Over 65% of all new drugs undergo expedited drug approval in the USA.[1] Such drugs have been linked to a higher prevalence of adverse drug reactions, raising concerns about safety.[2] It is well documented that women generally report a higher frequency of adverse drug reactions than men.[3] However, it is unknown whether women have more adverse drug reactions than men from drugs approved via expedited pathways. I conducted a systematic literature review to assess sex differences (male or female, as reported in clinical trials) in data reporting. The review focused on the cardiovascular drug Multaq (dronedarone), which received expedited approval in 2009, intended as a safer replacement for amiodarone, a known proarrhythmic drug linked to severe arrhythmias, including Torsade de Pointes.[4] Womens' naturally longer QT intervals make them more susceptible to the proarrhythmic effects of drugs, which is well documented in the case of amiodarone.[4,5]

My research focused on assessing the extent of female participants' inclusion in both pre-approval and post-approval trials, and it scrutinised the availability of sex-disaggregated data on proarrhythmic effects. Female participants were under-represented in five of the six pre-approval trials, averaging at 32% of the sample. None of the pre-approval trials provided sex-disaggregated data on adverse drug reactions, which is concerning as the trials substantiate the drug's proarrhythmic potential. Post- approval observational evidence showed a greater occurrence of Torsade de Pointes among female than male participants,[6] with approximately two-thirds of cases attributed to the female group. Notably, the drug recorded the highest number of reported Torsade de Pointes cases in the USA in 2011—surpassing its predecessor, amiodarone.

These findings question the preventability of these outcomes through thorough sex-disaggregated reporting of adverse drug reactions in pre-approval stages. I highlight a knowledge gap that leaves the question of whether women face a higher risk of harm through expedited approval pathways than men.

I declare no competing interests.

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