

María Montoya-Martínez, MD¹

¹ Geriatrician, Hospital universitario Morales Meseguer, Servicio Murciano de Salud, Murcia, Spain.

Reporting of Sex- Related Differences on Depressive Symptoms and Brain Morphology in Older Population

1 BACKGROUND

Depressive symptoms (DS) is the most prevalent clinical condition in the field of mood disorders in older population. In addition, there is a broad evidence on how sex differences are found in the field of Neuro and Geroscience. It is proved that there are sex-related differences in brain morphology and that sex-related factors like: hormones, stress or socio-economic status differently affect the neurodevelopment. Nevertheless, studies focused on DS often overlook them.

Objective: evaluate how sex-related differences have been accounted for in studies focusing on Magnetic Resonance Imaging (MRI) markers associated to DS in older population.

2 METHODS

I looked for original articles on (i) older population (mean age ≥65 years old), (ii) measuring DS or any of its scoring tools, (iii) having assessed neuroimaging through brain MRI within the past 5 years and published in English and Spanish. Sex and Gender Equity in Research (SAGER) Guidelines (table 1) from the EASE were used to assess consideration of sex related-differences and its reporting in the studies included.

Table 1 Sex and Gender Equity in Research (SAGER) guidelines

General principles	
•	Authors should use the terms <i>sex</i> and <i>gender</i> carefully in order to avoid confusing both terms.
•	Where the subjects of research comprise organisms capable of differentiation by sex, the research should be designed and conducted in a way that can reveal sex-related differences in the results, even if these were not initially expected.
•	Where subjects can also be differentiated by gender (shaped by social and cultural circumstances), the research should be conducted similarly at this additional level of distinction.
Recommendations per section of the article	
Title and abstract	If only one sex is included in the study, or if the results of the study are to be applied to only one sex or gender, the title and the abstract should specify the sex of animals or any cells, tissues and other material derived from these and the sex and gender of human participants.
Introduction	Authors should report, where relevant, whether sex and/or gender differences may be expected.
Methods	Authors should report how sex and gender were taken into account in the design of the study, whether they ensured adequate representation of males and females, and justify the reasons for any exclusion of males or females.
Results	Where appropriate, data should be routinely presented disaggregated by sex and gender. Sex- and gender-based analyses should be reported regardless of positive or negative outcome. In clinical trials, data on withdrawals and dropouts should also be reported disaggregated by sex.
Discussion	The potential implications of sex and gender on the study results and analyses should be discussed. If a sex and gender analysis was not conducted, the rationale should be given. Authors should further discuss the implications of the lack of such analysis on the interpretation of the results.

3 RESULTS (table 2)

After application of the SAGER guidelines it was found that 10 studies used the term “sex” and 2 used “gender”. Although sex is considered relevant to the topic, no study referred it in the introduction section. Six studies had samples in which one of both sexes represents less than 40% of the sample: male participants were underrepresented being 14%, 29%, 30.3%, 30.3% and 37%, of the sample and in other female ones were 14%. For all studies sex was a confounder and one account for it as an effect modifier, and found that sex interaction for grey matter was significant, whereas for white matter was not. None of the studies stratified results by sex. Only one study discussed the unequal sex distribution sample as a generalisability issue.

Table 2 Reporting of sex in included studies according to SAGER guidelines.

AUTHORS	SEX and/or GENDER RELEVANT to THE TOPIC	USE of THE TERMS « SEX » and « GENDER »	INTRODUCTION Report of the expected sex-differences	METHODS			RESULTS Data disaggregation	DISCUSSION	
				Method for determining sex	Sample sex distribution female sex %	Gender Based Analysis (GBA)		Generalizability issue	Reasons for lack of GBA
Kumar et al., 2015	Yes	Appropriate use of « sex »	Not reported	Not reported	57.6%	No	No	Not reported	
Chang et al., 2015	Yes	Appropriate use of « sex »	Not reported	Not reported	63%	No	No	Not reported	
McClaren et al., 2016	Yes	Appropriate use of « sex »	Not reported	Not reported	71%	No	No	Not reported	
Szymkowicz et al., 2016	Yes	Appropriate use of « sex »	Not reported	Not reported	69.7%	No	No	Not reported	
Zhou et al., 2016	Yes	Inappropriate use of “gender”	Not reported	Not reported	86%	No	No	Not reported	
Szymkowicz et al., 2017	Yes	Appropriate use of « sex »	Not reported	Not reported	69.7%	No	No	Not reported	
Pink et al., 2017	Yes	Appropriate use of « sex »	Not reported	Not reported	50%	No	No	Not reported	
Szymkowicz et al., 2018	Yes	Appropriate use of « sex »	Not reported	Not reported	62%	No	No	Not reported	
Tudorascu et al., 2015	Yes	Inappropriate use of “gender”	Not reported	Not reported	44%	No	No	Not reported	
Uden et al., 2015	Yes	Appropriate use of « sex »	Not reported	Not reported	45.4%	No	No	Not reported	
Allan et al., 2016	Yes	Appropriate use of « sex »	Not reported	Not reported	17%5	No	No	Discussed	
Sloten et al., 2015	Yes	Appropriate use of « sex »	Not reported	Not reported	56.6	No	No	Not reported	No

4 DISCUSSION

The lack of reporting of most of the SAGER guidelines items for each section, shows that reporting of sex-related differences, was insufficient. The unequal sample distribution of sex, as the absence of a gender based analysis could potentially affect the inferences coming from these studies.

Take away messages

- Assessing reporting of sex-related differences, raise awareness about whether the inferences coming from studies are affected by sex-related bias, which eventually limit their generalisability and applicability to clinical practice.
- Lack of interest in sex differences may not only be harmful but also present missed opportunities for innovation.