

**UNIVERSITY OF BIRMINGHAM AND YORK HEALTH
ECONOMICS CONSORTIUM
(NICE EXTERNAL CONTRACTOR)**

Health economic report on piloted indicator

Pilot QOF indicators:

The percentage of women with schizophrenia, bipolar affective disorder or other psychoses under the age of 45 years who have been given information and advice about pregnancy, conception or contraception tailored to their pregnancy and contraceptive intentions recorded in the preceding 12 months.

Potential output: Recommendations for NICE Menu

Contents

Contents	1
Introduction	2
Guideline References for the Indicator.....	2
Economic Rationale for the Indicator	3
Evidence on Pooled Estimate of Abnormality Risk	5
Evidence on Effects of Specific Drugs	7
Evidence on Costs of the Indicator	8
Summary	8
References	10

Introduction

This briefing paper presents a cost-effectiveness analysis for a potential indicator from pilot 8 of the NICE Quality and Outcomes Framework (QOF) indicator development programme:

The percentage of women with schizophrenia, bipolar affective disorder or other psychoses under the age of 45 years who have been given information and advice about pregnancy, conception or contraception tailored to their pregnancy and contraceptive intentions recorded in the preceding 12 months.

This paper sets out our assessment of the economic evidence on the indicator.

Guideline References for the Indicator

The NICE guideline on bipolar disorder refers to the risk of abnormalities and malformation in babies due to medication for mental illness [1]. The guideline does not refer to pregnancy advice itself but rather specifies drugs (in particular valproate, carbamazepine and lamotrigine), that should be stopped if a woman is planning to get pregnant or on becoming pregnant if the pregnancy was unplanned. The guidance states that valproate should not be routinely prescribed to women of child bearing age.

The NICE guideline on antenatal and postnatal mental health gives the following recommendation [2]:

“Women with an existing mental disorder who are pregnant or planning a pregnancy, and women who develop a mental disorder during pregnancy or the postnatal period, should be given culturally sensitive information at each stage of assessment, diagnosis, course and treatment about the impact of the disorder and its treatment on their health and the health of their foetus or child. This information should cover the proper use and likely side effects of medication.”

The NICE guideline on schizophrenia makes no mention of advice on contraception or pregnancy [3].

Economic Rationale for the Indicator

None of the NICE guidance referred to includes an economic model of advice on pregnancy to women with serious mental illness or on the cessation of drug treatment if a woman with serious mental illness is planning for pregnancy or becomes pregnant. No other relevant economic models could be identified through a literature search of the databases of the Centre for Reviews and Dissemination.

The indicator states that the advice given to women of child bearing age with schizophrenia, bipolar affective disorder or other psychosis is to be tailored to their pregnancy and contraceptive intentions. It does not state that the advice should be tailored to their current pharmaceutical treatment for their condition. For the purposes of this analysis, however, it has been assumed that the advice being offered is around pharmaceutical treatment. To produce an economic analysis, evidence in several key areas is required.

Stopping or swapping efficacious medication or treatment either before a planned pregnancy or during the pregnancy itself may have an impact on a woman's (and potentially unborn child's) quality of life. The NICE guidance on bipolar disorder suggests that patients may be offered an antipsychotic as an alternative to other drugs [1]. For an economic model an estimate is required of the potential quality adjusted life years (QALY) loss from women stopping taking medications where either:

- No harm would have arisen to the foetus should a woman have continued on a specific medication or;
- Harm did arise to the foetus or mother because mental health issues escalated when effective treatment was stopped.

No evidence was found for either of these situations.

ITEM 17d – Serious mental illness – YHEC report

An economic model would require a link between the drugs being prescribed to treat the conditions identified in the indicator and health or economic outcomes for either the mother (potential or actual) and the baby (born or unborn). In this case, the available guidance suggests that the economic argument is one of avoided birth defects caused by medications for mental illness. There are two ways to potentially model the economic consequences of avoided birth defects.

The first is to assume a flat rate of birth defects for any medication that is avoided when a woman eligible to be included in the indicator is given appropriate conception, contraception and pregnancy advice. This relies on a pooled estimate of abnormality risk from medications for mental illness.

The second approach to economic modelling is to examine evidence on the rates and nature of foetal abnormalities of the specific drugs that the NICE guidance on bipolar disorder recommends should be discontinued or modified when women plan to become or do become pregnant.

Evidence on Pooled Estimate of Abnormality Risk

Evidence on the pooled estimate of abnormality risk is not available, although the US Food and Drug Administration reported in 2012 that a range of anti-psychotic drugs should be prescribed with precaution to pregnant women¹. This was due to concerns about withdrawal symptoms in babies whose mothers had been taking these drugs, especially during the third trimester.

There is some evidence that anti-epileptic drugs, some of which are prescribed for women with serious mental illness, can cause still births and developmental delay [4]. However, these studies are small and of poor methodological quality for evidencing causality. In the absence of robust data this 'pooled' approach is therefore not feasible.

¹ <http://www.webmd.com/mental-health/news/20110222/antipsychotics-in-pregnancy-risky-for-newborns>

ITEM 17d – Serious mental illness – YHEC report

Evidence on Effects of Specific Drugs

Valproate

Valproate in pregnancy has been reported to result in delayed cognitive development at three years of age and in significantly higher rates of autism [5, 6]. This evidence is likely to have led NICE to recommend that valproate should not be offered to women of child bearing age and it is thought that only a very small number of women are receiving this drug for serious mental illness [7].

As women under 45 should not routinely be prescribed valproate (and where they are prescribed the drug, they should be advised of the risks should they become pregnant), it seems unreasonable to include advising on this drug as part of any economic analysis of the indicator.

Carbamazepine

There is some evidence from a meta-analysis of over 1,000 births that carbamazepine may result in foetal abnormalities including neural tube defects, cardiovascular and urinary tract anomalies, and cleft palate [8]. The meta-analysis was undertaken across studies that used the drug for a range of uses including anti-epileptic purposes. Whilst the dosages for the drug appear to be the same regardless of the condition being treated², it is not clear what the difference in outcome is from stopping women taking the drug when they have bipolar disorder compared to stopping them taking the drug if they have epilepsy.

Lamotragine

The evidence on foetal abnormalities from lamotragine is mixed, with no unequivocal evidence found in human studies that it causes harm during pregnancy. Lithium is also mentioned in the NICE guidance but it states that the drug can be continued if closely monitored.

² http://www.drugs.com/dosage/carbamazepine.html#Usual_Adult_Dose_for_Epilepsy
Primary Care Quality and Outcomes Framework Advisory Committee
11 and 12 June 2014
Agenda item 17d: Serious mental illness – YHEC report

Little evidence, therefore, exists to link changes in use of specific drugs for serious mental illness to specific outcomes for mother and baby. The exception is valproate but this should not be routinely prescribed to women of child bearing age in any case and if it is they should be advised of the importance of contraception at the time of prescription.

Evidence on Costs of the Indicator

To develop an economic model evidence would also be needed on the cost of advice to women with serious mental illness of either altering a woman's medication use or on their use of contraception. No relevant evidence could be found from guidelines or studies reviewed.

Workload diaries received from pilot practices provide some evidence that the delivery of the indicator involves a face to face discussion with a GP, within a standard GP appointment time. For modelling purposes this would be recorded as a 17.2 minute consultation with a cost of £66 [9]. However this does not disaggregate the various activities that might be involved (advice on contraception, conception or pregnancy).

If a patient receives advice on pregnancy then there may also be an impact on drug costs. If patients cease taking SMI drugs then there would be a reduced cost or if their drugs were switched for different drugs then there would be a change in costs. This cannot be accurately estimated from the evidence available.

Summary

There is a lack of evidence to support economic modelling for the indicator.

This includes:

- The effect of advice to women to alter their medication use or to effectively use contraception;
- The costs involved in offering alternative drug treatments to women when they are planning a pregnancy or become pregnant

ITEM 17d – Serious mental illness – YHEC report

- The outcomes for mothers and children (both born and unborn) when pre-pregnancy treatment is withdrawn or altered;
- Evidence from randomised (or indeed observational) studies on the dosages of drugs given for anti-psychotic purposes and the impact these have on the unborn child.

In the absence of this evidence, economic modelling of the indicator would only be possible with assumptions across costs, effectiveness and utility. Such a model would be of limited use and could be misleading. As such, no economic analysis has been undertaken for this indicator. The lack of evidence does not necessarily mean that the intervention is not cost-effective.

The following table gives a summation of the considerations in this paper:

INDICATOR ADVICE	ADVICE COSTS	ADDITIONAL INTERVENTION	UNCERTAINTY
Advice about pregnancy	Consultation cost	Change or stop SMI drugs (leads to reduced costs if stopped or change in costs if swapped)	Likelihood of harm to baby or mother, or no harm or benefits to baby or mother
Advice about conception	Consultation cost	None	None
Advice about contraception	Consultation cost and prescription costs of contraceptives	None	None

References

- [1] National Institute for Health and Care Excellence. Clinical Guideline 38: Bipolar disorder. The management of bipolar disorder in adults, children and adolescents, in primary and secondary care. 2006
- [2] National Institute for Health and Care Excellence. Clinical Guideline 45: Antenatal and postnatal mental health. 2007
- [3] National Institute for Health and Care Excellence. Clinical Guideline 178: Psychosis and schizophrenia in adults. 2014
- [4] Moore SJ, Turnpenny P, et al. A clinical study of 57 children with fetal anticonvulsant syndromes. *J. Med. Genet* 2000. 37 (7): 489–97
- [5] Meador KJ et al. for the NEAD Study Group. Cognitive function at 3 years of age after fetal exposure to antiepileptic drugs, *N Engl J Med.* 2009 360:1597
- [6] Rasalam AD, Hailey H, et al. Characteristics of fetal anticonvulsant syndrome associated autistic disorder. *Dev Med Child Neurol* 47 2005 (8): 551–5
- [7] National Institute for Health and Care Excellence. Implementation uptake report. Lithium and valproate prescribing for bipolar disorder
- [8] Prakash, Prabhu LV, et al. Lamotrigine in pregnancy: safety profile and the risk of malformations. *Singapore Med J.* 2007;48(10):880-3.
- [9] Unit Costs of Health & Social Care 2013. Personal Social Services Research Unit (PSSRU). Compiled by Lesley Curtis. University of Kent.