Scoping Review

The Plastics Pandemic: Diseases of unknown origin, declining fertility, and the wider implications

Ok Pannenborg[1], Richard Seifman[2]

[1] Former World Bank Chief Health Scientist (Retired), Washington DC, USA
[2] Honorary Diplomate of the American Veterinary One Health Society (AVOHS), Washington DC, USA

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Corresponding author:
Richard Seifman, Washington DC, USA. Email: seifmanrichard@gmail.com

Abstract

Introduction: In this article we explore:

1. The potential significance of plastics in an expanding series of diseases of unknown causes.
2. The longer-term effects of plastics on (in)fertility patterns across the world.
3. The possible effects, including wider implications for the future of mankind.

Methods: We use the explorative format of a scoping review to evidence synthesis.

Review: Macro, micro- and nano-plastics proliferation so far figures only marginally in the determination of the etiology of major modern disease incidence and prevalence. Similarly, the significant reduction of total fertility rates (TFR) around the world since the 1960s and the subsequent disconcerting increase in infertility patterns remain largely unexplored in terms of micro- and nano-plastics (MNP) as a major contributing or causative factor. The combination of some deteriorating mortality, morbidity and disability rates from major disease groups of unknown or unresolved origin on the one hand and dramatically decreasing fertility levels on the other, both with an increasing probability of micro- and nano-plastics playing a role in terms of their dynamics, may have long-term political, social, developmental and evolutionary consequences currently not considered.

We reviewed a wide array of scientific, social, political, financial, industrial, policy and media sources as to the importance of macro, micro- and nano-plastics with regard to their role as causes of a wide range of current pathologies of increasing incidence or age-group shifting prevalence. We found an increasing rate of coverage in the scientific literature worldwide, but little evidence of policy-sensitive relevance. An astounding lack of translational research in this field results in global plastics only being considered from a superficial pollution point of view.

Discussion: The increasing probability that MNP plays an important role in the origins of such everyday diseases as Alzheimer's, Parkinson's, many cancers etc., remains seriously underappreciated with a disproportionate absence of relevant research in this respect. This pattern equally applies to the global patterns of changing fertility and infertility levels. When extrapolated to the marine environment, plant biology and human biology from conception to day one of birth, it seems reasonable and proportionate to suggest that much more scientific inquiry, applied research across the sciences and translational and policy research will be required worldwide.

Conclusions: We conclude, partly in view of the global UN Plastics Negotiations in November 2024 in Busan, South Korea, that the potentially large scale implications of macro-, micro- and nano-plastics for human health, fertility, animal health, biological and plant survival dynamics need to be addressed at a more urgent and senior policy and decision-making level across national and international public, private, financial, industrial and socio-political levels in order to prevent the probability of major long-term damage to mankind. We call for greater involvement of applied material sciences and engineering, deepening of biomedical etiological research and the consideration of an International Plastics Control Agency and its establishment along the lines of the International Energy Agency.

Keywords: Global Plastics Negotiations, Plastic-induced Diseases, Environmental Health, One Health, Population Dynamics, Evolutionary Changes, International Plastics Control Agency.

Conflict of interests: None declared

Introduction

A steady number of publications and research findings are being shared around the world about the increasing global plastics problems. Many of these focus on the proliferation of plastics everywhere, the tons produced, by which industry, how discarded plastics has become one of the more ubiquitous pollution aspects, and perhaps how solutions or mitigations can be found and implemented.

For instance, more than 430 million tons of plastic are produced each year, two-thirds of which is cast aside as waste after just one use. If trends continue, plastic waste will triple by 2060. Eleven million metric tons of plastics enter our ocean alone each year, in addition to the estimated 200 million metric tons that already flow through our marine environments. At the current rate of production, there will be more plastic than fish in the ocean by mid-century (1, 2).

There is also the occasional paper or article on the potentially negative health aspects of plastics. More recently the issue of micro and nano plastics has been highlighted in a variety of scientific, clinical, political, industrial and social circles.

We will highlight a few dimensions of the plastics universe (3) [1] that we consider insufficiently emphasized and as such need to be prioritized, namely,

1. The potential significance of plastics in a series of diseases whose causes remain unknown or unresolved
2. The longer-term effects of plastics on (in)fertility patterns across the world
3. The possible effects, including wider and possibly evolutionary implications

We also touch on plastic alternatives and include thoughts as to ways forward with regard to scientific and applied research priorities, as well as global institutional policies and institutions.

Methods

We examined the literature and policy documents regarding the emerging and evolving issue of plastics and health, fertility and the wider implications for geopolitical and even evolutionary consequences, including the identification of both research and policy gaps. This commentary does not claim to reflect a systematic review, nor to be comprehensive. We explicitly extended our review efforts to get a scope of worldwide instances of scientific efforts, policy research and both social and political economy publications. This included systematic efforts to review macro-, micro- and nano-plastics topics published by OECD institutions and media, as well as those in Sub-Saharan Africa, South Asia, East- & South-East Asia, China, the Middle East and Latin-America & the Caribbean. We equally targeted publications from both public and private sector sources, including industrial and commercial financial sources. This also covered all global and multilateral investment and policy research papers and reports by, for example, UN

[1] This commentary will use, for ease of reference and inclusiveness, the term plastics and macro-, micro- and nano-plastics to include materials consisting of synthetic or semi-synthetic high molecular mass polymers, phthalates, bisphenols and PFAS and related per- and polyfluoroalkyl substances (the latter are not necessarily always plastic-related)

institutions and the multilateral Bretton Woods and related institutions or the World Economic Forum (WEF).
Our approach hopes to contribute to the synthesis of evidence with regard to the unexplored and potentially insidious effects of MNP on human health, all other biological species, incl. plants, and ultimately the sustainability of current plastic and MNP practices and policies.

For scientific public sector publications, we mostly used the repository of the U.S. National Library of Medicine, its European counterparts and the Chinese Academy of Medical Sciences (English language). Similarly, we explored a large number of scientific chemical journals, as well as policy publications by the gas- and oil industry. For daily or periodic media reporting we reviewed several years editions of the Washington Post, the New York Times, the Financial Times, the Frankfurter Allgemeine Zeitung, the Neue Zuricher Zeitung, Le Monde, Le Figaro, the Yomiuri Shimbun (English language), The Economist, and others. For regulatory publications we reviewed EU, OECD, ASEAN, GCC, AU and G20 policy documents, as well as records of the European Court of Justice, the ICJ, the PCA, the ICC Court of Arbitration, the ICSID and the US Federal Court Electronic Records system (PACER).

We did not include any review of social media (e.g. Facebook, Instagram, Messenger, TikTok, Telegram, Weibo, WeChat, LinkedIn, etc.) in this respect.

Scoping Review

Plastics and Health

The health and medical status of populations around the world over the last 100 years has improved dramatically, partly driven by most countries becoming richer, jointly with higher levels of education, knowledge and the expansion of research and scientific findings. Numerically the world is blessed with ever better health outcomes in terms of average life expectancy, lower death rates and in many or even most cases significant increases in quality-of-life[2] (4).

At the same time, we are seeing a longer and longer list of diseases the origins or causes of which we have little or no idea about. In scientific language, *etiology: unknown*. In many cases contributing factors are identified, but what the real cause is of many of these often remains unresolved or a mystery. Many of these illnesses are familiar: Parkinson's disease, Alzheimer's, pancreatic cancer, many other cancers, multiple sclerosis, schizophrenia, brain tumors, and a host of autoimmune diseases. Even diabetes is officially unknown in terms of its origin: lots of contributing factors, yes, but *real cause*: no. As to cancers, many of them are shifting down[3] to younger generations and cohorts (5). Similarly, the rise in inflammatory bowel diseases have

[2] This is not to discount the enormous suffering we have seen in terms of wars and conflicts. But until recently most countries experienced poverty *reductions* and positive socio-economic development. Only recently these trends have stalled.
[3] For pancreatic and kidney cancer, for example, the incidence rate among those born in 1990 was two to three times the rate of those born in 1955.

overtaken the earlier Crohn's disease prevalence by many factors. The developments of fibromyalgia, migraines, myeloma and other bone cancers, myalgic encephalomyelitis, and the expanding patterns of Attention deficit/hyperactivity disorder (ADHD) all can be seen in this light[4]: we remain unable to specify a true cause (6). This is very different from, for example, malaria or many infectious diseases: here we know the parasite or the virus, we know the vector, and we know the disease as a result of them; the response is to neutralize the pathogen, or the vector and you have prevented the disease.

The timing of these patterns appears to coincide with the great plastics expansion. Few of the readers' grandparents or great grandparents were exposed to plastics during their youth, with macro plastics coming into their lives only in their middle- or old age. Those born in the 1940s and 1950s equally had little exposure to plastics in their youth, but from the 1960s and 1970s increasingly became more prevalent.[5] The X, Y and Z generations, however, were born with macro and increasingly micro plastics surrounding them literally everywhere.

Most material objects in the world of the earlier generations consisted of wood, metal, glass, natural textiles, rubber, ivory, paper, stone, ceramic products, and plant-or animal-based items: think cars, milk bottles, houses, furniture, beddings, almost everything in the home, wool, cotton, leather, and so on. Now think of today: your car is mostly plastic or plastic-based composite material, most textiles are polymer-based or- mixed, most furniture is plastic-composite material, almost all packaging and bottles are synthetic, even food and drinks contain many synthetic and petro-chemical derived products, and so on. A baby born today enters into a plastic world (most materials in the obstetric department or clinic are plastic-based) and is wrapped in plastic and breathes and drinks plastics (7, 8);[6] plastic particles are there from the first minute one is on earth, not to mention fetal nano-plastic exposure while still in the womb (nano plastics pass through both the brain-blood and the placental barriers (9, 10).

As with the rate of cancerous growth, *time* and *accumulation* are major variables. Older generations, even when exposed later in life, simply did not have enough time in their life to be sufficiently affected by plastic and other petrochemical products. Younger generations have been exposed increasingly throughout their lives, allowing accumulation and time to create build-ups of micro- and nano-plastics in their bodies. In fact, few humans in the world are free from micro and nano plastics in their bodies and, with nano plastic particles, even in their brains. Mind you, many of these may settle in the body cumulatively, not break-down and belong to the so-called category of for-ever plastics.

[4] To be sure, these are just a few examples of disorders without a known or resolved cause: while difficult to put a precise number on the total, they run into the thousands, all at different prevalence levels (approx. 6,800 rare diseases, for most of which the cause remains unknown)

[5] In the 1967 famous movie, "The Graduate", career advice is given to the young man played by Dustin Hoffman star, that "the plastic industry" was the promising future.

[6] Most breast milk in richer countries now contains micro- and nano-plastics, directly compromising neonatal and child health form the start, with potential long-term consequences for the rest of their lives

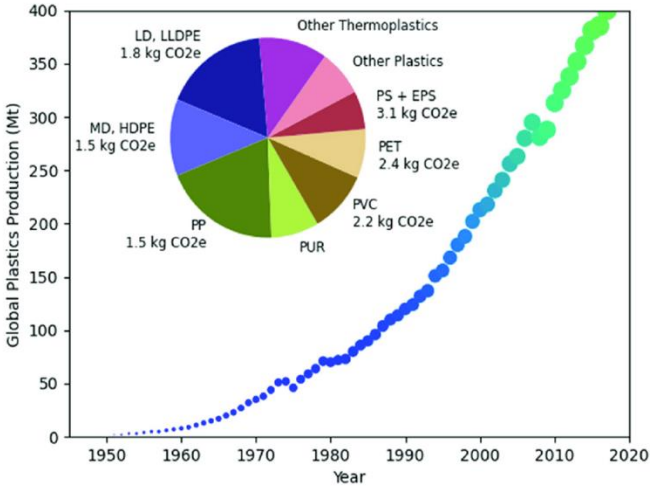
Thus, it doesn't take rocket science to ask, *"are these related?"*. Might there be a correlation or even causal link between the incidence and prevalence rates of diseases of unknown or unresolved etiology and the proliferation of plastics over time? In short, are plastics causative for these diseases?

The big surprise here is actually not the question or the findings, but the level of timidity and disproportional absence of the question asked. The number of studies looking into, for example, to what extent nano plastics may play a role in the amyloid-beta (Aβ) accumulation in the brain of Alzheimer's patients is astoundingly small (11, 12. Similarly, chronic inflammatory bowel syndromes (and related diseases) have significantly increased in numbers when compared with earlier generations: micro- and nano-plastic particles interfering and modifying the molecular and absorption dynamics of the intestinal linings and membranes has been highlighted (13) but are obscure in clinical and policy publications when it comes to identifying culprits and addressing them. With colorectal (or bowel), kidney, gallbladder, and testicular cancers in the under-50s on the rise (small intestine and liver cancers especially among women), one would expect an interest in examining the correlation or any causal effects with the micro and nano plastics exposure that these cohorts underwent as distinct from their generational forebears. And one would anticipate a significant number of basic and applied research papers on *the potential causal links between micro- and nano-plastics and* the long and increasing list of prevalent and less prevalent *diseases of unknown or unresolved origin*. Fortunately, there are some early signs that this challenge is being taken up are emerging. For instance, older populations with longer-term exposure to nano-plastics may disproportionally suffer from premature heart aging, inflammation, and oxidative stress. Plastic particles lodged in a key blood vessel were more likely to experience heart attack, stroke, or death during a recent seminal three-year study in Nature (14, 15).

Nevertheless, the absence of serious, robust and widespread attention to the role of macro-, micro- and nano-plastics as the cause of a very large number of severe diseases afflicting mankind, with enormous costs in terms of mortality, morbidity and disability and huge social and economic losses remains disconcerting, to say the least and likely, when looking back in a decade, highly irresponsible.[7]

[7] For instance, policy-influential publications like *The Washington Post* or *The Financial Times* typically include an article on the problem of plastics only *two or three times a year*; similar frequencies apply to the Frankfurter Allgemeine Zeitung, Le Monde, the Yomiuri Shimbun and even The Economist; ***compared with priorities such as climate change, war and conflict, human rights, pandemic threats and so on, this is astoundingly modest and disproportional to the potential damage and harm taking place and to be expected from micro- and nano-plastics contamination.***

Figure 1: World plastic production throughout the years (1950-2019)[8] (16).



Micro- and nano-Plastics and Fertility

The effects plastics have on fertility dynamics have been studied and known a bit longer. Early publications emerged in the 1980s and 1990s looking at broken-down remnants of macro plastics affecting women and men in terms of their reproductive capacity. Unfortunately, these early insights emerged in a field notorious in medical science for being among the least dynamic in research and innovation: obstetrics and gynecology even today remain less addressed (17)[9] and in the 1980s the field of male fertility hardly yet existed (18)[10].

At the same time, while gynecological and obstetric risks were well known to the early and middle generations of the 20th century and fertility concerns focused mostly on limiting fertility – and *infertility concerns* were rare– from the 1970s and 80s onward infertility patterns grew more prominent and since the 2000s have become a major medical and social industry. While it would have been difficult to find infertility clinics 50 years ago, they are now manifold for both women and men.

[8] Mt: megaton; PS: polystyrene; EPS: expandable polystyrene; PP: polypropylene; MD, HDPE: medium-density/high-density polyethylene; LLDPE: linear low-density polyethylene; LDPE: low-density polyethylene; PUR: polyurethane; PET: poly(ethylene terephthalate); PVC: poly(vinyl chloride); other plastics include acrylonitrile butadiene styrene resin (ABS), polybutylene terephthalate (PBT), polycarbonate (PC), polymethyl methacrylate (PMMA), and polytetrafluoroethylene (PTFE).

[9] The earlier mentioned breast milk example goes to show: see the recent research by Professor Meghan Azad's group at the University of Manitoba, which more rigorously analyzed the various human breast milk components (incl. the discovery of around 50,000 small molecules previously unknown)

[10] The field of Andrology in the opinion of the authors even today remains underdeveloped

The coincidence of the emergence of micro- and nano-plastics and the emergence of global infertility patterns seems reasonable, and the timeline and prevalence distribution coincide well (19).

First the biomedical aspects and then the global distribution effects. Early concerns how pesticides, agricultural hormones and microplastics might influence fertility emerged in the 1960s: the fields of endocrinology (a new field at the time, with a high innovation index reputation) and toxicology were relatively successful in alerting society, governments and regulating agencies to the potential risks for human health of the first two. The result was fairly dramatic reductions of the use of pesticides and hormones in the food chain from the 1960s onward. Microplastics came into their own regarding fertility concerns somewhat more since the 2000s, but less successful in terms of subsequent industrial or regulatory policy measures. The concerns, among others, focused on effects on ovaries and testes, on germ cell and other somatic cell development, on synergistic sperm toxicity, on oxidative stress and apoptosis related gene expression, and impaired spermatogenesis. (20, 21, 22) Similarly, more specific female reproductive damage, metabolic abnormalities in offspring and female reproductive and infertility disorders are beginning to move up the priority list in global health (23, 24, 25, 26).

In the words of professor Hagai Levine (27), head of the Environmental Health Track at the Hebrew University-Hadassah Braun School of Public Health and Community Medicine in Jerusalem, and professor Shanna H. Swan (28) of New York's Icahn School's Department of Environmental Medicine and Public Health and their research colleagues in Brazil, Denmark, Israel, Spain and the United States, when discussing specifically the role of plastics in sperm decline: *"We do see a dramatic decline: Cut in half—99 million per milliliter in 1973 and down to 47 million per milliliter in 2011. That's 39 years. It's a decline of 52% which is faster than 1% per year, and if you thought about anything else, like breast cancer or ADHD or anything else increasing or changing at that rate people would be up in arms. But for some reason, they're not so alarmed about this decline".*

More direct in terms of longer-term consequences, Professor Swan sounded the alarm in 2017 on sperm levels trending towards zero by 2045 (29). In 2021, she authored the book "*Count Down: How Our Modern World is Threatening Sperm Counts, Altering Male and Female Reproductive Development, and Imperiling the Future of the Human Race*" (underlining by the authors) (29).

Now, the growth and proliferation of the infertility patterns started primarily in the rich economies, for easy sake of argument, in the OECD countries. More recently, both the reduction of fertility -as measured by the total fertility rate (TFR)- and the increase in *in*fertility can be observed in East- and South-East Asia, in South Asia, in Latin-America and, to some extent, even in Sub-Saharan Africa. A reasonable hypothesis would be that the drop in TFR and increase in infertility is following the introduction and use of macro, micro, and nano plastics in all these societies. The highest TFRs can still be found in rural villages in remote African and Asian areas, communities where the introduction of plastics is either recent or still absent (visit a Congolese village North of Isiro, West of Mangadian in Mali, North of Kapultete in Zambia, or a

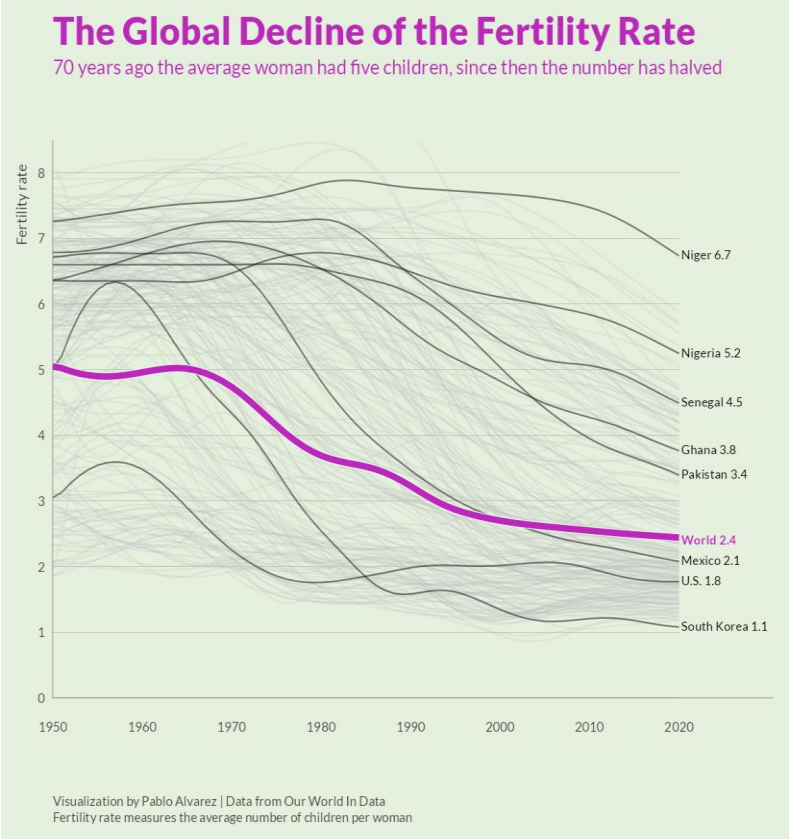
Sudanese/Ethiopian settlement in the area of Arbodi and you'll find hardly any plastic or synthetic goods or materials, with the exception of some macro plastic items). TFR in Nigeria remains somewhat of an exception, although similar mostly in rural areas, not in the large urban developments where plastics have found their way now as well since over a decade.

As can be seen from Figure 2, the onset of the drop in the world's fertility coincides with the wider introduction of macro-plastics in the world, around the early 1960s (see Figure 1). A short steep drop in the 1950s may well reflect the introduction of modern contraceptive technology in 1953, that is the oral contraceptive pill (discovered and developed by Carl Djerassi and others) (30). The subsequent steep drop from 1963 onwards and the accelerated drop from 1993 onward could well reflect wider introduction and proliferation of micro- and nano-plastics over the last 30 years.

Traditionally demographers, population specialists and family planning experts, as well as those in the field of gynecology and obstetrics have attributed falling fertility levels around the world to economic growth and higher incomes/caput, higher female education and female workforce participation, women's emancipation, increasing costs of child-rearing, better purchasing power (PPP), and increases in contraceptive prevalence rates. Government concerns regarding dropping TFRs, a converted national population pyramid and a future shortage of a younger generation labor force have focused on policy measures addressing these underlying factors or causes (31, 32, 33)[11], in addition to immigration policies. But plastics – rarely, if at all.

Figure 2: The global decline of the fertility rate (34**)**

[11] Examples include subsidies for additional children, free nursery and primary education, child care and subsidized nanny programs, and wider population growth incentive programs; France, South-Korea and more recently China are leading in these respects.



So far almost no policy documents, government strategies, academic or institutional analytical papers have included considerations of micro- and nano-plastics on global dynamics of decreasing fertility levels and increasing infertility levels and linked them to the proliferation of plastics and their products at ever higher levels in even the most remote households around the world.

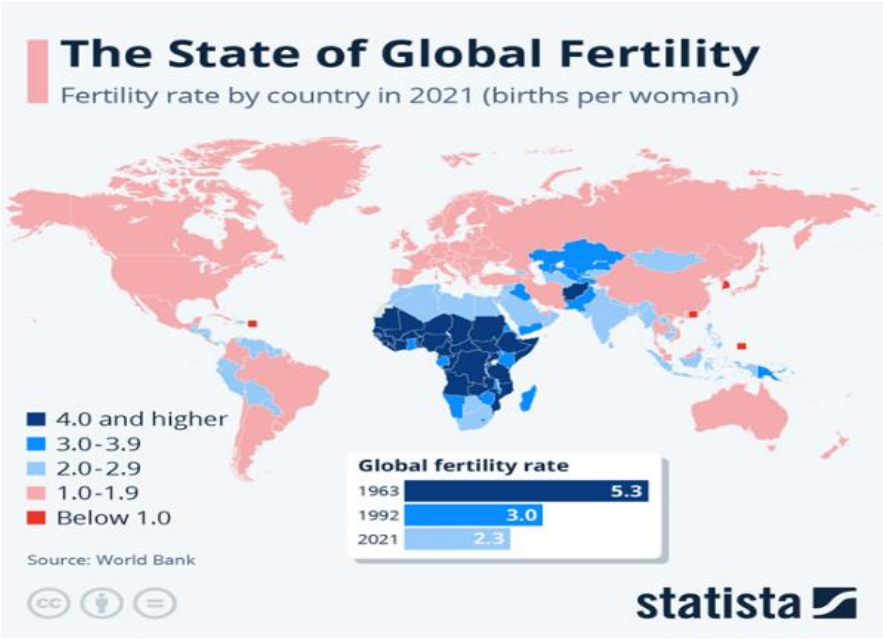
Wider Considerations and beyond

To push the argument a bit further to engage strategic colleagues, one could argue that, based on the above observed global trends of fertility in conjunction with the plastics epidemic going around the world, this so-far fairly silently spreading phenomenon could have significant global consequences. One can envisage an initial potential drop in fertility in OECD countries to almost zero and a subsequent slower, in phases, reduction of fertility and increase in infertility in East- and South-East Asia (well underway in China and Indo-China, going for zero in the Koreas and Japan and starting in Indonesia and even the Philippines), then in South Asia, then across Sub-Saharan Africa (towards the 2060s or 2070s perhaps) and ultimately also in the Middel East. Latin America already is at low levels that may go into negative territory.

The result of plastic contributing to the fertility decline bearing on the world's population dynamics and concentrations, would see a Europe with less than 5% of world population, with the U.S. and Canada faring a bit better. China would fail to grow to be the nominally largest

economy in the world; India may remain a question mark for a while to come (many very promising trends, but equally many structural obstacles to grow into a modern and leading economy, with plastics use increasing almost exponentially); Latin America and the Middle East may remain secondary in many respects; while Sub-Saharan Africa would become the largest entity in terms of people, but still diminishing in absolute numbers by early next century.

Figure 3: The state of global fertility (35)



Projecting further in the future, if plastics will not be contained, in conjunction with other major factors such as climate change and its consequences, the effect would be a shrinking world population in absolute numbers. While some may argue from an *ecological and evolutionary* point of view that this may or would be desirable and a positive development, in terms of geopolitical power distribution the world would fundamentally change in ways it is hard to imagine.

Potential Scenarios

Doomsday scenarios are nothing new, so how does this potential plastic risk figure *vis-à-vis* earlier and other global risks? Let's consider three similar developments: climate change, pandemics and pollution-and-the-chemical-revolution.

Climate change as a systemic global risk: fortunately, it has been recognized, and measures to mitigate it have been codified by the 2015 Paris Treaty. Implementation of these and other measures are under way, albeit with significant obstacles, delays and continuing resistance playing a major role. Recognition of the damaging effects of greenhouse gases took decades, but in the end their identification, risks and long-term damage effects did get the global priority necessary, and mankind has a chance of limiting those effects.

Pandemics have long been recognized as single most deadly events: They can kill over a million people and more in a very short time, apart from (nuclear) war, earthquakes, volcanic eruptions or an asteroid. While formal efforts and lots of advance operational disaster plans had been agreed upon and enacted (36)[12] as a result of the analytical pandemic work undertaken, when push came to shove with the 2020 COVID-19 pandemic, almost none of the International Health Regulations (IHR) turned out to be effective, as most countries simply ignored earlier international law commitments and responded to national panic mode concerns (by closing their borders). The latest Pandemic Treaty proposals submitted to the 77th World Health Assembly (37) earlier this year similarly came to nought (38).

Chemical products can be toxic to man and nature goes back to historic times and the Middle Ages (think, for example, lead and arsenic). But more serious analytical insights -and subsequent measures to control or mitigate their harm started in the mid-19th Century[13]. Subsequently a series of laws and regulations around the world were enacted to outlaw or manage toxicity risks, mostly nationally, but also internationally (e.g. the Montreal Protocol [re: ozone], the Minamata Convention [mercury], the Basel Convention [hazardous waste disposal], the Stockholm Convention on Persistent Organic Pollutants [POPs], the FAO Code of Conduct on Pesticides, and several others (39).[14]

Regarding macro, micro and nano-plastics so far, the sad reality is that many of the above regulations are self-assessed by the chemical industry itself and remain exceptionally ineffective. The Stockholm Convention illustrates this well: "since it became effective in 2004, the Stockholm Convention has managed to examine and ban only 26 out of potentially 350,000 synthetic chemicals (<0.01%), with nine more under review in Annex B (restriction) and C (unintentional production)" (40). To put this in perspective, in the U.S. alone approximately 1,500 new chemical substances are introduced every year (*U.S. Government Accountability* Office (41).

With the 20th century chemical revolution, we are much closer to today's global plastic challenge, as plastics are synthetic chemical polymer compounds (made from molecules mostly derived from oil and gas (and coal) in the petrochemical industry).

Current Plastic Control Efforts

To be sure, various efforts are underway to bring global attention and proposals for a course of action. The UN Environment Program (UNEP) 2023 Report, "*Turning off the Tap: How the*

[12] From the early Sanitary Conventions in the late 1800s to the International Health Relations (IHRs) of the 1990s and early 2000s and the Pandemic Treaty drafts of 2023/2024

[13] For example, the Royal Chemical Society was established in 1841

[14] Major examples include the EU REACH (2006) Regulation, the US Toxic Substances & Control Act (1976) and the US EPA Procedures for Prioritization of Chemicals for Risk Evaluation Under the Toxic Substances Control Act, the Japan 1973 Act on the Regulation of Manufacture and Evaluation of Chemical Substances, the China 2011 Regulations on Safe Management of Hazardous Chemicals in China (Decree 591), or the India 2000 Manufacture, Storage And Import Of Hazardous Chemical (Amendment) Rules.

world can end plastic pollution and create a circular economy" maps out a plan to reduce global plastic waste by 80% within two decades. It created an Intergovernmental Negotiating Committee to Develop an International Legally Binding Instrument on Plastic Pollution, including in the Marine Environment, to produce a proposed agreement by the end of this year (its fourth session took place in April 2024). These current international efforts to address plastics reflect many good intentions. However, it seems to be primarily limited to plastics pollution and the management thereof and remain unusually superficial in terms of harmful effects on humans and the environment in a more systemic and structural way, as argued above (*UNEP* (42). Taking into account the fairly peripheral position of these negotiations in the overall UN structure and among the list of global multilateral priorities[15], not too much should be expected from the upcoming 5th round of negotiations anticipated for November 25 in Busan, South Korea (as illustrated by the plastic production reduction proposals by Peru and Rwanda, which failed) (UNEP (43).

Nevertheless, these negotiations offer an opportunity to deepen global concerns about the plastic pandemic and perhaps, can give rise to a subsequent Global Plastics Treaty II later on, that will go beyond pollution and would recognize the likely evolutionary costs of plastic proliferation worldwide. This would need to include analytics on the nano-plastic coverage and accumulation in plants, trees and aquatic life, as nano-plastics by now are ubiquitous in water and thus would enter the life cycles of trees and all other biological organisms (44, 45). This is fully consistent with the One Health approach, which is increasingly gaining traction.

In line with the first dimension outlined above, hopefully it would stimulate research into the link between micro and nano plastics and the long list of diseases of unknown and unresolved origin, including many cancers, *at an order of magnitude many times larger than today*.

Assessment of Plastics Compared to Other Similar Threats

When comparing all these dimensions, are plastics really that much different from the earlier warnings about pesticides, chemical air-, ground- and water-pollution with toxic substances, the potential risks of thousands of pandemic viruses, processed foods, or war and conflict and their consequences in terms of poverty, malnutrition and starvation or even nuclear effects? Are the plastic nano particles much different from the soot particles from coal, oil and diesel fuel (*WHO*

[15] While the plastic negotiations are attended by large numbers of observer organizations (NGOs, CSOs and others in the hundreds, including from petrochemical industry trying to limit or frustrate the negotiations, many delegations from low- and middle-income countries often are less than vocal or supportive, as in their view plastic problems are still mainly rich countries' problems - and their own problems (security, malnutrition, drought, youth education and unemployment, etc.) are more immediate and urgent; in view of the silent, insidious and increasingly ubiquitous nature of micro- and nano-plastics effects also in the poorest communities, this is a seriously misinformed position (based on personal communication with a UN Under-Secretary-General, 14 Aug. 2024, New York)

(46)[16], as we knew them from the 19th century onward in terms of seriously damaging to your health (47)?

Our sense is that the answer depends on to what extent micro- and nano-plastics intake is cumulative, their degree of accumulation, their molecular dynamics, what the clearance rates of plastic particles from tissue or organic matter is, and what pathology rates emerge for human, animal or plant cells (48, 49). If these turn out to be as damaging as bad case scenarios -as outlined above- would indicate, the issue could actually be more dangerous to the survival of mankind than current climate change concerns.

We see a need for a much larger, in-depth, global research and investigative effort by countries around the world to clarify the answers to these questions. A positive development in this respect concerns the European Commission's funding of the *Research Cluster to Understand the Health Impacts of Micro- and Nano-plastics*, which currently covers five collaborating research projects: Aurora, ImpTox, Plasticheal, PlasticsFatE and Polyrisk (*EU-CUSP* (50). Findings from these and other research projects could have far-reaching implications for policies and regulations on chemicals, plastics, food, and water in terms of carcinogenicity, mutagenicity, reproductive toxicity, and respiratory toxicity.

The UN Plastic Pollution Treaty, if enacted, would be similarly good news, but likely limited in terms of compliance authority; the countries that have outlawed plastic bags remain just a handful and many more countries need to go much further in plastic restrictive policies regarding thousands of products. But first and foremost, we need to better understand the real underlying mechanisms of micro- and nano-plastics effects on human, animal and plant health, fertility and progeny and the various models of rates of progression of each of them. Unless we understand and take action we will be like frogs in a slowly warming pot, ultimately boiling to death.[17]

Discussion

Future Options in the Material Sciences. As with most problems and critiques, we also need to consider "if not plastics, then what?". In view of how plastics are literally ubiquitous, it is no use arguing "just get rid of them".

Are there alternatives?

The comparison that seems appropriate is climate change and energy. During the early days of awareness of energy pollution and later their climate change implications, alternatives to fossil fuels were scarce (e.g. geothermal, hydro) or controversial (nuclear). The solar cell, battery technology and wind turbine and blade revolutions had hardly been conceived of, whereas now,

[16] Plastic nano particles: 1 nm to 1 μm; soot particles range from about 10 nm to 1 mm in size. Fine particulate matter is defined as particles that are 2.5 microns or less in diameter (PM2.5).

[17] The boiling frog is an apologue describing a frog being slowly boiled alive. The premise is that if a frog is put suddenly into boiling water, it will jump out, but if the frog is put in tepid water which is then brought to a boil slowly, it will not perceive the danger and will be cooked to death. The story is used as *a metaphor for the inability or unwillingness of people to react to or be aware of sinister threats that arise gradually rather than suddenly*

if narrow political, self-interest and trade perceptions could be overcome, the world could easily do away with almost all fossil fuel sources and have abundant solar cell energy for all of mankind[18] – a material science innovation and advance that was difficult to envisage 50 and a 100 years ago. Similarly, the semiconductor transformation over the last 60 years and their emerging AI effects shows the power of sustained R&D efforts with unforeseen new products.

We are aware of the biochemical efforts and progress in the field of bacterial and bioremediation solutions to plastic waste and pollution. While these fields of science should equally be mobilized to address the issue, we remain somewhat skeptical as to their potential in view of the historical record and its seemingly limited ability for scaling up and large-scale implementation. Nevertheless, these efforts should equally be pursued vigorously (51).

The world of research and development in the material sciences, among the technological fields with a significant innovation index, should be more prominently engaged with regard to development of *plastic alternatives*, across the spectrum of macro, micro and nano plastics (52, 53*)*. To become long-term effective, efficient and socially productive such efforts should reflect joint undertakings by industrial and academic R&D, supported by government agencies such as the U.S. NIH, BARDA and DARPA, the EU's Horizon Program and the many public R&D and innovation funding agencies in other OECD and G20 countries. Hopefully this can be achieved in more collaborative and less mendicity-prevalent situation than we have seen with some industry in their dealings with earlier plastic toxicity findings (54)[19].

Conclusions

As former senior global health executives, we seek to raise awareness of the risks of micro and nano plastics. Our hope is that those who can share new research and act on public concerns will do so with a wider audience around the world, and will convince local, national and global leaders to act more vigorously in taking on the task of protecting their citizens from excessive macro and nano plastic risk. This should also be accompanied, at the same time, with efforts to stimulate and invest in ways to find substitutes or new approaches for those areas where plastic materials currently are difficult to replace.

Depending on what will be learned, and needs identified, it could generate sufficient support for the creation of an "International Plastics Control Agency", in a similar manner to how first the

[18] One of the authors (OP) recently traveled by air from Southern California to Washington D.C.: when flying over the enormous deserts of Southern California, Nevada, New Mexico, Arizona and Utah, he was struck by the observation that essentially NO large solar panel grits are visible across huge areas where almost no communities are present, 300+ days a year the sun is shining and transmissions would be stable (technologically and politically). Similarly, the solar cell energy potential over hundreds of thousands square kilometers of desert land in the Americas, the Middle-East and most of Saharan Africa remains unused (politically less stable). In combination with ever higher efficiencies of batteries and battery volumes, future history will likely judge this as an unusually dense period of myopic failings.

[19] Examples include the documentary *Dark Waters (2019)*, as well as the more comprehensive overviews of US Federal and State Regulatory and Legislative Action

International Atomic Energy Agency (IAEA) was created and subsequently the International Energy Agency. They increasingly play an instrumental role in the progress of the Paris Climate Change Accords.

If we consider how deadly micro and nano plastics could turn out to be as originators or crucial contributors to the increasing number of acute or chronic diseases of unknown origin, as well as being a main culprit of reducing human reproduction to negative fertility levels, the challenge may be equal to or even surpass climate change in urgency.

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