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and preterm birth, occur in women with mild thyroid dysfunction receiving levothyroxine treatment has been shown in a large cohort study.[9]

Obstetric clinicians do not routinely carry out growth scans to estimate fetal weight for mothers with subclinical hypothyroidism or isolated hypothyroxinaemia. The findings of this study should be taken into consideration when assessing for risk of SGA and determining a plan for fetal growth screening in pregnancy. Clinicians should also consider dose adjustments to titrate to low-normal FT_4 concentrations, while maintaining normal TSH levels.

Fetal birthweight is a complex entity that is driven by multiple factors, both maternal and fetal. The authors have accounted for important confounders in the prediction of SGA in their analyses but have missed some significant confounders because of unavailable data. Examples are previous SGA, previous stillbirth, and maternal renal or hypertensive disease. It is possible that the association of maternal thyroid function with SGA risk would be modified were these confounders to be accounted for, which should be considered when interpreting the results.

Individual-participant data meta-analyses are considered the gold standard because they can improve the quality of data and the type of analyses that can be done. In this study, this approach has allowed the authors to standardise the definition of thyroid function test abnormalities and analyse potential dose-dependent associations. Future studies in the field should consider this methodological approach and include data from randomised trials to strengthen the quality of the study's findings.

In summary, this is a well conducted systematic review and meta-analysis on a clinically important and highly prevalent problem. It should prompt clinicians to be cautious with overenthusiastic prescription of levothyroxine to women with subclinical hypothyroidism and to include discussions on the risk of SGA in antenatal counselling.

I declare no competing interests.

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1 Hollowell JG, Staehling NW, Flanders DW, et al. Serum TSH, T(4), and thyroid antibodies in the United States population (1988 to 1994): national health and nutrition examination survey (NHANES III). *J Clin Endocrinol Metab* 2002; **87:** 489–99.
2 Stagnaro-Green A. Overt hyperthyroidism and hypothyroidism during pregnancy. *Clin Obstet Gynecol* 2011; **54:** 478–87.
3 Derakhshan A, Peeters RP, Taylor PN, et al. Association of maternal thyroid function with birthweight: a systematic review and individual-participant data meta-analysis. *Lancet Diabetes Endocrinol* 2020; **8:** 501–10.
4 Haddow JE, Craig WY, Neveux LM, et al. Implications of high free thyroxine (FT4) concentrations in euthyroid pregnancies: the FaSTER trial. *J Clin Endocrinol Metab* 2014; **99:** 2038–44.
5 Medici M, Timmermans S, Visser W, et al. Maternal thyroid hormone parameters during early pregnancy and birth weight: the Generation R Study. *J Clin Endocrinol Metab* 2013; **98:** 59–66.
6 Johns LE, Ferguson KK, Cantonwine DE, Mukherjee B, Meeker JD, McElrath TF. Subclinical changes in maternal thyroid function parameters in pregnancy and fetal growth. *J Clin Endocrinol Metab* 2018; **103:** 1349–58.
7 Tong Z, Xiaowen Z, Baomin C, et al. The effect of subclinical maternal thyroid dysfunction and autoimmunity on intrauterine growth restriction: a systematic review and meta-analysis. *Medicine (Baltimore)* 2016; **95:** e3677.
8 Alexander EK, Pearce EN, Brent GA, et al. 2017 guidelines of the American Thyroid Association for the diagnosis and management of thyroid disease during pregnancy and the postpartum. *Thyroid* 2017; **27:** 315–89.
9 Maraka S, Mwangi R, McCoy RG, et al. Thyroid hormone treatment among pregnant women with subclinical hypothyroidism: US national assessment. *BMJ* 2017; **356:** i6865.

How fossil fuel-derived pesticides and plastics harm health, biodiversity, and the climate

Three global challenges menace survival as we know it: climate change, loss of biodiversity, and chemical pollution (including endocrine-disrupting chemicals [EDCs]). These threats are more strongly interlinked than previously thought by their common origins in fossil fuels such as coal, oil, or gas, including that derived from fracking. It is well established that accumulation of anthropogenic greenhouse gases (CO_2, methane, and N_2O) in the atmosphere is the main driver of climate change. However, policy makers and the general public need to better appreciate the links of each of these threats to life.

The foremost threats are chemical pollution, plastic pollution, and loss of biodiversity, as each is largely linked to the fossil fuel industry. The argument is that not only can these threats be averted, but also by reducing our dependence on fossil fuel usage we can simultaneously mitigate and eventually reverse the current climate crisis and improve environmental wellbeing and human health. If we are to embrace these economic transitions which are so urgently required, a deeper understanding of the interlinked mechanisms is needed. These outcomes can be achieved by investing in alternative energies—eg, solar, wind, or geothermic. Development of these renewable energy sources will in turn substantially reduce biodiversity loss, chemical pollution, and plastic pollution.

Although not all chemicals are EDCs, overexploitation of fossil fuels can be linked to atmospheric and chemical pollution, and their closely linked corollary—endocrine disruption. Food contact plastics, some pesticides, flame retardants, perfluorinated compounds, and other endocrine-disrupting compounds are derived from oil, coal, or gas. Moreover, shale gas, obtained by fracking, produces multiple EDCs (figure).[1]

Nearly 60 years ago, Carson[2] showed that the decline in bird and fish populations was due to the pesticide dichlorodiphenyltrichloroethane (DDT)—a finding that predated the concept of EDCs by 30 years. Later research showed that DDT acted through endocrine mechanisms.[3] Oil is used to make chlorobenzene, which in turn is used to synthesise DDT. Similarly, many pesticides such as neonicotinoids, pyrethryoids, and glyphosate formulants are produced from gas and oil.

The massive increase in chemical production since 1950 corresponds to a steep rise in the incidence of non-infectious diseases including obesity, diabetes (with an increased cardiovascular-disease risk), fertility problems, reproductive cancers—particularly cancers occurring at early ages, thyroid disease, neurodevelopmental disorders including autism spectrum disorder and attention deficit or hyperactivity disorders, and IQ loss. These disorders are certainly multifactorial; however, both epidemiology and experimentation has linked all these disorders to EDCs.[3]

Loss of IQ across highly-exposed populations and individuals is perhaps the most worrying. As with most pollution-related problems, this loss can be more severe in lower socioeconomic classes. In addition to costing Europe over €150 billion annually[4] and the US proportionally more, this IQ loss could mask a decline in human ingenuity.

Major contributors to endocrine disruption are some types of plastic and microplastic pollutants. Plastic can be considered a visible component of pollution, whereas microplastic is the invisible component. Both adversely affect human health and the environment. The most visible—frequently used single-use plastic—contributes to the degradation of marine, freshwater, and terrestrial life, and their ecosystems.[5] To what extent microplastics damage the environment and health has yet to be determined. The term plastics covers a plethora of products from food contact materials, medical devices, foam in mattresses, phthalates often used for toys, cosmetics, and coatings for computer screens, to uses such as plasticulture (plastics for agricultural use).

Establishing the hierarchy of production for these petrochemical-derived sectors is difficult. Currently, about 20% of oil is used for petrochemicals and 24% is used for

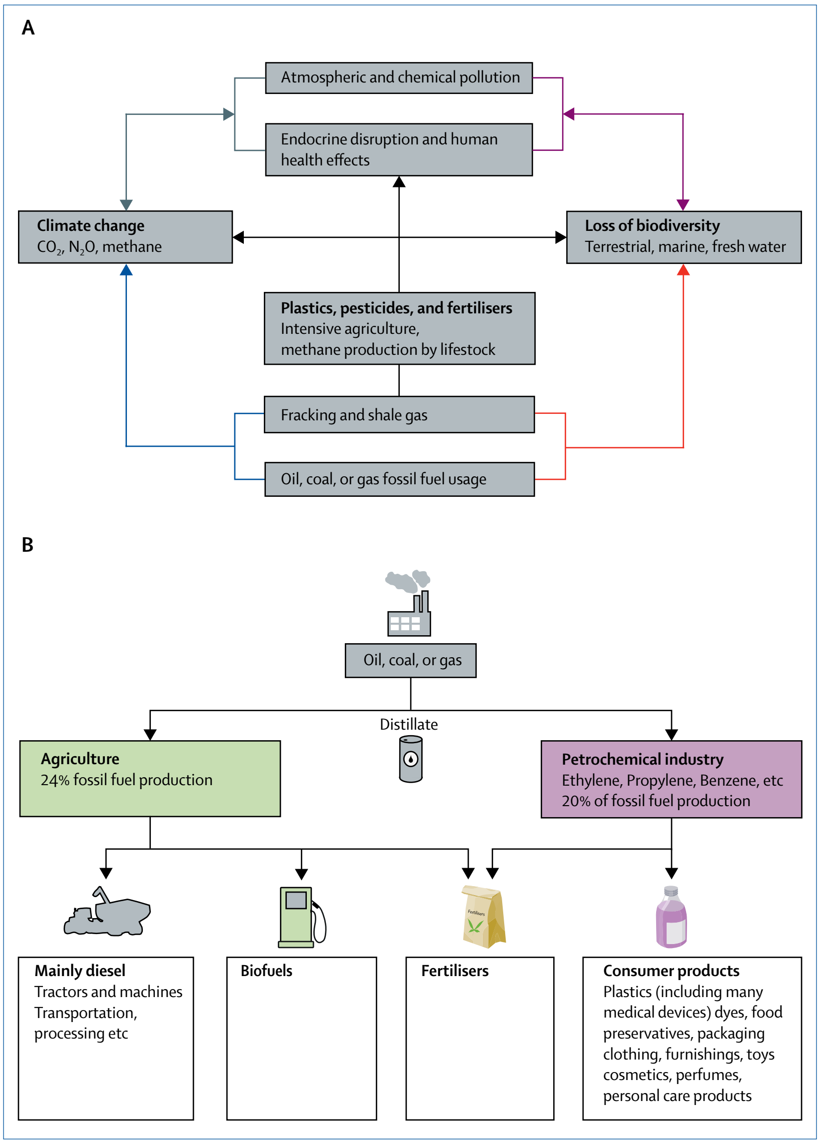

Figure: **Interrelationships and consequences arising from fossil fuel usage**
(A) Link between climate change, loss of biodiversity, and atmospheric or chemical pollution. All fossil fuels including shale gas from fracking can be used to derive plastics, pesticides, and fertilisers. (B) Derivation of plastics, pesticides, and fertilisers from fossil fuels and from fracking.

For more on the **Energy-smart food for people and climate report** see http://www.fao.org/family-farming/detail/en/c/285125/

agriculture, which includes manufacturing, production, processing, transportation, marketing, and consumption. Both percentages could shift markedly as a result of government incentives for renewable energy sources, mainly for private cars and other forms of transport. Potentially, the oil and gas industry could use petrochemicals to restore profitability by increasing production of plastics and fertilisers.

Gas derived from fracking is rapidly driving the development of new petrochemical and plastics plants worldwide. Petrochemicals can be used to derive numerous chemicals, fertilisers and fibres. Many of these petrochemicals also contain EDCs—eg, plastics and consumer goods such as cosmetics and cleaning products; floorings such as polyvinylchloride; also pesticides and fertilisers. Data from the United Nations Environment Programme state that chemical production has increased 300 times since 1970; therefore, unless political and consumer awareness increases, demand for these products will continue to grow. The current coronavirus disease 2019 (COVID-19) pandemic, with oil plunging in price and industrial production plummeting, is clearly leading to a substantial decrease in CO_2 emissions. However, this environmental upside could be negated by producers seizing the opportunity to increase petrochemical production.

For more on the **United Nations Environment Programme data** see https://www.unenvironment.org/explore-topics/chemicals-waste/what-we-do/policy-and-governance/global-chemicals-outlook

For more on the **sustainable development goals** see https://sustainabledevelopment.un.org/?menu=1300

Intensive agriculture is also linked to climate change and fossil fuel consumption, mainly through the use of fertilisers, pesticides, herbicides, and machine fuel. Excessive fertiliser use, whether petrochemical-derived or manure-based, increases nitrate levels and promotes eutrophication in rivers and oceans, which has consequences for wildlife and the climate because of increased N_2O emissions.[6] Pesticide use significantly contributes to biodiversity loss.[7]

Biodiversity can contribute to reversing climate change. An edifying example of that is the "Little Ice Age" in the 16th century.[8] The conquest of America resulted in an increase in fallow land related to the reduced burning of biomass and pandemics. A direct consequence was that the CO_2 in the atmosphere declined by 10 parts per million (ppm) (at present it is around 410 ppm) and temperature decreased by 0·6°C.[9] Currently, the effects of intensive agriculture (use of pesticides and fertilisers) and deforestation are the main drivers of biodiversity loss.[6] Unfortunately, climate change is enabling previously inaccessible regions to be exploited for agriculture, often justified by the argument that the growing population needs to be fed.[10] Conversion of previously unavailable land to arable land is often referred to as the climate-driven farming frontiers. Unfortunately, arable land, if thawed and tilled, contains readily-releasable carbon (>177 gigatonnes)—as much as the amount of CO_2 emitted throughout the 20th century by the USA.[10]

Felling of forests results in a vicious circle of increased intensive agriculture due to climate change, accompanied by greater pesticide and fertiliser usage. This combination leads to even greater loss of biodiversity, soil degradation, and more chemical pollution. Solutions to these problems exist: there is no need to go back to tilling or weeding by hand! For instance, robots using alternative-derived energy sources can be expected. Although solutions are readily available, they require strong political support for their application. The industrial sector often threatens large-scale unemployment and governments tend to focus on growth statistics. Yet, increased investment in alternative energies combined with boosting research on more readily biodegradable plastics and less harmful chemicals (including pesticides), will ensure growth and employment, and also provide a better environment for humans and biodiversity. As a result, such pleiotropic efforts will not only reduce climate change, limit biodiversity loss, and reduce health costs from endocrine disruption, but also help attain the United Nations sustainable development goals.

The author holds a patent under the name "Transgenic clawed frog embryos and use thereof as detectors of endocrine disruptors in the environment", filed in 2002 (number FR020669) and extended by a Patent Cooperation Treaty filed in 2003.

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1 Kassotis CD, Nagel SC, Stapleton HM. Unconventional oil and gas chemicals and wastewater-impacted water samples promote adipogenesis via PPARγ-dependent and independent mechanisms in 3T3-L1 cells. *Sci Total Environ* 2018; **640–641:** 1601–10.
2 Carson R. Silent spring. New York: Houghton Mifflin Riverside Press, 1962.
3 Demeneix B, Slama R. Endocrine disruptors: from scientific evidence to human health protection. Brussels, Belgium: European Parliament, 2019.
4 Bellanger M, Demeneix B, Grandjean P, Zoeller RT, Trasande L. Neurobehavioral deficits, diseases, and associated costs of exposure to endocrine-disrupting chemicals in the European Union. *J Clin Endocrinol Metab* 2015; **100:** 1256–66.
5 Rochman CM, Browne MA, Halpern BS, et al. Policy: classify plastic waste as hazardous. *Nature* 2013; **494:** 169–71.
6 Tilman D, Cassman KG, Matson PA, Naylor R, Polasky S. Agricultural sustainability and intensive production practices. *Nature* 2002; **418:** 671–77.
7 Wagner DL. Insect declines in the anthropocene. *Annu Rev Entomol* 2020; **65:** 457–80.
8 Mann ME, Zhang Z, Rutherford S, et al. Global signatures and dynamical origins of the Little Ice Age and Medieval Climate Anomaly. *Science* 2009; **326:** 1256–60.
9 Nevle RJB, Bird DK, Ruddiman WF, Dull RA. Neotropical human-landscape interactions, fire and atmospheric CO2 during European conquest. *Holocene* 2011; **21:** 853–64.
10 Hannah L, Roehrdanz PR, K C KB, et al. The environmental consequences of climate-driven agricultural frontiers. *PLoS One* 2020; **15:** e0228305.