**Introduction/Background & aims**

Adverse drug reactions (ADRs) are a significant cause of morbidity and mortality worldwide, with females experiencing higher rates of reported ADRs compared to males [1]. Statins are a cornerstone of primary and secondary prevention for cardiovascular disease and are the most commonly prescribed medication in the UK. Previous surveys have shown that females have higher rates of myalgia with statin therapy compared to males, and higher rates of stopping statin therapy [2]. It is unclear how sex influences statin ADR reporting in the UK Yellow Card Scheme. The aim of this study was therefore to explore sex-specific ADR signals for statin therapy.

**Method/Summary of work**

ADR data from January 2001 – March 2021 were downloaded from the Yellow Card Scheme website. Serious or fatal ADRs with a recorded sex were included. Proportional reporting ratios (PRR) and 95% confidence intervals were calculated for ADRs associated with atorvastatin and simvastatin in males or females [3]. ADRs with 3 or less reports were excluded. A sex-reporting ratio (SRR) for each ADR was calculated using the formula: PRRfemale/PRRmale with propagation of error to create 95% confidence intervals. A SRR > 1 suggests a higher reporting of the ADR compared to background signal in females versus males for the same drug. Significant SRRs (adjusted for multiple testing with Bonferroni’s correction) were grouped according to clinical relevance to establish patterns in sex-specific ADR reporting.

**Results/Discussion**

A total of 1,397,968 unique reports of 10,707 ADR types were included, covering 2,250 drugs. There was a higher proportion of ADRs among females (57.2%) compared to males. There were 12,243 and 10,842 ADRs for simvastatin and atorvastatin respectively, with greater reporting of statin ADRs among males (54.4% simvastatin and 53.7% atorvastatin reports from males). Signals for inflammatory muscle disorders were disproportionately higher in females compared to males. Reports of liver function abnormalities were associated with atorvastatin use in females (SRR 2.4, 95% CI 2.1 – 2.9), with trends for other measurements of hepatic dysfunction in women taking atorvastatin, but not simvastatin (figure). Consistent across both statins, signals for arthralgia and gastrointestinal side-effects were disproportionately higher in males compared to females.

Chart, table

Description automatically generated with medium confidence

Figure: Forest plot showing the sex-reporting ratio (SRR) and 95% confidence intervals for various adverse drug reactions with simvastatin and atorvastatin, grouped according to body system. A SRR > 1 indicates that the ADR is reported at higher levels in females compared to background signal versus males. Significance is denoted by point-estimate shape. P-value threshold adjusted for multiple comparisons using Bonferroni’s correction.

## Conclusion(s)

There are sex-related differences in reporting of ADRs for statins. This could be related to biological susceptibility, pharmacokinetic differences in drug metabolism or confounding associated with spontaneous reporting, such as from females having an increased polypharmacy burden, longer life expectancy and greater healthcare attendances. Disproportionality analysis does not infer causality and sex-specific ADR signals should be interrogated in further studies.

## Reference(s)

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