



UNDERSTANDING GP ATTITUDES TO CANCER PREVENTING DRUGS

FEBRUARY 2017



**CANCER
RESEARCH
UK**

ACKNOWLEDGEMENTS

Cancer Research UK commissioned a consortia of academic researchers led by the Wolfson Institute of Preventive Medicine, Queen Mary University of London to carry out the study.

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ABOUT CANCER RESEARCH UK

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LIST OF ACRONYMS

BNF	British National Formulary
CCG	Clinical Commissioning Group
HIS	Healthcare Improvement Scotland
NICE	National Institute for Health and Care Excellence
SERMs	Selective Oestrogen-Receptor Modulators

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EXECUTIVE SUMMARY

Around four in 10 cases of cancer could be prevented in the UK, largely through lifestyle changes. In addition, chemoprevention – the use of cancer-preventing drugs – has the potential to save many lives by stopping cancer developing in the first place.¹

Chemoprevention is a relatively new approach to cancer prevention and we know that there is considerable variability in the uptake of different medicines. In response, the Cancer Strategy for England recommends a more systematic approach to making chemoprevention available.²

Ensuring evidence-based chemoprevention is routinely discussed with and offered to the relevant people should be a priority across the UK. For example, an estimated quarter of a million women in the UK are at increased risk of breast cancer and are eligible for preventive medications.ⁱ And research demonstrates that chemoprevention using Selective Oestrogen-Receptor Modulators (SERMs) such as tamoxifen and raloxifene can reduce incidence of breast cancer by around a third or more among women with a clear family history of the disease.³

However, it is not currently possible to understand on a national level what the level of uptake of chemoprevention currently is. Or indeed how many cases of cancer could be prevented should uptake increase. Published studies suggest there may be problems with making chemoprevention part of routine clinical practice.⁴

Our study aimed to increase our understanding of GP attitudes towards offering the use of tamoxifen and aspirin to lower the risk of cancer, or to prevent cancer.ⁱⁱ This is important because it's an area where there is little research around clinician attitudes and knowledge.

We focussed on the prevention of breast and bowel cancer via the use of tamoxifen and aspirin for two reasons.

Firstly, because of the high level of evidence demonstrating the efficacy of both these drugs. Among patients taking tamoxifen for five years, the preventive effects are expected to last at least 20 years.⁵ Evidence from randomised controlled trials have shown the benefits of aspirin in preventing bowel cancer in population riskⁱⁱⁱ participants and in reducing the incidence of bowel cancer for people with Lynch Syndrome.^{iv}

Secondly, we intentionally chose one drug that is covered by National Institute for Health and Care Excellence (NICE) and Healthcare Improvement Scotland (HIS) guidance (tamoxifen) and, as a comparator, one drug that is not (aspirin), despite the weight of evidence for its efficacy.

In 2013 NICE recommended the use of tamoxifen and raloxifene for women at an increased risk of breast cancer due to their family history (NICE Guideline CG164). Wales and Northern

ⁱ Figures calculated in reference to the PROCAS study (www.ncbi.nlm.nih.gov/pubmed/25047362) that found approximately 10-12% of women met NICE thresholds and assuming two million women per annum are screened.

ⁱⁱ This study in this instance did not explore clinician attitudes towards the use of chemoprevention in preventing secondary cancer. This would be a valuable area for follow up research.

ⁱⁱⁱ Population risk' for an individual refers to their risk of disease assuming they are not at high risk, for example they don't have a genetic or familial predisposition.

^{iv} Lynch Syndrome is also known as hereditary non-polyposis colorectal cancer (HNPCC) and is estimated as affecting between 1 in 400 and 1 in 1,200 people in the UK. Figures will not be exact as people aren't routinely tested. The CaPP2 trial has shown the long term use of daily aspirin (600mg) by people with Lunch Syndrome can reduce the incidence of bowel cancer and other cancers associated with the syndrome.

Ireland follow NICE guidelines.

However, there are not yet formal guidelines for prescribing aspirin in the UK and there is no process established to ensure consistency in prescribing tamoxifen in England, Wales or Northern Ireland.¹¹

Local policies in England are in place. For example, the Greater Manchester Medicines Management Group have established a shared care protocol whereby GPs prescribe tamoxifen and raloxifene, but this is after it is prescribed by a secondary care clinician first (via the family history clinic).

In Scotland, there is an established pathway for GPs to prescribe tamoxifen in a shared care agreement for high risk women between primary and secondary care.

The Cancer Strategy for England includes two recommendations (6 and 7) which set out the need to improve appropriate prescribing of chemopreventive agents, as well as the need to update NICE guidelines on the use of aspirin for individuals with hereditary non-polyposis colorectal cancer (HNPCC) or Lynch Syndrome.

THE STUDY

Cancer Research UK commissioned a consortia of academic researchers led by the Wolfson Institute of Preventive Medicine, Queen Mary University of London, to carry out the study.

A sample of 1,007 GPs from across the UK completed an online survey in May 2016 investigating GPs':

- Awareness of familial breast cancer guidelines and confidence in prescribing tamoxifen for women with a strong family history of breast cancer. Respondents were asked to consider a number of scenarios describing a patient.^v
- Awareness of Lynch Syndrome and the preventive effects of aspirin among those with Lynch Syndrome and their comfort in discussing the risks and benefits of the drug.
- Attitudes towards recommending the use of aspirin for individuals at population risk of bowel cancer.

In this instance, the term chemoprevention was used to refer to the use of medicines to prevent disease among people not previously affected.

KEY FINDINGS: TAMOXIFEN

AWARENESS

Strikingly for a drug that is covered by guidance, there was low awareness of the potential of tamoxifen.

Nearly half of the responding GPs (48%) were unaware tamoxifen could be used for the prevention of breast cancer among women with a clear family history of the disease.

Only 24% were aware of the NICE familial breast cancer guidelines. A similar level of awareness (20%) for the HIS guidelines was reported among Scottish GPs.

^v This included difference in lifetime risk of developing breast cancer and if the GP was responsible for writing the first prescription to the patient, or if this originated from a family history clinician.

WILLINGNESS TO PRESCRIBE

Despite low levels of awareness, GPs were willing to prescribe tamoxifen. 77% reported they would be willing to prescribe tamoxifen for a patient at increased risk of breast cancer.^{vi}

In fact, the GPs that were aware of the NICE or HIS guideline relating to tamoxifen were more willing to prescribe tamoxifen. Plus willingness to prescribe was higher among GPs who were told they would be continuing a prescription initiated by a secondary care clinician (in this instance by a family history clinician).

COMFORT

A third of GPs said they would be quite uncomfortable (30%) or very uncomfortable (4%) managing a patient who decides to take tamoxifen.

GPs were asked about their level of comfort in discussing the risks and benefits of tamoxifen with patients.

As above, respondents were more likely to report they were comfortable if they were told a secondary care clinician would write the first prescription. And the GPs aware of the NICE or HIS guideline also reported greater comfort in discussing the risks and benefits of the drug.

INFLUENCES ON DECISION MAKING

A particular issue in chemoprevention is that these drugs will generally be old ones that have been investigated for new uses so will likely have come off-patent. As such, prescribing will often be 'off-label'. Our survey shows that off-label prescribing is a factor in the decision-making of GPs – but several other factors had a greater influence.

The factors GPs reported as most likely to affect their decision to decision to prescribe tamoxifen were the evidence for the benefits of the drug; existence of the NICE or HIS guideline; and the patient's awareness of the risks and benefits.

On the flipside, the financial costs; the prescribing budget in their practice; and attitudes of more senior colleagues, were reported as least likely to affect their decision.

SUPPORT REQUIRED

GPs wanted support in prescribing tamoxifen.

63% wanted to speak with someone else before they decided to write a prescription. It was most common to want to speak with a specialist in secondary care (68%), a colleague in primary care (26%) or the local CCG or medicines management team (22%).

COMMISSIONER ATTITUDES

The survey also included 192 English GPs with a role in commissioning. Only ten reported that their Clinical Commissioning Group (CCG) had discussed tamoxifen and only a third believed CCGs were responsible for making local policy decisions about the drug.

In fact, over half (56%) believed it was actually the responsibility of the local medicines management group and 42% believed their CCG would have concerns about GPs prescribing tamoxifen.

^{vi} The remaining GPs said they were "probably not willing" (18%) or "not at all willing" (5%) to prescribe tamoxifen.

KEY FINDINGS: ASPIRIN

AWARENESS

In contrast to the low levels of awareness of the potential of tamoxifen, the majority of GPs (73%) were aware that aspirin could reduce the risk of bowel cancer in population risk individuals. This is despite the fact that there is no clinical guideline relating to aspirin. Furthermore, around one quarter had previously discussed the use of aspirin for cancer prevention with a patient at population risk.

The study did not ask GPs why they were aware of the preventative effects of aspirin. The higher level of knowledge in this instance could be due to widespread media coverage of the benefits together with the fact that aspirin is an older drug.

A third of the GPs had not heard of Lynch Syndrome or any of its associated names. Among those GPs who had heard of it, nearly half (47%) were aware of the preventive effects of aspirin for those with the syndrome.

COMFORT

Most GPs (64%) reported they would feel comfortable discussing the benefits and risks of aspirin with a patient at population risk who wanted to take it to prevent bowel cancer.

After reading information supplied by our survey describing the preventive effects of aspirin among people with Lynch Syndrome, 68% of the GPs surveyed indicated that they would be comfortable discussing the risks and benefits of aspirin with a patient with the syndrome.

WILLINGNESS TO PRESCRIBE

A part-funded Cancer Research UK randomised controlled trial (the CaPP2 trial) showed a significant reduction in bowel cancer among those with Lynch Syndrome who took 600mg per day of aspirin for at least two years.⁶ However 600mg is the dose that GPs participating in this study reported as being least willing to prescribe, compared to lower doses of aspirin.^{vii}

Those who were aware of the preventive effects of aspirin for people with Lynch Syndrome were more willing to prescribe at 600mg.

RECOMMENDATIONS

Our study shows that more needs to be done to promote evidence and guidance on chemoprevention. This is particularly important in regard to existing familial breast cancer guidelines in order to increase GP awareness and their confidence in prescribing tamoxifen.

We also need a better understanding of the way in which the interaction between primary and secondary care can be improved to facilitate the use and uptake of chemoprevention. And patients, when considering the use of tamoxifen or aspirin, need high quality information in order to make informed decisions.

Finally, providing GPs with more information about chemoprevention is key to ensure they are better prepared for these conversations and enabled to take appropriate action.

^{vii} 62% of respondents were willing to prescribe 600mg. Most were willing to prescribe at the lowest dose, 100mg (91%).

1. THE PREVENTIVE EFFECTS OF TAMOXIFEN AND ASPIRIN, AND TAMOXIFEN'S ASSOCIATED NATIONAL GUIDELINE, REQUIRE BETTER PROMOTION

- NICE and NHS England (and national equivalents) should develop a programme of work to increase GP awareness of the guidelines relating to tamoxifen together with awareness of the benefits and risks of chemoprevention using tamoxifen.
- NHS England (and national equivalents) should commission NICE to develop guidelines for the use of drugs for the prevention of bowel cancer, in line with the recommendation of the Cancer Strategy for England.⁷ This should consider the use of aspirin for individuals with Lynch Syndrome. Once published, Clinical Commissioning Groups should ensure that GPs appropriately implement them.
- A decision-aid that can be used by both patients and clinicians when discussing the decision to use medication for the primary prevention of cancer should be developed. Local decision-aids are currently in use. NHS England (and national equivalents) should assess these. The Cancer Alliance leads should then ensure these resources are made available for their local populations – ensuring proper information is provided for patients on which to base their decision.
- For the appropriate patient groups, primary prevention should be listed as an unlicensed indication for tamoxifen and aspirin in the British National Formulary (BNF). The BNF does not have the authority to licence a medication but it frequently describes alternative unlicensed indications for medications.

2. GPs REQUIRE MORE SUPPORT AND INTERACTION WITH THEIR SECONDARY CARE COLLEAGUES

The Cancer Alliances should work with research scientists, clinical networks and NICE to develop standardised pro-formas for secondary care clinicians, such as those from the breast cancer department, family history or clinical genetics clinic, to send to GPs when they are referring high-risk patients to discuss chemoprevention. These could be adapted from existing templates within the HIS guidelines for tamoxifen.⁸

3. SHARED CARE AGREEMENTS BETWEEN PRIMARY AND SECONDARY CARE COULD FACILITATE PRESCRIBING

To facilitate greater use of chemoprevention, prescriptions could be initiated in secondary care and continued in primary care. Areas of work should include:

- NHS England, NHS Wales and the Department of Health in Northern Ireland should seek to replicate the national prescribing policy developed within the HIS guidelines for tamoxifen, adapting this policy for use within their respective nations.
- The approach used by the Greater Manchester Medicines Management Group for tamoxifen and raloxifene^{viii} prescribing should be explored to understand if this could be

^{viii} While both tamoxifen and raloxifene are available as chemoprevention agents to women at increased risk of breast cancer, evidence available suggests the majority of discussions with patients are about tamoxifen. We therefore decided to base our study around the use of this drug.

considered as a model for the rest of England. The Cancer Alliances are a route for this to happen.

- In England, local medicines management groups and CCGs, alongside family history clinics and genetics centres, should prioritise shared care agreements for the prescription of tamoxifen and raloxifene. The Cancer Alliances could facilitate these discussions.
- Further research is required to investigate how local prescribing policies are formed in Wales and Northern Ireland. The role of cancer networks in local policy development should be explored.

4. IMPROVE DATA COLLECTION RELATING TO CHEMOPREVENTION

- NHS England (and national equivalents), working with relevant partners, should lead in ensuring national level data on the numbers of people who are eligible for preventive medicines is collected, together with information on the subsequent level of uptake.

AREAS FOR FUTURE FOCUS

Our short study specifically explored the perceptions and attitudes of GPs towards chemoprevention. It did not collect information on the perspectives of patients, an area of equally important focus – particularly if we are to understand more about why people may choose to take (or not to take) preventive medicines.

This study also only focussed on chemoprevention for those that have not been previously affected by cancer. Further research in terms of the role of preventive medicines in preventing secondary cancer is needed.

To move forward, more work is required to understand what support mechanisms would boost GP confidence in making proper use of chemoprevention. Plus, greater exploration of the implications that many cancer preventing drugs will have come off-patent – but will have been proven effective in new uses for which they haven't been licensed.

1. BACKGROUND

The number of cases of cancers diagnosed each year is increasing, largely due to the fact that more people are living longer, reaching older ages when cancer is more common. Around 357,000 people in the UK were diagnosed with cancer in 2014⁹ and research has suggested that by 2035 the number of diagnoses each year could reach 500,000.¹⁰

Lifestyle factors also play a role though – around four in 10 cases of cancer in the UK could be prevented, largely through lifestyle changes.

Chemoprevention is a relatively new approach to cancer prevention. Traditionally, doctors have used a variety of cancer drugs to manage and treat cancer, but now there is growing use of utilising existing drugs to try to prevent cancer. Along with lifestyle changes, cancer-preventing drugs have the potential to save many lives.¹¹

Ensuring chemoprevention is appropriately prescribed in the NHS is a priority of the Cancer Strategy for England, and Cancer Research UK considers it a priority in all UK nations.¹²

This study is aimed at increasing our understanding of GP attitudes towards offering the use of tamoxifen and aspirin to lower the risk of cancer, or prevent cancer, in people who may be at increased risk, either due to family history or genetic factors.^{ix} This is important because it is an area where there is little research around clinician attitudes and knowledge.

In this instance, we focussed on the prevention of breast and bowel cancer via the use of tamoxifen and aspirin for two reasons.

Firstly, because of the high level of evidence demonstrating the efficacy of both these drugs. Among patients taking tamoxifen for five years, the preventive effects are expected to last at least 20 years.¹³ Evidence from randomised controlled trials have shown the benefits of aspirin in preventing bowel cancer in population risk^x participants and in reducing the incidence of bowel cancer for people with Lynch Syndrome.^{xi}

Secondly, we intentionally chose one drug that is covered by National Institute for Health and Care Excellence (NICE) and Healthcare Improvement Scotland (HIS) guidance (tamoxifen) and, as a comparator, one drug that is not (aspirin), despite the weight of evidence for its efficacy.

In 2013 the National Institute for Health and Care Excellence (NICE) recommended the use of tamoxifen and raloxifene for women at an increased risk of breast cancer due to their family history (NICE Guideline CG164). Wales and Northern Ireland follow NICE guidelines.

However, there are not yet formal guidelines for prescribing aspirin in the UK and there is no process established to ensure consistency in prescribing tamoxifen in England, Wales or Northern Ireland.¹¹

^{ix} This study in this instance did not explore clinician attitudes towards the use of chemoprevention in preventing secondary cancer. This would be a valuable area for follow up research.

^x Population risk' for an individual refers to their risk of disease assuming they are not at high risk, for example they don't have a genetic or familial predisposition.

^{xi} Lynch Syndrome is also known as hereditary non-polyposis colorectal cancer and is estimated as affecting between 1 in 400 and 1 in 1,200 people in the UK. Figures will not be exact as people aren't routinely tested. The CaPP2 trial has shown the long term use of daily aspirin (600mg) by people with Lunch Syndrome can reduce the incidence of bowel cancer and other cancers associated with the syndrome.

Local policies in England are in place. For example, the Greater Manchester Medicines Management Group have established a shared care protocol whereby GPs prescribe tamoxifen and raloxifene, but this is prescribed by a secondary care clinician first (via the family history clinic)

In Scotland, there is an established pathway for GPs to prescribe tamoxifen in a shared care agreement for high risk women between primary and secondary care.

1.1 CHEMOPREVENTION FOR WOMEN AT INCREASED RISK OF BREAST CANCER

Each year in the UK around 53,300 women are diagnosed with breast cancer, and around 11,600 die of the disease.¹⁴

An estimated 250,000 women in the UK are at increased risk of breast cancer and are eligible for preventive medications.^{xii} However, it is not currently possible to understand on a national level what the level of uptake of chemoprevention currently is (see section 1.1.1 below). Or indeed how many cases of cancer could be prevented should uptake increase.

Chemoprevention using Selective Oestrogen-Receptor Modulators (SERMs) such as tamoxifen and raloxifene can reduce incidence of breast cancer by 30% or more among women with a clear family history of the disease.¹⁵

Among patients taking tamoxifen for five years, the preventive effects are expected to last at least 20 years.¹⁶ Despite long-term follow-up in two large tamoxifen prevention trials, it is still too early to observe mortality reductions.¹⁷ SERMs also increase the risk of a thromboembolic event, endometrial cancer, and side effects similar to menopausal symptoms.¹⁸

In 2013 the National Institute for Health and Care Excellence (NICE) recommended the use of tamoxifen and raloxifene for women at moderate^{xiii} and high^{xiv} risk of breast cancer due to their family history (NICE Guideline CG164).^{xv,xvi,19} Wales and Northern Ireland follow NICE guidelines.

In Scotland, the guideline was developed by Healthcare Improvement Scotland (HIS) and is based on the NICE recommendations. However, in Scotland only high risk women are eligible for tamoxifen (not raloxifene), and there is an established pathway for GPs to prescribe in a shared care agreement between primary and secondary care.

1.1.1 UPTAKE OF BREAST CANCER CHEMOPREVENTION

There is no nationally collected data on uptake of breast cancer chemoprevention. However, we know from individual studies that this is low. For instance, a systemic review of published

^{xii} Figures calculated in reference to the PROCAS study (www.ncbi.nlm.nih.gov/pubmed/25047362) that found approximately 10-12% of women met NICE thresholds and assuming two million women per annum are screened.

^{xiii} 17-30% lifetime risk of breast cancer

^{xiv} ≥30% lifetime risk of breast cancer

^{xv} The Scottish guideline was developed by Healthcare Improvement Scotland and are based on the NICE recommendations. However, in Scotland only high risk women are eligible for tamoxifen, and there is an established care pathway for GPs to prescribe in a shared care agreement.

^{xvi} While both tamoxifen and raloxifene are available as chemoprevention agents to women at increased risk of breast cancer, evidence available suggests the majority of discussions with patients are about tamoxifen. We therefore decided to base our study around the use of this drug.

articles reporting uptake and adherence to therapeutic agents to prevent breast cancer among women at increased risk, which was undertaken by Smith et al (the author of this study also), found only 16% of eligible women deciding to use preventive therapy.²⁰

Their analysis of uptake data shows only one in 6 women accepted the offer of breast cancer chemoprevention.²¹ Excluding the enrolment rates from clinical trials, uptake was one in 10 women, suggesting there may be problems with making chemoprevention part of routine clinical practice.

A previous research study funded by Cancer Research UK aimed to find out more about the choices of women who had a high risk of developing breast cancer, in particular if they had considered using tamoxifen to prevent it.

This showed that the uptake for 1,279 women attending the Family History Clinic at the Nightingale and Genesis Prevention Centre, Manchester was 10%. The study team found that four issues influenced their decisions: the impact of possible side effects; their association of tamoxifen as a cancer drug (this stirred up painful memories of family members experiencing cancer); the opinions of others; and an unwillingness to take a drug that would be a reminder of their cancer risk.²²

An interview study with GPs and family history clinicians conducted in 2015 highlighted some major barriers to implementing the NICE clinical guideline (CG164) for tamoxifen and raloxifene.²³ This included the unlicensed status of tamoxifen, low knowledge of this area and concerns about the pathway for prescribing.

1.2 CHEMOPREVENTION FOR BOWEL CANCER

In 2016, the US Preventive Services Task Force released a recommendation for the prevention of cardiovascular disease and bowel cancer using aspirin among population risk individuals.²⁴

The recommendation applies to healthy adults aged 50 years and over who have a 10% or greater 10-year cardiovascular disease risk, are not at increased risk of bleeding, have a life expectancy of at least 10 years, and are willing to take a low dose aspirin daily for at least 10 years.

No UK guidance for aspirin in this context currently exists and there are not yet formal guidelines for prescribing aspirin.

Overall, there is growing evidence that aspirin could join the small number of preventive drugs already in use. The Cancer Strategy for England recommends (recommendation seven) that NHS England should commission NICE to develop guidelines for the use of drugs for the prevention of bowel cancer. This should consider the use of aspirin for individuals with Lynch Syndrome (see section 1.3 below).²⁵

However, aspirin use is associated with an age-dependent increased risk of bleeding, particularly gastrointestinal bleeding, and therefore risks and benefits must be carefully considered.²⁶ Due to the risks for some people when taking aspirin for a prolonged period, it is important to further understand who should and should not be using these drugs, and for what length of time.

1.3 CHEMOPREVENTION FOR LYNCH SYNDROME

There is also ongoing research into the use of aspirin to prevent cancer among people with Lynch Syndrome.²⁷ Lynch Syndrome, also known as hereditary non-polyposis colorectal cancer (HNPCC), is thought to affect between 1 in 400 and 1 in 1200 people in the UK.²⁸

Approximately 80% of men and 40% of women with Lynch Syndrome develop bowel cancer by age 70 years. Carriers are also susceptible to other cancers including endometrial, ovarian and stomach cancer.²⁹

A part-funded Cancer Research UK randomised controlled trial (the CaPP2 trial) has shown a significant reduction in bowel cancer among those with Lynch Syndrome by taking 600mg per day of aspirin for at least two years. There were also promising effects of aspirin on other cancers associated with the syndrome.³⁰

Following on from this, a dose non-inferiority study (the CaPP3 trial) comparing doses of 100mg, 300mg or 600mg of aspirin per day is now underway to determine the optimal dose of aspirin for those with Lynch Syndrome. The results of the CaPP3 trial are expected in 2020.

For those who are ineligible for the CaPP3 trial or who do not wish to enter, the 2013 European Guidelines for the clinical management of Lynch Syndrome recommend patients should use low-dose aspirin (≤ 100 mg).

1.4 STUDY AIMS AND FOCUS

Our study explores GP awareness and attitudes to cancer chemoprevention, focussing specifically on tamoxifen and aspirin. In this instance, the term chemoprevention was defined as the use of medicines to prevent disease among people not previously affected.

The research was carried out for Cancer Research UK by an academic consortia, led by Queen Mary University of London, and aimed to explore the following research questions:

- **How do primary care clinicians and commissioners^{xvii}**
 - **become aware of research evidence?**
 - **use national guidance in their decision-making?**
- **What barriers do GPs face in speaking to patients about cancer chemoprevention?**
- **What attitudes do GPs and commissioners have towards off-label prescribing?**

Specifically, the research investigated awareness of the NICE and HIS familial breast cancer guidelines and GP confidence in prescribing tamoxifen as a chemoprevention for women with a moderate or high risk of breast cancer. It also explored GP awareness of prescribing aspirin for chemoprevention and confidence in prescribing for carriers of Lynch Syndrome.

The researchers collected online survey data from 1,007 GPs.^{xviii} The GPs were from all four UK countries. A subset of English GPs (192 respondents) who said they had a role on commissioning services were asked additional questions.^{xix}

^{xvii} Only English GPs were asked about their commissioning role, as GPs from Scotland, Wales and Northern Ireland do not take on this responsibility. All references to commissioners are therefore based on the responses of 192 English GPs who have a commissioning role.

^{xviii} Conducted May 2016.

^{xix} Scottish GPs were shown slightly different information because of differences between the NICE guideline (CG164) and 2014 Familial Breast Cancer Guideline produced by Healthcare Improvement Scotland ¹¹

The survey was designed by the authors following stakeholder interviews³¹ and a literature review. Appendix two provides the survey and appendix three gives more information on respondents.

GPs were asked to review four case study scenarios describing a female patient at increased risk of breast cancer (see section 2.2 and appendix two). The survey includes 79 responses from Scottish GPs. All Scottish GPs were allocated the same case study describing a high risk patient, with the GP initiating the prescription, as this matches the current context in Scotland.

Due to the lack of a definitive guideline around the use of aspirin and Lynch Syndrome, and because a large dose non-inferiority trial is ongoing (the CaPP3 study), a case study manipulation was not carried out for the aspirin scenario.

2. FINDINGS: TAMOXIFEN

Our survey respondents were provided with an introduction to chemoprevention with tamoxifen. This included the availability of the NICE or HIS clinical guideline^{xx} and the risk categories of patients eligible for tamoxifen.

The risks and benefits of tamoxifen were described and GPs were informed that there is no established process to ensure consistency in prescribing tamoxifen in England, Wales and Northern Ireland. Patients are typically referred back to primary care after discussing the topic with a secondary care clinician (such as a member of the breast clinic). The status of the licence for tamoxifen and the need to prescribe 'off-label' was outlined.

More detailed information, developed for the purpose of this study, titled 'Tamoxifen: The Facts' was also available to GPs by clicking a second link. The information was similar, but contained statistical information around the risks and benefits and a more extensive list of the side-effects. Both sets of information ('The Essentials' and 'The Facts') were available to GPs throughout the survey. Appendix two provides a copy of this information.

2.1 AWARENESS

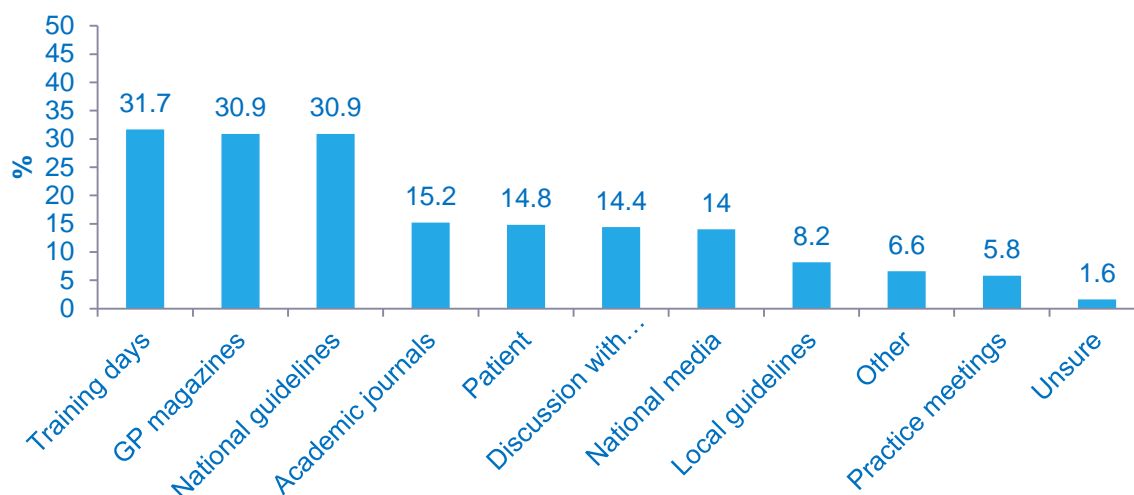
Approximately half (52%) of the survey respondents were aware tamoxifen could be used to reduce the risk of breast cancer but less than a quarter (24%) were aware of either the NICE guideline (CG164) or the HIS equivalent (20%).^{xxi}

The most common sources of information about tamoxifen among GPs who had heard of it were training days (32%), GP magazines (31%) and national guidelines (31%) (Figure 1).

^{xx} Scottish GPs were told about the HIS guideline instead of the NICE clinical guideline. They are largely similar, but moderate risk women are not eligible for tamoxifen in Scotland and there is an established pathway for GPs to prescribe in a shared care agreement between primary and secondary care.

^{xxi} GPs in England, Wales and Northern Ireland were asked about the NICE guideline (CG164) and Scottish GPs were asked about the Healthcare Improvement Scotland guideline.

FIGURE 1: REPORTED SOURCES OF INFORMATION ABOUT TAMOXIFEN (N=243)^{xxii}



2.2 PERSPECTIVES ON PRESCRIBING

GPs were invited to review one of four case study scenarios describing a female patient at increased risk of breast cancer (available in appendix two).

Information on the patient's age (45 years), her premenopausal status, and her lack of contraindications were identical in each case study. Two aspects of the descriptions were changed across the four case studies. In two of the case studies, the patient was described as having a moderate risk (17-30% lifetime risk) and in two case studies she was described as having a high risk ($\geq 30\%$ lifetime risk).

The second factor to be changed was the description of the clinician responsible for writing the first prescription for the patient. In two case studies a clinician from primary care (a GP) was the first prescriber, and in two case studies a secondary clinician (a family history clinician) was the first prescriber.

In Scotland, as noted in the previous chapter, a formal pathway exists for prescribing tamoxifen for high risk women.³² As such, they could not be randomised to three of the conditions within the vignettes as they describe situations that would not occur in their country.

It should be noted that Scottish GPs are therefore excluded from analysis below and instead are described in a separate section (section 2.6).

2.2.1 WILLINGNESS TO PRESCRIBE

Overall, the majority of GPs questioned (77%) were willing to prescribe tamoxifen for the patient in their case study.^{xxiii} The remaining GPs said they were 'probably not willing' (18%) or 'not at all willing' (5%) to prescribe tamoxifen.

^{xxii} Multiple responses were permitted.

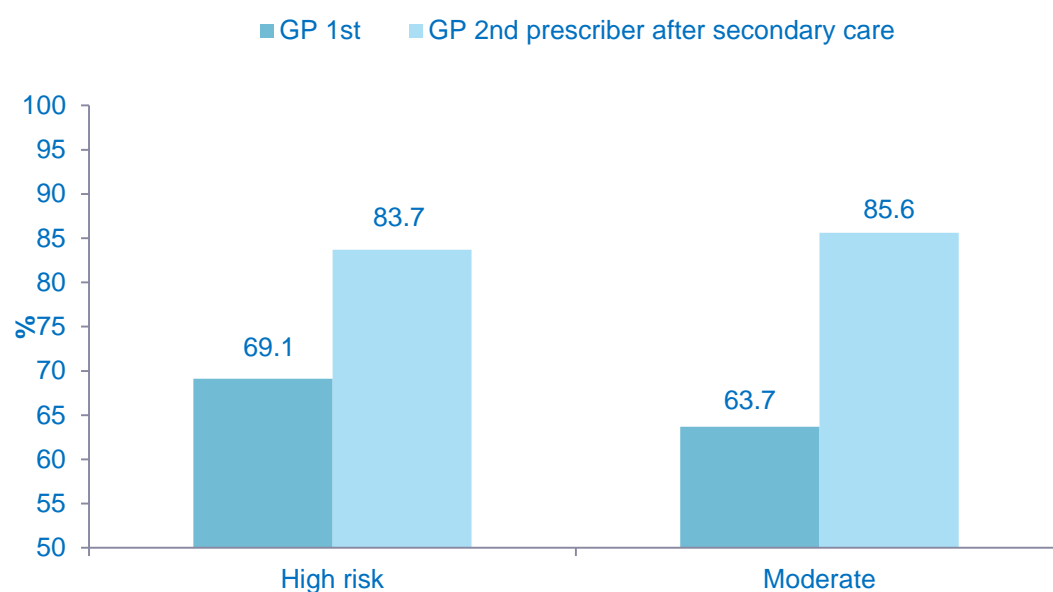
^{xxiii} 17.6% said they were "definitely willing" and 59.8% were "probably willing".

2.2.2 INFLUENCES ON WILLINGNESS

There was a difference in willingness to prescribe depending on whether GPs were told they would be asked to continue a prescription initiated by a secondary care clinician or if they were prescribing tamoxifen first.

The GPs that were told that they were the second prescriber were more willing to prescribe tamoxifen (see Figure 2).

FIGURE 2. WOULD YOU BE WILLING TO WRITE THE PRESCRIPTION FOR THE PATIENT? (% WILLING) (N=928)



Interestingly, willingness to prescribe was not affected by the patient’s risk level. There were no significant differences in GP’s willingness to prescribe for patients at different levels of risk (moderate risk: 77% vs. high risk: 78%).

2.3 COMFORT LEVELS

Most GPs reported being either quite comfortable (52%) or very comfortable (7%) discussing the risks and benefits of tamoxifen with patients. The remaining GPs were either quite uncomfortable (37%) or very uncomfortable (5%)^{xxiv}.

GPs were more likely to report being comfortable with discussing the risks and benefits of tamoxifen if they were told a secondary care clinician would write the first prescription (63%) compared with those who were told they would be asked to prescribe first (53%).

As above, there were no differences in reported comfort discussing the risks and benefits according to the patient’s risk level (moderate risk: 57% vs. high risk: 60%).

^{xxiv} Due to rounding numbers add up to more than 100%.

Overall, comfort in discussing the potential risks and benefits of tamoxifen was higher for:

- GPs older than 50 years
- GPs with more than 10 years' experience
- GPs with a special interest in cancer and preventive medicine
- GPs who were aware of the NICE or HIS guideline.

2.3.1 COMFORT IN MANAGING THE PATIENT

GP's comfort in managing the hypothetical patient, should she choose to start taking tamoxifen, was also explored.

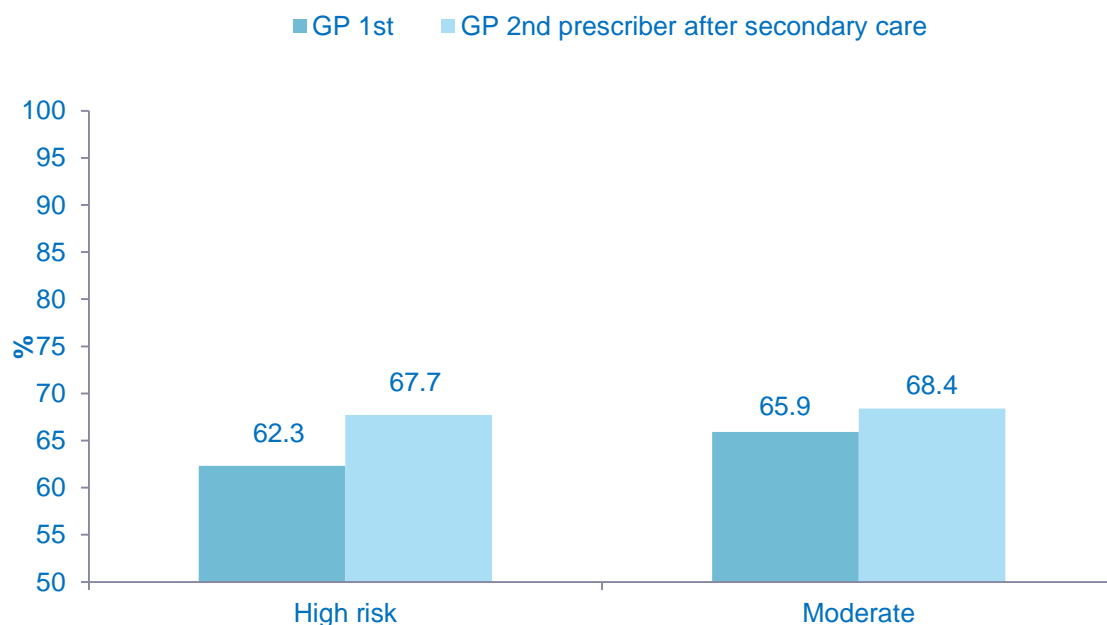
Overall, the majority of GPs indicated they would be very comfortable (8%) or quite comfortable (59%) managing the patient in the case study, should she decide to take tamoxifen. A third of GPs however said they were quite uncomfortable (30%) or very uncomfortable (4%).

There were no significant differences in reported comfort managing the patient when comparing GPs who were told they would be asked to continue a prescription initiated by a secondary care clinician with the GPs who were told they would be asked to prescribe first.

Furthermore, there was little difference when comparing the responses from GPs who were told the patient was at moderate risk compared with those who were told the patient was at high risk.

GP's comfort in managing the patient across each of the four case studies presented in the survey is shown in Figure 3.

FIGURE 3. IF THE PATIENT STARTED TAKING TAMOXIFEN, HOW COMFORTABLE WOULD YOU FEEL MANAGING HER CARE FOR THE DURATION OF THE PRESCRIPTION? (% COMFORTABLE) (N=928)



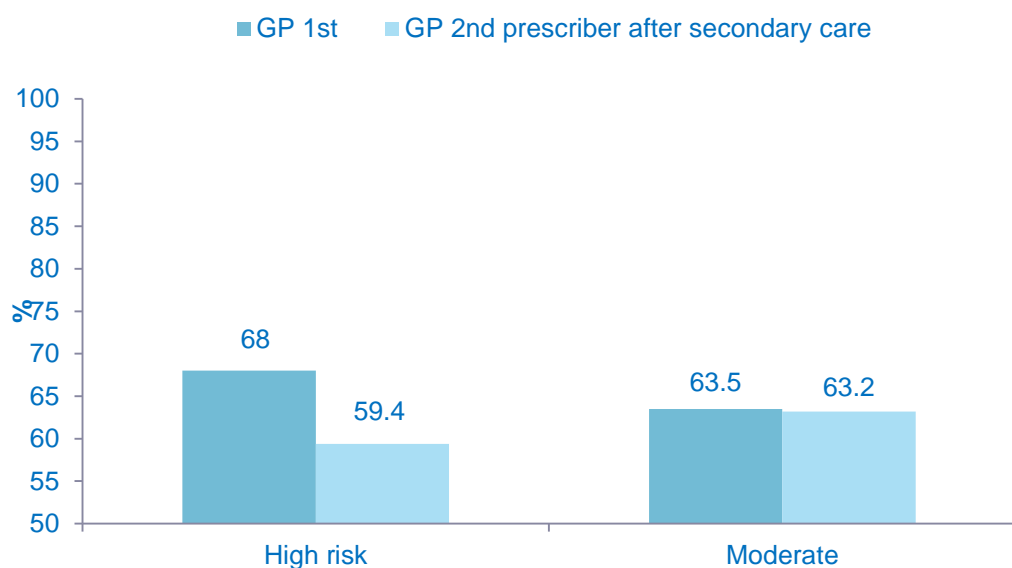
Overall comfort managing the hypothetical patient if she were to initiate tamoxifen was higher among GPs older than 50 years and the GPs with a special interest in preventive medicine.

2.4 INFLUENCES ON DECISION MAKING

Almost two thirds of GPs (63%) indicated they would want to speak with someone else before they decided whether to write the tamoxifen prescription for the patient. This was not affected by who was described as the first prescriber or by the description of the patient's risk.

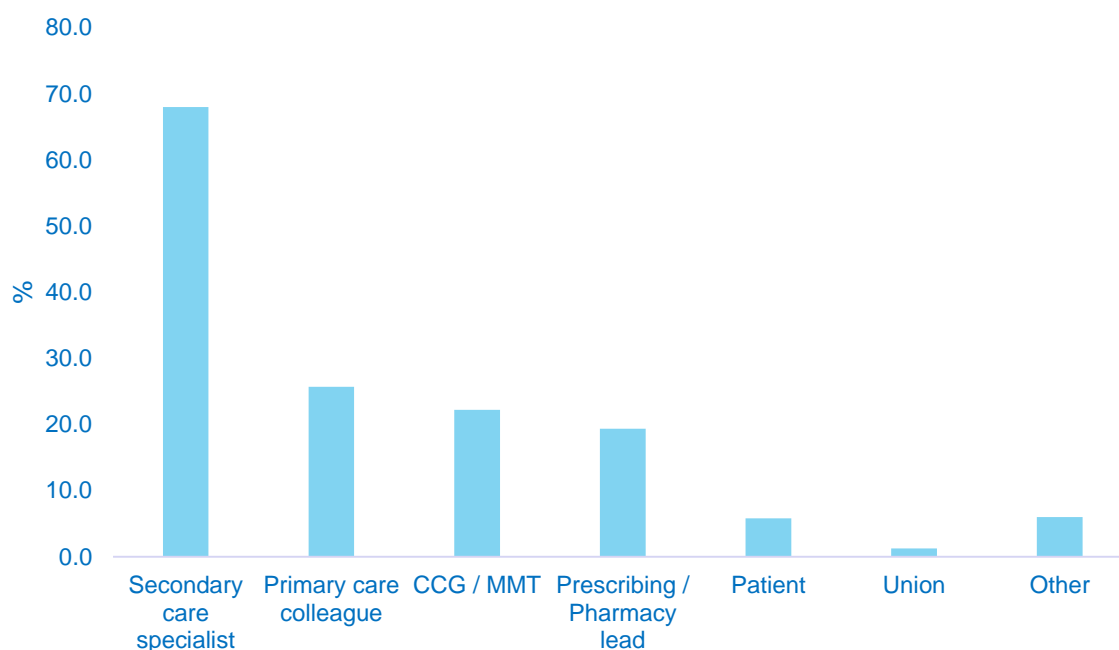
Figure 4 shows the proportion of GPs who indicated they would want to speak with someone else before making a prescribing decision.

FIGURE 4. WOULD YOU WANT TO SPEAK WITH ANYONE ELSE BEFORE YOU DECIDED WHETHER TO WRITE THIS PRESCRIPTION? (% YES) (N=928)



GPs most commonly wanted to speak with a specialist in secondary care (68%), around a quarter wanted to speak to a colleague in primary care (26%) and 22% reported that they would want to speak to their local CCG or medicines management team.

FIGURE 5. PLEASE DESCRIBE WHO YOU WOULD WANT TO SPEAK WITH BEFORE YOU DECIDED WHETHER TO WRITE A TAMOXIFEN PRESCRIPTION (% , N=635)



Willingness to prescribe tamoxifen was higher for male GPs and GPs who were aware of the NICE or HIS guideline.

GPs were also asked to indicate the extent to which a range of factors would influence whether they would be willing to prescribe tamoxifen for a patient. The factors most likely to influence a decision to prescribe tamoxifen for a woman at increased risk of breast cancer were:

- Evidence for the benefits of the drug (95%)
- Existence of the NICE or HIS guideline (95%)
- Patient awareness of the risks and benefits (94%).

The factors least likely to influence a decision to prescribe tamoxifen for a woman at increased risk of breast cancer were:

- The financial costs of tamoxifen (41%)
- The prescribing budget in their practice (42%)
- The attitude of more senior colleagues (59%)

Table 1 provides the full list of factors, in order of those reported to be most likely to influence the decision.

TABLE 1. FACTORS AFFECTING THE DECISION TO PRESCRIBE TAMOXIFEN FOR PATIENT (% AGREEMENT, EXCLUDING SCOTLAND N=928)

	Overall (%)	Willingness to prescribe		p-value
		Unwilling	Willing	
The evidence for the benefits of the drug	95.0	87.6	97.2	.000
The existence of NICE guideline (or national equivalent)	95.0	87.6	97.2	.000
The patient's awareness of the possible harms and benefits	94.1	81.9	97.6	.000
The patient's level of risk for breast cancer	93.8	82.9	96.9	.000
The patient's interest in taking tamoxifen	90.6	74.8	95.3	.000
Your confidence in your knowledge of tamoxifen	89.5	83.3	91.4	.001
The evidence for the harms of the drug	89.3	89.0	89.4	.879
The patient's support from the family history clinician	88.6	69.0	94.3	.000
First prescription being made by family history clinician ^{xxv}	86.0	72.7	88.4	.000
The policy of your Clinical Commissioning Group	80.2	82.4	79.5	.361
Prescribing 'off-label'	74.6	91.4	69.6	.000
The first prescription being made by you	71.9	85.0	66.0	.000
The attitudes of your colleagues at the same career stage	61.6	57.6	32.8	.173
The attitudes of your colleagues more senior than you	59.4	58.1	59.7	.668
The prescribing budget in your General Practice	42.1	41.4	42.3	.814
The financial costs of tamoxifen	41.4	37.6	42.5	.208

In terms of those GPs who indicated that they were willing to prescribe tamoxifen, a number of factors were more commonly considered which included the:

- Benefits of tamoxifen
- Patient's risk of breast cancer
- Patient's support from the family history clinician.

GPs who said they were unwilling to prescribe tamoxifen were significantly more likely to consider the:

- Issue of 'off-label' prescribing
- Fact that they were being asked to write the first prescription^{xxvi}.

There were no statistical differences between the GPs, across the four case studies, in regard to the consideration of the evidence of the risks of tamoxifen.

^{xxv} This item was only asked to those GPs allocated to conditions where the GP was asked to continue a prescription from secondary care (n=501)

^{xxvi} This item was only asked to those GPs allocated to conditions where the GP was described as being the first prescriber (n=427).

2.5 COMMISSIONER ATTITUDES

Our study asked GPs involved in commissioning in England additional questions about whether their local clinical commissioning group (CCG) had discussed and approved tamoxifen for prevention; their perception of who was responsible for making local policy decisions regarding tamoxifen, and; whether they felt there would be concerns about the prescription of tamoxifen from a CCG perspective.

In total, 192 of the survey's English respondents said that they had a role in commissioning and completed the additional questions.

2.5.1 CCG LOCAL POLICY

Of the 192 commissioner respondents, only ten (5%) reported that their CCG had discussed tamoxifen and of these ten, only two reported that a local policy was in place. The remaining eight respondents said that either no policy was formed (two people) or that tamoxifen was still under discussion (six people).

This compares with 63% who said that their CCG had not discussed tamoxifen, and a third (32%) who were unsure.

2.5.2 RESPONSIBILITY FOR LOCAL POLICY

Our survey data suggests there may be local differences in terms of the groups responsible for creating prescribing policy.

The low proportion of CCGs discussing tamoxifen may be due to the fact that only 32% of the commissioners responding to our survey believed CCGs were responsible for making local policy decisions about the drug.

The remaining commissioners thought responsibility for such decisions rests with the local medicine managements group (56%) or their own general practice (9%).

However, despite over half of the responding commissioners suggesting the local medicines management group were responsible, 42% believed their CCG would have concerns about GPs prescribing tamoxifen.

Analysis of free text comments from commissioners recorded respondent concerns relating to the level of evidence for tamoxifen; the lack of expertise in primary care to make the local policy decision; the need for shared care agreements and issues around off-label prescribing and cost.^{xxvii}

2.6 RESPONSES FROM SCOTTISH GPs

Our survey received 79 responses from Scottish GPs. Due to the fact that a formal pathway exists for prescribing tamoxifen for high risk women in Scotland our survey allocated all Scottish GPs to the vignette describing a high risk patient, with the GP initiating the prescription.³³

Scottish GPs reported a low level of awareness regarding the HIS guidelines for the

^{xxvii} Comments provided were very brief and more depth of analysis is unfortunately not possible in the context of this study.

management of women at increased risk of breast cancer (20% of respondents).

Among all respondents reviewing the case study describing a high risk patient (a total of 254), GPs from England, Wales and Northern Ireland were:

- Less willing to prescribe tamoxifen than their Scottish counterparts (69% vs. 81%)
- Broadly equally comfortable discussing tamoxifen (53% vs. 57%)
- Broadly equally comfortable managing the patient (62% vs. 65%)
- Broadly equally likely to want to speak with someone else before deciding to write a prescription (32% vs. 38%).

2.7 ATTITUDES TO OFF-LABEL PRESCRIBING

A particular issue in chemoprevention is that these drugs will generally be old ones (and have come off patent) and have also been proven effective in new uses for which they haven't been licensed (so called 'off-label').

Evidence from a previous interview study (carried out by the lead researcher for this report) has suggested GPs who are unwilling to prescribe tamoxifen are concerned about the drug not being licensed for a prevention indication.³⁴

However, current prescribing arrangements allow for 'off-label' drugs found to have new uses to be prescribed if considered to be clinically appropriate for an individual. There are no legal or regulatory barriers to prescribing off-label.

While our survey data shows that off-label prescribing is a factor in the decision-making of GPs, several other factors had a greater influence. Indeed, off-label prescribing was featured eleventh in the most common factors GPs considered (see table one above).

Interestingly, GPs who were unwilling to prescribe tamoxifen were far more likely to consider this factor than those who were willing.

The greater willingness to prescribe tamoxifen among those GPs who were told in the survey they would be continuing a prescription from secondary care may be at least partially explained by the issue of off-label prescribing. To quote a GP from the previous interview study:

"...The main issue is obviously with it being off-licence. If it had come from secondary care and I had a letter, and discussed that it was off-licence, I feel happy that the responsibility is...they've [secondary care] taken the primary decision, and we are supporting it by prescribing."³⁵

3. FINDINGS: ASPIRIN

Aspirin is proven to help prevent heart attacks and strokes in some people, and research has suggested that it also prevents some types of cancer. For instance, the CaPP2 trial showed a significant reduction in bowel cancer among those with Lynch Syndrome by taking 600mg per day of aspirin for at least two years. There were also promising effects of aspirin on other cancers associated with the syndrome.³⁶

As part of our survey we wanted to explore GP awareness of prescribing aspirin to reduce the risk of bowel cancer in population risk^{xxviii} individuals and their level of confidence in prescribing for people with Lynch Syndrome.

Due to the lack of a definitive guideline around the use of aspirin and Lynch Syndrome, and because a large dose non-inferiority trial is ongoing (the CaPP3 study outlined in chapter one), a case study manipulation was not carried out for the aspirin scenario.

Instead, GPs were asked to:

'Imagine the CaPP3 study shows that [100mg/300mg/600mg] of aspirin is the optimal dose for reducing the incidence of cancer in Lynch Syndrome carriers. How willing would you be to prescribe aspirin [100mg/300mg/600mg] for a patient with Lynch Syndrome?'

The order in which the three doses within the CaPP3 study were presented to GPs was randomised to prevent order effects, with each GP indicating how willing they would be to prescribe at that dose.

3.1 USE OF ASPIRIN IN POPULATION RISK INDIVIDUALS

The majority of respondents (73%) were aware aspirin could reduce the risk of bowel cancer in population risk individuals. Approximately one quarter (26%) had previously discussed the use of aspirin for cancer prevention with a patient.

Most GPs (64%) said they would feel comfortable discussing the benefits and risks of aspirin with a patient at population risk who wanted to take it to prevent bowel cancer.

3.2 AWARENESS OF LYNCH SYNDROME

A quarter (27%) of GPs had heard of Lynch Syndrome, 61% had heard of hereditary non-polyposis colorectal cancer (HNPCC) and 4% had heard of Muir-Torre Syndrome (associated names for Lynch Syndrome). Almost one third of GPs (29%) had not heard of any of the names for the syndrome.

Lynch Syndrome affects between 1 in 400 and 1 in 1200 people in the UK³⁷ and the majority of our respondents (63%) reported they had not seen a patient with Lynch Syndrome in their practice. A total of 19% were unsure.

^{xxviii} Population risk' for an individual refers to their risk of disease assuming they are not at high risk, for example they don't have a genetic or familial predisposition.

Among those GPs who had heard of Lynch Syndrome, or any of its associated names, just under half (47%) were aware aspirin could reduce the risk of cancers associated with Lynch Syndrome. In this same group, 4% reported having previously discussed aspirin with a patient with the syndrome.

3.3 COMFORT DISCUSSING RISKS AND BENEFITS

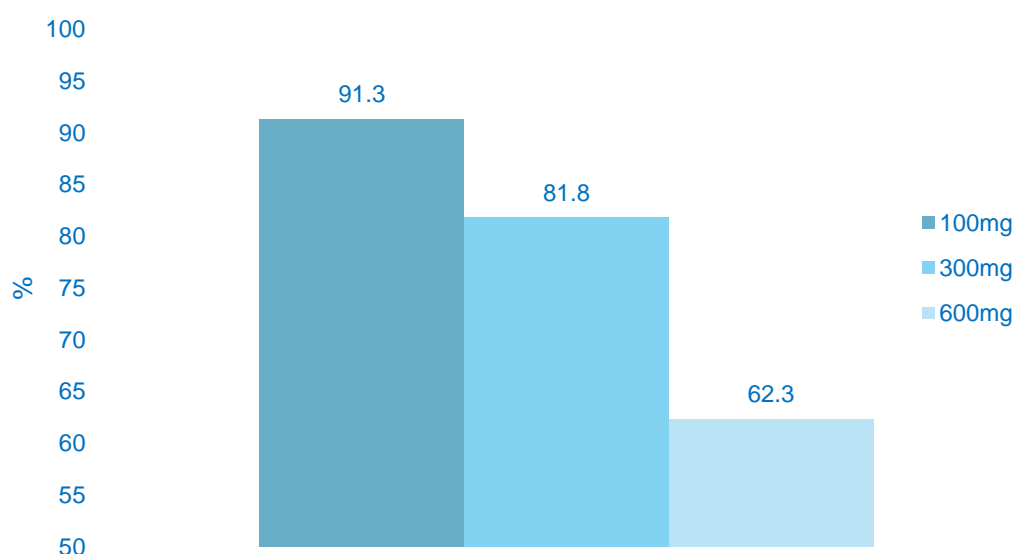
After reading information describing the preventive effects of aspirin among Lynch Syndrome carriers (appendix two details the information provided), 68% of all respondents indicated they would be comfortable discussing the risks and benefits of the drug with a patient.

3.4 WILLINGNESS TO PRESCRIBE

Although 600mg was the dose proven to reduce the risk of bowel cancer and other cancers associated with Lynch Syndrome in the CaPP2 study, it is the dose GPs were least willing to prescribe compared to lower doses of aspirin.

GPs were most willing to prescribe aspirin for people with Lynch Syndrome at the lowest dose, with almost all respondents indicating they were 'probably willing' or 'definitely willing' to prescribe aspirin at 100mg (91%). There was then a graded decline in willingness to prescribe aspirin at 300mg (82%) and 600mg (62%).

FIGURE 6. WILLINGNESS TO PRESCRIBE ASPIRIN AT 100MG, 300MG AND 600MG IF THE DOSE WAS SHOWN TO BE OPTIMAL IN THE CAPP3 STUDY (% WILLING) (N=1007)



Further analysis was undertaken to understand the factors associated with willingness to prescribe the 600mg dose of aspirin was higher among:

- GP partners
- Older GPs
- Those with more years of experience
- GPs who were aware aspirin could be used for this particular indication (69% vs. 58%).

Willingness to prescribe the highest dose was lower among GPs with a special interest in family history. Appendix three provides a more detailed breakdown by respondent characteristics.

Finally, awareness of the preventive effects of aspirin for those with Lynch Syndrome was associated with a greater willingness to prescribe at the highest dose described (600mg).

4. CONCLUSION AND RECOMMENDATIONS

Around four in 10 cases of cancer in the UK could be prevented, largely through lifestyle changes. Additionally, cancer-preventing drugs have the potential to save many lives by reducing the risk of cancer developing in the first place.³⁸

Chemoprevention is a relatively new approach to cancer prevention and we know that there is considerable variability in the uptake of different medicines. The Cancer Strategy for England recommends a more systematic approach to making chemoprevention available as a way of significantly improving outcomes.³⁹

This study was aimed at increasing our understanding of GP attitudes towards recommending the use of tamoxifen and aspirin to lower the risk of cancer or prevent cancer.

Overall, we found low-to-moderate awareness of the potential for drugs such as tamoxifen and aspirin to be used as chemoprevention agents.

Strikingly for a drug that is covered by national guidance, nearly half (48%) of the GPs questioned were unaware tamoxifen could be used for chemoprevention and only a quarter were aware of the NICE familial breast cancer guidelines.^{xxix} A similar level of awareness for the HIS guidelines were seen among Scottish GPs.

In contrast to the low levels of awareness of the potential of tamoxifen - the majority of GPs (73%) were aware aspirin could reduce the risk of bowel cancer in population risk individuals. This is despite the fact that there is no clinical guideline relating to aspirin.

The study did not ask GPs why they were aware of the preventative effects of aspirin. The higher level of knowledge in this instance could be due to widespread media coverage of the benefits together with the fact that aspirin is an older drug.

The study also found that awareness of the NICE or HIS guideline was associated with a greater willingness to prescribe tamoxifen, and greater comfort in discussing the risks and benefits of the drug. Awareness of the preventive effects of aspirin for people with Lynch Syndrome was also associated with a greater willingness to prescribe at the highest dose described (600mg).

A large number of GPs wanted to speak with someone else (for instance a practice partner or secondary care clinician) before deciding whether to prescribe tamoxifen for the patient in the case study vignette.

Furthermore, only 7% of GPs described themselves as being 'very comfortable' discussing the risks and benefits of tamoxifen with a patient.

^{xxix} Only 20% of Scottish GP respondents reported that they were aware of the Healthcare Improvement Scotland guidelines for the management of women at increased risk of breast cancer.

RECOMMENDATIONS

Our study shows that more needs to be done to promote evidence and guidance on chemoprevention. This is particularly important in regard to existing familial breast cancer guidelines in order to increase GP awareness and their confidence in prescribing tamoxifen.

We also need a better understanding of the way in which the interaction between primary and secondary care can be improved to facilitate the use and uptake of chemoprevention. And patients, when considering the use of tamoxifen or aspirin, need high quality information in order to make informed decisions.

Finally, providing GPs with more information about chemoprevention is key to ensure they are better prepared for these conversations and enabled to take appropriate action.

1. THE PREVENTIVE EFFECTS OF TAMOXIFEN AND ASPIRIN, AND TAMOXIFEN'S ASSOCIATED NATIONAL GUIDELINE, REQUIRE BETTER PROMOTION

- NICE and NHS England (and national equivalents) should develop a programme of work to increase GP awareness of the guideline relating to tamoxifen together with awareness of the benefits and risks of chemoprevention using tamoxifen.
- NHS England (and national equivalents) should commission NICE to develop guidelines for the use of drugs for the prevention of bowel cancer, in line with the recommendation of the Cancer Strategy for England.⁴⁰ This should consider the use of aspirin for individuals with Lynch Syndrome. Once published, Clinical Commissioning Groups should ensure that GPs appropriately implement them.
- A decision-aid that can be used by both patients and clinicians when discussing the decision to use medication for the primary prevention of cancer should be developed. Local decision-aids are currently in use. NHS England (and national equivalents) should assess these. The Cancer Alliance leads could then ensure these resources are made available for their local populations – ensuring proper information is provided for patients on which to base their decision.
- For the appropriate patient groups, primary prevention should be listed as an unlicensed indication for tamoxifen and aspirin in the British National Formulary (BNF). The BNF does not have the authority to licence a medication but it frequently describes alternative unlicensed indications for medications.

2. GPs REQUIRE MORE SUPPORT AND INTERACTION WITH THEIR SECONDARY CARE COLLEAGUES

The Cancer Alliances should work with research scientists, clinical networks and NICE to develop standardised pro-formas for secondary care clinicians, such as those from the breast cancer department, family history or clinical genetics clinic, to send to GPs when they are referring high-risk patients to discuss chemoprevention. These could be adapted from existing templates within the HIS guidelines for tamoxifen.⁴¹

3. SHARED CARE AGREEMENTS BETWEEN PRIMARY AND SECONDARY CARE COULD FACILITATE PRESCRIBING

To facilitate greater use of chemoprevention, prescriptions could be initiated in secondary

care and continued in primary care. Areas of work should include:

- NHS England, NHS Wales and the Department of Health in Northern Ireland should seek to replicate the national prescribing policy developed within the HIS guidelines for tamoxifen, adapting this policy for use within their respective nations.
- The approach used by the Greater Manchester Medicines Management Group for tamoxifen and raloxifene^{xxx} prescribing should be explored to understand if this could be considered as a model for the rest of England. The Cancer Alliances are a route for this to happen.
- In England, local medicines management groups and CCGs, alongside family history clinics and genetics centres, should prioritise shared care agreements for the prescription of tamoxifen and raloxifene. The Cancer Alliances could facilitate these discussions.
- Further research is required to investigate how local prescribing policies are formed in Wales and Northern Ireland. The role of cancer networks in local policy development should be explored.

4. IMPROVE DATA COLLECTION RELATING TO CHEMOPREVENTION

- NHS England (and national equivalents), working with relevant partners, should lead in ensuring national level data on the numbers of people who are eligible for preventive medicines is collected, together with information on the subsequent level of uptake.

AREAS FOR FUTURE FOCUS

Our short study specifically explored the perceptions and attitudes of GPs towards chemoprevention. It did not collect information on the perspectives of patients, an area of equally important focus – particularly if we are to understand more about why people may choose to take (or not to take) preventive medicines.

This study also only focussed on chemoprevention for those that have not been previously affected by cancer. Further research in terms of the role of preventive medicines in preventing secondary cancer is needed.

To move forward, more work is required to understand what support mechanisms would boost GP confidence in making proper use of chemoprevention. Plus, greater exploration of the implications that many cancer preventing drugs will have come off patent – but will have been proven effective in new uses for which they haven't been licensed.

^{xxx} While both tamoxifen and raloxifene are available as chemoprevention agents to women at increased risk of breast cancer, evidence available suggests the majority of discussions with patients are about tamoxifen. We therefore decided to base our study around the use of this drug.

APPENDIX ONE: METHODOLOGY

SAMPLE

A national survey of GPs practicing in the UK was undertaken in April, 2016. Members of the M3 Global Research Panel (n≥33,000) were invited to take part and sent a link to access the online survey. Respondents were eligible if general practice was their speciality. GPs were excluded if they were not practicing in the UK.

The target sample size was 1,000 GPs, of whom a minimum of 80 would be involved in commissioning.

Respondents were compensated a total of £15 for completing the questionnaire.

STUDY PROCEDURE AND DESIGN

After agreeing to participate, respondents were invited to confirm their speciality and the country they practice in to ensure inclusion and exclusion criteria were met. GPs were also asked to indicate whether they had a role in commissioning, and their response was used to route them to the appropriate items in the survey.

A brief introduction to the topic of chemoprevention was given. This emphasised that in this instance, chemoprevention was referring to the use of medicines to prevent disease among people not previously affected by the disease.

All GPs completed the tamoxifen section first. A brief introduction to chemoprevention with tamoxifen was given. This included the availability of the NICE clinical guideline^{xxxi} and the risk categories of patients eligible for tamoxifen.

More detailed information, titled 'Tamoxifen: The Facts' was available to GPs by clicking a second link. The information was similar, but contained statistical information around the risks and benefits, a more extensive list of the side-effects, and a longer description of the current care pathways that are used. Both sets of information ('The Essentials' and 'The Facts') were available to GPs throughout the survey.

GPs were invited to review one of four case studies describing a patient at increased risk of breast cancer (see below)

The case studies were manipulated using a between-subjects 2 x 2 factorial design. The first between-subjects factor was the risk level of the patient (moderate risk [17-30% lifetime risk] vs. high [≥30% lifetime risk]). The second between-subjects factor was the description of the clinician responsible for initiating the prescription (GP vs. secondary care clinician).

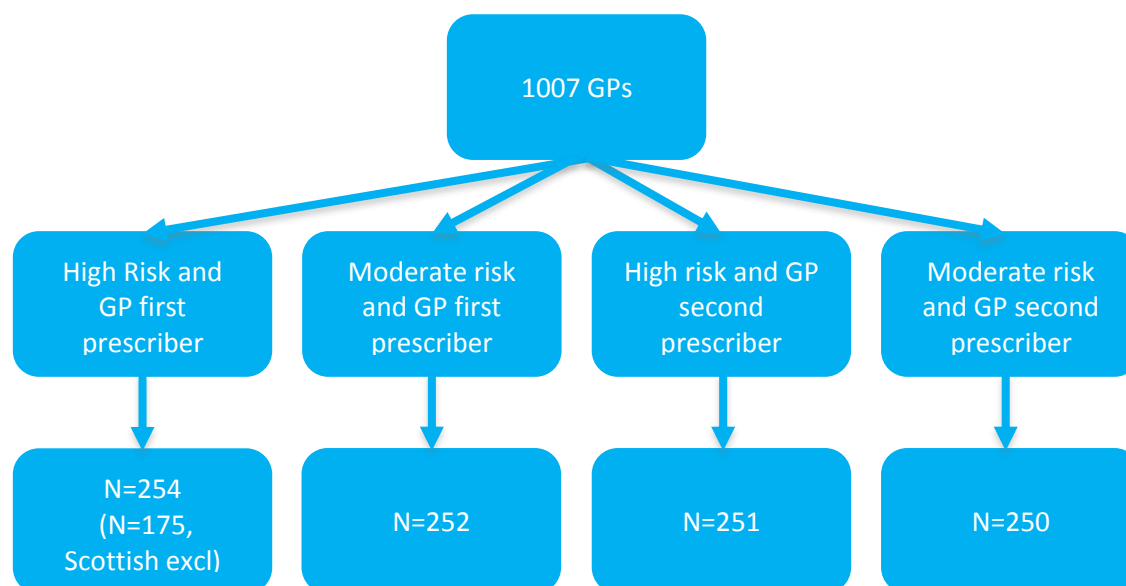
The GPs were randomised to a single case study using the ratio 1:1:1:1. The case study viewed by the GP was available to them throughout the appropriate questions, and was designed to mirror a typical scenario of a patient seeking a prescription for tamoxifen.

After viewing the case study, GPs were presented with a series of items assessing their willingness and comfort in prescribing tamoxifen for the hypothetical patient, and the factors they considered in the decision.

^{xxxi} Scottish GPs were told about the Healthcare Improvement Scotland guideline instead of the NICE clinical guideline. They are largely similar, but moderate risk women are not eligible for tamoxifen in Scotland and there is an established care pathway for GPs to initiate prescribing.

GPs involved in commissioning were asked additional questions.

Randomisation of GPs to four case studies:



After completing the remaining tamoxifen items, GPs were presented with brief information about Lynch Syndrome. Information was presented on the evidence for the cancer preventive effects of aspirin. Specifically, GPs were presented with information regarding the outcomes of the CaPP2 trial, the recommended dose according to European guidelines, and the current status of the CaPP3 dose-inferiority trial. Respondents were informed of the major adverse events that can occur among people taking aspirin, and that aspirin was a generally accepted recommendation among this population group.

GPs were able to consult the background information on Lynch Syndrome and aspirin throughout the items in this section.

The final component of the survey asked questions relating to aspirin use among the general population for bowel cancer prevention. Evidence from the latest systematic review on the topic was presented.⁴²

Respondents were informed that no UK policy on aspirin use is available, but that the US Preventive Services Taskforce have released draft guidelines supporting its use for bowel cancer prevention in adults aged 50-59 years with no contraindications.⁴³

SURVEY DEVELOPMENT

Prior to starting this project, Dr Smith and colleagues completed a qualitative interview study with family history and clinical genetics (FHCG) staff (n=15) and general practitioners (n=10). The findings from these interviews are reported elsewhere.⁴⁴

The data collected from these key informants were supplemented by a further six interviews with GPs and a FHCG clinician.

The survey was co-designed by the authors of this report. Together, they have expertise in

behavioural science, health policy, statistics, epidemiology, clinical genetics, primary care and public health.

STATISTICAL ANALYSES

The data were described using percentages, means and standard deviations. For the vignette part of the study, the main effects of risk and prescriber were tested using the chi-square statistic.

To calculate the interaction effect, the main effects of risk and prescriber were entered simultaneously into a logistic regression model, along with the interaction term. The same process was used for the outcomes relating to comfort discussing tamoxifen and comfort managing the patient for the duration of the prescription. The Chi-Square statistic was used to compare sub-group differences on study outcomes. For example, willingness to prescribe by participant characteristics such as age.

The trend for willingness to prescribe aspirin across the three doses was analysed using an extension of the Wilcoxon rank-sum test.⁴⁵

CASE STUDIES

Case studies describing a patient at increased risk of breast cancer:

GP	Secondary care clinician
Sarah is a 45-year- old woman with a family history of breast cancer. She consulted you previously and was referred to a local family history clinic for risk assessment. A family history clinician assessed her as having a high risk of breast cancer. This means she has a lifetime risk of $\geq 30\%$. Sarah has discussed the potential harms and benefits of taking tamoxifen for five years with the family history clinician. She has expressed an interest in taking tamoxifen. Sarah is premenopausal with no menstrual dysfunction, is not planning pregnancy, has no contraindications, and is taking no other medications. The family history clinician supports her decision to take tamoxifen and has also referred her for additional screening. The family history clinician has written the first prescription, and has requested that you take over as the main prescriber.	Sarah is a 45-year- old woman with a family history of breast cancer. She consulted you previously and was referred to a local family history clinic for risk assessment. A family history clinician assessed her as having a high risk of breast cancer. This means she has a lifetime risk of between 17% and 30%. Sarah has discussed the potential harms and benefits of taking tamoxifen for five years with the family history clinician. She has expressed an interest in taking tamoxifen. Sarah is premenopausal with no menstrual dysfunction, is not planning pregnancy, has no contraindications, and is taking no other medications. The family history clinician supports her decision to take tamoxifen and has also referred her for additional screening. The family history clinician has written the first prescription, and has requested that you take over as the main prescriber.

Sarah is a 45-year-old woman with a family history of breast cancer. She consulted you previously and was referred to a local family history clinic for risk assessment. A family history clinician assessed her as having a high risk of breast cancer. This means she has a lifetime risk of $\geq 30\%$. Sarah has discussed the potential harms and benefits of taking tamoxifen for five years with the family history clinician. She has expressed an interest in taking tamoxifen. Sarah is premenopausal with no menstrual dysfunction, is not planning pregnancy, has no contraindications, and is taking no other medications. The family history clinician supports her decision to take tamoxifen and has also referred her for additional screening. The family history clinician requested that you write the first prescription and continue to act as the main prescriber.

Sarah is a 45-year-old woman with a family history of breast cancer. She consulted you previously and was referred to a local family history clinic for risk assessment. A family history clinician assessed her as having a high risk of breast cancer. This means she has a lifetime risk of between 17% and 30%. Sarah has discussed the potential harms and benefits of taking tamoxifen for five years with the family history clinician. She has expressed an interest in taking tamoxifen. Sarah is premenopausal with no menstrual dysfunction, is not planning pregnancy, has no contraindications, and is taking no other medications. The family history clinician supports her decision to take tamoxifen and has also referred her for additional screening. The family history clinician requested that you write the first prescription and continue to act as the main prescriber.

RESEARCH LIMITATIONS

The survey was cross-sectional, and therefore we cannot infer causality with these data. The GPs were well-matched to national estimates, but we cannot rule out the possibility that respondents to our survey were more motivated and interested in the topic of chemoprevention than non-respondents.

While cross-sectional surveys do not allow causal inferences, it is possible that increasing awareness of chemoprevention medications could facilitate appropriate prescribing behaviour.

Finally, the questions asked of GPs were hypothetical, and we do not know the extent to which their responses to the survey items reflect their prescribing behaviour in a real clinical situation.

APPENDIX TWO: SURVEY

Before we start, we are interested in some basic information about you and your practice to ensure the study is relevant for you.

Please confirm your specialty.

- a) GP
- b) Other

Please confirm the region you practice in.

- a) England
- b) Scotland
- c) Wales
- d) Northern Ireland

Do you have a role in commissioning?

- a) Yes
- b) No

1 CHEMOPREVENTION

We are interested in the use of chemoprevention drugs in the NHS. In this instance, chemoprevention is the use of medication to lower the risk of cancer in people not previously affected by the disease. We are particularly interested in chemoprevention using tamoxifen and aspirin.

We have supplied some information below for you to read, with some follow-up questions.

Please take your time to read this information.

We would like to provide two levels of detail for the survey – one ‘gist’ version of one paragraph and then a second ‘detailed’ version that can be accessed if they click a link. The information below will be the ‘detailed’ version, and the new text here is the ‘gist’ version.

Tamoxifen: The Essentials

NICE guidelines suggest women at high risk of breast cancer ($\geq 30\%$ lifetime risk) should be offered tamoxifen for primary prevention and clinicians should consider offering the drug to moderate risk women (17–30% lifetime risk). Women would take tamoxifen for 5 years. Tamoxifen can reduce the risk of getting breast cancer among women at increased risk by at least one third. Women taking tamoxifen have an increased risk of endometrial cancer, venous thromboembolic events and menopausal side-effects. There is no generally accepted nationwide care pathway for prescribing tamoxifen for primary prevention. Tamoxifen will

usually be discussed with patients in secondary care, and interested patients will typically be referred back to primary care. Tamoxifen is not licensed for a primary prevention indication, and therefore prescriptions are made 'off-label'.

Tamoxifen: The Facts

Background

In 2013, NICE endorsed the use of tamoxifen as a therapeutic agent for women at increased risk of breast cancer because of a family history of the disease (see Clinical Guideline 164: Familial breast cancer: classification, care and managing breast cancer and related risks in people with a family history of breast cancer). The guidelines suggested that women at high risk of breast cancer ($\geq 30\%$ lifetime risk) should be offered tamoxifen and that clinicians should consider offering tamoxifen to women at moderate risk of breast cancer (17–30% lifetime risk). Women initiating therapy would take the medication for up to 5 years.

Benefits and harms

A meta-analysis of women at increased risk of breast cancer who were taking Selective Oestrogen Receptor Modulators (SERMs) (the class of medication that includes tamoxifen), showed a relative risk reduction of 38% for breast cancer incidence. Women taking tamoxifen had a higher rate of endometrial cancer (Hazard ratio [HR]=2.18), venous thromboembolic events (HR=1.60) and cataracts (HR=1.10). Tamoxifen can also increase the likelihood of experiencing gynecological, sexual and vasomotor symptoms, as well as weight gain and headaches.

Prescribing

There is no generally accepted nationwide pathway for prescribing tamoxifen for primary prevention. Patients at increased risk of breast cancer will generally be seen in clinical genetics clinics, family history clinics, or breast cancer departments. The option of tamoxifen will be discussed in secondary care and patients who are interested in taking tamoxifen will typically be referred back to primary care. Tamoxifen is not licensed for a primary prevention indication, and therefore all prescriptions have to be made 'off-label'.

Please confirm you have read and understood the above by clicking on the next button.

Tamoxifen: The Essentials (Scottish respondents only)

Healthcare Improvement Scotland guidelines suggest women at high risk of breast cancer ($\geq 30\%$ lifetime risk) should be offered tamoxifen for primary prevention. Women would take tamoxifen for 5 years. Tamoxifen can reduce the risk of getting breast cancer among women at increased risk by at least one third. Women taking tamoxifen have an increased risk of endometrial cancer, venous thromboembolic events and menopausal side-effects. The recommendations for chemoprevention are supported by a shared-care framework. Tamoxifen will be discussed with patients in secondary care, and interested patients will be referred back to primary care for prescribing. Tamoxifen is not licensed for a primary prevention indication, and therefore prescriptions are made 'off-label'.

If you would like more detailed information about tamoxifen, please click here.

Please confirm you have read and understood the above by clicking on the next button.

Tamoxifen: The Facts

Background

Healthcare Improvement Scotland guidelines from 2014 endorsed the use of tamoxifen as a therapeutic agent for women at increased risk of breast cancer because of a family history of the disease (see Familial Breast Cancer Report: Implementation of the National Institute of Health and Care Excellence (NICE) clinical guideline 164 on ‘familial breast cancer’ in Scotland). The guidelines suggested that women at high risk of breast cancer ($\geq 30\%$ lifetime risk) should be offered tamoxifen. Women initiating therapy would take the medication for up to 5 years.

Benefits and harms

A meta-analysis of women at increased risk of breast cancer who were taking Selective Oestrogen Receptor Modulators (SERMs) (the class of medication that includes tamoxifen), showed a relative risk reduction of 38% for breast cancer incidence. Women taking tamoxifen had a higher rate of endometrial cancer (Hazard ratio [HR]=2.18), venous thromboembolic events (HR=1.60) and cataracts (HR=1.10). Tamoxifen can also increase the likelihood of experiencing gynecological, sexual and vasomotor symptoms, as well as weight gain and headaches.

Prescribing

The recommendations for chemoprevention are supported by a shared-care framework. Patients at increased risk of breast cancer will generally be seen in clinical genetics clinics, family history clinics, or breast cancer departments. The option of tamoxifen will be discussed in secondary care and patients who are interested in taking tamoxifen will be referred back to primary care for their GP to initiate prescription. Tamoxifen is not licensed for a primary prevention indication, and therefore all prescriptions have to be made ‘off-label’.

Please confirm you have read and understood the above by clicking on the next button.

Before today, were you aware that tamoxifen can be used to reduce the risk of breast cancer in women with a family history of the disease?

- a) Yes
- b) No

Before today, were you aware of the ‘NICE clinical guidelines’ or ‘Healthcare Improvement Scotland guidelines’ outlining recommendations regarding the use of tamoxifen for primary prevention?

- a) Yes

b) No

How did you first become aware that tamoxifen could be used to reduce the risk of breast cancer in women with a family history of the disease?

Tick all that apply

	Yes	No
Previously raised by a patient		
Training days / Educational meetings		
Academic journals		
GP magazines e.g. Pulse		
Informal discussion with colleagues		
National media		
Local guidelines		
National guidelines (e.g. NICE or national equivalent)		
Practice meetings		
Other (please specify)		
Unsure		

Would you be willing to write the prescription for Sarah?

- a) Not at all willing
- b) Probably not willing
- c) Probably willing
- d) Definitely willing

Would you want to speak with anyone else before you decided whether to write this prescription?

- a) Yes
- b) No

Please describe who you would want to speak with and why before you decided whether to write this prescription.

A number of factors have been identified in interviews with GPs that could influence whether they would be willing to prescribe tamoxifen. How much do you **agree or disagree** that the following factors affected your decision of whether or not to write a prescription for Sarah?

	Strongly disagree	Disagree	Agree	Strongly agree
The evidence for the benefits of the drug				
The evidence for the harms of the drug				
Prescribing 'off-label' because tamoxifen is not licensed for primary prevention				
The first prescription being made by a family history clinician				
The first prescription being made by you				
The financial costs of tamoxifen				
Sarah's level of risk for breast cancer				
Sarah's interest in taking tamoxifen				
Sarah's awareness of the possible harms and benefits				
Your confidence in your knowledge of tamoxifen				
Sarah's support from the family history clinician				
The attitudes of your colleagues who are at the same career stage as you				
The attitudes of your colleagues who are more senior than you				
The prescribing budget in your General Practice				
The policy of your Clinical Commissioning Group				
The existence of NICE guidelines (or national equivalent)				
Are there any other factors not listed here that you believe would influence your decision-making? (Please Specify)				
If you do not have any further comments, please type 'n/a'				

How comfortable would you feel discussing the possible benefits and harms of tamoxifen with Sarah?

- a) Very uncomfortable
- b) Quite uncomfortable
- c) Quite comfortable
- d) Very comfortable

If Sarah started taking tamoxifen, how comfortable would you feel managing her care for the duration of the prescription?

- a) Very uncomfortable
- b) Quite uncomfortable
- c) Quite comfortable
- d) Very comfortable

Do you have any comments regarding the prescription of tamoxifen for women at increased risk of breast cancer?

If you do not have any further comments, please type 'n/a'

Has your clinical commissioning group discussed the use of tamoxifen for primary prevention?

- a) Yes
- b) No
- c) Don't know

What was the outcome?

- a) Local policy in place
- b) Still under discussion
- c) No policy formed
- d) Unsure
- e) Other (please describe)

In your opinion, who is responsible for making local policy decisions regarding the use of tamoxifen for primary prevention?

- a) Local clinical commissioning groups
- b) Your own General Practice
- c) Local Medicines Management Group, Drug and Therapeutic Committee or equivalent
- d) Other (please specify)

In your opinion, would clinical commissioning groups have any concerns about GPs prescribing tamoxifen for primary prevention?

- a) Yes
- b) No

What concerns do you think the clinical commissioning groups would have about GPs prescribing tamoxifen for primary prevention?

Aspirin: The Facts

Background – Lynch Syndrome

Lynch Syndrome was formerly known as hereditary non-polyposis colorectal cancer (HNPCC) and Muir Torre syndrome. In the UK, between 1 in 400 and 1 in 1200 people are affected by Lynch Syndrome. Approximately 80% of men and 40% of women with Lynch Syndrome develop colorectal cancer by age 70 years. They are also susceptible to other cancers including endometrial, ovarian and stomach cancer.

Please confirm you have read and understood the above by clicking on the next button.

Before today, had you heard of Lynch Syndrome, HNPCC or Muir Torre syndrome? (tick all that apply)

- a) Yes, Lynch Syndrome
- b) Yes, HNPCC
- c) Yes, Muir Torre syndrome
- d) No, hadn't heard of any

Aspirin and Lynch Syndrome

A randomised controlled trial (the CaPP2 trial) has shown the long term use of daily aspirin (600mg) by people with Lynch Syndrome can reduce the incidence of colorectal cancer and other cancers associated with the syndrome. A dose non-inferiority study (the CaPP3 trial) comparing 100mg, 300mg or 600mg of aspirin per day is underway to determine the optimal dose of aspirin for Lynch Syndrome carriers. For those who are ineligible for the CaPP3 trial or who do not wish to enter, the 2013 European Guidelines for the clinical management of Lynch Syndrome recommend patients should use low-dose aspirin (≤ 100 mg).

At all doses, there is an age-dependent increased risk of bleeding, especially gastrointestinal bleeding, and peptic ulcer. Despite the potential for side-effects and the uncertainty regarding dose, use of aspirin among Lynch Syndrome carriers is a generally accepted recommendation.

Please confirm you have read and understood the above by clicking on the next button.

Before today, were you aware aspirin could reduce the risk of cancers associated with Lynch Syndrome?

- a) Yes
- b) No

Have you ever seen a patient with Lynch Syndrome in your practice?

- a) Yes
- b) No
- c) Unsure

Have you ever discussed the use of aspirin with a Lynch Syndrome carrier?

- a) Yes
- b) No
- c) Unsure

If a patient was recommended to take aspirin by a clinician in secondary care, how comfortable would you feel discussing the possible benefits and harms of aspirin with a Lynch Syndrome carrier?

- a) Very uncomfortable
- b) Quite uncomfortable
- c) Quite comfortable
- d) Very comfortable

Imagine the CaPP3 study shows that 100mg of aspirin is the optimal dose for reducing the incidence of cancer in Lynch Syndrome carriers.

How willing would you be to prescribe aspirin (**100mg**) for a patient with Lynch Syndrome?

- a) Not at all willing
- b) Probably not willing
- c) Probably willing
- d) Definitely willing

Imagine the CaPP3 study shows that 300mg of aspirin is the optimal dose for reducing the incidence of cancer in Lynch Syndrome carriers.

How willing would you be to prescribe aspirin (**300mg**) for a patient with Lynch Syndrome?

- a) Not at all willing
- b) Probably not willing
- c) Probably willing
- d) Definitely willing

Imagine the CaPP3 study shows that 600mg of aspirin is the most effective dose for reducing the incidence of cancer in Lynch Syndrome carriers.

How willing would you be to prescribe aspirin (**600mg**) for a patient with Lynch Syndrome?

- a) Not at all willing
- b) Probably not willing
- c) Probably willing
- d) Definitely willing

Background - Population risk

Aspirin has been tested as a chemoprevention medication among population risk subjects. Two high dose aspirin trials ($\geq 500\text{mg}$) have shown an overall 37% reduction in colorectal cancer incidence in population risk participants who took aspirin for at least 5 years. Three trials of

low-dose aspirin (75-300mg) found a 25% reduction in colorectal cancer incidence. Data from seven pooled trials suggests a 40% reduction in colorectal cancer mortality, and this is unrelated to dose.

In the UK, there is no national policy around the use of aspirin for cancer prevention among people at population risk. Draft guidance from the US Preventive Services Task Force in the United States recommends offering low-dose aspirin ($\leq 100\text{mg}$) to adults at age 50–59 years for the prevention of colorectal cancer and cardiovascular disease.

Before today, were you aware aspirin could reduce the risk of colorectal cancer in population risk individuals?

- a) Yes
- b) No

Have you ever discussed the use of aspirin for cancer prevention with a patient at population risk?

- a) Yes
- b) No
- c) Unsure

How comfortable would you feel discussing the benefits and harms of aspirin with a patient at population risk who wanted to take it to prevent colorectal cancer?

- a) Very uncomfortable
- b) Quite uncomfortable
- c) Quite comfortable
- d) Very comfortable

Thank you very much for your time so far, your contribution is very much appreciated, just a few demographic questions and your study will be complete.

Please fill these next few questions out carefully, they will be important in helping us to analyse the regional data and patterns essential to this research.

Please be assured once more that your responses are aggregated to provide an overall picture of attitudes and prescribing in the area discussed. We will not attempt to identify individual GPs from the data we are provided with.

About your General Practice

What is the name of your General Practice?

What is the postcode of your General Practice?

What is the list size in your General Practice? (approx. patient numbers)

Is your General Practice a training practice? Yes/ No

Please indicate your gender

- a) Male
- b) Female

Please indicate your age.

- a) Under 30
- b) 30 – 39
- c) 40 – 49
- d) 50 – 59
- e) 60 or over

Do you have a MRCGP qualification?

- a) Yes
- b) No

Year Gained?

Which of the following best describes you?

- a) GP specialist trainee
- b) GP Partner
- c) Salaried GP
- d) Other (please specify)

What year did you qualify in the area of General Practice?

Where are you currently practising?

How many sessions per week do you work?

Do you have a special interest in any of the following?

- a) Cancer
- b) Preventive medicine
- c) Family history
- d) Genetics
- e) None of the above

Please indicate if you are willing to be re-contacted in the event that we need to ask any follow up/ clarifying questions on this topic?

- a) Yes
- b) No

Please indicate if you would like to a summary of the results of this survey? These would be sent to you via email after completion of analysis.

- a) Yes
- b) No

Your answers will remain anonymous. However, if you want to see a summary/analysis of everyone's answers, then please feel free to leave your name and email address here.

APPENDIX THREE: RESPONDENTS

Overall, 13,764 GPs were sent an email link to the questionnaire. Data from 1007 GPs were available for analysis.

An overview of the respondents is shown in Table 2. The sample closely matched the overall proportion of GPs in each country according to national estimates from 2013.⁴⁶ By comparison with national data, the GPs responding to this survey were more likely to be a salaried GP, younger, male and from practices with larger list sizes and less deprivation. Almost one quarter (22.3%) of the English GPs reported having a role in commissioning.^{xxxii}

Country	Sample (%)	National data (%)
England	85.6	82.8
Scotland	7.8	9.8
Wales	3.9	4.7
Northern Ireland	2.7	2.7
Occupation^{xxxiii}		
GP partner	58.4	67.6
Salaried / locum GP	38.5	21.2
GP retainers	0.3	0.9
GP specialist trainee	2.0	10.3
Other	0.8	-
Gender^{xxxiv}		
Male	57.8	50.8
Female	42.2	49.2
Age^{xxxv}		
<50	72.3	57.2
50+	27.7	38.0
List size of practice (mean, SD)^{xxxvi}	9515 (5878)	7338 (4422) (England only)
IMD score (mean, SD)^{xxxvii}	14891 (9457.5)	13736 (9403) (England only)

^{xxxii} Only English GPs were asked about their commissioning role, as GPs from Scotland, Wales and Northern Ireland do not take on this responsibility.

^{xxxiii} Data source: Table 3 in BMA briefing document.¹⁴

^{xxxiv} Data source: Table 4 in BMA briefing document.¹⁴

^{xxxv} Data source: Table 6 in BMA briefing document.¹⁴

^{xxxvi} Data source: Public Health England (<http://bit.ly/27sadYT>)

^{xxxvii} Note: N=467 due to missing data. Data were missing because of refusal to provide postcode data (n=456), unavailable IMD data for specific postcodes (n=2). The remaining missing data are because IMD equivalents in Scotland (n=49), Northern Ireland (n=14) and Wales (n=19) are not comparable to the English Index.

A minority had a special interest in cancer (12.4%), preventive medicine (14.2%), family history (5.4%) and genetics (3.3%).

	High risk, GP % (N)	Mod. risk, GP % (N)	High risk, other % (N)	Mod. risk, other % (N)
Overall	175 ^{xxxviii}	252	251	250
Nation				
England	93.1	91.7	92.0	94.8
Scotland	-	-	-	-
Wales	4.0	5.2	4.0	3.6
Northern Ireland	2.9	3.2	4.0	1.6
GP Status				
GP Partner	59.4	56.3	56.2	59.6
Salaried / locum GP	39.4	39.3	41.4	36.8
GP retainers	0	0	0.4	0.4
GP Specialist trainee	0.6	3.2	1.6	2.4
Other	0.6	1.2	0.4	0.8
Gender				
Male	57.1	57.9	55.8	58.4
Female	42.9	42.1	44.2	41.6
Age				
<50	72.0	73.0	73.7	70.4
50+	28.0	27.0	26.3	29.6
Specialisms				
Cancer	14.9	14.7	10.4	11.6
Preventive medicine	14.7	13.1	18.2	28.0
Family history	10.4	4.4	2.8	7.2
Genetics	11.6	3.6	1.2	3.6

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