



Sex differences in the humoral response to vaccine in multiple sclerosis a meta-analysis

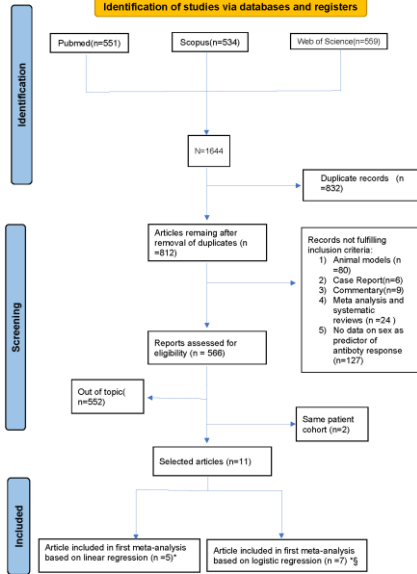
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Background

Biological sex influences immune function and vaccine response, differently throughout the lifetime, in relationship to chromosomal and hormonal differences between sexes. However, little is known about sex differences in immune response to vaccination in patients with multiple sclerosis (MS). This meta-analysis evaluates available evidence on the differences in antibody response to vaccination between men and women with MS.

MATERIALS AND METHODS

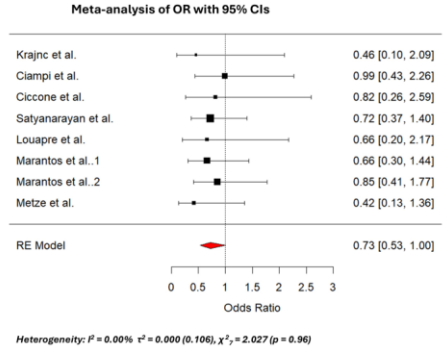
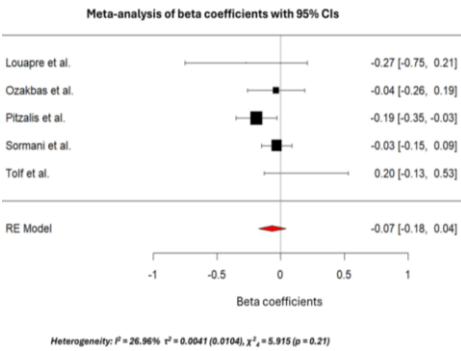


*one shared article
Some article included two separate analyses for two different vaccines

Two separate meta-analyses were conducted using the metafor package in R, focusing on studies reporting sex-specific antibody data in MS patients post-vaccination. A linear regression meta-analysis was performed for studies providing β coefficients, and a logistic regression meta-analysis for studies reporting odds ratios, to ensure methodological consistency. Effect sizes were extracted or calculated and pooled using a Restricted Maximum Likelihood estimator. Heterogeneity was assessed via I^2 , τ^2 , and Cochran's Q test. Eleven articles were included.

First Author	Title	DOI	Year
Ciccone A, et al.	Serology results after COVID vaccine in multiple sclerosis patients treated with fingolimod	10.1016/j.neuro.2022.2023	2023
Ciampi E, et al.	Safety and humoral response rate of inactivated and mRNA vaccines against SARS-CoV-2 in patients with Multiple Sclerosis	10.1016/j.msard.2022.10	2022
Krajnc N, et al.	Humoral immune response to SARS-CoV-2 third vaccination in patients with multiple sclerosis and healthy controls: A prospective multicenter study	10.1016/j.msard.2022.10	2022
Louapre C, et al.	Anti-CD20 therapies decrease humoral immune response to SARS-CoV-2 in patients with multiple sclerosis or neuromyelitis optica spectrum disorders	10.1136/jnnp-2021-326904	2023
Marantos T, et al.	Immunogenicity of a seasonal influenza and a pneumococcal polysaccharide vaccine in multiple sclerosis patients under disease-modifying therapies: A single-center prospective study	10.1016/j.vaccine.2024.0	2024
Metze C, et al.	Immunogenicity and predictors of response to a single dose trivalent seasonal influenza vaccine in multiple sclerosis patients receiving disease-modifying therapies	10.1111/acs.13034	2018
Ozakbas S, et al.	Comparison of SARS-CoV-2 antibody response after two doses of mRNA and inactivated vaccines in multiple sclerosis patients treated with disease-modifying therapies	10.1016/j.msard.2022.10	2022
Pitzalis M, et al.	Effect of Different Disease-Modifying Therapies on Humoral Response to BNT162b2 Vaccine in Sardinian Multiple Sclerosis Patients	10.3389/fimmu.2021.781	2021
Satyanarayan S, et al.	Differential antibody response to COVID-19 vaccines across immunomodulatory therapies for multiple sclerosis	10.1016/j.msard.2022.10	2022
Sormani MP, et al.	Effect of SARS-CoV-2 mRNA vaccination in MS patients treated with Effect of SARS-CoV-2 mRNA vaccination in MS patients treated with disease-modifying therapies	10.1016/j.ajtm.2021.10	2021
Tolf A, et al.	Factors Associated With Serological Response to SARS-CoV-2 Vaccination in Patients With Multiple Sclerosis Treated With Rituximab	10.1001/jama.2022.11497	2022

RESULTS



A comprehensive literature search yielded a total of 1644 records. Ultimately, 15 studies met the eligibility criteria, which were reduced to 11 after excluding follow-up studies. The pooled beta from five studies showed no significant sex effect ($\beta = -0.07$, 95% CI: -0.18 to 0.04 ; $I^2 = 27\%$). Logistic regression across eight estimates suggested a non-significant trend toward lower seroconversion in males (OR = 0.73, 95% CI: 0.53 to 1.00; $I^2 = 0\%$). None of the included studies evaluated menopausal status and hormonal replacement treatment.

CONCLUSION

This meta-analysis underscores the overlook of the importance of sex on vaccination response in MS. Indeed, out of 1644 records only very few evaluated the effect of sex on the efficacy of vaccinations, and none considered the possible influence of hormonal status (i.e. specifying whether women were pre- or post-menopausal). The two meta-analyses of the few included studies showed no statistically significant difference in antibody production against the vaccine between female and male subjects, and a non-significant lower effect in males in the logistic regression meta-analysis. Further research accounting for sex differences and including hormonal status, particularly menopause, are needed to better characterize sex-specific immune responses in this population.

