

General Practitioner attitudes towards prescribing tamoxifen for the primary prevention of breast cancer

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ABSTRACT

Background: The Cancer Strategy for England (2015-2020) recommends general practitioners (GPs) prescribe tamoxifen for breast cancer primary prevention among women at increased risk.

Aim: To investigate GP attitudes towards prescribing tamoxifen.

Design and Setting: In an online survey, GPs in England, Northern Ireland and Wales (n=928) were randomised using a 2x2 between-subjects design to read one of four vignettes describing a healthy patient seeking a tamoxifen prescription (ISRCTN14292000).

Method: In the vignette, the hypothetical patient's breast cancer risk ('moderate' vs. 'high') and the clinician initiating the prescription ('GP prescriber' vs. 'secondary care clinician [SCC] prescriber') were manipulated in a 1:1:1:1 ratio. Outcomes were willingness to prescribe, comfort discussing harms and benefits, comfort managing the patient, factors affecting the prescribing decision, and awareness of tamoxifen and the NICE guideline CG164.

Results: Half (51.7%) of the GPs knew tamoxifen can reduce breast cancer risk, a quarter (24.1%) were aware of NICE guideline CG164. Respondents asked to initiate prescribing ('GP prescriber') were less willing to prescribe tamoxifen than those continuing a prescription initiated in secondary care ('SCC prescriber') (68.9% vs. 84.6%, $p<0.001$). The GP prescribers reported less comfort discussing tamoxifen (53.4% vs. 62.5%, $p=0.005$). GPs willing to prescribe were more likely to be aware of the NICE guideline ($p=0.039$) and to have acknowledged the benefits of tamoxifen ($p<0.001$) and were less likely to have considered its 'off-licence' status ($p<0.001$).

Conclusions: Initiating tamoxifen prescriptions for preventive therapy in secondary care before asking general practitioners to continue the patient's care may overcome some prescribing barriers.

Key words: primary care; general practice; tamoxifen; chemoprevention; preventive therapy; breast cancer

How this fits in

The Cancer Strategy for England recommends GPs prescribe tamoxifen for breast cancer primary prevention among women at increased risk. We showed that GPs are largely unaware of using tamoxifen for primary prevention, and a significant minority may be unwilling to prescribe the drug for eligible patients. Our data show that a shared care agreement between primary and secondary care could alleviate a number of concerns, and facilitate appropriate prescribing.

INTRODUCTION

In the UK, over 53,000 women are diagnosed with breast cancer each year and 11,000 die of the disease (1). Women with a family history of the disease are at increased risk, and this accounts for 5-10% of all breast cancer cases (2). The majority of women with an increased risk of breast cancer are ineligible for prophylactic surgery, and therefore prevention by other means is a priority (3).

In 2013, the UK National Institute for Health and Care Excellence (NICE) issued recommendations regarding the use of two Selective Oestrogen-Receptor Modulators (SERMs), tamoxifen and raloxifene, for women at increased risk of breast cancer due to their family history (3). SERMs reduce breast cancer incidence by 30% or more (4). **The number needed to treat to prevent one diagnosis of breast cancer in the first 10 years is 42.** However, the decision to prescribe SERMs is complicated because current preventive therapy trials are not designed to detect effects on mortality (5), and the medications are not licenced for primary prevention. SERMs also increase the risk of thromboembolic events, endometrial cancer, and menopausal side-effects (4). Only one in 6 women accept the offer of breast cancer preventive therapy, and uptake is significantly lower in non-trial settings (6). The Cancer Strategy for England (2015-2020) has recommended that action be taken to ensure preventive therapy is appropriately prescribed in the National Health Service (NHS) (7).

Our previous qualitative work has suggested GPs and family history clinicians experience barriers to implementing the NICE clinical guideline for familial breast cancer (CG164) (8). Concerns were raised relating to licencing, interpretation of the NICE guideline and responsibility for prescribing. GPs suggested they may be more comfortable continuing a preventive therapy prescription, providing it had been initiated in secondary care. To validate and quantify these findings, we surveyed a national sample of GPs who were randomised to view one of four case studies of a hypothetical patient seeking a tamoxifen prescription for primary prevention.

METHODS

Study design and sample

A national survey of GPs practising in the UK was undertaken in April, 2016. Members of a research panel with over 33,000 members were emailed an invitation to take part. Sampling was done by inviting panellists on an unfiltered random basis to avoid over-sampling. GPs practising in Scotland were excluded from these analyses because an agreed care pathway already exists there for the prescription of tamoxifen (9). GPs practising outside of the UK were excluded. The study was prospectively registered (ISRCTN14292000).

Questionnaire design

Respondents were randomised in a 1:1:1:1 ratio to one of four case study vignettes describing a hypothetical patient at increased risk of breast cancer (Supplementary Table 1). **The vignettes were designed with input from clinical geneticists, medical oncologists, general practitioners and public health specialists. They were intended to be representative of a typical patient attending a family history clinic, and were informed by our earlier research (8).** The vignettes described a hypothetical patient's age (45 years), risk level, premenopausal status, her lack of contraindications, and her discussion in secondary care. The case studies were presented using a between-subjects 2x2 factorial design, where patient risk level (moderate lifetime risk of 17-30% vs. high lifetime risk of $\geq 30\%$) and the clinician responsible for initiating the prescription (GP vs. secondary care clinician) were manipulated. The secondary care clinician was described as a family history clinician. The case study was available to them throughout the survey.

Prior to the vignettes, respondents were informed about the NICE guidelines, the eligibility criteria for tamoxifen, the harms and benefits of the drug, the typical patient pathway, and the licencing status.

This information was available throughout the survey.

Measures

Chemoprevention awareness

Respondents were asked if they were aware tamoxifen could be used for risk reduction in women with a family history of breast cancer, and, if they were aware of the relevant NICE guideline. Respondents answering 'yes' to the second question were asked how they became aware that tamoxifen could be used for primary prevention. Example options are shown in the supplementary material.

Willingness to prescribe

GPs' willingness to prescribe tamoxifen was assessed, and response options were, 'definitely not willing', 'probably not willing', 'probably willing' and 'definitely willing'. Data were combined to reflect unwilling and willing responses.

Comfort discussing harms and benefits of long-term management

GPs were asked to report their comfort in discussing the harms and benefits of tamoxifen with a patient, as well as their comfort in managing the patient for the duration of the prescription. Response options were 'very uncomfortable', 'quite uncomfortable', 'quite comfortable' and 'very comfortable'. Data were combined to reflect GPs who were uncomfortable and comfortable.

Barriers to prescribing

Respondents were offered a series of factors that could potentially affect the willingness of GPs to write a prescription for the hypothetical patient. Respondents were provided with the response categories, 'strongly disagree', 'disagree', 'agree' and 'strongly agree'. Data were combined to reflect agreement and disagreement.

Respondent characteristics

GPs self-reported their gender, age in 10-year bands, status within the practice, region of practice, year qualified in general practice, and special interests.

Statistical analysis

The data were described using percentages. For the vignettes, the main effects of risk and prescriber on willingness to prescribe, comfort discussing tamoxifen and comfort managing the patient were tested using unadjusted logistic regression. Logistic regression models with the interaction between risk and prescriber were also tested. Multivariable logistic regression adjusted for nation, GP status, gender, age, experience and specialisms was used to compare sub-group differences on study outcomes. Unadjusted logistic regression was used to compare differences in endorsement of barriers between GPs who were and were not willing to prescribe tamoxifen. Statistical significance was set at $p < 0.05$. Analyses were conducted using SPSS version 22.

RESULTS

Sample overview

In total, 13,764 of approximately 33,000 GPs were approached via email, and 1,321 started the survey (9.6%). Respondents were excluded if they did not agree to the terms and conditions ($n=35$), did not complete the survey ($n=143$), completed the survey after the deadline ($n=35$) or failed a data quality check ($n=101$). Scottish GPs ($n=79$) were also excluded, leaving data from 928 GPs for this analysis. An overview of the sample compared with national data is shown in Table 1. Participant characteristics across the study arms were comparable (Table 2).

Awareness of tamoxifen and the NICE guidelines

Approximately half (51.7%) of the respondents were aware tamoxifen could be used to reduce the risk of breast cancer, and a quarter (24.1%) were aware of the NICE guideline CG164. Among those who were aware of the NICE guideline, common sources of information about tamoxifen were training days (31.7%), GP magazines (30.9%), and the NICE guideline (30.9%) (Figure 1).

Barriers to prescribing and discussing breast cancer preventive therapy

Willingness to prescribe

The majority of GPs (77.4%) were willing to prescribe tamoxifen for the hypothetical patient (definitely willing, 17.6%; probably willing, 59.8%). The remaining GPs were either probably not

willing (18.1%); not at all willing (4.5%) to prescribe tamoxifen. Male GPs were more likely to report a willingness to prescribe tamoxifen than female GPs (OR=1.38, 95% CI 1.00-1.90, p=0.05).

Willingness to prescribe was unaffected by the other GP characteristics (Table 3).

Table 4 shows the proportion of GPs willing to prescribe tamoxifen in each condition. GPs told they would be asked to be the first prescriber were significantly less willing to prescribe tamoxifen than GPs told they would be asked to continue a prescription initiated in secondary care (68.9% vs. 84.6%, OR=0.40, 95% CI, 0.29-0.55, p<0.001). There were no differences in respondents' willingness according to patient risk (moderate risk: 77.1% vs. high risk: 77.7%; OR=1.04, 95% CI, 0.76-1.41, p=0.83). There was no interaction between the two factors.

Comfort in discussing harms and benefits of tamoxifen

The majority of GPs were either very comfortable (6.5%) or quite comfortable (51.8%) discussing the harms and benefits of tamoxifen. The remaining GPs were either quite uncomfortable (36.6%) or very uncomfortable (5.1%). In multivariable analysis, comfort in discussing the harms and benefits of tamoxifen with a patient was higher among GPs older than 50 years (OR=1.53, 95% CI, p=0.02), with more than 10 years' experience (OR=1.39, 95% CI 1.02-1.91, p=0.04), and those with a special interest in cancer (OR=1.79, 95% CI 1.12-2.85, p=0.02). Comfort discussing tamoxifen was unaffected by the remaining GP characteristics (Supplementary Table 2).

GPs were more likely to report they were comfortable in discussing the harms and benefits of tamoxifen if they were told a secondary care clinician would write the first prescription, compared with those who were told they would be asked to prescribe first (62.5% vs. 53.4%, OR=0.69, 95% CI, 0.53-0.90, p=0.01). There were no significant differences in reported comfort discussing the harms and benefits according to the patient's risk (moderate risk: 56.6% vs. high risk: 60.3%; p=0.25), and there was no interaction between the two factors.

Comfort in managing the patient's care

The majority of GPs were very comfortable (7.8%) or quite comfortable (58.6%) managing the patient, should she decide to take tamoxifen. The remaining GPs were quite uncomfortable (29.8%) or very uncomfortable (3.8%). Comfort managing the hypothetical patient was higher among GPs with a special interest in preventive medicine (OR=1.66, 95% CI 1.03-2.69, p=0.04). Comfort managing the patient was unaffected by all other GP characteristics (Supplementary Table 3).

There were no differences in comfort managing the patient comparing the prescriber manipulation or the patient risk manipulation. There was also no interaction between these variables.

Tamoxifen attitudes according to knowledge of the national guideline

GPs who were aware of the NICE guideline were more willing to prescribe tamoxifen, with 82.4% who were aware being willing to prescribe, compared with 75.7% who were unaware (OR=1.50, 95% CI, 1.02-2.19, p=0.04). Awareness of the NICE guideline also affected reported comfort in discussing the potential harms and benefits of tamoxifen, with 66.5% of those who were aware being comfortable, compared with 55.6% of those who were unaware being comfortable (OR=1.58, 95% CI, 1.16-2.17, p<0.01). There was no difference in comfort in managing the patient according to awareness of the guidelines (OR=1.25, 95% CI, 0.90-1.73, p=0.18).

Factors affecting prescribing decisions

GPs were most likely to agree that the evidence for the benefits of the drug (95.0%), the existence of the NICE guideline (95.0%) and the patient's awareness of the harms and benefits (94.1%) affected their decision (Table 5). GPs who were willing to prescribe were more likely to consider a number of factors than those who were unwilling. Key differences were observed with regard to their consideration of prescribing 'off label' (unwilling=91.4% agreed that it affected their decision, willing=69.6%, OR=4.65, 95% CI, 2.8-7.73, p<0.001), the patient's awareness of the harms and benefits (unwilling=81.9%, willing=97.6%, OR=9.11, 95% CI=5.02-16.53, p<0.001) and the evidence for the benefits of the drug (unwilling=87.6%, willing=97.2%, OR=4.93, 95% CI = 2.69-9.03, p<0.001).

DISCUSSION

Summary

The Cancer Strategy for England (2015-2020) has recommended that work should be done to ensure tamoxifen is appropriately prescribed as preventive therapy to interested patients. Our national study showed that only three-quarters of UK GPs reported that they would be willing to prescribe tamoxifen for a hypothetical patient at increased risk of breast cancer. Willingness was significantly lower among GPs who were told that they would be asked to initiate the drug prescription, compared with GPs who were asked to continue a prescription from a clinician in secondary care. Levels of reported comfort in discussing the harms and benefits of tamoxifen were low, and respondents who were asked to prescribe first reported significantly lower levels of comfort. The most commonly reported barrier among GPs who were unwilling to prescribe was concern about off-label prescribing.

Strengths and limitations

This study was strengthened by its randomised design and large national sample. We were able to compare our sample with the UK GP workforce (10), which showed that the current sample were more likely to be salaried GPs, younger and male. Recruitment was from an online panel, and not all UK GPs are affiliated with the company responsible. Our response rate was low, which may further limit generalisability. Multiple barriers to prescribing tamoxifen were investigated, and therefore the possibility of a type I error is increased. The patient vignette was designed to be representative of a typical patient in this context, but specific characteristics may not match all patients. **Similarly, the healthcare professional was described as a family history clinician, and attitudes towards prescribing may have been different if alternative clinical positions were described.** The vignette was hypothetical, and prescribing behaviour may be different in a clinical setting.

Comparison with existing literature

Our previous qualitative work suggested that a shared care agreement between primary and secondary care would reduce ambiguity for prescribing, and encourage discussions about preventive therapy with high risk patients (8). Our current data support this conclusion. Our earlier work also suggested

GPs are concerned about the lack of licence for tamoxifen when used for prevention (8). The survey responses showed that this is considered in the decision-making of GPs, but other factors had a greater influence. Together, our interview and survey data help to explain why uptake of preventive therapy is lower in routine clinical settings compared with trial participation (6).

Implications for practice

Guidance for prescribing tamoxifen in Scotland has been produced (9), but there is no formal care pathway for the rest of the UK. Developing a pathway involving both primary and secondary care in a shared care agreement could substantially increase GPs willingness to prescribe. While GPs may become more familiar with tamoxifen as a preventive agent over time, shared care agreements could form one facet of a longer term implementation strategy. Consideration would however have to be given to the fact that genetic counsellors do not have prescribing rights, and therefore a supervising clinician would have to be responsible for prescribing in secondary care. The approach we describe is similar to the national prescribing policy developed within the Health Improvement Scotland guidance for tamoxifen (11). We recommend that NHS England, NHS Wales and the Department of Health in Northern Ireland should replicate and adapt the Scottish guidelines.

One of the major barriers to implementing the tamoxifen guidelines is the low awareness of its potential to be used as preventive therapy. While cross-sectional surveys do not allow causal inferences, our data suggest increasing awareness of preventive medications could facilitate appropriate prescribing behaviour. The most common sources of information were training days, GP magazines and national guidelines. Strategies to promote awareness of tamoxifen for primary prevention should consider ways to target these sources. Providing an up-to-date and accurate source of information for GPs so they are prepared to have informed conversations with patients may reduce prescribing barriers. While local decision-aids are currently in use, a single national resource could ensure all patients are provided with the same information.

Developing standardised pro-formas for secondary care clinicians to send to GPs when referring patients to discuss preventive therapy could be a useful strategy to improve GP awareness. These pro-formas could be adapted from those included in the Health Improvement Scotland guidelines (9). Our data suggest encouraging GPs to consider the evidence for the benefits of the drug may encourage prescribing. Perceiving that patients may be lacking awareness of the harms and benefits of tamoxifen was also shown to be a barrier to prescribing among GPs. Highlighting that harms and benefits have already been communicated to the patient by a specialist may alleviate these concerns.

Our data suggest the lack of licence for tamoxifen factors within decision-making, and is the most commonly reported barrier among those who are unwilling to prescribe. One strategy to overcome anxieties related to off-label prescribing is through acknowledgement in the British National Formulary (BNF). While the BNF does not have the authority to licence a medication, it frequently describes alternative unlicensed indications for medications. We suggest that primary prevention is listed as an indication for tamoxifen in the BNF for the appropriate patient groups.

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