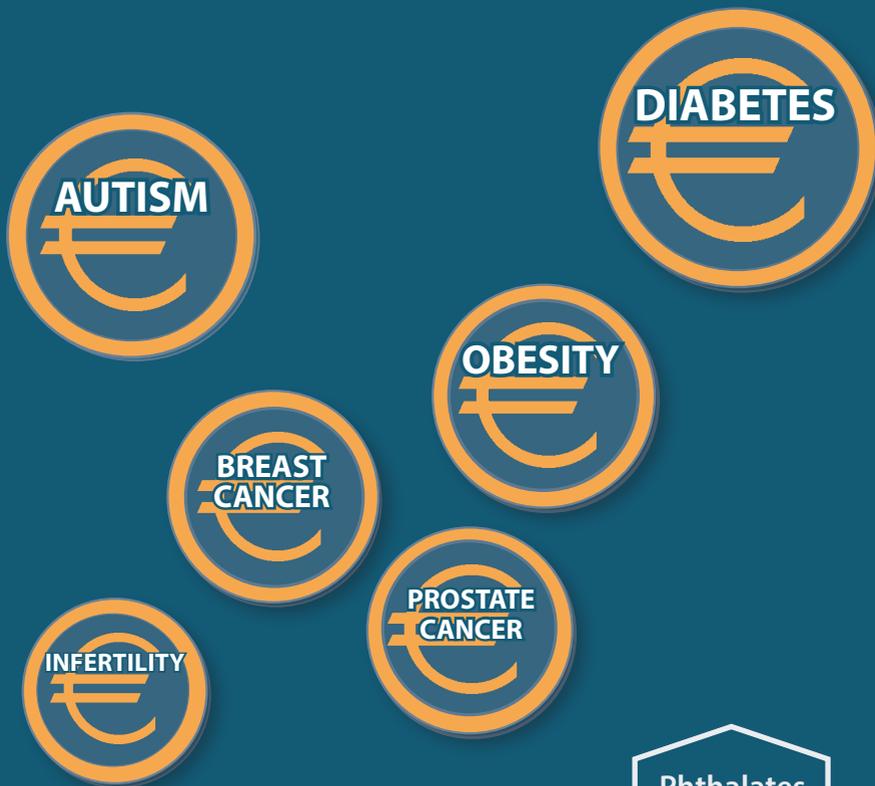


HEALTH COSTS IN THE EUROPEAN UNION



HOW MUCH IS RELATED TO EDCS?



About HEAL

The Health and Environment Alliance (HEAL) is a leading European not-for-profit organisation addressing how the environment affects health in the European Union (EU). With the support of its more than 65 member organisations, HEAL brings independent expertise and evidence from the health community to different decision-making processes. Our broad alliance represents health professionals, not-for-profit health insurers, doctors, nurses, cancer and asthma groups, citizens, women's groups, youth groups, environmental NGOs, scientists and public health research institutes. Members include international and Europe-wide organisations as well as national and local groups.

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HEAL policy statement

The opportunity for prevention that should not be missed



EU health savings up to 31 billion per year possible from reducing EDC exposures

The Health and Environment Alliance (HEAL) has commissioned the technical report which follows this policy statement as a first step towards estimating of the costs of a major menace to public health in Europe – the health impacts from exposure to endocrine disrupting chemicals (EDCs).

Over the past 20 years, scientific research has built up a body of evidence linking synthetically-produced EDCs to a wide range of diseases and conditions, including hormone-related cancers, type 2 diabetes, and infertility.

Endocrine disrupting chemicals, or EDCs, are synthetic chemicals used in a range of manufacturing processes, consumer products and agricultural applications to which everyone is exposed in everyday life.



European comparative human biomonitoring has shown mothers and children have several chemicals in their bodies, including EDCs, which are chemicals of concern¹. Other analyses have found dozens of chemicals in human blood.

In an expert report published last year, the World Health Organization (WHO) and United Nations Environment Programme (UNEP) said evidence linking hormone-mimicking chemicals to human health problems had grown stronger over the past decade. It stated that human exposure to EDCs now represented a “global threat” that should be addressed.

¹ <http://www.eu-hbm.info/euresult/media-corner/press-kit>

The calculation

The technical report compiles a cost calculation for a list of diseases and conditions that are related to the human endocrine system. The human endocrine system is essential for healthy functioning of many processes in the body, from prenatal development to most tissue and organ functions in adulthood. Scientists tell us that people's bodies taking up EDCs (i.e. being exposed) from food, drink and everyday products may be contributing to the number of cases of these diseases.

The conditions include:

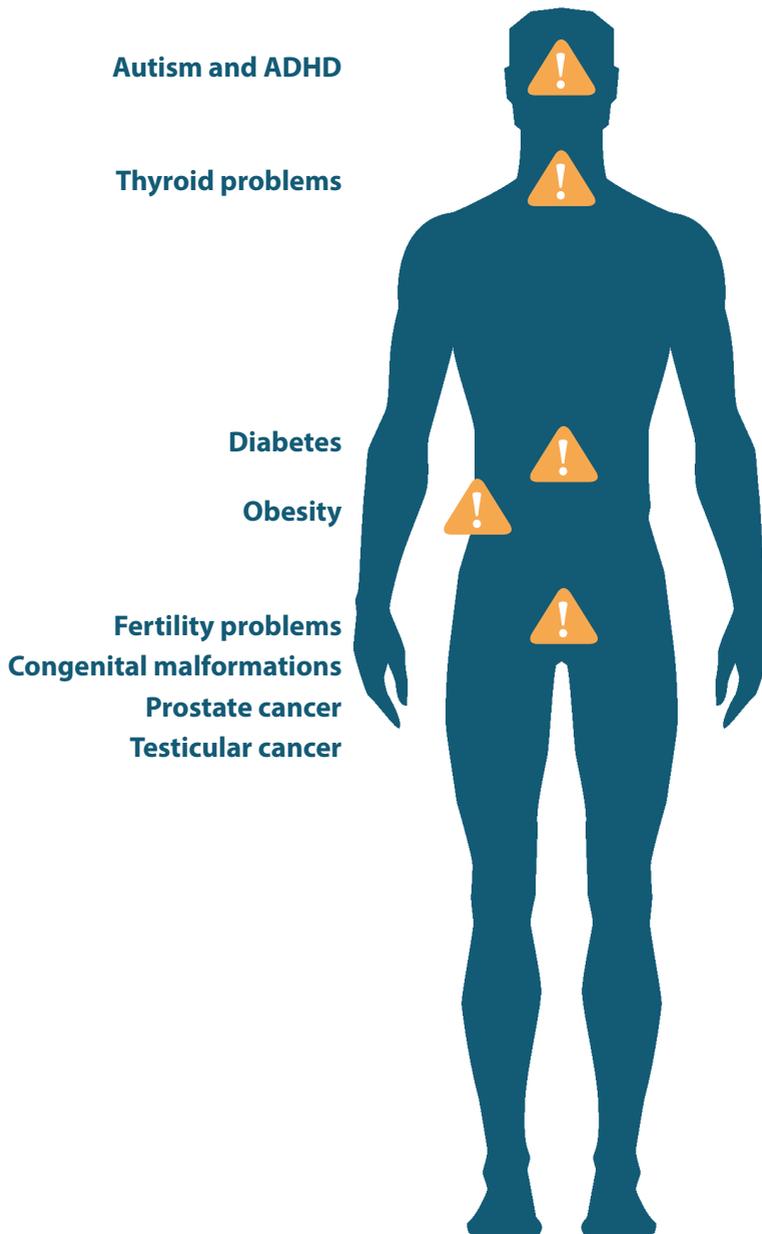
- Reproductive and fertility problems
- Abnormalities of the penis and testicles in baby boys
- Cancer of the breast, prostate, testes
- Children's behavioural disorders, such as autism and attention deficit hyperactivity disorder (ADHD)
- Obesity and diabetes.

University of Bath environmental economist, Dr Alistair Hunt, and Dr Julia Ferguson, Visiting Fellow at the Cranfield School of Management have produced an estimate of total costs in the European Union (EU) based on cost figures available for the above conditions. Their technical report puts the total of costs for the selected endocrine-related diseases and conditions at €636 – 638 billion per year in the EU.

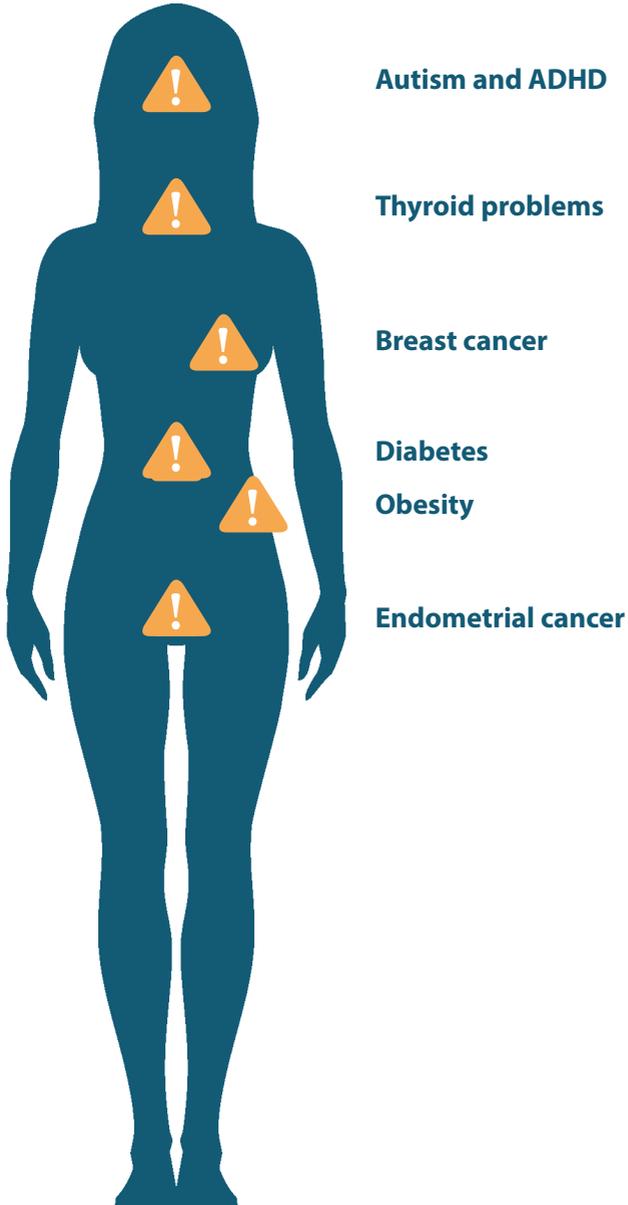
It is worth noting that the total cost calculation is probably a gross underestimate despite some of the assumptions and generalisations involved in calculating it.

- Figures were not available for all the endocrine-related health problems.
- Some figures are estimates for costs to the health care system but do not include the costs to families arising from illness and to employers from lost working days.
- None of the figures cover the costs of misery and pain associated with these conditions.

The Endocrine System: Health problems for men related to EDCs?



The Endocrine System: Health problems for women related to EDCs?



Linking the costs to exposure

Only a proportion of this total cost figure can be attributed to EDC exposure since major contributors to these diseases include genetics and lifestyle factors, such as diet, smoking or insufficient physical activity.

No-one knows exactly what contribution EDC exposure makes to the overall costs of the chronic diseases and health problems covered. A pioneering US scientific paper estimated the contribution of exposure of a single EDC to two different health conditions. Scientists found that BPA exposure in food contact materials may be responsible for 1.8% or 12,000 cases of child obesity and almost 39,000 cases of new incident coronary heart disease in the USA, with associated costs of US\$2.98 billion.

The above paper is limited to one EDC and two conditions and applies only to food contact materials. In reality, humans of all ages are exposed to many EDCs via many different exposure pathways – one source lists nearly 1,000 potential EDCs². Moreover many diseases and conditions have been identified as potential consequences of that exposure (hormonal cancers, reproductive problems, metabolic diseases, neuro-behavioral disorders). In addition, the WHO has noted that the ‘environmental burden of disease’ from chemicals is likely to be underestimated because of lack of data³.

It therefore seems possible that 2-5% would be a more realistic proportion. Whilst this percentage is a speculation, in the absence of more scientific work on what proportion of diseases could be attributed to EDC exposure, the hypothetical 2-5% figure can be instructive for policy makers considering the potential benefits accruing from reducing exposure and preventing diseases.

² See the Endocrine Disruption Exchange (TEDX) List of Potential Endocrine Disruptors: <http://endocrinedisruption.org/endocrine-disruption/tedx-list-of-potential-endocrine-disruptors/overview>

³ “Knowns and unknowns on burden of disease due to chemicals: a systematic review”, Prüss-Ustün et al., *Environmental Health* 2011, 10:9. <http://www.ehjournal.net/content/10/1/9>

If EDCs contribute to only 2-5% of the total health costs from endocrine-related chronic diseases, EU policy change such as the phasing out of these hazardous substances and promoting safer alternatives could save Europeans up to €31 billion each year in health costs and lost productivity.

Here, there are also factors that could make these figures of between 13 and 31 billion an underestimate. For example, future costs are likely to be even higher than today's because:

- Current exposure may not appear as cancer or diabetes until decades later.
- Certain EDC-related conditions imply future health risks. For example, a baby boy born with a genital defect known as hypospadias has a higher risk of becoming infertile or developing testicular cancer later in life.
- Trans-generational, or epigenetic, effects may occur. This means that future generations may be affected by damage caused by EDC exposure in the current generation.

What are endocrine disrupting chemicals?

The following endocrine disrupting chemicals (EDCs) are all related to familiar objects in our daily lives. They are present in the environment and in our bodily fluids, such as urine, blood, the umbilical cord and breast milk.

Bisphenol A (BPA): a constituent part of polycarbonate plastic and epoxy resins. Polycarbonate is found in hundreds of everyday objects, such as eye glasses, computer casing and plastic food containers and dishes from which BPA can leach into food. Epoxy resins are used as a food preservative, as internal coatings inside tins, jars and lids, in water supply pipes and wine vats. There are other uses such as the thermal paper receipts from supermarkets. Researchers associate BPA exposure with breast and prostate cancer, metabolic disorders (diabetes, obesity), cardiovascular risk, problems with reproduction and neuro-behavioural problems.

Certain phthalates: plasticising additives principally found in flexible polyvinylchloride (PVC) (used in flooring, medical tubing for drips, shoes and gadgets), texturing agents, solvents and fixatives, fragrances in cosmetics and perfumes. Some phthalates, e.g. DEHP, DBP, and BBP are classified in Europe as toxic to reproduction, and have the potential to exert endocrine disruption, which may cause birth defects, harm to reproduction, organ damage, obesity, early puberty or cancer of the breast or testis.

Parabens: propyl and butyl paraben are preservatives used in personal care products or as food additives. Propylparaben has estrogenic and anti-androgenic properties and has been shown to decrease the production of sperm in male rats. Butylparaben shows a stronger estrogenic activity than propylparaben and also has effects on thyroid hormones; it affects the number and mobility of sperms and the metabolism of fats.

Perfluorinated chemicals (PFOA, PFOS): a family of halogenated polymers used in non-stick cookware (e.g. frying pans); textiles and products which have been treated to resist stains; packaging; and cosmetics. A Danish study published in 2009 links them to the decrease in sperm count in men.

Perchloroethylene: the chlorinated solvent often used in dry cleaning. Classified as a probable carcinogen (CMR 2A) by the World Health Organization's specialist cancer agency (IARC), exposure among pregnant mice affects the weight of the uterus and the fetus, and alters the behaviour of male offspring. In humans, an epidemiological investigation suggested links between occupational exposure and neurological disorders.

Ultraviolet (UV) filters: several common ultra-violet filters used in sun-tan products and other cosmetics, such as oxybenzone (also known as benzophenone) compounds and derivatives of camphor, can cause endocrine disruption and affect the reproduction of the offspring of exposed male rats.

Butylated hydroxyanisole (BHA): this antioxidant and preservative is commonly used in food, for example, chewing gum, and in food packaging and cosmetics. Rats fed with BHA are found to have lower levels of hormones (testosterone and thyroid hormones) and sperm abnormalities. Their offspring are smaller, have delayed sexual maturation, and smaller than normal reproductive organs.

Brominated flame retardants (BFRs): a family of compounds used as flame retardants in electronic components, plastics and synthetic textiles. Some are proven to disrupt thyroid hormones in mammals.

Heavy metals: such as mercury which is still used in dental fillings. According to researchers, the endocrine disturbance would affect the ovaries and testicles provoking immune disorders, reproductive disorders and an increase in breast cancer.

Certain pesticides: Many agricultural pesticides are suspected endocrine disruptors, which can be ingested as residues from processing fruits and vegetables. They include thiram, methoxychlor, mancozeb, zineb, fenarimol, resmethrin, deltamethrin, metribuzin, ketoconazol, carbaryl, terbutyn, fenitrothion, and chlorpyrifos.

Where to find out more about which chemicals are EDCs

European Union Institutions and Agencies:

- EU Joint Research Centre Database on EDCs⁴:
http://ihcp.jrc.ec.europa.eu/our_activities/food-cons-prod/endocrine_disruptors/eas_database
- European Chemicals Agency REACH Candidate List⁵:
<http://echa.europa.eu/candidate-list-table>

Member State Governments:

- Sweden's list of pesticides⁶:
http://www.kemi.se/Documents/Bekampningsmedel/Docs_eng/SE_positionpaper_annenll_sep08.pdf

Public Interest / Non Profit Organisations:

- SIN (Substitute It Now!) List by the International Chemical Secretariat (ChemSec)⁷:
<http://www.chemsec.org/what-we-do/sin-list>
- TEDX (The Endocrine Disruption Exchange) list of potential EDCs⁸:
<http://endocrinedisruption.org/endocrine-disruption/tedx-list-of-potential-endocrine-disruptors/overview>
- Pesticide Action Network Europe: <http://www.disruptingfood.info/en/consumer-guide>

⁴ 428 substances suspected of endocrine disruption, and more will be added in an update

⁵ as of June 2014, 4 EDCs listed due their EDC properties, and more listed for their reproductive toxicity

⁶ both EDCs and other hazardous properties (carcinogens, mutagens and reproductive toxicants)

⁷ as of June 2014, 47 substances not including substances classified for reproductive toxicity

⁸ As of June 2014, nearly 1,000 substances

Understanding EDCs

While it was long accepted that “the dose makes the poison” (meaning that the concentration of the chemical determines the severity of its effect), EDCs have the five following characteristics that contradict the simplicity of this traditional dictum:

- Low doses may be more harmful than higher doses in certain circumstances
- Critical windows of exposure exist (e.g., exposure may be more harmful during phases of sensitive, rapid development such as the fetal period, puberty and pregnancy)
- The combined effects of several EDCs working together may be greater than would result from the individual EDCs acting alone (mixtures or the “cocktail” effect)
- The “poison” can be latent rather than immediate (e.g., exposure in utero may increase risk of breast cancer later in life)
- Effects from exposure of the current generation may be carried on to the next and later generations in trans-generational, or epigenetic, effects.

Existing regulation

The manufacture and use of chemicals has increased enormously over the past 40 years, and the levels in our bodies likewise. The “chemicalisation” of our lives has prompted increased scrutiny by policy-makers and regulatory bodies of the potential hazards of certain substances, including some limited regulatory action on EDCs.

The EU has in the past and can still cite the precautionary principle as a rationale for protecting human health or the environment when the existing evidence of harm is worrying but not absolutely conclusive. For example, the use of certain phthalates in soft PVC toys and child care articles, which are intended to be placed in the mouth by children under three years of age, have been banned since 1999. In 2009, the law was revised to include more substances. EU law has prohibited Bisphenol A (BPA) in plastic feeding bottles for babies since 2011.

Some EU countries like Austria, Belgium, Denmark, France and Sweden have taken further action nationally, for example on BPA in food contact materials, or on other substances. Some countries are also very active in promoting regulatory action on EDCs at EU level. For example, France has proposed the restriction of BPA in thermal paper (e.g., in cash receipts) under the EU REACH chemicals law.

However, many known and suspected EDCs remain in food, drink, food contact materials, body care products, furniture, electronics, carpets and many other products. They are released into air, onto our skins, and move into our bodies in other ways allowing interaction with our hormone systems repeatedly in our daily lives.

Regulatory action by the EU could be effective in reducing human exposures in a relatively short period of time. Even though some EDCs are “persistent”, that is, they stay lodged in the environment and our bodies for a long time, monitoring shows that levels fall after a ban. For example, traces of DDT in breast milk in Europe have declined in the years since the ban.

Where regulatory action to protect or improve health has been taken in the past - even if there was not 100% scientific proof of harm - hindsight and further science has shown it to be justified⁹. Examples include early controls on smoking, which were introduced before scientists were able to show a biological explanation of the causal link.

What should be done now?

The leading scientists on endocrine disruption have made clear that enough evidence now exists to justify acting to protect human health and the environment.

HEAL is working hard to achieve the following changes as soon as possible. In this effort, HEAL is joined by many concerned groups and individuals, including more than 50 partner organisations of the EDC-Free Europe alliance.

⁹ Late Lessons from early warnings, 2013, EEA, <http://www.eea.europa.eu/publications/late-lessons-2>

- Swiftly establish official European methods for identifying and categorising EDCs across all uses
- Overhaul all relevant, existing EU laws to reduce exposure to EDCs
- Set out a timetable by which EDCs must be identified, the tests to identify them made mandatory, and safer alternatives phased in
- Reform risk assessment processes to ensure the characteristics of EDCs are fully taken into account and reflected in final assessments and risk management decisions
- Promote safer alternatives and thereby stimulate safer, greener innovation
- Include the phasing out of EDCs in national plans to tackle chronic diseases and other disease prevention efforts
- Educate health professionals, medical experts and health affected groups so they can better assist their patients/members in exposure reduction, conduct clinical research, and participate in relevant policy making fora.

Reducing exposure could bring huge health benefits

As an alliance of over 65 member organisations, representing health professionals, not-for-profit health insurers, doctors, nurses, cancer and asthma groups, citizens, women's groups, youth groups, environmental NGOs, scientists and public health research institutes, HEAL advocates for urgent policy and regulatory action to swiftly reduce exposure, particularly for the most vulnerable like women before and during pregnancy, infants and children.

Taking action now rather than later could help reduce the spiralling rates of certain hormone-related conditions. It would also offer huge financial benefits alongside the avoided pain and suffering.

Technical report

Introduction

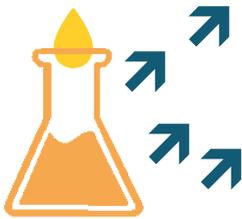
Scientists are currently investigating the links between people's exposure to EDCs and the following chronic diseases and conditions:

- reproductive problems including poor semen quality;
- congenital malformations of male sexual organs such as hypospadias (birth defect of the penis) and cryptorchidism (undescended testes);
- cancer, including of the breast, prostate, testes, endometrium, ovaries and thyroid;
- neurobehavioural disorders, such as autism and attention deficit hyperactivity disorder (ADHD), as well as thyroid diseases, and disorders affecting the brain development of children; and
- obesity, diabetes and metabolic syndrome.

The health effects listed above are linked to exposure to EDCs and have been referred to as “endocrine-related”. (1) Whilst these diseases and conditions are recognised as having multiple causes, current science demonstrates exposure to synthetic chemicals in the everyday environment can interfere with the hormone (endocrine) system. The role of these chemicals is an increasing concern not only because of the emerging evidence of harm but also because of the rising levels of many of these endocrine-related diseases in Europe. This report presents data on the incidence and prevalence of these conditions and their associated costs.

Context

Sales of manufactured chemicals have increased steadily over the past 40 years. Insofar as production is a useful proxy for exposure, human exposure directly and via the environment is steadily increasing. Between 1970 and 2010, the chemical industry worldwide grew in value from US\$171 billion to US\$4120, according to the United Nations Environment Programme (UNEP). (2) Today, Europeans are exposed to synthetic chemicals through what they eat and drink, through consumer products, such as body care products



Chemical sales have increased 24 times over the past 40 years

rubbed into the skin, via the air they breathe (both indoors and outdoors), and through drinking and bathing water.

Synthetic chemicals are inextricably linked to modern comfort but some are also harmful to animal and human health. Damage to wildlife from EDCs includes what is called “gender bending” effects. The negative effects on human health are those related to disruption of the human endocrine system. Special concerns apply to the exposure of the unborn child during pregnancy, which may have irreversible, life-long health effects. EDCs are suspected of contributing to the current growth of “endocrine-related” diseases and conditions listed above.

The endocrine-related conditions listed on the previous page is taken from the Berlaymont Declaration. On 24 May 2013, a group of the world’s leading scientific experts on EDCs launched an urgent plea calling on the European Commission “to implement regulatory measures that are in line with the best available science”. (1)

The signatories to “The 2013 Berlaymont Declaration on Endocrine Disruptors” noted that there are alarming signs of a growing public health burden in Europe. They stated that:

.....
“the prevalence of endocrine-related diseases is higher than it has ever been and [that] this disease burden continues to increase in the EU and globally.”
.....

Four major scientific reports have all assessed the state of the science regarding the role of EDCs in the development of endocrine related diseases and disorders and highlighted a number of key concerns (see box below).

What scientists are saying

World Health Organization and United Nations Environment Programme

Time to act to improve human health by limiting the use of EDCs

"It is now time to move forward and act on EDCs along the lines of future needs presented in the UNEP/WHO State of the Science of Endocrine Disrupting Chemicals report. I hope we can all work together to improve human health and the environmental conditions of wildlife by limiting use of and/or formation of anthropogenic EDCs."¹⁰

Professor Ake Bergman, Stockholm University, and lead author of UNEP/WHO report.

Berlaymont Declaration signed by 89 expert scientists (1)

EU policy should change

"Important pieces of EU chemicals regulation are entirely inadequate for capturing endocrine disrupting effects."

"We call on the European Commission to implement a regulatory regime for EDCs that is based on sound scientific principles."

"Scientific uncertainty should not delay regulatory action and commercial interests must not take precedent over concerns about risks associated with endocrine disrupters."

¹⁰ "Industry-funded review highly critical of WHO/Unep EDC report", Chemical Watch, 24 April 2014 <http://chemicalwatch.com/19407/industry-funded-review-highly-critical-of-whounep-edc-report>

The four key reports

- United Nations Environment Programme and World Health Organization (UNEP/WHO) report, State of the Science of Endocrine Disrupting Chemicals – 2012 (published in 2013) (4)
- European Environment Agency, The impacts of endocrine disruptors on wildlife, people and their environments (2012) (3)
- European Commission, State of the art assessment of endocrine disruptors, Final report (2011) (5)
- The Endocrine Society, Endocrine-Disrupting Chemicals: An Endocrine Society Scientific Statement (2009). (2)



The concerns identified include the fact that endocrine related diseases are increasing at a rate that cannot be attributable to genetic factors alone, and so are likely to involve environmental factors which may include EDCs. Whilst these reports highlight the difficulties involved with scientific study in this area, the evidence for the role of EDCs in such diseases is mounting. Although much of the research is based on laboratory studies on animals, this type of toxicological data, when combined with evidence from wildlife studies and epidemiological data, gives reasonable grounds for assuming that the adverse effects from EDC exposures seen in animals are relevant to humans. Thus there is evidence to suppose that EDCs are involved in some endocrine-related diseases in humans.

Expanding on the list of diseases and conditions identified by the authors of the Berlaymont Declaration, each disease section of this report provides data on the incidence and prevalence of these conditions in Europe, as well as estimates of the health care costs associated with their treatment. Within the scope of this report, it is not possible to attribute a specific proportion of these costs to exposure to EDCs. However, the scale of the costs indicates that any attribution that is subsequently demonstrated implies that effective regulation may have a sizeable influence on public health budgets.

This report therefore provides a first step in estimating the potential health benefits, and potential reduction in disease and health costs, for individuals, families and governments. The benefits could be achieved from strengthened EU policy action to prevent endocrine-related diseases via measures to reduce use and exposure to EDCs.

Methodology

- 1 Five broad types of health effect suggested as being associated with EDCs were identified by HEAL, based on a review of the scientific literature to date (above mentioned four reports), and selected as providing the focus for analysis in this report.
- 2 For each health effect type, the justification for its analysis is summarised by a short quote from the Berlaymont Declaration. (1) This also provides the starting point for the presentation and discussion of the incidence and economic data gathered for each health effect under the heading, "Incidence and Costs".
- 3 The section, "Incidence and Costs" first provides a summary overview of the recent incidence rates, and their trends, of the identified health effect across Europe. It should be noted that many trends are upward. However, it is not always possible to distinguish between environmental factors – and EDCs specifically – and improved diagnostics for the increases in incidence.

The section "Incidence and Costs" then documents evidence on the costs of treating the health effect. Cost studies tend to comprise of national level studies – which may be European or non-European (primarily US) – and EU-wide estimates. We present the principal cost estimates from these studies having adjusted them for inflation. They are reported here as the price levels existing in 2012.
- 4 For each health effect considered, the summary table then presents total cost estimates for the EU28 countries. These are generated by scaling up, on the basis of population size, from the estimates derived from the documented cost studies. For example, since the population of the UK comprises 12.6% of the EU28 population, a cost estimate of €1 billion for the UK would be multiplied by a scaling factor of 7.9 (100/12.6) to give an EU28 total of €7.9 billion.
- 5 There is an important caveat regarding the comparability of the EU28 total cost estimates between diseases. This is because economic cost studies differ substantially in both their coverage of cost types and

their methods¹¹. For our purposes, the more important difference is in the types of economic costs included. The main types of cost are direct and indirect costs. Direct economic costs comprise the costs of medicines and other treatment costs such as the time of medical professionals (doctors, nurses, etc.). Indirect economic costs include lost productivity resulting from absenteeism and premature retirement, the lost productivity or leisure time spent by family and friends in care, and the costs of rehabilitation and retraining or additional educational resources devoted to the individual, as well as subsequent losses in their own productivity (e.g. as affected children enter the workforce).

Intangible costs such as the pain and suffering associated with these health effects are not considered. However, in a legal case of liability, they would almost certainly be considered in relation to damages awarded.

Whilst there remain further distinctions in coverage, the aggregate estimates in the subsequent sections of this report are compiled from studies that consider the components mapped in the table immediately below.

¹¹ In this study, the terms “economic costs” and “financial costs” are understood to be inter-changeable.

Table 1
EU28 Total Cost Estimates – Coverage of Cost Types

Health Effect	Direct Cost	Indirect Cost
Human infertility – ART treatment	√	-
Cryptorchidism and Hypospadias	√	-
Breast Cancer	√	√
Prostate cancer	√	√
Autism	√	√
ADHD	√	-
Obesity	√	-
Diabetes	√	√

6 For each health effect, a table presents a summary of the incidence and economic evidence gathered. Health care costs are presented for the EU28. These have been derived by scaling existing country-level and regional-level cost data up to the EU28 level on the basis of population and serve to allow for an initial comparison of the size of the cost burden between individual health effects. Clearly, scaling on the basis of population is a simplifying process that abstracts from the realities of local and national differences in a) treatment costs, and b) varying incidence rates between countries.

Diseases and conditions

Reproductive problems

HUMAN INFERTILITY

What the Berlaymont Declaration says:



In some EU Member States, large proportions of young men have semen quality so poor that it will seriously affect their chances of siring children.

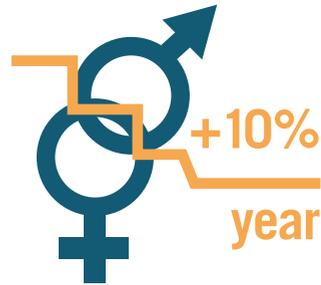
Incidence & Costs

By 1992, sperm quality across the European population was reported to have declined by 50% in the previous 50 years. (7) A recent study of 26,600 men in France showed sperm count had fallen by a third between 1989 and 2005. (8) Furthermore, a Spanish study found that even in young men, sperm concentration was falling by an average of two percent a year. (9)

An effect of low sperm count is to reduce the chances of conception in human reproduction, thereby increasing infertility rates across the affected population. Consequently, medical treatment such as Assisted Reproductive Technology (ART) may be sought. Clearly, though, not all ART results from male sperm deficiency. Women in Europe similarly face risks of infertility due to common female reproductive problems. For example endometriosis which increases the risks of infertility may be rising in incidence and appearing in younger women. (5)

An estimated one in six couples seeks help in conceiving a child. (10) The demand worldwide in 2010 was 48.5 million couples seeking treatment. (10) In the UK, one in 50 babies (2%) is born each year as a result of IVF. (11) In Belgium, Slovenia, Denmark, Netherlands and Sweden more than 3% of all babies born are conceived by ART. (10) Another study shows more than one in 25 children (4.2%) being born following ART treatment during 2002. (12)

The rate at which couples are seeking medical assistance due to infertility is increasing at more than 10% per year



The demand for treatment in Europe – as expressed in treatment cycles performed in European countries – has increased by 59% in the five years from 1997 to 2002 (from 204,000 to 324,000 cycles). (13) By 2009, the number of treatment cycles had increased to just over 537,000. (14) Recent reviews of trends in infertility predict that rates will continue to rise. (15, 16)

The 11,000 assisted pregnancies/births taking place in Denmark during 2010 cost more than €40 million. (17) A number of studies have developed a cost of ART per live birth resulting from this treatment, the costs comprising medical treatment costs only. For example in Denmark this is €11,310 (18) and in the Netherlands €51,822 in 2010. (19) Furthermore, ART typically costs up to 0.25% of public health service budgets. (14)

Table 2
Costs and trends in human infertility

Endocrine- related disease or condition	Incidence/ prevalence trends	Cost of illness
Human fertility problems – sperm quality	Sperm quality has declined by 50% over the past 50 years	No cost data available
Human infertility inability to produce a live birth	An estimated one in six couples seeks help in conceiving a child Demand for ART is growing by 1-2% a year in Europe	Total annual ART cycle cost in EU28: €2.4 billion - €3.1 billion

Congenital malformations of male sex organs

What the Berlaymont Declaration says:



Congenital malformations, such as hypospadias (birth defect of the penis) and cryptorchidism (non-descending testes), are increasing or levelling off at unfavourably high levels.

Ten years ago, cases of undescended testicles (or cryptorchidism) were said to affect 2-4% of new-born boys. More recent studies suggest rates are now much higher with estimates in the UK at 6% and in Denmark at 9%. (20) These disorders may require early surgery of affected infants. What is certain is that this condition increases the risks of infertility and testis cancer later in life. (21)

The phenomenon of increasing incidence of four conditions: cryptorchidism (undescended testes), hypospadias (congenital malformations in baby boys), testis cancer, and failure of spermatogenesis (infertility) has been labelled “testicular dysgenesis syndrome” (TDS). (22)

Calculated on the basis of medical treatment costs, orchiopexy to correct undescended testicles is estimated to cost €5,715 – 8,415 per case in the US in 2009. (22)

Table 3
Costs and trends in congenital malformations of male sex organs

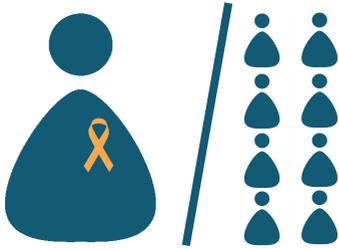
Endocrine- related disease or condition	Incidence/ prevalence trends	Cost of illness
Cryptorchidism and Hypospadias	As many as one in 15 boys are born with cryptorchidism (22) Annual cases of cryptorchidism have doubled in 10 years	Cost: €0.9 – €1.5 billion per annum in EU28, assuming 6% rate of incidence*

*Since this condition either corrects itself or is often treated in the first year of life, incidence is assumed to equate to prevalence. This incidence rate is further adjusted to 3% to take account of the fact that by 3 months of age, the incidence is usually more than halved due to spontaneous descent of the originally cryptorchid testes (21).

Cancers in women and in men

WOMEN

Breast cancer



One in eight women in Europe will develop breast cancer during her lifetime

What the Berlaymont Declaration says:



There is a dramatic rise in incidence of breast cancer in Eastern and Southern European EU Member States. In northern and western European countries, where breast cancer is more prevalent, incidences increase more slowly or are levelling off at rates much higher than 30 years ago.

Breast cancer is the most common cancer in women. (23) Over the past 30 years, breast cancer has increased dramatically throughout Europe. (3) In the UK, female breast cancer incidence increased from 83 per 100,000 women to 156 per 100,000 women during this period. Rates more than doubled between 1980 and 2010 in Bulgaria, Croatia, Finland, Latvia, Lithuania and Poland. (24) By 2010, the lifetime risk for women in the UK of developing breast cancer was one in eight. (25) We note also that breast cancer does occur in the male population, though incidence rates are not currently quantified across Europe on a reliable basis.

A recent Europe-wide study of cancer published in the Lancet estimated the total economic cost of breast cancer to be €16 billion in 2009, the healthcare component amounting to €6.4 billion (productivity losses due to mortality equalling €3.5 billion, cost of informal care being €3.4 billion and productivity losses due to morbidity equating to €1.9 billion). (27) In the UK the total cost is €1.7 billion, including a healthcare component of €0.7 billion. (27)

Other female cancers

Similarly, endometrial cancer incidence rates have risen over the last 30 years, specifically for the estrogen-dependent type. (3) The incidence of thyroid cancer has significantly increased in most industrialised countries over the last 30 years. In Europe, rates increased by between 5.3% (Switzerland) and 155.6% (France) with an average increase of 7% across Europe between 1980 and 2010. (3)

Table 4
Costs and trends in cancers in women

Endocrine- related disease or condition	Incidence/ prevalence trends	Cost of illness
Breast Cancer	1 in 8 women in Europe will develop this condition during her lifetime (25) 90 per 100,000 – EU28 (23)	Total economic cost in EU28: €16 billion
Endometrial cancer estrogen-dependent type	Incidence rates have increased, specifically for estrogen-dependent type	No cost data available
Thyroid Cancer	Incidence increasing at 7% per year in Europe (25) Particularly high and increasing burden in women, children and adolescents (3)	No cost data available

MEN

Prostate cancer



Prostate cancer represents one in four of all cancers diagnosed in men

What the Berlaymont Declaration says:



All EU countries are experiencing strong rises in prostate cancer, with the exception of high prevalence countries, such as The Netherlands and Austria.

Prostate cancer is the most common cancer in men in the EU representing 25% of all male new cancer cases diagnosed. (26)

All European countries (except those with high incidence already) have seen dramatically increasing incidence trends in recent years. Although the trend may be partly explained by improved diagnostic methods, environmental factors such as EDC exposure are also thought likely to be determinants. The highest rates occur in Finland, Sweden and Austria (114, 112 and 106 cases per 100,000, respectively), while Poland, Croatia, Slovenia, Malta and Denmark have comparatively low incidence rates (24, 35, 37, 46 and 50 cases per 100,000, respectively).

Cancer Research UK states that the incidence of prostate cancer in the UK has trebled in 25 years and that this trend is expected to continue. Lifetime risk of prostate cancer is projected to rise from 5% (1 in 20) to just over 14% (1 in 7) in 2015. This means that boys born in the UK in 2015 will have almost three times the risk of being diagnosed with prostate cancer at some point during their lives than those born in 1990. (28)

The European Society of Medical Oncology (ESMO) has estimated the total costs of prostate cancer in Europe to be €9 billion in 2009, with health care costs amounting to €5.8 billion. (27) Total UK costs equate to £0.8 billion, comprising of healthcare costs of £0.4 billion, productivity costs of £0.2 billion and costs of informal care of £0.2 billion.

Testicular cancer



Cancer of the testes is now the most common cancer of young men, peaking at 25-30 years.

What the Berlaymont Declaration says:



All EU countries are experiencing strong rises in prostate cancer... Similar trends exist for other hormonal cancers, including those of the testes....

Cancer of the testes is now the most common cancer of young men, peaking at 25-30 years. This trend in a cancer among the young has prompted interest because it is unusual - most cancers affect older people. The emergence of this cancer has been rapid over the past 60 years, with incidence doubling over the past 25 years in many western countries. Almost 1% of men in Denmark can now expect to be diagnosed with this cancer during their lifetime. (20)

Testicular cancer, low sperm counts and genital birth defects share common risk factors of fetal origin and are known as "testicular dysgenesis syndrome" (TDS), as referred to above. (20)

No studies have been undertaken to identify the costs associated with testicular cancers.

Table 5
Costs and trends in cancers in men

Endocrine-related disease or condition	Incidence/ prevalence trends	Cost of illness
Prostate cancer	<p>1 in 7 men in UK will develop this condition during his lifetime (29)</p> <p>61 per 100,000 incidence in EU28 (age standardised rates) (23)</p> <p>Boys born in UK in 2015 face a three-fold increase in risk compared with those born in 1990 (29)</p>	Total cost in EU28: € 9.04 billion
Thyroid Cancer	2.5 per 100,000 incidence in EU28 (age standardised rates) (23)	No cost data available
Testicular Cancer	<p>5 per 100,000 incidence in EU28 (age standardised rates) (23)</p> <p>Incidence has doubled over the past 25 years</p>	No cost data available

Neurological disorders affecting child brain development and behaviour

What the Berlaymont Declaration says:



Neuro-behavioural disorders and thyroid disease and disorders affecting brain development represent a high and increasing paediatric disease burden in countries where these disease trends have been followed.

Much of the impact of EDCs on brain development is a downward trend in children's IQ, which is not normally measured. (30) We therefore focus on autism and Attention Deficit Hyperactivity Disorder (ADHD) since these are conditions that are diagnosed and reported.

AUTISM SPECTRUM DISORDERS (ASD)



The prevalence of autistic disorders is currently around one in 500

Incidence & Costs

A number of recent studies show an increase in the incidence and prevalence of autism over the last 50 years. For example, a review of studies from a variety of countries concluded that the prevalence of autistic disorders has increased, and is currently around 20 per 10,000 population. (31) The increases in incidence in these and other studies is explained in part by the inclusion of milder cases or the reduction in the age of diagnosis over this time period. (32) However, other factors such as EDCs are not precluded. (33)

WHO (2013) estimate ASD to account for 0.3% of the global burden of disease. (34)

A small number of studies have estimated the economic costs associated with ASD. Most of these studies are from the US. One found that the average cost of ASD per child is €12,445, of which health care costs constitute 20% and education costs constitute 50%. (35) A study undertaken in the UK estimated costs of ASD to both children and adults. It distinguished between cases with and without intellectual disability. The study found that for someone with autism without intellectual disability the undiscounted lifetime cost was €3.5 million. The undiscounted lifetime cost for someone with autism who was also intellectually disabled was 50% higher at €5.2 million. The aggregate national cost of supporting children with ASD was €3.1 billion, of which 60% was comprised of educational costs. Aggregate national cost for adults excluding benefit payments was €28.4 billion. For adults with intellectual disability, approximately 50% of the costs were associated with accommodation for which the main cost component for those without disability was lost productivity, of circa 60%. (36)

ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD)

Attention Deficit Hyperactivity Disorder (ADHD) is now the most common neuro-developmental disorder in children in Europe. (36) One in twenty of school-aged children in England and Wales are currently affected by some form of ADHD. (37) The worldwide prevalence of ADHD is estimated to be 5.3% (4), with a rate of 11% (equivalent to 6.4M children) in the USA. (38)

Costs associated with ADHD in Europe are currently significant and expected to rise. A study published in 2007 suggested that a projected 10-fold increase in the prevalence of this condition over the 10-year period to 2012 would drive overall annual costs of treating ADHD to €311 million in Germany and to €91 million in the UK (39), (40). It is acknowledged that increasing prevalence is likely to be, in part, due to better diagnosis. These European cost estimates only include direct treatment; US evidence suggests that these costs comprise 5% - 20% of the total costs. Thus, in the US, total costs per person (children) equate to €10,650. (41) These costs include medication, educational facilities and formal and informal care by professional providers and family.

The number of prescriptions for one common medication for this condition (methylphenidate, trade name Ritalin) increased more than 55 times in 10 years to 2003 in the UK. Educational costs for children with ADHD are considerably higher than for other children. (41) Costs often endure beyond childhood because children do not always grow out of ADHD. Up to 65% of adolescents with this condition will continue to present with the disorder as adults. (41)

Table 6
Costs and trends in neurological disorders affecting children

Endocrine- related disease or condition	Incidence/ prevalence trends	Cost of illness
Autism	Studies in several countries show a population rate of one in 500 (31, 32)	Total annual cost in EU28: €226 billion (36)
Attention Deficit Hyperactivity Disorder (ADHD)	In the UK, 3.62% of boys and 0.85% of girls aged 4-15 are affected Incidence rates in EU countries range from 2-10% (42)	Total cost in EU28: €0.72 billion (treatment costs only)

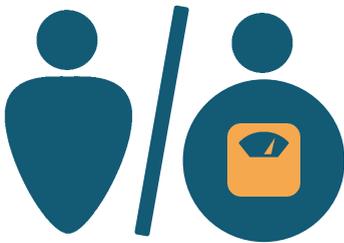
Obesity and diabetes

What the Berlaymont Declaration says:



The prevalence of obesity and its co-morbidity factors, type 2 diabetes and metabolic syndrome have increased dramatically in almost all EU Member States.

OBESITY



Over half the adult population in the EU is overweight or obese

The rate of obesity (defined as a “Body Mass Index” or BMI of 30 or above) has more than doubled over the past 20 years. According to World Health Organization statistics, over 50% of men and women are overweight, and 20% men and 23% women are obese. (43)

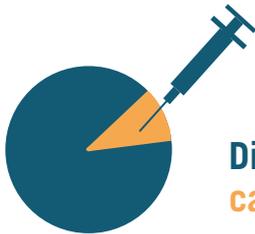
As many as 200 million adults may be overweight or obese in the EU – that is, over half the adult population. (44) Almost one-quarter (24%) of children aged 6-9 years are overweight or obese across Europe, albeit with regional variations. (45)

Total healthcare costs of overweightness and obesity to the UK National Health Service are currently estimated to be €6.1 billion per annum, whilst the European Commission estimated that obesity costs in the EU represent 7% of its total health care spending in 2006. (44) This equates to around €81 billion per year in 2012. (43) These estimates are in broad agreement with the World Health Organization who estimated that obesity accounts for 2-8% of health care spending in the 53 countries of the European region. (43)

Obesity also causes a range of very serious physical and mental health problems, ranging from diabetes to cancers, heart diseases, infertility to psychological disorders. (43) Because obesity is associated with higher risks of chronic illnesses,

it also adds significantly to health care costs indirectly. (45) Related to this, there is potential overlap between the costs of obesity as presented above, and those for diabetes presented below since diabetes type 2 may result from obesity. However, we do not know the extent of this potential overlap and so assume in this calculation that the two costs are separable and additive.

DIABETES



Diabetes absorbs up to 10% of health care budgets in some EU countries

Diabetes is one of the most common non-communicable diseases in Europe. The vast majority of cases are Type 2. Current prevalence of diabetes in adults aged 20-79 years is about 6% across the EU and ranges from close to 5% in the UK, 6% in France, Greece, Italy and Spain to over 7.5% in Poland and Portugal, and around 9% in Germany and Cyprus. (46) Prevalence is predicted to increase by 17% by 2030 across all age groups in Europe. (47) The burden on health care systems is currently equivalent to more than 10% of national healthcare expenditure and is expected to rise. (47) This figure hides national variations: the burden ranges from 15% of the health care budget in the Czech Republic, 11% in Lithuania and Finland, 6% in Italy and Spain, 5% in France and 3% in Netherlands. (48)

A study by the London School of Economics (49) calculated the direct cost burden of people with diabetes across five EU countries to be €90 billion. This figure includes “the cost of complications or medical conditions some of which may not necessarily be caused by diabetes, but can be exacerbated by it.” Indirect costs, (absenteeism, early retirement, social benefits), for the five countries - Germany, UK, Spain, France and Italy – comprised a further €98.4 billion in 2010. The study also showed that health care expenditures on diabetes in France, Germany, Italy, Spain and UK increased rapidly between 2000 and 2008. The greatest spending growth on diabetes per capita in the eight-year period was in Spain (85%), followed by Italy (43%), France (41%), UK (39%) and Germany (22%).

Table 7
Costs and trends in overweightness and obesity, and diabetes

Endocrine-related disease or condition	Incidence/ prevalence trends	Cost of illness
Obesity	<p>Prevalence of obesity in EU has more than doubled over the past 20 years</p> <p>Over 50% of men and women are overweight, 20% men and 23% women obese</p>	<p>Costs of obesity in EU28: €81 billion</p>
Diabetes	<p>30 million people in EU = 6% of population between ages 20-79 (46)</p> <p>Upward trend: prevalence increasing by approx. 1% every 3 years (47)</p>	<p>Costs of diabetes in EU28: €300 billion</p>

Total cost of health burden from endocrine-related diseases and conditions

The following table summarises annual costs of prevalence for the diseases and conditions outlined above. As noted in the Methodology section above, the estimates differ in their inclusion of cost types. Most significantly, indirect costs such as productivity losses are sometimes, but not always, included. In the table, those estimates marked with an asterisk include

indirect effects. Summed, they give a first indication of the relative economic burdens though given the partial coverage of indirect costs, the total is an under-estimate of the true cost. The main value of this exercise can be seen to be an exploration of the economic cost data which currently exists that might be utilised to generate EDC-related cost estimates in the event of attributable fractions becoming available. The differences in coverage and method in the cost estimates gathered here suggest a need for methodological guidance to inform such future studies and ensure their comparability.

To give context to these figures, total healthcare expenditure in the European Union (EU28) in 2010 represented 9.5% of GDP (OECD Factbook, 2013), or €1,166 billion (Eurostat, 2012). The healthcare bill for chronic disease is €700 billion. (50) These figures do not include indirect health costs.

Table 8
Summary of costs of endocrine-related diseases and conditions

Endocrine- related disease or condition	Total burden in the EU28: (Annual)
Human infertility – assisted reproduction technology	€2.4 - €3.1 billion
Cryptorchidism and Hypospadias	€0.9 – €1.5 billion
Breast Cancer	€16 billion*
Prostate Cancer	€9 billion*
Attention Deficit Hyperactivity Disorder (ADHD)	€0.7 billion
Autism	€226 billion
Overweightness and obesity	€81 billion
Diabetes	€300 billion*
ALL DISEASES ABOVE	€636-638 BILLION

Table 9
Cost estimates of endocrine-related diseases and conditions by country

Country	Cost per person (€)	Total costs (€ Millions)
Austria	1278	10 804
Belgium	1262	14 083
Bulgaria	1244	9 063
Croatia	1223	5 212
Cyprus	1401	1 213
Czech Republic	1272	13 381
Denmark	1259	7 051
Estonia	1389	1 833
Finland	1285	6 972
France	1260	82 634
Germany	1263	101 714
Greece	1269	14 038
Hungary	1273	12 612
Ireland	1257	5 772
Italy	1264	75 452
Latvia	1264	2 558
Lithuania	1281	3 808
Luxembourg	1217	653
Malta	1232	519
Netherlands	1260	21 141

Poland	1262	48 638
Portugal	1275	13 367
Romania	1252	25 070
Slovak Republic	1169	6 327
Slovenia	1240	2 554
Spain	1261	58 914
Sweden	1269	12 125
UK	1262	80 641
TOTAL	1266	638 150

Method to construct Table 8 & 9

Table 9 presents estimates of total costs associated with health effects of interest in the EU28. These are derived from the aggregate cost estimates presented in Table 8 on the basis of population. (51) Thus, the EU28 totals in Table 8 are disaggregated and apportioned according to the population of the country relative to the population of the EU28. In the case of the two health effects where a range of cost values are presented for the EU28 aggregate, we use the mid-point in this range for subsequent disaggregation.

The two most important caveats to be noted are: a) that those health effects marked with asterisks (*) include both direct and indirect costs; all others include direct costs only, and b) the country-disaggregated costs do not reflect differences in either prevalence or unit costs. As a priority, future work should refine these estimates by addressing these limitations.

Conclusion

This report shows that chronic endocrine-related diseases represent an enormous cost for both Europeans and health care systems in the EU. We conclude that: If exposure to EDCs accounts for just a small part of the incidence of endocrine-related chronic diseases and conditions, then stronger controls on endocrine disrupting chemicals could generate better health and significant financial savings each year for health care services and labour productivity in the EU.

Furthermore, if no action is taken, the magnitude of these EDC-related costs is likely to accelerate over time assuming exposure to EDCs continue at current levels or rise, and latent effects become manifest. Moreover, latent effects may continue to appear in the future as EDCs appear to have the potential to cause epigenetic effects, i.e. changes in the genetic programming that manifest in the next and subsequent generations. Hence, the possible financial savings from reductions of exposure have the potential to grow as a result of action that is taken now.

Legislative changes in Europe aimed at protecting health have been shown to deliver health cost savings in the past. For example, thanks to legislative and educational changes related to smoking and to the prevention of passive smoking, tobacco smoking is falling in Europe and the incidence of lung cancer is also declining or stagnant in some European countries. Strong political and regulatory action by the European Commission and by individual Member States could help slow - or possibly even stop - the current upward trend in endocrine-related chronic disease. Better family health, a healthier workforce, and reduced health care budgets would be the benefits.

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