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プラスチックのパラドックス：なぜプラスチックは健康に対する緊急の脅威なのか？

The Plastic Paradox: Why Plastic is an Urgent Threat to Health and What We Can Do About It

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- 科学顧問：Beautycounter、IS-Global、Footprint、食品包装フォーラム、Ahimsa

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- Scientific Advisory Roles: Beautycounter, IS-Global, Footprint, Food Packaging Forum, Ahimsa

プラスチックは医療を一変させた

Plastics have transformed health care.

プラスチックは世界を変えた
Plastics have transformed the world.

- 1950年代に毎年200万トンを生産
  2 million tons produced each year in 1950s

- 今日年間生産量4億トン
  Today: 400 million tons produced each year

- 新興国からの需要の高まり
  Growing demand from emerging economies

2020年に世界で生産されるバージンプラスチックのうち、52%がアジア（中国の32%）で生産され、次いで北米（19%）、欧州（17%）、中東・アフリカ（7%）、中南米（4%）と続く。

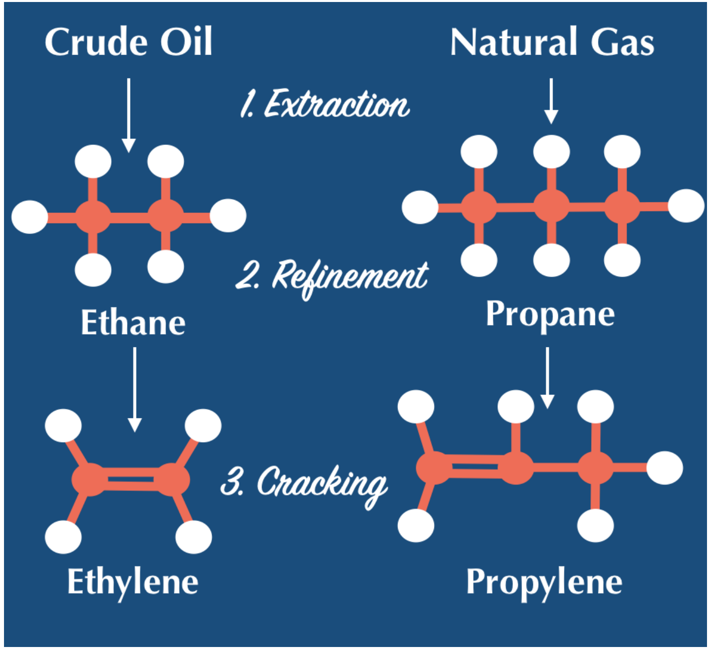
Of the virgin plastics produced globally in 2020, 52% produced in Asia (32% in China), followed by North America (19%), Europe (17%), the Middle East and Africa (7%), and Latin America (4%)

プラスチックの原料は化石燃料
Plastics come from fossil fuels

- ほとんどすべてのプラスチックは化石燃料から作られている
Nearly all plastics are made from fossil fuel feed stocks

- ポリエチレン・プラスチックは、天然ガスから容易に分離できるエタンを分解して製造される
Polyethylene plastics are produced by cracking ethane, which is readily separated from natural gas.

- 実際、多国籍化石企業は、燃料製造からプラスチック製造に軸足を移している。
In fact, multinational fossil companies are pivoting from making fuels to plastic
  - シノペック（2020年から2025年にかけてプラスチック生産が36%増加）、
Sinopec (+36% growth in plastic production between 2020-2025),
  - エクソンモービル (+35%) ExxonMobil (+35%)
  - ペトロチャイナ (+38%) PetroChina (+38%)
  - ロシア資本のSIBUR (+240%)、 Russian-owned SIBUR (+240%),
  - オマーン製油所・石油 (+269%) Oman Oil Refineries and Petroleum (+269%)
  - インドHPLCミッタル (+343%) Indian HPLC-Mittal (+343%)



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プラスチックは危機をもたらした。
Plastics have created a crisis.

- 生態系への影響 Ecosystem effects
- 気候変動 Climate change
- 化学物質と人の健康 Chemicals and human health

生態系への影響 Ecosystem effects

- 年間2,200万トンのプラスチック廃棄物が環境に流入
  22 million tons of plastic waste enter the environment annually

- 現在までに使用されたプラスチックの9%がリサイクルされている
  9% of all plastic used to date has been recycled

リサイクルされないプラスチックの運命
Fates for unrecycled plastic:

- 管理された埋立地と管理されていない埋立地
  Controlled and uncontrolled landfills
- 焼却（これについては人間の健康について述べるときに詳しく述べる）
  Burning (more on this when we address human health)
- 輸出 Export

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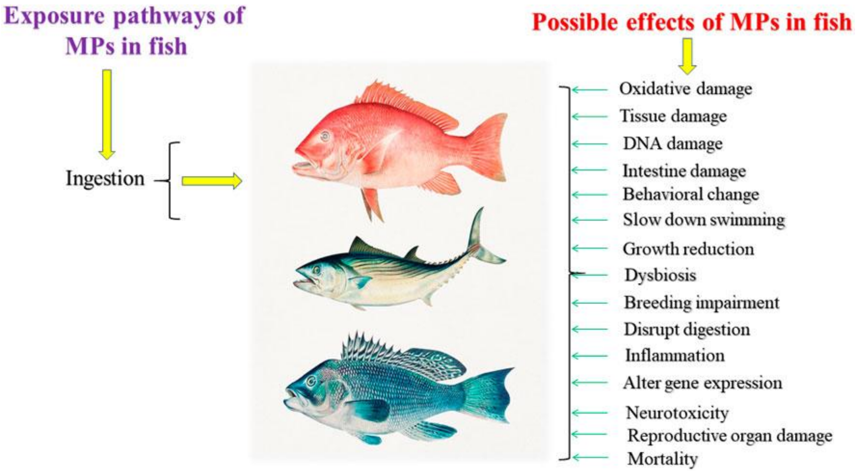
野生生物に含まれる目に見えるプラスチックとマイクロプラスチックVisible and micro-plastics in wildlife



Bhuyan Front. Environ. Sci., 16 March 2022 | https://doi.org/10.3389/fenvs.2022.827289

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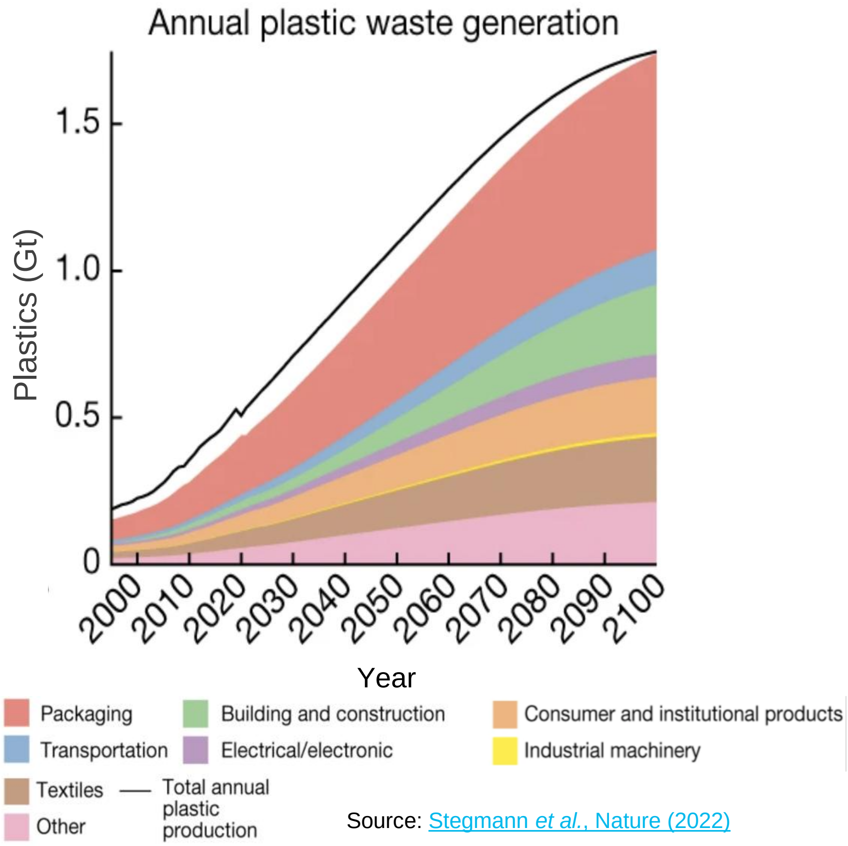
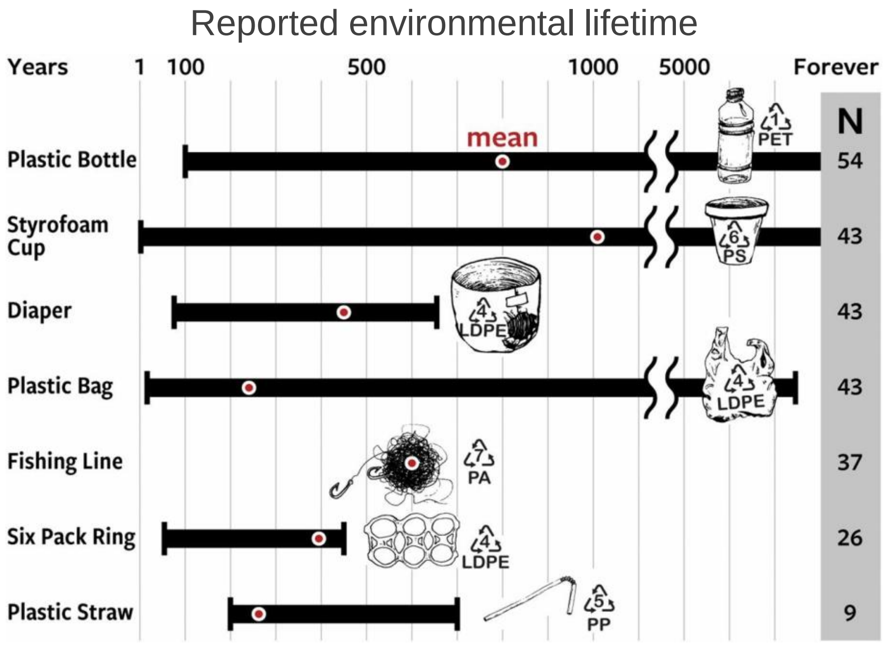
より多くの（マイクロ）プラスチックが環境に蓄積される

More (micro)plastics will accumulate in the environment



Source: Stegmann *et al.*, Nature (2022)



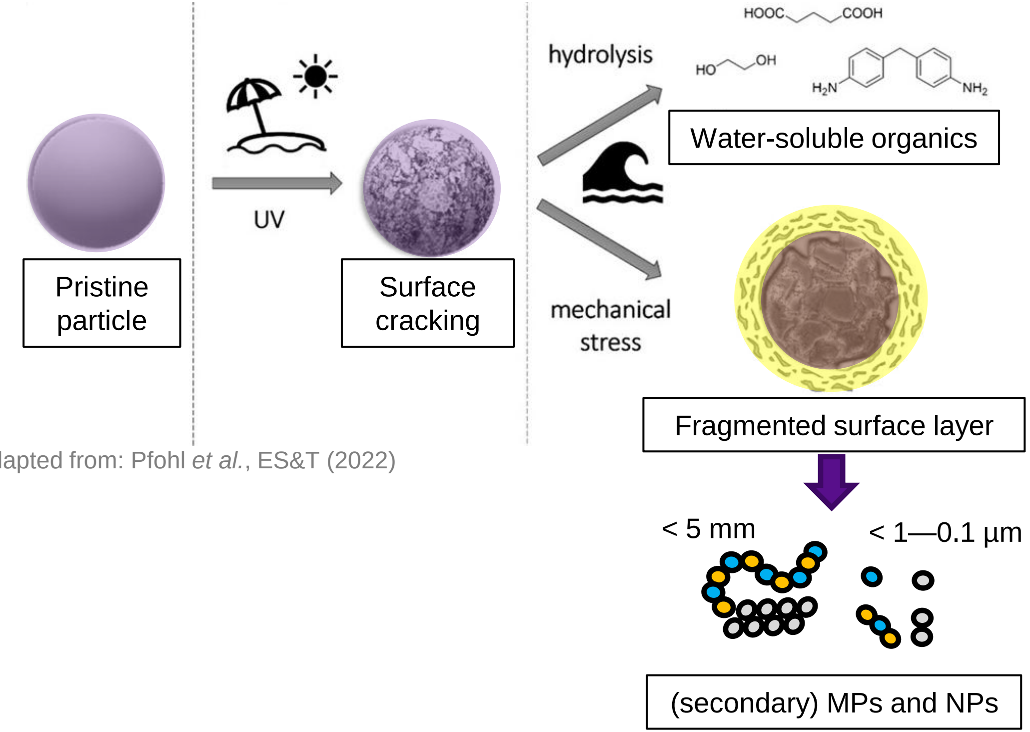
Source: Ward & Reddy, PNAS (2020)

より多くの（マイクロ）プラスチックが環境に蓄積される

More (micro)plastics will accumulate in the environment

環境悪化と断片化

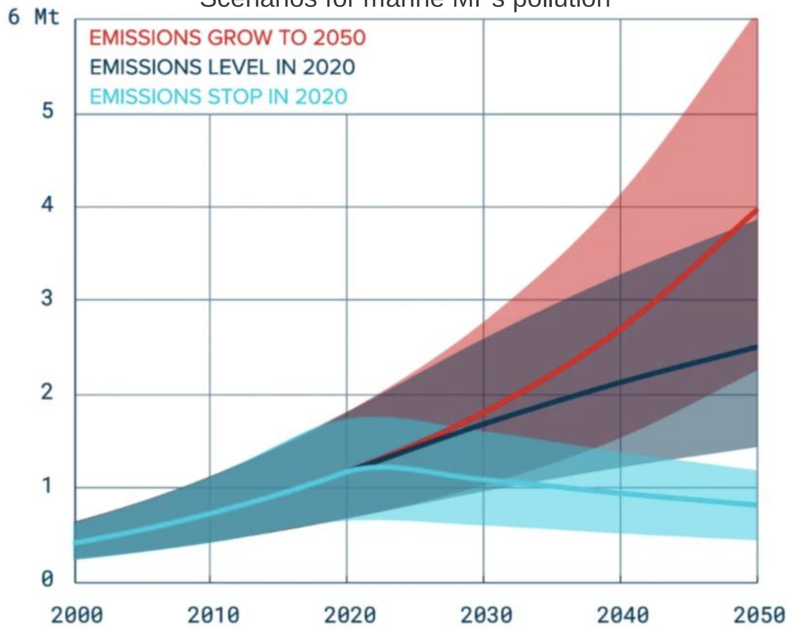
Environmental degradation and fragmentation



Adapted from: Pfohl *et al.*, ES&T (2022)

海洋マイクロプラスチック汚染のシナリオ

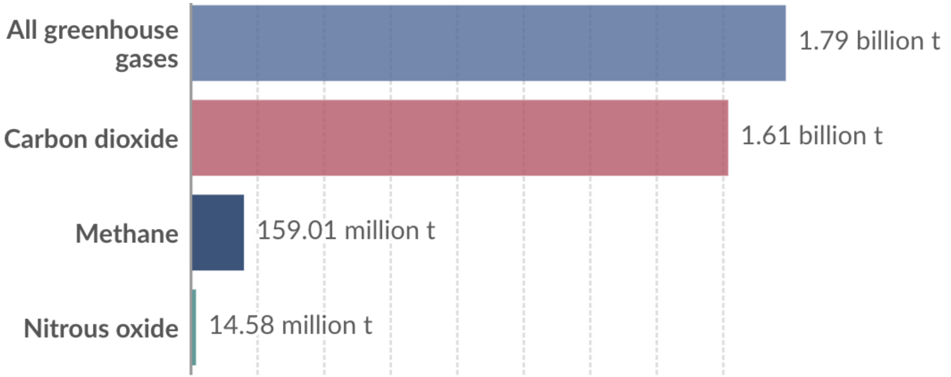
Scenarios for marine MPs pollution



Source: Lebreton *et al.*, Nature Scientific Reports (2019)

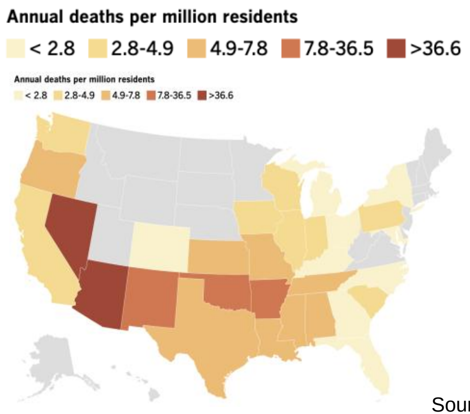
プラスチックが気候変動の原因に
Plastics contribute to climate change

プラスチックのライフサイクルからの温室効果ガス排出量（2019年）
Greenhouse gas emissions from plastics lifecycle (2019)



Source: OECD (2022)

米国における地球温暖化と熱関連死亡率
Global warming and heat-related mortality in the U.S.



Source: CDC (2022)

~2019年の温室効果ガス総排出量の～3%～4　~3% to 4% of total greenhouse emissions in 2019

UNCCは2040年までに排出量が～20%に増加すると予測している。
UNCC anticipates emissions to raise to ~20% by 2040

光により劣化するプラスチックが強力な温室効果ガスを放出（Royer et al.）
Photo-weathered plastics release potent greenhouse gases (Royer et al., PLoS ONE, 2018)

プラスチック使用によるその他の下流への影響としての事故
Accidents as other downstream consequences of plastic use

- オハイオ州イースト・パレスタイン
  East Palestine, Ohio

- 塩化ビニールが広範囲で燃焼（鉄道車両5両分）
  Vinyl chloride burned widely (five rail cars worth)

- 新たに発表されたデータによると、土壌中のダイオキシン濃度は、米国環境保護庁が設定した発がんリスク基準値の数百倍である。
  Newly released data shows soil contains dioxin levels hundreds of times greater than cancer risk threshold set by US Environmental Protection Agency

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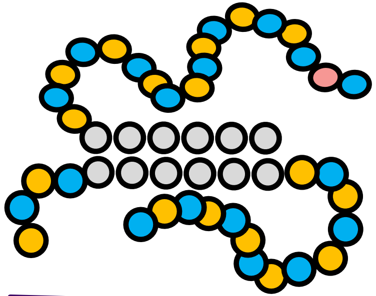
プラスチックへの人体暴露：2つの領域の問題

Human Exposure to Plastics: a two-domain issue

合成ポリマーの破片と粒子
Synthetic polymer debris and particles

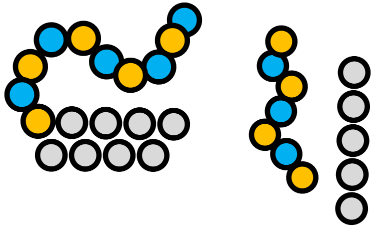
マクロプラスチック片
Macroplastics fragment

> 5 mm



(二次)MPとNP
(secondary) MPs and NPs

< 5 mm　　< 1—0.1 µm



溶存有機化学物質
Dissolved organic chemicals

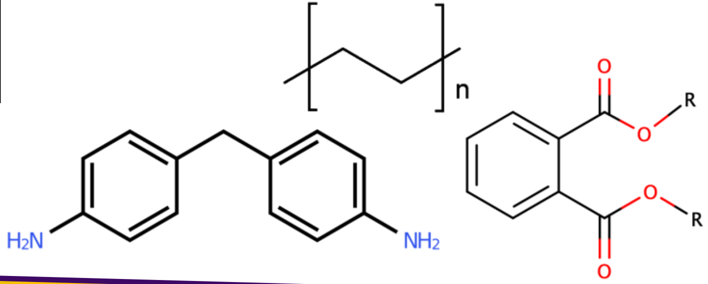
プラスチック由来の溶存有機化学物質
浸出物:オリゴマー、モノマー、添加剤、吸着・脱離した汚染物質

< 1-10 kDa

Plastic-derived Dissolved Organic Chemicals

Leachates: oligomers, monomers, additives, adsorbed/desorbed pollutants

< 1—10 kDa



分子量 (Da) Molecular weight (Da)

人体暴露
human exposure

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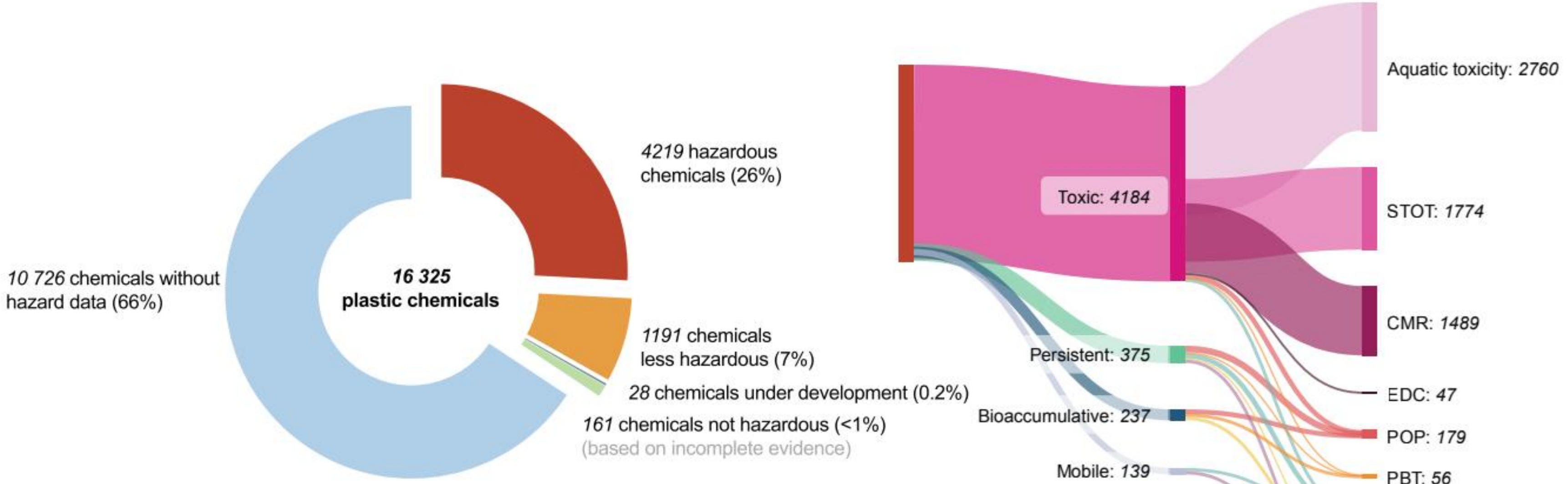


Wagner et al (2024)

プラスチックは内分泌かく乱化学物質の重大な発生源である
Plastics are a crucial source of endocrine disrupting chemicals

- ビスフェノール類（ポリカーボネートプラスチック、アルミ缶ライニング
  Bisphenols (polycarbonate plastics, aluminum can linings)

- フタル酸エステル類（食品包装） Phthalates (food packaging)

- パーフルオロアルキル物質およびポリフルオロアルキル物質（PFAS、調理具の焦げ付き防止加工、フッ素樹脂プラスチック）
  Per- and polyfluoroalkyl substances (PFAS, nonstick cooking and fluoropolymer plastics)

- 臭素系難燃剤（引火性を低下させる添加剤）
  Brominated flame retardants (additives to reduced flammability)

- プラスチックを燃やす → ダイオキシン
  Burning plastics → dioxins

内分泌かく乱化学物質とは何か？

What are endocrine disrupting chemicals?

- 内分泌かく乱化学物質（EDC）はホルモンのシグナル伝達系を阻害する
  Endocrine disrupting chemicals (EDCs) interfere with hormonal signaling systems
- 現在、ホルモンの働きを乱し、病気や障害の原因となる合成化学物質が1,000種類以上あることがわかっている
  We now know of >1,000 synthetic chemicals that can disrupt hormonal functions and thereby contribute to disease and disability
  - 天然ホルモンの合成、放出、輸送、代謝、結合、排泄を模倣、阻害、調節する
    Mimic, block, or modulate the synthesis, release, transport, metabolism, binding, or elimination of natural hormones
  - 脳、下垂体、性腺、甲状腺、その他内分泌系の構成要素
    Brain, pituitary, gonads, thyroid, and other components of the endocrine system

	Representative EDCs
Pharmaceuticals	Trenbolone acetate, ethinylestradiol, dexamethasone, levonorgestrel, rosiglitazone
Cosmetics, personal care products	DBP, benzophenones, parabens, triclosan, DEET
Pesticides, herbicides, fungicides	Chlorpyrifos, glyphosate, pyraclostrobin, DDT, atrazine
Industrial chemicals	BPA, PCBs, triphenyl phosphate, PBDEs
Metals	Lead, cadmium, mercury, arsenic
Synthetic and naturally occurring hormones	Progesterone, testosterone, cortisol, oestrone

Representative EDCs from diverse functional use categories. EDC=endocrine-disrupting chemical. DBP=dibutyl phthalate. DEET=N,N-diethyl-m-toluamide. DDT=dichlorodiphenyltrichloroethane. BPA=bisphenol A. PCB=polychlorinated biphenyl. PBDE=polybrominated diphenyl ether.

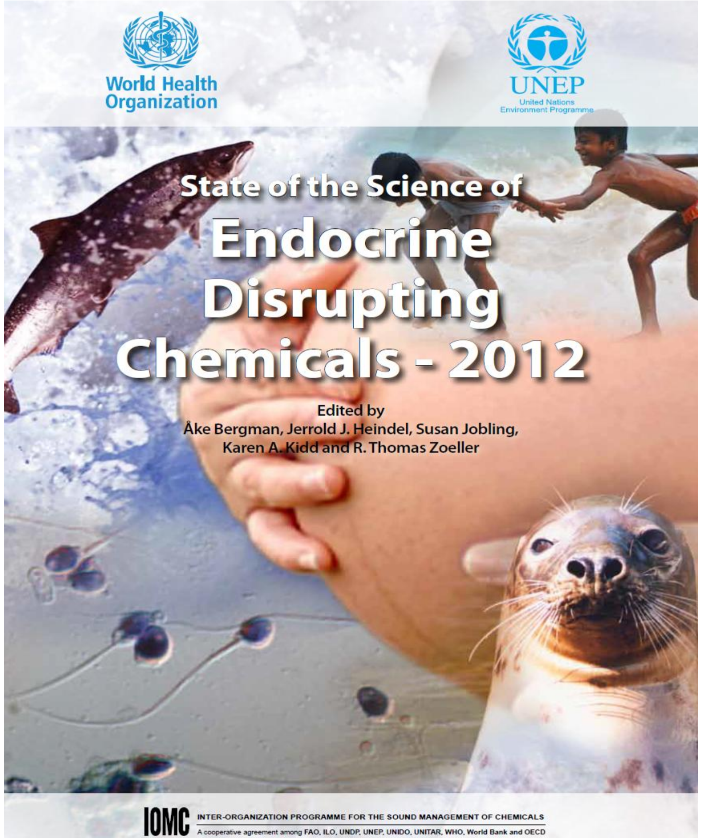
***Table 1:* List of representative EDCs in use**

Endocrine-Disrupting Chemicals: An Endocrine Society Scientific Statement

Evanthia Diamanti-Kandarakis, Jean-Pierre Bourguignon, Linda C. Giudice, Russ Hauser, Gail S. Prins, Ana M. Soto, R. Thomas Zoeller, and Andrea C. Gore

Endocrine Section of First Department of Medicine (E.D.-K.), Laiko Hospital, Medical School University of Athens, 11527 Athens, Greece; Department of Pediatrics (J.-P.B.), Centre Hospitalier Universitaire de Liege, 4000 Liege, Belgium; Department of Obstetrics, Gynecology, and Reproductive Sciences (L.C.G.), University of California San Francisco, San Francisco, California 94131; Department of Environmental Health (R.H.), Harvard School of Public Health, Boston, Massachusetts 02115; Department of Urology (G.S.P.), University of Illinois at Chicago, Chicago, Illinois 60612; Department of Anatomy and Cell Biology (A.M.S.), Tufts University School of Medicine, Boston, Massachusetts 02111; Biology Department (R.T.Z.), University of Massachusetts, Amherst, Massachusetts 01003; and Division of Pharmacology and Toxicology (A.C.G.), The University of Texas at Austin, Austin, Texas 78712

There is growing interest in the possible health threat posed by endocrine-disrupting chemicals (EDCs), which are substances in our environment, food, and consumer products that interfere with hormone biosynthesis, metabolism, or action resulting in a deviation from normal homeostatic control or reproduction. In this first Scientific Statement of The Endocrine Society, we present the evidence that endocrine disruptors have effects on male and female reproduction, breast development and cancer, prostate cancer, neuroendocrinology, thyroid, metabolism and obesity, and cardiovascular endocrinology. Results from animal models, human clinical observations, and epidemiological studies converge to implicate EDCs as a significant concern to public health. The mechanisms of EDCs involve divergent pathways including (but not limited to) estrogenic, antiandrogenic, thyroid, peroxisome proliferator-activated receptor γ, retinoid, and actions through other nuclear receptors; steroidogenic enzymes; neurotransmitter receptors and systems; and many other pathways that are highly conserved in wildlife and humans, and which can be modeled in laboratory *in vitro* and *in vivo* models. Furthermore, EDCs represent a broad class of molecules such as organochlorinated pesticides and industrial chemicals, plastics and plasticizers, fuels, and many other chemicals that are present in the environment or are in widespread use. We make a number of recommendations to increase understanding of effects of EDCs, including enhancing increased basic and clinical research, invoking the precautionary principle, and advocating involvement of individual and scientific society stakeholders in communicating and implementing changes in public policy and awareness. (*Endocrine Reviews* 30: 293–342, 2009)



WHO/UNEP報告書への対応

Response to WHO/UNEP Report

- WHO/UNEP報告書(2012年) 2015年 SAICM 国際的な化学物質管理のための戦略的アプローチで全参加国が "歓迎"

WHO/UNEP report (2012) “welcomed” by all participant countries at 2015 Strategic Alliance for International Chemicals Management

EDC-2: The Endocrine Society’s Second Scientific Statement on Endocrine-Disrupting Chemicals

A. C. Gore, V. A. Chappell, S. E. Fenton, J. A. Flaws, A. Nadal, G. S. Prins, J. Toppari, and R. T. Zoeller

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The Endocrine Society’s first Scientific Statement in 2009 provided a wake-up call to the scientific community about how environmental endocrine-disrupting chemicals (EDCs) affect health and disease. Five years later, a substantially larger body of literature has solidified our understanding of plausible mechanisms underlying EDC actions and how exposures in animals and humans—especially during development—may lay the foundations for disease later in life. At this point in history, we have much stronger knowledge about how EDCs alter gene-environment interactions via physiological, cellular, molecular, and epigenetic changes, thereby producing effects in exposed individuals as well as their descendants. Causal links between exposure and manifestation of disease are substantiated by experimental animal models and are consistent with correlative epidemiological data in humans. There are several caveats because differences in how experimental animal work is conducted can lead to difficulties in drawing broad conclusions, and we must continue to be cautious about inferring causality in humans. In this second Scientific Statement, we reviewed the literature on a subset of topics for which the translational evidence is strongest: 1) obesity and diabetes; 2) female reproduction; 3) male reproduction; 4) hormone-sensitive cancers in females; 5) prostate; 6) thyroid; and 7) neurodevelopment and neuroendocrine systems. Our inclusion criteria for studies were those conducted predominantly in the past 5 years deemed to be of high quality based on appropriate negative and positive control groups or populations, adequate sample size and experimental design, and mammalian animal studies with exposure levels in a range that was relevant to humans. We also focused on studies using the developmental origins of health and disease model. No report was excluded based on a positive or negative effect of the EDC exposure. The bulk of the results across the board strengthen the evidence for endocrine health-related actions of EDCs. Based on this much more complete understanding of the endocrine principles by which EDCs act, including nonmonotonic dose-responses, low-dose effects, and developmental vulnerability, these findings can be much better translated to human health. Armed with this information, researchers, physicians, and other healthcare providers can guide regulators and policymakers as they make responsible decisions. (*Endocrine Reviews* 36: 0000–0000, 2015)

主な認識 Mainstream recognition

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ETIOLOGY AND PATHOPHYSIOLOGY

OBESITY WILEY

Endocrine-disrupting chemicals and obesity risk: A review of recommendations for obesity prevention policies

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[2]Boden Collaboration, University of Sydney, Camperdown, New South Wales, Australia
[3]Duke World Food Policy Center, Sanford School of Public Policy, Durham, North Carolina, USA

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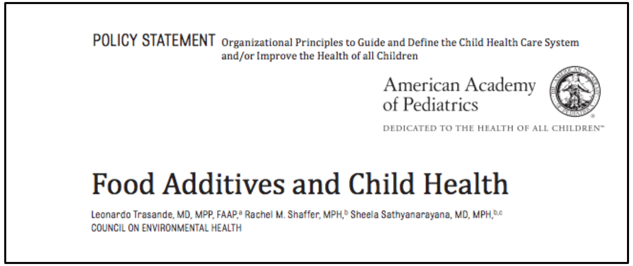
Summary
Emerging evidence indicates that industrially produced endocrine-disrupting chemicals (EDCs) may be as obesogenic as poor dietary patterns and should be considered in obesity prevention policies. The authors conducted two reviews: (a) a systematic search of four electronic databases for papers published since January 2010 to identify the policy recommendations contained in scientific reviews of EDC exposure and obesity risk and (b) a narrative review of obesity policy documents published since January 2012 to identify the recommendations of national and international agencies. A search of four electronic databases found 63 scientific reviews with policy recommendations, of which 26 suggested individual responsibility to avoid exposure, 11 suggested medical interventions to counter the effects of exposure, and 42 suggested regulatory control of hazardous chemicals. Of sixty policy documents examined, six mentioned pollutants as a possible risk factor for obesity, and only one made explicit reference to strategies for reducing exposure to EDCs. The UN Sustainable Development Goals include targets to prevent ill health from hazardous chemicals (Targets 3.9 and 12.4) and to remove unsafe industrial chemicals from the environment (Targets 6.3, 11.6, 12.4, and 14.1). The authors suggest these should be explicitly linked to World Health Assembly targets to halt the rise in obesity.

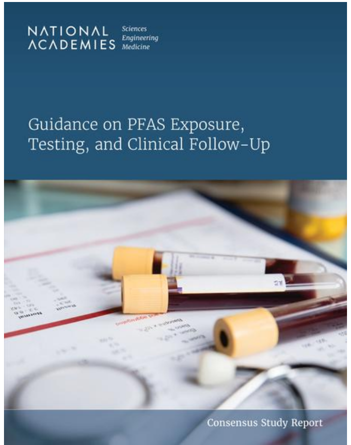


POLICY STATEMENT Organizational Principles to Guide and Define the Child Health Care System and/or Improve the Health of all Children

American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN™

Food Additives and Child Health

Leonardo Trasande, MD, MPP, FAAP,[a] Rachel M. Shaffer, MPH,[b] Sheela Sathyanarayana, MD, MPH,[b,c]
COUNCIL ON ENVIRONMENTAL HEALTH



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プラスチックはEDCの重要な発生源である
Plastics are a crucial source of EDCs

- ビスフェノール類（ポリカーボネートプラスチック、アルミ缶ライニング
  Bisphenols (polycarbonate plastics, aluminum can linings)
- フタル酸エステル類（食品包装） Phthalates (food packaging)
- パーフルオロアルキル物質およびポリフルオロアルキル物質（PFAS、ノンスティック調理、フッ素樹脂プラスチック）
  Per- and polyfluoroalkyl substances (PFAS, nonstick cooking and fluoropolymer plastics)
- 臭素系難燃剤（引火性を低下させる添加剤）
  Brominated flame retardants (additives to reduced flammability)
- プラスチックを燃やす → ダイオキシン
  Burning plastics → dioxins

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ビスフェノール類　Bisphenols

- ポリカーボネート樹脂、エポキシ樹脂に使用（アルミ缶、感熱紙レシート）
  Used in polycarbonate plastics and epoxy resins (aluminum cans, thermal paper receipts)

- ビスフェノールAは、ヒトによく見られるレベルで、複数の内分泌作用を撹乱する
  Bisphenol A disrupts multiple metabolic mechanisms, at levels commonly seen in humans
  - 脂肪細胞のサイズを大きくし、アディポネクチンの機能や、（BPAなどの）エストロゲン作用が弱目の合成エストロジェン活性物質の働きを撹乱する
    Increases fat cell size, disrupts adiponectin function and low-grade synthetic estrogen

- 懸念が高まる中、現在、化学的に類似した約40種類の代替品が使用されてる：ビスフェノールS（BPS）、BPF、BPAF、BPZ、BPP...
  As concern has increased, ~40 chemically similar replacements now in use: bisphenol S (BPS), BPF, BPAF, BPZ, BPP…
  - BPS：同様のエストロゲン撹乱作用、胎児への有害性（他の可能性もある）
    BPS: similar estrogenicity, embryotoxicity (potentially others)

Masuno et al. *J Lipid Res.* 2002;43(5):676-684; Sakurai K et al. *Br J Pharmacol.* 2004;141(2):209-214;

フタル酸エステル類　Phthalates

シャンプー、化粧品、ローション、その他のパーソナルケア製品に香りを保つために使用される低分子量（LMW）フタル酸エステル類
Low-molecular weight (LMW) phthalates used in shampoos, cosmetics, lotions and other personal care products to preserve scent

- 抗アンドロゲン作用（アンドロゲン受容体の転写低下）
  Anti-androgenic properties (reduced transcription of the androgen receptor)

高分子量（HMW）フタル酸エステル類は、床材、透明食品ラップ、点滴チューブ用のビニールプラスチックに使用されている
High molecular weight (HMW) phthalates used to produce vinyl plastic for flooring, clear food wrap and intravenous tubing.

- 食品包装に使用されるフタル酸ジ-2-エチルヘキシル（DEHP）の代謝産物であるフタル酸モノ（2-エチルヘキシル）（MEHP）は、脂質および糖質代謝に重要な役割を果たす受容体の発現を増加させる
  Mono-(2-ethylhexyl) phthalate (MEHP), a metabolite of one HMW phthalate used in food packaging, di-2-ethylhexylphthalate (DEHP), increases expression of receptors which play key roles in lipid and carbohydrate metabolism

Bornehag and Nanberg 2010; Colon et al. 2000; Engel et al. 2010; Miodovnik et al. 2011; Sathyanarayana 2008; Swan 2008; Swan et al. 2005; Desvergne et al. 2009, Grun and Blumberg 2007, Philips et al Repro Tox 2019

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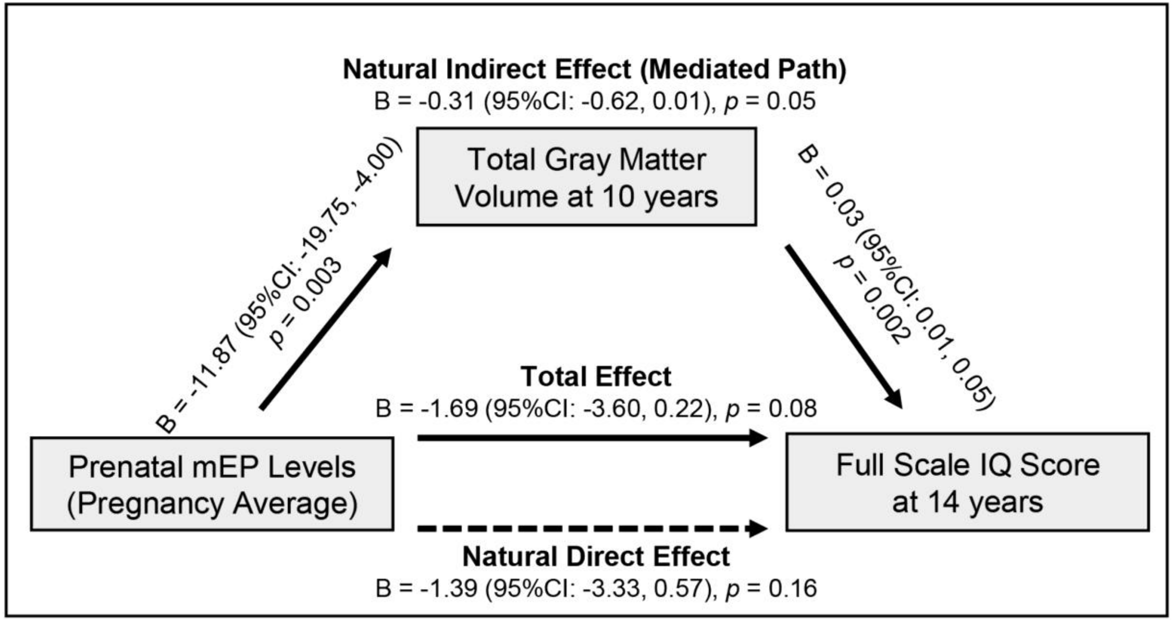
脳の総灰白質の減少が、フタル酸エステル類によるIQ低下を説明する

Reductions in total gray matter explain lower IQs due to phthalates



Ghassabian et al Mol Psychiatry. 2023 Nov; 28(11): 4814–4822.

妊娠中の化学物質曝露と甲状腺機能

Chemical exposure and thyroid function in pregnancy

	Free T4 (ng/dL) beta [95% CI]	Total T4 (ng/dL) beta [95% CI]	Free T4/Free T3 (pg/mL) beta [95% CI]	TSH (mU/L) beta [95% CI]	TSH/Free T4 (ng/dL) OR [95% CI]
∑Bisphenols	-0.01 [-0.02, 0.00]	-0.16 [-0.32, -0.00]*	0.00 [-0.00, 0.00]	0.05 [-0.03, 0.13]	0.06 [-0.03, 0.14]
OP pesticides ∑DM	0.01 [-0.01, 0.02]	0.12 [-0.06, 0.29]	0.00 [-0.00, 0.01]	-0.08 [-0.16, 0.01]	-0.12 [-0.23, -0.01]*
OP pesticides ∑DE	0.01 [-0.01, 0.02]	0.06 [-0.12, 0.23]	0.00 [-0.00, 0.01]	-0.08 [-0.16, 0.01]	-0.13 [-0.24, -0.02]*
OP pesticides ∑DAP	0.01 [-0.01, 0.02]	0.14 [-0.04, 0.31]	0.01 [0.00, 0.01]*	-0.09 [-0.18, -0.00]*	-0.15 [-0.26, -0.04]*
∑PAHs	-0.01 [-0.02, 0.01]	0.04 [-0.14, 0.22]	0.00 [-0.01, 0.01]	-0.03 [-0.12, 0.06]	-0.03 [-0.14, 0.09]
Phthalates ∑LMW	-0.01 [-0.02, 0.00]	-0.08 [-0.24, 0.08]	-0.00 [-0.01, 0.00]	-0.01 [-0.09, 0.07]	-0.02 [-0.11, 0.06]
Phthalates ∑HMW	-0.02 [-0.03, -0.00]*	-0.22 [-0.38, -0.06]*	-0.00 [-0.01, 0.00]	-0.01 [-0.09, 0.06]	0.00 [-0.08, 0.09]
Phthalates ∑DEHP	-0.02 [-0.03, -0.01]*	-0.32 [-0.48, -0.16]*	-0.00 [-0.01, 0.00]	-0.04 [-0.11, 0.04]	-0.01 [-0.10, 0.08]
Phthalates ∑DnOP	-0.02 [-0.03, -0.00]*	-0.23 [-0.39, -0.08]*	-0.00 [-0.01, 0.00]	0.07 [-0.01, 0.15]	0.09 [0.01, 0.18]*
Phthalates ∑DiNP	-0.00 [-0.02, 0.01]	-0.03 [-0.19, 0.12]	-0.00 [-0.01, 0.00]	0.03 [-0.04, 0.11]	0.05 [-0.04, 0.13]

モデルは、年齢、教育レベル、人種・民族、分娩数、保険の種類、タバコへの環境暴露、抑うつ症状、甲状腺測定時の妊娠年齢で調整した。

Models were adjusted for age, educational levels, race and ethnicity, parity, insurance type, environmental exposure to tobacco, depressive symptoms, and gestational age at the time of thyroid measurement

ジェネレーションRファースト（胎児期から成人期までの前向きコホート研究）のフタル酸エステル類とビスフェノール類：胎児と出生後の成長

Phthalates and bisphenols in Generation R First: fetal and postnatal growth

- 妊娠中平均のフタル酸（PA、全フタル酸エステルの最終代謝物；-0.08 SD：95% CI -0.14、-0.02）およびLMW（-0.09 SD：95% CI -0.16、-0.02）：分娩後40週までの胎児の体重減少
  Pregnancy-averaged phthalic acid (PA, end metabolite of all phthalates; -0.08 SD: 95% CI -0.14, -0.02) and LMW (-0.09 SD: 95% CI -0.16, -0.02): lower fetal weight through 40 weeks postpartum.
- 妊娠期間平均MEOHP（DEHP代謝物）：早産リスク増加（OR 1.43；95% CI：1.03-1.97）
  Pregnancy-averaged MEOHP (DEHP metabolite): increased risk of preterm birth (OR 1.43; 95% CI: 1.03-1.97)
- 第1期BPS：10歳時の骨密度（6.13mg/cm^2、95%CI：-10.02、-2.23）および骨量（0.12g、95%CI：-0.20、-0.04）の減少（性差なし、多重試験に耐えた）。(van Zwol-Janssens et al Env Res 2020）
  First trimester BPS: decreased bone mineral density (6.13 mg/cm^2; 95% CI: -10.02, -2.23) and content (0.12 g, 95% CI: -0.20, -0.04) at age 10 (no sex specific differences, endured multiple testing). (van Zwol-Janssens et al Env Res 2020)

ジェネレーションRファーストにおけるフタル酸エステル類とビスフェノール類：脂肪量、インスリン抵抗性、血圧

Phthalates and bisphenols in Generation R First: fat mass, insulin resistance and BP

- 妊娠第1期のフタル酸エステル：心膜脂肪指数のSD偏差スコア増加0.13（95%CI：0.04、0.21）（男児で強く、多重比較後に有意）(Sol et al Int J Obesity 2020）。
  First trimester PA: 0.13 (95% CI: 0.04, 0.21) SD deviation score increase in pericardial fat index (stronger among boys, significant after multiple comparison). (Sol et al Int J Obesity 2020)
- 妊娠第2期の母親の尿中の総ビスフェノールとBPA：男児で収縮期血圧が高い（0.13；95%CI 0.03、0.23、0.14；95%CI 0.04、0.23）
  Second trimester maternal urine total bisphenol and BPA: higher systolic BP (0.13; 95% CI 0.03, 0.23 and 0.14; 95% CI 0.04; 0.23) among boys.
- 妊娠第3期のフタル酸エステル：0.20（95%CI 0.07、0.34）SD 10歳時点の男子で中性脂肪が高い。(Sol et al Env Int 2020）
  Third trimester PA: 0.20 (95% CI 0.07, 0.34) SD higher triglycerides among boys at age 10. (Sol et al Env Int 2020)

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フタル酸エステル類と早産：NIH ECHOプログラム

Phthalates and preterm birth: NIH ECHO Program

- ECHOプログラムの13コホートから5006組の母子が参加
  5006 mother–child dyads from 13 cohorts in the ECHO Program
- フタル酸、フタル酸ジイソデシル（DiDP）、フタル酸ジ-n-オクチル（DnOP）、フタル酸ジイソノニル（DiNP）は、特にDEHPや他の代謝物群と比較して、妊娠期間、出生身長、出生体重と最も強く関連していたPhthalic acid, diisodecyl phthalate (DiDP), di-n-octyl phthalate (DnOP), and diisononyl phthalate (DiNP) were most strongly associated with gestational age, birth length, and birthweight, especially compared with DEHP or other metabolite groupings.
- DEHPは早産と関連していたが（オッズ比1-45［95%CI 1-05-2-01］）、log$_{10}$ 増加あたりのリスクは、フタル酸（2-71［1-91-3-83］）、DiNP（2-25［1-67-3-00］）、DiDP（1-69［1-25-28］）、DnOP（2-90［1-96-4-23］）の方が高かった
  Although DEHP was associated with preterm birth (odds ratio 1·45 [95% CI 1·05–2·01]), the risks per log$_{10}$ increase were higher for phthalic acid (2·71 [1·91–3·83]), DiNP (2·25 [1·67–3·00]), DiDP (1·69 [1·25–2·28]), and DnOP (2·90 [1·96–4·23]).
- 2018年のフタル酸エステル起因の早産症例は56,595例（感度分析24,003-120,116例）、関連コストは30-840億米ドル（感度分析1-63-80-140億米ドル）と推定された
  We estimated 56 595 (sensitivity analyses 24 003–120 116) phthalate-attributable preterm birth cases in 2018 with associated costs of US$3·84 billion (sensitivity analysis 1·63– 8·14 billion).

Trasande et al Lancet Planet Health
. 2024 Feb;8(2):e74-e85. doi: 10.1016/S2542-5196(23)00270-X.

フタル酸エステル → 心血管系死亡率
Phthalates → cardiovascular mortality

- 成人男性における心血管系死亡の予測因子あるいはマーカーとなる低T値
  Low T either predictor of or marker of cardiovascular mortality in adult men

- 高分子量フタル酸エステルは、60歳以上の男性において、テストステロンの総量、遊離体、有効量の低下と関連していた
  High molecular weight phthalates were associated with lower total, free, and bioavailable testosterone among men age ≥60.

  - Attina et al Lancet Diab Endo 2016; Hauser et al JCEM 2015

心血管死亡率は、DEHP代謝物であるフタル酸モノ（2-エチル-5-オキソヘキシル）ばく露で有意に増加した
Cardiovascular mortality was significantly increased in relation to a prominent DEHP metabolite, mono-(2-ethyl-5-oxohexyl)phthalate.

- 55～64歳のアメリカ人に当てはめると、50,200人が死亡し、234億ドルの経済生産性が失われる
  Extrapolating to the population of 55-64 year old Americans, 50,200 attributable deaths and $23.4 billion in lost economic productivity.

Trasande et al Env Pollution 2021

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ビスフェノール → 心血管系死亡率
Bisphenols → cardiovascular mortality

BPAが関連：BPA associated with:

- 12～30歳および70歳以上の頸動脈内膜中膜厚の増加
  Increased carotid intima-media thickness of 12-30 and >70 year olds

  Lin et al Atherosclerosis 2015, Lind et al Atherosclerosis 2011)

- 血管造影における冠動脈疾患の重症度
  Severity of coronary artery disease in angiography

  Melzer et al PLOS One 2012

- 成人における心拍変動の減少
  Reduced heart rate variability in adults

  Bae et al Hypertension 2012

- 全死因死亡率、心血管疾患死亡率
  All-cause mortality, and cardiovascular disease mortality

  Bao et al JAMA Network Open 2020

Table 3. Adjusted associations between exposure to BPA and BPS and the risk of type 2 diabetes in the D.E.S.I.R. cohort (single-pollutant models).

	At baseline		At year 3		Average exposure at baseline-year 3	
Bisphenol exposure/detections	n/N[a]	aHR (95% CI)[b]	n/N[a]	aHR (95% CI)[c]	n/N[a]	aHR (95% CI)[d]
BPA exposure		N = 726		N = 623		N = 623
BPA-G concentration (ng/mL)						
<0.71	62/233	1	11/94	1	10/75	1
0.71–1.75	48/182	0.80 (0.53, 1.21)	28/162	1.42 (0.66, 3.07)	33/176	2.56 (1.16, 5.65)
1.75–3.78	39/158	1.01 (0.65, 1.55)	44/190	2.40 (1.16, 4.98)	36/198	2.35 (1.07, 5.15)
≥3.78	38/153	0.85 (0.54, 1.35)	25/177	0.99 (0.44, 2.21)	29/174	1.56 (0.68, 3.55)
BPS detection		N = 644		N = 579		N = 529
BPS-G concentration ≥LOD						
No	139/546	1	92/522	1	61/389	1
Yes	32/98	1.68 (1.09, 2.58)	15/57	1.92 (1.02, 3.62)	38/140	2.81 (1.74, 4.53)

Note: Groups of BPA exposure were defined on the pooled baseline and year 3 BPA-G concentrations in subcohort members. aHR, adjusted hazard ratio; BMI, body mass index; BPA-G, BPA-glucuronide; BPS-G, BPS-glucuronide; CI, confidence interval; D.E.S.I.R., Data from an Epidemiological Study on the Insulin Resistance Syndrome; LOD, limit of detection (0.3 ng/mL).

[a]n/N indicates the numbers of type 2 diabetes cases relative to the total number of participants in each exposure category.

[b]aHRs quantify the association between exposure to BPA/BPS and incidence of diabetes between baseline and year 9. Cox models with age as the timescale and stratified on smoking status were adjusted for sex and the following variables from baseline: urinary creatinine level, education level, employment, marital status, physical activity, caloric intake, family history of diabetes, hypertension, and BMI.

[c]aHRs quantify the association between exposure to BPA/BPS and incidence of diabetes between year 3 and year 9. Cox models with age as the timescale and stratified on smoking status were adjusted for sex and the following variables from year 3: urinary creatinine level, education level, employment, marital status, physical activity, caloric intake, family history of diabetes, hypertension, and BMI.

[d]aHRs quantify the association between exposure to BPA/BPS and incidence of diabetes between year 3 and year 9. Cox models with age as the timescale and stratified on smoking status were adjusted for sex, average urinary creatinine level, and the following variables from year 3: education level, employment, marital status, physical activity, caloric intake, family history of diabetes, hypertension, and BMI.

Ranciere et al EHP 2019

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パーおよびポリフルオロアルキル化合物（PFAS）
Per- and polyfluoroalkyl substances (PFAS)

高い安定性と耐熱性を持つ有機フッ素化合物
Synthetic organic fluorinated compounds with high stability and thermal resistance

米国人口の98%以上の血液から検出可能
Detectable in blood of >98% of the US population.

食品包装は暴露の主な経路である（焦げ付き防止調理器具、電子レンジ用ポップコーン袋）。
Food packaging is a major route of exposure (nonstick cooking, microwaveable popcorn bags)

24研究のメタ分析：母体または臍帯血PFAS増加1ng/mlあたり出生体重-10.5g（95%CI：-16-7、-4-4）
Meta-analysis of 24 studies: −10·5 g (95% CI: −16·7, −4·4) birth weight per ng/ml increase in maternal or cord blood PFAS

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PFASと成人の体重増加／糖尿病
PFAS and adult weight gain/diabetes

糖尿病予防プログラムの生活習慣介入試験：Diabetes Prevention Program lifestyle intervention trial:

- 総PFASは、対照群でのみ体重増加と関連していた
  Total PFAS were associated with increased weight gain exclusively among the control group.

カルデナスら 2018

成功したPOUNDS LOST試験のフォローアップ：
Follow-up of the successful POUNDS LOST trial:

- ペルフルオロオクタンスルホン酸（PFOS）とペルフルオロノナン酸（PFNA）は、安静時代謝率の低下と関連していた
  Perfluorooctane sulfonate (PFOS) and perfluorononanoic acid (PFNA), were associated with reductions in resting metabolic rate.

リウら 2018

PIVUS（スウェーデン）、Nurses（米国）、DPPOS（米国）：PIVUS (Sweden), Nurses (US), DPPOS (US):

- PFASと糖尿病発症との関連 PFAS associated with incident diabetes

Cardenas et al 2018

Liu et al 2018

Cardenas et al 2019, Sun et al 2018, Liu et al 2014

乳がん関連化学物質（BCRC）リスト

Breast Cancer Relevant Chemicals (BCRC) List

乳がんに関連する2つの作用は、**内分泌かく乱作用**（体内ホルモンに干渉する）と**遺伝毒性**（DNAに損傷を与える）である。BCRCのリストでは、各化学物質を以下のように分類している：

2 activities relevant to breast cancer are **endocrine disruption** (interference with bodily hormones) and **genotoxicity** (cause DNA damage). BCRC list classifies each chemical as follows:

Endocrine Disrupting Chemicals (EDC)

	Estradiol/Progesterone Steroidogenesis (*in vitro* H295 assay screen)	Estrogen Receptor Agonism (integration of 18 assays concerning cell proliferation and receptor binding)
EDC +	Positive in concentration-response screen	Area Under the Curve ≥ 0.1
EDC ~	Borderline in concentration-response or positive in single-dose	0.1 > Area Under the Curve ≥ 0.01
EDC-	Did not increase E2/P4 production	Area Under the Curve < 0.01

Steroidogenesis: process that synthesizes chemicals
Agonism: activates receptor
Concentration-response: multiple chemical doses are tested

Genotoxicity (GT)

In vitro or in vivo assay hit-calls in public databases:

NTP Bioassay Genetox Conclusions, EURL ECVAM, OECD eChemPortal, NLM GENE-TOX, CCRIS

GT+: any positive result in any assay
GT-: only negative results

リストに載っている化学物質は、**乳腺発がん**物質か**内分泌かく乱物質**である：

Chemicals on the list are either **mammary carcinogens** or **endocrine disruptors**:

Rodent Mammary Carcinogens (MCs)

278 chemicals, Ionizing radiation

IARC Monographs; NTP Technical Reports, 15th RoC; EPA IRIS, OPP, ToxRefDB, ToxValDB; LCDB; CCRIS

+

Non-MC BCRCs

642 chemicals

Estradiol/Progesterone Steroidogens
515 chemicals
Karmaus 2016, Haggard 2018, Cardona 2021

Estrogen Agonists
267 chemicals
Judson 2015

=

BCRC List

920 chemicals, ionizing radiation

Kay et al., EHP 2024, DOI 10.1289/EHP13233

プラスチックのBCRC BCRCs in Plastics

- PlastChemデータベースには、プラスチックに含まれる化学物質とその危険性データ、規制状況が掲載されている：
The PlastChem database contains chemicals in plastic and their hazard data and regulation status:

Grouping Plastics		Hazard Information	Regulation Status	
Keyword Search Identifies arsenic containing chemicals, lead containing chemicals, DDT, etc.	**Existing Lists** EPA CompTox Dasboard, European Chemicals Agency, Australia Industrial Chemicals Introduction Scheme and experts	**Uses 15 databases** including IARC and ECHA to identify **carcinogens, mutagens and reproductive toxicants, EDCs**, etc.	**MEA List** _*Global Regulations* Stockholm Convention, Montreal Protocol, Minamata Protocol, Basel Convention	**Precedent List** *Regional and National Regulations* Ex. EU's REACH restriction, Japan's ISHA, USA's California P65

414の化学物質がBCRCであり、PlastChemデータベースにも登録されている： 414 chemicals are both BCRCs and in the PlastChem database:

- 227は遺伝毒性がある 227 are genotoxic
- 166は内分泌かく乱作用が強く、175はどちらともいえない（つまり341は内分泌かく乱作用がある） 166 are strongly endocrine disrupting and 175 are equivocal (so 341 are endocrine disrupting)
- 98種がMCで、239種は未検査。テストされていないもののうち、81は遺伝毒性があり、97は強い内分泌かく乱作用がある 98 are MCs, 239 are not tested. Of the not tested, 81 are genotoxic and 97 are strongly endocrine disrupting.
- 88のBCRCは、plastchem state of science reportで指摘された15の優先懸念グループ（芳香族アミン、アラルキルアルデヒド、アルキルフェノール、サリチル酸エステル、芳香族エーテル、ビスフェノール、フタル酸エステル、ベンゾチアゾール、有機金属、パラベン、アゾ染料、アセト/ベンゾフェノン、塩素化パラフィン、PFAS）に含まれる
88 BCRCs are in the 15 priority groups of concern noted in the plastchem state of science report (Aromatic amines, Aralkyl aldehydes, Alkylphenols, Salicylate esters, Aromatic ethers, Bisphenols, Phthalates, Benzothiazoles, Organometallics, Parabens, Azodyes, Aceto/benzophenones, Chlorinated paraffins, PFAS)
- 309のBCRCがレッドリスト（国際的規制のない懸念化学物質）に掲載されている309 BCRCs are on the red list (chemicals of concern without international regulation)

Wagner et al., Zenodo 2024, DOI 10.5281/zenodo.10701706
Kay et al., EHP 2024, DOI 10.1289/EHP13233

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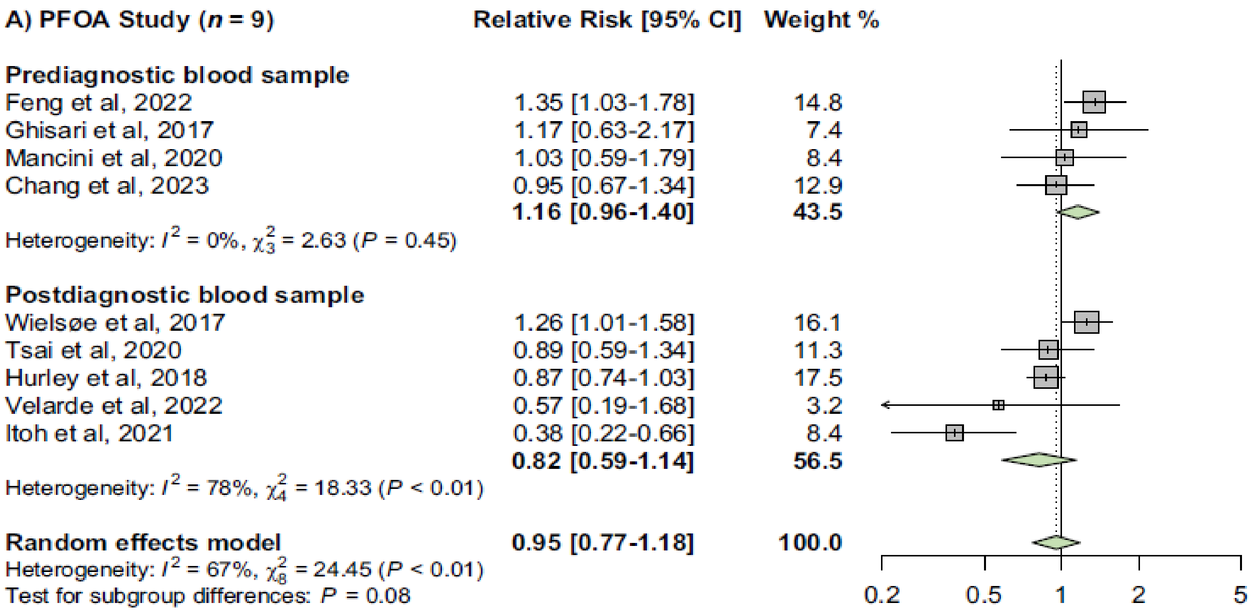
PFASと乳がん PFAS and Breast Cancer



Chang CJ et al. Exposure to per- and polyfluoroalkyl substances and breast cancer risk: a systematic review and meta-analysis of epidemiologic studies. AJE 2024

EDCと甲状腺がん EDCs and Thyroid Cancer

- 尿中BPA濃度は、甲状腺乳頭癌患者対健康対照群で有意に高かった：3.57; 95%信頼区間: 1.37-9.30 (Zhou et al. 2017)
  Urinary BPA levels were significantly higher in patients with papillary thyroid cancer vs health controls, OR: 3.57; 95% CI: 1.37–9.30 (Zhou et al. 2017)
- 血清中BPAF（BPAの類似物質）は分化型甲状腺がんと正の相関があり、OR：15.07、95% CI：1.59-142.13であった（Marotta et al 2019）
  Serum levels BPAF (an analogue to BPA) was positively associated with differentiated thyroid cancer, OR: 15.07; 95% CI: 1.59–142.13 (Marotta et al 2019)
- 一部の難燃剤（BDE-209およびTCEP）の高レベルは、甲状腺乳頭がんのリスク上昇と関連していた（Hoffman et al.2017）
  Higher levels of some classes of flame retardants (BDE-209 and TCEP) were associated with an increased risk of papillary thyroid cancer, (Hoffman et al. 2017)
- 血清BDE-28高値（最高三分位値）は、検出限界以下の血清レベルと比較して、甲状腺乳頭癌のリスク上昇と関連していた（OR：2.09；95%CI：1.05-4.15、Huangら、2020年）
  High serum BDE-28 level (highest tertile) was associated with increased risk of papillary thyroid cancer compared to serum levels below the limit of detection (OR: 2.09; 95% CI: 1.05–4.15, Huang et al. 2020)

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EDCと前立腺がん EDCs and Prostate Cancer

- 前立腺癌患者187人とPSA4未満の50歳以上の対照男性151人を対象とした症例対照研究
  Case-control study of 187 patients with prostate cancer versus 151 male controls age >50 with PSA <4
- ビスフェノールとフタル酸エステル代謝物の尿中濃度を調査
  Examined urine levels of bisphenol and phthalate metabolites
- 年齢、BMI、配偶者の有無、学歴、喫煙、アルコールとの多変量モデルにおいて前立腺がんとの有意な関連性
  Significant association with prostate cancer in multivariable models with age, BMI, marital status, education, smoking, alcohol

Metabolite µg/g creatinine	Adjusted OR (95% CI), p-value
BPA (≥1.43 vs <0.45)	7.33 (2.63-20.43), p<0.001
ΣDEHP (≥45.42 vs <21.75)	33.02 (10.66-102.28), p<0.001

Wang et al. Journal of Hazardous Materials 2024

内分泌かく乱作用と生殖能力
Endocrine disruption and fertility

- 妊孕性（にんようせい）とは、夫婦の状態であり、両性の生殖に関する健康が重要な役割を果たす
  Fertility is a condition of a couple, where reproductive health of both sexes plays a role

Louis et al 2013

- フタル酸エステル類への胎児暴露と乳児の肛門性器距離（AGD）の減少
  Fetal exposure to phthalates with reduced infant anogenital distance (AGD)

Swan et al EHP 2005, Bornehag et al EHP 2014

- 成人のAGD短縮は精液の質およびテストステロン値の低下と関連する
  Shortened adult AGD is associated with reduced semen quality and testosterone level

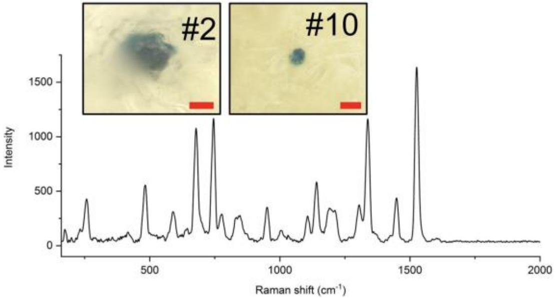
- 複数の研究で、フタル酸エステル、ビスフェノールA、ポリフルオロ化学物質を含む複数のEDCによる男性の生殖能力の低下と精液の質の低下が確認されている
  Multiple studies have identified reduced male fertility and poor semen quality with multiple EDCs, including phthalates, bisphenol A, and polyfluorinated chemicals

Juul et al Nat Rev Endo 2014

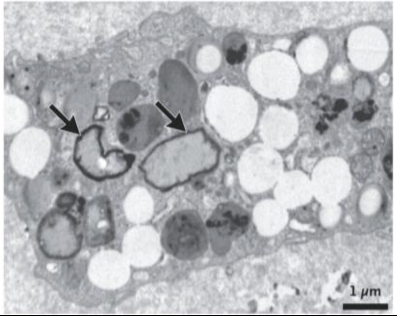
ヒト試料からのマイクロ・ナノ プラスチック検出が増加している

MNPs are increasingly detected in human samples

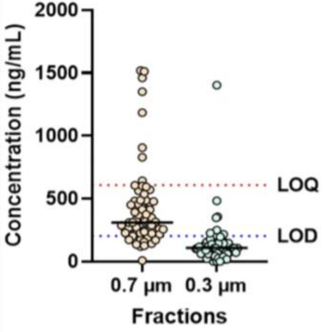
胎盤　Placenta:
Stained PP, coating, dyes.
MPs size 5—10 μm
Ragusa *et al.*, Env. Int. (2021)



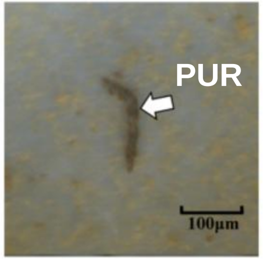
頸動脈プラーク
Carotid artery plaque:
PE and PVC.
Up to 22 μg/mg plaque
Marfella *et al.*, N Engl J Med (2024)

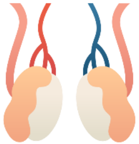


血液Blood:
PE, PVC, PET, PMMA.
Σ_{MNPs}: 170—2490 ng/mL
Brits *et al.*, Micropl.&Nanopl. (2024)

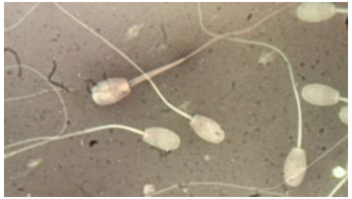


肺　Lungs:
PP, PET, PE, PFTE, PS, PUR.
Up to 1.65 MP/g
(49% fiber, 43% fragment)
Jenner *et al.*, *STotEN* (2022)





精巣　Testicles
PE>>ABS, N66, PVC, PU
Up to 328.44 μg/g
Hu *et al.*, *Tox. Sci.* (2024)



HASSENFELD CHILDREN'S HOSPITAL AT NYU LANGONE

マイクロ･ナノプラスチックの分析方法を早急に調整する必要がある

Urgent need for harmonization of MNPs analysis protocols

Sample collection
- *How to prevent contamination?*

Sample preparation
- *Removal of biological matrix: 10% KOH, H_2O_2, Fenton, Trypsin, Proteinase-K*
- *Isolation of MNPs: vacuum filtration, density separation*

Analysis
- *Physical Characterization*
- *Chemical Characterization*

Report results
- *Which data should always be included?*

Currently, there is no standard procedure for MNPs analysis in human biospecimens

Environmental MNPs reference materials, controls needed for method development/validation

現状では、人体におけるマイクロ･ナノプラスチックの標準的な分析方法が確立されていない
環境中マイクロ・ナノ プラの標準物質、方法の開発や検証にコントロールが必要

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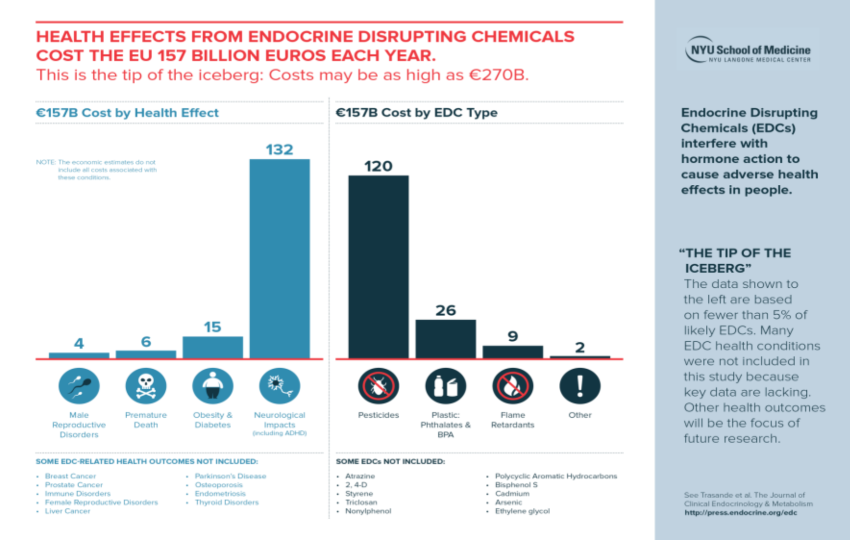
EDCによる疾病負担と医療費は？

What is the burden of disease burden and are the health costs due to EDCs?

- 専門家委員会は、因果関係を示す証拠が最も強い疾患を特定した
  Expert panels identified conditions where the evidence is strongest for causation
  - EDCに起因する疾病負担の割合の範囲を開発
    Developed ranges for fractions of disease burden that can be attributed for EDCs
  - 疫学的エビデンスを評価するためのGRADE作業部会およびWHOの基準の適応Adapted GRADE Working Group and WHO criteria for evaluating epidemiologic evidence
  - 毒性学的エビデンスを評価するためのデンマークEPA基準の採用Adapted Danish EPA criteria for evaluating toxicology evidence
  - 疫学と毒物学の証拠を統合し、因果関係の確率を推定するためにIPCCのアプローチを採用したAdapted IPCC approach to integrate epidemiology and toxicology evidence and estimate probability of causation



EDCの5%未満　Fewer than 5% of EDCs

EDCによる疾患のサブセットを選択
Subset of diseases due to EDCs selected

調査された条件による費用の一部
Subset of costs due to conditions examined

総コストの大幅な過小評価
Severe underestimate of total costs

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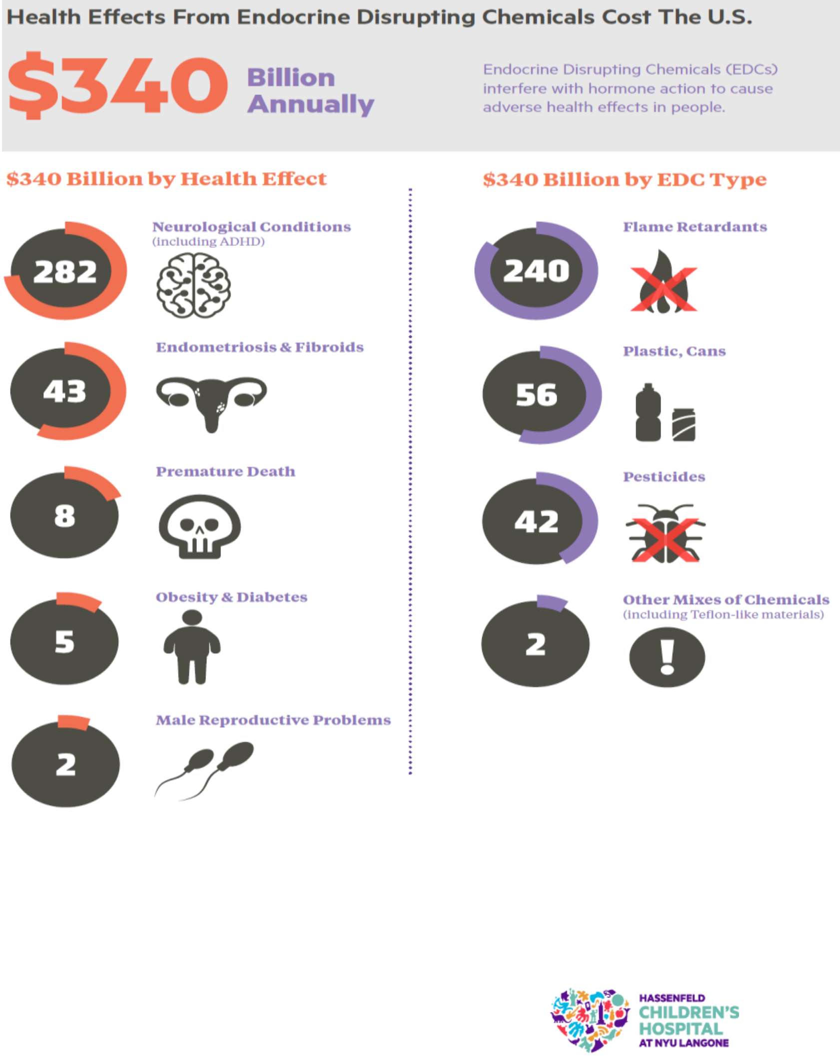
政策はばく露を予測する
Policies predict exposure.

ばく露は病気を引き起こす
Exposure contributes to disease.

病気は私たち全員に影響する。
Disease affects us all.

- 米国のコストはEUより高い
  Costs in US higher than EU
  - PBDEレガシーによるところが大きい
    Largely due to PBDE legacy
- 米国の農薬によるコスト低下
  Lower costs due to pesticides in US
  - 食品品質保護法のおかげだ！
    Thanks to the Food Quality Protection Act!



PFASの疾病負担とコスト PFAS disease burden and costs

米国におけるPFASに起因する疾病コスト：13の症状で年間55億2000万ドル～626億ドル

PFAS-attributable disease costs in the US: $5.52-62.6 billion/year across 13 conditions

- 出生前ばく露によるLBW
  LBW due to prenatal exposure
- 出生前のばく露による小児肥満
  childhood obesity due to prenatal exposure
- 生涯ばく露による腎臓がん
  kidney cancer due to lifetime exposure
- 生涯ばく露による精巣がん
  esticular cancer due to lifetime exposure
- 生涯ばく露による女性の甲状腺機能低下症
  hypothyroidism in females due to lifetime exposure
- 生涯ばく露による成人肥満
  adult obesity due to exposure over the lifespan
- 生涯ばく露による女性のT2D
  T2D in females due to exposure over the lifespan
- 妊娠中に測定されたばく露によるGDM
  GDM due to exposure measured in pregnancy
- 生涯ばく露による子宮内膜症
  endometriosis due to exposure over the lifespan
- 生涯ばく露によるPCOS
  PCOS due to exposure over the lifespan
- 女性の生涯ばく露による夫婦不妊
  couple infertility due to lifetime exposure in females
- 生涯ばく露による女性の乳がん
  female breast cancer due to lifetime exposure,
- と And
- 胎内ばく露による小児肺炎
  pneumonia in children due to prenatal exposure

Obsekov et al Exposure and Health 2022

70カ国のデータから、PFASへのばく露が過去20年間に年間約461,635例（95%信頼区間：57,418-854,645例）の乳幼児死亡に寄与したことが示唆され、その主な原因はアジア地域であった

Data from 70 countries suggest exposure to PFAS contributed to approximately 461,635 (95% CI: 57,418-854,645) cases per year of LBW during the past two decades, predominantly from Asian regions

Fan et al ES&T 2022

EDCによる疾病負担のうち、プラスチックに関係するものはどのくらいあるのか？
How much of the disease burden due to EDCs is related to plastic?

- ビスフェノールAの97.5%（感度分析では96.25～98.75） 97.5% for bisphenol A (96.25-98.75% for sensitivity analysis)
- ジ-2-エチルヘキシルフタレートに対して98% (96%-99%) 98% (96%-99%) for di-2-ethylhexylphthalate
- フタル酸ブチルとフタル酸ベンジルは100%（71%-100%） 100% (71%-100%) for butyl phthalates and benzyl phthalates,
- PBDE-47に対して98% (97%-99%) 98% (97%-99%) for PBDE-47
- PFASについては93%（16%～96%） 93% (16%-96%) for PFAS

Chemicals Used in Plastic Materials: An Estimate of the Attributable Disease Burden and Costs in the United States

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Abstract

Context: Chemicals used in plastics have been described to contribute to disease and disability, but attributable fractions have not been quantified to assess specific contributions. Without this information, interventions proposed as part of the Global Plastics Treaty cannot be evaluated for potential benefits.

Objective: To accurately inform the tradeoffs involved in the ongoing reliance on plastic production as a source of economic productivity in the United States, we calculated the attributable disease burden and cost due to chemicals used in plastic materials in 2018.

Methods: We first analyzed the existing literature to identify plastic-related fractions (PRF) of disease and disability for specific polybrominated diphenylethers (PBDE), phthalates, bisphenols, and polyfluoroalkyl substances and perfluoroalkyl substances (PFAS). We then updated previously published disease burden and cost estimates for these chemicals in the United States to 2018. By uniting these data, we computed estimates of attributable disease burden and costs due to plastics in the United States.

Results: We identified PRFs of 97.5% for bisphenol A (96.25-98.75% for sensitivity analysis), 98% (96%-99%) for di-2-ethylhexylphthalate, 100% (71%-100%) for butyl phthalates and benzyl phthalates, 98% (97%-99%) for PBDE-47, and 93% (16%-96%) for PFAS. In total, we estimate $249 billion (sensitivity analysis: $226 billion-$289 billion) in plastic-attributable disease burden in 2018. The majority of these costs arose as a result of PBDE exposure, though $66.7 billion ($64.7 billion-67.3 billion) was due to phthalate exposure and $22.4 billion was due to PFAS exposure (sensitivity analysis: $3.85-$60.1 billion).

Conclusion: Plastics contribute substantially to disease and associated social costs in the United States, accounting for 1.22% of the gross domestic product. The costs of plastic pollution will continue to accumulate as long as exposures continue at current levels. Actions through the Global Plastics Treaty and other policy initiatives will reduce these costs in proportion to the actual reductions in chemical exposures achieved.

- 合計で、2018年のプラスチックに起因する疾病負担は2,490億ドル（感度分析：2,260億ドル～2,890億ドル）と推定される
  In total, we estimate $249 billion (sensitivity analysis: $226 billion-$289 billion) in plastic-attributable disease burden in 2018.
- これらの費用の大部分はPBDE暴露の結果として生じたが、667億ドル（647億～673億ドル）はフタル酸エステル暴露によるものであり、224億ドルはPFAS暴露によるものであった（感度分析：38.5～601億ドル）
  The majority of these costs arose as a result of PBDE exposure, though $66.7 billion ($64.7 billion-67.3 billion) was due to phthalate exposure and $22.4 billion was due to PFAS exposure (sensitivity analysis: $3.85-$60.1 billion).

Trasande et al J Endo Soc 2024

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高所得国における格差Disparities in high-income countries

- 非ヒスパニック系黒人（568億ドル、総費用の16.5%）とメキシコ系アメリカ人（5001億ドル、14.6%）では、EDC暴露レベルとそれに関連する疾病負担および費用が、総人口に占める割合（それぞれ12.6%、13.5%）に比べて高い
  EDC exposure levels and associated burden of disease and costs higher in non-Hispanic Blacks ($56.8 billion; 16.5% of total costs) and Mexican Americans ($50.1 billion; 14.6%) compared with their proportion of the total population (12.6% and 13.5%, respectively).

- 非ヒスパニック系白人の関連費用は総費用の52.3%（1,798億ドル）を占めたが、彼らは米国人口の66.1%を占めている
  Associated costs among non-Hispanic whites comprised 52.3% of total costs ($179.8 billion) although they comprise 66.1% of the US population.

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中低所得国における不平等な影響Unequal impacts in low- and middle-income countries

- OECDは、2030年までに化学製品の生産と消費の大半が中低所得国で行われると予測している
  OECD predicts majority of chemical production and consumption will occur in low- and middle-income countries by 2030

- 低・中所得国の埋立地にもプラスチックごみがあふれている
  Landfills in low- and middle-income countries are teeming with plastic waste as well.

- ゴミ拾いは、こうした地域の人々にとって、ますます生活の一部になっている
  Waste picking increasingly a way of life for people in these communities.

- 出産適齢期の女性がゴミ拾いをする人のかなりの割合を占め、プラスチックの生産と消費が多世代に及ぶ結果を引き起こしている
  Women of childbearing age comprise a substantial proportion of waste pickers, setting in motion multigenerational consequences of plastic production and consumption.

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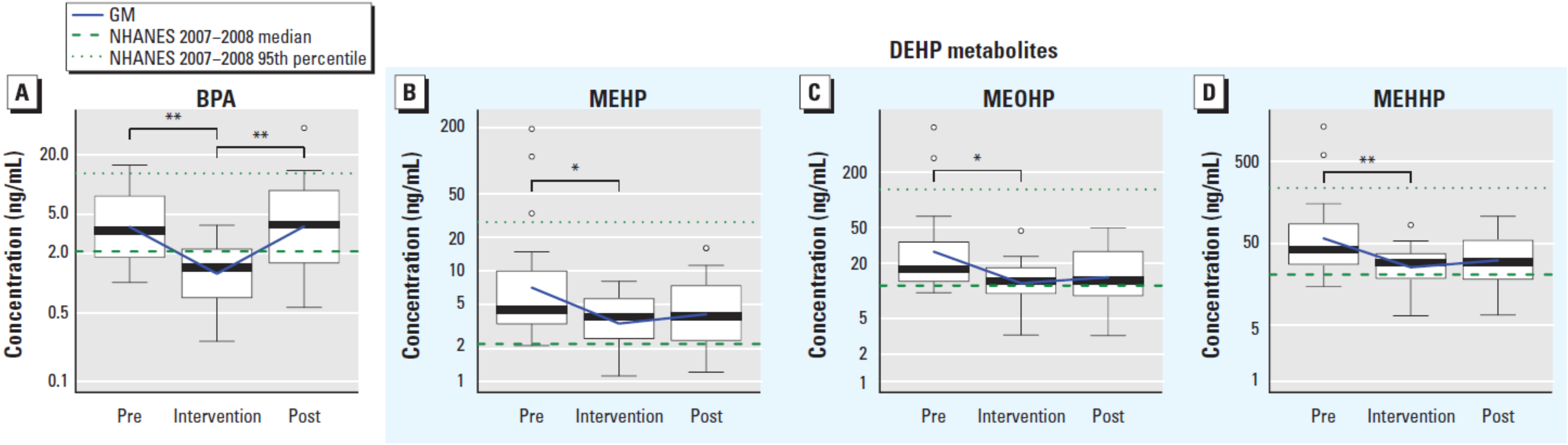
EDCばく露を制限するために、私たちにできることは何か？
What can we do limit EDC exposures?

- **幸いなことに、家庭でできる安全で簡単な対策がある**
  Fortunately, there are safe and simple steps families can take at home to limit these exposures.

- また、ばく露を制限する先を見越した政策を提唱することもできる
  We can also advocate for proactive policies that limit exposures.



Rudel et al EHP 2011

ビスフェノールとフタル酸エステルへの暴露は予防可能である（SES（socioeconomic status、社会経済状況）の高い集団においても）

Bisphenol and phthalate exposures are preventable (also in high SES populations)…

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- 青少年主導の地域参加型調査介入
  Youth-led, community-based participatory research intervention

- ラベルにこれらの化学物質が含まれていないと記載されたパーソナルケア製品を3日間使用したラテン系女子100名
  100 Latina girls using personal care products whose labels stated they did not contain these chemicals for 3 days

- フタル酸モノエチルの尿中濃度は、3日間の介入で平均27.4%減少した（95%CI：-39.3、-13.2）
  Urinary concentrations of monoethyl phthalate decreased by 27.4% (95% CI: –39.3, –13.2) on average over the 3-day intervention

Harley et al EHP 2016

…低資源地域も同様である
…and low-resource communities as well

- 15種類のPFAS、8種類のPBDE、19種類の有機リン酸エステル（PBDE代替物質）が、オフィス、共用スペース、教室の粉塵から測定された：
  15 PFAS, 8 PBDEs, and 19 organophosphorus esters (PBDE replacements) measured in dust from offices, common areas, and classrooms having undergone:
  - 無介入（厳しい消防法に適合した古い建物の従来の部屋）
    no intervention (conventional rooms in older buildings meeting strict fire codes)
  - より健康的な」素材への全面的な介入（最近建設された建物や全面改装された建物で「より健康的な」素材を使用した部屋）、または
    full “healthier” materials interventions (rooms with “healthier” materials in buildings constructed more recently or gut-renovated), or
  - 部分的な介入（少なくとも「より健康的な」発泡家具はあるが、建物汚染の可能性がより高い他の部屋）partial interventions (other rooms with at least “healthier” foam furniture but more potential building contamination).
- より健康的な」材料が全面的に介入された部屋は、介入されていない部屋よりもPFASの埃レベルが78%低かった（$p<0.01$）
  Rooms with full “healthier” materials interventions had 78% lower dust levels of PFAS than rooms with no intervention ($p<0.01$).
- 断熱材、電子機器、家具に関する共変量で調整した結果、「より健康的な」完全介入を行った部屋は、介入を行わなかった部屋よりも埃中のOPE濃度が65%低く（$p<0.01$）、部分的介入のみを行った部屋よりもPBDE濃度が45%低かった（$p<0.1$）
  Rooms with full “healthier” interventions also had 65% lower OPE levels in dust than rooms with no intervention ($p<0.01$) and 45% lower PBDEs than rooms with only partial interventions ($p<0.1$), adjusted for covariates related to insulation, electronics, and furniture.

Young et al Env Int 2020

家庭環境も重要だ！
Household environment matters too!

ばく露を抑える安全で簡単な方法

Safe and simple steps to limit exposure

- 缶詰は避ける。 ビスフェノールA（BPA）は、ソーダ、野菜、ツナなど缶詰の種類によって区別されない。食品に吸収される最大の要因はおそらく酸味だが、どのタイプの缶詰にも検出可能なレベルのBPAが含まれている
  Avoid canned foods. Bisphenol A (BPA) doesn't discriminate by the type of can – soda, vegetables, tuna. Acidity is probably the biggest driver of absorption into food, but all types of canned food have detectable levels of BPA.
- プラスチック容器を電子レンジで温めたり、食器洗浄機に入れたりしないでください。 プラスチックから化学物質を取り除くには、熱と刺激の強い洗浄剤が効果的です
  Don't microwave plastic containers or put them in the dishwasher. Heat and harsh cleaning agents are effective at getting the chemicals out of plastic.
- 3 （ポリ塩化ビニル） 、6 （ポリスチレン） 、7 （他の有害化学物質が含まれている） の数字のついたペットボトルは避ける Avoid plastic bottles with the numbers 3, 6 or 7.
- ペットボトルは1回しか使わないのであれば、そのまま使いましょう。 それに、再利用すると細菌汚染の可能性が高まる
  If plastic bottles were meant for single use, keep them that way. Besides, reusing them raises the chance of bacterial contamination.
- プラスチックの食品容器にエッチングが施されていたら、捨てる時です。 エッチングは溶出の確率を高める
  If plastic food containers are etched, it's time to throw them away. Etching increases the odds of leaching
- ステンレス製か鋳鉄製の調理器具を使う. Use stainless steel or cast iron cookware.
- HEPAフィルターで定期的に掃除機をかけ、ウェットモップでモップをかけ、ホコリがたまらないようにする
  Vacuum regularly with a HEPA filter and mop with a wet mop to prevent dust from accumulating.

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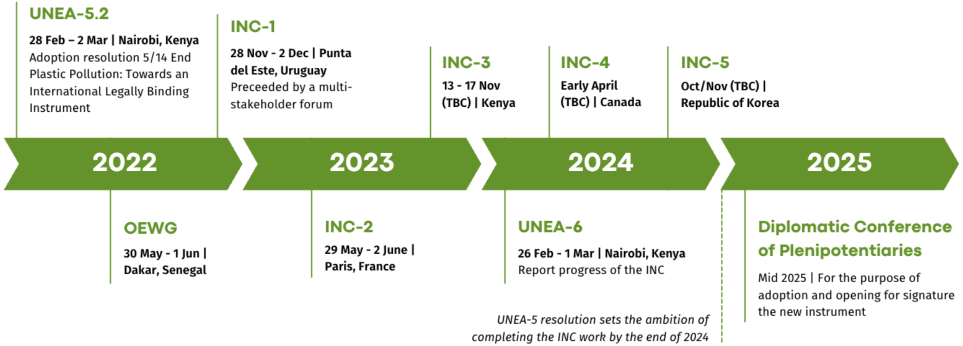
  Fortunately, there are safe and simple steps families can take at home to limit these exposures.

- **また、ばく露を制限する先を見越した政策を提唱することもできる**
  We can also advocate for proactive policies that limit exposures.

国際プラスチック条約　A Global Plastics Treaty

- 2022年3月、再開された第5回国連環境総会：決議が国連環境計画事務局長に政府間交渉委員会の開催を要請
  March 2022 at resumed fifth session of the UN Environment Assembly: resolution requested the Executive Director of the UN Environment Programme to convene an Intergovernmental Negotiating Committee

- 目的：海洋環境を含むプラスチック汚染に関する国際的な法的拘束力のある文書を作成する
  Purpose: to develop an international legally binding instrument on plastic pollution, including in the marine environment, which addresses the full life cycle of plastic, including its production, design, and disposal.



リデュース、リユース、リサイクル？
Reduce, reuse or recycle?

- リサイクルされたプラスチック自体にも健康上の脅威がある
Recycled plastics themselves present health threats.

- リサイクルそのものにエネルギーが必要で、化石燃料からプラスチックを作るよりもコストがかかる
Recycling itself is energy intensive and more expensive than creating plastic from fossil fuels.

- リサイクルされたポリエチレン・プラスチック・ボトルは、廃棄、回収、再加工の際の二次汚染により、新たに製造されたボトルよりも高レベルのビスフェノール類、フタル酸エステル類、金属類を含むことが確認されている
Recycled polyethylene plastic bottles also have been identified to contain higher levels of bisphenols, phthalates and metals than newly-produced bottles due to cross-contamination during disposal, collection and reprocessing.

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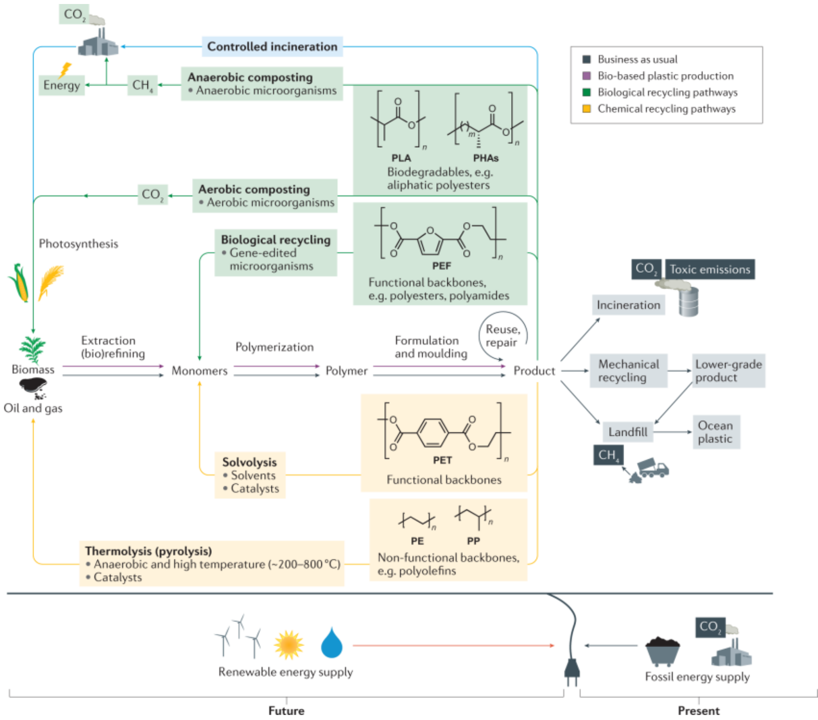
バイオプラスチック？Bioplastics?

- 植物やその他のバイオベースのプラスチックもまた、地球に優しい代替品であり、持続可能なイノベーションの一形態として注目されている
  Plant- and other bio-based plastics have also been touted as a planet-friendly alternative and form of sustainable innovation.
- しかし、リサイクルするためには高温が必要であり、コストが高いためにバイオプラスチックが埋立地に押し込められると、気候変動を引き起こす二酸化炭素よりも強力なメタンを発生させる
  However, they require high temperature to be recycled, and when the high costs force bioplastics into landfills, they produce methane, which is more potent than carbon dioxide in driving climate change.
- 実験室での研究でも、バイオプラスチックボトルから採取された液体に含まれる化学物質の酸化ストレスや抗アンドロゲン性がより高いことが示唆されている
  Laboratory studies also suggest greater oxidative stress and antiandrogenicity of chemicals found in liquids obtained from bioplastic bottles.



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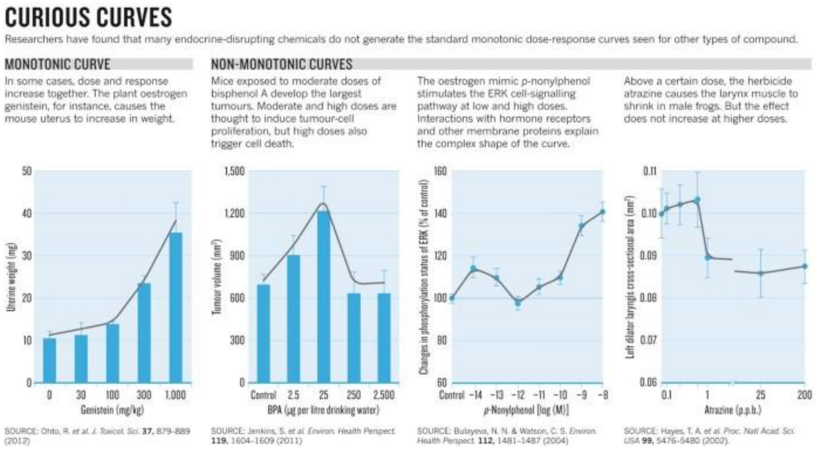
科学的知見：EDCのリスク評価は失敗した（ハザードベースのパラダイムが必要）

Scientific knowledge: risk assessment fails for EDCs (hazard-based paradigm needed)

特に糖尿病やがんなどの潜伏期間が長い疾病の転帰については、新たなばく露の特定から影響に関するヒトでの研究の完了までが遅れている
Lag from identifying new exposures to completing human studies of effects, especially for disease outcomes with longer latencies such as diabetes or cancers

EDCを含む多くの合成化学物質には、非単調な曝露反応関係が存在する → 有害影響のないレベルまで外挿できない
Non-monotonic exposure-response relationships exist for many synthetic chemicals including EDCs → inability to extrapolate to no adverse effect levels

リスクに基づくアプローチの中には、年齢に関連した脆弱性を考慮しようとするものがあるが、それらは、集団の感受性（子ども、高齢者）を*先験的に*定量化できるという誤った前提に立っている
While some risk-based approaches try to account for age-related vulnerability, they falsely presume that the population sensitivity (children, elderly) can be quantified *a priori*



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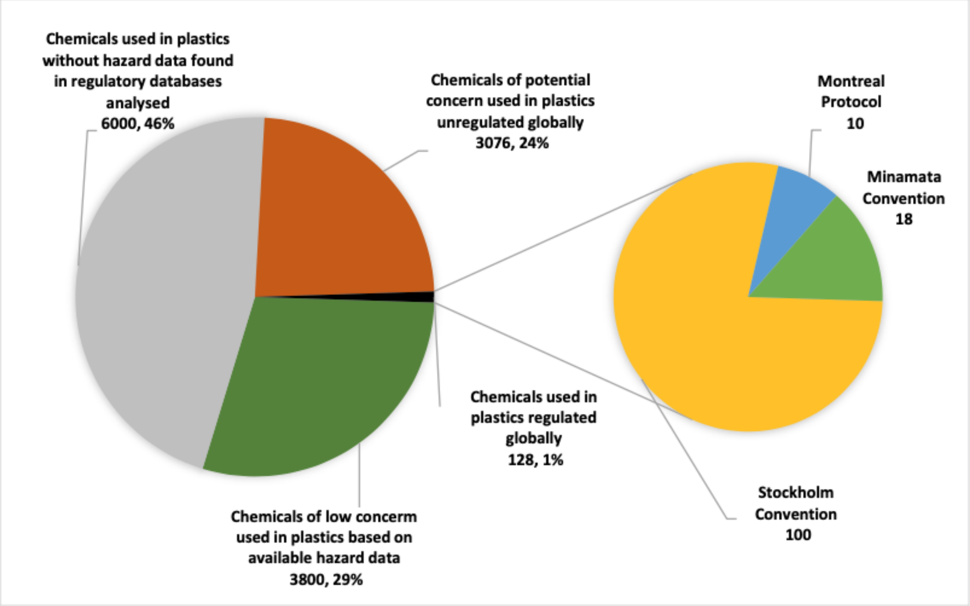
化学物質規制の手段？A vehicle for chemicals regulation?



バイオモニタリングの世界的拡大
Expanding biomonitoring globally

リスクベースのアプローチを続けるのであれば、より広範で強力なヒトのバイオモニタリング・プラットフォームが必要である
If persist with risk based approach, need broader and stronger human biomonitoring platform

- 特に中低所得国での格差に対処するため
  Particularly to address gaps in low- and middle-income countries
- 被ばくを抑えるための安全で簡単な方法に関する教育キャンペーンを知らせることもできる
  Can also inform educational campaigns about safe and simple steps to limit exposure

- 成分の開示も重要（知る権利）
  Disclosure of ingredients also crucial (right-to-know)

EDC*に関する国際研究機関An International Agency for Research on EDCs*

私たちは、内分泌かく乱作用を含む新たな国際機関の設立、あるいは国際がん研究機関（IARC）の科学的責任の拡大を提案する
We suggest the establishment of a new international agency, or a broadening of the International Agency for Research on Cancer (IARC)'s scientific charge, to include endocrine disruption

- 1965年に設立されたIARCは、環境有害物質による発がんの証拠を評価することを任務としている
  Established in 1965, IARC tasked with evaluating the evidence of carcinogenesis due to environmental hazards
- IARCのような自律的な機関は、EDCに関する国際的な共同報告書のために多様な専門家を集めることができ、規制に関する世界的な動きを促進する
  Autonomous body like IARC can bring together diverse experts for international collaborative reports on EDCs would foster global movement on regulations
- 内分泌かく乱作用の国際研究機関は、2020年以降の国際化学物質管理戦略同盟のプロセスをさらに支援する
  An International Agency for Research in Endocrine Disruption would further support post-2020 process of Strategic Alliance for International Chemicals Management

*プラスチックにEDCが大量に使用されていることから、農薬を除外する以外はプラスチックを代替できる
*Given the substantial use of EDCs in plastics, could substitute plastics here except that it would exclude pesticides

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国際的なプラスチック条約が必要だ：
We need a global plastics treaty that:

- プラスチック生産量の削減 Reduces plastic production
- バイオプラスチックのリサイクルや使用がもたらす危険性を認識する
  Recognizes hazards posed by recycling and use of bioplastics
- 内分泌かく乱化学物質の評価とプラスチックからの除去には、リスクではなくハザードを用いる
  Uses hazard rather than risk to evaluate and remove endocrine disrupting chemicals from plastic
- バイオモニタリングをグローバルに拡大
  Expands biomonitoring globally
- 内分泌かく乱化学物質の危険性を評価する独立科学機関を設立
  Establishes an independent scientific body to evaluate hazards of endocrine disrupting chemicals

Thank you

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