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ECONOMICS AND POLICY IN DIABETES (ES HUANG AND AA BAIG, SECTION EDITORS)

Underutilized and Under Threat: Environmental Policy as a Tool to Address Diabetes Risk

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Abstract

Purpose of Review Diabetes is a burgeoning threat to public health in the USA. Importantly, the burden of diabetes is not equally borne across society with marked disparities based on geography, race/ethnicity, and income. The etiology of global and population-specific diabetes risk remains incompletely understood; however, evidence linking environmental toxicants acting as endocrine-disrupting chemicals (EDCs), such as particulate matter and arsenic, with diabetes suggests that environmental policies could play an important role in diabetes risk reduction.

Recent Findings Evidence suggests that disproportionate exposures to EDCs may contribute to subgroup-specific diabetes risk; however, no federal policies regulate EDCs linked to diabetes based upon diabetogenic potential. Nevertheless, analyses of European Union data indicate that such regulation could reduce diabetes-associated costs and disease burden.

Summary Federal laws only regulate EDCs indirectly. The accumulating evidence linking these chemicals with diabetes risk should encourage policymakers to adopt stricter environmental standards that consider both health and economic impacts.

Keywords Diabetes · Pollution · Toxicant · Endocrine-disrupting chemical · Environmental policy · Environmental justice

> By their very nature chemical controls are self-defeating, for they have been devised and applied without taking into account the complex biological systems against which they have been blindly hurled.
>
> Rachel Carson, *Silent Spring*, 1962

Introduction

Human health is predicated on the delicate balance of nutrient delivery with nutrient utilization. Disruptions in this carefully choreographed regulation can result in hyperglycemia and the clinical diagnosis of diabetes. The consequences of developing this condition are grave. In the USA, diabetes is the leading cause of adult blindness, kidney failure, and non-traumatic amputations while also catalyzing the development of cardiovascular disease, the country's leading cause of death [1]. Importantly, diabetes rates have increased dramatically over the last several decades with 30.3 million individuals or nearly one in ten Americans currently afflicted by the disease and another 84.1 million Americans with prediabetes and at heightened risk for developing diabetes [2]. In addition to the tremendous impact of this condition on the quality of life for individuals and families, the societal costs are significant with the economic impact in the USA alone exceeding $245 billion annually [3]. It is critical to recognize, however, that the impact of diabetes extends beyond the USA as nearly 630 million individuals worldwide are projected to have the disease by 2045 [4]. In addition to these disturbing

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Table 1 Endocrine-disrupting chemicals linked to diabetes and sources of exposure

Endocrine disrupting chemical	Direct (primary) sources of exposure	Indirect (secondary) sources of exposure
Phthalates	Plastic food and beverage containers	
	Personal care products (perfumes, hair sprays, deodorants, nail polishes, insect repellents, and most consumer products containing fragrances)	Air
	Contaminated food and water	Water
	Plastic toys; plastic coatings; PVC-containing products; carpeting and vinyl flooring	Soil
Bisphenol A (BPA)	Polycarbonate plastics	Water
	Some coatings in food and beverage containers	
Polybrominated diphenyl ethers (PBDEs)	Flame retardants	Air, only when borne on particulate matter
Persistent organic pollutants (POPs)	Industrial chemicals	Air
	Pesticides	Soil
	Pharmaceuticals	Water
Polychlorinated biphenyls (PCBs)	Old building materials, including some paints and caulking	Air
	Toxic waste sites	Soil
	Old submersible pumps containing PCBs	Water
	Contaminated fish, meat, and dairy products; freshwater fish	
Organochlorine (OC) pesticides	Some fatty fish	Soil
	Some high-fat meats and dairy products	
DDT	Agricultural products	Air
		Soil
		Water
Dioxins	Industrial waste	Air
	Pesticides	Soil
	Meat, dairy, fish	Water
Perofluoroalkyl substances	Non-stick cookware	Air
	Flame retardant	Soil
	Stain- or water-resistant products	Water
Atrazine	Herbicide	Soil
Tolylfluanid	Pesticides	Soil
Organotins	Plasticizers	
	Marine and agricultural pesticides	Soil
		Water
Arsenic	Insecticides	Air
	Herbicides	Soil
	Glass manufacturing	Water
Cadmium	Pigments	Air
	Plasticizers	Soil
	Steel plating	Water
Mercury	Burning of fossil fuels	Air
	Contaminated fish	Soil
		Water
Particulate matter	Burning of fossil fuels	Air

global trends, there are important disparities in the distribution of diabetes across the population. There are stark differences based on income, education, race and ethnicity, as well as geography that create disproportionate burdens on vulnerable populations. Emerging contributors to overall diabetes trends as well as these disparities include exposures to diabetogenic chemicals, making environmental policies potential tools for modifying diabetes risk.

Environmental Exposures and Diabetes

Traditional concepts of diabetes pathogenesis center on the disease-promoting effects of physical inactivity, caloric excess, and genetic susceptibility; however, a burgeoning body of scientific evidence now suggests that exposures to diabetogenic environmental endocrine-disrupting chemicals (EDCs) may be additional contributors to the global diabetes epidemic [5••, 6, 7]. The Endocrine Society defines an EDC as an

exogenous chemical or mixture of chemicals that interferes with any aspect of hormone function [8]. In addition to the capacity of EDCs to alter traditional hormonal signaling cascades (e.g., estrogen, androgen, and thyroid axes), increasing evidence suggests that a number of EDCs have the capacity to disrupt metabolic regulation and promote diabetes pathogenesis (Table 1 and Refs. [5••, 6, 7]). These compounds include both organic and inorganic chemicals, such as arsenic, pesticides, flame retardants, industrial chemicals and waste products, plasticizers, phytochemicals, pharmaceutical agents, and various chemical constituents in air pollution.

Air Sources

Air pollution includes a number of chemical components, including particulate matter (PM, which is subcategorized by size (PM_{10}, < 10 μm in size; $PM_{2.5}$, < 2.5 μm)), nitrogen oxides (NO_X, including NO_2), and ground-level ozone (O_3). A number of these measures have been associated with diabetes risk and outcomes (reviewed in Ref. [9••]). For example, some studies have demonstrated that increased exposure to fine particulate matter ($PM_{2.5}$) is associated with dynamic changes in insulin resistance [10, 11] and prevalent diabetes [12, 13]. PM_{10} and nitrogen dioxide (NO_2) have been shown to be associated with increased insulin resistance in young children [14], while exposure to PM_{10}, NO_X, and living in close proximity to areas with high levels of traffic have been associated with increased risk of incident diabetes [15–17]. Air pollution has also been linked to diabetes-related mortality [18, 19]. Additionally, air is an underappreciated exposure source for other diabetogenic EDCs, including polyaromatic hydrocarbons (PAHs) and organochlorine compounds (e.g., polychlorinated biphenyls (PCBs) and organochlorine (OC) pesticides) [20].

Water Sources

Various common water contaminants have also been associated with diabetes outcomes. For example, arsenic is thought to contaminate the drinking water of millions of individuals in the USA and globally; moreover, it is known to disrupt metabolic function. Indeed, a number of cell-based and animal studies demonstrate that arsenic impairs glucose homeostasis and has the capacity to alter both insulin secretion and action [21–25]. In addition, epidemiological studies associate arsenic with diabetes risk [26–28]. In addition to arsenic, water-borne exposure is an important source of human contact with other putative metabolism-disrupting chemicals, such as triclosan, perchlorate, alkylphenols, phthalates, cadmium, lead (Pb), and mercury.

Agricultural Sources

Agricultural practices create exposures to diabetes-associated EDCs through both runoff into water and food-borne transmission. For example, OC pesticides like dichlordiphenyltrichloroethane (DDT), used extensively in agriculture from the 1940s through the 1960s, have resulted in measurable human levels persisting decades after elimination of use. Several of these OC pesticides have been linked to diabetes risk. In a meta-analysis of eight studies, plasma hexachlorobenzene was associated with a twofold increased risk of diabetes [29]. Dichlorodiphenyldichloroethylene (DDE), a metabolite of DDT, has also been shown to be associated with incident diabetes in a population of Great Lakes sport fish consumers [30] and a population of Swedish women [31]. Additionally, other OC pesticides have also been associated with incident diabetes, including *trans*-nonachlor, oxychlordane, and mirex [32, 33], as well as dieldrin [34].

Industrial Sources and Challenges

Outside of the USA, environmental catastrophes underscore the metabolic risk of industrial chemical releases [35, 36]. In 1976, a chemical plant explosion in Seveso, Italy resulted in the release of a toxic cloud containing 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD). A study followed exposed populations who either resided in the contaminated areas or immigrated to the area within 10 years of the accident and compared them to those in unaffected areas [36]. In addition to excess malignancy risk, women in the contaminated zones had increased diabetes-related mortality [36]. While this is an extreme example, a number of other industrial products have been linked to diabetes risk in cell-based, animal, and epidemiological studies [5••, 6, 7]. Importantly, industrial practices are an important source of air and water releases, underscoring the complexity of source-based regulations.

Geographic Variations in the Burden of Diabetes

A striking aspect of agricultural and industrial activity in the USA is its geographic distribution, raising important questions about whether that distribution may influence regional differences in diabetes risk. Indeed, pronounced geographic disparities in diabetes exist in the USA and globally [37]. In the USA, age-adjusted diabetes prevalence rates differ by more than twofold across states and threefold across counties [2]. Americans living in rural areas are more likely to develop diabetes than those living in urban areas [38]. Furthermore, there are distinct geographic regions that are diabetes "hot spots." The Centers for Disease Control and Prevention have identified a "diabetes belt" that spans regions of the South and Appalachia in which 11.7% of the population has diabetes compared to 8.5% outside this region [39, 40]. While obesity and physical inactivity are thought to underlie much of diabetes risk, these factors explain less than one third of the

increased risk of diabetes in this region [40]. While certainly multifactorial in origin, these data suggest that aspects of the ambient environment may contribute to diabetes risk and that local and federal environmental regulations may be tools to modify this risk.

Federal Environmental Policy Related to Endocrine-Disrupting Chemicals

Chemicals that have been shown to act as EDCs are managed under myriad federal policies and a patchwork of state and local mandates and guidance. However, existing federal policy does not regulate EDCs based specifically on their endocrine-disrupting properties nor based on their link to diabetes. Furthermore, there is no overarching approach that integrates exposures that occur via multiple routes of exposure. Instead, existing regulatory frameworks are largely based on indirect exposure sources and the non-diabetes-related toxicities of specific chemicals. Despite these imperfect constructs, current data provide insights into how established regulatory approaches may consider exposures to diabetogenic EDCs.

Federal environmental laws began to emerge in the 1950s, with some previously enacted at the federal level to manage disease and water prior to the invention of modern sewage systems. Spurred by the activism of the 1960s, high-profile environmental incidents like that at Love Canal oxford, and the publication of *Silent Spring*, the environmental movement in the USA took flight over the next decade, heightening public awareness of the connections between pollution and health. In 1970, the National Environmental Policy Act was the first law passed to require federal agencies to consider the environmental impacts of their actions. From this emerged new laws and significant amendments to existing ones to regulate many chemicals of concern for human health (see Fig. 1 and Table 2 for a timeline and characterization of milestone legislation). While a fuller appreciation of the links between chemical exposures and diabetes risk would not emerge for another 40 years, many chemicals regulated by these laws were subsequently shown to also be related to diabetes risk.

Air Quality

The first federal legislation on air pollution was the Air Pollution Control Act of 1955, though its scope was limited and states were responsible for regulation. In 1963, the Clean Air Act was enacted to regulate stationary sources of pollution. These initial federal steps were critical because they prompted research programs on air pollution effects and the development of air quality criteria. The Motor Vehicle Air Pollution Control Act was then passed in 1965 and established uniform mobile emissions standards based on cost and feasibility. The Clean Air Act amendments of 1970 marked the beginning of the extensive air quality regulation that exists today. These amendments established the National Ambient Air Quality Standards (NAAQS) for stationary sources and set limits for mobile pollution sources. NAAQS set maximum concentration levels of each criteria pollutant (O_3, carbon monoxide, NO_X, Pb, $PM_{2.5}$, PM_{10}, sulfur oxides (SO_X)) listed within the Clean Air Act, based solely on health risks. This

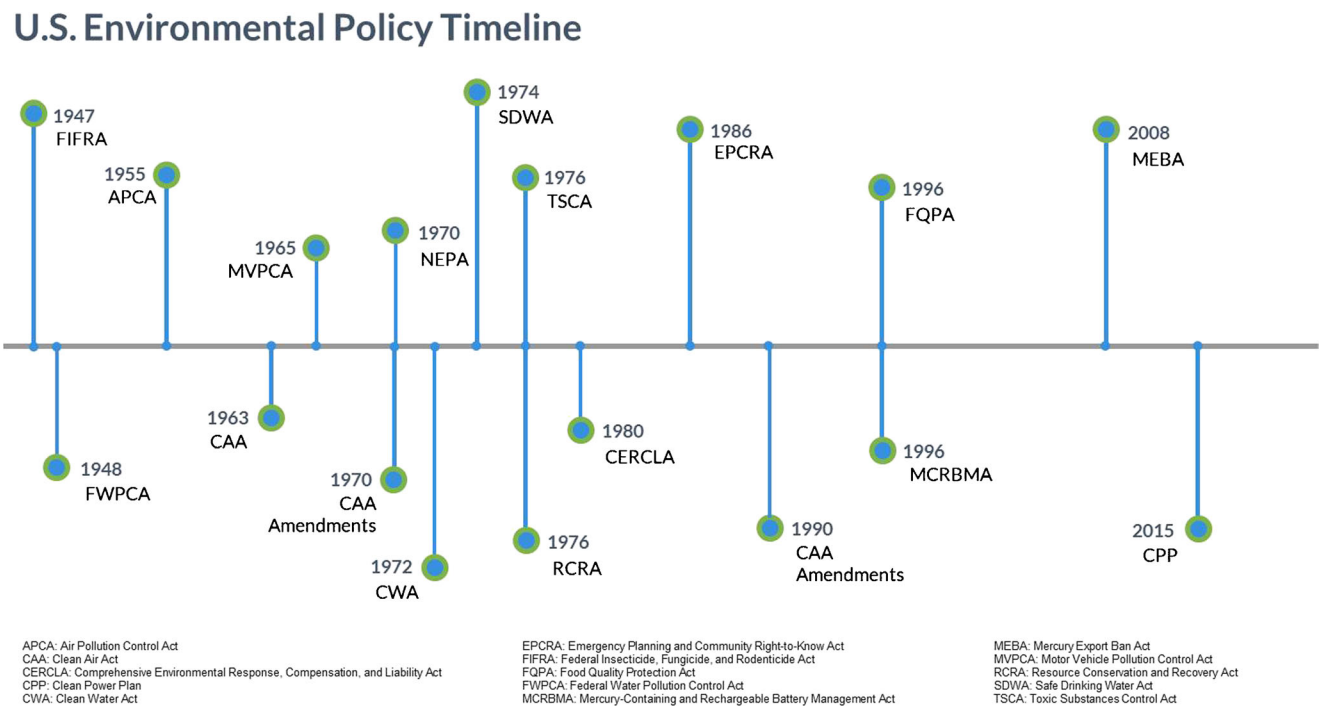

Fig. 1 Milestones in the United States Environmental Policy

Table 2 Major federal environmental legislation related to diabetes-associated endocrine-disrupting chemicals

Policies that regulate or address	Regulatory mechanisms or standards	EDCs regulated
Clean Air Act (CAA)	National Ambient Air Quality Standards (NAAQS) and National Emissions Standards for Hazardous Air Pollutants (NESHAP)	Arsenic Cadmium Dioxins Mercury Perofluoroalkyl substances Phthalates Particulate matter
Clean Water Act (CWA)	National Pollutant Discharge Elimination System	Arsenic Cadmium Dioxins Mercury
Safe Drinking Water Act (SDWA)	Maximum contaminant levels; best available technologies for removal	Arsenic Atrazine Cadmium Mercury Perofluoroalkyl substances Phthalates
Resource Conservation and Recovery Act (RCRA)	Hazardous Waste Program	Arsenic Cadmium Dioxins Mercury Phthalates
Toxic Substances Control Act (TSCA)	New and existing chemicals program; significant new use rules (SNURs)	Perofluoroalkyl substances Phthalates
	Polychlorinated biphenyls (PCBs) program	Polychlorinated biphenyls (PCBs)
Emergency Planning and Community Right-to-know Act (EPCRA)	Chemical substances inventory	Bisphenol A (BPA) Phthalates
	Toxic release inventory	Mercury
Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA)	Enforcement of levels consistent with other regulations	Arsenic Dioxins Perofluoroalkyl substances Phthalates
Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA)	Regulation of registration, distribution, and sales by the EPA; however, states have most authority in enforcement	Arsenic Atrazine Dioxins OC pesticides Organotins Persistent organic pollutants (POPs) Polybrominated diphenyl ethers (PBDE) Tolylfluanid
Direct ban or specialized policies	Regulated by the EPA	DDT Mercury

law became more specific in its regulation of criteria air pollutants and hazardous air pollutants (HAPs), through NAAQS. The law was sweeping and established a requirement that each state submit and implement a state

implementation plan (SIP). SIPs, which continue today, require states to determine which regulations and technologies will be used within the state to meet NAAQS. Once approved by the EPA, the provisions of the SIP are enforceable by federal law. The Clean Air Act was further amended in 1990 to require that HAPs, a different class of pollutants that cause serious health effects, be regulated through technology-based approaches using health standards as support and to establish more cost-effective compliance options for criteria pollutants through the use of market-based mechanisms [41•].

Water Quality

The basis of the modern Clean Water Act was enacted in 1948 as the Federal Water Pollution Control Act. It was significantly amended in 1972 when it became known as the Clean Water Act. The revised law was a sweeping protection of navigable waters from any point source of pollution and established standards for wastewater treatment and sewage infrastructure. Through the establishment of a permitting system called the National Pollutant Discharge Elimination System (NPDES), the Clean Water Act required a permit under NPDES for the discharge of any pollutants from point sources. Further amendments added in 1987 included regulatory measures for non-point source water pollution. In addition to the Clean Water Act, an essential piece of water legislation that relates to diabetes-linked chemicals is the Safe Drinking Water Act, which originally passed in 1974 and was subsequently amended in 1986 and 1996. Governed by the EPA, the law establishes and regulates drinking water standards and bans the use of Pb in drinking water systems. Within the Safe Drinking Water Act, maximum contaminant level goals (MCLG) are set based upon known risks to human health with particular attention on at-risk populations including infants and the elderly. For microbial contaminants and carcinogenic contaminants, the MCLG is set at zero. For non-carcinogenic contaminants, MCLGs are established based on known health effects and with attention to vulnerable populations [42]. The maximum contaminant level (MCL) is then set as close to the MCLG as possible, also taking costs into account. In some cases, like for Pb and copper, treatment techniques are specified to reflect the best available technologies and relative costs of the techniques, instead of MCLs. Importantly, both MCLs and treatment techniques are intended to be adjusted as new information is released. A recent study considered the impact of changes in the MCL for arsenic from the decades-old EPA level in public water systems at 50 to 10 μg/L in January 2006. While arsenic policy changed for public water, it did not change for well water where the arsenic MCL is not enforced. Following the adoption of the lower MCL for arsenic, public water users experienced a 17% reduction in dimethylarsinate (DMA) levels, the main metabolite of inorganic arsenic in humans, following the change in MCL, while levels among private well users were unchanged; this indicates both inadequate protection where arsenic MCLs were not enforced and reductions in exposure for those under the new MCL [43••, 44••]. Importantly, the MCLs and treatment technique requirements under the Safe Drinking Water Act allow available technology and economic costs to be considered along with risks to public health when determining targets and remediation techniques.

Pesticides and Toxic Chemicals

A key piece of legislation related to agricultural and food exposures is the Federal Insecticide, Fungicide, and Rodenticide Act (FIRFA), which was first passed in 1947 and later underwent numerous amendments. Also governed by the EPA, this law regulates pesticides through controls on all aspects of use, including application, storage and containment, transportation, disposal, and labeling [45]. The standards of FIFRA are generally monitored and enforced under States' authorities. A related policy, the Food Quality Protection Act of 1996, regulates pesticide use in the consumption phase, by establishing maximum contamination levels for pesticide residues in food sources.

Under EPA's jurisdiction, the Toxic Substances Control Act (TSCA) of 1976 creates and maintains an inventory of most chemicals, excluding the ones that are exempt from the law for various reasons. The law regulates chemicals like mercury and PCBs, but not others like pesticides or food additives that are managed under other legislation. While the law is designed to identify and regulate any chemicals that pose a risk to human health, it is often criticized because of the marked gaps in knowledge on the effects of chemicals on health, particularly endocrine-disrupting ones, and for not being utilized to its full authority and jurisdiction for testing new chemicals [46].

The Emergency Planning and Community Right-to-Know Act (EPCRA) was established in 1986 to create reporting standards on the storage, use, and releases of hazardous substances. The Act assists communities in planning for chemical emergencies through increased transparency of the chemicals used in facilities and requiring local and state authorities to establish plans for handling spills or leaks. It includes a toxic release inventory as part of which certain chemicals are reportable.

Hazardous Waste

The Comprehensive Environmental Response, Compensation, and Liability Act, generally referred to as CERCLA or informally as "Superfund", was a landmark law passed in 1980 and reauthorized by the Superfund Act in 1986 [47]. Passed partly in response to incidents like Love Canal, the law authorizes the EPA to manage remediation and redevelopment efforts for

hazardous waste sites, specifically those contaminated sites that pose the greatest threat to human health. Listed by the EPA on the National Priorities List, these sites are generally no longer operational; thus, a major component of CERCLA implementation focuses on identifying responsible parties and legally mandating clean-up measures. The Resource Conservation and Recovery Act oversees the storage, treatment, and disposal of certain listed hazardous substances [48]. CERCLA includes a list of hazardous substances, some of which must be reported when in excess of a certain quantity.

A few chemicals proven to exert sufficient adverse effects have merited outright bans or specific restrictions (e.g., DDT and mercury). DDT was banned by the EPA in 1972. The Mercury-Containing and Rechargeable Battery Management Act of 1996 phased out the use of mercury in batteries, while the Mercury Export Ban Act of 2008 aims to reduce the accessibility of mercury in domestic and international markets [49].

Indirect, Incomplete, and Inconsistent Regulatory Milieu

As noted, no specific federal regulation accounts for the links between EDCs and diabetes in rule-making. Indeed, metabolic effects are not part of hazard identification; thus, where restrictions are implemented (e.g., MCLs) on EDCs, those rules are based on alternative toxicities that do not consider diabetes or endocrine effects. Furthermore, these assessments generally do not consider effects during sensitive windows of development that program long-term metabolic health. An additional complication is that EDCs linked to diabetes risk span various types of environmental sources, with exposure to many compounds occurring via multiple routes. As such, diabetogenic EDCs are indirectly regulated under a panoply of federal laws including the Clean Air Act, Clean Water Act, and Safe Drinking Water Act, which do not take specific metabolic effects into consideration. In addition, exposures also arise from foods, pesticide use (e.g., arsenic, atrazine, POPs), or from by-products of industrial practices (e.g., arsenic, dioxins, PCBs, POPs). These exposures are partially addressed indirectly by a combination of federal policies regulating chemical exposure including TSCA, CERCLA, and the Food Quality Protection Act. While in theory these policies appear to cover multiple sources, implementation and enforcement measures have proven to be difficult to coordinate across government agencies or across states. Thus, even with standards established by federal policies, compliance is not always guaranteed. Furthermore, even in instances where a diabetogenic EDC happens to be regulated, these policies fail to adequately account for *cumulative* exposures that occur across multiple sources. Moreover, because humans are exposed to a variety of chemicals, many of which have been shown to augment diabetes risk; policies that take into account *simultaneous* exposures to metabolically toxic chemicals are biologically warranted; however, federal policies fail to account for this.

Other prominent sources of exposure to EDCs are chemicals in household products, including paints, plastics and packaging (e.g., bisphenol A (BPA), phthalates), and furnishings (e.g., perofluoroalkyl substances). Many of these EDCs are identified as such by the Food and Drug Administration, but control varies across states or relies on voluntary action. For example, BPA is only included on the Toxic Release Inventory of the Emergency Planning and Right-to-Know Act, and policies do not address its presence in daily household items and food and beverage packaging through which most exposure occurs. Instead, there is a patchwork of state- and city-level policies in CT, MN, WI, WA, Chicago, and Suffolk County (NY) that directly prohibit the sale of BPA-containing food containers, cups, and baby bottles [50]. However, these are not standardized across states or localities, which complicates enforcement and compliance with minimum guidelines. Similarly, among polybrominated diphenyl ethers (PBDE), c-PentaBDE, and c-octaBDE are addressed by requiring a notice to the EPA before articles containing these chemicals are manufactured or imported [51]; however, some individual states have implemented outright bans on these chemicals. Further illustrating the complexities of these multilayered policies, the flame-retardant decaBDE, another PBDE, lacks any substantial federal action to restrict its use; however, WA, ME, MD, and OR have issued varying bans on its use [52]. While beyond the scope of the present review, these examples illustrate the marked variance in policies regulating environmental health across the USA, raising important questions about the contributions of environmental inequalities to differences in diabetes risk.

Diabetes Disparities and Environmental Justice

In addition to geographic variation, it has long been recognized that marked racial, ethnic, and socioeconomic differences exist in diabetes rates across the USA. Indeed, while 9.1% of non-Hispanic Whites have diabetes, age-adjusted rates among African Americans and Mexican Americans are markedly higher (17.9 and 20.5%, respectively) [53]. The risk of diabetes is 66% higher in Hispanic Americans and 77% higher in African Americans than in non-Hispanic White Americans [54]. Furthermore, the consequences of diabetes are greater in these populations with age-adjusted diabetes mortality rates significantly higher among Hispanics and non-Hispanic blacks than non-Hispanic whites [55]. Compared to non-Hispanic Whites, rates of diabetes and its complications are also markedly elevated in American Indians

and Native Alaskans [56]. Similarly, individuals with lower incomes and less education are more likely to have diabetes [57]. While several factors have been proposed to contribute to these differences [37], a recent analysis suggests that differential exposures to diabetes-promoting EDCs may contribute to disease disparities among African Americans, Hispanics, and those with low incomes [9••].

A variety of factors have been suggested to explain these exposure disparities (reviewed in Ref. [9••]), including the historical construction and consolidation of chemical production facilities and toxic waste sites in low-income and minority neighborhoods across the country [58]. This creates unavoidable exposures to many chemicals, including some linked to diabetes risk. From the perspective of federal policy, CERCLA is often tied to environmental justice concerns because of the disproportionate burden of contaminated and abandoned sites in Native American and African-American communities. Remediation of these areas is an important step within the framework of environmental justice. In addition to CERCLA, federal policies active in this area include Executive Order 12898: Federal Actions to Address Environmental Justice in Minority Populations and Low-Income Populations. Signed in 1994 by President Clinton as an executive order, this directive requires federal agencies to consider "disproportionately high and adverse human health or environmental effects of its programs, policies, and activities on minority populations and low-income populations" [59]. However, the executive order does not require any specific actions related to environmental justice in siting, implementing, or designing policy. Therefore, despite the fact that policies connecting pollution and diabetes could help address diabetes disparities, doing so will require concerted executive and legislative commitment that is currently flagging.

Challenges in Environmental Policy Influencing Diabetes Risk

Existing regulatory frameworks that influence exposures to diabetogenic EDCs have important gaps that must be addressed to reduce diabetes risk. In addition, there are additional challenges that limit the capacity of regulation to address these deficits.

Identification of Diabetogenic EDCs

As mentioned above, federal laws regulate diabetes-associated EDCs indirectly and without regard to their impact on diabetes risk. Furthermore, current federal programs that investigate the potential for chemicals to act as EDCs are inadequate. The Endocrine Disruptor Screening Program (EDSP) was created under the authority of the 1996 Food Quality Protection Act and includes provisions calling for the screening of chemicals for their possible endocrine-disrupting properties. Importantly, this program determines endocrine-disrupting action but is not accompanied by enforcement authority. Furthermore, similar to efforts by the Organisation for Economic Cooperation and Development, EDSP is principally concerned with endocrine effects on the estrogen, androgen, and thyroid hormone axes. While these pathways influence metabolism, dedicated programs to investigate diabetes per se are needed.

Executive Actions

Beyond policies established in federal regulations via legislative action, implementation of environmental policy has increasingly been conducted through presidential actions. Two salient examples relevant to diabetes risk include the Clean Power Plan (CPP) and actions related to oil and gas exploration. In 2015, the Obama administration's EPA enacted the CPP to establish guidelines for states to follow in reducing greenhouse gas emissions from fossil fuel-fired power plants [60]. In 2017, the Trump administration issued an executive order on energy independence (E.O. 13783) with a plan to repeal the CPP after a public comment period. While the CPP was intended to address climate change by reducing greenhouse gas emissions, it would have also further affected ancillary air pollutants, including those linked to diabetes risk. Similarly, intriguing evidence now suggests that chemicals used in oil and gas extraction (e.g., hydraulic fracturing or "fracking") function as EDCs with effects that include metabolic disruptions [61, 62]. Furthermore, these processes increase leaching of diabetogenic arsenic into groundwater [63]. Consequently, recent executive actions to liberalize oil and gas exploration on federal lands and in coastal waters may adversely affect diabetes risk [64, 65]. Thus, federal policies meant to address anthropogenic climate change as well as energy independence must be considered in light of their impact on diabetes risk.

Consumer Knowledge and Consent

Behaviors of individuals determine exposure to many of the chemicals linked to diabetes risk. While federal, state, and local policies influence specific exposures, current policy gaps ensure that many individuals will continue to be exposed to diabetes-promoting EDCs because of a lack of consumer knowledge. Many individuals are inadvertently exposed to EDCs because the chemical content of many products (e.g., foods, beverages, personal care products, and cleaning

chemicals) is not sufficiently labeled to provide informed consent to consumers prior to purchase. In addition, information about the risks of EDCs is not readily accessible or understandable to consumers. Large knowledge gaps exist in our understanding of diabetogenic chemicals; however, this should not preclude implementation of policies that improve consumer knowledge of chemical use, as failing to do so violates core principles of medical ethics [66].

Translating Knowledge to Care

The Endocrine Society has drawn attention to the health threat posed by EDCs [67, 68], and the American Diabetes Association has established a robust annual statement on best practices in diabetes care [1]. However, at present, the connection between awareness and practice is completely absent. To meaningfully reduce the burden of diabetes, health care providers, professional organizations, and patient advocacy groups will need to better recognize the links between environmental policies and diabetes risk.

The Transformative Impact of Diabetes-Conscious Policy

Formal recognition that environmental degradation contributes to diabetes risk means that policies aimed at reducing pollution to improve human health related to cancer, cardiovascular disease, respiratory illnesses, and developmental disorders have the potential to also benefit metabolic health. This has significant implications for the rule-making process for EDCs based both on human health as well as economic considerations. Given the lack of consideration for the relationship between EDCs and metabolic diseases, rule-making decisions do not reflect full health impacts and as a result understate economic benefits from additional control. Since economically efficient environmental policy maximizes benefits over costs, inclusion of diabetes-related health improvements from EDC-targeted environmental policy could create more economically sound policy. On a pure financial basis, improved environmental quality could reduce diabetes-associated healthcare costs. In an analysis of the Prospective Investigation of the Vasculature of Uppsala Seniors (PIVUS) study, 25% reductions in exposure to several EDCs associated with diabetes were predicted to reduce the prevalence of diabetes in Europe by 13% with a projected cost savings of €4.51 billion annually [69••]. At the federal level, inclusion of pollution-associated diabetes risk would justify strengthening national environmental standards. Aligning state and local policies to maintain federal standards with more specific attention on local populations, geographic disparities, land use decisions, and urban and rural planning would ultimately encourage more sustainable economic development.

Conclusions

Current federal policy is not yet well aligned with the increasing scientific evidence linking environmental exposures with diabetes risk, and recognition of these associations strengthens both the health and economic basis for policy interventions directing control of EDCs. This is crucially important today given the current administration in 2018 is attempting to roll back more than 400 rules and regulations that protect the environment and human health [43••], including those related to HAPs under the Clean Air Act. Since criteria air pollutants and some others are regulated on the basis of human health, it is critically important to identify all linkages of pollution to diabetes and metabolic health. Additionally, the identification of these linkages will enhance estimates of the economic benefits related to pollution control, many of which are measured as avoided costs of illness and premature death, potentially changing the outcomes of cost-benefit analyses in favor of enhanced and more targeted environmental regulations. Increasing support for research into EDC-diabetes connections and consequently revising public policy to address these relationships is urgently needed. Furthermore, because of the disproportionate burden of pollution and diabetes risk borne by critical subpopulations, the distribution of policy costs and benefits should also be considered through appropriate spatial, geographic, and distributional analyses that would better inform targeted policy measures and actions to improve environmental justice. Finally, our increasing recognition that environmental quality is intimately linked to metabolic health strongly argues for an active role of the diabetes community in issues related to land use, energy policy, industrial practices, and other development issues that influence exposures to pollutants linked to diabetes and other adverse health effects.

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Compliance with Ethical Standards

Conflict of Interest Sabina Shaikh, Jyotsna S. Jagai, Colette Ashley, and Shuhan Zhou declare that they have no conflict of interest.

Robert M. Sargis reports honoraria from CVS.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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- • Of importance
- •• Of major importance

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