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Peer reviewed by two members of Breast Cancer UK independent Science Panel

1. Summary

Bisphenols are a group of endocrine disrupting chemicals used mainly in the production of polycarbonate plastics, epoxy resins and increasingly, flame retardants. Low levels of bisphenols are widespread in the environment and in human tissues and body fluids, including breast milk. Bisphenols have been linked to an increased risk of developing breast cancer; this is thought to be associated with their ability to mimic the natural hormone oestradiol. Animal and in vitro (breast cell culture) studies have shown bisphenol A (BPA) can increase breast cancer growth and development and potentially contribute to breast cancer onset. BPA is now restricted for many uses, resulting in its replacement with other, structurally similar bisphenols. These bisphenol substitutes are currently unregulated. Studies suggest they have similar properties to BPA and constitute “regrettable substitution”. Bisphenols may also have adverse effects on babies in the womb, which could potentially lead to breast cancer during adulthood. This should be investigated further as a matter of urgency.

2. Introduction

Female breast cancer is the most common cancer worldwide (1). Around, 55,500 breast cancer cases in females and 370 in males are diagnosed every year in the UK (2). A person’s risk of developing breast cancer depends on many factors for example age, family history (including evidence of the BRCA1/2 mutations), diet, lifestyle and the environment, including exposure to harmful chemicals (3). The majority of breast cancers are hormonally driven, mainly through natural oestrogens binding to oestrogen receptors (ERs) within breast cells, which results in enhanced growth of oestrogen receptor positive (ER+) breast tumours.

Endocrine disrupting chemicals (EDCs) are predominantly man-made chemicals, or mixtures of chemicals, that interfere with any aspect of hormone action (4). EDCs are frequently identified as environmental contaminants, meaning they are released into the environment, often unintentionally. Many EDCs have the ability to mimic the actions of specific hormones in the body. Those that mimic the actions of the natural hormone oestrogen are of particular concern regarding breast cancer risk.

Bisphenol compounds are probably the most studied class of EDCs in relation to breast cancer. They can mimic the actions of oestrogen, which is part of the tightly controlled endocrine system.

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Lifetime exposure to high levels of oestrogen increases breast cancer risk and exposure to compounds that mimic oestrogen can also increase risk (5, 6).

Bisphenols are used ubiquitously to form polycarbonate plastics used in the packaging of food, drink and toiletries, and epoxy resins which are used as can linings, as well as in various coatings and adhesives (7). Certain halogenated bisphenols (which contain a halogen element such as bromine or chlorine) such as tetrabromobisphenol A [TBBPA] are commonly used as flame retardants, for example on furniture and clothing (8).

Bisphenols are known to leach into consumer products and the environment in general, leading to unintentional exposures (9). Flame retardants can be absorbed through the skin from cloths and furniture (10). Evidence suggests that a chronic, low-level exposure to environmental chemicals, including bisphenols, could influence breast cancer risk (11).

In this brief we will evaluate recent scientific studies investigating how the most studied bisphenol compound, bisphenol A (BPA) may contribute to breast cancer development. We will also explore bisphenols that are increasingly being used to replace BPA (known as BPA substitutes) and consider why we should be concerned about their continued usage in everyday products. We also discuss why the mechanistic actions of bisphenols in the body are still incompletely understood.

3. Bisphenol A (BPA)

Arguably, the most commonly known EDC is BPA. This compound is ubiquitously used worldwide with demand continuing to rise (12). The UK consumption of BPA is also predicted to steadily increase year on year (13). BPA is used in the production of many materials that are used to manufacture numerous consumer items (7, 14) as shown in Table 1.

Table 1: Uses of bisphenol A (13)

BPA uses and products	% Total BPA use
Polycarbonate Plastic - Construction materials - Household electronics (DVDs/TVs/mobile phones) - Personal protective equipment (protective eyewear/gloves) - Plastic food containers (Tupperware) - Plastic bottles (including some reusable ones) - Sports equipment (racquets/helmets/goggles)	75%
Epoxy resins - Can linings - Coatings (industrial/nonslip) - Water pipes - Adhesives (e.g., glue) - Electronics (circuit boards)	17%
Additive to other materials - Polyvinyl chloride (PVC; used in food packaging film) - Thermal paper (used for till receipts)*	17%
Other	<8%

*In 2020, the EU and UK restricted the amount of BPA that could be used in thermal paper to less than 0.02% (total weight) (30).

BPA was first identified as an artificial oestrogen in 1936 (15), but was never used medically for this purpose. Its uses in commercial products began in the late 1940/ early 1950s (16).

BPA has a similar structure to diethylstilboesterol (DES, Figure 1), another synthetic oestrogen formerly prescribed to pregnant women for treating hormone imbalances and preventing miscarriage (17).

Children born to these women were subsequently found to have a higher incidence of rare vaginal cancers (18) and breast cancer (17, 19). DES is now classed as a group I carcinogen by the International Association for Research on Cancer (IARC) (20) meaning 'there is enough evidence to conclude it can cause cancer in humans' (21).

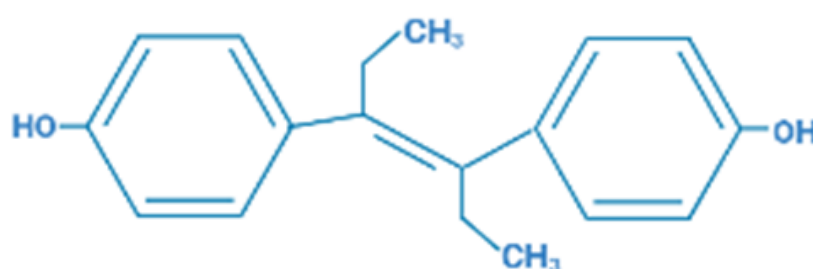
Phthalates can also be found in polyethylene terephthalate (PET) plastic bottles. PET plastic does not require plasticisers, but these can enter the plastic due to cross-contamination during plastic production and recycling [30,31]. Migration of phthalates from the bottle into the liquid may result in drinks containing high levels of phthalates, especially if they are acidic liquids (e.g., soft drinks, vinegar and alcohol) [28,31,32].

3.1 Exposure to BPA

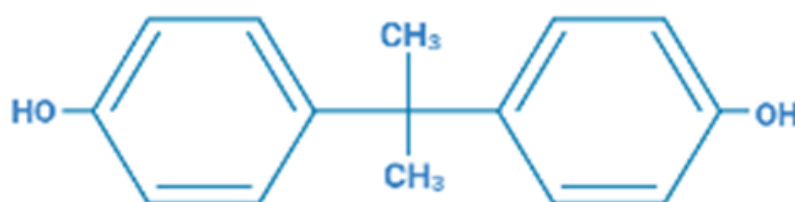
The ubiquitous use of BPA in everyday items provides a means for widespread human exposure. BPA exists as a single unit known as a monomer (Figure 2).

To produce consumer products, BPA monomers need to be linked together to form polymers, these can contain several thousand monomer units.

Diethylstilboesterol (DES)



Bisphenol A (BPA)



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Figure 1: Chemical structures of Diethylstilboesterol (DES) and Bisphenol A (BPA)

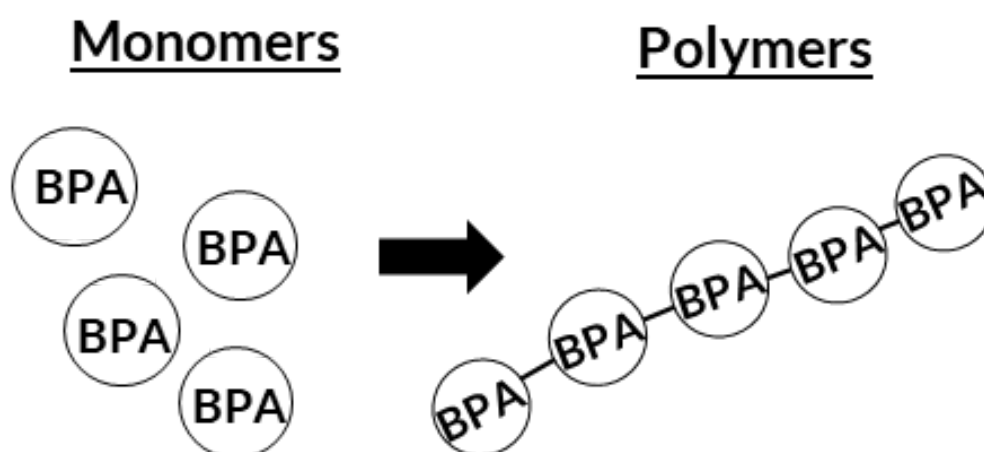


Figure 2: BPA polymer formation. Individual BPA monomers are chemically bonded together to form polymers which form the basis of many plastics and resins used in commercial products (114)

Humans are exposed to BPA in its monomer form, meaning that the bonds linking the units within polymers are broken (due to processes such as excessive heating- see next paragraph). BPA can then migrate into the environment, food, drink or directly onto skin, leading to unintentional exposures. This is known as BPA leaching and has been well documented (22).

Dietary exposure primarily occurs through leaching of BPA into food and drink from packaging, and food/body care contact materials. This has been identified as the primary exposure route in humans (9). BPA leaching into food and drink may be accelerated by other contributing factors including high temperature, degree of acidity (pH) and extended contact time; all of which weakens the individual bonds between BPA units within polymers, promoting their release (23). Indeed, numerous studies have identified higher levels of BPA migration from polycarbonate food packaging/containers (e.g., Tupperware)

in response to elevated temperatures (24–26). Moreover, BPA is the main component of epoxy resins, used to line the inside of cans for both food and drink. The sterilisation process used to prolong the life of canned foods involves heating to high temperatures which can also increase BPA migration into food (27–29).

BPA was until recently used as a developer in thermal paper for till receipts (see Table 1 and Footnote 1) (30). Here it was present in its unpolymerized (monomer) form, making migration upon contact with skin much more likely (31, 32). Dermal transfer was identified as the second most common source of BPA exposure after dietary routes (22, 32).

Less is known about atmospheric BPA, but it can represent an additional exposure route through inhalation. BPA has been detected in indoor air as it has a particular affinity to dust particles (33). Furthermore, the release of BPA into the atmosphere can occur through incineration of BPA-containing

household plastic/ electrical waste (34). Studies have shown that airborne BPA levels are higher in developing countries in comparison to developed countries. This has been attributed to waste disposal methods (e.g., open burning) and less advanced recycling processes (35, 36).

3.2. BPA in the body

Biomonitoring studies have shown BPA to be universally present in the general population (37). BPA is present in many bodily fluids including human urine, serum, plasma, sweat, amniotic fluid (liquid that surrounds the unborn baby during pregnancy), foetal cord serum and breast milk (38). Furthermore, BPA has also been identified in human tissues including liver, brain, fat and breast tissues (39, 40). Worryingly, the placenta can also facilitate BPA transfer into foetal tissues (38, 41–43).

One way BPA disrupts the endocrine system, which tightly controls the balance of hormones in the body, is through binding to oestrogen receptors (ERs, mechanism described in Figure 3) (4, 44, 45). Briefly, after BPA or oestrogen binds to an ER, this complex must bind to another before it can migrate to the nucleus, bind to DNA and alter the expression of certain genes. Despite BPA having a lower affinity (meaning it binds less strongly to ERs) it can still result in activity normally associated with the natural hormone and this disruption can lead to adverse effects (8, 38, 39).

BPA also affects oestrogenic signalling independent of the effects associated with ER binding. This includes acting on non-genomic ERs; that is, BPA does not bind to the ERs present inside the cell as illustrated in Figure 3 but instead binds to receptors on the outer cell surface. This cell surface BPA-receptor binding triggers a molecular signalling cascade of events within the cell, which can lead to enhanced cell growth just like genomic ER binding (46).

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Reporter gene assays (which can assess whether EDCs promote a response upon binding to specific receptors) have also demonstrated BPA can bind to both the androgen (male hormone) (47) and thyroid hormone (48) receptors. Both are thought to act “antagonistically”, meaning they can block the natural hormones from binding to androgen or thyroid receptors and producing a response. This disrupts the delicate signalling balance that normally exists in the body, which for thyroid receptors can lead to altered metabolism including imbalance in energy levels and for androgen receptors to adverse effects on the male reproductive system (49).

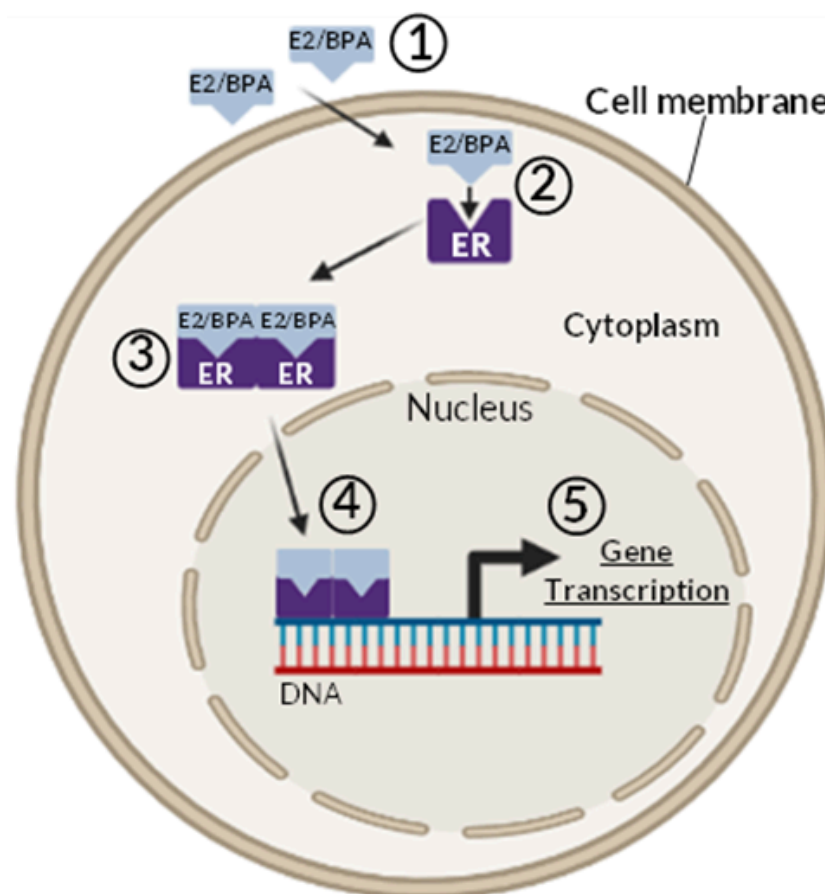


Figure 3: Mechanism of oestrogen/BPA action on oestrogen receptors.

Oestradiol (a form of oestrogen, abbreviated E2) and BPA cross cell membranes (1) and bind to oestrogen receptors (ERs) (2). This complex then binds to another in a process known as dimerization (3). Together, these receptors travel to the nucleus and bind specific DNA sequences (4) to alter gene expression (5). This can result in enhanced cell division (increased number of cells), migration (cells move from the primary site), survival (cells escape destruction); all of which can fuel breast cancer progression.

BPA can also cause epigenetic effects. Epigenetics refers to molecular structures and mechanisms associated with DNA, which control the function (expression) of genes without altering the sequence of the underlying DNA. Thus, alterations in epigenetic molecular structures can lead to dramatic changes in gene expression. Epigenetic-mediated changes in gene function caused by exposure to environmental pollutants have now been linked with a range of illnesses including cancer (50). A key element of epigenetics is DNA methylat-

-ion. This is where methyl (CH₃) groups are attached to certain base units of DNA, particularly regions controlling gene function (51). This can have significant implications for the way in which genes are expressed to produce important proteins in the body. Studies have revealed BPA can induce DNA methylation changes in both non-cancerous (52) and ER positive breast cancer cells; with the latter potentially contributing to the increased proliferation seen in these cells (53).

3.3 BPA and breast cancer

Continuous exposure to high levels of circulating oestrogens is considered an important breast cancer risk factor (36), particularly in post-menopausal women (37–39). This is because oestrogen can stimulate cell division through controlling specific genes within normal breast cells. This increases the chances of mutation (alterations in the DNA sequence) which could promote breast cancer onset.

Numerous in vitro (using cell culture) and animal studies[†] have shown that BPA can accelerate the progression of already established breast cancers through oestrogen-related mechanisms (Figure 2) including increasing the growth and invasion capabilities of tumour cells (54–58). This not only increases tumour size but also the possibility of metastasis (the development of secondary cancers away from the primary site). Metastasizing tumour cells involves them travelling through the primary cancerous tissue and into the blood by a process known as migration. Migration is also important for breast cancer development since tumour cells eventually breach the membrane of enclosed normal breast structures and invade the surrounding tissue (shown in Figure 4).

Interestingly, increased tumour cell migration does not just occur in ER positive breast cancer cells; recent studies have also seen this effect in hormone receptor negative breast cancer

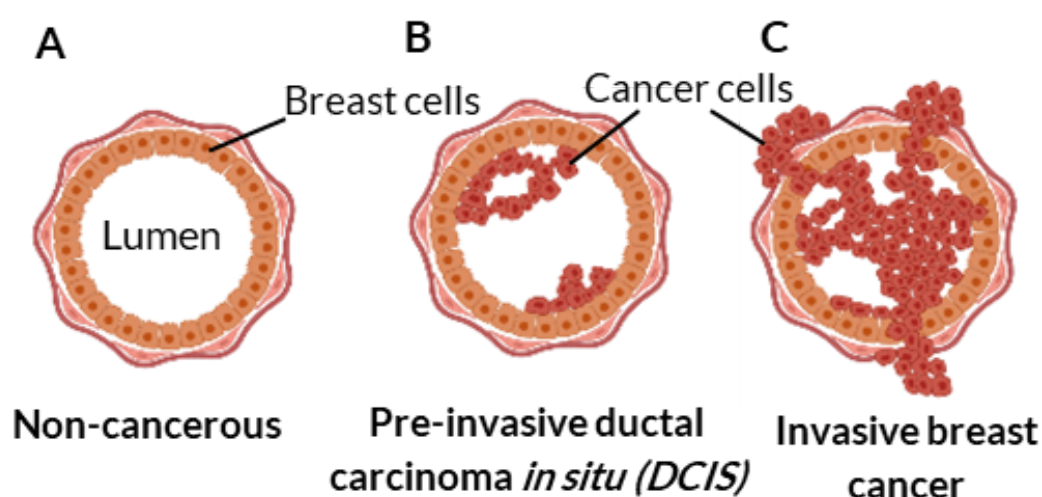
cells (59, 60). This indicates BPA may act through mechanisms other than oestrogen signalling to invoke this process.

Evidence is also emerging that BPA may contribute to breast cancer development. In cell culture studies using breast epithelial cells performed in 2D (where cells grow in a single layer attached to the surface of the culture vessel, dish or flask), some scientists have shown BPA can promote cell division of normal breast cells (61, 62), although others have not (63, 64). However, exposing these non-cancerous cells to BPA for longer time periods promotes characteristics reminiscent of a cancerous breast (61, 64).

In 3D studies, breast epithelial cells are maintained in an environment that permits them to form “spheroids” (cells attach to each other and self-assemble to grow in sphere-like formations). Growing cells this way is a much better representation of human breast tissue 2D systems. BPA can disrupt the organisation of normal breast structures when grown in 3D and promote cell invasion into the lumen (the hollow structures found in the normal breast,) (63, 65, 66). These alterations are reminiscent of ductal carcinoma in situ (DCIS); an early form of breast cancer usually seen before breast cancer becomes invasive (Figure 4B-C).

Importantly, many of these results were seen when exposing cells to a low concentration of BPA, which is physiolo-

[†]Breast Cancer UK does not support research projects which involve animal experiments or materials derived from animal experiments.



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Figure 2: Schematic depicting the stages of breast cancer development. Non-cancerous (healthy) breast structures consist of a hollow space known as the lumen which is surrounded by breast cells (A). Invasion of breast cells into the lumen is characteristic of pre-invasive breast cancer known as ductal carcinoma in situ (DCIS, B). DCIS progresses to invasive breast cancer once cells breach the basement membrane and invade the surrounding areas of the breast (C).

-gically relevant (concentrations used were similar to levels detected in the human body). BPA has also been associated with increased breast density (which itself is an important breast cancer risk factor) (67–69) and reduced response to certain chemotherapy drugs (70–73). Although much less studied, BPA can affect other cells of the breast including fibroblasts, adipocytes (fat cells) and immune cells, all of which can create a more favourable environment for breast epithelial cells to become cancerous (74).

3.4 BPA regulation

The early reports of BPA's potential adverse effects resulted in a tolerable daily intake (TDI, the daily amount of a chemical that can be consumed without causing any health risks) being established in 2006 by the European Food Safety Authority (EFSA), set at 50

µg/kg of body weight/day (75). The first restrictions of BPA use came in 2011 when it was banned from being used in the manufacture of infant feeding bottles (76). BPA was then strictly limited in the production of children's toys from 2014 (77).

In 2015, recognition of adverse effects caused by BPA below the established tolerable level led the EFSA to set a substantially lower tolerable daily intake of 4µg/kg of body weight/day (9). More recently, at the end of 2021, the EFSA published a draft opinion to further reduce the tolerable daily intake to 0.04ng/kg of body weight/day (78). This is yet to come into force but represents a 100,000-reduction compared to the level implemented in 2015, reiterating the concerns of scientists that BPA can exert its effects at extremely low concentrations. After BREXIT, the UK

government (with the exception of Northern Ireland) maintained the EU daily tolerable intake at 4µg/kg of body weight/day.

4. Bisphenol substitutes

Given the tighter regulations for BPA mentioned above, manufacturers began to source alternatives to use in their products. Products, for example reusable water bottles, made from BPA alternatives, are often marketed as 'BPA free'. Unfortunately, in most cases, BPA has been replaced with bisphenol substitutes such as bisphenol S, F or AF (BPS, BPF, BPAF respectively). Another example is the recent restriction in 2020 on the amount of BPA permitted in thermal paper used for till receipts, to less than 0.02% total weight (30, 79). Manufacturers simply substituted BPA for the structurally similar BPS (see appendix 1 for structures), as its use is currently unregulated (30).

Most (including BPF, BPS and BPAF) but not all bisphenol substitutes are structural analogues of BPA, meaning their structures are comparable (Appendix 1). The similarities between some substitutes would suggest they may exert the same or similar adverse effects to BPA. Indeed, many of these alternatives have already been detected in human urine (80–82), demonstrating they are able to leach into the environment and lead to unintentional exposures.

Recent evidence has shown that almost all bisphenol substitutes have oestrogenic activity with some even demonstrating elevated activity compar-

-ed to BPA. Thus, these alternatives appear to constitute what is known in the field of toxicology as "regrettable replacement" as they may also potentially increase the risk of breast cancer (83, 84). To date, only one bisphenol substitute, tetramethyl bisphenol F (TMBPF), has been shown not to be oestrogenic in in vitro assays (85). Moreover, both BPF and BPS have been shown to affect androgen activity (83). Androgen receptors are expressed in 70-90% of all breast cancers and likely contribute to its development and subsequent progression (86). Thus, disruption to androgen as well as oestrogen signalling mediated by bisphenols may work together to increase breast cancer risk; however more research is required to confirm this.

4.1 Bisphenol substitutes and breast cancer

Research into bisphenol substitutes has substantially increased over the past 20 years. Laboratory in vitro studies using breast cell culture systems have found many of these substitutes increase tumour cell division (58, 84, 87–89), migration (58, 84), cell cycle progression (58, 89), and DNA alterations (90) including DNA damage (87). Several of these processes are regulated by oestrogen receptors (mechanism shown in Figure 3).

Similar to BPA, initial research into bisphenol substitutes focused on their potential to accelerate fully manifested breast cancers. However, more recent research has shown these substitutes can also adversely affect non-cancerous

breast cells and tissue. In fact, BPS, like BPA, promotes lumen invasion characteristic of DCIS (63), the pre-invasive form of breast cancer (Figure 4B). Furthermore, both BPF and BPS can disrupt normal breast architecture to a higher degree than BPA (66).

5. Bisphenol exposures, obesity and mammographic density

Bisphenols have been associated with obesity, which is a standalone risk factor for breast cancer in post-menopausal women and in men (3). Bisphenol compounds are lipophilic, which means they preferably travel and accumulate in fat tissue. Since the female breast is rich in fat tissue, bisphenols and other EDCs likely also accumulate here (39, 40, 91).

Within cancerous breast tissue, tumour cells are immediately adjacent to fat (92), creating an easily accessible route for bisphenols to adversely affect breast cancer cells and promote carcinogenic (cancerous) characteristics. In the normal breast, multiple bisphenols may accumulate within fat tissue (93), creating a total concentration higher than the tolerable daily intake of BPA. This could result in the promotion of a pre-cancerous environment and therefore may increase the risk of breast cancer.

The levels of oestrogenic EDCs including bisphenols in the body have been associated with mammographic density. Mammographic (or breast) density is a measure of how dense your breasts are, determined by the amounts of non-fat

fibroglandular tissue in relation to fat tissue, using a mammogram scan. A high mammographic density (i.e., having high amounts of fibroglandular tissue compared to fat tissue) is a strong risk factor for breast cancer (94).

Circulating serum (blood) and urinary concentrations of BPA have been identified as having a positive association with mammographic density (95, 96). Hence, BPA may increase breast cancer risk through influencing other established risk factors such as mammographic density. However more research is required to confirm this.

6. Timing of exposure affects breast cancer risk

Timing of exposure to bisphenols is a critical factor to consider when assessing the impact of these chemicals on breast cancer and other health problems. Animal studies[†] are suggestive that critical exposure windows for individuals include in utero (in the womb), during puberty, and finally during pregnancy, as this is when the mammary gland fully matures.

Biomonitoring studies (assessment of individual exposures to chemicals) have detected EDCs, including bisphenols, in the placenta, amniotic fluid and breast milk of pregnant women and nursing mothers (38, 97), which suggests infants are exposed to a variety of chemical pollutants both before and immediately after birth. Several studies have suggested prenatal exposure to chemicals such as BPA could promote metabolic disease such as obesity and diabetes as well as breast cancer onset

during adulthood (69, 98–102).

7. Bisphenol mixtures

The majority of research has focused on the oestrogenic potential of single bisphenols in isolation. However, given that numerous bisphenols and other EDCs are present in low concentrations in the environment, determining how exposure to multiple, low concentrations of these compounds affects human health would be more relevant.

Exposure to EDCs can result in an “additive” response, meaning each chemical’s response can add up to produce an effect where their individual concentration alone would have been insufficient to do so (103). For example, at low concentrations, five parabens (EDCs used as preservatives and commonly found in cosmetic products) in combination have a more measurable effect on the proliferation of breast cancer cells, compared to when these compounds were tested in isolation (104).

Similar effects have been seen for bisphenols in animal studies[†]. BPA, BPF and BPS have demonstrated a higher activation of ERs compared to each bisphenol alone (105). Furthermore, EDC mixtures can elevate both BPA and oestrogen concentrations in the body, demonstrating their ability to interact (106).

The concern for bisphenols and their potential combined effects has resulted in them being adopted as priority substances for the Human Biomonitoring for Europe project (HBM4EU) (107, 108)

This scheme co-ordinates biomonitoring studies across Europe in order to collate and assess data on the actual exposure to multiple chemicals with the overall aim of identifying and implementing measures for reduced exposures and improved human health (109, 110).

8. Bisphenol mixtures with other EDCs

Human exposures are not just isolated to bisphenol compounds, but also include many other EDCs such as parabens (used as preservatives in cosmetic products) and phthalates (used as plasticisers to produce soft plastics). These EDCs can also influence breast cancer progression by affecting hormone action. Thus, exposure to other EDC classes in combination with bisphenols will likely amplify the effects of the latter resulting in a further increased risk of breast cancer (111, 112).

9. The effects of bisphenol exposures are not fully understood

Despite the increase in research related to bisphenols, their mechanisms of action are still not entirely understood. This is due in part to the focus of most studies on commonly known EDCs such as BPA and their well-established actions on hormone receptors including oestrogen and androgen receptors. Less is known about their effects on other receptors located in the nucleus or embedded in cell membranes (11). Even less is known about new and emerging EDCs including some of the bisphenol substitutes (11).

Many experiments (particularly those investigating in utero effects of bisphenols) are performed in animals[†]. Despite the endocrine system being highly conserved (meaning there are limited differences in how this system works between species) across mammals, important variations do exist, including reproductive cycle length, duration of pregnancy and number of offspring (11). Results are therefore not always translated in humans.

Additionally, more studies that are longitudinal (involve repeated observations over a certain time period) or multigenerational (the same observations taken across multiple generations) are required to determine the lifelong risk of exposure to EDCs, as well as pinpointing the mechanisms of bisphenol exposure in the womb that may promote carcinogenesis (the process of healthy cells transforming into cancer cells) during adulthood (11).

10. Links to other diseases

BPA has been linked to many other conditions including diabetes, cardiovascular disease, thyroid disruption, neurodevelopmental and neurological effects (primarily as a result of early life exposures), and hormone-dependant cancers such as prostate cancer in males and ovarian and cervical cancer in females (11). Animal studies[†] have shown BPA to be associated with both male and female fertility problems including decreased sperm (113) and viable oocyte (114) counts respectively. Bisphenol substitutes have also been linked to many of these disorders (101, 115, 116).

11. Bisphenol and aquatic life

Bisphenols have been detected in numerous bodies of water across the globe including rivers, lakes and oceans. The source of these bisphenols is largely through plastic pollution as when these plastics are exposed to high UV radiation or salt content, they degrade and release harmful chemicals into the water (117).

The effects on marine life can be serious. BPA has been detected in numerous aquatic species including fish, amphibians, birds and crustaceans. EDCs including bisphenols can cause reproductive, developmental and behaviour abnormalities in marine life (118). Meanwhile the consumption of microplastics (fragments of plastics less than 5mm in size) which can contain a myriad of harmful chemicals can damage and block the digestive tract (119). The detection of bisphenols in fish and shellfish also identifies a route to enter the food chain and cause unintentional human exposures (120).

12. Regulation of bisphenol substitutes

All bisphenol substitutes are currently unregulated in the UK/EU and US, despite their increased use. However, the UK government has chosen bisphenols in thermal paper as one of their five priorities for the 2022-2023 UK REACH (registration, evaluation, authorisation and restriction of chemicals) work programme (121). This means evidence on the potential adverse

effects of bisphenols will be reviewed and a potential restriction evaluated.

In the EU, the European Chemicals Agency (ECHA) is proposing a group restriction of 34 bisphenols, which they have deemed as very likely to be EDCs and therefore require regulation (122). Group restrictions speed up the process of identifying chemicals that require restrictions, whilst also promoting consistency between different chemical groups.

Germany has also recently proposed to restrict BPA and structurally related bisphenols in all consumer products (123). Meanwhile BPA, BPB and another less known and used bisphenol, 2,2-bis(4'-hydroxyphenyl)-4-methylpentane have been identified as substances of very high concern (SVHC) by the EU and UK REACH (124, 125).

12. Conclusion

Bisphenols have consistently been identified in many human tissues and fluids, demonstrating their ability to leach from everyday products into the environment. Furthermore, studies have consistently demonstrated that low concentrations of bisphenol compounds can accelerate the growth and progression of breast cancer by influencing some of the key cancer hallmarks including cell division, migration and invasion.

Recent research has also demonstrated the potential for bisphenol compounds to contribute to breast cancer development by adversely affecting the structure of normal breast tissue and promoting characteristics traditionally seen before breast cancer becomes invasive. Additionally, animal studies[†] have shown potential for these chemicals to cause adverse effects in utero which could lead to the manifestation of breast cancer during adulthood. Moreover, the impact of these bisphenols being released into the environment is not just a concern for humans, but also wildlife, for which ingestion of these chemicals and plastics can have a devastating impact.

Finally, the effects of bisphenols will, in all likelihood, be exacerbated by other EDCs, which people are exposed to on a daily basis.

Further studies are required to assess the long-term impact of bisphenol compounds on breast cancer risk; in addition to ascertaining the complete mechanistic action of these compounds in the body and how this may contribute to breast cancer development.

While uncertainties remain regarding the safety of bisphenols and other EDCs at tolerable daily intake levels set by regulators, it would seem prudent to avoid exposure to these substances as much as is practical by avoiding, for example, food and drink packaged in cans and plastic containers.

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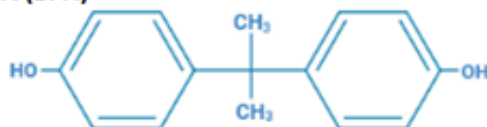
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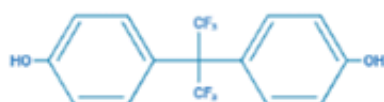
Appendix

Appendix 1: Chemical structures of some commonly used bisphenol compounds

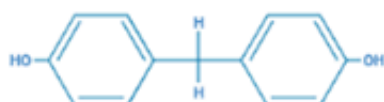
Bisphenol A (BPA)



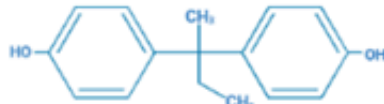
Bisphenol AF (BPAF)



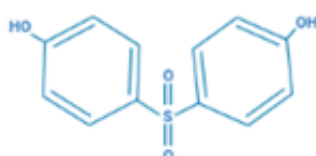
Bisphenol F (BPF)



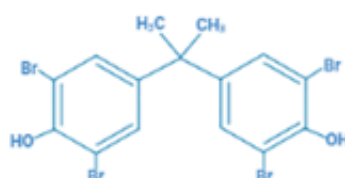
Bisphenol B (BPB)



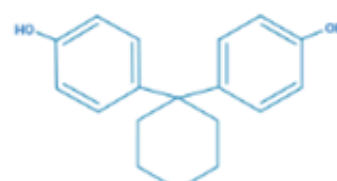
Bisphenol S (BPS)



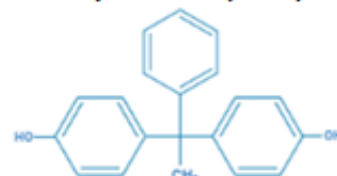
Tetrabromobisphenol A (TBBPA)



Bisphenol Z (BPZ)



Bisphenol AP (BPAP)



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About Breast Cancer UK

Who we are?

Breast Cancer UK aims to prevent breast cancer through scientific research, collaboration, education and policy change. We educate and raise awareness of the risk factors for breast cancer and provide practical information to help people reduce these risks. We campaign to ensure government policies support the prevention of breast cancer. And we fund scientific research that helps to better understand what risk factors contribute to breast cancer, and how to address them. For further information on breast cancer risk factors please visit our website www.breastcanceruk.org.uk

To view this information in a more accessible format or to provide feedback, please contact us.

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We welcome your feedback, if you have any comments or suggestions about this review please contact us at info@breastcanceruk.org.uk or on 0208 1327088.

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