ASSET
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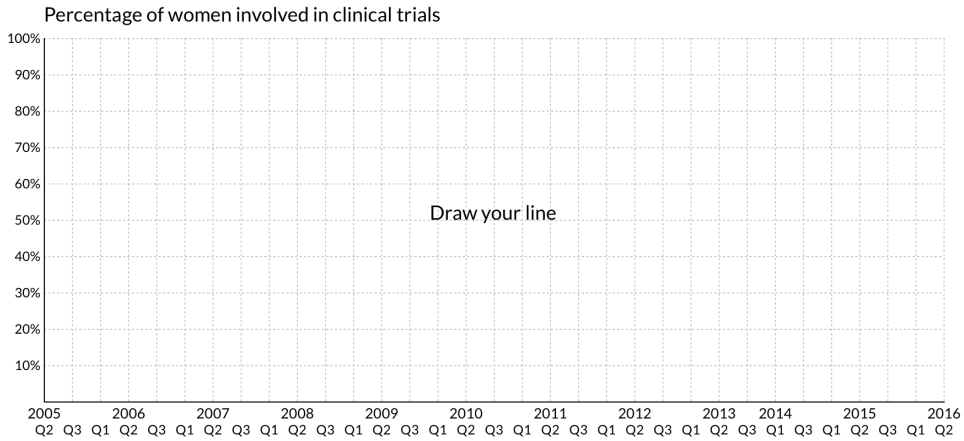
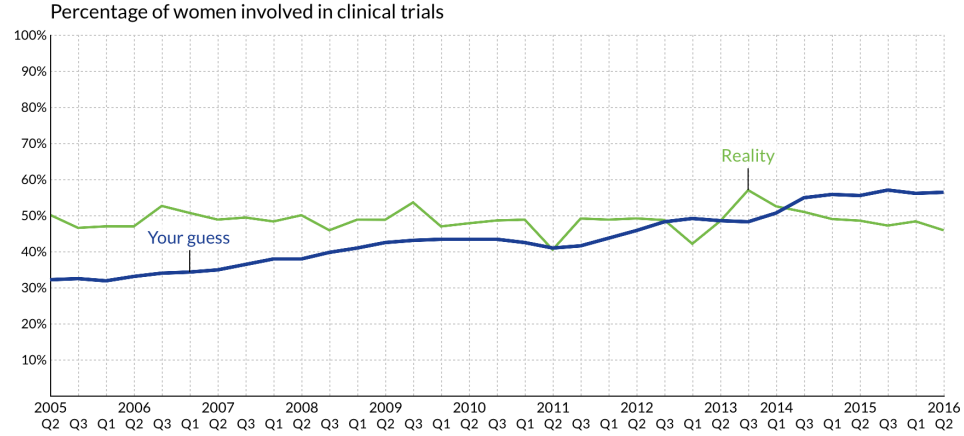
Sex and gender in clinical trials

Data Visualization

It is often said that sex and gender differences are perceived as overlooked in research design and in clinical trials, even those on vaccines.
Experts from the ASSET project performed a study to compare participation rates of males and females in clinical vaccine trials.

All readers are invited to actively participate to the data visualization, drawing a line that show a supposed females participation rates in clinical vaccine trials according to their opinion and comparing it with the actual graphical representation of data (see graphs below).





The following graphs show, on the Y axis, the females participation rates in clinical vaccine trials and, on the X axis, the years in which the trials were conducted (since 2005, the year from which data are available). Data are aggregated in four month period. Users are invited to draw a line representing the estimated females participation rates in clinical vaccine trials according to your opinion.
Two coloured lines will appear in the graphs, the blue one indicating users' bias regarding females participation rates in clinical trials, and the green one indicating the true females participation rates.
These data were taken from EU Clinical Trials Register, downloading clinical trials containing the word vaccine and excluding those related to cancer vaccines.
Only 198 of the 440 trials extracted reported data related to the rates of males and females participants. Among these, only 160 reported data related to different phases of the trial (see the box).

Background

Despite the acknowledged importance of sex and gender in most areas of research, the gap in the representation of women in studies on human subjects has been well documented, as reported by Heidari et al. For example, a 2009 review of cardiovascular treatment trials included in Cochrane Reviews reveals that only 27% of the total participants to the 258 clinical trials were women. More importantly, only one third of the trials that recruits both men and women reported a gender-based analysis. The underrepresentation of women in research can result in adverse consequences. For instance, it is well known that pharmacokinetics and pharmacodynamics of pharmaceutical agents differ between sexes, resulting in different safe dosage range and side effects.
In 2010, the World Health Organisation (WHO) published the document "Sex, gender and influenza", which states that many reports of influenza vaccination rates as well as the safety, efficacy and effectiveness of vaccines around the world do not disaggregate data by sex.
Katie Flanagan, senior lecturer of the Department of Immunology at Monash University in Melbourne, Australia, explained in a video that almost all the clinical vaccine trials would combine males and females together and report the data according to the males and females combined. However, according to her, it would be very helpful if researchers actually reported the sexes separately or did an analysis by sex with the aim of being able to give different types of vaccines according to the different persons' immune system, their immune status and possibly their sexes.
Female participation in clinical trials has improved in recent years, as stated in Sex, clinical trials and medicines regulation: part I. The United States adopted a regulation early on to increase the participation of women in clinical trials (Sex, clinical trials and medicines regulation: part II) and Europe recently adopted the EU Clinical Trial Regulation, which regulates the transparency of clinical trials data, including the

population groups for whom the medicines are intended (also in terms of gender and age). It also contains new rules for including pregnant and breastfeeding women under strict protective measures (Sex, clinical trials and medicines regulation: part III). Besides, a panel of 13 experts representing nine countries developed an international set of guidelines to encourage a more systematic approach to the reporting of sex and gender in research, and to enforce existing policies. The Sex and Gender Equity in Research (SAGER) guidelines are a comprehensive procedure for reporting sex and gender information in study design, data analyses, results, and interpretation of research findings.

Results

Based on available data, this comparison shows that there are no significant differences in participation rates of males and females in clinical vaccine trials, also analyzing data by trial phase.
The data visualization indicates that men and women are equally represented in the clinical vaccine trials analyzed in this work.
This analysis has some limits: most of the trials did not include the participation rates of males and females, and the specific phases of some clinical trials extracted. Moreover, in many cases it was not possible to determine if the data examined were disaggregate by sex or gender, since this information was not reported.
However, the fact that only a minority of the trials disaggregated data by sex and gender is a highly relevant finding, for it indicates that such a distinction was not perceived as important.
It would be interesting to know why these data have not been reported and if the inclusion of sex-disaggregated data and gender analysis would have given different results.

Final Considerations

Despite these limits and even if the clinical trials reporting of sex-specific and gender-specific data are still a minority, ASSET analysis shows that increased female participation subjects in clinical trials seems to have been reached, and also highlights that many studies will not have been designed to analyse sex and gender differences. Sex and gender should be considered when evaluating the safety and efficacy of treatments with the aim of improving health and healthcare for every person. Since the scientific knowledge on sex differences is now well known, it is desirable that researchers will take into account the biological characteristics and the evolving social/cultural features of both women and men, and conduct sex and gender analysis in each stage of the research cycle as the Guidance on Gender Equality in Horizon 2020 claims. In fact, one of the three objectives of gender equality in Horizon 2020 is to integrate the gender dimension in research and innovation (R&I) content, in order to

improve the scientific quality and societal relevance of the produced knowledge, technology and innovation.
The ASSET work encourages researchers to consider sex and gender as relevant to the topic of the study, such as in clinical vaccine trials, and to collect and present data separately on men and women.

CONTACTS

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