

# Preventing the co-prescription of tamoxifen and fluoxetine in General Practice

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## Abstract

In 2010 a population-based cohort study showed that there was decreased efficacy of the breast cancer drug tamoxifen when used in combination with fluoxetine, a commonly used SSRI antidepressant. The aim of this project was to identify patients who may be affected by this co-prescription and suggest a change in medication. The project was conducted across two GP practices in Clevedon (The Riverside Practice & The Green Practice), Bristol. The patients were all from the active patients register at each surgery. A search was conducted to find all those on tamoxifen and fluoxetine, using the EMIS computer system. These patients would then be sent a letter to attend clinic. The new data would then be discussed with them before recommending a change of antidepressant (typically to sertraline). Three patients were found to be on both medications. They were all called into clinic and changed from fluoxetine to sertraline. Furthermore a presentation was given to all GPs at the two surgeries alerting them to the new guidelines. A message was also set up to flash on the computer system whenever an attempt was made to co-prescribe the two drugs. All the patients on tamoxifen in these two practices are now receiving the optimum treatment. Furthermore interventions have been put in place to ensure that this remains the case in future. Another data collection should be conducted in one year. This project provides a good example of how this problem could be resolved at other GP surgeries.

## Problem

Tamoxifen and fluoxetine are two of the most commonly prescribed medicines in the UK and as such there is likely to be some overlap of the two drugs in individual patients. A recent study has shown that fluoxetine could actually reduce the action and effectiveness of tamoxifen in preventing the growth of breast cancer.

## Background

Some breast cancer requires oestrogen to grow. Tamoxifen is an endocrine therapy that inhibits the oestrogen-receptor in breast tissue, and thus effectively stops the growth of the cancer. It is currently used in both pre- and post-menopausal women with oestrogen receptor-positive breast cancer and since it came off patent in 2002 it has become the world's largest selling hormonal drug for breast cancer.

Fluoxetine, meanwhile, is approved for the treatment of major depression as well as other psychological disorders. It is currently the third most prescribed antidepressant.

In 2010 a population-based cohort study showed that there was an increased risk of death from breast cancer in patients on both tamoxifen and fluoxetine (SSRI) as opposed to tamoxifen alone (Andersohn & Willich, 2010). The risk of death was also shown to increase the longer the patient was taking both drugs. This is because tamoxifen is a pro-drug that requires conversion to an active metabolite via the cytochrome P450 system. Thus drugs such as fluoxetine, that inhibit this system, also reduce the amount of active drug, endoxifen. The study showed that other drugs that could have similar interactions are paroxetine, bupropion, quinidine and cinacalcet.

## Baseline Measurement

The problem was quantified across two GP practices in Clevedon, Bristol (The Riverside Practice and the Green Practice). This was done by auditing the active patient population to seek those patients on both tamoxifen and one of the drugs above. This was done using the EMIS computer system used at both practices with the search terms Tamoxifen [AND] Fluoxetine [OR] Paroxetine [OR] Bupropion [OR] Quinidine and [OR] Cinacalcet.

In the Green Practice there were 7,424 registered patients, of whom five were on tamoxifen. One of these patients was on both tamoxifen and fluoxetine. Meanwhile in the Riverside Practice there were 9,228 active patients, 13 of whom were on tamoxifen. Two of these patients were on both tamoxifen and fluoxetine. Thus in total in our cohort there were three patients on both tamoxifen and fluoxetine.

## Design

It was clear from a baseline data and process flow that changes were required to firstly alter the medication of those patients at risk of the drug interactions. Furthermore there was a need to implement a system to ensure no further prescriptions would create such risk.

Three interventions were decided upon. Firstly the three patients found to be on both tamoxifen and fluoxetine would be called in for a review of medication. Secondly a warning message would be put onto the EMIS computer system that is used for drug prescriptions; this both flashes and makes a sound when an attempt is made to prescribe tamoxifen with one of the above drugs (or visa versa). Finally the drug interactions and this audit would be discussed at a

staff meeting.

## Strategy

### PDSA Cycle 1

Those patients on both tamoxifen and fluoxetine were called into the surgery. The relevant new information was discussed and change from fluoxetine to sertraline was recommended and accepted by all. This achieved the goal of removing those currently at risk but did not deal with the possibility of future recurrences.

### PDSA Cycle 2

Two interventions were performed to stop future co-prescriptions. Firstly a prompt was put on the EMIS computer system used by the GPs at both practices. This will appear and make a sound when an attempt is made to prescribe the two drugs together. Furthermore the GPs were informed about the new data.

See supplementary file: ds1557.doc

## Post-Measurement

Our intervention has provided a 100% reduction in those at risk from the interaction of the two drugs in our population. A further check was performed using the same EMIS system four weeks after the intervention and showed that there were no new cases on both tamoxifen and fluoxetine. This will be re-checked in 12 months time.

## Lessons and Limitations

This project had few problems. The GP practices were fortunate enough to have a computer technician who was comfortable with the EMIS system to implement the new prompt, although this would be a consideration for other practices.

A further theoretical problem would be encouraging the patients to attend the clinic to have their medication changed, but this was not the case in the project. A further consideration for other practices would be the wording of the letter or phone call that goes out to their affected patients. This is a delicate situation as the implication is the patient has not been receiving the optimum treatment for their breast cancer during the time they have been on fluoxetine.

This project is definitely scaleable and should be implemented in all GP practices in the UK. We have outlined a template that worked across these two practices; however, given the small number of affected patients there may be further unforeseen complications if implemented in a larger practice.

## Conclusion

The problem that we started with was the recent discovery of an interaction between fluoxetine and tamoxifen that caused the latter

to be less effective. This has a large implication on affected patients as it means they are receiving substandard treatment for their breast cancer.

We implemented two quality improvement cycles. The first helped us identify those patients that were affected and change their medication to eradicate the problem. The second allowed us to put in place measures that should stop the co-prescription of these two drugs in the future.

The project was successful in that at the current time there are no people across the active databases for the two GP practices who are at risk of the interaction. There is plenty of scope for this project to be implemented in all GP practices in the UK and we strongly encourage this. Furthermore the database will be re-checked for these two practices in one year to ensure the ongoing success of our interventions, reflecting the continual nature of quality improvement.

## References

Andersohn F., Willich S. Interaction of serotonin reuptake inhibitors with tamoxifen. BMJ 2010;340:c783