited in the Protein Data Bank (PDB), www.pdb.org (PDB ID codes 5L8Q, 5MV5, 5MUP, and 5MV6). The crystal structures of the DWV virion and P domain have been deposited under PDB ID codes 5G52 and 5G51.

[1]To whom correspondence should be addressed. Email: pavel.plevka@ceitec.muni.cz.

This article contains supporting information online at www.pnas.org/lookup/suppl/doi:10.1073/pnas.1615695114/-/DCSupplemental.

corresponding to SBPV VP4 was not identified in the SBPV virion structure (13).

Here, we present the structure of the DWV virion and show that, similar to SBPV, it contains a C-terminal extension of capsid protein VP3 that forms a globular domain with a putative receptor-binding site located at the virion surface. We show that, unlike SBPV, DWV's putative active site not only is flexible but also adopts two alternative conformations. Furthermore, bases from the RNA genome interact with the DWV capsid close to the fivefold axes. These structural details provide potential targets for development of antiviral compounds.

Results and Discussion

Structure of DWV Virion and Capsid Proteins. The structure of the DWV virion was determined to a resolution of 3.5 Å using cryo-electron microscopy and to 3.8 Å using X-ray crystallography (Table S1 and Fig. S1). The DWV virion is built from subunits VP1, VP2, and VP3 arranged in a capsid with pseudo-T3 icosahedral symmetry (Fig. 1). The major capsid proteins have jellyroll β-sandwich folds with β-strands named according to the virus jellyroll fold convention B to I (Fig. 1*A*) (15, 16). The complete structures of the major capsid proteins could be built except for residues 1 and 254 to 258 out of the 258 residues of VP1, 251 to 254 out of the 254 residues of VP2, and 1 and 416 out of the 416 residues of VP3. Iflaviruses were suggested to harbor short VP4 subunits consisting of about 20 residues (11, 14). Nevertheless, the electron density corresponding to VP4 could not be identified in either of the two DWV virion structures.

Subunit VP3 of DWV contains a C-terminal extension that forms a P domain positioned on the virion surface (Fig. 1). Because of the P domains, the maximum diameter of the DWV virion (397 Å) is similar to that of SBPV (398 Å) and bigger than those of other picornaviruses and dicistroviruses (about 300 Å). The cryo-EM and X-ray structures of the capsid shell of DWV are similar, with an rmsd of Cα-atoms of 0.77 Å; however, the positioning of the P domains on the surface of the virions is different (Fig. 1 *B* and *C*). The location of the P domains in the crystal structure is not affected by crystal contacts, indicating that it depends on the composition of the solution surrounding the virus. The cryo-EM images were collected on virions in PBS (137 mM NaCl, 2.7 mM KCl, 10 mM Na_2HPO_4, 2 mM KH_2PO_4, pH 7.4) whereas the crystallization conditions contained 0.8 M KH_2PO_4, 0.8 M NaH_2PO_4, and 0.1 M sodium Hepes, pH 7.5. The movement of the P domain between the two alternative attachment sites at the virion surface involves a 39-Å shift of its center of mass and 145° rotation. This change in position is possible due to a 20-residue-long linker that connects the P domain to the core of the VP3 subunit.

Host cell entry of iflaviruses has not been studied, but it probably includes receptor-mediated endocytosis, as has been demonstrated for some picornaviruses (17, 18). Endosomal entry involves exposure of the virions to a solution differing in composition (e.g., low pH), which could trigger detachment of the P domain from the virion surface. It is possible that, during cell entry, the P domain functions without being fixed to a specific position at the virion surface. Instead, it may be anchored by its polypeptide linker to the core of the VP3 subunit. Similar, alternative attachment sites of the P domain at the virion surface have been observed previously for SBPV, reinforcing the possibility that movement of the P domains might be required for their biological function (13). It was speculated previously that the movements of the SBPV P domains were induced by differences in pH. In contrast, the DWV structures were determined at similar pH; however, the crystallization solution was of high ionic strength (0.8 M KH_2PO_4, 0.8 M NaH_2PO_4). It is therefore possible that the movements of the P domain of DWV that we observed were induced by these high, nonphysiological ion concentrations.

Structure of the P Domain. The P domain of the VP3 subunit of DWV is globular, with a diameter of 30 Å (Fig. 1). In both cryo-EM and X-ray structures of the DWV virion, the residues of the P domain have higher average temperature factors than residues from the remainder of the capsid, indicating a higher mobility of the P domain. As a result, electron density maps of the P domains are less well-resolved than other parts of the capsid. We therefore used X-ray crystallography to determine the structure of the isolated P domain to a resolution of 1.45 Å (Table S1). In addition to the globular core, the P domain of DWV contains a finger-shaped loop with four-residue-long antiparallel β-strands β8 and β9 (Fig. 2*A*). The core of the P domain consists of a central antiparallel β-sheet formed from strands β5 and β6 surrounded by the 11-residue-long α-helix α1, the 5-residue long α2, and two β-sheets containing strands β1 and β2 and β3 to β7 (Fig. 2*A*). The β-strands are connected by loops that vary in length between

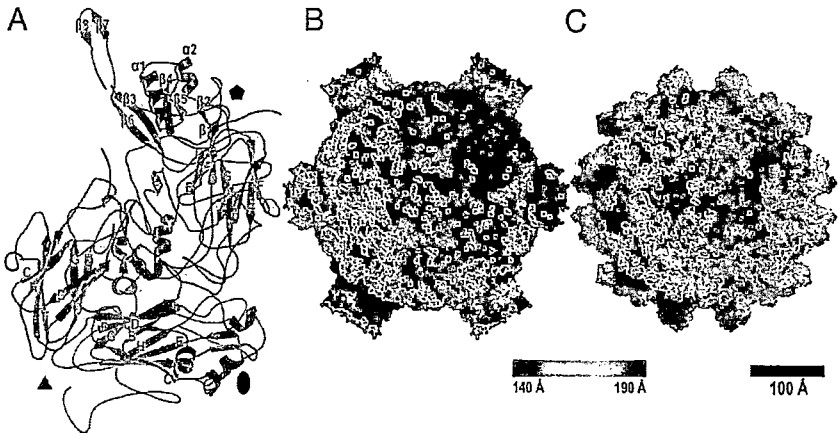

Fig. 1. Structures of the icosahedral asymmetric unit of DWV and its virions in alternative conformations. Icosahedral asymmetric unit of DWV in schematic representation (*A*) with major capsid protein VP1 colored in blue, VP2 in green, and VP3 in red. The P domain, which is part of VP3, is highlighted in magenta. Selected secondary structure elements are labeled. The locations of the fivefold, threefold, and twofold symmetry axes are denoted by a pentagon, triangle, and oval, respectively. Molecular surfaces of DWV virions determined by (*B*) cryo-EM and (*C*) X-ray crystallography. The virion surfaces are rainbow-colored according to their distance from the particle center. (Scale bar: 100 Å.)

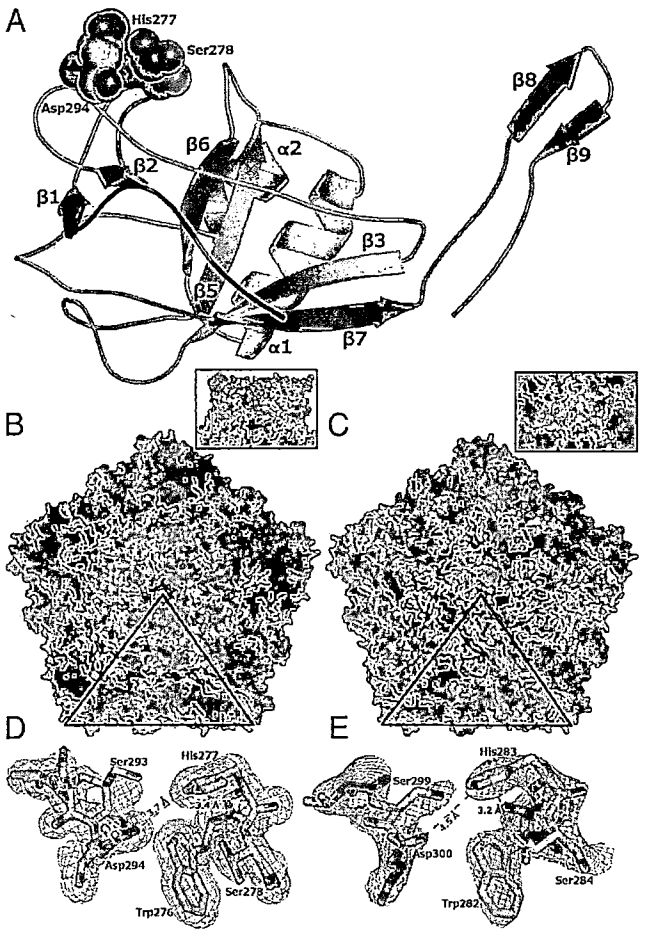

Fig. 2. Structure of the DWV P domain, its localization on the virion surface, and details of the putative catalytic or receptor-binding site. Schematic representation of the crystal structure of the P domain (*A*), rainbow-colored from residue 260 in blue to 416 in red. Atoms of residues forming the putative active site Asp294, His277, and Ser278 are shown as spheres. Please note that β-strand 4, which is present in the P domain of SBPV, is missing in the DWV structure. Surface representation of pentamers of capsid protein protomers of (*B*) native cryo-EM structure and (*C*) X-ray structure of DWV virions. VP1 subunits are shown in blue, VP2 in green, VP3 in red, and the P domain in magenta. Positions of the conserved residues that form a putative active or receptor-binding site of DWV are highlighted in cyan. The borders of one icosahedral asymmetric unit are highlighted with a black triangle. (*Insets*) Detailed views of the conserved residues forming a compact patch at the P domain surface. In the *Inset* of *B*, one of the P domains was removed to allow a view of the inside of the crown formed by the P domains. The P domains of DWV (*D*) and SBPV (*E*) contain putative Ser-His-Asp active sites, which are parts of groups of seven residues that are conserved among iflaviruses. The residues are displayed in stick representation. The conserved residues are shown with carbon atoms in cyan. Residues that are not conserved are shown with carbon atoms in magenta. Residues Ser278, Ala292, Ser293, and Asp294 of DWV adopt alternative conformations that are shown with carbon atoms in yellow. Distances between the side chains constituting the putative catalytic triad are shown as orange dashed lines. The electron density maps are contoured at 1 σ.

6 and 45 residues. The high-resolution structure of the P domain was fitted into the corresponding regions of the cryo-EM and crystallographic electron density maps of the DWV virion and refined against the experimental data. The resulting P domain structures are similar, with an rmsd in atom positions smaller than 0.50 Å. However, residues 399 to 416 forming the P domain "finger" were not resolved in either of the virion electron density maps, probably due to the flexibility of the loop.

Comparison of DWV and SBPV Virion Structures. DWV shares 32% sequence identity in capsid proteins with SBPV (13). The two viruses have similar surface topologies with capsids decorated with P domains. The differences between the SBPV and DWV capsids are predominantly in the loops of the major capsid proteins exposed at the outer virion surface. Capsid protein VP1 of DWV has a GH loop that is five residues shorter than that of SBPV and lacks an α-helix α6 (Fig. S2 *A* and *B*). The GH loop of the VP2 subunit of SBPV contains the integrin-recognition motif Arg192-Gly193-Asp194 (RGD) and is four residues longer than that of DWV (Fig. S2 *C* and *D*). Integrins serve as cell entry receptors for numerous viruses, including the foot and mouth disease virus and several parechoviruses (19–21). However, the RGD motif is not present in DWV and other iflaviruses. Differences in the structure of the GH loop between DWV and SBPV might reflect different functions of the loops in receptor recognition.

DWV and SBPV differ in the structures of both the core and P domains of their VP3 subunits (Fig. S2 *E* and *F*). The β-sandwich cores of VP3 subunits of DWV and SBPV can be superimposed with an rmsd of 1.35 Å for 94% of the residues whereas the P domains have an rmsd of 1.69 Å for 80% of the residues. The P domain of DWV contains 18 structured residues at the C terminus that form a finger with a 4-residue-long antiparallel beta sheet (Fig. 2*A* and Fig. S2*G*). Notably, these residues are not resolved in the crystal structures of SBPV virions (Fig. S2*H*). The sequence identity within the P domains of the two viruses is 17% whereas it is 33% for the remaining parts of the capsid proteins. Thus, it seems that the P domain is more tolerant to mutations than the parts of the virus proteins forming the capsid shell. Nevertheless, the P domains of DWV and SBPV contain 8 conserved residues that are also shared with several other iflaviruses and that might form a catalytic or receptor-binding site as discussed below.

Comparison of the P Domain with Other Proteins. A search for structures similar to the DWV P domain (22) identified a globular surface domain of a virus from the *Astroviridae*, an additional family of nonenveloped viruses like the picornaviruses and caliciviruses, all of which possess a single-stranded positive sense RNA genome (Table S2) (23). The domain is similar to the P domain of DWV in terms of having a core formed by β-strands that are complemented by short α-helices located at the periphery of the domain. Nevertheless, the two domains are quite different and could not be meaningfully superimposed. Several additional proteins could be detected, but their structural similarities to the DWV P domain were low and the alignments always included only a small fraction of the structures (Table S2). Therefore, it seems that the P domains of iflaviruses might have evolved de novo as C-terminal extensions of the capsid proteins and therefore have a unique fold.

Position of the P Domain at the Virion Surface. In the cryo-EM structure of DWV, the P domains related by one icosahedral fivefold axis form a crown-like arrangement at the virion surface (Figs. 1*B* and 2*B*). The crowns have a diameter of 80 Å and protrude 40 Å above the capsid surface. The P domains within the same crown contact each other with a buried surface area of 380 Å^2, and each of them binds to the capsid through a 430-Å^2 interface located next to the fivefold axis. In contrast, the P domains of native SBPV, which also forms crowns, are not in contact with each other (Fig. S3). In the crystal structure of DWV, the P domains are positioned approximately in between the icosahedral fivefold, threefold, and twofold axes and interact with the capsid through a 1,000-Å^2 interface (Fig. 2*C*). The P domains in this structure do not interact with each other, and, therefore, we refer to them as being in "centered" arrangement. The movements of the P domains between the two positions

seem to be accomplished by "rolling" over the virion surface (Fig. 2 *B* and *C* and Movies S1 and S2). The residues forming the 430 Å^2 of the VP1 surface that became exposed after the P domain movements do not contain any specific motives to indicate their function in receptor binding. Similar movements of the P domains have been observed previously in SBPV crystallized in low pH conditions (13). Unlike in the case of SPBV, movements of the DWV P domain could not be induced by exposing DWV to pH 5.0 (Fig. S4 *A* and *B*). However, the structures of the P domains determined by cryo-EM of DWV at low pH are less resolved and therefore more mobile than those of the virus in neutral pH (Fig. S5 *A* and *B*). To determine whether the movements of the P domains are reversible, we exposed DWV virions to the crystallization condition and subsequently dialyzed them back against PBS. Cryo-EM reconstruction of these particles determined to a resolution of 3.8 Å showed P domains in the crown arrangement similar to native virions (Figs. S4*C* and S5*C*). It was not possible to calculate cryo-EM reconstruction of the DWV virions in the crystallization buffer because the 1.6-M phosphate salts prevent preparation of grids with vitreous ice of sufficient quality for cryo-EM data collection. In an attempt to directly observe the virus with P domains in the centered arrangement, DWV virions were exposed to the crystallization condition and cross-linked by addition of 1% glutaraldehyde. The particles were then dialyzed against PBS and used for cryo-EM reconstruction that was determined to a resolution of 3.1 Å. These particles had P domains in the crown arrangement (Figs. S4*D* and S5*D*). Three-dimensional classification using the program RELION did not identify a subclass of particles with P domains in the centered arrangement. Thus, the cryo-EM analysis did not confirm the positioning of P domains in the centered arrangement observed in the crystal structure (Fig. 1*C*). The differences in the virion structures obtained by the two types of structural analysis could be caused by low-efficiency of cross-linking of the P domains. Furthermore, it is likely that the movements of P domains within a single virus particle are not synchronized with each other. Cryo-EM analysis, even in combination with 3D classification, may therefore not allow detection of a subset of the P domains in the centered arrangement. In contrast, crystallization, which required 5 months, probably specifically selected for particles with a centered P domain arrangement.

P domains of DWV virions that were exposed to high salt or low pH became more mobile than those of native virions or viruses cross-linked by 1% glutaraldehyde (Fig. S5). We speculate that it is the mobility of the P domains rather than their precise positioning that is important for DWV cell entry, during which the virus is likely to encounter low pH. Our results provide evidence of the possible extent of movements of the P domains.

Putative Role of the P Domain in Cell Entry. The P domain of DWV contains residues Asp294, His277, and Ser278 located close to each other, and the arrangement of their side chains indicates that they constitute a catalytic triad (Fig. 2 *A* and *D*) (24). The distances between the side chains of the residues are larger than ideal for catalyzing a hydrolytic reaction (Fig. 2*D*) (24). However, the 1.45-Å-resolution structure of the DWV P domain shows that residues Ser278, Ala292, Ser293, and Asp294 adopt alternative conformations (Fig. 2*D*), indicating local flexibility of the structure. It is therefore possible that the optimal configuration of the active site might be achieved upon binding the as-yet-unknown substrate. This type of catalytic triad has been previously identified in proteases, lipases, and esterases (24–26). Therefore, DWV may use the putative catalytic activity of its P domains in cell entry. The P domains might bind to virus receptors or disrupt membranes and thus allow the virus to deliver its genome into the cell cytoplasm.

The putative catalytic triad and five additional residues, which form a compact patch on the P domain surface, are conserved among iflaviruses containing P domains (Figs. 2 *B* and *C* and 3*A*) (11, 27–29), which is in contrast to the limited 3% overall sequence identity of the remaining residues of the P domains. Conservation of these residues indicates that they constitute a functionally important receptor-binding or substrate-binding site. The Asp294-His277-Ser278 catalytic triad of SBPV also has a 3D arrangement indicative of an active site (Fig. 2*E*) (13). A similar group of residues in the P domains of noroviruses was shown to bind glycans (30, 31). Alternatively, the putative catalytic site may facilitate the escape of DWV virions from endosomes in a manner analogous to the lipase activity present in the N-terminal domain of the capsid protein VP1 from parvoviruses (32).

The conserved residues in the iflavirus P domain provide a potential target for antiviral compounds. The putative active site faces the interior of the crown in the native virus; however, it is exposed at the apex of the P domain in the virion structure with the centered arrangement of the P domains (Fig. 2 *B* and *C*). The exposure of the active site after the P domain rotation reinforces the possibility that movements of the P domain might be required for efficient DWV infection.

Evolutionary Relationship to Other Viruses from the Order *Picornavirales*. The availability of the DWV and SBPV virion structures enabled the construction of a structure-based phylogenetic tree comparing the iflaviruses to other viruses from the families *Dicistroviridae* and *Iflaviridae* (Fig. 4). The structural comparison shows that iflaviruses are most similar to the insect-infecting dicistroviruses Israeli acute bee paralysis virus, cricket paralysis virus, and triatoma virus (33–35). The viruses most similar to DWV and SBPV from the *Picornaviridae* family are hepatitis A virus and human parechovirus 1 (HPeV-1), which were previously suggested to form evolutionary intermediates between human and insect viruses (21, 36) (Fig. 4). The closer structural similarity of DWV and SBPV capsid to the viruses from the *Dicistroviridae* family than to viruses from the *Picornaviridae* family might be because of similarities in the processing of the polyprotein precursor of capsid proteins. The amino acid sequence of the VP4 subunit is located in front of the N terminus of VP3 in viruses from the family *Dicistroviridae* whereas it is located in front of the VP2 sequence in viruses of the family *Picornaviridae*. The VP4 sequences of iflaviruses were predicted to be located in front of VP3 in the polyprotein (11, 14). Even though the VP4 subunits of DWV and SBPV are not resolved in the virion structures, the similar cleavage pattern of the capsid

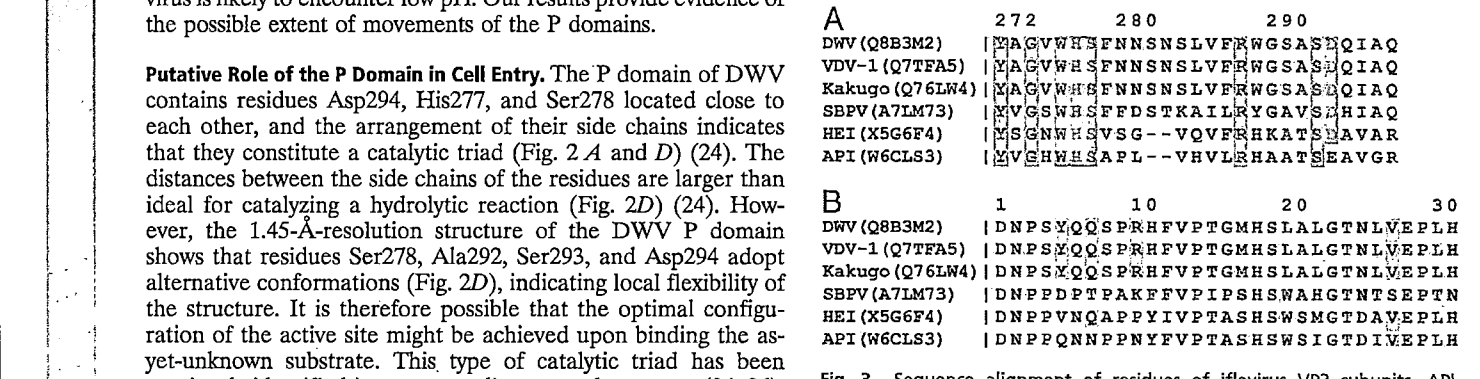

Fig. 3. Sequence alignment of residues of iflavirus VP3 subunits. API, *Antherae pernyi* iflavirus; HEI, *Heliconius erato* iflavirus. UniProt accession numbers of the sequences used in the alignment are provided. (*A*) Conserved residues constituting the putative catalytic triad Asp-His-Ser are highlighted with an orange background; other conserved residues located in the structure close to the putative active site are highlighted with a gray background. (*B*) Conserved residues involved in the interaction with genomic RNA are highlighted with a yellow background.

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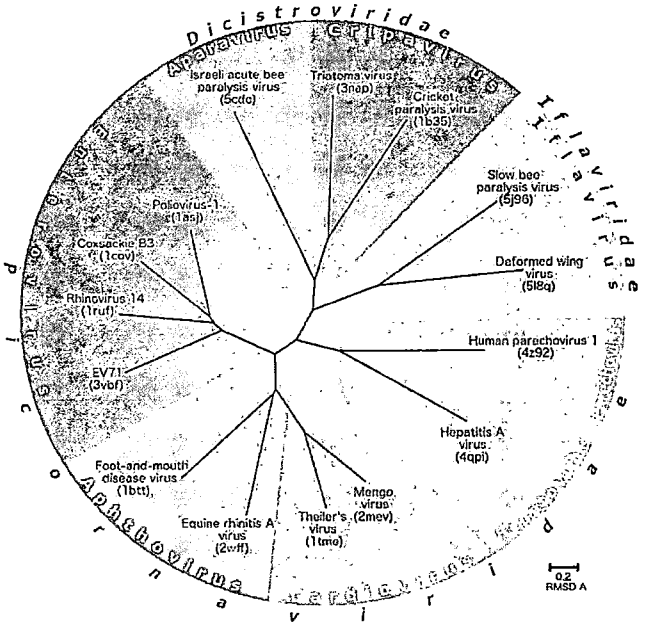

Fig. 4. Evolutionary relationship among viruses from the families *Iflaviridae*, *Picornaviridae*, and *Dicistroviridae* based on structural alignment of their capsid proteins. Phylogenetic tree based on structural similarity of icosahedral asymmetric units of indicated viruses. For details on the construction of the diagram, please see *Materials and Methods*.

protein subunits from the precursor polyprotein P1 might impose constraints on the organization of the capsid, resulting in the closer similarity of iflaviruses to dicistroviruses.

Iflaviruses are structurally and genetically related to vertebrate picornaviruses, for which numerous capsid-binding inhibitors have been developed. Compounds that bind into a hydrophobic pocket within VP1 can inhibit receptor binding and/or genome release of some picornaviruses (37–39). However, such a hydrophobic pocket is not formed in DWV VP1 subunits. Similarly, the hydrophobic pocket was not observed in VP1 of SBPV (13), which suggests that capsid binding inhibitors that intercalate into VP1 subunits may not be effective as antivirals against honey bee viruses of the family *Iflaviridae*.

Capsid–RNA Interactions. The DWV genome is a 10,140-nt-long linear RNA molecule (11) that forms unique interactions with the inner surface of the icosahedral capsid. The virus RNA does not affect the packing of particles within the crystal or the determination of particle orientations performed in the course of the cryo-EM reconstruction. Therefore, both X-ray and cryo-EM maps contain information about the icosahedrally averaged RNA structure.

Clearly defined electron density corresponding to an RNA nucleotide is associated with each VP3 subunit of DWV close to the fivefold icosahedral axis (Fig. 5*A*). The shape of the density indicates that the base of the nucleotide is a pyrimidine, and it was therefore modeled as a uridine (Fig. 5*B*). The nucleotide has 90% occupancy, showing that the genome binds to nearly all of the 60 available positions within the virion. Each nucleotide interacts with residues from three VP3 subunits belonging to different protomers within one pentamer (Fig. 5*B*). The residues that bind the RNA are conserved among several honey bee Iflaviruses (Fig. 3*B*). However, the structured RNA was not observed in the SBPV virion, which does not have the conserved RNA-binding residues (Fig. 3*B*) (40). Reminiscent of the RNA–protein interactions in DWV are structured RNA oligonucleotides that have been recently described in the parechoviruses HPeV-1, HPeV-3, and Ljungan virus, where they also mediate contacts among capsid proteins from different protomers (21, 41, 42). The conservation of the RNA-binding residues among some of the honey bee iflaviruses, together with the near-complete occupancy of the RNA, indicates that the RNA–capsid binding might play a role in virion stability. In addition, RNA–capsid interactions may play a role in DWV virion assembly, as was previously suggested for related picornaviruses (43). Therefore, future mutational analyses of the residues involved in the RNA binding may lead to determination of the mechanism that ensures packaging of the DWV genome into newly forming particles, and which may offer alternative targets for antiviral compounds.

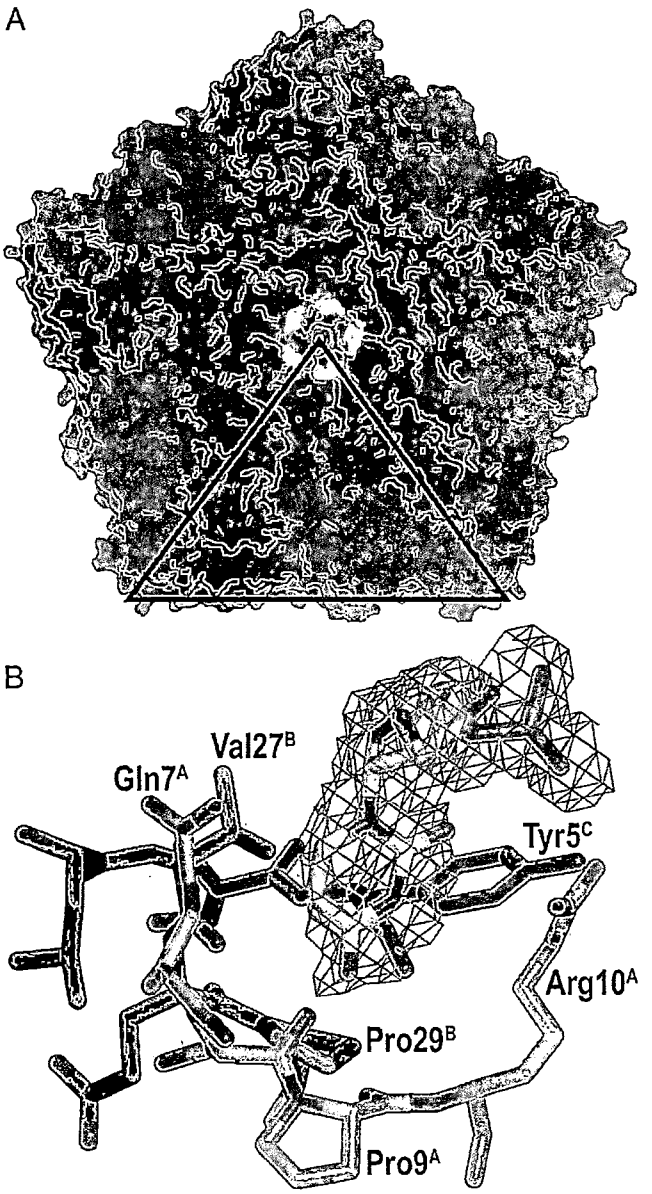

Fig. 5. Interactions of DWV genomic RNA with capsid. Location of RNA nucleotides displayed in yellow within the pentamer of capsid protein protomers as seen from the inside of the virion (*A*). VP1 subunits are shown in blue, VP2 in green, and VP3 in red. The borders of one icosahedral asymmetric unit are highlighted with a triangle. (*B*) Detail of the interaction of viral RNA with the VP3 subunits. The electron density map of the nucleotide is contoured at 1 σ. VP3 subunits from different icosahedral asymmetric units are distinguished by color shades and superscripts "A," "B," and "C."

Materials and Methods

The propagation of DWV was carried out as described in the COLOSS BeeBook (44). A suspension of DWV was applied onto holey carbon grids and vitrified by plunging into liquid ethane. Images were recorded with an FEI Falcon II camera in an FEI Titan Krios electron microscope. The images were processed using the package RELION (45). The P domain was expressed in *Escherichia coli* BL21(DE3). Crystals of the DWV P domain were obtained using the sitting-drop technique with a bottom solution containing 4.3 M sodium chloride and 0.1 M Hepes, pH 7.5.

ACKNOWLEDGMENTS. We thank synchrotron "Soleil" Proxima-1 and beamline scientist Dr. Pierre Legrand for help with X-ray data collection and processing. This research was carried out under the project CEITEC 2020 (LQ1601), with financial support from the Ministry of Education, Youth and Sports of the Czech Republic under National Sustainability Program II. Access to computing and storage facilities owned by parties and projects contributing to the National Grid Infrastructure MetaCentrum, provided under the program "Projects of Large Infrastructure for Research, Development, and Innovations" Grant (LM2010005), is greatly appreciated. This work was supported by the IT4Innovations Centre of Excellence project Grant (CZ.1.05/1.1.00/02.0070), funded by the European Regional Development Fund and the national budget of the Czech Republic via the Research and Development for Innovations Operational Program, as well as the Czech Ministry of Education, Youth and Sports via the project Large Research, Development and Innovations Infrastructures Grant (LM2011033). The research leading to these results received funding from the European Research Council under the European Union's Seventh Framework Program Grant (FP/2007-2013)/ERC Grant Agreement 355855 and from EMBO Grant Agreement European Molecular Biology Organization (EMBO)-IG 3041 (to P.P.).

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The Lancet Commission on pollution and health

Article *in* The Lancet · October 2017

DOI: 10.1016/S0140-6736(17)32345-0

The *Lancet* Commission on pollution and health

Philip J Landrigan, Richard Fuller, Nereus J R Acosta, Olusoji Adeyi, Robert Arnold, Niladri (Nil) Basu, Abdoulaye Bibi Baldé, Roberto Bertollini, Stephan Bose-O'Reilly, Jo Ivey Boufford, Patrick N Breysse, Thomas Chiles, Chulabhorn Mahidol, Awa M Coll-Seck, Maureen L Cropper, Julius Fobil, Valentin Fuster, Michael Greenstone, Andy Haines, David Hanrahan, David Hunter, Mukesh Khare, Alan Krupnick, Bruce Lanphear, Bindu Lohani, Keith Martin, Karen V Mathiasen, Maureen A McTeer, Christopher J L Murray, Johanita D Ndahimananjara, Frederica Perera, Janez Potočnik, Alexander S Preker, Jairam Ramesh, Johan Rockström, Carlos Salinas, Leona D Samson, Karti Sandilya, Peter D Sly, Kirk R Smith, Achim Steiner, Richard B Stewart, William A Suk, Onno C P van Schayck, Gautam N Yadama, Kandeh Yumkella, Ma Zhong

Executive summary

Pollution is the largest environmental cause of disease and premature death in the world today. Diseases caused by pollution were responsible for an estimated 9 million premature deaths in 2015—16% of all deaths worldwide—three times more deaths than from AIDS, tuberculosis, and malaria combined and 15 times more than from all wars and other forms of violence. In the most severely affected countries, pollution-related disease is responsible for more than one death in four.

Pollution disproportionately kills the poor and the vulnerable. Nearly 92% of pollution-related deaths occur in low-income and middle-income countries and, in countries at every income level, disease caused by pollution is most prevalent among minorities and the marginalised. Children are at high risk of pollution-related disease and even extremely low-dose exposures to pollutants during windows of vulnerability in utero and in early infancy can result in disease, disability, and death in childhood and across their lifespan.

Despite its substantial effects on human health, the economy, and the environment, pollution has been neglected, especially in low-income and middle-income countries, and the health effects of pollution are underestimated in calculations of the global burden of disease. Pollution in low-income and middle-income countries that is caused by industrial emissions, vehicular exhaust, and toxic chemicals has particularly been overlooked in both the international development and the global health agendas. Although more than 70% of the diseases caused by pollution are non-communicable diseases, interventions against pollution are barely mentioned in the Global Action Plan for the Prevention and Control of Non-Communicable Diseases.

Pollution is costly. Pollution-related diseases cause productivity losses that reduce gross domestic product (GDP) in low-income to middle-income countries by up to 2% per year. Pollution-related disease also results in health-care costs that are responsible for 1·7% of annual health spending in high-income countries and for up to 7% of health spending in middle-income countries that are heavily polluted and rapidly developing. Welfare losses due to pollution are estimated to amount to US$4·6 trillion per year: 6·2% of global economic output. The costs attributed to pollution-related disease will probably increase as additional associations between pollution and disease are identified.

Pollution endangers planetary health, destroys ecosystems, and is intimately linked to global climate change. Fuel combustion—fossil fuel combustion in high-income and middle-income countries and burning of biomass in low-income countries—accounts for 85% of airborne particulate pollution and for almost all pollution by oxides of sulphur and nitrogen. Fuel combustion is also a major source of the greenhouse gases and short-lived climate pollutants that drive climate change. Key emitters of carbon dioxide, such as electricity-generating plants, chemical manufacturing facilities, mining operations, deforestation, and petroleum-powered vehicles, are also major sources of pollution. Coal is the world's most polluting fossil fuel, and coal combustion is an important cause of both pollution and climate change.

In many parts of the world, pollution is getting worse. Household air and water pollution, the forms of pollution associated with profound poverty and traditional lifestyles, are slowly declining. However, ambient air pollution, chemical pollution, and soil pollution—the forms of pollution produced by industry, mining, electricity generation, mechanised agriculture, and petroleum-powered vehicles—are all on the rise, with the most marked increases in rapidly developing and industrialising low-income and middle-income countries.

Chemical pollution is a great and growing global problem. The effects of chemical pollution on human health are poorly defined and its contribution to the global burden of disease is almost certainly underestimated. More than 140 000 new chemicals and pesticides have been synthesised since 1950. Of these materials, the 5000 that are produced in greatest volume have become widely dispersed in the environment and are responsible for nearly universal human exposure. Fewer than half of these high-production volume chemicals have undergone any testing for safety or toxicity, and rigorous pre-market evaluation of new chemicals has become mandatory in only the past decade and in only a few high-income countries. The result is that chemicals and pesticides whose effects on human health and the environment were never examined have repeatedly been responsible for episodes of disease, death, and environmental degradation. Historical examples include lead, asbestos, dichlorodiphenyltrichloroethane (DDT), polychlorinated biphenyls (PCBs), and the ozone-destroying chlorofluorocarbons. Newer synthetic chemicals that have entered world markets in the past

Published Online October 19, 2017 http://dx.doi.org/10.1016/S0140-6736(17)32345-0

See Online/Comment http://dx.doi.org/10.1016/S0140-6736(17)32588-6 and http://dx.doi.org/10.1016/S0140-6736(17)32545-X

Arnhold Institute for Global Health (Prof P J Landrigan MD), Mount Sinai Heart (V Fuster MD), and Department of Environmental Medicine and Global Health (Prof A S Preker PhD), Icahn School of Medicine at Mount Sinai, New York, NY, USA; Pure Earth, New York, NY, USA (R Fuller BE, D Hanrahan MSc, K Sandilya LLB); Office of the President, Manila, Philippines (N J R Acosta PhD); Department of Health, Nutrition, and Population Global Practice (O Adeyi DrPH), and Office of the US Executive Director (K V Mathiasen MALD), The World Bank, Washington, DC, USA; Department of Chemical and Environmental Engineering, University of Arizona, Tucson, AZ, USA (R Arnold PhD); Faculty of Agricultural and Environmental Sciences, McGill University, Montreal, Canada (Prof N Basu PhD); Ministry of Environment and Sustainable Development, Dakar, Senegal (A B Baldé MS); Scientific Committee on Health, Environmental and Emerging Risks of the European Commission, Luxembourg City, Luxembourg (R Bertollini MD); Office of the Minister of Health, Ministry of Public Health, Doha, Qatar (R Bertollini); Institute and Outpatient Clinic for Occupational, Social and Environmental Medicine, University Hospital of LMU Munich, Munich, Germany (S Bose-O'Reilly MD); Department of Public Health, Health Services Research and Health Technology

Assessment, University for Health Sciences, Medical Informatics and Technology, Hall in Tirol, Austria (S Bose-O'Reilly); New YorkAcademy of Medicine, New York, NY, USA (J I Bouffourd MD); Department of Environmental Health and Engineering, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA (P N Breysse PhD); School of Social Work (Prof G N Yadama PhD), and Department of Biology (T Chiles PhD), Boston College, Chestnut Hill, MA, USA; Chulabhorn Research Institute, Bangkok, Thailand (HRH Princess C Mahidol PhD); Ministry of the Health and Social Affairs, Dakar, Senegal (A M Coll-Seck MD); Department of Economics, University of Maryland, College Park, MD, USA (Prof M L Cropper PhD); Resources for the Future, Washington, DC, USA (Prof M L Cropper, A Krupnick PhD); Department of Biological, Environmental and Occupational Health Sciences, School of Public Health, University of Ghana, Accra, Ghana (J Fobil DrPH); Centro Nacional de Investigaciones Cardiovasculares Carlos III, Madrid, Spain (V Fuster); Department of Economics, University of Chicago, Chicago, IL, USA (M Greenstone PhD); Department of Social and Environmental Health Research and Department of Population Health, London School of Hygiene & Tropical Medicine, London, UK (Prof A Haines FMedSci); Nuffield Department of Population Health, University of Oxford, Oxford, UK (Prof D Hunter MBBS); Department of Civil Engineering, Indian Institute of Technology, Delhi, India (Prof M Khare PhD); Faculty of Health Sciences, Simon Fraser University, Burnaby, BC, Canada (B Lanphear MD); Centennial Group, Washington, DC, USA (B Lohani PhD); The Resources Center, Lalitpur, Nepal (B Lohani); Consortium of Universities for Global Health, Washington, DC, USA (K Martin MD); Faculty of Common Law, University of Ottawa, Ottawa, ON, Canada

2–3 decades and that, like their predecessors, have undergone little pre-market evaluation threaten to repeat this history. They include developmental neurotoxicants, endocrine disruptors, chemical herbicides, novel insecticides, pharmaceutical wastes, and nanomaterials. Evidence for the capacity of these emerging chemical pollutants to cause harm to human health and the environment is beginning to become evident. These emerging chemicals are of great concern, and this concern is heightened by the increasing movement of chemical production to low-income and middle-income countries where public health and environmental protections are often scant. Most future growth in chemical production will occur in these countries. A further dimension of chemical pollution is the global archipelago of contaminated hot-spots: cities and communities, homes and schoolyards polluted by toxic chemicals, radionuclides, and heavy metals released into air, water, and soil by active and abandoned factories, smelters, mines, and hazardous waste sites.

Cities, especially rapidly growing cities in industrialising countries, are severely affected by pollution. Cities contain 55% of the world's population; they account for 85% of global economic activity and they concentrate people, energy consumption, construction activity, industry, and traffic on a historically unprecedented scale.

The good news is that much pollution can be eliminated, and pollution prevention can be highly cost-effective. High-income and some middle-income countries have enacted legislation and issued regulations mandating clean air and clean water, established chemical safety policies, and curbed their most flagrant forms of pollution. Their air and water are now cleaner, the blood lead concentrations of their children have decreased by more than 90%, their rivers no longer catch fire, their worst hazardous waste sites have been remediated, and many of their cities are less polluted and more liveable. Health has improved and people in these countries are living longer. High-income countries have achieved this progress while increasing gross domestic product (GDP) by nearly 250%. The challenge for high-income nations today is to further reduce pollution, decarbonise their economies, and reduce the resources used in achieving prosperity. The claim that pollution control stifles economic growth and that poor countries must pass through a phase of pollution and disease on the road to prosperity has repeatedly been proven to be untrue.

Pollution mitigation and prevention can yield large net gains both for human health and the economy. Thus, air quality improvements in the high-income countries have not only reduced deaths from cardiovascular and respiratory disease but have also yielded substantial economic gains. In the USA, an estimated US$30 in benefits (range, $4–88) has been returned to the economy for every dollar invested in air pollution control since 1970, which is an aggregate benefit of $1·5 trillion against an investment of $65 billion. Similarly, the removal of lead from gasoline has returned an estimated $200 billion (range, $110 billion–300 billion) to the US economy each year since 1980, an aggregate benefit to-date of over $6 trillion through the increased cognitive function and enhanced economic productivity of generations of children exposed since birth to only low amounts of lead.

Pollution control will advance attainment of many of the sustainable development goals (SDGs), the 17 goals established by the United Nations to guide global development in the 21st century. In addition to improving health in countries around the world (SDG 3), pollution control will help to alleviate poverty (SDG 1), improve access to clean water and improve sanitation (SDG 6), promote social justice (SDG 10), build sustainable cities and communities (SDG 11), and protect land and water (SDGs 14 and 15). Pollution control, in turn, will benefit from efforts to slow the pace of climate change (SDG 13) by transitioning to a sustainable, circular economy that relies on non-polluting renewable energy, on efficient industrial processes that produce little waste, and on transport systems that restrict use of private vehicles in cities, enhance public transport, and promote active travel.

Many of the pollution control strategies that have proven cost-effective in high-income and middle-income countries can be exported and adapted by cities and countries at every level of income. These strategies are based in law, policy, regulation, and technology, are science-driven, and focus on the protection of public health. The application of these approaches boosts economies and increases GDP. The strategies include targeted reductions in emissions of pollutants, transitions to non-polluting, renewable sources of energy, the adoption of non-polluting technologies for production and transportation, and the development of efficient, accessible, and affordable public transportation systems. Application of the best of these strategies in carefully planned and well resourced campaigns can enable low-income and middle-income countries to avoid many of the harmful consequences of pollution, leapfrog the worst of the human and ecological disasters that have plagued industrial development in the past, and improve the health and wellbeing of their people. Pollution control provides an extraordinary opportunity to improve the health of the planet. It is a winnable battle.

The aim of this *Lancet* Commission on pollution and health is to raise global awareness of pollution, end neglect of pollution-related disease, and mobilise the resources and the political will needed to effectively confront pollution. To advance this aim, we make six recommendations. Additional recommendations are presented at the end of each Section. The key recommendations are:

(1) Make pollution prevention a high priority nationally and internationally and integrate it into country and city

www.thelancet.com Published online October 19, 2017 http://dx.doi.org/10.1016/S0140-6736(17)32345-0

planning processes. Pollution can no longer be viewed as an isolated environmental issue, but is a transcendent problem that affects the health and wellbeing of entire societies. Leaders of government at all levels (mayors, governors, and heads of state) need, therefore, to elevate pollution control to a high priority within their agendas; to integrate pollution control into development planning; to actively engage in pollution planning and prioritisation; and to link prevention of pollution with commitments to advance the SDGs, to slow the pace of climate change, and to control non-communicable diseases.

Targets and timetables are essential, and governments at all levels need to establish short-term and long-term targets for pollution control and to support the agencies and regulations needed to attain these goals. Legally mandated regulation is an essential tool, and both the polluter-pays principle and an end to subsidies and tax breaks for polluting industries need to be integral components of pollution control programmes.

(2) Mobilise, increase, and focus the funding and the international technical support dedicated to pollution control. The amount of funding from international agencies, binational donors, and private foundations that is directed to control of pollution, especially pollution from the industrial, transport, chemical, and mining sectors in low-income and middle-income countries is meagre and needs to be substantially increased. The resources directed to pollution management need to be increased within cities and countries as well as internationally. Options for increasing the international development funding directed to pollution include expansion of climate change and non-communicable disease control programmes to include pollution control and development of new funding mechanisms.

In addition to increased funding, international technical support for pollution control is needed in prioritisation and planning of processes to tackle pollution within rapidly industrialising cities and countries; in development of regulatory and enforcement strategies; in building technical capacity; and in direct interventions, in which such actions are urgently needed to save lives or can substantially leverage local action and resources. Financing and technical assistance programmes need to be tracked and measured to assess their cost-effectiveness and to enhance accountability.

(3) Establish systems to monitor pollution and its effects on health. Data collected at the national and local levels are essential for measuring pollution levels, identifying and apportioning appropriate responsibility to each pollution source, evaluating the success of interventions, guiding enforcement, informing civil society and the public, and assessing progress toward goals. The incorporation of new technologies, such as satellite imaging and data mining, into pollution monitoring can increase efficiency, expand geographic range, and lower costs. Open access to these data is essential, and consultation with civil society and the public will ensure accountability and build public awareness. With even limited monitoring programmes, consisting of only one or a few sampling stations, governments and civil society organisations can document pollution, and track progress toward short-term and long-term control targets. Pollution control metrics should be integrated into SDG dashboards and other monitoring platforms so that successes and experiences can be shared.

(4) Build multi-sectoral partnerships for pollution control. Broad-based partnerships across several government agencies and between governments and the private sector can powerfully advance pollution control and accelerate the development of clean energy sources and clean technologies that will ultimately prevent pollution at source. Cross-ministerial collaborations that involve health and environment ministries, but also ministries of finance, energy, agriculture, development, and transport are essential. Collaborations between governments and industry can catalyse innovation, create incentives for cleaner production technologies and cleaner energy production, and incentivise transition to a more sustainable, circular economy. The private sector is in a unique position to provide leadership in the design and development of clean, non-polluting, sustainable technologies for pollution control, and to engage constructively with governments to reward innovation and create incentives.

(5) Integrate pollution mitigation into planning processes for non-communicable diseases. Interventions against pollution need to be a core component of the Global Action Plan for the Prevention and Control of Non-Communicable Diseases.

(6) Research pollution and pollution control. Research is needed to understand and control pollution and to drive change in pollution policy. Pollution-related research should:

- Explore emerging causal links between pollution, disease, and subclinical impairment, for example between ambient air pollution and dysfunction of the central nervous system in children and the elderly;
- Quantify the global burden of disease associated with chemical pollutants of known toxicity such as lead, mercury, chromium, arsenic, asbestos, and benzene;
- Identify and characterise the adverse health outcomes caused by new and emerging chemical pollutants, such as developmental neurotoxicants, endocrine disruptors, novel insecticides, chemical herbicides, and pharmaceutical wastes;
- Identify and map pollution exposures particularly in low-income and middle-income countries;
- Improve estimates of the economic costs of pollution and pollution-related disease; and
- Quantify the health and economic benefits of interventions against pollution and balance these benefits against the costs of interventions.

(M A McTeer LLM); Institute for Health Metrics, Seattle, WA, USA (C J L Murray MD); Ministry of Environment, Ecology and Forests, Antananarivo, Madagascar (J D Ndahimananjara MD); Columbia Center for Children's Environmental Health, Department of Environmental Health Sciences (F Perera DrPH), and Department of Health Policy and Management (Prof A S Preker), Mailman School of Public Health, Columbia University, New York, NY, USA; UN International Resource Panel, Paris, France (J Potočnik PhD); SYSTEMIQ, London, UK (J Potočnik); Health Investment & Financing Corporation, New York, NY, USA (Prof A S Preker); Parliament of India, New Delhi, India (J Ramesh MS); Stockholm Resilience Centre, Stockholm University, Stockholm, Sweden (J Rockström PhD); Mexico City, Mexico (C Salinas PhD); Department of Biological Engineering and Department of Biology, Center for Environmental Health Sciences, Koch Institute for Integrative Cancer Research, Massachusetts Institute of Technology, Cambridge, MA, USA (Prof L D Samson PhD); Children's Health and Environment Program, Child Health Research Centre, University of Queensland, Brisbane, QLD, Australia (Prof P D Sly DSc); Environmental Health Sciences Division, School of Public Health, University of California, Berkeley, CA, USA (K R Smith PhD); Oxford Martin School, University of Oxford, Oxford, UK (A Steiner MA); Guarini Center on Environmental, Energy, and Land Use Law, New York University, New York, NY, USA (Prof R B Stewart LLB); Division of Extramural Research and Training, National Institute of Environmental Health Sciences, National Institutes of Health, Research Triangle Park, NC, USA (W A Suk PhD); Care and Public Health Research Institute, Maastricht University, Maastricht, the Netherlands (Prof C P van Schayck PhD); United Nations Industrial Development Organization, Vienna, Austria

(K Yumkella PhD); and School of Environment and Natural Resources, Renmin University of China, Beijing, China (Prof M Zhong PhD)

Correspondence to: Prof Philip J Landrigan, Arnhold Institute for Global Health, Icahn School of Medicine at Mount Sinai, New York, NY 10029, USA philip.landrigan@mssm.edu

Introduction

Pollution is one of the great existential challenges of the Anthropocene epoch. Like climate change, biodiversity loss, ocean acidification, desertification, and depletion of the world's fresh water supply, pollution endangers the stability of the Earth's support systems and threatens the continuing survival of human societies.[1] Pollution, especially pollution caused by industrial emissions, vehicular exhausts, and toxic chemicals, has increased sharply in the past 500 years, and the largest increases today are seen in low-income and middle-income countries. Yet despite its great and growing magnitude, industrial, vehicular, and chemical pollution in developing countries has been largely overlooked in international development and global health agendas, and programmes for pollution control have received little attention or resources from either international agencies or philanthropic donors. Pollution is now a substantial problem that endangers the health of billions, degrades the Earth's ecosystems, undermines the economic security of nations, and is responsible for an enormous global burden of disease, disability, and premature death.

Pollution is intimately linked to global climate change.[2,3] Fuel combustion—fossil fuel combustion in high-income and middle-income countries, and biomass burning in inefficient cookstoves, open fires, agricultural burns, forest burning,[4,5] and obsolete brick kilns in low-income countries—accounts for 85% of airborne particulate pollution and for almost all pollution by oxides of sulphur and nitrogen. Fuel combustion is the major source of greenhouse gases and short-lived climate pollutants that are the main anthropogenic drivers of global climate change (appendix pp 1–11).[6]

See Online for appendix

Pollution is very costly; it is responsible for productivity losses, health-care costs, and costs resulting from damages to ecosystems. But despite the great magnitude of these costs, they are largely invisible and often are not recognised as caused by pollution.[7] The productivity losses of pollution-related diseases are buried in labour statistics. The health-related costs of pollution are hidden in hospital budgets.[8] The result is that the full costs of pollution are not appreciated, are often not counted, and are not available to rebut one-sided, economically based arguments against pollution control.[7,9]

The nature of pollution is changing and, in many places around the world, it is worsening. These changes reflect increased energy consumption, the increased use of new materials and technologies, the rapid industrialisation of low-income and middle-income countries, and the global movement of populations from rural areas into cities. Household air and water pollution, the forms of pollution that were historically associated with profound poverty and traditional lifestyles, are slowly declining. However, ambient air pollution, chemical pollution, and soil pollution, are all increasing.[10,11] Key drivers of these types of pollution are: the uncontrolled growth of cities;[12] rising demands for energy; increasing mining, smelting, and deforestation; the global spread of toxic chemicals; progressively heavier applications of insecticides and herbicides; and an increasing use of petroleum-powered cars, trucks, and buses. Increases in ambient air, soil, and chemical pollution over the past 500 years can be directly attributed to the currently prevalent, linear, take-make-use-dispose economic paradigm—termed by Pope Francis "the throwaway culture"[13]—in which natural resources and human capital are viewed as abundant and expendable, and the consequences of their reckless exploitation are given little heed.[14,15] This economic paradigm focuses single-mindedly on GDP[14] and is ultimately unsustainable: this model fails to link the economic development of human societies to social justice or to maintenance of the Earth's resources.[1,2,15]

Scientific understanding of pollution and its effects on health have greatly advanced.[16,17] New technologies, including satellite imaging,[18] have enhanced the ability to map pollution, measure pollution levels remotely, identify sources of pollution, and track temporal trends.[17] Sophisticated chemical analyses have refined understanding of the composition of pollution and elucidated links between pollution and disease.[19] Large prospective, multi-year epidemiological studies, beginning with the studies by Pope and colleagues[20] in Utah and the Harvard Six-Cities study,[21] have showed that pollution is associated with a much wider range of diseases, particularly non-communicable diseases, than was previously recognised. Pollution is now understood to be an important causative agent of many non-communicable diseases including asthma, cancer, neurodevelopmental disorders, and birth defects in children (appendix p 11); and heart disease, stroke, chronic obstructive pulmonary disease, and cancer in adults.[22–34] In the absence of aggressive intervention, the number of deaths due to ambient air pollution are on track to increase by more than 50% by 2050.[35]

Despite these advances in knowledge, there are still many gaps in information about pollution and its effects on health. These gaps include an absence of information in many countries on pollution levels and the prevalence of pollution-related disease; poor knowledge of the toxic effects of many chemicals in common use, especially newer classes of chemicals;[36,37] incomplete information on the scope of exposures and burden of disease associated with toxic exposures at contaminated sites;[38] and inadequate information on the possible delayed effects of toxic exposures sustained in early life.[39] Also unknown is the exact shape of the dose-response functions used to estimate the relative risk of disease associated with pollution. In the case of fine-particulate air pollution, for example, the shape of the exposure–response association at both very low and very high exposure levels and the assumptions that underlie the integrated exposure–response function[40] used to estimate the relative risks of fine particulate ($PM_{2.5}$) exposure in

both the Global Burden of Disease (GBD) study[41,42] and WHO analyses are not precisely known.[23]

The good news is that, despite the great magnitude of pollution and current gaps in knowledge about its effects on human health and the environment, pollution can be prevented. Pollution is not the inevitable consequence of economic development. High-income and some middle-income countries have enacted legislation and issued regulations that build on new scientific knowledge about pollution and its health effects. These laws and regulations are based on the polluter-pays principle; they mandate clean air and clean water and set standards at levels that prevent disease, have established policies for chemical safety, have banned certain hazardous pollutants such as lead, asbestos, and DDT, and have effected clean-up of the worst of the hazardous waste sites.

Many of these proven, cost-effective control strategies are now ready to be exported and adapted for use by cities and countries at every level of income. Their application in carefully planned and well resourced campaigns can enable developing and industrialising countries to avoid many of the harmful consequences of pollution—to leapfrog over the worst of the human and ecological disasters that have plagued industrial development in the past—and to improve human health and wellbeing.

Contrary to the oft-repeated claim that pollution control stifles economic growth, pollution prevention has, in fact, been shown repeatedly to be highly cost-effective. In the USA, for example, concentrations of six common air pollutants have been reduced by about 70% since passage of the Clean Air Act in 1970 and, in the same time period, GDP has increased by nearly 250% (figure 1).[43] Every dollar invested in control of ambient air pollution in the USA not only improves health,[44] but also is estimated to yield US$30 in economic benefits (95% CI $4–88).[45]

Another example of the economic benefits of addressing pollution is seen in the consequences of removing lead from gasoline in the USA. This intervention began in 1975 and, within a decade, had reduced the mean blood concentration of lead in the population by more than 90% (figure 2), almost eliminated childhood lead poisoning, and increased the cognitive capacity of all American children born since 1980 by 2–5 IQ points.[46] This gain in intelligence has increased national economic productivity and will yield an economic benefit of US$200 billion (range $110 billion–300 billion) over the lifetimes of each annual cohort of children born since 1980,[46] an aggregate benefit to-date of over $6 trillion.[47,48]

Yet, despite its harmful effects on human health, the economy, and the environment and, notwithstanding the clear evidence that it can be cost-effectively controlled, pollution (especially industrial, vehicular, and chemical pollution in low-income and middle-income countries) has been largely neglected.[49,50] Work to control the biological contamination of drinking water[51–54] and to curb

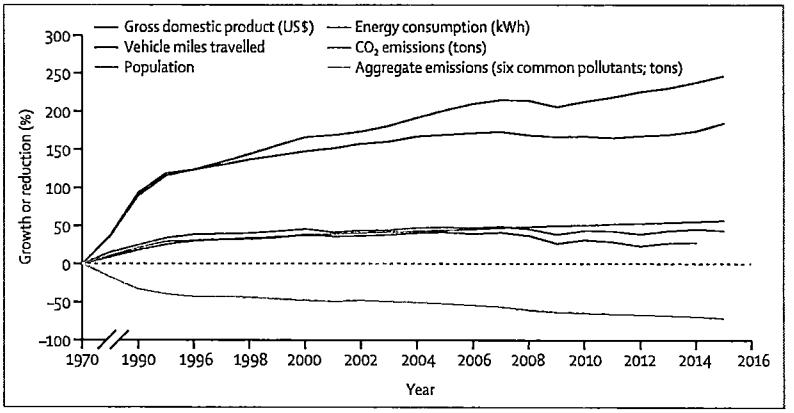

Figure 1: **Pollution, population, and GDP in the USA, 1970–2015**
Figure taken from reference 43, with permission.

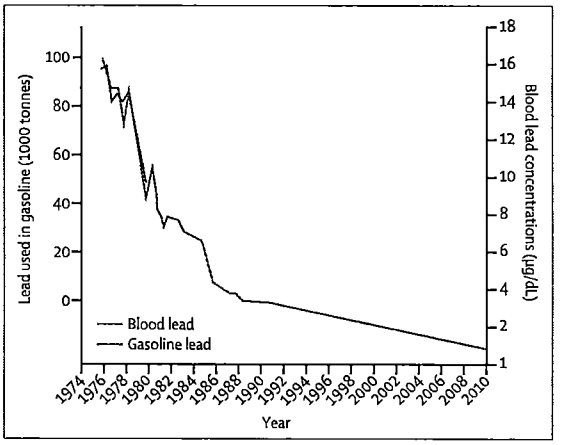

Figure 2: **Correlation between population mean blood concentration of lead and lead use in gasoline in the USA, 1974–91**
Taken from data that is publicly available from the Centers for Disease Control.

household air pollution produced by poorly ventilated cookstoves[55–57] has occurred over many years and those efforts, along with new vaccines, antibiotics, and treatment protocols, have contributed to promising reductions in the morbidity and mortality associated with the traditional forms of pollution.[58–60] However, the burgeoning problems of air, water, and soil pollution produced by modern industry, electricity generation, mining, smelting, petroleum-powered motor vehicles, and chemical and pesticide releases in low-income and middle-income countries have received almost no international attention or resources.[49,50] Budgets for foreign aid from the European Commission, the US Agency for International Development, and most bilateral development agencies, private philanthropists, and major foundations have not included substantive funding for control of industrial, mining and transport-related pollution.[50,61] The national and local resources directed toward the study and control of industrial, chemical, and vehicular pollution and the diseases that they cause within cities and countries are

For the Global Alliance for Clean Cookstoves see http://cleancookstoves.org/

For the US Agency for International Development see https://explorer.usaid.gov/

often meagre.[62] Lastly, interventions against pollution are barely mentioned in the Global Action Plan for the Prevention and Control of Non-Communicable Diseases,[63] which is a major missed opportunity.

Several factors have contributed to the neglect of pollution. A persistent impediment has been the flawed conventional wisdom that pollution and disease are the unavoidable consequences of economic development, the so-called "environmental Kuznets hypothesis" (panel 1).[64–73] This Commission vigorously challenges that claim as a flawed and obsolete notion formulated decades ago when populations and urban centres were much smaller than they are today, the nature, sources, and health effects of pollution were very different, and cleaner fuels and modern production technologies were not yet available.

Fragmentation of the agendas for environmental health and pollution control is another factor that has contributed to neglect of pollution. In many countries, responsibility for pollution-related disease falls between ministries of health and ministries for the environment, and too often belongs to neither. Air, water, soil, and chemical pollution are each regulated by different agencies and studied by different research groups. The consequence is that the full scale of pollution and its contribution to the global burden of disease are not recognised. The separation of public health from environmental protection has also slowed the growth of research on pollution-related disease, led to the virtual elimination of coursework in environmental health science from the curricula of most medical and nursing schools, and impeded the development of environmental health policy.

In the international development agenda, neglect of the modern forms of pollution can be traced to the historical origins of overseas development assistance programmes whose goals, when they were launched at the end of World War 2, were to reduce poverty, improve maternal and child health, and combat infectious diseases in an era when much of the world was devastated and more than 50% of countries were classified as low-income.[49,50] At that time, the predominant health problems of the developing world were infectious diseases and maternal and child mortality, and many overseas development programmes have been highly successful and have contributed to the control of these problems.[74] However, these programmes were never intended to address the more modern forms of pollution.

Finally, the opposition of powerful vested interests has been a perennial barrier to control of pollution, especially industrial, vehicular, and chemical pollution. These entrenched interests, which often exert disproportionate influence on government policy, impugn the science linking pollution to disease, manufacture doubt about the effectiveness of interventions, and paralyse governmental efforts to establish standards, impose pollution taxes, and enforce laws and regulations.[75] These interests act both within countries and internationally.

The aim of this *Lancet* Commission on pollution and health is to end the neglect of pollution, especially of the modern forms of pollution, in low-income and middle-income countries, to focus the world's attention onto the silent threat of pollution-related disease, and to mobilise the national and international resources and the political will needed to effectively confront pollution.

To accomplish this aim and to mobilise the resources that will be needed to control pollution around the world, we have reviewed data on the health effects and economic costs of all forms of pollution: pollution of air, water, and soil, pollution in the workplace, and pollution by toxic chemicals (appendix p 15). We have also examined the links between pollution and poverty, injustice, and inequality. Finally, this Commission presents examples of cost-effective, proven strategies that can be adapted by cities and countries at every level of income to control pollution and prevent disease (appendix pp 63–107).

The work of this Commission on pollution and health builds upon work undertaken in the past decade by international organisations and bi-national funders to address the challenges of modern-day pollution, such as the World Bank Water and Sanitation Programme.[76,77] WHO has established a Department of Public Health

For the World Bank Water and Sanitation Programme see http://www.wsp.org/

Panel 1: The environmental Kuznets curve

The Kuznets curve, developed by economist Simon Kuznets (1901–85), describes the association between economic inequality and per capita income over the course of economic development.[64] This curve illustrates Kuznets' hypothesis that, as a society develops from a primarily agrarian to an urban, industrialised economy, market forces first increase and then, at a so-called "turning point" of per-capita income, decreases the overall degree of economic inequality in the society. These trends are shown as an inverted U-shaped curve.[65]

The Kuznets hypothesis has been extended to environmental economics. Here, it is postulated that pollution and environmental degradation must increase in early stage economic development, that pollution will continue to increase up to a threshold of per-capita income, and that pollution will then decrease as the economy continues to grow. The postulated result is that high income and economic growth eventually lead to environmental improvements. This extension of Kuznets' hypothesis has become entrenched as conventional wisdom in global environmental policy.[66,67]

Despite the great certitude with which the environmental Kuznets hypothesis is sometimes promulgated, empirical and theoretical research finds that the historical evidence in support of this hypothesis is uneven, and that the underlying statistical methods are weak.[70–72] Additional shortcomings are that the environmental Kuznets hypothesis fails to consider the movement of polluting industries from high-income to low-income and middle-income countries,[68] does not consider the health and environmental effects of modern classes of pollutants such as chemical carcinogens, neurotoxicants, and endocrine-disrupting chemicals,[69–73] and does not consider the potential benefits to human health and the environment of newer, non-polluting energy sources.

The conclusions from this analysis are that pollution is not the unavoidable consequence of economic development, and that it is much more important to formulate sound laws, policies, and regulations to control pollution than to wait for an economy to reach a magical tipping point that will solve the problems of environmental degradation and pollution-related disease. The goal of this Commission is to catalyse the formulation of such policies.

and the Environment, which has become a global leader in documenting the effects of environmental threats to children's health.[78,79] The UN Development Programme has taken on many components of the pollution control agenda. The World Bank financially supports several projects to control pollution. The UN Environment Programme also supports several programmes to control chemical pollution, some in partnership with WHO, and supports and oversees international agreements limiting the manufacture, environmental release, and global transport of persistent pollutants,[80] pesticides, hazardous waste, and mercury. The Strategic Approach to International Chemicals Management, housed within the UN Environment Programme, provides a platform for discussion on control of chemical pollution and toxic waste among a broad range of stakeholders (appendix pp 13–14). These global advances in controlling ambient air, chemical, and vehicular pollution are welcome[81] and have produced important gains, such as phasing lead out from gasoline, endorsed by the Partnership for clean fuels and vehicles, incorporating air pollution into the health agenda,[82] establishing programmes to control the addition of lead to paint,[83] and creating a pollution-focused trust fund within the World Bank.

Pollution defined

This Commission defines pollution as unwanted, often dangerous, material that is introduced into the Earth's environment as the result of human activity, that threatens human health, and that harms ecosystems; this definition is based on a definition of pollution developed by the European Union.[84]

To provide a framework for organising scientific knowledge about pollution and its effects on human health and to help focus pollution-related research, this Commission has developed the concept of the pollutome (figure 3). The pollutome is defined as the totality of all forms of pollution that have the potential to harm human health. The pollutome can be viewed as a fully contained (nested) subset of the exposome.[85,86] This model includes pollutant exposures during gestation, infancy, childhood, adolescence, adult life (including occupational exposures), and old age.

Because knowledge about the health effects of pollution varies by pollution type and ranges from the well characterised and quantified to the still emerging, we have divided the pollutome into three zones.

Zone 1 includes well established pollution–disease pairs, for which there are robust estimates of their contributions to the global burden of disease. The associations between ambient air pollution and non-communicable disease are the prime example.[23]

Zone 2 includes the emerging effects of known pollutants, where evidence of causation is building, but associations between exposures and disease are not yet fully characterised and the burden of disease has not yet been quantified. Examples include associations between $PM_{2.5}$ air pollution and diabetes,[24–26] pre-term birth,[27–29] and diseases of the central nervous system, including autism in children,[3,30–32] and dementia in the elderly.[29,33] Soil pollution by heavy metals and toxic chemicals at contaminated industrial and mining sites provides another example of a potentially important, but not yet fully characterised or quantified source of pollution-related disease.[38,87]

Zone 3 includes new and emerging pollutants,[36,37] most of them chemical pollutants whose effects on human health are only beginning to be recognised and are not yet quantified. Several of these chemicals have become widely disseminated in the environment, and many are detectable in the bodies of most persons examined in national surveys, such as the Centers for Disease Control's national biomonitoring programme in the United States. At least some of these chemical pollutants appear to have potential to cause global epidemics of disease, disability, and death. This zone includes developmental neurotoxicants;[37,88] endocrine disruptors;[89–92] new classes of pesticides such as the neonicotinoids;[93] chemical herbicides such as glyphosate and nano-particles; and pharmaceutical wastes.[94–96] These emerging chemical pollutants are discussed in detail in the appendix of this report (pp 2–11).

The list of diseases attributed to pollution will probably continue to expand as the environmental distributions and health effects of newer chemical pollutants are better defined and new exposure–disease associations are discovered. The health effects of pollution that are currently recognised and quantified could thus be the tip of a much larger iceberg.[88] As more research becomes available, some pollution–disease pairs that are currently placed in zones 2 and 3 of the pollutome could move up to

For the **Strategic Approach to International Chemicals Management** see http://www.saicm.org/

For the **Centers for Disease Control and Prevention national biomonitoring programme** see https://www.cdc.gov/biomonitoring/

For the **Partnership for clean fuels and vehicles** see http://www.unep.org/transport/pcfv/

For the **World Bank pollution management and environmental health programme** see http://www.worldbank.org/en/programs/pollution-management-and-environmental-health-program

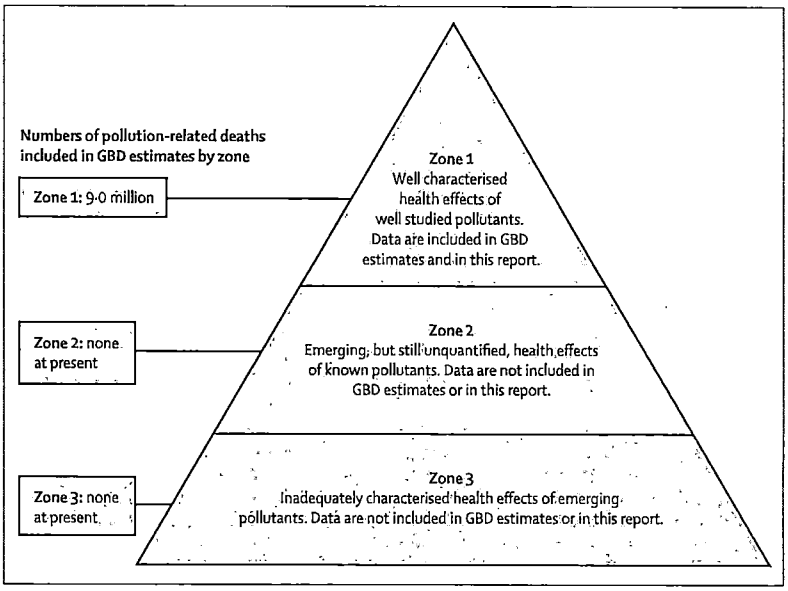

Figure 3: The pollutome

zone 1 and be included in future estimates of the global burden of disease. The numbers of deaths attributable to the forms of pollution included in zones 2 and 3 are unknown.

This Commission's work has been informed by the work of previous *Lancet* Commissions and Series, notably the Commission on Investing in Health,[72] the Commission on the Political Origins of Health Inequity,[73] the Commission on Health and Climate Change,[97] and the Series on Public Health Benefits of Climate Change Mitigation Policies.[98] This Commission's deliberations were guided particularly closely by the findings of The Rockefeller Foundation-*Lancet* Commission on Planetary Health[15] whose 2015 report described how human activity is changing the global environment, increasing risk of disease, and threatening the conditions that, ultimately, sustain all life on Earth.

This Commission was guided further by influential reports from international agencies, among them the 2016 report from WHO,[99] Preventing Disease through Health Environments, the World Bank's Shock Waves report[100] on climate change and global poverty, the World Bank's report,[77] Clean Air and Healthy Lungs, and the United Nations Environment report,[101] Costs of Inaction on the Sound Management of Chemicals.

This report is organised into five Sections. Section 1 synthesises information on the burden of disease attributable to pollution using data from the GBD 2015 Study[41,42] coordinated by the Institute for Health Metrics and Evaluation, and supplemented by data from WHO[99,102] and from Pure Earth.[38] Section 2 examines data on the economic costs of pollution and presents a detailed analysis of the economic losses that result from pollution-related disease. Section 3 examines the links between pollution, disease, and poverty and documents the marked inequities that characterise the global distribution of pollution and pollution-related disease and the disproportionate effects of pollution on children, the poor, the elderly, and other vulnerable populations. Section 4 presents pathways and priorities, case studies, and proven interventions that can be adopted and deployed to control pollution, prevent disease, and advance economic development. Section 5 outlines the Commission's plans for future initiatives.

Sustainable long-term control of pollution will require that societies at every level of income move away from the prevalent resource-intensive, and inherently wasteful, linear take-make-use-dispose economic paradigm, towards a new paradigm rooted in the concept of the circular economy (panel 2).[15,103,104] In a circular economy, pollution is reduced through the creation of durable, long-lasting products, the reduction of waste by large-scale recycling, reuse, and repair, the removal of distorting subsidies, the replacement of hazardous materials with safer alternatives, and strict enforcement of pollution taxes.[105] A circular economy conserves and increases resources, rather than taking and depleting them. This societal transition is essential for promoting smart, sustainable, and inclusive growth that reduces pollution, promotes health, and prevents disease.[104]

Panel 2: Circular economy

A circular economy is an economic model that decouples development from the consumption of non-renewable resources and minimises the generation of pollution and other forms of waste by recycling and reuse.[104] In a fully circular economy, the only new inputs are renewable materials, and all non-renewable materials are recycled. The underlying assumption is that waste is an inherent inefficiency, a loss of materials from the system, and thus a cost.[104] Transition towards a circular economy will reduce pollution-related disease and improve health.

The three core principles of the circular economy are preservation of natural capital by reducing use of non-renewable resources and ecosystem management; optimisation of resource yields by circulating products and materials so that they are shared and their lifecycles extended; and fostering system effectiveness by designing out pollution, greenhouse gas emissions, and toxic materials that damage health.

The steps needed for transition towards a circular economy include large-scale transition to non-polluting sources of energy (wind, solar, and tidal), the production of durable products that require lower quantities of materials and less energy to manufacture than those being produced at present; incentivisation of recycling, re-use, and repair; and replacement of hazardous materials with safer alternatives.[15]

Limitations of the Commission

The Commission's economic analysis does not include information about the costs of environmental damage caused by pollution. The Commission recognises that the ecological damages due to pollution are substantial, but considered analyses of the costs of these damages to fall outside of the scope of our work.

Levels of pollution are changing and pollution caused by industrial, vehicular, and chemical emissions is increasing in many rapidly developing countries, but the Commission's analysis is based on data from the 2015 Global Burden of Disease study, information that is now 2 years old.

Section 1: The burden of disease attributable to pollution

In this Section, we review data for the global burden of disease and death attributable to pollution.[23,38,42,99,106]

Methods

This review of the burden of disease and premature death due to pollution is based on a method for assessing disease burden that was developed in the 1980s by

WHO.[107,108] The core of this approach is the disability-adjusted life-year (DALY) concept, a summary metric of population health that combines information on mortality and disease into a single number to represent the health of a population, thus permitting comparisons of disease burden between countries, between diseases, and over time. The DALY method is at the core of the GBD project, a multinational study initiated by WHO in partnership with the World Bank and the Harvard School of Public Health,[108] and sustained today by WHO[102] and the Institute for Health Metrics and Evaluation.[41,42]

To examine the global burden of disease attributable to pollution risk factors, this Commission has relied principally on the 2015 estimates from the GBD study,[41,42,106] coordinated by the Institute for Health Metrics and Evaluation. We also examine data from the 2012 WHO analysis[99,102,109,110] of the global burden of disease caused by living and working in unhealthy environments.

Following the standard conservative practice of the GBD study[42,106] and WHO,[99] this Commission has restricted its review to combinations of pollution risk factors and disease for which there is convincing or probable evidence of causal association. For this reason, numbers presented are likely to be underestimates of the full burden of disease attributable to the pollutome (figure 3).

In reviewing data on the burden of disease attributable to soil pollution caused by toxic chemicals and heavy metals at contaminated sites, this Commission has relied on information provided by the Blacksmith Institute/Pure Earth Toxic Sites Identification programme.[38] This programme obtains data on pollution caused by chemicals and metals at contaminated sites through field studies that use a protocol adapted from a US Environmental Protection Agency assessment tool.[111] Two particularly common types of contaminated sites are used lead-acid battery recycling sites, where lead is the principal pollutant, and artisanal and small-scale gold mining sites, where the principal pollutant is elemental mercury (which is used to extract gold from ore). We used the methods of Ericson and colleagues[111] to assess the burden of disease associated with lead-acid battery recycling sites, and the methods and data of Steckling and colleagues[112,113] to assess the burden of disease associated with gold mining sites[114–116] These methods are described in detail in the appendix (pp 16–19).

The pollution risk factors examined by the Commission were: (1) air pollution: household air pollution, ambient fine particulate pollution ($PM_{2.5}$), and tropospheric ozone pollution; (2) water pollution: unsafe sanitation, and unsafe water sources; (3) soil, chemical, and heavy metal pollution: lead (including contaminated sites polluted by lead from battery recycling operations), and mercury from gold mining; and (4) occupational pollution: occupational carcinogens, and occupational particulates, gases, and fumes.

In reviewing disease burden in relation to national income, we have relied on the 2015 World Bank income classifications (high, upper middle, lower middle, and low). In reviewing disease burden in relation to geographical region, we have grouped countries using the regional groupings defined by WHO (Africa, eastern Mediterranean, Europe, Americas, southeast Asia, and western Pacific).

To examine temporal trends in the global burden of disease that are attributable to different forms of pollution, we have divided pollution into two broad categories: pollution linked to poverty and pollution linked to industrial development. Pollution linked to poverty includes household air pollution, unsafe water sources, and inadequate sanitation, the forms of pollution associated with profound poverty and traditional lifestyles in low-income and middle-income countries. Pollution linked to industrial development includes pollution produced by industrial emissions, vehicular exhausts, and chemical releases, and includes ambient fine particulate ($PM_{2.5}$) pollution, tropospheric ozone pollution, toxic occupational exposures, and soil pollution caused by heavy metals and toxic chemicals, including lead.

Main findings

The GBD study[42] estimates that pollution-related disease was responsible for 9 million premature deaths in 2015—16% of total global mortality (table 1).[42,99,102] The GBD study also estimates that disease caused by all forms of pollution was responsible for 268 million DALYs—254 million years of life lost and 14 million years lived with disability.[106] This information is available by country and region and is presented in the appendix.

WHO estimates that, in 2012, unhealthy environments were responsible for 12·6 million deaths worldwide—23% of total global mortality—and for 26% of deaths in children younger than 5 years.[99,102,109,110]

The most important finding to be drawn from these two analyses is that both the GBD study and WHO find that pollution is a major cause of disease, disability, and premature death. The GBD study reports that pollution was responsible for an estimated 9·0 million deaths in 2015, whereas the WHO analysis concludes that living in unhealthy environments was responsible for 12·6 million deaths in 2012.

The difference between these two estimates of total mortality attributable to environmental factors mainly reflects differing definitions of environment. This Commission focuses strictly on pollution-related disease, as defined above. By contrast, the WHO definition of environment is broader and encompasses several risk factors that were not included in this Commission's analysis, including road accidents, ultraviolet and ionising radiation, noise, electromagnetic fields, occupational psychosocial risks, built environments, agricultural methods, and man-made climate and ecosystem change. Risk factors that were included

	GBD study best estimate (95% CI)	WHO best estimate (95% CI)
Air (total)	6·5 (5·7–7·3)	6·5 (5·4–7·4)
Household air	2·9 (2·2–3·6)	4·3 (3·7–4·8)
Ambient particulate	4·2 (3·7–4·8)	3·0 (3·7–4·8)
Ambient ozone	0·3 (0·1–0·4)	..
Water (total)	1·8 (1·4–2·2)	0·8 (0·7–1·0)
Unsafe sanitation	0·8 (0·7–0·9)	0·3 (0·1–0·4)
Unsafe source	1·3 (1·0–1·4)	0·5 (0·2–0·7)
Occupational	0·8 (0·8–0·9)	0·4 (0·3–0·4)
Carcinogens	0·5 (0·5–0·5)	0·1 (0·1–0·1)
Particulates	0·4 (0·3–0·4)	0·2 (0·2–0·3)
Soil, heavy metals, and chemicals	0·5 (0·2–0·8)	0·7 (0·2–0·8)
Lead	0·5 (0·2–0·8)	0·7 (0·2–0·8)
Total	9·0	8·4

Note that the totals for air pollution, water pollution, and all pollution are less than the arithmetic sum of the individual risk factors within each of these categories because these have overlapping contributions—eg, household air pollution also contributes to ambient air pollution and vice versa.

Table 1: **Global estimated deaths (millions) due to pollution risk factors from the Global Burden of Disease study (GBD; 2015)[42] versus WHO data (2012)[99,101]**

in the WHO analysis and not in this Commission account for more than 3 million deaths each year, thus explaining most of the apparent discrepancy between the two estimates (panel 3).[117–120]

Some specific differences are seen between the two sets of estimates (figure 4).[42,99] For example, the GBD study estimates that 4·2 million deaths in 2015 were because of ambient air pollution, whereas WHO attributes 3·7 million deaths in 2012 to this risk factor. The two analyses relied on similar approaches to comparative risk assessment, on the same sources of exposure data, and on the same integrated exposure–response functions[40] but, in 2014, the GBD study made changes to their computational methodology,[42] which appears to account for most of the divergence.

The GBD study estimated that 2·9 million deaths in 2015 were associated with household air pollution, whereas WHO estimated 4·3 million related deaths in 2012. This difference can partly be explained by different approaches in quantifying exposure–outcome associations. The GBD study relied on the integrated exposure–response curve[40] to provide evidence for the effect size of non-communicable diseases, whereas WHO adapted relative risks for certain non-communicable diseases based on epidemiological evidence. Additionally, the GBD study has expanded data sources for personal exposure values for women, men, and children in the past 2 years.

The GBD study estimated that, in 2015, 1·8 million deaths resulted from diseases related to water pollution, whereas WHO estimated 0·84 million related deaths in 2012. This divergence appears largely to reflect differing definitions of access to safe water. The GBD study considers access to safe water at both the water's source and at the point of use, whereas WHO only considers access to an improved water source.

Diseases caused by all forms of pollution were responsible for an estimated 9 million deaths in 2015.[41] Pollution is thus responsible for more deaths than a high-sodium diet (4·1 million), obesity (4·0 million), alcohol (2·3 million), road accidents (1·4 million), or child and maternal malnutrition (1·4 million). Pollution was also responsible for three times as many deaths as AIDS, tuberculosis, and malaria combined (figure 5)[41] and for nearly 15 times as many deaths as war and all forms of violence.[41] Only dietary risk factors (all combined) (12·1 million) and hypertension (10·7 million) caused more deaths than pollution; however, the Commission notes that approximately 2·5% of deaths due to hypertension are attributable to lead.

Pollution and non-communicable diseases

Non-communicable diseases account for most of the total burden of disease due to pollution—approximately 71%.[41] In 2015, all forms of pollution combined were responsible for 21% of all deaths from cardiovascular disease, 26% of deaths due to ischaemic heart disease, 23% of deaths due to stroke, 51% of deaths due to chronic obstructive pulmonary disease, and 43% of deaths due to lung cancer (figure 6).[42]

The relative risks of all non-communicable diseases associated with pollution increase as exposure to pollution increases. An integrated exposure–response function has been developed to describe these associations, and the health effects of air pollution are quantitatively consistent with those of tobacco smoke when their relative risks are plotted against a common metric of exposure to airborne fine particulates.[121]

The sources and nature of pollution change as countries develop and industrialise (figure 7).[10,42] An unsafe water source, unsafe sanitation, and household air pollution are considered to be forms of pollution linked to poverty and the early stages of industrial development. Airborne fine particulate pollution, tropospheric ozone pollution, occupational chemical pollution, and soil pollution by heavy metals and chemicals (including lead) are considered to be forms of pollution linked to industrial development.

Changes to the distribution of pollution-related diseases occur in response to the changes that accompany development.[11] Thus deaths from pneumonia and diarrhoeal diseases—the diseases associated with household air pollution, water pollution, and poor sanitation—are slowly declining worldwide, although they still kill millions of people, particularly children in poor countries. These declines reflect reductions in the forms of pollution associated with traditional lifestyles in low-income and middle-income countries, and the advent of new vaccines such as the pneumococcal vaccine and the rotavirus vaccine;[59] new approaches to paediatric

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Panel 3: WHO's programme on pollution and health

WHO has, for several decades, been a leader in conducting crucial evaluations of the health effects of pollution, and these assessments provide the scientific basis for pollution control policies in many countries. WHO is also a global leader in providing guidelines and in coordinating health-focused partnerships for pollution control.

WHO is now further expanding this work through the framework of the Sustainable Development Goals (SDGs). WHO is the custodian agency that monitors progress towards six SDG targets; this monitoring includes tracking several targets measuring the environmental health-related burden of disease within SDG 3. The following are examples of this work:

Ambient air pollution

- WHO has periodically reviewed the international literature on air pollution and developed Global Air Quality Guidelines.[117] These are the primary reference points for air pollution standards worldwide. The latest version was published in 2006,[117] and a committee has been formed to create an updated version in 2018.
- WHO hosts one of the largest databases of ambient air pollution measurements in cities. Currently, the publicly available WHO Global Urban Ambient Air Pollution Database contains air quality measurements from 3000 cities, representing 103 countries. In the past 2 years alone, the database has nearly doubled in size, with more cities now measuring air pollution concentrations and recognising the associated health effects than ever before. This database also provides inputs to the integrated models that use satellite remote-sensing and chemical transport models to estimate ambient air pollution exposure globally, including estimates for regions without any ground-level monitoring (eg, smaller cities and rural areas). The Global Urban Ambient Air Pollution Database also supports monitoring of urban air quality for SDG 11 indicator 11·6: "to reduce the adverse per capita environmental impact of cities, including by paying special attention to air quality and municipal and other waste management".[118]

Household air pollution

- WHO has developed guidelines[119] for indoor air quality regarding household fuel combustion, which clarified the enormous health risks of burning kerosene, coal, and wood in the home, and has provided emission standards for home energy equipment used in cooking, heating, and lighting. This work filled a gap in health guidance for household energy interventions and is increasingly being adopted by development partners investing in improving access to energy in the homes of the poor worldwide.
- WHO has developed several tools and training programmes to build the capacity and understanding of countries and actors working in different sectors to effectively address household energy as a health risk. WHO is currently developing a Clean Household Energy Solution Toolkit (CHEST) to provide the guidance and tools necessary for countries to implement the WHO Guidelines for Indoor Air Quality: Household Fuel Combustion.[119]
- Monitoring access to clean energy in the home is led by WHO in close cooperation with partners performing household surveys (UNICEF, USAID, and the World Bank). The associated indicator, 7·1·2—the "proportion of population with primary reliance on clean fuels and technology"—is part of the Global Tracking Framework of Sustainable Energy for All and is used to show progress towards SDG 7, which follows WHO guidelines criteria.

Climate, pollution, and health

- WHO, the Climate and Clean Air Coalition, and UN Environment Programme have joined forces in the BreatheLife campaign to address the associated crises of air pollution and climate change. The campaign was announced in July, 2016, and launched at Habitat III in Quito, Ecuador.

Urban health

- WHO has established the Urban Health Initiative to reduce deaths and diseases associated with air and climate pollutants in cities, while enhancing health benefits from the policies and measures used to tackle climate pollution.

Water and sanitation

- WHO has produced authoritative guidelines and technical assistance on management of water quality, sanitation, and wastewater, and health for decades. Along with UNICEF, WHO is responsible for tracking the extent of human exposure to poor water, inadequate sanitation, and poor hygiene.

Toxic chemicals

- WHO is the leading international agency for chemical safety through its Intergovernmental Panel on Chemical Safety, which sets guidelines for dozens of commonly used chemicals. The importance of chemicals management is reflected by SDG target 3·9 on reducing deaths and illness from hazardous chemicals, and links to target 12·4 on the sound management of chemicals and wastes. Achievement of sound chemicals management requires a multisector, multistakeholder approach. To advance this work, the 2017 World Health Assembly approved a Chemicals Road Map to enhance the engagement of the health sector in the management of international chemicals.

For the WHO Global Urban Ambient Air Pollution Database see www.who.int/phe/health_topics/outdoorair/databases/cities

For the WHO Chemicals Road Map see www.who.int/ipcs/saicm/roadmap

(Continues on next page)

(Panel 3 continued from previous page)

Mercury

- WHO is supporting implementation of the Minamata Convention on Mercury and has developed guidance for phasing out mercury-containing instruments in the health sector.[120] Urgent attention by health departments and ministries is needed to address the phase out of import, export, and manufacture of mercury thermometers, sphygmomanometers, and other mercury-containing instruments in health care.

Cancer

- WHO's International Agency for Research on Cancer (IARC) has the responsibility of determining whether chemicals are human carcinogens and conducts a range of research on cancer worldwide. IARC provides evidence-based guidance on cancer control to countries around the world.

For the Health Effects Institute special report on the state of global air see https://www.stateofglobalair.org

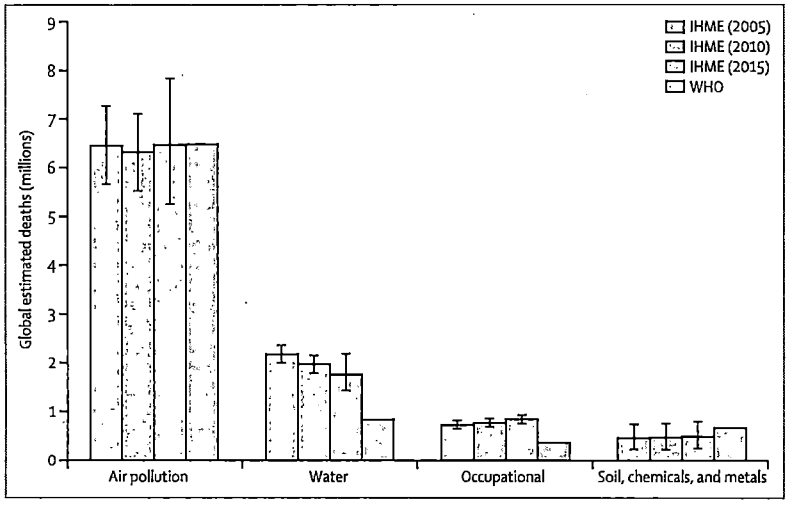

Figure 4: Global estimated deaths (millions) by pollution risk factor, 2005–15
Using data from the GBD study[41] and WHO.[99] IHME=Institute for Health Metrics and Evaluation.

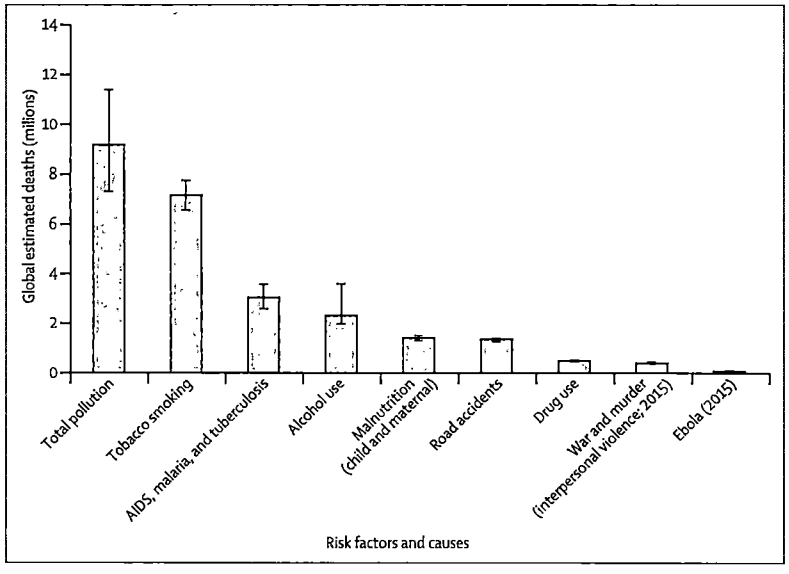

Figure 5: Global estimated deaths by major risk factor and cause, 2015
Using data from the GBD Study, 2016.[41]

therapy such as oral rehydration therapy;[60] and improved nutrition of young children and pregnant women.[61]

By contrast, the numbers of deaths caused by ambient air, chemical, and soil pollution—the forms of pollution associated with modern industrial and urban development—are increasing. The number of deaths attributable to $PM_{2.5}$ air pollution is estimated to have risen from 3·5 million (95% CI 3·0 million–4·0 million) in 1990 to 4·2 million (3·7 million–4·8 million) in 2015, a 20% increase. Among the world's 10 most populous countries in 2015, the largest increases in numbers of pollution-related deaths were seen in India and Bangladesh, as reported by the Health Effects Institute. The increase in the absolute number of deaths and DALYs attributable to pollution reflects an increased population size, an ageing population, and increased levels of air pollution in low-income and middle-income countries.[23]

An analysis of future trends in mortality associated with ambient $PM_{2.5}$ air pollution finds that, under a "business as usual scenario", in which it is assumed that no new pollution controls will be put into place, the numbers of deaths due to pollution will rise over the next three decades, with sharpest increases in the cities of south and east Asia.[35,121] These trends are projected to produce a more than 50% increase in mortality related to ambient air pollution, from 4·2 million deaths in 2015 to 6·6 million deaths in 2050 (95% CI 3·4 million–9·3 million).[35,122] These projections are corroborated by an analysis[107] of the health effects of coal combustion in China. Population ageing are major contributors to these projections of growth and absolute increased numbers of deaths from pollution-related disease.

A second analysis[123] examining the potential benefits of reducing $PM_{2.5}$ pollution projects that aggressive controls could avoid 23% of current deaths related to air pollution. However, because of population ageing and consequent increases in age-related mortality from cardiovascular disease, chronic obstructive pulmonary disease, and lung cancer, and also because the exposure–response association between $PM_{2.5}$ pollution and non-communicable diseases is relatively strong at lower levels of exposure but weaker at higher levels, Apte and colleagues[124] note that it will be easier to achieve reductions in mortality in less heavily polluted areas of western

Europe and North America than in heavily polluted regions in Asia.

Geography of pollution

In 2015, the greatest numbers of deaths due to pollution occurred in southeast Asia (3·2 million deaths) and the western Pacific (2·2 million deaths; figure 8).[42] In this definition, southeast Asia includes India and the western Pacific region includes China. The highest population-based estimates of premature death and disease due to pollution are seen in the low-income countries of sub-Saharan Africa.[42]

Pollution and poverty

92% of all pollution-related mortality is seen in low-income and middle-income countries, with the greatest numbers of deaths from pollution-related disease occurring in rapidly developing and industrialising lower-middle-income countries (figure 9).[42] In the most severely affected countries, pollution is responsible for more than one in four deaths.[42] In countries at every level of income, the health effects of pollution are most frequent and severe among the poor and the marginalised. Further discussion of the links between pollution, disease, and poverty is presented in section 3 of this report.

Disease and death due to pollution occur most frequently in the very young and the very old. Deaths due to all forms of pollution show a peak among children younger than 5 years of age, but most pollution-related deaths occur among adults older than 60 years of age (figure 10).[42] By contrast, DALYs resulting from pollution-related disease are highly concentrated among infants and young children, reflecting the many years of life lost with each death and case of disabling disease of a child (figure 11).[42]

Air pollution

Two types of air pollution—household air pollution and ambient air pollution—and two airborne pollutants—fine particulates and ozone—are considered in this Commission.[23] Pollution caused by oxides of nitrogen and by some short-lived climate pollutants is not fully accounted for in this Commission because the burden of disease due to these forms of air pollution is not separately quantified in the GBD study.

Although household and ambient air pollution are considered separately in deriving estimates of disease burden,[42,99] they are both comprised of many of the same pollutants and often co-exist; for example, in low-income and middle-income countries, household cooking contributes to ambient particulate air pollution.[55,56] Accordingly, the total numbers of deaths attributed to air pollution in the GBD study and in the WHO estimates are less than the arithmetic sum of the number of deaths attributed to each form of pollution alone.[35,99,125]

Air pollution disperses globally. Airborne pollutants travel across national boundaries, continents, and oceans.[126–128] An analysis[129] of emissions from Chinese export manufacturers found that, on days with strong westerly winds (winds blowing from China across the Pacific), 12–24% of sulphate concentrations, 2–5% of ozone, 4–6% of carbon monoxide, and up to 11% of black carbon pollution detected in the western USA were of Chinese origin.

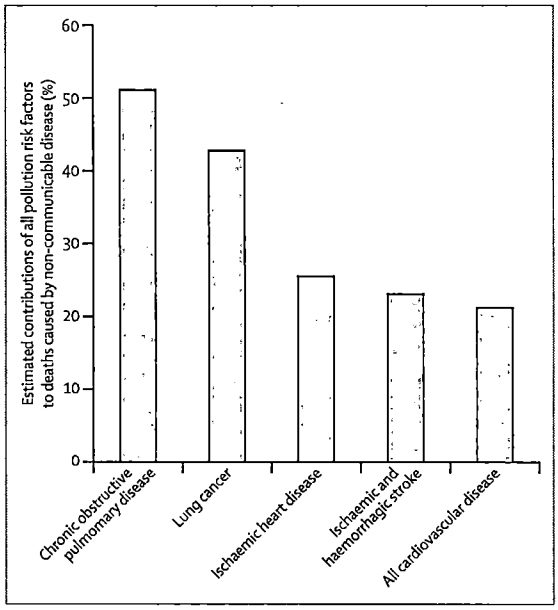

Figure 6: **Estimated contributions of all pollution risk factors to deaths caused by non-communicable diseases, 2015**
GBD Study, 2016.[42]

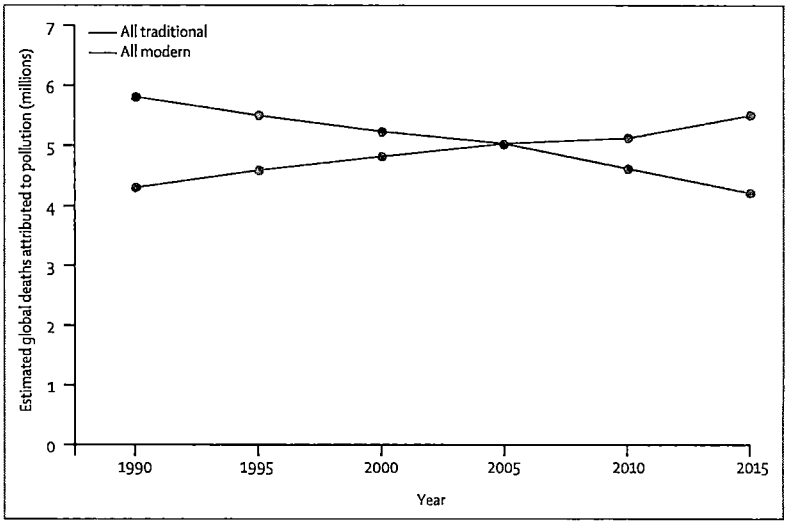

Figure 7: **Estimated global deaths (millions) by pollution category, 1990–2015**
GBD Study, 2016.[42] All modern=modern forms of pollution, comprising ambient air, chemical, occupational, and soil pollution. All traditional=traditional forms of pollution, comprising household air and water pollution.

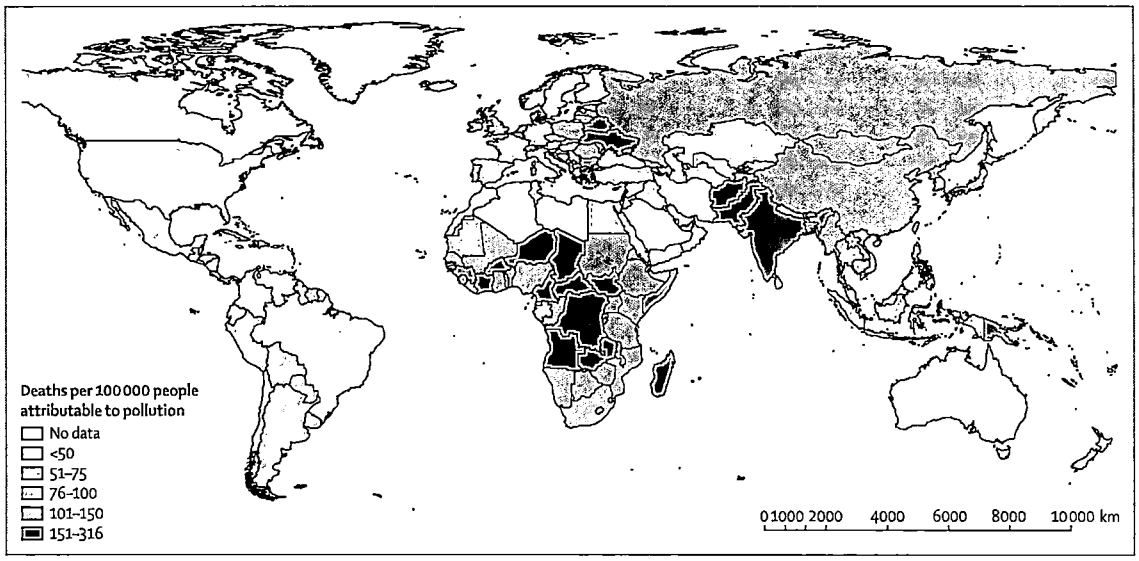

Figure 8: Number of deaths per 100 000 people that are attributable to all forms of pollution, 2015
GBD Study, 2016.[42]

Air pollution and disease

$PM_{2.5}$ is the best studied form of air pollution and is linked to a wide range of diseases in several organ systems.[23,130] The strongest causal associations are seen between $PM_{2.5}$ pollution and cardiovascular and pulmonary disease. Specific causal associations have been established between $PM_{2.5}$ pollution and myocardial infarction,[131–137] hypertension,[138] congestive heart failure, arrhythmias,[139] and cardiovascular mortality.[24,140–143] Causal associations have also been established between $PM_{2.5}$ pollution and chronic obstructive pulmonary disease and lung cancer.[42] The International Agency for Research on Cancer has reported that airborne particulate matter and ambient air pollution are proven group 1 human carcinogens.[34,40,144]

Fine particulate air pollution is associated with several risk factors for cardiovascular disease, including: hypertension,[138] increased serum lipid concentrations,[145] accelerated progression of atherosclerosis,[146–148] increased prevalence of cardiac arrhythmias,[139] increased numbers of visits to emergency departments for cardiac conditions,[132,133] increased risk of acute myocardial infarction,[131] and increased mortality from cardiovascular disease[142] and stroke.[149]

Clinical and experimental studies suggest that fine airborne particles increase risk of cardiovascular disease by inducing atherosclerosis, increasing oxidative stress, increasing insulin resistance, promoting endothelial dysfunction, and enhancing propensity to coagulation.[145,147,148,150]

Emerging evidence suggests that additional causal associations may exist between $PM_{2.5}$ pollution and several highly prevalent non-communicable diseases. These include diabetes,[25] decreased cognitive function, attention-deficit or hyperactivity disorder and autism in children,[30,31,151,152] and neurodegenerative disease, including dementia, in adults.[28,29,33] $PM_{2.5}$ pollution may also be linked to increased occurrence of premature birth and low birthweight.[27,153–159] Some studies have reported an association between ambient air pollution and increased risk of sudden infant death syndrome.[160] These associations are not yet firmly established, and the burden of disease associated with them has not yet been quantified, and they are therefore included in zone 2 of the pollutome (figure 3).

Water pollution

This Commission considers two types of water pollution: unsafe water source and inadequate sanitation.[51] Many areas in low-income and middle-income countries lack

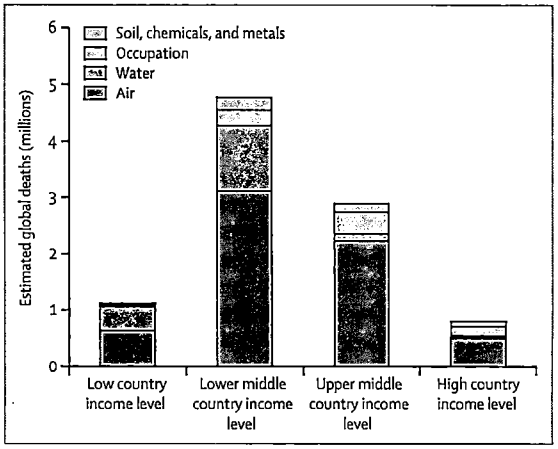

Figure 9: Estimated deaths by pollution risk factor and country income level, 2015
GBD Study, 2016.[42]

www.thelancet.com Published online October 19, 2017 http://dx.doi.org/10.1016/S0140-6736(17)32345-0

acceptable water supplies and many people, particularly in rural areas in poor countries, have inadequate sanitation.[52] Prevention technologies and systems exist, but poverty, lack of knowledge, and other priorities constrain the adoption of improvements.[161]

The problems of water supply and health are intensified where industrial pollutants contaminate water systems because treatments that control infectious agents are not effective in removing many toxic chemicals from drinking water. Improved analytical techniques have allowed identification of hundreds of industrial chemicals, pharmaceuticals, and pesticides in water systems. Some of the worst biological and chemical pollution of drinking water is seen in rapidly urbanising and industrialising lower-middle-income countries, where local waterways and groundwater are heavily polluted and serious health conditions are widely reported, but no alternative water sources exist.[53]

The principal diseases linked to water pollution are acute and chronic gastrointestinal diseases, most importantly diarrhoeal diseases (70% of deaths attributed to water pollution), typhoid fever (8%), paratyphoid fever (20%), and lower respiratory tract infections (2%).[42] These estimates include diseases associated with an unsafe water source, inadequate sanitation, and inadequate hand-washing. Polluted water and inadequate sanitation are linked, additionally, to a range of parasitic infections. These diseases affect more than 1 billion people, predominantly in low-income and middle-income countries.[41]

Water pollution also has effects on planetary health that extend beyond its effects on human health.[15] Pollution of rivers, lakes, and the oceans from agriculture, manufacturing, and the extractive industries can have catastrophic effects on freshwater and marine ecosystems that result in the collapse of fisheries and the diminished livelihood of indigenous populations and others who rely upon fish as a major food source.[162,163]

Most of the deaths caused by unsafe sanitation and unsafe water sources occur in children younger than 5 years of age. Increased numbers of deaths from waterborne pollution-related disease are also seen in adults older than 60 years of age.

Burden of disease due to water pollution

The GBD study[42] estimates that, in 2015, 1·8 million deaths were attributable to water pollution, including unsafe water sources, unsafe sanitation, and inadequate handwashing. Of this total, 0·8 million deaths were estimated to be caused by unsafe sanitation and 1·3 million to unsafe water sources. The total burden of disease attributable to water pollution is less than the sum of the diseases attributable to each of its components because of overlaps between unsafe water source, unsafe sanitation, and inadequate handwashing. WHO data indicate that 0·28 million deaths were attributable to unsafe sanitation in 2012 and that unsafe water sources were responsible for 0·5 million deaths.[99] As in the case of air pollution, the total number of deaths attributed to all forms of water pollution combined is less than the arithmetic sum of the deaths due to the individual types of water pollution because the various types of water pollution often co-exist and overlap with each other.

Trends in disease from water pollution

Targeted interventions to provide modern water and sanitation infrastructure began in the developing world as early as the 1950s, in the early days of international development assistance programmes. The Millennium

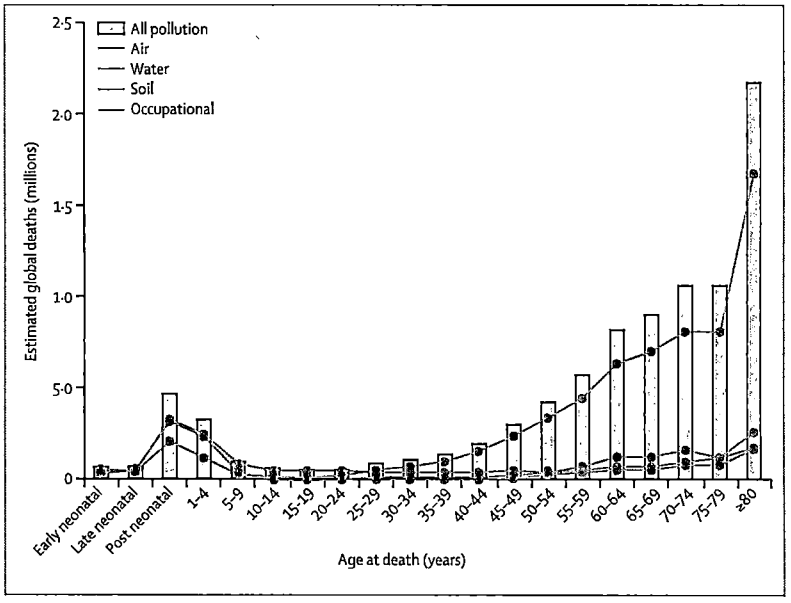

Figure 10: Estimated global deaths by pollution risk factor and age at death, 2015 GBD Study, 2016.[42]

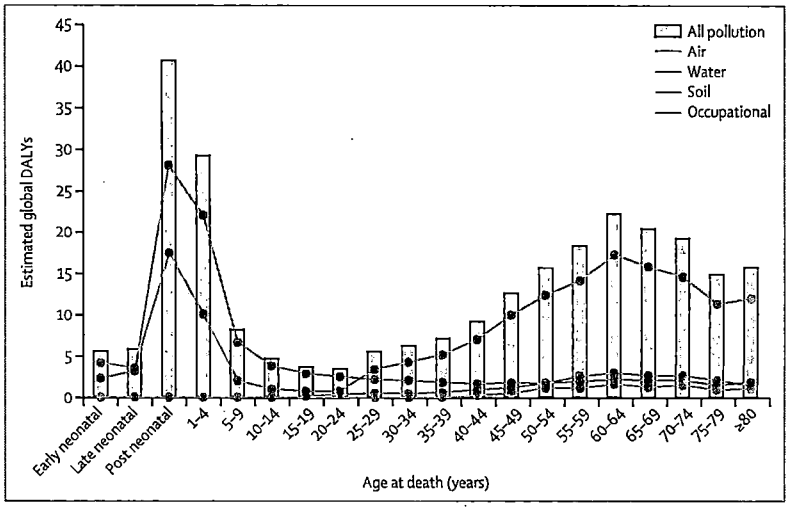

Figure 11: Estimated global DALYs by pollution risk factor and age at death, 2015 GBD Study, 2016.[42] DALYs=disability-adjusted life-years.

Development Goals (MDGs) accelerated this work, and MDG Target 7C called on the global community "by 2015, to halve the proportion of the population without sustainable access to safe drinking water and basic sanitation". To track interventions against water pollution and waterborne disease, WHO and UNICEF established the Joint Monitoring Programme for Water Supply and Sanitation.[54]

Substantial progress has been made in reducing water pollution and waterborne disease. Between 1990 and 2015, 2·6 billion people gained access to improved drinking water sources, 2·1 billion people gained access to improved sanitation, and the MDG Target 7C was met 5 years ahead of schedule. In this time, the number of children dying from diarrhoeal diseases decreased by almost 60%, from approximately 1·5 million deaths in 1990 to slightly greater than 0·6 million deaths in 2012. However, despite this progress, 2·4 billion people are still using unimproved sanitation facilities, including 946 million people who still practise open defecation.

For WHO data on numbers of water pollution-related mortalities see http://www.who.int/healthinfo/mortality_data/en/

Geography of water pollution and disease

Population-based estimates of the number of deaths from water pollution are highest in sub-Saharan Africa (figure 12).[42] Large numbers of deaths are seen also in some southeast Asian countries. In the past two decades, China has greatly reduced mortality from waterborne infectious disease.[42]

Importantly, these data do not reflect deaths from chemical pollution of water, because data for levels of chemical contamination of drinking water are not available for most low-income and middle-income countries. Disease due to chemical contamination of drinking water is included in zone 2 of the pollutome (figure 3).

Soil, heavy metal, and chemical pollution

Comprehensive assessments of the health effects of most forms of soil, heavy metal, and chemical pollution have not yet been published. Lead is an exception, and has been studied extensively. Newer research on a few contaminated sites is beginning to report data for disease burden at these sites; at present, these estimates are limited to DALYs and do not include deaths.

Lead

People have used lead for centuries but, until the modern era, it was largely an occupational poison.[164] In the 19th and 20th centuries, lead moved beyond the workplace into air, water, and soil in countries around the world as a consequence of sharp increases in lead production that accompanied the Industrial Revolution. In the early 20th century, lead was incorporated, for the first time, into mass-market consumer products such as lead-based paint and gasoline. Global contamination of air, water, and soil resulted. Global production of lead has more than doubled since the 1970s and continues to rise. Increasing global manufacture of batteries for products ranging from mobile phones to cars, is the main driver of this increase.[165] 82% of deaths due to lead occur in low-income and middle-income countries.

In adults, chronic exposure to lead is an established risk factor for hypertension, renal failure, cardiovascular

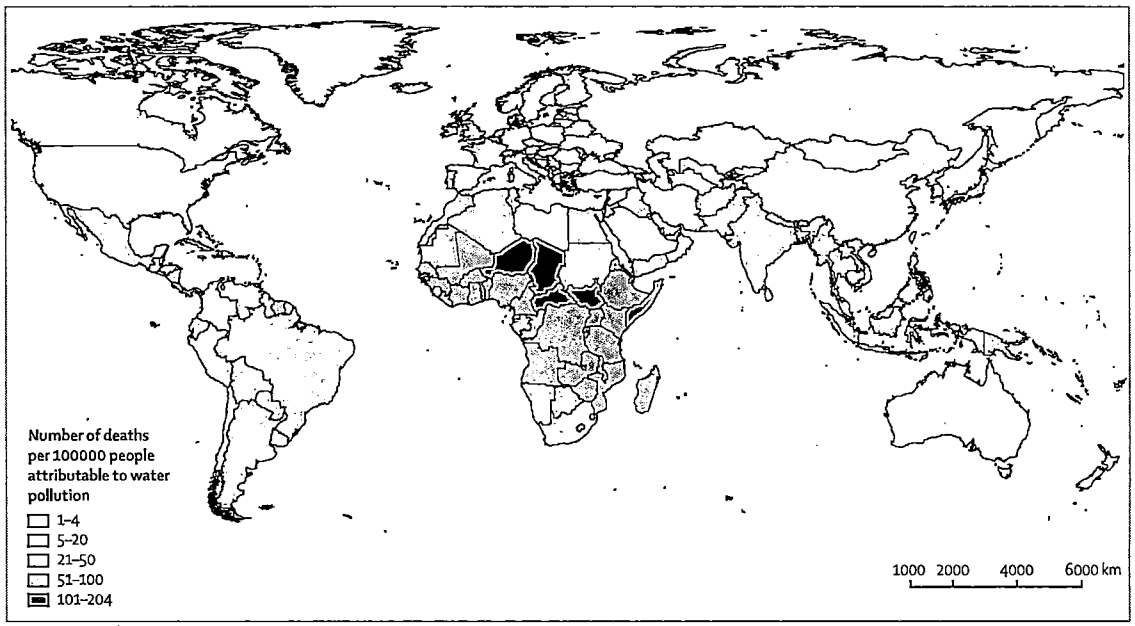

Figure 12: Number of deaths per 100 000 people due to water pollution, 2015
GBD Study, 2016.[42]

disease, and stroke, especially among workers exposed in their occupations. Large-scale epidemiological studies[26] based on a national probability sample have confirmed that the causal association between lead, hypertension, and mortality from cardiovascular disease is evident even at very low blood lead concentrations.

Neurodevelopmental toxicity is the most important consequence of lead toxicity in children.[166] The neurobehavioural sequelae of paediatric lead exposure include cognitive impairment,[167–170] shortening of attention span with increased risk for attention deficit or hyperactivity disorder,[171] and increased risk for antisocial and criminal behaviours.[172,173] These effects can persist across the entire lifespan and result in decreased school performance, increased risk of drug abuse and incarceration, and decreased economic productivity. Lead causes neurobehavioural damage in children at even the very lowest blood concentrations. WHO states that "there is no known level of lead exposure that is considered safe" (panel 4).[30,32,37,88,91,173–177]

Trends in lead exposure

Despite continuing increases in global lead production, bans on the use of lead in petrol, paint, plumbing, and solder have produced substantial reductions in lead exposure and disease burden. Lead has now been removed from gasoline in more than 175 countries.

Despite these advances, several sources of occupational and community exposure to lead persist.[38,178,179] Lead-glazed pottery is a notable source of exposure in several countries.[169,180] Infants in the womb can be exposed to lead via transplacental transfer, and nursing infants can be exposed to lead in breastmilk.[181] Children are at risk of exposure to lead-based paint in older housing[182,183] and to lead that leaches into drinking water from lead pipes and solder.[184] Informal (so-called "backyard") recycling of used lead-acid batteries is a widespread source of lead exposure for both workers and communities.[185]

Estimates from the GBD study[42] indicate that lead was responsible for 0·5 million premature deaths and for 9·3 million DALYs in 2015. This estimate is based entirely on adult deaths (15 years and older). Half of these deaths occurred in people aged 70 years and older. These estimates do not reflect exposures to lead at contaminated sites.[186] Although lead has caused child mortality in episodes of acute poisoning at heavily contaminated sites in low-income and middle-income countries,[187] it is not a major contributor to child mortality globally.

Cardiovascular diseases, including hypertension, coronary artery disease, stroke, cardiac arrhythmias, and peripheral arterial disease, account for the overwhelming majority of deaths attributable to lead in adults.[26,188] These associations are evident at blood lead concentrations as low as 5 µg/dL.[188,189] The GBD study[42] estimates that lead exposure accounts for 2·5% of the global burden of ischaemic heart disease. Lead is also estimated to account for 12·4% of the global burden of idiopathic intellectual disability (panel 4). The GBD analysis indicates that deaths in 2015 that were attributable to lead are as follows: cardiovascular disease (465 000 deaths), ischaemic heart disease (240 000), cerebrovascular disease (155 000), ischaemic stroke (68 000), haemorrhagic stroke (87 000), hypertensive heart disease (47 000), and chronic kidney disease (28 000).[42]

WHO estimates that, in 2012, lead was responsible for 13·9 million DALYs[109] and that childhood lead exposure is responsible for mild to moderate mental retardation of 0·6 million children annually.[190]

Pollution at contaminated sites

Polluted soil at contaminated sites threatens the environment and human health in communities worldwide. Most contaminated sites are relatively small, but the aggregate number of people affected globally by the many hundreds of thousands of extant sites is large.[191] Polluted sites are most commonly contaminated by informal, small-scale, unregulated local industry or artisanal activity.[191–193] Sites can be contaminated by current industrial and mining activity, or they can be abandoned, legacy sites that were contaminated by previous operations.[194]

The contaminants at polluted sites that pose the greatest threats to health are environmentally persistent substances such as metals, persistent organic pollutants (including persistent pesticides), and radionuclides. The metals most commonly encountered at polluted sites include mercury, lead, chromium, and cadmium.

***Panel 4:* Pollution and neurodevelopment**

Foetuses, infants, and children are particularly sensitive to neurotoxic pollutants, even at very low levels of exposure, because of the vulnerability of early-stage development of the human brain.[91,174–176] Toxic exposure during so-called windows of vulnerability in early life can cause lasting damage to brain function. Lead poisoning in childhood has, for example, been linked to reduced cognitive function and also to juvenile delinquency, violent crime in adulthood, and lifelong reduction in economic productivity.[37] Neurotoxic pollutants are also linked to autism,[152] attention deficit and hyperactivity disorder,[89,177] and conduct disorders.[173]

Exposure to neurotoxic pollutants is widespread as a result of fossil fuel combustion, industrial and agricultural production, and the extensive use of toxic chemicals in consumer products.[30] Routine biomonitoring studies have detected many dozens of toxic pollutants in the bodies of children and pregnant women.[175]

Pollutants known to be toxic to the developing brain (in addition to lead) include mercury, combustion by-products such as polycyclic aromatic hydrocarbons and fine particulate matter, organophosphate pesticides, brominated flame retardants, phthalates, and polychlorinated biphenyls.[88] Many more commonly used chemicals, whose developmental neurotoxicity has not yet been discovered could be causing undetected damage to children today.

The social and economic costs of early life exposure to neurodevelopmental toxicants are great. Large economic and social gains can be realised through prevention of these disorders.[32]

Panel 5: Superfund legislation

Legislation to control contaminated waste sites was enacted in the USA in the aftermath of a series of environmental and public health disasters.[199] The major trigger occurred at the Love Canal (Niagara County, NY, USA), an unused channel between Lake Erie and Lake Ontario into which the Hooker Chemical Company had dumped toxic wastes from the 1940s until the 1960s. When it was full, the canal was covered with a clay seal, and homes and a school were built on top of this clay. However, the waste did not stay underground. The canal filled with water and, by 1976, heavy rain regularly caused toxic sludge to bubble up into the basements of the overlying homes and into nearby streams. By the time this site was recognised as a hazardous waste site, Love Canal contained an estimated 21 000 tonnes of discarded chemicals. Within a few years, a second major waste site was discovered near Louisville, KY. Known as the Valley of the Drums, the site contained thousands of steel drums full of chemical wastes that had accumulated over several decades.

These events made it clear to policy makers and the public that hazardous waste was an environmental and public health emergency. In response, the US Congress passed the Comprehensive Environmental Response Compensation and Liability Act on Dec 11, 1980. The law became known as the Superfund Act because it authorised the creation of a large fund that, from 1980 to 1995 was supported by a tax on the chemical manufacturing and petroleum industries, the two major producers of toxic chemical wastes. Many of the new hazardous waste sites subsequently being discovered were the result of actions by polluters who no longer existed. The tax was based on the polluter-pays principle and was intended to provide resources to remediate abandoned sites. In 1995, the US Congress allowed the tax on the chemical and petroleum industries to expire. Since that time, remediation of hazardous waste sites in the USA has been supported through general tax revenues.

	Artisanal small-scale gold mining		Used lead-acid batteries		Total median DALYs (range)
	Population exposed	Median DALYs	Population exposed	Median DALYs	
Africa	10·90	1·91	4·11	0·32	2·23 (0·97–3·49)
Eastern Mediterranean	0·30	0·05	1·54	0·10	0·15 (0·04–0·27)
Europe	2·35	0·43	1·45	0·07	0·19 (0·09–0·28)
Americas	0·37	0·07	5·53	0·22	0·50 (0·24–0·76)
Southeast Asia	0·37	0·07	3·73	0·13	0·29 (0·08–0·50)
Western Pacific	0·19	0·35	3·73	0·13	0·48 (0·20–0·76)
Total	16·70	2·96	16·80	0·87	3·83 (1·61–6·06)

DALYs=disability-adjusted life-years.

Table 2: Estimated exposed populations (millions) and DALYs attributable to artisanal and small-scale gold mining and used lead-acid battery recycling by region, 2016[112,113,203]

Human exposure to contaminated soil at toxic sites can result from ingestion, inhalation, or dermal absorption.[195] Ingestion is the most common pathway. Children are at greatest risk of exposure because they play close to the ground and because of their common oral exploratory behaviour.[196–198]

In high-income countries, substantial progress has been made in identifying and remediating contaminated industrial sites and, thus, in reducing exposures and associated disease. In the USA, the Superfund programme (panel 5),[199] a national programme for site remediation, has been funded by the US Federal Government since 1980[199,200] and additionally by state governments. In Europe, similar programmes have been created and, since 2004, they have been subsumed under the Environmental Liability Directive of the European Commission, which establishes a framework to prevent damage and remediate hazardous sites based on the polluter-pays principle.[201]

Burden of disease due to soil pollution by metals and chemicals at toxic sites

Based on data from the Blacksmith Institute/Pure Earth Toxic Sites Identification programme, we estimate that about 61 million people in the 49 countries surveyed to-date are exposed to heavy metals and toxic chemicals at contaminated sites. Because this estimate reflects exposures at only a fraction of the total number of contaminated sites worldwide, further investigation will be required before the full magnitude of exposures at such sites and their contribution to the global burden of disease can be estimated.[202]

Two types of contaminated sites that have begun to be studied in detail are used lead-acid battery recycling sites and artisanal and small-scale gold mining sites (table 2).[112,113,203] Lead poisoning from informal battery recycling is seen in low-income countries in all regions of the world.[187,204–206] Artisanal and small-scale gold mining takes place worldwide, but is most highly concentrated in Africa.[207] Details on methods for these analyses can be found in the appendix (pp 17–18).

We estimate that between 6 million and 16 million people are exposed to dangerous concentrations of lead each year at used lead-acid battery recycling sites.[185,203] These exposures result in the loss of an estimated 0·87 million DALYs annually.[203] We also estimate that between 14 million and 19 million artisanal and small-scale gold miners are at risk of occupational exposure to elemental mercury.[112] These exposures result in an estimated 2·9 million DALYs lost annually to elemental mercury poisoning.[112]

Occupational pollutants

Recognition of the health consequences of toxic occupational exposures dates to 200 BC,[164] and many of the diseases caused by occupational exposures were well known by the 1700s.[208,209] The major epidemics of industrial disease that ravaged workers' health in the 19th and 20th centuries are, however, of relatively recent origin. Such diseases include coal workers' pneumoconiosis,[210] silicosis,[164] bladder cancer in dye workers[211] leukaemia and lymphoma in workers exposed to benzene,[212] and asbestosis, lung cancer, mesothelioma, and other malignancies in workers exposed to asbestos.[213] These conditions can be traced to the rapid, initially largely uncontrolled, industrialisation and reckless exploitation of natural resources that characterised the Industrial Revolution in western Europe, North America, Japan, and Australia.

In high-income countries, the worst occupational exposures have now been controlled by legislation and regulation, backed by strong enforcement, and rates of occupational disease are down.[164,214] Substantial progress has been made in controlling exposures to occupational carcinogens. Central to this success has been the work of WHO's International Agency for Research on Cancer, which has produced independent and objective analyses of the carcinogenicity of hundreds of chemicals. These analyses guide cancer control programmes in countries around the world

By contrast, occupational exposures to toxic pollutants have become highly prevalent in the past 50 years in low-income and middle-income countries.[42] The worst of these exposures tend to occur in informal, small-scale, locally owned establishments where child labour is also a frequent problem.[176]

Burden of disease due to toxic occupational pollutants

Occupational pollutants cause a wide range of diseases.[164,215–217] The GBD study[42] considers the burden of disease attributable to two types of occupational pollutants. These are occupational carcinogens—asbestos, polycyclic aromatic hydrocarbons, silica, sulphuric acid, trichloroethylene, arsenic, benzene, beryllium, cadmium, chromium, diesel exhaust, second-hand smoke, formaldehyde, and nickel—and occupational particulates, gases, and fumes.

The GBD study[42] estimates that, in 2015, toxic occupational risk factors (not including occupational injuries or ergonomic factors) were responsible for 0·88 million deaths globally and for 18·6 million DALYs. Carcinogens were responsible for 0·49 million (55%) of the deaths from occupational exposures to toxicants and for 9·8 million DALYs. Asbestos was responsible for nearly 40% (0·18 million) of all deaths caused by occupational carcinogens. Exposures to particulates, gases, and fumes in the workplace were responsible for an estimated 0·36 million deaths and for 8·8 million DALYs.

WHO data indicate that, in 2012, occupational pollutants were responsible for 0·36 million deaths.[110] Occupational respiratory carcinogens (arsenic, asbestos, beryllium, cadmium, chromium, diesel exhaust, nickel, silica) were responsible for 0·1 million of these deaths; occupational leukaemogens (benzene, ethylene oxide, ionising radiation) for 3000 deaths; occupational particulates, dusts, fumes, and gases for 0·23 million deaths; and acute occupational poisonings for 27 000 deaths. WHO estimates that, in 2012, occupational exposures were responsible for 13·6 million DALYs.[109]

Age distribution of deaths linked to toxic occupational pollutants

Most deaths attributable to occupational pollutants and, especially, to occupational carcinogens occur in people aged 50 years and older (figure 13).[42] This pattern reflects the long latency of most occupational cancers.[213]

Pollution sources not currently quantified

Many hundreds of new synthetic chemicals have entered world markets in recent decades, come into widespread use, and are now beginning to be recognised as potential threats to health. These chemicals have become extensively disseminated in the environment, are detectable in the bodies of almost all people examined in national surveys, and have the potential to cause global epidemics of disease, disability, and death. Most chemicals have undergone little or no assessment of their safety or potential hazards to human health.

For IARC monographs on the evaluation of cancer risks to humans see http://monographs.iarc.fr/

Because the effects of these new chemicals on human health are only beginning to be recognised and their contributions to the global burden of disease are not yet quantified, they are currently placed within zone 3 of the pollutome (figure 3). Such emerging chemical pollutants are described below.

Developmental neurotoxicants

Evidence is strong that widely used chemicals and pesticides have been responsible for injury to the brains of millions of children and have resulted in a global pandemic of neurodevelopmental toxicity.[37,88] The manifestations of exposure to these chemicals during early development include loss of cognition, shortening of attention span, impairment of executive function, behavioural disorders, increased prevalence of attention deficit and hyperactivity disorder, learning disabilities, dyslexia, and autism.[37]

Prospective epidemiological birth cohort studies have been a powerful instrument for detecting associations between prenatal exposures to developmental neurotoxicants and disease.[218] Examples of pollution-related diseases in children that have been identified through prospective studies are: cognitive impairment, with decreased IQ in children exposed prenatally to

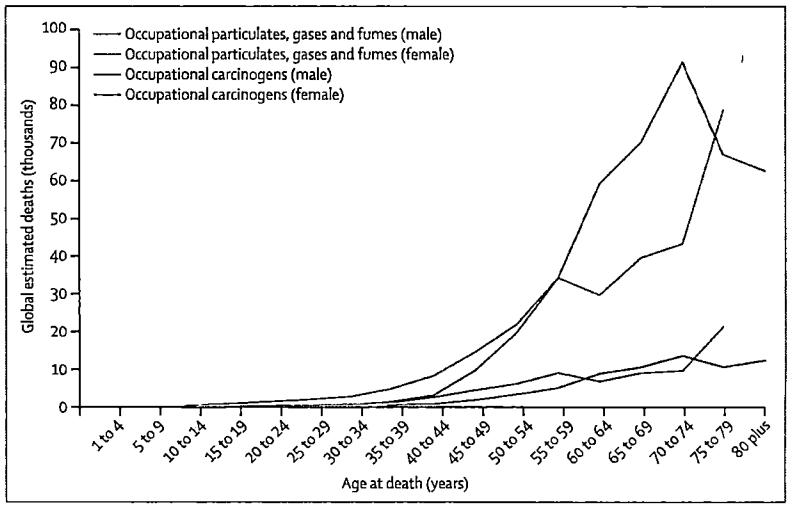

Figure 13: **Global estimated deaths due to occupational carcinogenic and particulate exposures by age at death and gender, 2015**
GBD Study, 2016.[42]

PCBs;[219] reduced IQ and shortening of attention span in children exposed prenatally to methyl mercury;[37] microcephaly at birth, anatomical and functional delays in brain development, and autistic behaviours in children exposed prenatally to the organophosphate pesticide, chlorpyrifos;[220,221] autistic behaviours in children exposed prenatally to phthalates;[89] cognitive impairment, shortened attention span, and disruptive behaviour in children exposed prenatally to brominated flame retardants;[177] and neurodevelopmental delays in children exposed prenatally to polycyclic aromatic hydrocarbons.[32,175]

An important unanswered question is whether there are additional chemicals in use today whose ability to cause silent injury to the developing human brain has not yet been discovered.[88,222,223]

Endocrine disruptors

Endocrine disruptors are chemical pollutants that mimic, block, or alter the actions of normal hormones.[78,90–92] They include phthalates, bisphenol A, perchlorate, several pesticides, such as the orthophosphates, brominated flame retardants, and dioxins. Many endocrine disruptors are also developmental neurotoxicants. These chemicals are manufactured in volumes of millions of kilograms per year and are used widely in consumer products such as soaps, shampoos, perfumes, plastics, and food containers. Exposures in utero to even extremely low doses of endocrine-disrupting chemicals during early development can lead to permanent impairments in organ function and increased risk of disease. Prenatal exposures have been linked to autistic behaviours in children[224] and to anomalies of the reproductive organs in baby boys.[225]

Pesticides

More than 20 000 commercial pesticide products, including insecticides, herbicides, fungicides, and rodenticides are available on world markets. More than 1·1 billion pounds of these products are used in the USA each year and an estimated 5·2 billion pounds globally.[226] Some of the heaviest applications occur in low-income and middle-income countries where use and exposure data are scant. Experience with three categories of pesticides—the organophosphate insecticides, the neonicotinoid insecticides, and the synthetic herbicide glyphosate—illustrate the challenges posed by these new and inadequately tested pesticide chemicals.

The organophosphate insecticides are a large and widely used class of pesticides. Members of this class of chemicals are powerful developmental neurotoxicants, and prenatal exposures are associated with persistent deleterious effects on children's cognitive and behavioural function and with long-term, potentially irreversible, changes to brain structure that are evident on MRI.[220] Toxicological studies of rodents exposed perinatally to organophosphates produce parallel findings.[227]

The neonicotinoids are a novel class of neurotoxic pesticides that were developed in the 1980s and whose use has risen substantially in the past decade. The neonicotinoid imidacloprid is now the most widely used insecticide in the world.[228] In the USA, agricultural use of neonicotinoids was nearly 4 million kg in 2014.[229]

Neonicotinoids target nicotinic acetylcholine receptors in the insect nervous system.[230] They are water-soluble and can persist for years in soils, dust, wetlands, and groundwater and are detected in commonly consumed foods. Substantial evidence indicates that neonicotinoids can have negative effects on the behaviour and health of bees and other pollinators at environmentally relevant concentrations.[231,232] These chemicals are a suspected cause of bee colony collapse disorder. Despite their extensive use and known neurotoxicity to insects, very little information is available on the possible human health effects of the neonicotinoids.[228]

Chemical herbicides account for nearly 40% of global pesticide use and applications are increasing.[226] A major use is in production of genetically modified food crops engineered to be resistant to glyphosate (Roundup), the world's most widely used herbicide. Glyphosate-resistant, so-called "Roundup Ready" crops, now account for more than 90% of all corn and soybeans planted in the USA, and their use is growing globally. Glyphosate is widely detected in air and water in agricultural areas, and glyphosate residues are detected in commonly consumed foods.

Epidemiological studies of agricultural workers who were exposed occupationally to glyphosate and other herbicides have found evidence for increased occurrence of non-Hodgkin lymphoma in these people. Toxicological studies of experimental animals exposed to glyphosate show strong evidence of dose-related carcinogenicity at several anatomical sites, including renal tubule carcinoma and haemangiosarcoma. On the basis of these findings, the International Agency for Research on Cancer has determined that glyphosate is a "probable human carcinogen";[233] this finding is contested by glyphosate's manufacturer.

Thousands of tonnes of pharmaceutical waste are released into the environment each year, especially in high-income and middle-income countries, and measurable concentrations of several pharmaceuticals are detected in urban wastewater.[95,96]

The sources of pharmaceutical waste pollution include discharges from pharmaceutical manufacturing plants, hospitals, agriculture, and aquaculture. Anti-inflammatory agents, antibiotics, oestrogens, anti-epileptics, caffeine, and cancer chemotherapy agents are among the compounds most commonly detected. In some locations, concentrations of the anti-inflammatory drug diclofenac have been reported to exceed predicted no-effect levels.[234,235] Concern is increasing that these compounds could damage freshwater and salt water marine species through a range of toxicological mechanisms, including endocrine disruption.

www.thelancet.com Published online October 19, 2017 http://dx.doi.org/10.1016/S0140-6736(17)32345-0

Further information on these emerging chemical pollutants is presented in the appendix (pp 2–11).

Research recommendations

To increase knowledge of pollution and its effects in human health, this Commission recommends that research be undertaken to: (1) define and quantify the burden of neurodevelopmental disease in children and the burden of neurodegenerative disease in adults attributable to $PM_{2.5}$ air pollution (zone 2 of the pollutome); (2) define and quantify the burden of diabetes attributable to $PM_{2.5}$ air pollution (zone 2 of the pollutome); (3) define and quantify the burden of preterm birth and low birth weight attributable to $PM_{2.5}$ air pollution (zone 2 of the pollutome); (4) better quantify the burden of disease caused by chemical pollutants of known toxicity at contaminated sites, such as lead, mercury, chromium, arsenic, asbestos, and benzene (zone 2 of the pollutome); and (5) discover and quantify health effects associated with new and emerging chemical pollutants, such as developmental neurotoxicants, endocrine disruptors, novel classes of insecticides, chemical herbicides, and pharmaceutical wastes (zone 3 of the pollutome).

Section 2: The economic costs of pollution and pollution-related disease

Premature death and disease due to pollution impose great costs on national budgets and health-care spending, especially in rapidly industrialising low-income and middle-income countries. Diseases caused and exacerbated by pollution result in medical expenditures and in pain and suffering. Pollution-related disease can reduce labour force participation, labour market productivity, and economic output. In children, pollution-related disease can cause failure in school and perpetuate intergenerational poverty. Early life exposures to neurotoxic pollutants such as lead and mercury can impair cognition, diminish the ability to concentrate, and disrupt behaviour, thus reducing lifetime earnings. The costs of disease and premature death caused by pollution, especially the more modern forms of pollution, are rising rapidly.[236]

The costs of pollution-related disease are often overlooked and undercounted because they are associated with non-communicable diseases of long latency that extend over many years, are spread across large populations, and are not captured by standard economic indicators.[7–9,237] These costs are much more difficult to calculate than the costs of pollution control, which are usually tangible and concrete.[238] Although the costs of pollution-related disease can have large effects on the budgets of health ministries and increase spending in health systems, they are typically buried in general health expenditures and hospital budgets, hidden in productivity reports, do not affect the budgets of environment ministries, and are not attributed to pollution.[9]

The costs of pollution-related disease include: (1) direct medical expenditures, including hospital, physician, and medication costs, long-term rehabilitation or home care, and non-clinical services such as management, support services, and health insurance costs; (2) indirect health-related expenditures, such as time lost from school or work, costs of special education, and the cost of investments in the health system (including health infrastructure, research and development, and medical training); (3) diminished economic productivity in persons whose brains, lungs, and other organ systems are permanently damaged by pollution; and (4) losses in output resulting from premature death.

Pollution-related disease is responsible also for intangible costs, such as those of poor health in people made ill by pollution, disruption of family stability when a person of working age becomes disabled or dies prematurely as a result of pollution, and the loss in years of life to the person themselves.

A method to estimate the tangible costs of pollution-related disease was developed in the early 1980s by an expert committee convened by the Institute of Medicine.[239] The core of this method is calculation of the so-called "fractional contribution" of pollution to causation of a particular disease.[41] This environmentally attributable fraction is defined as "the percentage of a particular disease category that would be eliminated if pollution was reduced to the lowest feasible levels."[240] This fractional contribution is then multiplied by the number of cases of pollution-related disease in a population and by the average cost per case to calculate the total costs of pollution-related disease.

The cost of a case of illness is often measured by the medical expenses incurred when a person is ill (the direct costs of illness) and by the loss in productivity when a person dies prematurely or is disabled (the indirect cost of illness).[241] This method has been used to estimate the costs of pollution-related disease in children[242–244] and of occupational disease in workers,[245] has enabled quantification of the effects of pollution-related disease on GDP, and has provided a means to calculate costs that are typically externalised and not captured by standard accounting methods, and thus were previously hidden.[7] Information derived from this so-called full-cost accounting method has proven to be a powerful lever for shaping public policy and is an effective antidote to one-sided arguments for not taking or delaying action against pollution that are based solely on the costs of pollution control.[7,9]

The cost of illness approach to calculating costs of pollution-related disease works reasonably well in countries with strong public health data systems and robust information about the costs of disease. However, it is less applicable in countries without those resources. Therefore, the GBD study and WHO estimates of the burden of disease due to pollution are based primarily on data for premature deaths and do not adequately

reflect the full burden of pollution-related disease because, in many countries, researchers are not able to capture information about pollution-related morbidity. In countries where data are available relating pollution to morbidity and to the costs of disease, these costs are often substantial. Such studies suggest that the morbidity costs resulting from pollution-related disease might conservatively increase mortality costs by 10–70%,[236,246,247] and some individual country studies suggest that the increment might be even greater: 25% for Colombia,[247] 22–78% for China,[248] and 78% for Nicaragua.[249]

A second shortcoming in using the cost of illness approach to estimate the health costs of pollution is that it can never capture the intangible losses caused by pollution-related disease, even when comprehensive data are available. For example, this method can neither measure the family disruption that follows the premature death of a mother or a father nor can it quantify the grief that follows the death of a child. Those losses are separate and qualitatively different from losses in income generated or in goods produced.[14] Similarly, a method that is based solely on the effect of pollution on GDP cannot fully describe the negative effects of pollution on societal health, on diminished visibility in national parks, on ecosystem services, or the benefits of pollution control in enhancing national welfare.[72]

To overcome these shortcomings in the cost of illness approach, economists have devised a second strategy to assess disease costs: the so-called "willingness-to-pay" method. This metric is a measure of how much people are willing to pay to reduce the risk of premature death.[250–252] This approach captures individuals' preferences for avoiding increases in risk of death by analysing their behaviour in risky situations (the revealed preference approach) or in hypothetical choice situations involving changes in their risk of death (the stated preference approach).

To aggregate data from willingness to pay (WTP) studies, economists have developed the Value of a Statistical Life (VSL) concept. The VSL is defined as the total of what many people would pay for small reductions in the probability of dying over the coming year that, together, add up to saving one life. For example, if each of 10 000 people were willing to pay US$100 over the coming year to reduce their risk of dying by 1 in 10 000, one statistical life would be saved and the VSL would equal $100×10 000, or $1 000 000.

Multiplying the number of lives lost to pollution by the VSL provides an estimate of the health costs associated with pollution. Multiplying the number of lives that pollution control would save by the VSL provides an estimate of the benefits of pollution control.

Although the VSL method has the disadvantage of relying on estimates of what people say they will pay to reduce mortality risks, it overcomes many of the limitations that hinder efforts to estimate pollution-related disease costs; for instance, by expanding estimates from those made solely in terms of productivity losses and effects on GDP. The VSL method has been used by governments in high-income countries and in Colombia, Malaysia, Mexico, and Peru, amongst others, to estimate the benefits of reducing pollution.[246]

Methods

This Commission uses both approaches in the current analysis. Economic losses from pollution-related disease are therefore measured in terms of lost productivity and health-care costs, and the costs of pollution-related disease are also presented using estimates derived from WTP studies. Costs associated with air, water, and lead pollution are included in this analysis, but costs associated with soil pollution are not yet available and are not included. To calculate the VSL in countries where no original studies are available, we have extrapolated estimates from other countries, taking differences in income levels into account.[246,253] This method is described in the appendix (pp 25–28).

The economic benefits that result from the control of pollution and prevention of pollution-related disease are the same as the costs that result from pollution-related disease. Losses in economic productivity are a key component of the costs of pollution-related disease. When pollution-related disease results in the death of children or adults of working age, the economic output that those people would have produced is lost forever. The productivity losses associated with premature mortality are measured by calculating the output that an individual would have produced over his or her working life, summing these losses to the present.

Pollution-related disease also reduces the productivity of ill people while they are working. Hanna and Oliva[254] estimated that the closing of a heavily polluting refinery in Mexico City, Mexico, increased the hours worked by people living near the refinery by 3·5%. Zivin and Neidell[255] found that a 10 ppb reduction in ground-level ozone increased the productivity of farm workers in California, USA, by 5·5%. Chang and colleagues[256] report that each 10 μg/m^3 increase in outdoor $PM_{2.5}$ concentrations reduced the productivity of factory workers by 6% in northern California, USA. Similarly, water pollution has also been shown to reduce adult productivity. An estimated 35 million people in Bangladesh are exposed to concentrations of arsenic in groundwater that exceed 50 μg/L and 57 million people are exposed to concentrations above the WHO standard of 10 μg/L. Carson and colleagues,[257] who performed this study, estimate that reducing arsenic concentrations to the WHO standard would increase annual hours worked by the average household in their sample by 6·5%.

A method to measure lost output is to calculate its effects on a worker's contribution to GDP. Table 3 shows reductions in GDP that result from pollution-related deaths as a percentage of a country's GDP. Losses are reported by World Bank income group and pollutant

www.thelancet.com Published online October 19, 2017 http://dx.doi.org/10.1016/S0140-6736(17)32345-0

category (lead exposure, ambient air pollution, household air pollution, unsafe water, and unsafe sanitation. Because the magnitude of productivity losses is sensitive to the interest rate used to discount losses to the present (discount rate), this Commission gives results using two different discount rates (1·5% and 3%). For country-level data see appendix (pp 43–47).

Because pollution-related disease is most common in heavily polluted, low-income countries, productivity losses due to pollution-related disease are disproportionately high in these countries. Thus, in low-income countries, productivity losses due to pollution-related disease represent between 1·3% and 1·9% of GDP. By contrast, in lower middle-income countries, these losses amount to between 0·6% and 0·8% of GDP. In low-income countries, the largest productivity losses due to pollution-related disease result from lack of access to safe water and sanitation, followed by exposures to air pollution. Household air pollution alone causes losses of between 0·49% and 0·68% of GDP in low-income countries.

In upper middle-income and high-income countries, most economic losses attributable to pollution-related disease are due to ambient air pollution. These losses comprise a smaller fraction of GDP than in low-income and lower middle-income countries because there is generally less pollution in these countries and prevalence of pollution-related disease is lower. An additional factor that reduces the estimated costs of pollution-related disease in high-income countries is that more than 82% of deaths due to air pollution in these countries occur in people age 65 years and older. This reduces the calculated costs because the international definition of working age is 15–64 years of age and, hence, the economic contribution of premature death in people older than 65 years is not counted. In upper middle-income and high-income countries, estimated economic losses due to pollution-related disease in 2015 were more than US$53 billion.

Additional economic costs of coal combustion not included in this analysis are costs related to disease and premature death in coal miners due to injuries and coal workers' pneumoconiosis; costs of lung cancer in coke oven workers; ecological and community costs of mountain top removal and strip mining; losses in property values near mines and along railroad rights-of-way; loss of timber resources; and crop losses due to water contamination.[9]

Pollution benefit-cost analyses

Benefit-cost analyses of water and sanitation improvements and improved cookstoves must account for the health benefits of these interventions, the time savings for households who no longer need to collect water or firewood, and the benefits associated with improved childhood health, such as greater educational achievement.

The health benefits associated with a project to improve water quality (eg, home disinfection of drinking water) exceed the reduced mortality risk and lost productivity measured in this chapter, and also include reductions in morbidity due to diarrhoea, especially among children, and associated reductions in malnutrition.

	Ambient air pollution and household air pollution	Unsafe water and unsafe sanitation*	Lead exposure	Total
High income	0·044% (0·048%)	0·0028% (0·0033%)	0·0027% (0·0029%)	0·050% (0·054%)
Upper-middle income	0·13% (0·15%)	0·019% (0·027%)	0·0054% (0·0059%)	0·15% (0·18%)
Lower-middle income	0·32% (0·40%)	0·28% (0·40%)	0·012% (0·013%)	0·61% (0·82%)
Low income	0·62% (0·86%)	0·70% (1·03%)	0·012% (0·013%)	1·33% (1·90%)
World	0·092% (0·11%)	0·033% (0·047%)	0·0042% (0·0046%)	0·13% (0·16%)

Results without parentheses discount future output at the rate of growth in per capita GDP plus 3%. Results in parentheses discount future output at the rate of growth in per capita GDP plus 1·5%. For the calculations see appendix (pp 25–26). *Includes, but is not limited to, no hand washing with soap.

Table 3: Productivity losses as a percentage of gross domestic product (GDP) by pollutant and World Bank income group

Two studies that combine results from the medical literature to estimate the global benefits of various water and sanitation interventions suggest benefit-cost ratios greater than 1 for many interventions on the basis of health benefits and time savings. The average benefit-cost ratio for deep borehole wells with hand pumps is 4·64, whereas household water treatment with bio-sand filters yields an average benefit-cost ratio of 2·48.[258,259] A cost–benefit analysis finds that improved water supplies, according to the WHO definition, yield a return of US$2 for every dollar invested.

Despite general acceptance that well targeted water and sanitation interventions have positive benefit-cost ratios,[260,261] the scale of these benefits can be questioned, given the number of uncertainties that are usually involved.[262,263] Site-specific analysis and examination of the range of probable benefit-cost ratios can provide useful input to the process of making policy and project decisions.[264]

Neurotoxic pollutants can reduce productivity by impairing children's cognitive development. It is well documented that exposures to lead and other metals (eg, mercury and arsenic) reduce cognitive function, as measured by loss of IQ.[168] Loss of cognitive function directly affects success at school and labour force participation and indirectly affects lifetime earnings. In the USA, millions of children were exposed to excessive concentrations of lead as the result of the widespread use of leaded gasoline from the 1920s until about 1980. At peak use in the 1970s, annual consumption of tetraethyl lead in gasoline was nearly 100 000 tonnes.

It has been estimated that the resulting epidemic of subclinical lead poisoning could have reduced the number of children with truly superior intelligence (IQ scores higher than 130 points) by more than 50% and, concurrently, caused a more than 50% increase in the number of children with IQ scores less than 70 (figure 14).[265] Children with reduced cognitive function

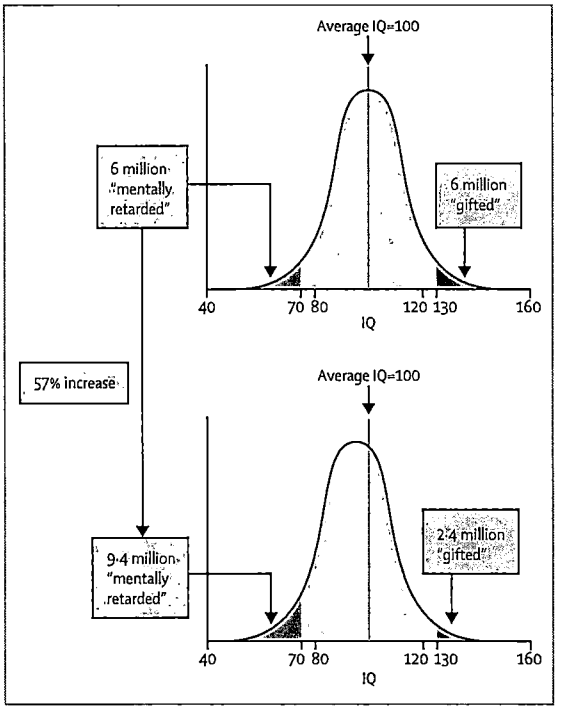

Figure 14: **Model of intelligence losses associated with a mean 5-point drop in IQ of a population of 100 million**
Figure taken from reference 265, with permission.

due to lead did poorly in school, required special education and other remedial programmes, and could not contribute fully to society when they became adults.

Grosse and colleagues[46] found that each IQ point lost to neurotoxic pollution results in a decrease in mean lifetime earnings of 1·76%. Salkever and colleagues[266] who extended this analysis to include the effects of IQ on schooling, found that a decrease in IQ of one percentage point lowers mean lifetime earnings by 2·38%. Studies from the 2000s using data from the USA[267,268] support earlier findings but suggest a detrimental effect on earnings of 1·1% per IQ point.[269] The link between lead exposure and reduced IQ[46,168] suggests that, in the USA, a 1 µg/dL increase in blood lead concentration decreases mean lifetime earnings by about 0·5%. A 2015 study in Chile[270] that followed up children who were exposed to lead at contaminated sites suggests much greater effects. A 2016 analysis by Muennig[271] argues that the economic losses that result from early-life exposure to lead include not only the costs resulting from cognitive impairment but also costs that result from the subsequent increased use of the social welfare services by these lead-exposed children, and their increased likelihood of incarceration.

Pollution-related disease has substantial effects on health-care expenditure. To quantify these costs, it is necessary to know the number of cases of each category of pollution-related disease in a population and the average health-care expenditure per case (appendix pp 29–31). These data are available for some high-income countries[272] but not for low-income and middle-income countries, except for Sri Lanka.[273]

Respiratory disease, cardiovascular disease, stroke, and cancer account for the largest proportion of the DALYs from pollution-related disease. Air pollution is responsible for half of the DALYs associated with lower respiratory tract infections and chronic obstructive pulmonary disease worldwide, and for a quarter of the DALYs resulting from ischaemic heart disease and stroke.[42,106] Globally, 24% of the DALYs associated with cancers of the trachea, bronchus, and lungs are attributed to air pollution. The proportions of DALYs linked to each of these non-communicable diseases are higher in low-income and middle-income countries than in high-income countries (table 4).[41,42] For country-level calculations see the appendix (pp 57–62).

Based on information from seven high-income countries, it can be estimated that air pollution, which accounts for 2·4% of all DALYs in these countries (panel 6),[42] accounts for 3·5% of their total health expenditure; in 2013, this amounted to US$100 billion. In Sri Lanka, a rapidly industrialising lower middle-income country where the burden of pollution-related disease is proportionately much larger than in high-income countries, air pollution accounts for 6·5% of all DALYs. Estimated expenditures on disease due to air pollution in Sri Lanka account for 7·4% of all health-care expenditures.

	Lower respiratory infections	Tracheal, bronchial, and lung cancer	Ischaemic heart disease	Ischaemic stroke	Haemorrhagic stroke	Chronic obstructive pulmonary disease	Cataracts
High income	12%	8%	13%	9%	11%	16%	1%
Upper-middle income	34%	30%	24%	20%	24%	41%	14%
Lower-middle income	57%	38%	35%	28%	31%	52%	25%
Low income	64%	48%	43%	36%	22%	51%	35%
Global	53%	24%	28%	37%	27%	44%	19%

Calculations based on data from the GBD 2015 Mortality and Causes of Death Collaborators (2016)[41] and the GBD 2015 Risk Factors Collaborators (2016).[42]

Table 4: **Percentage of disability-adjusted life-years attributable to air pollution (household air pollution plus ambient air pollution) by disease and country income group**

www.thelancet.com Published online October 19, 2017 http://dx.doi.org/10.1016/S0140-6736(17)32345-0

Globally, unsafe water and sanitation, including poor hand hygiene, are associated with 96% of DALYs due to diarrhoeal disease and with 95% of the DALYs linked to typhoid fever. In low-income countries, these percentages are even higher (97% for both diseases). Health-care expenditures on pollution-induced diarrhoea and typhoid are difficult to quantify due to inadequate data. However, the costs of treating these diseases, especially for children, represent only a small proportion of the health costs to society from these diseases[274,275] and the impoverishing effect of these diseases can be as great, if not greater, than the direct cost of illness. For example, in children who survive diarrhoea, effects on nutritional status and school attendance are likely to far outweigh the costs of treatment. Repeated bouts of diarrhoea interfere with the body's ability to absorb nutrients and, in countries where many children are malnourished, compound the effects of poor nutrition.[276] The negative effects of poor nutrition on labour force productivity[277] and the effects of diarrhoea and other childhood diseases on school attendance are well studied.[278] All of these effects are magnified in settings where poor households forego medical treatment but still suffer substantial impoverishment from the loss of household income or long-term disability, where the foregone treatment is a low-cost intervention that could have restored full labour market participation.

We define welfare losses from pollution-related disease as equal to household WTP to reduce pollution. When the VSL method is used to estimate the global costs of premature deaths attributable to pollution, the total in 2015 was more than US$4·6 trillion, or 6·2% of world GDP (table 5).[42]

This estimate of WTP to reduce pollution greatly exceeds the estimated costs of pollution-related disease that are derived from productivity losses alone for two reasons. Firstly, what people will pay to reduce their risk of death is much greater than the present value of lost output. When a person dies at age 35 years, the present value of productivity losses is about 20 times per capita GDP; in low-income countries, the ratio of the VSL to per capita GDP is between 40:1 and 50:1. Secondly, the VSL is applied to all premature deaths, not only those of adults at working age. Because 75% of deaths associated with lead pollution, 64% of deaths associated with ambient air pollution, 33% of deaths associated with unsafe water and sanitation, and 56% of the deaths associated with household air pollution occur at age 65 years or older, these deaths are excluded from economic calculations based on productivity losses. The VSL approach values these deaths by what people are willing to pay to avoid them. By contrast, the method based on productivity losses presented in table 3 assigns no value to deaths that occur at age 65 years or older.

Although pollution damages are highest, in absolute terms, in high-income countries, they are highest as a proportion of income in low and middle-income countries. Table 5 shows the damages associated with each pollutant category, measured in 2015 US dollars at market exchange rates and as a percent of gross national income (which represents the sum of incomes earned by all residents of a country), and summarised by World Bank income category. The method used to calculate these damages is identical to that used in the Institute for Health Metrics and Evaluation-World Bank study;[279] however, this Commission presents all figures converted to 2015 US dollars at market exchange rates rather than using purchasing power parity dollars. Because the ability to pay to reduce mortality risks increases with income, it is highest for high-income countries. The value of avoided mortality as a percent of income is, however, much higher as a proportion of income for low-income and middle-income countries—between 8·3% and 9·4% of gross national income, reflecting the fact that most pollution deaths occur in these countries.

Ambient and household air pollution together constitute the largest category of welfare damages for all groups of countries. In high-income and upper middle-income countries, the damages associated with ambient air pollution outweigh the damages associated with household air pollution—ie, eliminating all deaths due to ambient air pollution would yield higher benefits than eliminating all deaths due to household air pollution. The reverse is true in lower middle-income and low-income countries. The damages from unsafe water and sanitation remain substantial, constituting 39% of damages in low-income and 27% of damages in lower middle-income countries.

Panel 6: **Summary of Commission's estimates of the health costs of pollution-related disease**

- In high-income countries, health-care spending on diseases caused by air pollution alone amounted to 3·5% of total health expenditures in 2013.
- In Sri Lanka, the only low-income or middle-income country for which data are available, health-care spending on diseases due to air pollution accounted for an estimated 7·4% of health-care spending in 2013.
- The costs of lost productivity from pollution-related disease are estimated to be between 1·3% and 1·9% of gross domestic product (GDP) in low-income countries, and between 0·6% and 0·8% of GDP in low-middle income countries.
- In high-income and upper-middle-income countries, the cost of lost productivity associated with pollution-related disease is estimated to have exceeded US$53 billion in 2015.
- When the willingness-to-pay method is used to estimate the amount that people would be willing to pay to avoid premature death due to pollution-related disease, the total is estimated to be more than US$4·6 trillion, which is 6·2% of global economic output.

	Ambient air pollution and household air pollution	Unsafe water and unsafe sanitation*	Lead exposure	Total
High income	US$1691 (3·52%)	US$159 (0·33%)	US$303 (0·63%)	US$2153 (4·48%)
Upper-middle income	US$1691 (8·37%)	US$89 (0·44%)	US$118 (0·59%)	US$1898 (9·40%)
Lower-middle income	US$367 (6·38%)	US$143 (2·49%)	US$28 (0·49%)	US$538 (9·36%)
Low income	US$18 (4·83%)	US$12 (3·30%)	US$0·740 (0·20%)	US$31 (8·33%)
Total	US$3767 (5·06%)	US$404 (0·54%)	US$451 (0·61%)	US$4622 (6·21%)

For the calculations see appendix (pp 27–28). *Includes, but is not limited to, no hand washing with soap.

Table 5: Welfare damages (in billion US$) and as percentage of gross national income by pollutant and World Bank country income group (2015)[42]

The welfare losses presented in table 5 (for country-level calculations, see appendix pp 48–52) can also be used to estimate WTP for policies to control pollution. Table 6 shows estimates of the amount a person exposed to pollution would be willing to pay to reduce the risk of death from exposure to each pollutant source to zero, converted to 2015 US dollars at market exchange rates.[42] For country-level WTP calculations, see the appendix (pp 53–56). This WTP estimate is the product of the VSL and the mortality risk associated with the pollutant, which is also shown. The WTP values indicate what a person would be willing to pay to reduce their risk of death due to pollution, assuming that they understood the risk. Some of these numbers might appear low—for example, the WTP per person for an improved water source in low income countries is US$15 per person; however, this would almost be sufficient to cover the capital costs of installing a borehole well (approximately $20 per person).[280] Moreover, measures to control pollution yield benefits beyond reductions in mortality risk, such as convenience and comfort, in addition to health benefits. Reducing outdoor air pollution and smoke from burning solid fuels provides aesthetic and ecosystems benefits, and the health benefits of clean air.

Although high, these numbers almost certainly underestimate the full economic burden of pollution-related disease because of inadequate data in many countries on pollution and disease prevalence, poor knowledge of the toxic effects of many chemicals in widespread use,[36,37] and lack of information on the possible effects later in life of toxic exposures sustained in early life. An issue that contributes to this underestimate is that calculations of productivity losses due to pollution understate the total value of output lost due to premature mortality because deaths of persons over age 64 are not counted in these calculations. It should also be noted that the economic approach for calculating productivity effects reflects only losses in output that are captured in GDP, and thus does not capture productivity losses in domestic work (child care, cleaning, and cooking) or in the informal sector.[281] Finally, GDP does not measure societal wellbeing.[14,282]

The estimates presented here also do not capture the health savings that have been projected to result from the reductions in air pollution that will arise from strategies to slow the pace of global climate change.[2] The evidence for health benefits of climate mitigation was reviewed in the *Lancet* Commission on Health and Climate Change.[97] The annual marginal benefits of avoided mortality from reductions in air pollution that will result from greenhouse gas mitigation strategies are estimated to range from US$50–380 per ton of CO_2 abated, and are projected to exceed marginal abatement costs in both 2030 and 2050.

Research recommendations

We make several recommendations related to research on the economic costs of pollution. Research is needed to improve estimates of the morbidity costs of pollution. This requires measuring the morbidity associated with pollution, which is more difficult than estimating mortality. This improvement also requires valuing morbidity endpoints, which are more diverse than mortality.

Additionally, work is needed to improve estimates of the non-health benefits of reducing pollution. For traditional pollution problems, these estimates should include the value of time savings associated with water and sanitation interventions and improved cookstoves and the education benefits associated with reduced illness in children. For ambient air pollution, estimates should include the aesthetic value and the ecosystem benefits of cleaner air.

Section 3: Pollution-related disease, poverty, and the SDGs

The former Secretary General of the United Nations, Kofi Annan, has declared that "the biggest enemy of health in the developing world is poverty."[283] Pollution, poverty, poor health, and social injustice are deeply intertwined. Pollution and pollution-related disease most affect the world's poor and powerless.[284] Pollution's victims are often the vulnerable and the voiceless. To understand the links between pollution, poverty, and pollution-related disease, it is necessary to elucidate the complex and multidimensional nature of poverty.[285] Poverty is not simply a lack of money. Poverty results also in reduced access to education, health care, nutrition, and sanitation and impedes participation in legal and political processes, when such processes exist, and in civil society. When

www.thelancet.com Published online October 19, 2017 http://dx.doi.org/10.1016/S0140-6736(17)32345-0

	Ambient air pollution	Household air pollution	Unsafe water sources	Unsafe sanitation	Lead exposure
High income	US$1472 (4·0)	US$98 (0·7)	US$11 (0·1)	US$1 (0·007)	US$264 (0·7)
Upper-middle income	US$523 (6·8)	US$214 (2·9)	US$13 (0·2)	US$5 (0·1)	US$47 (0·6)
Lower-middle income	US$85 (6·9)	US$66 (5·7)	US$39 (3·1)	US$23 (1·9)	US$10 (0·7)
Low income	US$13 (4·1)	US$23 (7·4)	US$15 (4·8)	US$11 (3·6)	US$1 (0·4)
Average	US$459 (6·2)	US$123 (4·6)	US$25 (2·0)	US$14 (1·3)	US$64 (0·7)

Numbers in parentheses are number of deaths associated with the pollutant per 10 000 people associated with the pollutant. For the calculations see appendix (pp 27–28).

Table 6: "Willingness to pay" per person (in US$, 2015) to reduce risk of death associated with pollution, by World Bank country income group and pollution type[42]

families lack access to food, clothing, and shelter, they do not have the resources to support even a minimum level of health.

This Section of the Commission report presents data documenting that pollution and pollution-related disease are concentrated among the poor and contribute to the intergenerational perpetuation of poverty. Pollution-related disease can result in lost income and increased health-care costs, thus imposing disproportionately great economic burdens on poor families and communities.[286] In children, early-life exposure to neurotoxic pollutants can impair cognitive function and diminish the ability to concentrate, further contributing to school failure and reducing lifetime earnings. In example, a long-term follow-up study[144] of children exposed to lead reported that an elevated blood lead concentration at age 11 years was associated with lower cognitive function and reduced socioeconomic status at age 38 years, with diminished IQ, and downward social mobility. Moreover, poverty can worsen health, for example, by forcing people to live in environments that make them ill, without decent shelter, clean water, or adequate sanitation.[287] When people live near polluting factories or downstream from hazardous waste sites, or when poor women have no alternative but to cook with traditional stoves in close quarters, or when children are forced to pick by hand through electronic waste to recover precious metals to sustain themselves and their families,[288] poverty can exacerbate poor health.

Without political influence and with little power in most countries to control or prevent pollution, the poor have limited ability to determine the fate of their communities. Their dependence for survival on tight social networks further restricts their mobility and opportunities. The result of these interconnected forces is that poverty is a trap that often spans generations. The poor have disproportionately heavy exposures to pollution and disproportionately high amounts of disease, disability, and premature death.[289,290] A major challenge to enlightened heads of government is to balance economic development that lifts people and communities out of poverty against pollution control and the prevention of pollution-related disease.

Pollution threatens fundamental human rights: the rights to life, to health, and to wellbeing.[291] It jeopardises the rights of the child, the right to safe work, and the protection of the most vulnerable.[292] Pollution and pollution-related disease are often reflections of environmental injustice. Many countries recognise the right to a healthy environment as a basic human right linked to the right to life and other fundamental human rights.[293,294] The right to a healthy environment also includes the right to safe food and water and adequate housing.[293,294]

Recognition of the right to a healthy environment requires that all members of a society have unfettered access to information about sources and patterns of pollution; that they have the power to participate in environmental planning and decision making; and that there is an environmental regulatory agency and an independent judiciary that protect the environment from polluters, and the poor against pollution.[295]

Pollution and pollution-related disease are often reflections of environmental injustice. Robert Bullard, widely regarded as the father of the environmental justice movement,[296] defines a core principle of environmental justice as "all people and communities are entitled to equal protection of environmental and public health laws and regulations."[297] Bullard stresses that environmental justice is a far-reaching concept that involves much more than equal enforcement of laws and regulations. In Bullard's view, environmental justice is a basic human and civil right and requires meaningful and timely involvement of people and communities in decisions that affect their environment and wellbeing. In 1991 Bullard and his colleagues, at the first National People of Color Environmental Leadership Summit adopted 17 Principles of Environmental Justice.[298] These principles were developed as a guide for organising, networking, and relating to government and non-government organisations.

Environmental injustice is the inequitable exposure of poor, minority, and disenfranchised populations to toxic chemicals, contaminated air and water, unsafe workplaces and other forms of pollution, and the consequent disproportionate burden among these populations of pollution-related disease, often in violation of their human rights. Environmental injustice has been characterised as a form of structural violence.[299] In many instances, environmental injustice is linked to so-called "structural racism".[300]

Panel 7: **India's judicial system for pollution**

During the UN Conference on Environment and Development in 1992, India committed to providing judicial and administrative remedies for the victims of environmental damage. To fulfil this commitment, India became the third country in the world to start a National Green Tribunal, a judicial body exclusively established to judge environmental cases. The National Green Tribunal was formed on Oct 18, 2010. The focus of this body is on the effective and expeditious resolution of cases relating to environmental protection and conservation of forests and other natural resources. The National Green Tribunal is mandated to make final judgments on applications and appeals within 6 months of their filing. The National Green Tribunal is comprised of judges, who are supported by environmental experts to provide informed guidance on environmental issues, to validate the Tribunal's legal judgments.

Cases such as the Vedanta Bauxite Smelter in Orissa, the Thermal Power Plants in Andhra Pradesh, and the Jaitpur Nuclear Power Plant in Maharashtra have seen controversy and protests. The involvement of the National Green Tribunal has resulted in amicable solutions to these cases, ensuring the people of the affected regions a safe and liveable environment. Before establishment of the National Green Tribunal there were numerous cases in which large industries were confronted by local people fighting for the environment.

Global spread of extractive industries: oil and gas production, mining, and smelting

Social and economic factors that have contributed to the global spread of environmental injustice and the inequitable exposure of poor and marginalised populations to pollution and disease include globalisation, which has caused the movement of hazardous industries such as chemical manufacture, steel making, pesticide production, and shipbreaking from higher income countries to low-income and middle-income countries. This movement has entailed low wages, little or no environmental and occupational regulation, and weak public health infrastructure. The consequences of these occupational and environmental conditions are disease and injury in underprotected workers, diseases caused by toxic chemicals in residents of communities near polluting facilities, and industrial explosions. Examples include the chemical explosion in Bhopal, India where a pesticide production factory that had been trans-shipped from the USA detonated and killed and injured thousands or workers and local residents; the global trade in asbestos that results in shipment of 2 million tons of asbestos annually to the world's poorest countries, where it will produce epidemics of lung cancer, mesothelioma, and other malignancies;[214] and the global trade in banned and restricted pesticides.

Transboundary transfers of hazardous and toxic wastes, such as electronic wastes and chemical wastes, from high-income to low-income and middle-income countries are a further cause of the global spread of environmental injustice. The global spread of artisanal and small-scale gold mining and the concomitant spread of occupational and community-wide exposure to elemental mercury and methylmercury are another example.[112,113] The expansion of gold mining is driven by large increases in the global price of gold, which encourage poor people to leave agriculture and other traditional occupations. Although small-scale mining is relatively profitable for the miners, it is highly exploitative in that the majority of the profits accrue with brokers and retailers, and the burdens of disease and environmental degradation fall almost entirely upon mining communities. Regional conflicts and wars, frequently driven by a desire for natural resources (namely oil, minerals, and timber) further aggravate these problems.

Environmental injustice exists in countries at all levels of income and development and in all regions of the world,[284,301–303] as can be seen in the following examples and case studies.

Combating environmental injustice

To advance environmental justice and reduce the inequitable exposure of the poor and the marginalised, countries must develop legal mechanisms that provide recourse for environmental injustice. India's green court, for example, provides citizens with access to an independent judiciary that has the power to redress pollution injustices. Such a system, when connected with openly shared data on toxic exposures and health can serve as a powerful mechanism to address environmental injustice (panel 7).

Environmental injustice in North America is well documented. Recurrent racial and ethnic disparities have been documented in North America in exposures to various forms of pollution. A study of the ambient air pollution in New York City have documented that almost all diesel bus depots, places where buses idle their engines for hours while emitting pollutants, are in minority, mostly disadvantaged neighbourhoods. Disproportionately increased prevalence of asthma and other respiratory diseases have been documented among children in these communities.[304] In the so-called "Cancer Alley" region of Louisiana, an 85 mile stretch along the Mississippi River where 125 companies manufacture a quarter of all petrochemical products made in North America, the US Commission on Civil Rights determined that the African-American community was economically disadvantaged and disproportionately affected by pollution from hazardous facilities.[305] Another case study[306] of environmental injustice in the USA relates to the exploitative uranium mining operations on Native American (Navajo) lands. Mining operations there depleted and contaminated the scarce water supply and produced high prevalence of lung cancer in Navajo underground miners, who suffered intense occupational exposures to radon.[306] A final example involves the disproportionate exposures of Hispanic farm workers to acutely toxic organophosphate pesticides, such as parathion. Several cases of acute pesticide poisoning have resulted. Many of these workers are undocumented immigrants and, hence, afraid to protest environmental injustice and pollution.[307]

www.thelancet.com Published online October 19, 2017 http://dx.doi.org/10.1016/S0140-6736(17)32345-0

In Canada, environmental injustice occurs in the traditional lands of First Nations (indigenous peoples). First Nations are battling the Alberta Oil Sands Project in northern Alberta[308] and exposure to Canada's worst air pollution hotspot in Ontario's so-called "Chemical Valley", where 40% of the country's chemical manufacturing is located.[309]

Environmental injustice issues are also prevalent in Europe.[310] In central and eastern Europe, some minority Roma people and refugee and displaced communities from Kosovo have faced environmental injustice. In Kosovo, camps for displaced Roma were located in an area polluted by toxic tailings from a lead mine. In Durres, Albania, refugees from Kosovo were housed in a disused chemical plant that had previously produced sodium dichromate and lindane, compounds classified by the International Agency for Research on Cancer as class 1 (proven) human carcinogens.[311]

In Asia, the sustained economic growth that has enabled substantial reduction in poverty has simultaneously increased toxic pollution and environmental inequity.[312] In China, a highly publicised example involved a paraxylene chemical factory in the city of Dalian, where residents feared that typhoons could breach chemical storage tanks and flood lower socioeconomic areas of the city with toxic material.[313]

In India, a well studied example of environmental injustice is the disproportionate siting of mineral and metals extraction facilities in the Adivasi belt of central and northeast India where 70 million Adivasis—tribal people—live in extreme poverty and are disproportionately exposed to air, water, and soil pollution produced by these facilities.[313] In a landmark case linking the mining industry in the Adivasi belt to environmental injustice,[314] the Indian Supreme Court observed that the fundamental rights of citizens, guaranteed by the Constitution, included "the right of enjoyment of pollution-free water and air for full enjoyment of life".

In Africa, extraction of natural resources is a major driver of environmental injustice and pollution. In Zambia, the lead and zinc mines at Kabwe are among the world's most polluted places. Although these mines are no longer active, the residue left behind after decades of extraction by overseas-based companies have contaminated soil and the local water supply. Children in Kabwe have blood lead concentrations that are 5–10 times higher than the threshold concentration recommended by the US Centers for Disease Control and Prevention.[315] Mineral extraction has also been associated with environmental injustice in post-apartheid South Africa, where large-scale gold mining has resulted in epidemic silicosis among miners, many of them economic migrants from the poor countries of southern Africa surrounding South Africa.[313] Gold mining was also the cause of the 2010 tragedy in Zamfara State, Nigeria, in which 163 people in deeply impoverished communities, including 111 children, died of acute lead poisoning.[316] Similar events have been recorded in relation to gold mining in Ghana.

In Latin America, environmental inequality is evident in a series of clashes between extractive industries, particularly the mining industry but also oil and gas production, and indigenous communities. Examples include the Tia Maria copper project in Peru, operated by Mexico's Southern Copper Corporation, the world's second largest copper mining company, and the USA-based Newmont Mining Company's US$4·8 billion Conga gold-copper project, Peru's biggest mining investment. Protests against the inequitable placement of these enormous projects on lands belonging to native peoples and the resulting disproportionate burdens of pollution, environmental degradation, and disease are reshaping basic paradigms of resource-based development. These struggles have forced contemporary legal systems, including legal systems in the high-income home countries of mining conglomerates, to accommodate indigenous world views and to correct, rather than perpetuate the unjust effects of economic growth upon the poor.[313,317]

With the worldwide spread of toxic chemicals and modern-day pollution, interest has grown in investigating, documenting, and mapping environmental injustice. Information produced through these efforts, especially information documenting patterns of pollution at the local level, can provide powerful leverage to disproportionately exposed communities who are struggling to reduce their exposure and their inequitable burden of pollution-related disease.

In Europe, the Environmental Justice Atlas, a global online database, now lists information on about 2000 sites around the world where pollution and environmental injustice are documented or suspected. Linked to this database is Environmental Justice, Organisations, Liabilities and Trade, a global research project supported by the European Commission that is compiling The Map of Environmental Justice, an atlas of maps documenting the distribution of pollution and environmental injustice around the world.[318]

For the Environmental Justice Atlas see https://ejatlas.org/

Pure Earth, a New York-based environmental non-profit organisation has developed a Toxic Sites Inventory Program that includes information on about 3500 polluted sites—active and abandoned mines, smelters, factories, and hazardous waste dumps—a number that is still growing.[38] This database focuses on contaminated sites in low-income and middle-income countries and has served as a resource to the work of this Commission.

In the USA, the Environmental Protection Agency has developed an open-access mapping tool, EJSCREEN, that is available on the EPA website and makes data on environmental injustice publicly available. This tool overlays 12 environmental factors, including information on levels of airborne particulate matter, lead paint, and proximity to water discharges with six demographic factors, including income level and percentage of the population classified as minority. The resulting maps

For EJSCREEN see https://www.epa.gov/ejscreen

enable people to check their neighbourhoods and to directly examine the intersection of pollution with poverty.

The global distribution of pollution and pollution-related disease illustrates the connections between pollution, poverty, and environmental injustice. 92% of pollution-related deaths occur in low-income and middle-income countries (figure 8). In countries at every level of income, the health effects of pollution are most frequent and severe among the poor and the marginalised. By far, the largest share of pollution-related diseases is the outcome of urban and household air pollution. However, water pollution and toxic occupational exposures are also crucial contributors to mortality and morbidity.

Air pollution, poverty, and environmental injustice

In 2015, more than 99% of deaths due to household air pollution and approximately 89% of deaths due to ambient air pollution occurred in low-income and middle-income countries.[319,320] Several cities in India and China record average annual concentrations of $PM_{2.5}$ pollution of greater than 100 μg/m³, and more than 50% of global deaths due to ambient air pollution in 2015 occurred in India and China.

Ambient air pollution in rapidly expanding mega-cities such as New Delhi and Beijing attracts the greatest public attention; however, WHO documents that the problem of ambient air pollution is widespread in low-income and middle-income countries and finds that 98% of urban areas in developing countries with populations of more than 100 000 people fail to meet the WHO global air quality guideline for $PM_{2.5}$ pollution of 10 μg/m³ of ambient air annually.

Household air pollution offers an even starker example of the strong links between pollution and poverty.[57] Deaths due to household air pollution are highly concentrated in the world's poorest countries.[57] An estimated 3 billion people in low-income and middle-income countries, mostly in rural communities, use solid fuels (firewood, biomass, or charcoal) and traditional stoves for heating and cooking.[57] In sub-Saharan Africa, for example, firewood is the main source of fuel, as it is in many parts of south Asia. The use of biomass fuels is closely linked to gender inequality. Without access to the cleaner fuels and cookstoves available to many urban households, rural women in these regions and their children are disproportionately exposed to toxic fumes from smoky open fires. As they cook food for the family or study by the light of the stove, these women and children court sickness and premature death in a way their urban counterparts do not.

For the Basel convention see http://www.basel.int/

Water pollution, poverty, and environmental injustice

Poor water and inadequate sanitation and hygiene are also highly concentrated in the world's poorest countries. An estimated 2·5 billion people lack access to a basic toilet; 1 billion people defecate in the open; and 748 million people lack clean drinking water.[321] Poor people living in rural areas, indigenous peoples, people with disabilities, and other marginalised groups are especially likely to lack these basic services.

A sharp gender gap is evident in the health and social effects of water pollution and inadequate sanitation. Girls are particularly severely affected by inadequate access to safe water because the task of collecting water falls disproportionately on them and because lack of water introduces a problem with menstrual hygiene. The many hours that girls in poor communities must spend fetching water increase the risk that they will miss school and, thus, remain trapped in their communities by lack of education. If a school does not provide safe, private toilets, monthly periods can also force girls to miss class or to leave school altogether.[322]

Of all deaths due to toxic occupational exposures, 92% occur in low-income and middle-income countries. This distribution reflects the fact that high-income countries have largely solved their worst problems of occupational exposure and reflects the international migration of polluting industries from high-income countries to poor countries.[323,324]

As a consequence of globalisation and production outsourcing, pollution and pollution-related disease have become planetary problems.[325,326] Dumping hazardous materials produced in high-income countries in poorer countries is a clear intersection between global pollution and environmental injustice. This dumping includes shipment of pesticides, industrial waste, and toxic chemicals that are no longer permitted in North America or the European Union to poor countries. For example, in 2006, 500 tons of toxic waste were transported from Amsterdam in the vessel Probo Koala and dumped in sites around Abidjan, Côte d'Ivoire. The toxic gas produced by the release of these chemicals resulted in 17 deaths and in more than 100 000 cases of respiratory and gastrointestinal disease.[327,328] A second example has been documented at a large electronic waste site at Agbogbloshie in Accra, Ghana.[329] This site contains thousands of broken computers and other electronic components shipped from European countries in containers labelled "secondhand goods"; the European Union allows export of genuinely reusable electronic goods, but the material shipped to Agbobloshie is usually broken beyond repair and hardly reusable.[326] Electronic waste dumpsites in poor neighbourhoods can be found worldwide, especially in the Asia-Pacific region. It is estimated that the global electronic waste market will quadruple in the next decade, from US$9·8 billion in 2012 to $41·4 billion in 2019.[330]

International action to address the global problem of dumping led to development of the 1989 Basel Convention on the Transboundary Movement of Hazardous Wastes and to conventions on persistent organic pollutants,[80] pesticides, mercury, hazardous waste, and chemicals. The European Union also joined the cause and has issued directives to limit international

dumping that include restrictions on hazardous substances and on waste electrical and electronic equipment, both promulgated in 2002. Although these conventions and directives are limited by weak enforcement and by structural impediments, such as the requirement in the Rotterdam Convention for complete unanimity amongst all participating countries before a pollutant can be proscribed, they have, nonetheless, helped to slow the global movement of toxic substances and reduce toxic pollution.

Pollution, poverty, and the UN's SDGs

The SDGs were adopted by the United Nations in September 2015 to guide the international development agenda until 2030. The SDGs are intended to advance human dignity in countries around the world.[331] It is of note that the predecessor to the SDGs, the Millennium Development Goals that guided global action until 2015, made no mention of pollution at all. By contrast, SDGs focus on the issue to an extraordinary extent, as noted in the introduction, and as befits an issue so integral to the fight against poverty. The main provision is, appropriately, in SDG 3 on good health and wellbeing, where SDG 3·9 commits the world community, by 2030, to "substantially reduce the number of deaths and illnesses from hazardous chemicals and air, water, and soil pollution and contamination".[332] The other pollution-specific goal is SDG 6 on water and sanitation, in which SDG 6·3 calls, by 2030, to "improve water quality by reducing pollution, eliminating dumping and minimizing release of hazardous chemicals and materials, halving the proportion of untreated wastewater and substantially increasing recycling and safe reuse globally".

However, the SDGs do not leave the issue there. Given the close linkages between poverty and exposure to toxic pollution and the need to reduce, if not eliminate, both, the SDGs seem to recognise that some actions to achieve the broader goals, such as SDG 1 (end poverty) and SDG 2 (end hunger), could, if unchecked, result in exacerbation of pollution exposures. Hence, pollution control must be central to agricultural and industrial development, if development of these is to be truly sustainable. To this end, the SDGs make repeated references to preventing and reducing pollution. These include SDG 2·4 (improving soil quality), SDG 7 (clean energy), SDG 9·4 (clean technologies and industrial processes), SDG 11 (sustainable cities and communities), SDG 12 (responsible consumption and production), and SDGs 14–15 (water and land conservation). Achievement of these SDGs will also positively affect environmental justice and fulfil SDG 10 (reduced inequalities). Importantly, measures to reduce greenhouse gas emissions and short-lived climate pollutants, such as black carbon, will help achieve SDG 13 (climate action).

The SDGs are explicitly about sustainable development but, for development to be sustainable, it must both combat poverty and ensure equity. In 1987, the Report of the World Commission on Environment and Development on "our common future" stated that sustainable development must assure the poor that they receive a fair share of the resources required to sustain their economic growth.[333] With the growing recognition that pollution not only exacerbates poverty but leads to environmental injustice, sustainability of development is now also increasingly linked to equity. As observed in the Human development report 2011 by the United Nations Development Programme,[334] sustainability and equity might not always be mutually reinforcing (although they can sometimes be), and the most feasible alternative solutions might require explicit and careful consideration of the trade-offs involved. Such an approach to pollution control will not only yield positive synergies between sustainability and equity but also ensure that the SDGs regarding poverty, pollution, and environmental justice are comprehensively met.

For the Rotterdam convention see http://www.pic.int/

The Regional Action Plan for Intergovernmental Cooperation on Air Pollution for Latin America and the Caribbean, prepared by UN Environment Programme in the context of the Latin America and the Caribbean Forum of Ministers of Environment is an example of a high-level plan that sets out common directions for national governments to work together on broad issues.[335] This Action Plan promotes collaboration towards the creation and adoption of national and local policies and programmes to reduce emissions of key pollutants and to achieve improvements in urban air quality in the region. The Action Plan covers broad supportive activities such as technical assistance, policy cooperation, methods, research, and awareness raising and monitoring. The Regional Action Plan will support and encourage the national and local administrations to develop and implement practical local plans to reduce the effects of air pollution.

Research recommendations

To reduce the inequitable exposure of the poor and the marginalised to pollution, this Commission recommends two key strategies. First, we recommend funding of research to document and map the disproportionate effects of pollution upon the poor, women, and girls be adopted as a priority by international health agencies. Additionally, a special focus should be placed on overseas development assistance to protect indigenous peoples and their communities from pollution and its harmful effects.

Section 4: Effective interventions against pollution: priorities, solutions, and benefits

A key message of this Commission report is that, with leadership, resources, and a clearly articulated, data-driven strategy, much of the world's pollution can be controlled and pollution-related disease prevented. Strategies to curb pollution have been developed, field-tested, and proven cost-effective. These strategies were developed initially in high-income countries and are now moving into

middle-income countries. They are based on law and regulation, rely heavily upon technology, are subjected to continuous evaluation, are backed by strong enforcement, and incorporate the polluter-pays principle. These programmes are held accountable to targets and timetables. These successful, effective strategies for pollution control can be used as models and adapted to local circumstances in cities and countries at every level of income. Their application can enable developing cities and countries to leapfrog over the worst of the human and ecological disasters that have plagued economic development in the past.

For the Minamata convention see http://www.mercuryconvention.org/

A second key message is that control and prevention of pollution provide several benefits, both short-term and long-term, for societies at every level of income. The direct benefits of pollution mitigation include improvements in air and water quality and improvements in health. The health benefits include reductions in disease incidence and prevalence, improvements in children's health, reductions in the numbers of premature deaths, increasing longevity, and substantial enhancements in quality of life. Indirect benefits include enhancing gender equity, alleviating poverty, increasing tourism, improving education, and enhancing political stability. Pollution control makes cities more liveable and attractive, benefits ecosystems, improves the economy and, when coupled with efforts to transition to clean fuels and to control emissions of greenhouse gases, pollution control can help to slow the pace of global climate change and accelerate the transition to a cleaner, more sustainable, circular economy.[81,336,337]

These many benefits of pollution control underscore the reality that pollution is much more than merely an environmental challenge; pollution is a profound and pervasive threat that affects many aspects of human health and wellbeing.

Pollution control today builds on the successes of the past. The industrially developed countries were the first to control pollution, and many of their control strategies were adopted in the aftermath of environmental and public health disasters caused by pollution. Thus, in mid-19th century London, UK, putrid contamination of the River Thames and recurrent epidemics of cholera led to regulation of public drinking water sources[338] and to the construction of large conduits for the removal of human waste and industrial pollution that now form the Thames Embankment.[339] Episodes of severe air pollution with substantial loss of life, such as the Great Fog of London in 1952,[340] and the Donora, Pennsylvania episode in the USA led to the passage of clean air legislation. Occupational and mining disasters catalysed the development of worker health and safety legislation. The discovery of contaminated toxic sites in the USA at Love Canal in New York and the Valley of the Drums in Kentucky led to legislation mandating clean-up of hazardous waste sites—the Superfund legislation.[175] An epidemic of congenital methylmercury poisoning in Minamata, Japan[341] led to global action to protect human health and the environment against mercury and culminated in adoption of the Minamata Convention.[198]

In response to the rapid, poorly controlled growth of cities and the global spread of industrial production and chemically intensive agriculture, low-income and middle-income countries have become increasingly engaged in pollution control. Targeted interventions to control water pollution, improve sanitation, and reduce waterborne diseases were among the earliest efforts to control pollution in low-income and middle-income countries, and began as early as the 1950s. Bangladesh has long been in the forefront of this work,[342,343] China has made extraordinary progress in control of water pollution and prevention of waterborne infectious disease (panel 8),[344–354]

***Panel 8:* China's recent experience**

In its 13th Five-Year Plan, for 2016, the Government of China acknowledged the dangers posed by pollution[344] and set specific targets for environmental improvement and restriction of resource use.

Air pollution

- China adopted The Air Pollution Prevention and Control Law in 1987. This law and its subsequent revisions have resulted in an 10% national decline in particulate matter less than 2·5 μm ($PM_{2.5}$) between 2014 and 2016, despite extremely high particulate concentrations in certain cities such as Beijing.[345] A 2016 amendment to the law explicitly mentioned, for the first time, the connection between environmental protection and public health.[346]
- China has increased its reliance on non-fossil energy sources (predominantly renewables and nuclear) from 9·4% of total energy use in 2010 to 12·0% in 2015, surpassing the 12th Five-Year Plan target of 11·4% by 2015. The most recent Five-Year Plan[347] aims to increase non-fossil energy use to at least 15% by 2020, and to at least 20% by 2030.
- China has implemented a vast network of stations to monitor air quality in more than 400 cities. The capacity to track emissions has been central to developing policy and implementing data-driven regulatory frameworks.[348]

Water pollution

- China's most recent water pollution legislation, the Water Ten Plan, was adopted in April, 2015.[349] This plan sets metrics and targets for ten major polluting industries. Among key targets to be met by 2020 are: more than 70% of water in seven key rivers shall reach Grade III or above; more than 93% of urban drinking water sources shall reach Grade III or above; reduce groundwater extraction and control groundwater pollution; and use of groundwater falling under the "very bad" category shall decrease to around 15%.
- The Ministry of Environmental Protection estimates that the Water Ten Plan will boost GDP by ¥5·7 trillion (US$91 billion), with a ¥1·9 trillion benefit to the affected industries.[350]

Soil pollution

- The 13th Five-Year Plan calls for the establishment of laws to monitor, prevent, and remediate soil pollution. The goal is to make 90% of polluted arable land safe for agricultural use by 2020, increasing to 95% by 2030.[351] The Ministry of Environmental Protection estimates that the actions of the 13th Five-Year Plan could add ¥2·7 trillion ($411 billion) to the nation's GDP and create around 2 million jobs.[352]
- The Five-Year Plan also details a nationwide soil quality monitoring programme.[353,354]

and Peru has embarked on a programme to improve mine drainage.[355]

Air pollution control programmes are developing in cities in several low-income and middle-income countries, including Mexico City,[356] Ulaanbaatar,[357] and New Delhi.[358] China is embarking on a national effort to reduce air pollution that includes a plan to dramatically increase reliance on non-polluting, renewable energy sources, and is on track to nearly triple its solar capacity between 2015 and 2020, adding 15 to 20 GW of solar capacity per year.[123,359–361]

Most countries now have programmes in place to address some aspects of pollution, and almost all have established frameworks for regulatory control of industry, although staffing, resources, and enforcement capacity are variable.[362] This Section of the Commission report enumerates the benefits of pollution control, describes key elements of successful pollution control strategies and the responsibilities of stakeholders, and it concludes with recommendations.

The benefits of pollution control

Examples of pollution control and its benefits are presented in this section, panels 9 and 10,[119,131,363–367] and in the appendix (pp 63–107).

One benefit afforded by pollution control is reduction of household air pollution by providing liquefied petroleum gas and bio-gas and by providing affordable electricity that is produced by non-polluting, renewable energy sources to replace wood chips, coal, charcoal, and cow dung as cooking fuels. These interventions not only reduce exposures to airborne particulates, thereby improving health, but they also produce short-term and long-term economic returns to local communities because households (especially women) are able to spend less time collecting wood, or processing dung for cooking, and thus have more time to devote to economically productive activities (for women) or education (for girls).[368]

A second benefit is improvements in sanitation that are achieved by providing clean water and toilets. These interventions not only reduce prevalence of waterborne disease but they also allow more children, especially girls, to attend school.[369] These improvements benefit tourism and help lift the economy in developing countries, since a reputation for clean beaches, an unpolluted environment, biodiversity, and safe food and water can help to lure discerning tourists and increase their spending.[370]

Another benefit is seen in shifting the energy sector from coal-fired power plants to cleaner gas-fired plants, and, better yet, to low-polluting renewable energy sources such as wind, tidal, geothermal, and solar. These interventions not only reduce pollution and improve the cardiorespiratory health of entire populations, but they will also sharply reduce greenhouse gas emissions, and increase the efficiency of electricity generation. [371]

Additional benefits are produced by controlling urban air pollution by upgrading public transportation, encouraging active transport (walking and cycling), reducing sulphur content of motor fuels, promoting use of low-emission and zero-emission vehicles (while concurrently cleaning the energy supply), and restricting car and trucks from city centres. These interventions not only improve air quality, but will also reduce childhood asthma, reduce incidence of cardiovascular disease, stroke, and diabetes in adults, and enhance the quality of urban life.[372,373]

Another benefit in controlling pollution is that remediation of highly contaminated sites in densely

Panel 9: Partial successes in reducing air pollution from cookstoves

China's National Improved Stove Programme

- China's National Improved Stove Programme (1982–92) has distributed 180 million improved cookstoves to people in rural areas of China, in conjunction with provincial programmes. This programme is among the world's largest and most successful national programmes for improved stoves.[363] The initiative aimed primarily to increase efficiency and thus reduce the use of biomass fuel. Middle-income households were targeted in this programme, and households were expected to purchase the stoves themselves.[364] All improved cookstoves had chimneys, and some had blowers for more efficient combustion.
- With regard to the primary objective of achieving better fuel efficiency, China's programme lowered household air pollution levels, but, unfortunately, this reduction was not sufficient to meet China's indoor air quality standards and substantial exposures remained. A fundamental problem was that the stove designs did not reduce emissions, but focused on fuel efficiency and, at best, moved the smoke outside, where it still caused exposures. Nevertheless, the programme showed that large-scale effects could be achieved by a well organised and well supported effort that was coordinated nationally, but with substantial local participation. Additionally, an epidemiological study of household stove improvement that was undertaken in a cohort of 21 232 Chinese farmers followed from 1976 to–1992 showed that stove improvement was associated with a greater than 30% reduction in incidence of lung cancer.[365]

Indian National Programme on Improved Chulha

- A second national programme at a similar scale to the Chinese programme, the Indian National Programme on Improved Chulha stoves, which operated from about 1984 to2001, was reported to have had little effect on fuel efficiency nationally, and even less in reducing long-term exposure to smoke.[365]

Gyapa Stoves Project, Accra, Ghana

- An African example of a successful cookstove intervention was the Gyapa Stoves Project in Accra, Ghana. In 2000, 95% of Ghanaian households used solid fuels to power stoves.[367] This was a much higher percentage than the estimated 73·4% for the rest of northwest Africa. Many homes in Ghana were poorly ventilated and the burning of solid fuels, such as savannah wood, was inefficient and contributed to deforestation and ecosystem imbalance. To address this problem, EnterpriseWorks/VITA, Shell Foundation, and USAID partnered in 2002 to implement a programme to replace traditional coal-pots with improved stoves called the Gyapa Stove. The Gyapa stove requires 50–60% less fuel than traditional stoves and produces less smoke. This project was unusual in that it aimed to create a sustainable business model that helped the local economy by creating jobs to manufacture the stoves. In 2008, 68 000 stoves were sold in Accra and Kumasi. Air quality was found to have improved by 40–45%.

Panel 10: Cleaner fuels and indoor air

In the past 2 years, major advances have made clean fuels more available in several countries. Examples of programmes to introduce cleaner fuels are the following:

The Indian liquefied petroleum gas programme

- In 2016, India set a goal of providing access to liquefied petroleum gas to 50 million additional poor families in 3 years through a large programme that was operated through the national oil companies. In 2016, more than 10 million households have already been targeted through the national Give it Up campaign, in which middle class families voluntarily give up their liquefied petroleum gas subsidy to a family who are below the poverty line, and corporate responsibility funds are earmarked for the upfront costs.

Ecuador's electric induction stove programme

- In Ecuador, the national government has developed a major programme to change every traditional cookstove in the country to an electric induction stove. Electric induction stoves are 50% more efficient and faster than gas or normal electric cooking, and have other advantages, including improved safety. This transition is possible because Ecuador has nearly universal electrification, much of it derived from hydroelectric projects. Other countries, including Paraguay and Bhutan, also have hydropower potential, and both are currently undertaking preparatory studies.
- Ultimately, it is clear that any household use of solid fuel has negative effects on health and that the eventual goal should be the elimination of solid fuel and its replacement with cleaner sources of energy. In the interim, in areas and countries where elimination of solid fuel is not immediately possible, transition to the cleanest biomass stoves should be strongly encouraged.[119] Millions of lives can be extended every year among the poorest populations in the world by such a transition, but the challenges are still great.
- Progress in implementing clean energy is tracked by the International Energy Agency at both the national and sectoral levels, which has shown some advances in the generation of cleaner energy nationally, but inadequate progress in meeting transportation goals. The International Energy Agency concludes that "strong actions linked to stated targets need to be pushed forward to achieve the clean energy potential".

populated areas will reduce the prevalence of poisoning by toxic chemicals and heavy metals, will enhance land values, and encourage urban redevelopment. Brownfield remediation projects have been successful in covering the expense of clean-up by the private sector.[200]

Reductions of exposures to lead from pottery (panel 11)[374–376] and paint will reduce childhood lead poisoning and thus enhance the intelligence, creativity,[169] and economic productivity of entire societies.[46]

A final benefit of pollution control results from bans on the production and use of asbestos, which will reduce asbestosis, lung cancer, and malignant mesothelioma and will therefore produce substantial gains in economic productivity by preventing serious illness and premature death and will also result in reductions to health-care costs. In conclusion, well designed and executed pollution control strategies will advance attainment of many of the UN's SDGs.[16]

Essential components of pollution control programmes

Planning processes that prioritise interventions against pollution, link pollution control to protection of public health, and integrate pollution control into development strategies are the first step to dealing with pollution. Defining and prioritising interventions enables a focus on cost-effectiveness and creates roadmaps for comprehensive solutions.

The key societal underpinnings for successful pollution control at any level of development include courageous and visionary leadership by heads of government—mayors, governors, and heads of state—along with an engaged, informed, and empowered civil society. It is also important that there be a shared societal commitment to protecting human health and advancing social justice and a carefully designed, evidence-driven package of pollution control policies.

Effective plans to control pollution require support from many sectors of society and, therefore, must involve collaborations among many agencies and organisations within and outside governments, and nationally and internationally. These stakeholders must be fully integrated into a city's or a country's development agenda. If they are to be successful, these efforts must include not only ministries of health and environment, but also ministries of finance, energy, industry, agriculture, and transport. Pollution control policy cannot exist in isolation.

Successful strategies rely on a mix of primary prevention approaches that eliminate pollution at source, coupled with downstream pollution control technologies, such as filters and stack scrubbers, that remove pollutants from the waste stream after they have already been formed. Examples of highly transformative strategies for pollution control that are based on primary prevention include shifting the mix of energy sources in a city or country away from polluting fuels toward non-polluting, renewable fuels;[377] use of safer feedstocks in industrial production, such as feedstocks produced by the burgeoning technologies of green chemistry, which eliminate use of hazardous feedstuffs and production of materials that can cause injury to human health and the environment;[378] incentivising the adoption of clean production technologies; and enhancing access to efficient, affordable public transportation.[379] Primary prevention can also be achieved by banning highly hazardous and carcinogenic materials such as asbestos, benzene, PCBs, and DDT, as has been successfully achieved in many countries. Primary prevention of pollution based on the elimination of pollution at source is inherently more effective than downstream control technologies, such as stack scrubbers or water filters that reduce the amount and toxicity of pollutant emissions after they have already been formed. Primary prevention of pollution at source is also essential for accelerating transition to a more sustainable, circular economy.

Further elaboration of these themes and case studies on pollution control are presented in the appendix (pp 63–82). The key elements of all successful pollution control plans are discussed in the following sections.

www.thelancet.com Published online October 19, 2017 http://dx.doi.org/10.1016/S0140-6736(17)32345-0

Establish ambitious but attainable targets and timetables for pollution control

Targets and timetables are essential for programmes to control pollution; these provide benchmarks and metrics for assessing progress towards pollution control. This Commission recommends establishing specific numerical targets and deadlines for pollution control and prevention of pollution-related disease in every city and country, along with incentives for meeting deadlines and penalties for failing to meet them.

Pollution control targets must be appropriate for each country's level of income and development and guided by the WHO pollution control targets. These targets will be most effective when they are focused on pollution sources that are established to be priorities and must be integrated into commitments to meet the SDGs and to reduce greenhouse gas emissions.

Prioritise interventions

It is crucial that pollution control programmes establish and adhere to a robust, systematic, and transparent system for prioritising pollution control that is based on assessment of health effects, environmental damages, and cost-effectiveness of control of various pollution sources. A robust system for assigning priority will avoid the pitfall of prioritising interventions on the basis of political expediency[380,381] or because they happen to be an item in the evening news.

Quick, highly visible successes are extremely important in gaining public support for a pollution control programme. It is therefore essential that intervention plans identify pollution sources whose early control will result in quick wins. Rapid, measurable improvements in public health, especially in the health of children, are powerful levers for building public and political support.

Key steps in ranking pollution sources in terms of their health effects, a key process of an effective health and pollution action plan, are as follows: (1) examine the frequency and severity of disease attributed to various types of pollution using data from national sources and data from the GBD study, and use this information to prioritise interventions against pollution; (2) for each type of pollution apportion the relative contributions of different exposure sources; (3) evaluate the efficacy of new programmes that have potential to reduce health effects from each pollution source, review existing programmes for efficacy and reach, and identify performance gaps and legal, regulatory, and enforcement gaps; (4) identify potential interventions (new and expanded) for those exposures for which there are dramatic effects on health outcomes and measurable indirect benefits, and evaluate these interventions for cost-effectiveness; (5) focus not only on high-visibility sources of pollution, but also on pollution sources that historically have received less attention, such as household air pollution, contaminated sites, lead (including lead in pottery glazes, lead in paint, and lead from other sources that might be specific to a specific culture), and occupational risks, including asbestos; (6) review the benefits of interventions against pollution and health improvement, considering the roles of gender equity, alleviation of poverty, slowing of the pace of climate change, increased tourism, economic growth, improved education, and political factors (panel 12);[382–387] (7) bring all relevant agencies into the prioritisation process, including senior representatives of ministries of health, environment, industry, development, finance, transportation, energy, planning, and legislative branches, and civil society, if possible; and (8) begin implementation with those programme areas where past experience will be a strong return on investment, as measured by benefit to public health and the possibility for early victories: examples include removing lead from paint or pottery, cleaning up highly visible toxic hotspots, banning asbestos, or publishing a ranked list of the most important pollution sources in a city or country, involving the media in advertising early successes.

Panel 11: Mexico's challenge: combating lead pollution

Pottery is produced in more than 10 000 artisanal, mostly small scale, workshops across Mexico. Most workshops use inexpensive, low temperature kilns that are not capable of firmly binding lead glaze to the clay. Lead is therefore released from the glaze into food. Lead has been used for centuries to glaze pottery in Mexico, and pottery is a pervasive source of population exposure to lead.[374–376] Beginning in the 1990s, the Mexican Government determined that prevention of lead poisoning must be a national public health priority and launched a multipronged approach strategy that included interventions against the use of lead in pottery.

The following are key elements of the control strategy:

- Undertake a comprehensive survey of artisanal workshops, to identify those using lead-based glazes
- Track producers and distributors of lead-based glaze and distributors and producers of lead-free glaze to understand the routes to market
- Notify producers and intermediaries that Mexican federal standards impose an absolute prohibition on the use of lead-based glazes in ceramics used for preparing or serving food
- Engage with producers of lead-free glaze to assist them in improving their product to better match the appearance of lead-glazed ceramics and to facilitate distribution
- Create market incentives for use of lead-free ceramics
- Strengthen enforcement of the federal lead glaze standard through improved monitoring and targeted inspections
- Launch a broad communications campaign to educate pottery makers and the public about the dangers of lead-glazed pottery and to advertise the high quality and enhanced safety of lead-free glazes

Establish robust systems for environmental monitoring and public health tracking

High quality metrics that monitor pollution and track progress towards national and local pollution prevention and disease control goals are essential to the success of any health and pollution action plan. Early establishment of public health and environment monitoring systems should therefore be a priority. Evidence-driven updates at

Panel 12: Cost-effective policies to improve access to safe water and sanitation

Disinfection kits for home drinking water and ceramic filters are low-cost technologies for purifying drinking water in rural households without access to safe water. Latrines are a cost-effective solution to open defecation. Chlorination of home drinking water costs between US$50 and $125 per lifeyear saved; ceramic filters cost between $125 and $325.[382]

A seemingly attractive solution to improving access to safe drinking water and improving sanitation would be for donors to distribute chlorination kits, filters, and latrines free of charge. Empirical studies have shown, however, that this approach is ineffective and wastes resources because not all households will use disinfection kits for home drinking water, even when they are provided free of charge. A better solution would be to charge for the technology and subsidise the purchase. Studies suggest that people who pay something for a product are more likely to use it.[383] Another effective approach is to distribute vouchers to households that can be redeemed when a kit is purchased.[384] Requiring households to redeem the voucher separates the households that are likely to use the kit from those that are not.

Lowering the price of ceramic drinking water filters and latrines, which have a large upfront cost, can substantially increase their uptake.[385,386] However, subsidies can be expensive. Microfinancing schemes that spread the cost of water filters or latrines over time have been effective in increasing uptake at a lower cost to funders than total subsidies.[387] This approach allows a larger number of households to be covered for a given expenditure of funds and has the added benefit of gaining household and community ownership of the improvement. Composting toilets might have some advantages in some circumstances, for example where there is no sewage system.

regular intervals are crucial. We encourage governments to consider creation of a central data coordination system that acts as a focus and point of reference for all data on pollution—household, ambient, and occupational. This system should provide validated information and synthesised reports to the public and could be a basic source of raw data for regulators, researchers, and policy makers.

The economic costs of pollution include not only productivity and health costs, but also costs resulting from destruction of ecosystems and loss of key species such as pollinators and fish stocks that convey great benefits to human beings and are crucial to sustaining life on earth. Like the economic losses that result from pollution-related disease, the costs of environmental degradation are mostly invisible. These costs are not captured by standard economic indicators and are buried within the uncounted, unpaid costs of modern industrial and agricultural production.

For the Health Effects Institute http://www.wsp.org/

The Economics of Ecosystems and Biodiversity is a global initiative sponsored by the UN Environment Programme that addresses the challenge of quantifying the economic losses that result from environmental degradation. This initiative applies a structured approach to valuation of ecological losses, explores the visible and invisible costs and benefits that flow from ecosystems into the economy, and evaluates how these flows might change under different policy interventions. The initiative examines the potential consequences of policy reforms that realign incentives and fiscal policy in both negative (ie, polluter-pays) and positive (ie, beneficiary-pays) ways. These scenarios can be analysed and juxtaposed against a scenario in which no changes are made, to identify more sustainable pathways.[388–390]

Monitoring air pollution typically involves a combination of ground-level monitoring and atmospheric dispersion modelling to determine air pollution concentrations and their distribution.[391,392] Low-cost air pollution monitors to measure levels of pollutants on the ground represent an important advance.[393] The use of satellite-based remote sensing to estimate levels of air pollution is gaining increased attention, although the coverage and interpretation of satellite data is still being refined.[394]

The importance of accurate epidemiological data for the prevention and control of disease has been recognised since the work of pioneers such as William Farr,[338] who documented patterns of disease and death during the great cholera epidemic in Britain of 1848–49. National and international programmes for the systematic collection, consolidation, evaluation, and rapid dissemination of data on morbidity and mortality have become a core component of the global public health infrastructure.[395,396]

There are still many gaps in knowledge, especially in poor countries with insufficient resources for systematic data collection.[397] Therefore, only a third of the world's population and only 5% of Africa has usable information on causes of death. China and India have both been redeveloping their verbal autopsy registration systems, in which cause of death is based on data provided by field-trained personnel, and these data systems are improving.[398] Limitations in the quality of public health data reduce the accuracy of global estimates of the burden of disease related to pollution.

Accountability

Accountability is of paramount importance, and programmes for pollution control and prevention must be continuously assessed and held accountable to targets and deadlines using both process metrics (the number of regulations established, monitors installed, or tests performed) and outcome measures (reductions in levels of pollution in air and water, or improvements in health status). Monitoring data and data on progress toward achieving targets and timetables must be made publicly accessible to citizens and civil society.[399–401]

Carefully selected metrics provide an essential foundation to monitoring and accountability. The Health Effects Institute has developed a taxonomy of metrics that can be used to track the progress of pollution control programmes. Regarding air pollution programmes, a summary of metrics suggested by The Health Effects Institute include regulatory metrics, emissions metrics, and pollutant metrics.[399]

Establish a sound chemicals management programme

A high proportion of the 140 000 chemicals and pesticides in commerce have never been adequately tested for safety

or toxicity.[36] Information on potential toxicity is publicly available for only about half of the commercial chemicals with high production volume that are in widest use, and information on developmental or reproductive toxicity is available for fewer than 20% of these widely used chemicals.[402] Because of the failure to test chemicals for toxicity, populations around the world today are exposed to hundreds of untested chemicals and recurrent episodes of disease and environmental degradation have resulted.[36]

To address the problem of population exposure to untested chemicals of unknown hazard, high-income countries are beginning to develop chemicals management programmes.[403,404] Mandatory testing of chemicals for safety and potential toxicity, coupled with the imposition of controls or bans on the manufacture and use of toxic chemicals are the two linchpins of these policies.[36] High-income countries have the resources to establish their own chemical testing programmes such as those supported by the European Chemical Agency and the US National Toxicology programme. Low-income and middle-income countries must rely on results from those testing agencies and on findings on chemical safety and toxicity promulgated by international bodies of high repute that are independent of the chemical manufacturing industry such as WHO's International Programme on Chemical Safety,[109] the International Agency for Research on Cancer, UN Environment Programme,[101] and the Ramazzini Institute.

For the European Chemical Agency see https://echa.europa.eu/information-on-chemicals

For the Ramazzini Institute see http://www.ramazzini.org/en/

Establish and enforce environmental laws and regulations and base regulation on the polluter-pays principle

A strong body of law[405] and clear, transparent, impartially enforced regulations are crucial components of policy packages for pollution control in all countries.

Experience in the USA documents the importance of law and regulation in reducing pollution. Through national regulations established under the US Clean Air Act, the USA has reduced concentrations of six common air pollutants by 75% since 1970 while increasing GDP by nearly 250% (figure 1).[43] Every dollar invested in control of ambient air pollution in the USA is estimated to yield US$30 in benefits (95% CI $4–88).[45]

The State of California has also deployed a suite of laws and policies to control air pollution that, in some instances, are even stronger than US federal regulations.[406] California's policies to reduce traffic-related air pollution include low-emission vehicle standards, a low-sulphur gasoline standard, diesel emissions standards, and financial incentives for replacement and retrofit of high-polluting vehicles. Additional policies that have been very successful include requirements for cleaner diesel fuels in marine vessels and railroad locomotives, and requirements for cleaner diesel fuels for stationary diesel engines and agricultural equipment. Policies to reduce emissions from stationary pollution sources include legally mandated reductions in emissions of oxides of nitrogen and sulphur, mandatory reviews of emissions from new sources, and source-specific emissions standards. Application of these standards has resulted in reductions in levels of major air pollutants by more than 70% in California, produced measurable improvements in children's respiratory health,[44] and has accomplished these goals in a time when the GDP has risen sharply, thus documenting, yet again, that control of pollution does not stifle economic development or societal advancement.[43]

Application of the polluter-pays principle is an important component of environmental regulation. The imposition of legally mandated requirements that polluters pay for their pollution and its clean-up create a powerful incentive to adopt new, more efficient production technologies that will reduce pollution. Application of the polluter-pays principle forces polluting industries to acknowledge and account for the previously externalised costs of pollution. Lastly, application of the polluter-pays principle can generate revenues that help to support the costs of pollution control programmes.

As a corollary to imposing the polluter-pays principle, it is important that governments also end subsidies to polluting industries such as coal, oil, gas, and chemical production. When polluting industries are granted subsidies by governments, these governments and the taxpayers who support them are indirectly paying to be polluted.

A competent, independent, non-corrupt judiciary provides an essential back-up to environmental laws and regulation.[407] An independent judiciary is needed to ensure the fair and impartial application of regulatory standards and to protect people, especially indigenous people and their lands, from the damaging effects of polluting industrial activities. For further discussion on existing national and international chemical control legislation and agreements, see the appendix (pp 13–14).

Engage with the private sector

This Commission emphasises that multiple stakeholders should be involved in controlling pollution and preventing pollution-related disease, including top government leaders, but also key civil servants, business, academia, and civil society. Carefully listening to the views of the most important and influential stakeholders (both formal and informal) can help to ensure that all the parties who can advance (or derail) programmes are taken into account.[77]

Enlightened business leaders can be powerful advocates for pollution control and disease prevention. The creation of incentives by governments for non-polluting industries can be powerful catalysts for innovative action, as seen by the rapid development of solar power systems and the organic food industry.

Support city-level initiatives to encourage active transport: reward walking and cycling, increase access to and affordability of public transport, and minimise use of motorised transport

Cities now house more than half of the world's population, a fraction that is growing rapidly, are responsible for 75% of greenhouse gas emissions, and account for 85% of global economic activity.[408,409] Cities, especially rapidly growing cities in low-income and middle-income countries, have some of the world's highest concentrations of ambient air and chemical pollution and the highest prevalence of disease caused by these forms of pollution.

Important initiatives are now underway in cities around the world to reduce emissions of both pollutants and greenhouse gases, and to make cities more resilient and sustainable. Several organisations at the local, national, and global levels have contributed to this progress and they include the Regional Plan Association in New York, the World Bank's Eco2Cities initiative, and the UN Department of Economic and Social Affairs urbanisation planning programmes.

Mayors have been powerful actors in efforts to control pollution and pollution-related disease, and visionary mayors have resurrected formerly blighted cities and turned them into places of extraordinary beauty and high livability.[410] This Commission commends initiatives to launch urban design and planning initiatives that reimagine cities through building green spaces, parks, and walkways, encouraging active transport (such as walking and cycling), and increasing access to and affordability of public transport. Such programmes are discussed in detail in the 2016 *Lancet* Series on City Planning and Population Health.[411,412]

Willingness to confront vested interests

Planning and prioritisation processes regarding health and pollution do not always proceed smoothly. The analyses regarding trade-offs between economic development and pollution are nuanced and vary substantially from industry to industry and country to country. In general, when public health externalities are included in the assessment, even primary industries like heavy manufacturing and mining achieve better long-term macroeconomic performance when strong controls for pollution management are in place.[413,414] However, these analyses can be complex and often contentious. Projections of growth rates and of the burden of pollution-related disease should look at sliding ranges of benefit, since low-polluting industries might provide substantial net benefits to a community. Heads of government who successfully confront vested interests, bring agencies together, reduce environmental injustice, control pollution, and prevent pollution-related disease can reap great praise, build a legacy, help the world achieve the SDGs, and earn an honoured place in history.

The next section of this Commission report outlines the contributions that various stakeholders— government, civil society, and health professionals—can make to pollution control.

Responsibilities of governments and major foundations

National, state or provincial, and city governments are powerful actors in efforts to control pollution and prevent pollution-related disease. Governments in countries at all levels of income have made remarkable victories against pollution.

Leadership by the head of government—the President, Prime Minister, Governor or Mayor—is of the utmost importance. Heads of government are uniquely well positioned to educate the public and the media about the importance of preventing pollution-related disease and can create a vision for a country or a city without pollution. These heads of government also have the power to bring together several agencies within their governments—health, environment, finance, transport, industry, energy, and development—to make pollution control a priority.

Heads of government also have great power to address the so-called "political economy" of pollution.[415] Much pollution, especially industrial pollution, is produced by vested interests that profit by externalising the costs of production and discharging unwanted wastes into the environment. These individuals and organisations will typically resist efforts to control pollution. Heads of government have unique power to overcome this resistance and to negotiate just settlements that reduce pollution and achieve social justice. Experience in countries at all levels of income shows that pollution control can be accomplished in the face of powerful opposition, but that the task is seldom easy and requires committed leadership and broad partnerships across civil society.

Responsibilities of international agencies

International development organisations, including UN agencies, multilateral development banks, bilateral funding agencies, private foundations, and non-governmental organisations, have important responsibilities in pollution control and prevention of pollution-related disease that complement and extend the role of governments. These agencies should elevate pollution prevention within the agendas of international development and global health and substantially increase the resources they devote to pollution, establishing it as a priority in funding mechanisms.

These agencies should build on existing global data platforms to develop a central platform to monitor and coordinate information on all forms of pollution globally, and should consider convening a bi-annual conference on pollution.

International agencies should also provide resources to reduce pollution-related disease in low-income and middle-income countries by:

(1) encouraging the development of action plans regarding health and pollution, both nationally and

www.thelancet.com Published online October 19, 2017 http://dx.doi.org/10.1016/S0140-6736(17)32345-0

regionally, and of specific pollution control projects that set time targets; (2) building data tracking systems to collect information on pollution and disease; (3) supporting direct interventions against pollution where such actions are urgently needed to save lives; (4) supporting interventions against pollution when international action can leverage local action and resources; (5) building professional and technical capacity within governments; (6) strengthening the capacity of universities in low-income and middle-income countries to research environmental health science and to train future health and environmental professionals; and (7) supporting research programmes in environmental health science in partnership with international academic institutions, including clinical and epidemiological studies to learn more about the undiscovered links between pollution and non-communicable disease.

This Commission also calls on international foundations and private donors to come together with governments around the world to establish dedicated international development funding specifically dedicated to the control of industrial, vehicular, mining, and chemical pollution. Such funding will be most effective in curbing pollution when its award is contingent upon host countries' implementation of the polluter-pays principle and ending financial subsidies and tax breaks for polluting industries.

Several design options for dedicated pollution control funding could be considered. The first is a new standalone fund analogous to GAVI (the Vaccine Alliance) or the Global Fund to Fight AIDS, Tuberculosis and Malaria, in which private philanthropists and foundations provide start-up monies that are then periodically replenished by governments. Another option is a large trust fund that is hosted and managed by an existing global institution, such as a multilateral development bank or a foundation. Alternatively, a virtual fund with contributions based on explicit agreements could be used. Finally, expansion of existing funding instruments for international development assistance could be used, including funds specifically designated for pollution control.

Responsibilities of citizens and civil society

Citizens and civil society organisations in countries and cities around the world have important responsibilities in the prevention of pollution, and non-governmental organisations have an important role in many countries in holding governments and companies accountable for pollution control and prevention of pollution-related disease. Civil society organisations can contribute to pollution control by acting as watchdogs, by serving as representatives of the public interest, and by advocating for specific policies, regulations, and practices (panel 13).[350] Civil society groups, especially those that are well funded and science-based, are a powerful force to represent poisoned populations. These organisations can highlight omissions in policy and advocate for change.[416] The best of these organisations provide solid policy support to government action and take a long-term, broad view of issues in their actions and recommendations.[417]

Panel 13: Case study: the power of civil society in controlling urban air pollution

National and city governments have key roles in solving pollution problems. But governments cannot act alone. The political will to create, implement, and sustain successful pollution control policies over the long term requires the involvement of citizens and civil society from many sectors. For example, in the winter of 2010–11, hourly air quality data from Beijing began, for the first time, to be publicly released by both the Chinese Government and the United States Embassy. Soon thereafter, so-called "airpocalypses" during winter were documented, and Beijing's air quality data began to be discussed extensively in local and international media. This unprecedented access to real-time air quality data spurred software developers to build apps, pushing the data out to millions. Through apps, social media, and general media outlets, the citizens of Beijing began, for the first time, to feel the air pollution problem in new, immediately accessible, and data-driven ways.

Since that time, China has invested in several programmes to mitigate air pollution. An expanded network of air quality monitors has been installed in Beijing and across the country. Stricter regulatory policies have been implemented. New emergency action plans for high-pollution days have been developed and promulgated. Simultaneously, public interest in pollution has not waned. In 2015, a popular television journalist, Chai Jing, made an independent documentary "Under the Dome" that discussed the effects of air pollution on health, which went viral across the country and then the world. The number of research publications on air pollution in Beijing have exponentially increased.

It is difficult to pinpoint the exact contributions of the policy, activism, technology, research, and media communities to the successful pollution control effort in Beijing and their effects on each other, but clearly their combined efforts are beginning to make a positive difference. Since 2014, government sources in Beijing have reported year-to-year decreases in annual average $PM_{2.5}$ concentrations, and these findings are consistent with data for decreasing concentrations of $PM_{2.5}$, as calculated from the monitor on the United States Embassy.[359]

Although Beijing and China still have a long way to go to clean their air, this case study documents the power of community involvement in pollution control and the crucial importance of data.

Responsibilities of health professionals

Physicians, nurses, and other health professionals have important responsibilities in helping societies to confront the challenges of pollution and pollution-related disease as they have educated societies around the world about the dangers of nuclear war and global climate change.

Health professionals can begin by controlling pollution and reducing carbon emissions from hospitals and health-care facilities and by reducing pollution and carbon-intensive energy sources in their own lives. Health professionals can support local, regional, and national planning efforts and emphasise the links between pollution and health, develop new transdisciplinary educational curricula that build knowledge of environmental health science and about

the health effects of pollution, and support research in exposure science, environmental science, health policy research and health economics.

Partnerships between government, civil society, and the health professions have proven powerfully effective in past struggles to control pollution. For example, in the ultimately successful effort to remove lead from gasoline, which was fiercely resisted for many years by the lead industry, partnerships were built between government agencies, health professionals, and civil society organisations.

Interventions against pollution

Table 7 gives a brief overview of interventions, effective policy solutions, and institutional needs by pollution type. Strategies to improve water and sanitation and to reduce indoor air pollution typically take the form of subsidies, especially in low-income countries, whereas policies to reduce pollution from stationary and mobile sources usually rely on regulation, often in the form of standards. Many of these strategies are policy-based and enforcement-based,[4,18] not requiring large governmental investments.

Section 5: Conclusion—the way forward

Pollution is the largest environmental cause of disease and premature death in the world today. Pollution poses a massive challenge to planetary health[15] and deserves the concentrated attention of national and international leaders, civil society, health professionals, and people around the world. Yet, despite its far-reaching effects on health, the economy and the environment, pollution—especially the rapidly growing threat of industrial, vehicular, and chemical pollution in low-income and middle-income countries—has been neglected in the international assistance and the global health agendas. Strategies for control of industrial, chemical, and automotive pollution in developing countries have been deeply underfunded.[49,50]

The goal of this Commission is to raise global awareness of the importance of pollution, to end neglect of pollution-related disease, and to mobilise the resources and the political will that are needed to effectively confront pollution.

To achieve this aim and advance progress toward the elimination of pollution, members of this Commission

	Ambient air (outdoor) pollution	Household air pollution	Water pollution and sanitation	Contaminated soil and water
Short-term interventions	Identify sources of key pollutants to enable targeted interventions; target control of stationary sources and install dust management systems; establish monitoring systems; mandate improved fuel quality and engine standards; and design and implement effective enforcement systems	Review current interventions—eg, cleaner fuels and cookstoves—and determine the most scalable strategies; targeted education campaigns; expand support for successful current systems	Expand campaigns for handwashing and improved sanitation; review and expand successful small-scale facilities; develop planning for river basin-wide construction of sanitation facilities; initiate construction of expanded sanitation facilities	Create inventories of polluted sites; test solutions with low-cost pilots for highly toxic sites; clean-up of high-impact sites; provide technical assistance and training
Medium-term interventions	Establish requirements for cleaner vehicles, including testing stations (controls on diesel vehicles, catalytic converters, converting to gas); provide incentives for use of electric and hybrid vehicles; upgrade public transport fleets	Expand access to clean fuels and cleaner cookstoves; upgrade heating and other solid fuel systems	Expand individual household connections for water and sewers	Establish disposal facilities; expand remediation projects; develop remediation industry; support brownfields pilot projects
Long-term interventions	Expand or upgrade public transit; facilitate active commuting by constructing walkways and cycle paths; create mechanisms to discourage vehicle use	Full (possibly universal) access to clean fuels	Upgrade existing drainage and sewage treatment	Establish regional and national toxic sites remediation programmes
Policy and institutions	Undertake source apportionment to identify the most important sources of pollution; establish and prioritise control targets and timetables; establish a high-level intersectoral Steering Committee; involve the public and civil society organisations	Define the target population; identify the responsible government agency with a mandate for health improvement; formulate a practical strategy for upgrading or switching fuels; define financial incentives	Define the target population; calculate the level of service required to achieve goals; community involvement strategy; establish a financial strategy	Establish policy and targets; generate specific policies for small and medium-sized enterprises, artisanal and small-scale gold mining, and other sectors; provide a clear mandate to the responsible government agency; define local powers and responsibilities; define and enable structures of financial support
Building capacity	Achieve adequate monitoring and testing of major air pollutants and emission sources; develop understanding of source contributions; use vehicle testing stations	Establish monitoring mechanisms; identify, review, and support local distributors and providers	Contracts or agreements with utilities providers; and strengthen community-level partnerships	Establish regulations and standards; approve technical support providers—eg, laboratories, testing firms—; expand regulation of active polluters; impose the so-called polluter pays principle; end government subsidies for polluting industries
Common gaps and structural issues	Expansion to less well resourced secondary cities	Reduction or elimination of use of solid fuels for heating	Financial sustainability in an era of increasing water shortage	Requirement of special measures at large-scale sites, such as polluted rivers

Table 7: Short-term, mid-term, and long-term interventions against pollution and the infrastructure and actions required to support them

www.thelancet.com Published online October 19, 2017 http://dx.doi.org/10.1016/S0140-6736(17)32345-0

and contributors to this report have initiated a series of activities within different sectors and countries that will extend beyond the life of this Commission and are intended to prevent pollution and save lives. At a global level, several authors of this Commission are in early stages of designing a Global Pollution Observatory, to be housed within the Global Alliance for Health and Pollution. This new observatory will be an international, multidisciplinary collaboration that is focused on coordinating information regarding all forms of pollution in countries around the world and developing solutions based on successes already achieved in other countries. We intend that this observatory will operate in close partnership with the Institute for Health Metrics and Evaluation, UN agencies, Future Earth, the Planetary Health Alliance, and major non-governmental organisations concerned with the wellbeing of the Earth's environment. A major function will be to provide data that assist countries in prioritising pollution initiatives, tracking pollution, and using pollution control metrics, including investments against pollution in countries around the world and to make these data publicly and easily available. The precise metrics to be followed are under consideration, but possibilities include monitoring country-by-country data on the status of regulations against each type of pollution; measuring exposures to key pollutants, country-by-country and regionally; reporting detailed country-by-country statistics on disease and premature death by pollution risk factor, to track performance towards the goals suggested in this report; tracking national and international investment into expanded research on disease and death due to pollution (especially soil pollution caused by heavy metals and toxic chemicals), including studies to discover new and previously unrecognised health effects of pollutants; tracking investments related to interventions against pollution, country-by-country (which can be broken down by source of investment and whether the investment is national or international and public or private); and developing a database to report the cost-efficacy of interventions against pollution, measured in terms of health outcomes.

In partnership with *The Lancet*, the Global Alliance on Health and Pollution plans to revisit the data on health and pollution periodically, and to publish updated information on global trends in pollution, pollution-related disease, and pollution control on a regular basis. The Global Alliance on Health and Pollution will also explore hosting a biennial conference on pollution that will include UN agencies, governments, and representatives of civil society and will review pollution control strategies, share project successes, and explore opportunities and the most cost-effective strategies for pollution control.

At the country level, work is underway to expand health and pollution planning in partnership with governments in low-income and middle-income countries. This work involves multiple organisations and agencies, including the Global Alliance on Health and Pollution, the World Bank, WHO, the UN Environment Programme, and the UN Development Programme. New programmes to educate global leaders and government agencies about proven solutions to pollution are also in development.

Activities to strengthen the involvement of the public and civil society in pollution control are essential because public concern provides a major impetus for governments to act against pollution. A new website is being developed by the Global Alliance on Health and Pollution to show current and, in some cases, real-time data related to pollution in countries across the world. This geocoded website links databases showing air pollution, water pollution, and soil contamination. Users can zoom down to the communities where they live, see the available information, and post their own stories and pictures about pollution. The website will incorporate a link for people to connect with local government organisations for solutions.

For this pollution website see http://www.pollution.org

These efforts are only the beginning, and there is much more to be done. This Commission encourages all efforts to bring the issue of pollution to public attention and supports all solutions to reduce the enormous health burden of this major, yet often hidden, global threat.

Contributors

PJL and RF developed the concept and objectives for the Commission. The full Commission met on two occasions (Nov 9–11, 2015, and June 16–17, 2016) in New York, NY, USA, with an additional meeting in January, 2016 (limited to the Health and Pollution working group, also in New York). The Commission formed four working groups to examine the burden of disease associated with environmental pollution, to calculate the economic costs of documented pollution-attributable global deaths and DALYs, to explore the intersection between pollution and inequality, and to evaluate and develop strategies and roadmaps for successful pollution control. Each working group was responsible for the design, drafting, and review of their individual sections. Working Group 1 (Health) was led by PJL. Working Group 2 (Economics) was led by MLC and AK. Working Group 3 (Environmental Justice) was led by KS. Working Group 4 (Interventions) was led by DHa and RF. Working Group leaders, along with Yewande Awe of the World Bank and Tim Kasten of UN Environment comprised the Report Steering Committee. All authors contributed to the identification of key issues and the selection of four main report sections. As co-chairs of the Commission, PJL and RF planned and coordinated all activities of the Commission, the development and review of the report drafts, and the preparation for external peer review. PJL and RF reviewed and edited all sections of this report. All authors reviewed each stage of the report and approved the final version. PJL wrote the first and subsequent drafts of the Introduction, with input from OA, MLC, RF, AH, AK, KVM, JP, and KRS. For Section 1, PJL wrote the first and subsequent drafts, with input from NB, RB, SB-O'R, JIB, PNB, TC, CM, JF, VF, DHu, BLa, KM, CJLM, FP, LDS, PDS, KRS, WAS, OCPvS, and GNY. For Section 2, MLC and AK wrote the first and subsequent drafts, with input from MG, PJL, KVM, and ASP. For Section 3, KS wrote the first and subsequent drafts, with input from OA, AH, PJL, KVM, MAM, JRo, KRS, AS, and GNY. For Section 4, DHa wrote the first draft, with subsequent drafts written and edited by RF and PJL, with input from NJRA, OA, RA, ABB, NB, AMCS, JF, AH, DHu, MK, BLo, KM, MAM, JDN, JP, JRa, JRo, CS, KRS, AS, RBS, KY, and MZ.

Declaration of interests

BLa served as an expert witness in California for the plaintiffs in a public nuisance case of childhood lead poisoning, in a Proposition 65 case on behalf of the California Attorney General's Office, in a case involving lead-contaminated water in a new housing development in Maryland, in a Canadian tribunal on a trade dispute about using lead-free galvanised

wire in stucco lathing, and as a plaintiff on a case involving lead-poisoned children in Milwaukee, Wisconsin, but he received no personal compensation for these services. His expert witness fees are deposited in a research and training fund at Simon Fraser University (Burnaby, BC, Canada). MG reports grants from the US Agency for International Development, the National Science Foundation, the International Growth Centre, and the Laura and John Arnold Foundation outside the submitted work; MG also reports more than US$10 000 in stocks and bonds, including in firms that pollute and firms that are affected by pollution, as part of a diversified portfolio. All other authors declare no competing interests.

Acknowledgments
Overall coordination of the report was led by Elena Rahona, whose team included Amy Chart, Samantha Fisher, Rachael Kupka, Yaqi Li, Karen McGill, Myla Ramirez, Anthony Rivera, Petr Sharov, Angela Bernhardt, Russell Dowling, Eric Fecci, and Carol Sumkin at Pure Earth; Alvara McBean at Icahn School of Medicine at Mount Sinai; and Kelsey Pierce at Institute for Health Metrics and Evaluation. Several people lent their expertise to contribute to certain sections of the report: Bret Ericson, Christa Hasenkopf, Greg McGruder, and Nadine Steckling. The Commission received invaluable technical advice and input from many individuals, including Gilles Concordel and Marie Concordel, Elena Craft, James Godbold, Nathalie Gysi, Andrew McCartor, Sumi Mehta, Conrad Meyer, Radha Muthiah, Dietrich Plass, Ananya Roy, Baskut Tuncak, and Birgit Wolz. In particular, the authors would like to thank the following people for coordinating input from different teams: Yewande Awe, Jostein Nygard, Ernesto Sanchez-Triana, and Momoe Kanada (World Bank); Annette Prüss-Üstün (WHO); Jill Hanna and Maria Pachta (European Commission); Loïc Viatte (Swedish Ministry of Environment and Energy); Katherine Swanson and Andrea Pavlick (US Agency for International Development), Mathy Stanislaus (while serving for the US Environmental Protection Agency during the Obama Administration), Kara Estep, Mohammad (Mehrdad) Forouzanfar, and Jeff Stanaway (Institute for Health Metrics and Evaluation); Tim Kasten, Fanny Demassieux, Achim Halpaap, and Pierre Quiblier (UN Environment), Natalia Linou, and Douglas Webb (UN Development Programme); and Nilgün Tas (United Nations Industrial Development Organization). This Publication is made possible by financial assistance from the European Union, UN Industrial Development Organization, the Swedish Ministry of Environment and Energy, the German Federal Ministry for the Environment, Nature Conservation, Building and Nuclear Safety, Royal Norwegian Ministry of Health and Care Services, the US Agency for International Development, the US National Institute of Environmental Health Sciences, the Icahn School of Medicine at Mount Sinai, and Pure Earth. The Global Alliance on Health and Pollution (GAHP) served through Pure Earth as secretariat for the Commission. GAHP is a collaborative body that coordinates and advocates for solutions on pollution and health in low-income and middle-income countries. Members include international agencies such as World Bank, UN Environment, United Nations Development Programme, and United Nations Industrial Development Organization, and government agencies globally. The Commission sought input and consultation from the members of GAHP, experts at the World Bank, World Health Organization and the World Health Organization network of Collaborating Centers in Children's Health and the Environment, the Consortium of Universities in Global Health, the Pacific Basin Consortium for Environment and Health, the Superfund Research Program of the US National Institute of Environmental Health Sciences, and a number of Non-Governmental Organizations including the Global Alliance for Clean Cookstoves, Clean Air Asia, Human Rights Watch, the Environmental Defense Fund, Global Poverty Project, and World Resources Institute. The contents of this publication are the sole responsibility of Pure Earth/GAHP Secretariat, the Icahn School of Medicine at Mount Sinai, and *The Lancet*, and can in no way be taken to reflect the views of the European Union or other donors or individual GAHP member agencies. The authors note that they are serving in their personal capacity. The opinions expressed in this article are the authors' own and do not reflect the views of their respective employers.

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