



Values of adding the
DNBC to register
based studies on

SSRI use and risk of miscarriage

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Already known at that time

- Concerns about increased risk of miscarriage following SSRI use in pregnancy
- Studies with self-reported data in teratology information services had reported no statistically

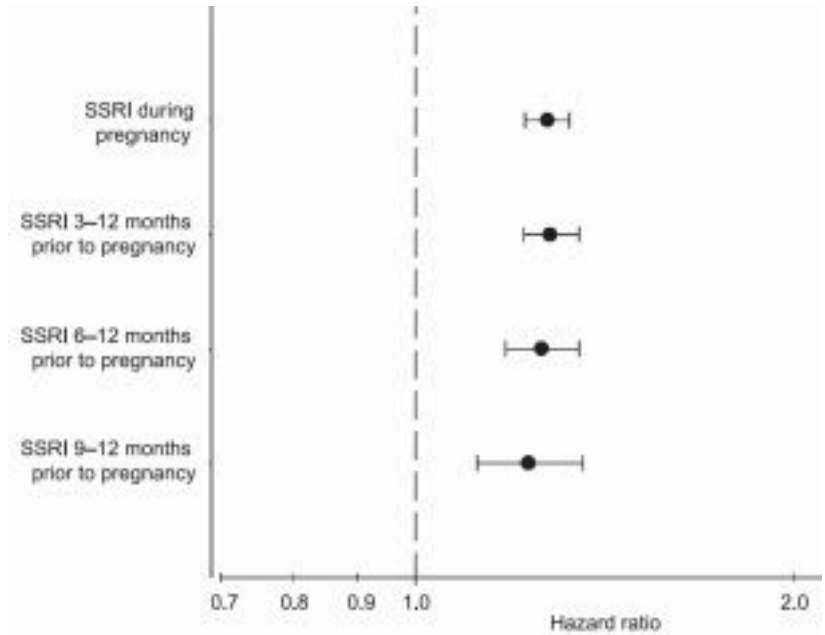
significant effect – properly due to sample size

- Register-based studies had indicated 20-60% increased risk of miscarriage following SSRI use in pregnancy

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Studies based on the Danish registries

Adjusted RR for miscarriage according to AD and depression



| | Diagnosis of depression | | No diagnosis of depression | | Marginal | |
|-------------------|-------------------------|-----------|----------------------------|-----------|------------------|-----------|
| | Exposed | Unexposed | Exposed | Unexposed | Exposed | Unexposed |
| Event | 218 | 105 | 2427 | 110377 | 2637 | 13482 |
| No event | 1465 | 715 | 11962 | 708049 | 12626 | 708794 |
| Risk ^a | 0.125 | 0.128 | 0.176 | 0.135 | 0.171 | 0.135 |
| RR | 0.98 (0.79;1.23) | | 1.31 (1.26;1.35) | | 1.36 (1.22;1.51) | |
| aRR ^b | 1.06 (0.80;1.24) | | 1.17 (1.13;1.23) | | 1.14 (1.10;1.18) | |

^aProbabilities of event.

^bAdjusted for maternal age, cohabitation, income, education, history of severe mental disorder and drug abuse in case of the marginal analysis and the stratified analysis for no diagnosis of depression.

Adjusted for maternal age, cohabitation, education, and history of severe mental disorder in case of the stratified analysis for a diagnosis of depression.

Crude RR for miscarriage according to specific types of AD

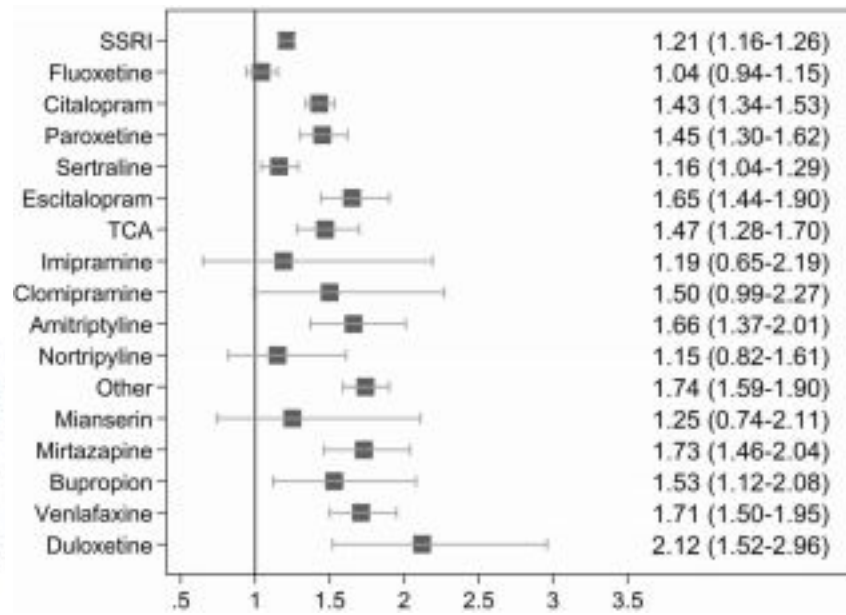


Fig. 2. The hazard of miscarriage in women exposed to selective serotonin reuptake inhibitors (SSRI) in different periods before and during pregnancy. Hazard ratios are adjusted for year of outcome or censoring, maternal age, educational length, income, and the number of previous miscarriages.

Kjaersgaard et al.

PLoS ONE 2013 Andersen et al. Obstet Gynecol 2014

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The association could be due to

- Misclassification – redeemed prescriptions \neq use •

Confounding by illness severity – hospital contacts

- Confounding by life-style – no information on health behaviors

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Aim

Advance previous studies by addressing:

Whether mental illness, lifestyle factors and misclassification of

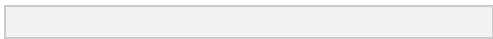


SSRI
explain the observed
association

within the registries



DNBC outline

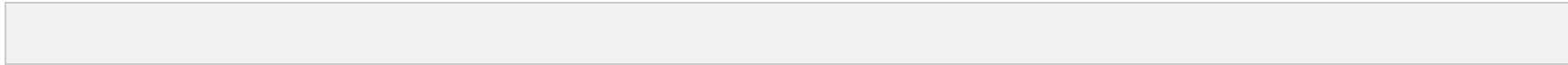


SSRI use

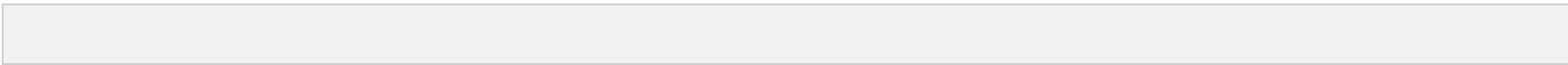
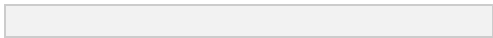
- First trim. use: -4 wks from LMP to termination or GA 84 days
- Discontinued use: -1 to -3 mo. from LMP and not in pregnancy
- Unexposed: no redemption from -3 mo. from LMP through end of 1st trim.
- First trim. use: -4 wks from LMP to enrollment or GA 84 days

Confounding by indication





Misclassification of SSRI



Conclusion

Information bias and especially confounding compete as explanations for the observed

- Higher risk among discontinued users and lower or identical risk among pregnancies exposed to SSRI compared to SSRI-unexposed pregnancies with a recent maternal depression/anxiety diagnosis
- Discontinued users seem to be a better comparison group to SSRI users than SSRI unexposed



Thank you for your attention

Questions?

- DNBC participants
- DNBC funders
- Co-authors

