Pesticides, organic food and breast cancer



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

1. Summary

Pesticides are chemicals used in agriculture and residential areas to repel or control certain forms of plant or animal life that are considered to be pests. Many of these chemicals are harmful and may damage the DNA, alter gene expression, induce oxidative stress, or act as Endocrine Disrupting Chemicals (EDCs). Some pesticides have also been classified as potentially promoting cancer by international regulatory bodies. People working with pesticides may be exposed to higher levels, whilst the rest of the population is primarily exposed through the diet or when pesticides are used in residential and private areas. Occupational and biomonitoring studies have shown that exposure to pesticides may increase breast cancer risk, especially for highly toxic pesticides that are no longer authorised but that may still persist in the environment. Very limited evidence suggests that dietary exposure to certain pesticides may increase breast cancer risk; meanwhile, some studies suggest that organic food may reduce risk. Whilst more research is needed on the health benefits of organic food, swapping conventional food with organic produce is an effective way to reduce pesticide exposure. Where this is not possible, fruit and vegetables should be washed with tap water.

2. Introduction

Breast cancer is the second most common cancer worldwide, with an estimated 2.3 million new cases in 2022 [1]. In the UK, around 56,000 women and 400 men are diagnosed with breast cancer each year [2]. A person's risk of developing breast cancer depends on many factors, including age, genetics and lifestyle [3]. Exposure to harmful chemicals may also play a role in breast cancer. Many chemicals are suspected Endocrine Disrupting Chemicals (EDCs) which can interfere with the endocrine (hormone) system in the body. EDCs that interfere with any aspect of

Glossary box:

Biomonitoring: studies that measure chemicals in biological fluids or tissues.

Carcinogen: a chemical, or another substance, that promotes cancer development.

Cocktail effect: when in mixtures, the harmful effects of chemicals may be added together resulting in higher toxicity.

Conventional food: food grown with the use of pesticides.

Epidemiological studies: human studies to assess if exposure to a certain factor is linked to a disease.

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oestrogen function may be linked to breast cancer [4], as oestrogen itself can increase breast cancer risk [5]. In this review, we will focus on chemicals that are used as pesticides, their potential link to breast cancer and whether organic food consumption may help reduce breast cancer risk.

3. Pesticides and their uses

Pesticides are chemicals used to repel or control certain forms of plant or animal life that are considered to be pests. They are divided into classes based on the type of pest, with the three main classes being [6]:

- Insecticides, to kill insects
- Herbicides (or weed killers), to kill weeds
- Fungicides, to kill fungi

Pesticides are used to kill pests and therefore improve crop yield, which is important for food security [7]. However, widespread use the of pesticides contaminates the where environment, they may accumulate and persist, and exposes wildlife and humans to their harmful effects. [7].

Pesticides are also classified based on their chemical structure as organochlorines, organophosphates, carbamates, and pyrethroids [6]. Many organochlorine pesticides are no longer authorised due to their toxicity but may still contaminate the environment years after their use has stopped [8]. A selected list of banned pesticides and their harmful effects can be found in Table 1 [9].

Glossary box (cont.):

Epigenetic changes: heritable changes affecting DNA expression but not the DNA sequence.

Fungicide: a chemical used to control fungi.

Herbicide: a chemical used to control weeds, also known as weed killer.

Insecticide: a chemical used to control insects.

In utero: Latin term for "in the womb".

Maximum Residue Level (MRL): maximum level of pesticide residue legally tolerated in food.

Metabolite: a substance formed from the breakdown of a chemical or substance during chemical processes (metabolism) in the body.

Non-occupational exposure: exposure to a chemical in settings not related to work.

Occupational exposure: exposure to a chemical in work-related settings.

Organic food: food grown without the use of pesticides.

Oxidative stress: imbalance between reactive oxygen species (highly reactive small molecules) and antioxidants that can damage cells.

Pesticide: a chemical used to control any type of pest.

Transcription: the process that copies DNA into RNA, ultimately resulting in the production of proteins.

The most well-known banned pesticide is dichloro-diphenyl-trichloroethane, also known as DDT, an insecticide used during the Second World War to control diseases that are spread by insects (e.g. malaria and typhus) [10]. After the war,



Table 1. Selection of pesticides banned in the UK colour-coded based on their class; Yellow: Insecticide, Blue: Herbicide, Pink: Fungicide. Pesticides are included if they have been evaluated by the International Agency for Research on Cancer (IARC, Appendix 1), have EDC properties, promote mammary tumours and/or DNA damage in laboratory studies. The symbol "-" is used for pesticides not evaluated by IARC, or when specific information is not available from the sources used to create the table (other sources may exist).

Pesticide	Class [9]	IARC [12]	EDC effects [4,9,13,14]	DNA damage [4]	Mammary tumours [14]
Asulam	Carbamate	-	Yes*	-	-
Atrazine	Other	3	Yes	Yes	Yes
Chlordane	Organochlorine	2B	Yes	Yes	Yes
Chlorpyrifos	Organophosphate	-	Yes	Yes	-
DDT	Organochlorine	2A	Yes	Yes	No
Dichlorvos	Organophosphate	2B	Yes	Yes	Yes
Dieldrin	Organochlorine	2A	Yes	Yes	Yes
Endosulfan	Organochlorine	-	Yes	Yes	No
Heptachlor	Organochlorine	2B	Yes	-	-
Hexachlorobenzene	Organochlorine	2B	Yes	-	-
Mancozeb	Carbamate	-	Yes*	Yes	-
Lindane	Organochlorine	1	Yes	-	-
Mirex	Organochlorine	2B	Yes	No	No
Parathion	Organophosphate	2B	Yes	Yes	Yes
Thiophanate-methyl	Carbamate	-	Yes*	-	-
Vinclozolin	Other	-	Yes	-	Yes

^{*}Officially recognised to be an Endocrine Disrupting Chemical by the EU [15].

it was used worldwide in large quantities in agriculture. DDT was banned in the UK in 1984 following the publication of Rachel Carson's 1962 book Silent Spring, which raised awareness of the environmental and health risks of DDT and revolutionised the environmental movement regarding regulation and policy [11]. While the use of DDT is banned in most countries, it is linked to numerous ecological and health effects, including breast cancer (see section 5.3.1).

Around 420 different chemicals are approved for use as pesticides in the UK [16], with a selection of these listed in Table 2. Glyphosate is the most used herbicide across all applications in the UK (see Box 1), whilst other examples of pesticides commonly used in the UK can be found in **bold** in Table 2 [17-23].

Among these, an area of concern is the rise in the use of pesticides classified as PFAS, such as flufenacet and lambdacyhalothrin [24,25]. PFAS are a group of



harmful chemicals also known as "forever chemicals" as they can remain in the environment for long periods (read our <u>PFAS</u> and breast cancer

review) [24]. Their use in agriculture has grown internationally, and in 2022, over 90% of UK-grown strawberries contained traces of PFAS [24,26].

Table 2. Selection of pesticides authorised in the UK colour-coded based on their class; Yellow: Insecticide, Blue: Herbicide, Pink: Fungicide. In bold some of the pesticides commonly used in the UK by farmers, local authorities and other businesses [17–23]. Pesticides are included if they are officially recognised as EDCs in the EU, have EDC effects, promote mammary tumours and/or DNA damage in laboratory studies. The International Agency for Research on Cancer (IARC) classification (Appendix 1) is also reported. The symbol "-" is for pesticides not evaluated by the EU or IARC, or when the information is not available from the sources used here (other sources may exist).

Pesticide	Class [9]	IARC [12]	Officially EDCs in EU [15]	EDC effects [4,13,27]	DNA damage [4]	Mammary tumours [14]
2,4-D	Other	2B	Not ED	Yes	-	Yes
Benthiavalicarb	Carbamate	-	ED**	-	-	-
Buprofezin	Other	-	ED	-	-	-
Clofentezine	Other	-	ED**	-	-	-
Cyprodinil	Other	-	ED (preliminary)	Yes	No	No
Deltamethrin	Pyrethroid	3	Under testing	Yes	-	Yes
Difenoconazole	Other	-	Under testing	Yes	Yes	Yes
Dimethomorph	Other	-	ED**	Yes	-	-
Fenoxaprop-P	Other	-	ED (preliminary)	Yes	-	-
Fludioxonil	Other	-	ED (preliminary)	Yes	-	No
Flufenacet	Other	-	ED (preliminary)	-	-	-
Folpet	Other	-	-	-	Yes	Yes
Glyphosate	Organophosphate	2A	Not ED	Yes	-	Yes
lmazalil	Other	-	-	Yes	-	No
Lambda-cyhalothrin	Pyrethroid	-	-	Yes [28]	-	-
Malathion	Organophosphate	2A	-	Yes	Yes	Yes
МСРА	Other	-	-	Yes	Yes	No
Mepanipyrim	Other	-	ED**	Yes	-	-
Metiram	Carbamate	-	ED**	-	-	-
Metribuzin	Other	-	ED	Yes	-	-
Thiabendazole	Other	-	ED	-	-	-
Triflusulfuron-methyl	Other	-	ED**	-	-	-

^{**}No longer authorised in the EU [27].



4. Exposure to pesticides

People can be exposed to pesticides occupationally through work-related tasks or non-occupationally (Figure 1) [29]. Occupational exposure includes working directly with pesticides (e.g., in agriculture) or being exposed at home when living with someone who works with these chemicals [29]. These people may be exposed to high levels of pesticides, whilst the rest of the population is more likely to be exposed to low levels, potentially for long periods, through the diet in or residential areas [30]. Pesticides can be absorbed through the skin, be ingested accidentally or with food, or be inhaled when they are sprayed [31,32].

4.1 Pesticides in food

Crops can be sprayed with multiple different pesticides several times per

year and may be exposed to complex pesticide mixtures [33]. After harvest, pesticide residues may remain on the food, making diet the main exposure route for the general population [34]. The maximum level of pesticide residue legally tolerated in food is known as the Maximum Residue Level (MRL) and it is set to intentionally leave a large gap between permitted and harmful levels [35].

The presence of pesticide residues in food is not uncommon. A 2023 report found 48% of food samples analysed in the UK contained at least one pesticide residue [36]. Although only about 1% of the samples had levels above the MRL, more than one pesticide residue was found in 33% of the food [36]. Because MRL values are set for individual pesticides, they likely underestimate the

Occupational exposure Non-occupational exposure Non-occupational exposure Residential and the workplace least a structural treatments Non-occupational exposure Non-occupational exposure Residential and the workplace least a structural treatments Non-occupational exposure

Figure 1. Examples of occupational and non-occupational exposure routes to pesticides.



so-called cocktail effect that occurs when multiple pesticides are present together, which may result in a higher overall toxicity [37].

The charity PAN UK periodically analyses which fruits and vegetables sold in the UK are the most likely to contain multiple pesticides. Their latest "Dirty Dozen list" found citrus fruits, strawberries, and grapes among the most likely produce to contain cocktails of residues [38].

4.2 Pesticides in the body

Once in the body, pesticides are mostly broken down and eliminated, but some may accumulate [39,40]. For example, organochlorines can accumulate in fat tissue, including the breast, where they may remain for long periods [40]. A review showed that organochlorines were detected in over 90% of cancerous and non-cancerous breast tissue, with DDE (metabolite of DDT) being the main component [41].

In addition to breast tissue, pesticides have been measured in many body fluids including breast milk, blood, placenta, sweat, and urine [42-46].

5. Pesticides and breast cancer

Some pesticides have been classified as probable (Group 2A) or possible (Group 2B) carcinogens by the International Agency for Research on Cancer (IARC) (Tables 1 and 2) [12], due to evidence suggesting they may promote cancer (Appendix 1).

Whilst only limited number а of pesticides have been evaluated by IARC, many display some more carcinogens characteristics" of [4]. These are 10 different biological mechanisms that contribute to transformation of normal cells into cancer cells. Whilst displaying these characteristics is not sufficient for an official classification from IARC, a

Table 3. Key characteristics of pesticides, observed in cells studies, that may contribute to the transformation of normal cells into cancer cells.

Key characteristic	Definition	Examples	
DNA damage [49]	Pesticides can damage the DNA altering its sequence and leading to DNA mutations, which are key for tumour development.	DDT, difenoconazole, glyphosate, malathion (Tables 1 and 2) [4]	
Oxidative stress [30]	Pesticides may form Reactive Oxygen Species increasing oxidative stress and cell damage, thus contributing to tumour development.	2,4-D, chlorpyrifos, glyphosate, mancozeb [50]	
Epigenetic changes [51]	"on" genes that are supposed to be "off" or vice versa		
Hormone receptor interference [30]	Pesticides can bind to hormone receptors and block or promote their activity (Section 5.1).	Chlordane, DDT, dieldrin, glyphosate [13,52]	



chemical that acts through one or more of these mechanisms may warrant further consideration [47]. The main characteristics displayed by pesticides are reported in Table 3. Through these mechanisms, pesticides may contribute to cell proliferation, which helps tumours to grow and spread [4,48].

5.1 Endocrine disrupting properties

Some pesticides may also act as Endocrine Disrupting Chemicals (EDCs) (Tables 1 and 2) and interfere with sex hormones such as androgens and oestrogens [30], ultimately affecting gene transcription, metabolism and cell proliferation [4].

Cell studies have shown that some pesticides can bind to androgen and oestrogen receptors leading to their activation, whilst others may block the receptors [4,13,14,30,53,54]. They may also interfere with the expression of the hormone receptors or with enzymes that control oestrogen (female sex hormone) levels [4,54–56]. Chemicals that mimic oestrogen or increase its levels might be involved in breast cancer, as high levels of oestrogen or prolonged exposure to it can increase breast cancer risk [4,57].

Pesticides also have antimay androgenic properties meaning that they block the action of androgen (main male hormone). amounts sex Small androgens are also produced in females and these may, according to some cell studies [58,59], inhibit breast cancer cell proliferation. Therefore, pesticides with anti-androgenic properties may play a role in breast cancer [60].

5.2 Mammary tumours in animals

In addition to cell studies suggesting pesticide involvement in breast cancer, some can also promote mammary tumours in animals or alter the development of the mammary gland (Tables 1 and 2) [4,14,61-63].

Whilst there are some limitations (including biological differences) on using results from animal studies to extrapolate if a chemical is carcinogenic to humans, they are often used to help assess the risk in humans [64].

Glyphosate, chlorpyrifos, and hexachlorobenzene have been shown to affect both the male and female rat mammary glands when exposure occurs during certain windows of susceptibility, such as in utero (in the womb) and postnatally (6-8 weeks after birth) [63]. A higher incidence of mammary tumours can occur in these animals as a result of this exposure [63].

5.3 Epidemiological studies

This section covers epidemiological studies (or human studies) investigated the link between pesticide exposure and breast cancer risk in women. Most of these studies have focused on occupational exposure to banned pesticides, whilst limited evidence is available for nonoccupational exposure to authorised pesticides. Biomonitoring studies, where levels of pesticides are measured in participants, and the possible link to breast cancer are also discussed here.



5.3.1 Occupational exposure

Most studies found that occupational exposure (e.g., direct use of pesticides, washing contaminated clothing) to organochlorines and organophosphates may increase breast cancer risk [55]. Examples include malathion, chlordane, dieldrin, and chlorpyrifos [55,65-68]. Occupational exposure to pesticides may also increase the risk of metastasis (spread of the tumour to other parts of the body) [69].

Studies evaluating women who live with someone regularly working with pesticides (e.g., organophosphates, dieldrin and chlorpyrifos) have shown that they may be at an increased risk of developing breast cancer due to indirect exposure [70,71]. No link was found with glyphosate [71]. Whilst exposure in the home may be significant for some individuals, these questionnaire-based studies should be interpreted with caution as they may not accurately reflect the women's exposure, which is not measured directly in the women but only estimated [55].

On the other hand, not all studies confirm a link between occupational exposure to pesticides and breast cancer [66,71,72]. This may partially be due to female agricultural workers smoking less and having higher levels of physical activity than the rest of the female population; both of these factors are known to reduce breast cancer risk [73].

5.3.2 Non-occupational exposure

Despite being the main exposure route to pesticides in the population [74], very

few studies have evaluated exposure through diet. This is due to challenges with the cost of measuring pesticide residues in food, difficulties in assessing mixtures, and imprecise data on how the food was grown [34].

One study found no association between dietary exposure to pesticides and breast cancer [75], whilst a second study found an increased risk in overweight postmenopausal women exposed to chlorpyrifos, imazalil, malathion, and thiabendazole [34].

Living near facilities where pesticides are produced, or fields where they are sprayed, may also increase breast cancer risk [55,76,77].

5.3.3 Biomonitoring

epidemiological Most studies on pesticides rely heavily on questionnaires or interviews to assess exposure, which can lead to errors due to participants reporting possibly information incorrectly [68]. Whereas studies that measure pesticide levels in biological samples (e.g., blood, fat tissue) can provide a better estimate of longer-term exposure and may help elucidate any link between pesticides and breast cancer [68].

High levels in biological samples of organochlorines, that are banned but still contaminate the environment (e.g., DDT, endosulfan, chlordane), were found to be associated with an increased breast cancer risk [78-83]. Importantly, when pesticides are in mixtures, they may have different effects on breast cancer risk [84]. For instance, a mixture



containing hexachlorocyclohexane and endosulfan, may increase breast cancer risk, whilst a mixture with DDT and chlordane metabolites may reduce risk [84]. However, this does not mean that exposure to these pesticides is safe.

[86]. A positive association was also found for in utero exposure, with high levels of DDT in the mother's blood linked to an increased breast cancer risk in daughters later in life [87].

5.3.4 Critical windows of susceptibility

As described in Section 5.2, pesticides can alter the development of the mammary gland and increase the risk of mammary tumours in animals [14,63].

Whilst research on this topic extremely limited, some human studies suggested that exposure have pesticides during certain critical life stages, such as in utero, may affect breast cancer risk [85-87] (see our Critical Windows of Susceptibility for Breast Development review for more information on life stages).

Another study found that maternal pesticides before exposure to conception or during the perinatal period (from pregnancy throughout the first year after birth) may be linked to breast cancer in daughters [85]. Paternal exposure may also affect breast cancer risk daughters in under certain circumstances [85,88].

Additionally, whilst most epidemiological studies found no association between adult exposure to DDT and breast cancer [89], exposure at a younger age may increase risk [82]. For example, women exposed to DDT (when still in use), before age 14, had a five-time increased breast cancer risk compared to women not exposed during childhood

Box 1. What is glyphosate?

Glyphosate represents 92% of all herbicides and 18% of all pesticides used worldwide [90]. In the UK, glyphosate is the most used herbicide across many applications, from crops to urban areas [17-19,22], and is also present in weedkiller products designed for the public [91]. Despite its classification as a probable human carcinogen in 2015, glyphosate remains authorised in the UK and EU [12,16].

Glyphosate can damage the DNA, increase oxidative stress, cause epigenetic changes, disrupt sex hormones, and interfere with the gland in animals mammary Whilst these indicate [55,63,92]. that it may play a role in breast cancer, evidence from epidemiological studies is very limited and inconclusive [71,93].

Exposure to glyphosate has been associated with the consumption of grains, wholemeal flour, soy, wine, and fast food [94]. After being sprayed on crops, glyphosate can enter the plant and accumulate in the seed and bran [95], meaning washing or peeling produce may not be sufficient. Buying organic alternatives where possible can help reduce exposure to glyphosate [95].



6. Organic food

Organic food is usually grown without synthetic (man-made) pesticides [96]. Whilst a diet consisting of conventional food (grown with pesticides) is the most common exposure route to pesticides, swapping produce for organic ones can reduce this exposure by around 90% [97-99].

Only under specific circumstances and with the correct approval can certain pesticides be used in organic farming. Around 30 different pesticides are currently approved for use, with the majority being non-toxic and natural substances (e.g., spearmint oil and citronella) [100].

Compared to conventional food, organic crops are four times less likely to residues. contain pesticide When pesticides are found on organic produce, these are generally below the MRLs and rarely include multiple residues [97,99,101]. If organic produce is not an option, due to availability affordability, it is important to wash and conventionally grown fruit vegetables with tap water in order to reduce pesticide exposure [102,103].

Organic food may also have a higher content of nutrients, such as vitamins, minerals, polyunsaturated fatty acids and antioxidants (e.g., polyphenols, flavonoids, and carotenoids) [104–106]. However, the overall evidence is not yet strong enough to conclude that organic produce is more nutritious than conventionally grown food [74,106].

6.1 Organic food and breast cancer

Despite the lower pesticide content, only a few studies have evaluated whether a higher consumption of organic food may reduce the risk of diseases such as breast cancer [107].

Two French studies found that postmenopausal participants with the highest consumption of organic food were less likely to develop breast cancer, compared to people conventional diets [34,108]. Conversely, a study on middle-aged UK women reported that avoiding food grown with pesticides made no difference to overall cancer or breast cancer risk [109].

Other studies found that organic food may reduce Body Mass Index (BMI) [106], a measure of body fat. This may reduce breast cancer risk indirectly, as being overweight post-menopause is associated with an elevated risk [110].

The perceived health benefits of organic food may not be attributable to the food people themselves. but to the Individuals who consume an organic diet generally have healthier habits, such as consumption higher of fruit vegetables, less processed food, and elevated physical activity [74,99].

Overall, the evidence that organic food positively impacts health or reduces the risk of breast cancer is currently considered insufficient [99,106,111].



7. Conclusions

Pesticide use in the UK is widespread and many of the chemicals used in agriculture and residential areas are highly toxic. In laboratory studies, pesticides have been shown to promote key cancerous characteristics including DNA damage, oxidative stress, epigenetic changes and hormone disruption. Pesticides can also interfere with the development of the mammary gland in animals and increase the risk of mammary tumours. However, evidence from human studies is currently too limited to make an accurate judgment on whether pesticides increase breast cancer risk, especially for nonoccupational exposure.

Future epidemiological studies should move away from estimating exposure

through questionnaires and instead measure pesticide levels in biological samples. Additional studies need to assess the risk of those pesticides commonly used in the UK, whilst also evaluating the effect of mixtures. Research should also further address if and how pesticides may be more harmful if exposure occurs during certain life stages.

There is, however, sufficient evidence that suggests pesticides are harmful, and, whilst the health benefits of organic food are still debated, eating organic food can effectively decrease pesticide exposure. When organic options are not available, fruit and vegetables should be washed thoroughly to reduce the presence of pesticide residues.

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Appendix

Appendix 1. Criteria for the IARC classification of carcinogens [112].

Group	Definition	Evidence
1	Carcinogenic	Enough evidence in humans to be conclusive that it can cause cancer.
2A	Probably carcinogenic	Enough evidence from animal studies that it can cause cancer, but limited evidence in humans.
2B	Possibly carcinogenic	Some evidence from animal studies that it can cause cancer and limited evidence in humans. Thus, evidence is far from being conclusive.
3	Unclassifiable	No evidence that it can cause cancer, as evidence from animals and humans is not adequate.
4	Probably not carcinogenic	Strong evidence that it does not cause cancer.



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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

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