WHY GENDER MATTERS FOR IMMUNIZATION

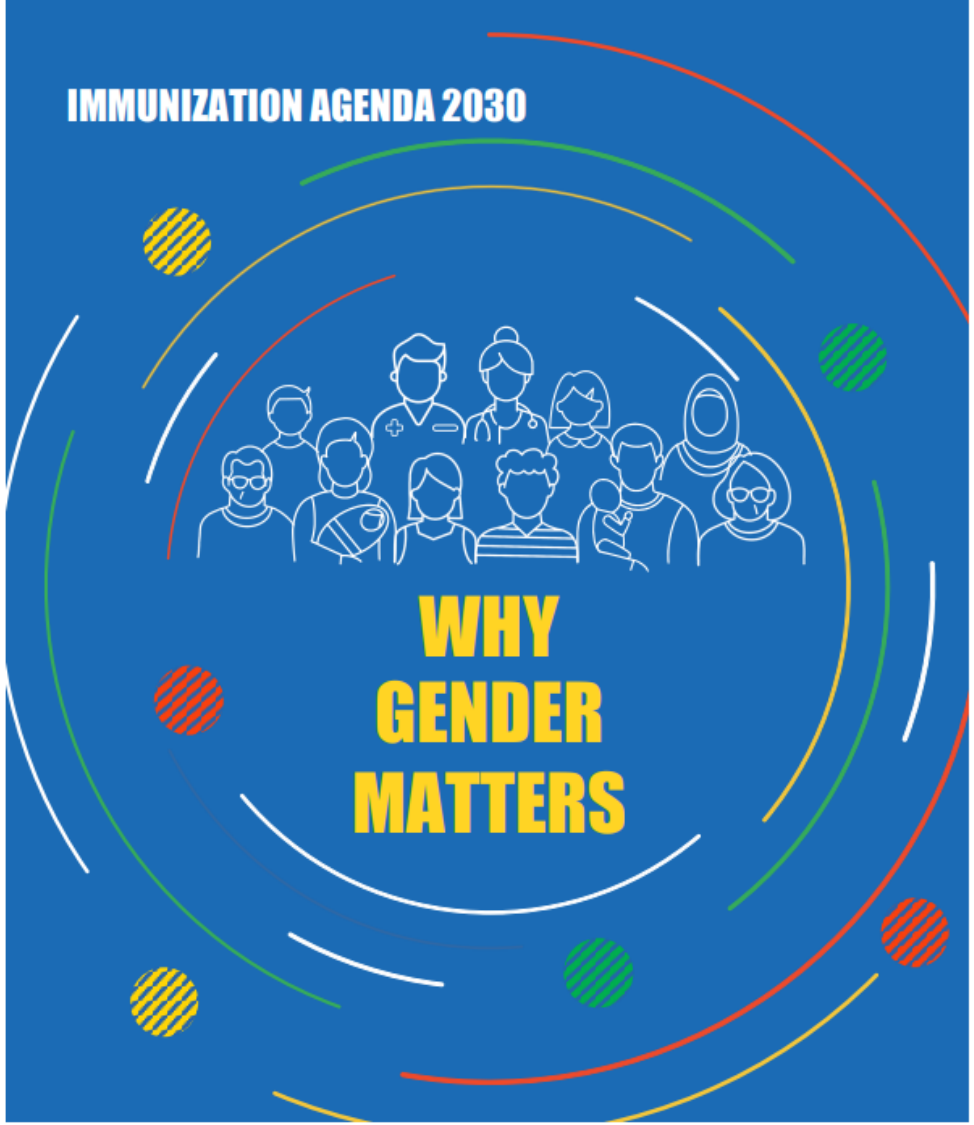
SECOND WEBINAR SERIES

World Health Organization

IMMUNIZATION AGENDA 2030

In association with

TechNet-21



WHY GENDER MATTERS for IMMUNIZATION: SECOND WEBINAR SERIES

IA2030 envisions a world where **everyone, everywhere, at every age**, fully benefits from vaccines to improve health and well-being. However, immunization programmes will only succeed in expanding **coverage and equity** when gender roles, norms and relations are understood, analyzed and accounted for as part of service planning and delivery.

Building upon the first webinar series organized in 2023, this second series of webinars aims to further **improve awareness and understanding** of how **gender-related barriers** impact immunization. The series will focus on **examples and best practices** of **gender-responsive programming** to improve coverage and equity from around the world.

Webinar 1: Gender responsive actions to improve the quality, accessibility and availability of services	Thurs 7 March 2024 15h-16h CET
Webinar 2: Empower and collaborate with civil society and change agents to overcome gender barriers	Thurs 4 April 2024 15h-16h CET
Webinar 3: Advance gender equality and improve coverage through integrated services and collaboration across sectors	Thurs 16 May 2024 15h-16h CET
Webinar 4: Apply a gender lens to research and innovation	Thurs 6 June 2024 15h-16h CET
Webinar 5: Implement gender-responsive immunization services in emergency settings	Thurs 11 July 2024 15h-16h CET

World Health Organization

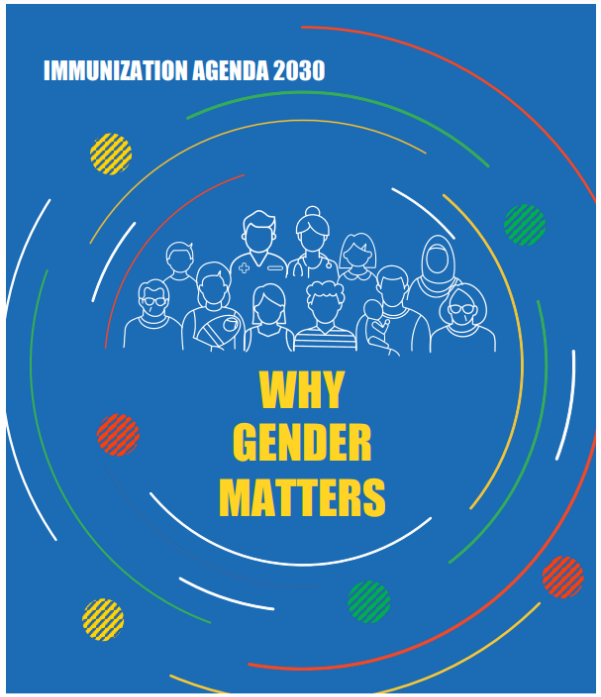
unicef for every child

Gavi The Vaccine Alliance

In association with TechNet-21 The Technical Network for Strengthening Immunization Services

All recordings and materials are available online:
https://www.technet-21.org/en/topics/programme-management/gender-and-immunization

Gender-responsive approaches to increasing immunization coverage



World Health Organization

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- Invest in gender data and analysis
- Make community engagement and social mobilization gender-responsive and transformative
- Engage with men to transform gender norms
- Empower and collaborate with civil society and change agents
- Implement gender-responsive actions for the health workforce
- Improve the quality, accessibility and availability of services
- Integrate services and collaborate across sectors
- Implement gender-responsive immunization services in emergency settings
- Apply a gender lens to research and innovation

Gender-responsive approaches to increasing immunization coverage

Apply a gender lens to research and innovation

Stephanie Shendale
Technical Officer
Lifecourse & Integration
IVB, WHO

Anna Ruggieri
Center for Gender Specific Medicine
Istituto Superiore di Sanità, Rome, Italy

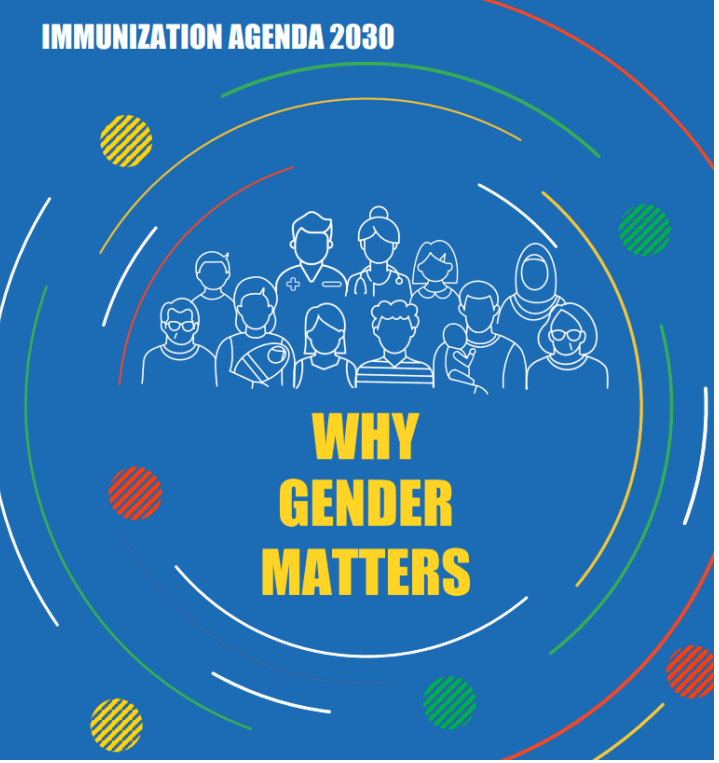
Shirin Heidari
Senior Technical Consultant on Gender IVB/GRE, WHO

Apply a gender lens to research and innovation

- *Sex and gender are important determinants of health and critical variables in scientific research, although too often disregarded.*
- *This oversight can significantly compromise study rigour and limit the relevance of research findings.*
- *Vaccine research and development should take into consideration sex and gender when developing and testing vaccine candidates for safety and efficacy, as well as when prioritizing products for development or roll-out.*

Action List

RESEARCH & INNOVATION	
☑	Investigate sex-based differences in immunology and vaccine response, including the importance of safety and efficacy data during pregnancy, as part of vaccine research and development *(54)*. *[Gender-sensitive]*
☑	Ensure that vaccine trials are designed to facilitate participation of both women and men, including specific groups such as pregnant and breastfeeding women. *[Gender-specific]*
☑	Strengthen local capacity to conduct implementation research to identify interventions and new technologies that enhance coverage and equity and support tailored solutions to address gender-related inequities and barriers. *[Gender-specific]*
☑	Share lessons learned on improved technologies, services and practices to address gender-related barriers. *[Gender-specific]*



"*Apply a gender lens to research and innovation*".

Sex differences in response to vaccination

Anna Ruggieri

Center for Gender Specific Medicine
Istituto Superiore di Sanità, Rome,
Italy

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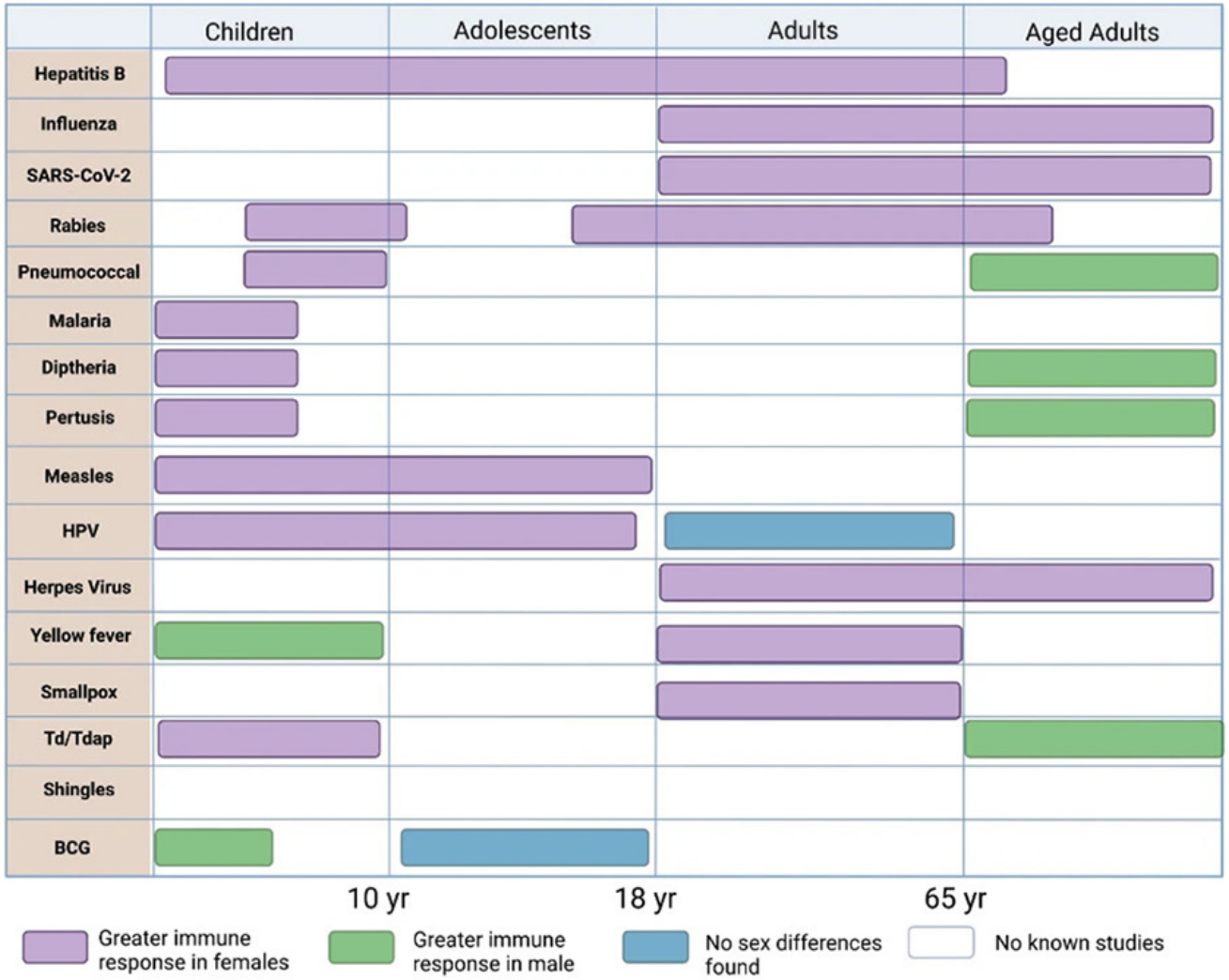
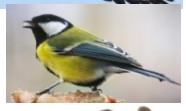
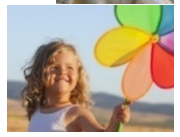
CENTRO DI RIFERIMENTO
MEDICINA DI GENERE

DIFFERENCES BETWEEN SEXES IN RESPONSE TO VACCINATIONS



St. Clair A., et al., Curr Top Microbiol Immunol, 2023

The sex difference in immune responses is preserved on the evolutionary scale in different animal species

	Common name	Species	Immune component	Sex difference
	Sea urchin	*Paracentrotus lividus*	Number of immunocytes, cytotoxic activity, phagocytosis and haemolysis	Greater in females than in males
	Fruit fly	*Drosophila melanogaster*	Activation of Toll and immune deficiency signalling	Greater in females than in males
	Scorpionfly	*Panorpa vulgaris*	Haemolysis and phagocytosis	Greater in females than in males
	Wall lizard	*Podarcis muralis*	Macrophage phagocytosis	Greater in females than in males
	Eurasian kestrels	*Falco tinnunculus*	Hypersensitivity responses	Greater in females than in males
	Great tit	*Parus major*	Hypersensitivity responses	Greater in females than in males
	House mouse	*Mus musculus*	Pro-inflammatory cytokine responses, T cell proliferation and antibody responses	Greater in females than in males
	Rhesus macaque	*Macaca mulatta*	Pro-inflammatory cytokine responses and antibody responses	Greater in females than in males
	Human	*Homo sapiens*	Type I interferon activity, T cell numbers and antibody responses	Greater in females than in males

Flanagan et al. 2017

…women are more immunoreactive than men

Adverse reactions to vaccines

….are more frequent in female recipients than in male recipients

Neither health surveillance nor vaccination plans presently take sex into account.

Rapporto Vaccini 2021
la sorveglianza postmarketing in Italia dei vaccini non-COVID-19

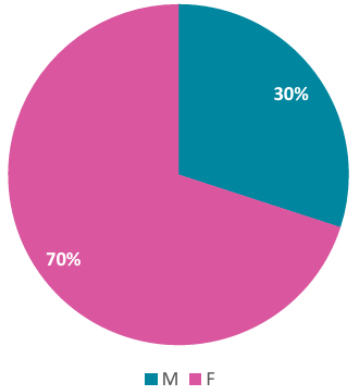
AIFA AGENZIA ITALIANA DEL FARMACO

Age and Sex distribution of the adverse reactions to vaccines in Italy (entered in 2021)

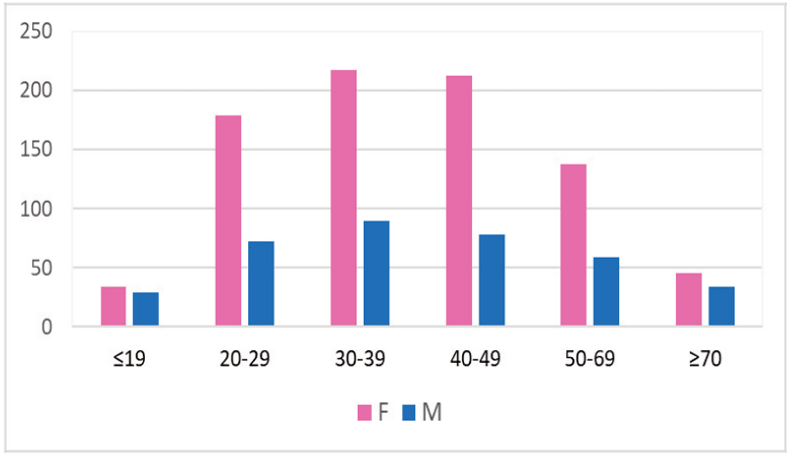
Age groups	Total		Males		Females	
years	N.	%	N.	%	N.	%
< 2 anni	15.376	91,9	8.172	93,8	7.204	89,7
2 - 11 anni	439	2,6	234	2,7	205	2,6
12 - 17 anni	186	1,1	96	1,1	90	1,1
18 - 64 anni	550	3,3	147	1,7	403	5,0
≥65 anni	187	1,1	61	0,7	126	1,6
Totale	**16.738**		**8.710**		**8.028**	

Sex differences in the frequency of adverse reactions to the COVID-19 vaccine reported to the Italian Pharmacovigilance Network

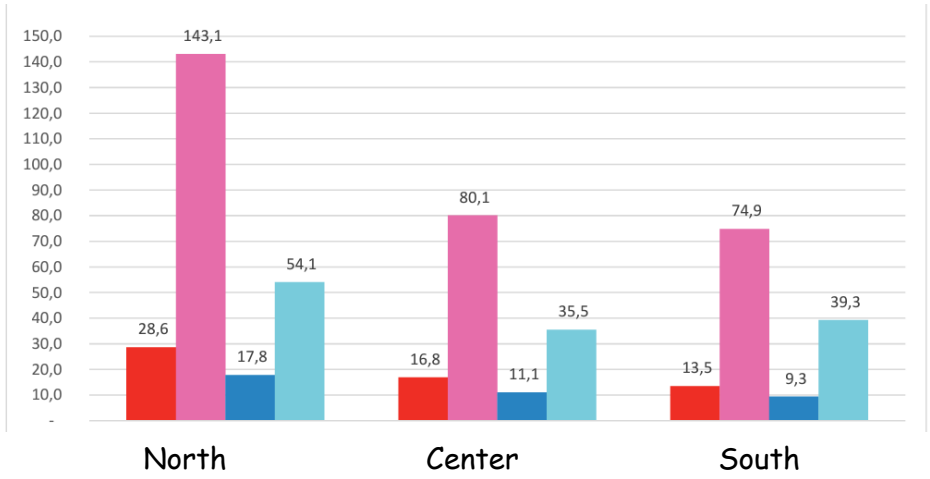
From dec. 2020 to dec. 2022



Reporting rate by gender and age groups



Reporting rate by gender severity and geographical area



F - severe ADR

F - mild ADR

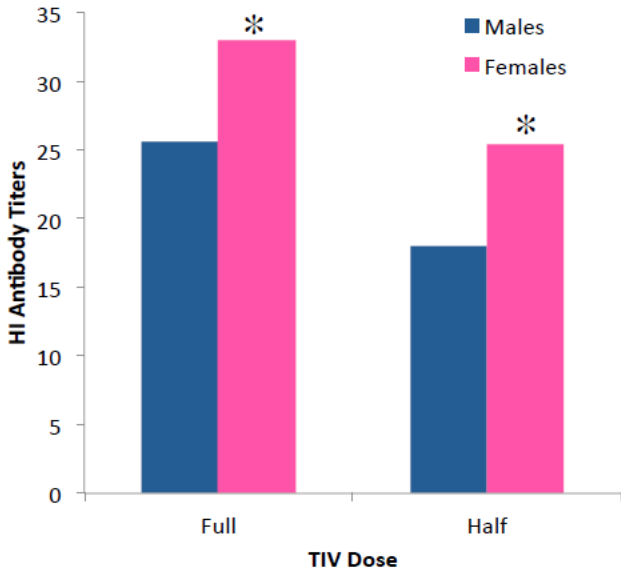
M - severe ADR

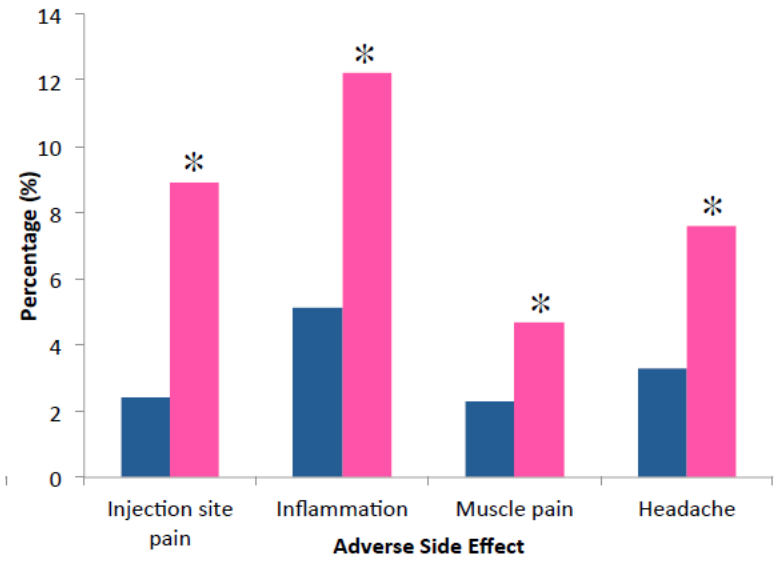
M - mild ADR

SEX DISPARITY IN RESPONSE TO VACCINES

- Historically, women have been underrepresented in vaccination trials as well as general clinical trials.
- Despite evidence that the sex of the recipient might have a significant impact on the immunological response, vaccinations are administered to males and females equally.
- This could have resulted in women receiving inadequate dosages of medications and vaccinations.

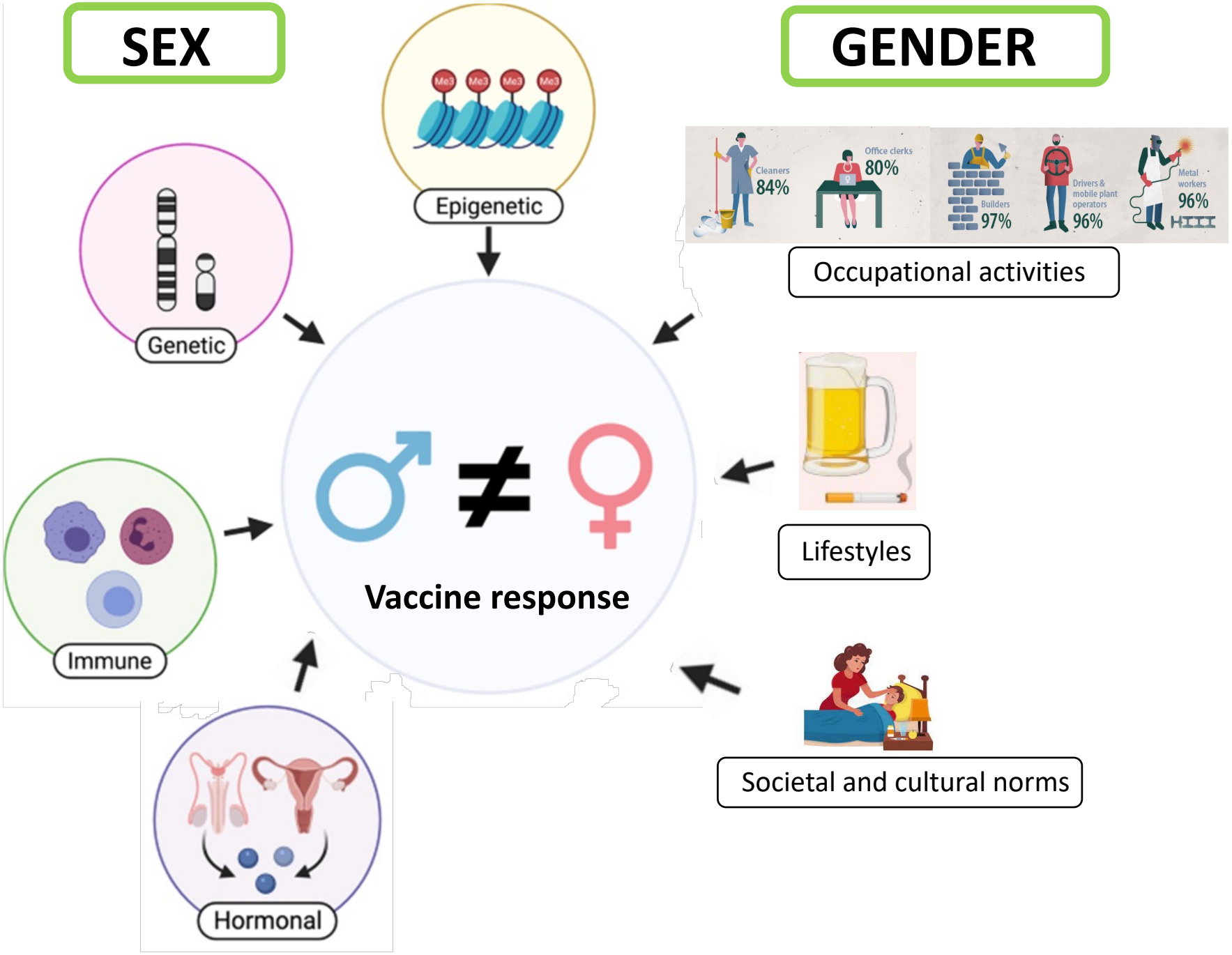
The response to seasonal influenza vaccine is sex specific





Engler RJ, et al. Arch Intern Med. 2008

When adult women receive a half dosage of the trivalent influenza vaccine, their antibody response is equal to that of men who receive the full dose of vaccine


SEX
GENDER
Epigenetic
Genetic
Occupational activities
Cleaners 84%
Office clerks 80%
Builders 97%
Drivers & mobile plant operators 96%
Metal workers 96%
Lifestyles
Immune
Vaccine response
Societal and cultural norms
Hormonal

Women have stronger innate and acquired immune response than men

Innate immune response

- More effective antigen presentation
- Stronger production of anti-microbial cytokines (e.g. IFN-alfa) in response to different antigens and pathogens
- More effective phagocytosis by neutrophils and macrophages

Adaptive immune response

- Higher number of activated T lymphocytes
- Increased number of B cells and higher levels of circulating antibodies

Sex hormones

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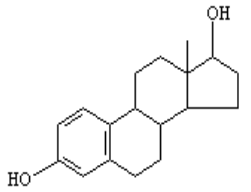
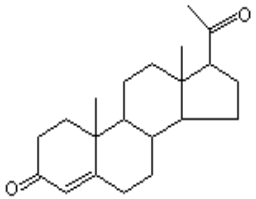
✓Sex steroid hormones receptors are present on immune cells, including lymphocytes, thus the immune response to infections and vaccines can be controlled by steroid hormones



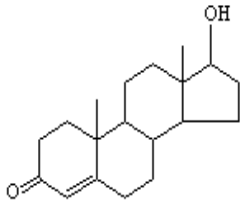
Estrogens

- **High concentration:**anti-inflammatory effects
- **Low concentration:** pro-inflammatory effects



Progesterone

- Anti-inflammatory effects



Testosterone

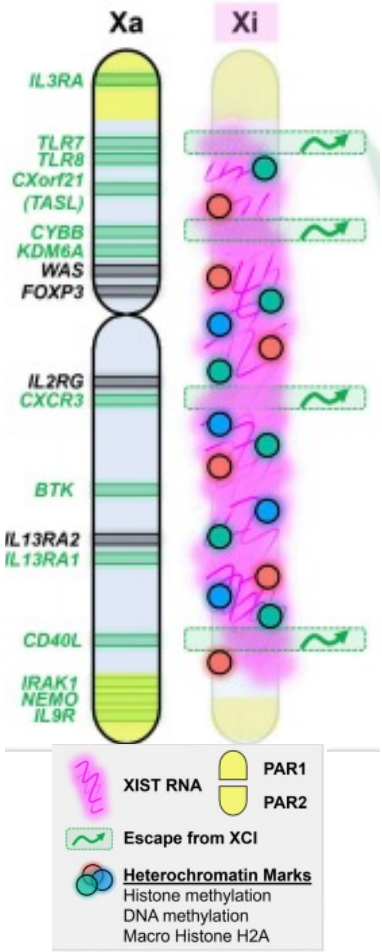
- Anti-inflammatory effects
- Immunomodulatory effects

Immuno-suppressive
Immuno-stimulatory

Genetic mechanisms:

Sex Chromosomes

- ✓ Female mammals have two X chromosomes in each cell. (Unlike males, who carry an X and a Y)
- ✓ Transcription of the genes present in both X chromosomes would lead to a harmful excess of their products, which is thus prevented by inactivating one of the two Xs, randomly chosen from the two available.
- ✓ Incomplete inactivation of the X chromosome (about 15%): overexpression of genes localized on the X chromosome
- ✓ More than 1100 genes are encoded on the X chromosome, including a **substantial number of genes associated with immunological responses** (CD40L, IL-9R, IL-2R, TLR7, TRL8, FOXP3, CXCR3, etc.).



COVID-19 Vaccine ?

Molecular Immunology 156 (2023) 148–155

Contents lists available at ScienceDirect

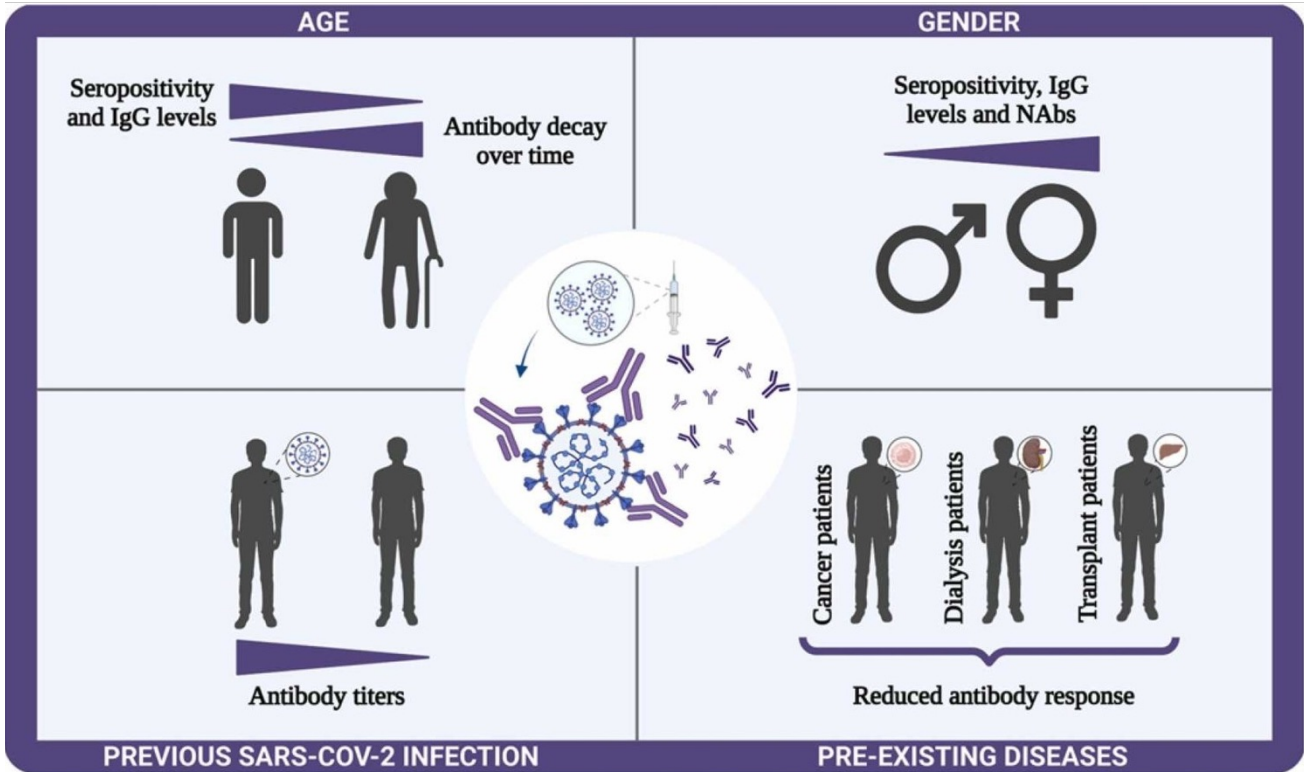
Molecular Immunology

journal homepage: www.elsevier.com/locate/molimm

Several Factors affect the antibody response to COVID-19 vaccination

Influence of age, gender, previous SARS-CoV-2 infection, and pre-existing diseases in antibody response after COVID-19 vaccination: A review

Maria da Conceição Rodrigues Fernandes, Germana Silva Vasconcelos, Amanda Campelo Lima de Melo, Tamires Cardoso Matsui, Ludmilla Freire Caetano, Fernanda Montenegro de Carvalho Araújo, Marcela Helena Gambim Fonseca *,1



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nature communications

Article

https://doi.org/10.1038/s41467-024-45468-9

Demographic and Clinical Factors Associated With SARS-CoV-2 Spike 1 Antibody Response Among Vaccinated US Adults: the C4R Study

Received: 5 May 2023

Accepted: 24 January 2024

Published online: 19 February 2024

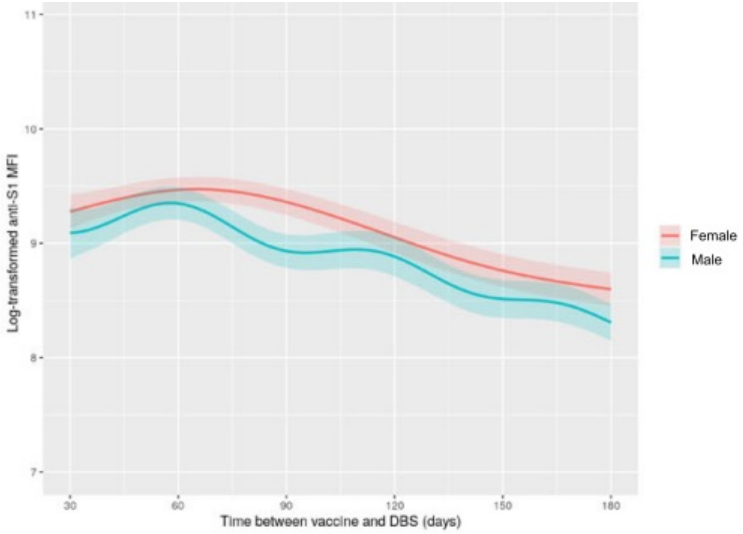
Check for updates

John S. Kim[1,2], Yifei Sun[3], Pallavi Balte[2], Mary Cushman[4,5], Rebekah Boyle[5], Russell P. Tracy[5], Linda M. Styer[6], Taison D. Bell[1], Michaela R. Anderson[7], Norrina B. Allen[8], Pamela J. Schreiner[9], Russell P. Bowler[10], David A. Schwartz[11], Joyce S. Lee[11], Vanessa Xanthakis[12,13], Margaret F. Doyle[5], Elizabeth A. Regan[14], Barry J. Make[10], Alka M. Kanaya[15], Sally E. Wenzel[16], Josef Coresh[17,18], Carmen R. Isasi[19], Laura M. Raffield[20], Mitchell S. V. Elkind[21,22], Virginia J. Howard[23], Victor E. Ortega[24], Prescott Woodruff[25], Shelley A. Cole[26], Joel M. Henderson[27], Nicholas J. Mantis[6,28], Monica M. Parker[5], Ryan T. Demmer[9,22,29,30] & Elizabeth C. Oelsner[2,30]

Anti-S response to COVID-19 vaccine is significantly greater in women than in men

- 6245 participants who received two doses of a mRNA COVID-19 vaccine
- anti-S1 IgG antibody levels in the meantime interval between the first vaccine dose and serosurvey of 4.0 months

Lower antibody levels were observed in older participants, men, and participants with a history of obesity, smoking, diabetes, or COPD



Sex differences in response to COVID-19 vaccination of Healthcare Workers (HCWs)

- Healthcare workers (HCWs) represent a significant target category for immunization since they are higly susceptible to contracting SARS-CoV-2 infection and are involved in nosocomial transmission.

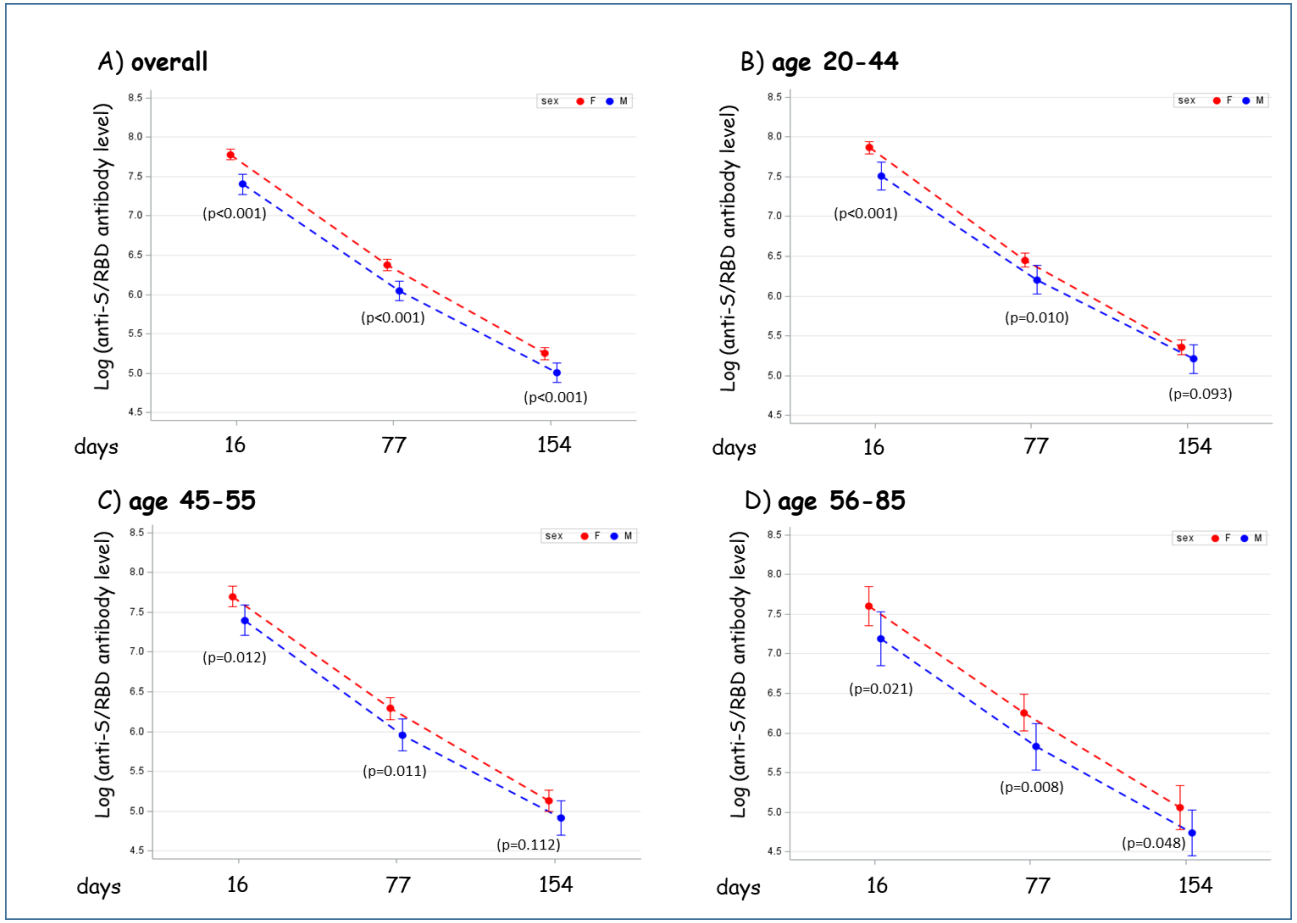
- At present, immunization schedules and health surveillance programs aimed at healthcare professionals are not sex-specific.

- ➢ **Evaluate sex differences of anti-S/RBD antibody responses to mRNA COVID-19 vaccine in HCWs**

- ➢ **Identify sex-specific biomarkers of serologic response to COVID-19 vaccine.**

In COVID-19 vaccinated HCWs, women develop anti-S Ab responses higher than men

- 521 HCWs (74% F, 26% M)



Anti-S/RBD Ab titers are higher in female HCWs than males HCWs for all age groups and for all post-vaccination (p.v.) intervals considered

A decline in anti-S titers is evident for either male and female HCWs over time interval considered

Anticoli S et al. 2023

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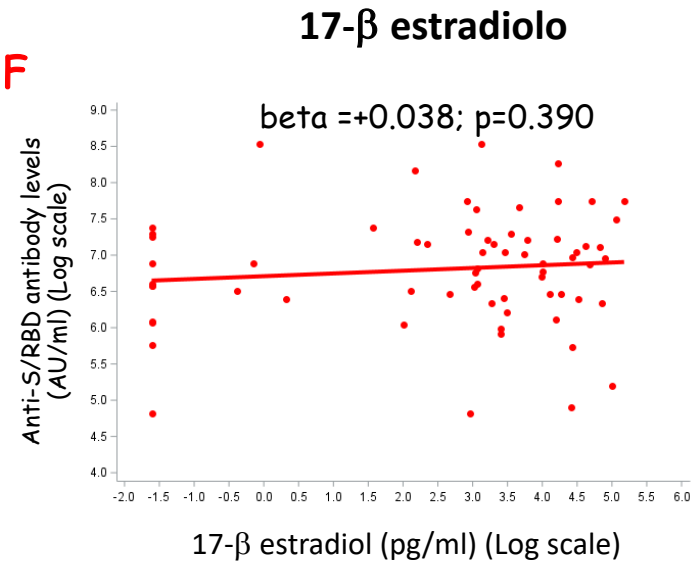
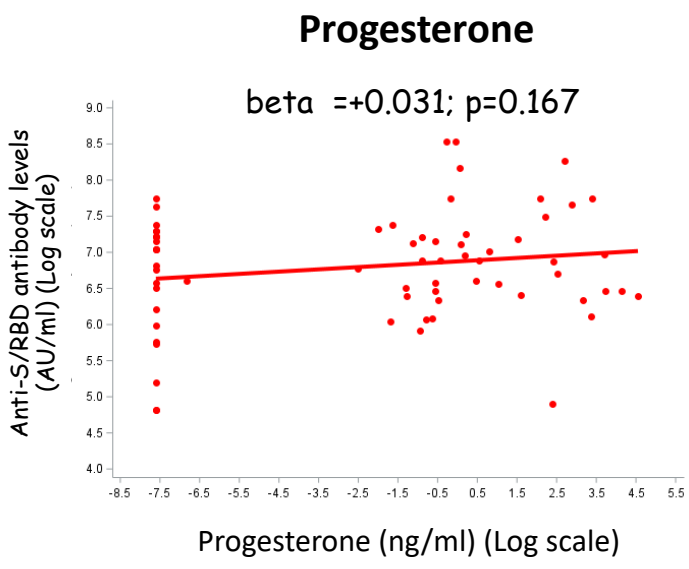
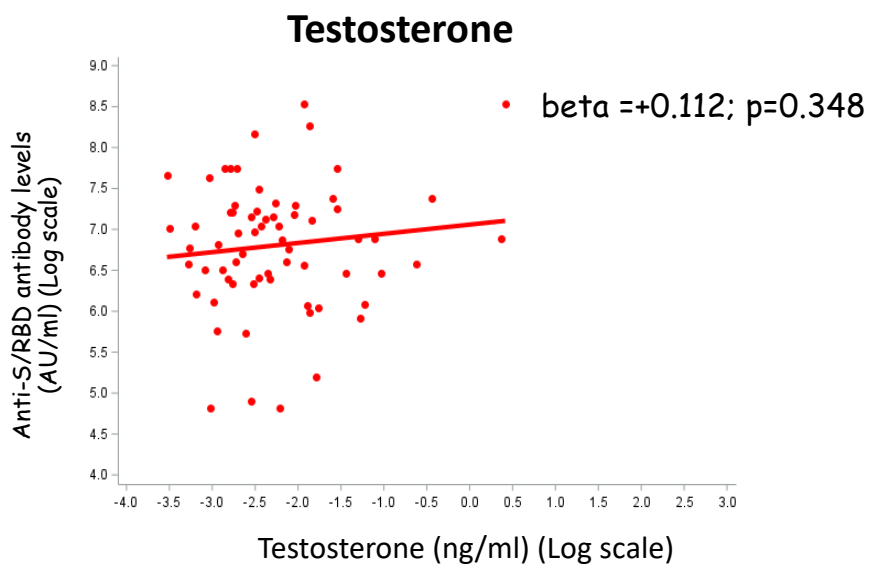
The role of sex hormones in gender disparities in anti-S titers

Multiple regression model to assess the effect of changes in sex hormone levels on anti-S titers

F







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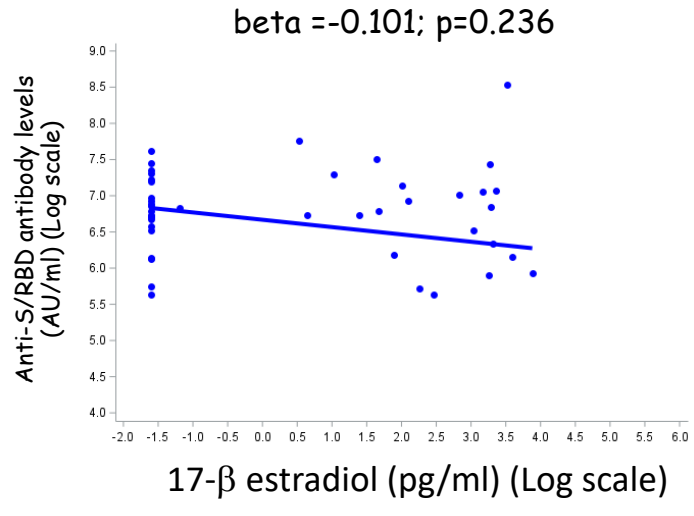
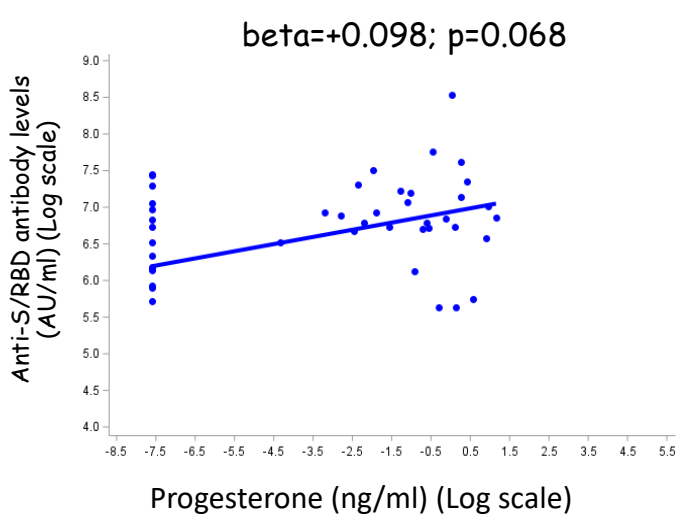
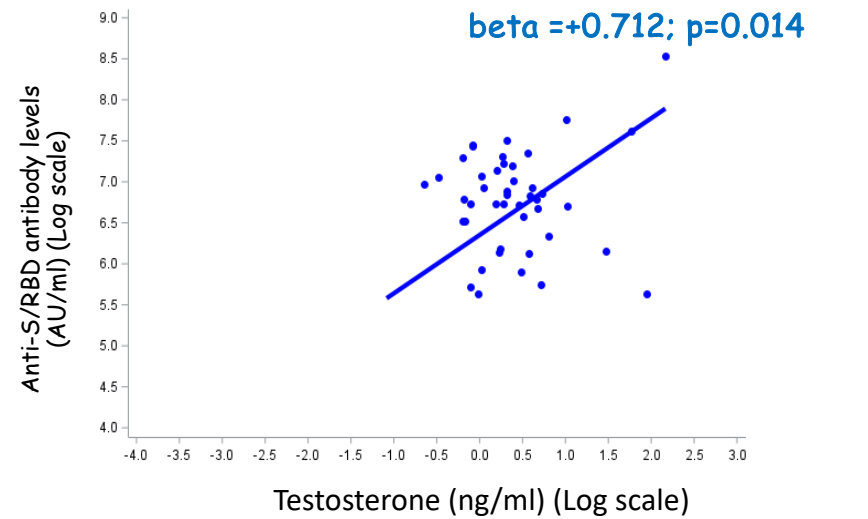






Anticoli S et al., 2023

Do sex differences in antibody responses to vaccinations impact vaccination effectiveness?

Sex differences in effectiveness of COVID-19 vaccines

- ✓ The results of phase II-III clinical trials have not revealed sex differences in the effectiveness of COVID-19 vaccines in preventing the development of the symptomatic disease (Vassallo A., Frontiers in Global Women's Health, 2021)

- ✓ As far as post-marketing studies are concerned, currently, sex-disaggregated data on the effectiveness of COVID-19 vaccines are scarce, difficult to retrieve and not consistently comparable

Reference	Vaccine	Vaccine effectiveness (VE) against SARS-CoV-2 infection	Effectiveness (VE) against symptomatic disease	Effectiveness against severe disease	Effectiveness with regard to hospitalization	Notes
Bjork et al., Infect Dis, 2021	BNT162b2	Equal between men and women	Not considered	Not considered	Not considered	
Butt et al ., Ann Intern Med, 2021	BNT-162b2 o mRNA-1273	Equal between men and women	Not considered	Not considered	Not considered	
Dagan et al., N Engl J Med, 2021	BNT-162b2 o mRNA-1273	Equal between men and women	Equal between men and women	Not considered	Not considered	
Young-Xu et al., JAMA Netw Open, 2021	BNT-162b2 o mRNA-1273	Not considered	Equal between men and women	Not considered	Not considered	
Chung et al., BMJ, 2021	BNT-162b2	Not considered	Slightly greater in men	Greater in females		
Li et al., Emerg Microbes Infect, 2021	CoronaVac vaccine	Not considered	Greater in women	Not considered	Not considered	Low number of subjects enrolled in the study (366)
Niessen et al., Vaccine, 2021	BNT-162b2, mRNA-1273 o ChAdOx1-S	Not considered	Not considered	Not considered	Greater in men (not statistically significant)	Low number of subjects enrolled in the study (45)
Nordströmet al., Lancet, 2022	BNT-162b2, mRNA-1273 o ChAdOx1-S	Not considered	• Equal in both sexes up to 4 months after vaccination • Greater in women 4-9 months after vaccination	Not considered	Not considered	

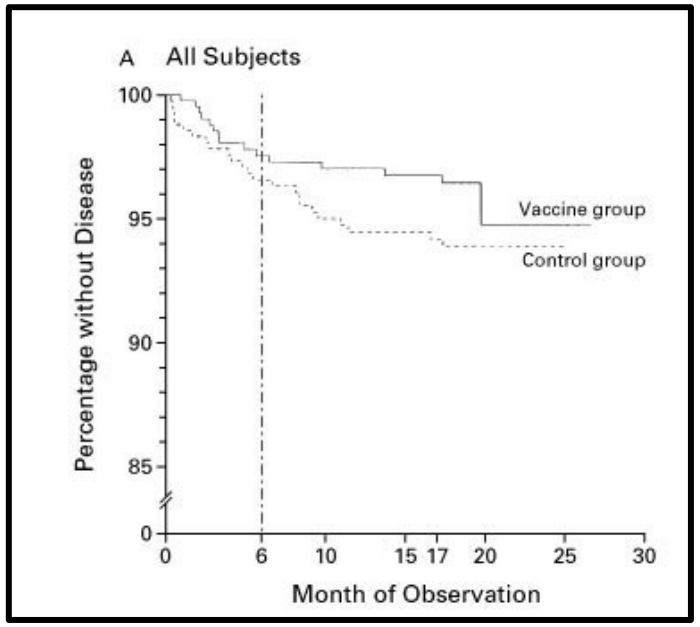
Nationwide retrospective population-based study on COVID-19 vaccine effectiveness (VE) towards infection and severe disease outcomes in Italy, during the pandemic period (SARS-CoV2 delta variant circulation was prevalent)

- Data were analyzed in relation to sex, age, and time since the last vaccination (≤ 120 days and >120 days).

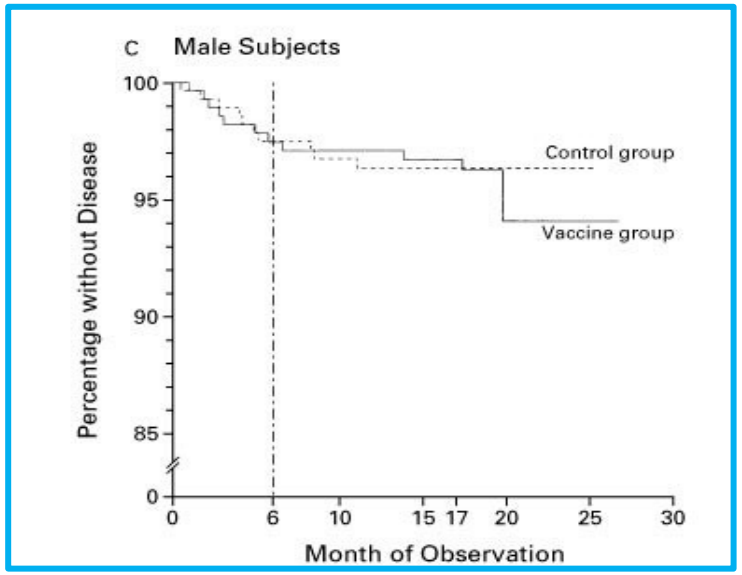
- Waning of the effectiveness of COVID-19 vaccine was observed in both males and females individuals who were vaccinated more than 120 days ago compared to those vaccinated within 120 days.

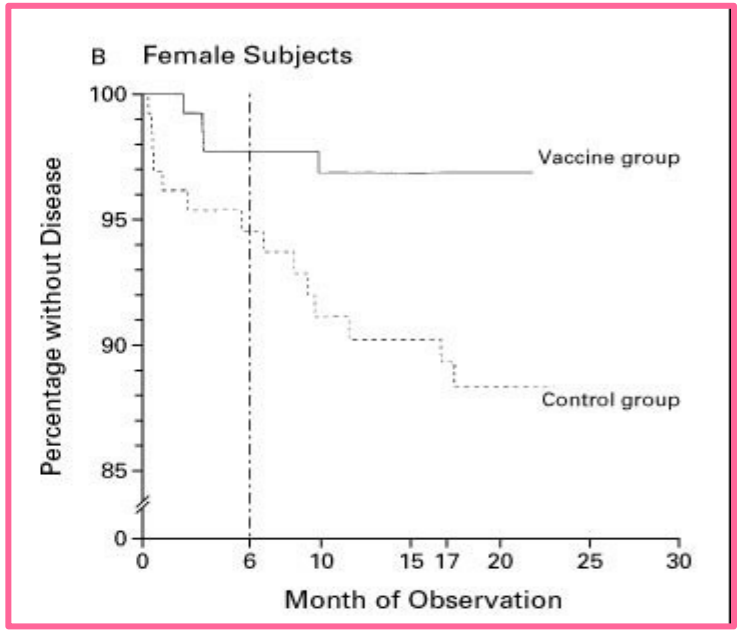
- **Vaccine effectiveness against infection was slightly higher in men than in women**

Sex specific effectiveness of the subunit vaccine for Genital Herpes (HSV- 1 e -2)



Stanberry LR et al., N Engl J MEd, 2002





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MEDICINA DI GENERE

Conclusions:

- Following immunization with two doses of mRNA COVID-19 vaccine in health workers, women develop higher anti-S titers than men, but adverse reactions to vaccines are more frequent and more severe in women than in men
- Anti-S Ab titer decreased over time intervals post vaccination
- Experimental evidence suggests that plasma testosterone levels are possible markers of anti-S response in men vaccinated with mRNA COVID-19 vaccine
- The sex-disaggregated evaluation of vaccine responses will contribute to achieve a more appropriate and personalized health surveillance programs in HCWs
- Sex-specific analysis of vaccines immunological response, effectiveness and adverse effects in large scale population studies will contribute to personalize vaccination campaign and may play a critical part in the design of future vaccine trials
- More extensive and specific investigations are still needed to explain the molecular mechanisms mediating these differences and modulating immune responses to vaccines.

...Thanks to you for your attention

anna.ruggieri@iss.it

Some people talk in their sleep. Lecturers talk while other people sleep

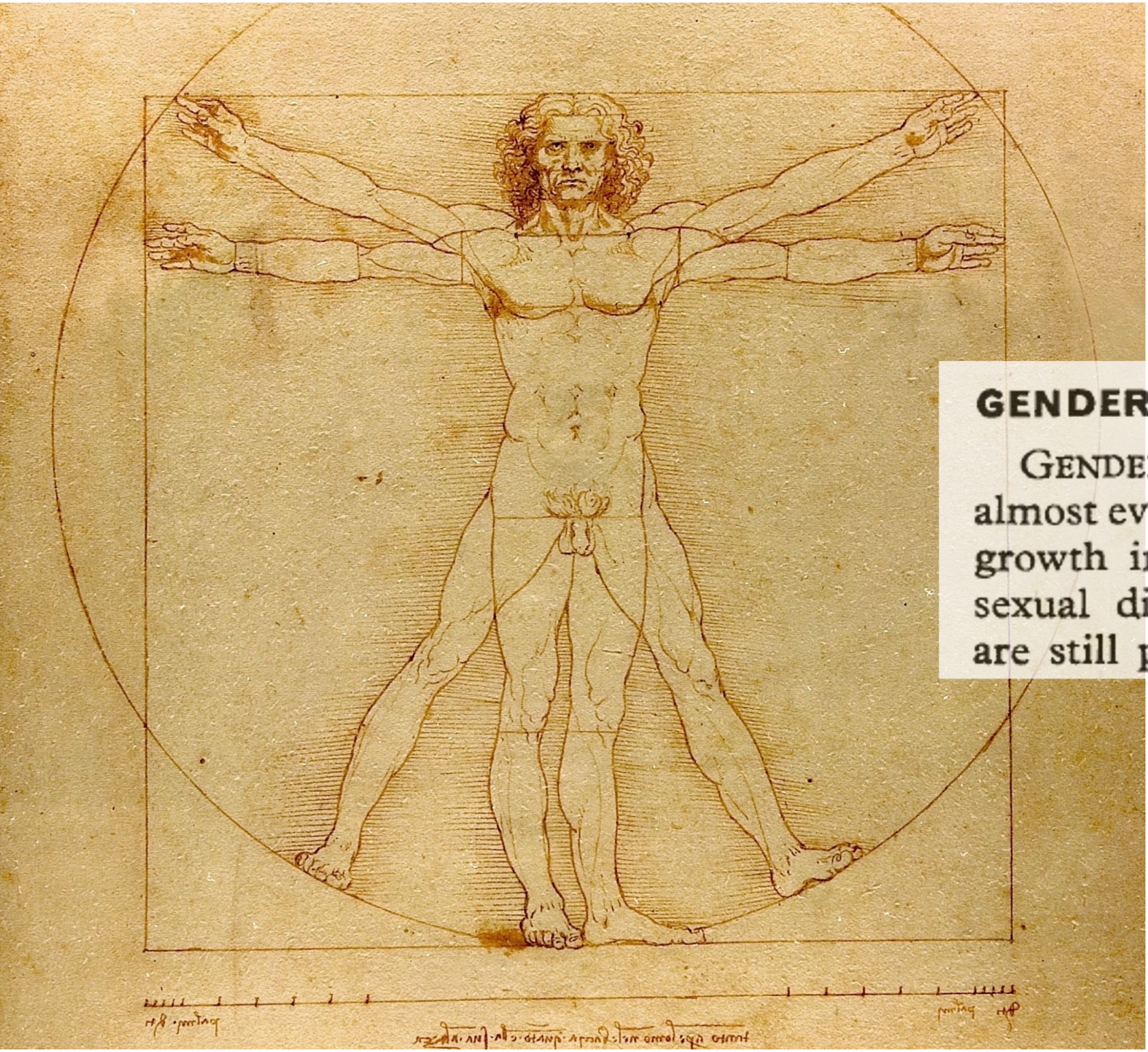
(Albert Camus)

Apply a gender lens to research and innovation: Implementation of Sex and Gender Equity in Research (SAGER) guidelines

06 June 2024

Shirin Heidari, Ph.D.
Department of Immunization, Vaccines and Biologicals & Department of Gender, Rights and Equity
Lead Author of the SAGER guidelines

World Health Organization



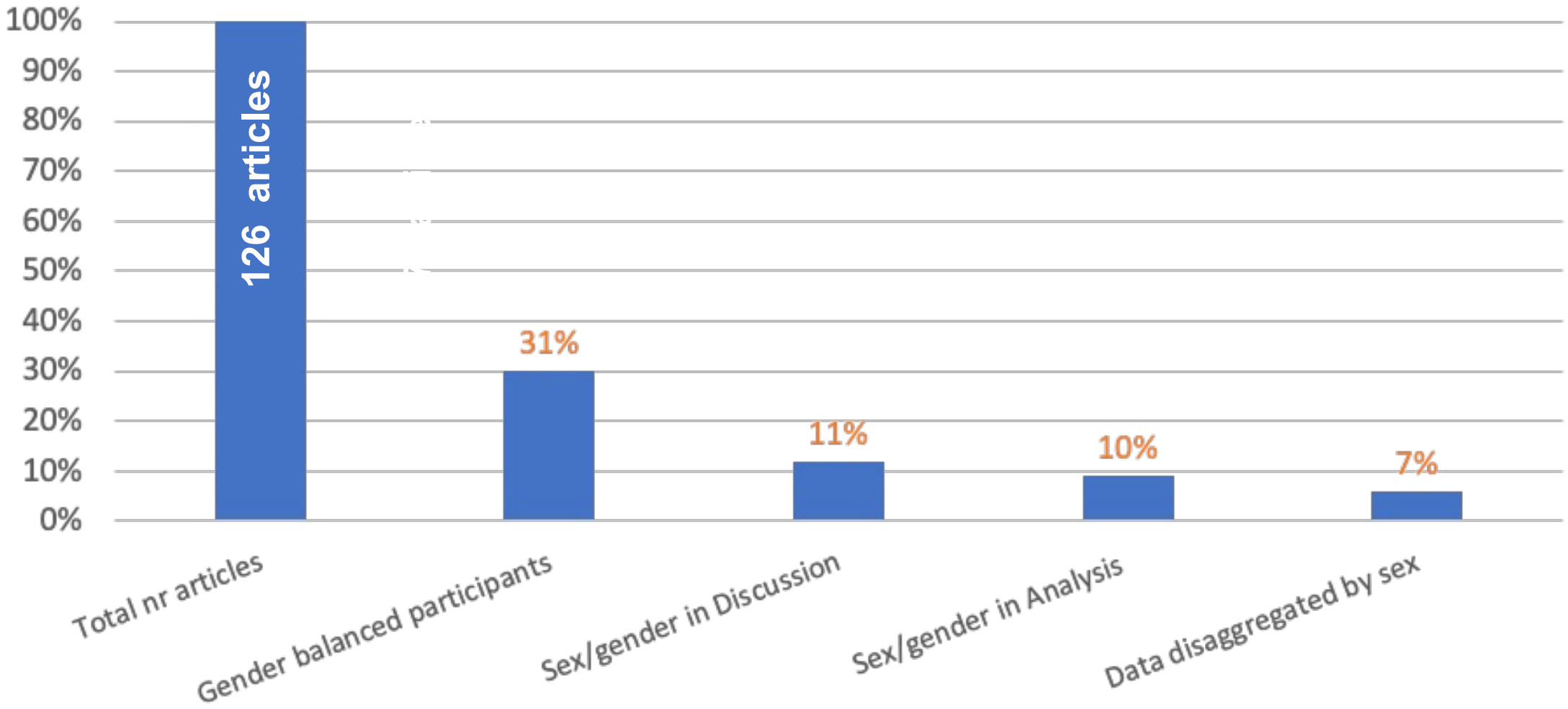
GENDER DIFFERENCES

GENDER or sex differences are well recognised in almost every area of medicine, but, despite an enormous growth in knowledge of the mechanisms underlying sexual differentiation over the past 25 years,[1] they are still poorly understood. One clinical sphere that

THE LANCET,

FEBRUARY 24, 1973

Gender blind reporting of clinical studies on COVID-19 (Jan-Sep 2020)



Pamler, Ovseiko, and Heidari BMJ GH 2021

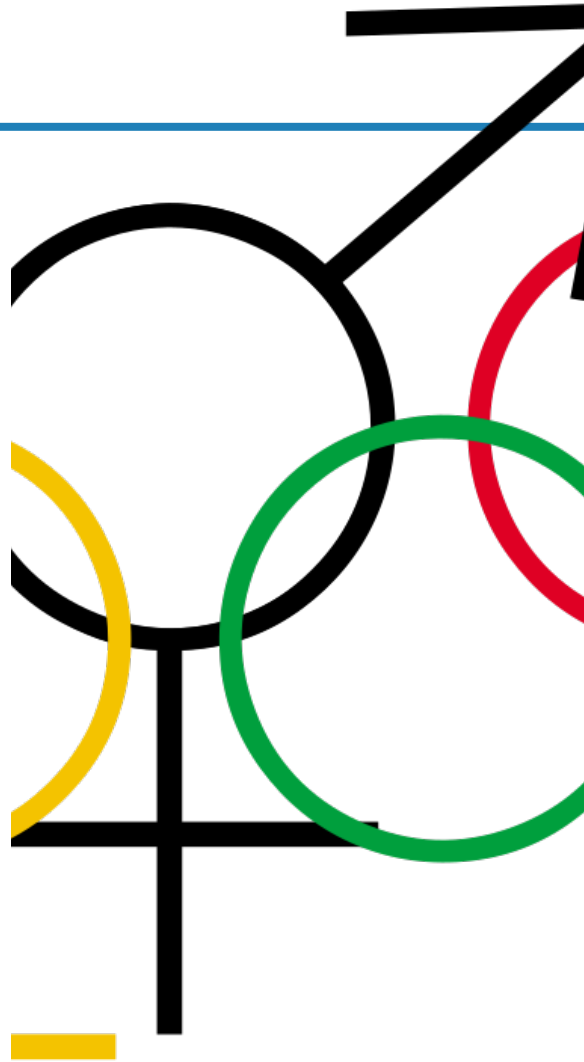
Are we turning a blind eye to gender blind research and reporting?

- Studies are rarely designed with sex and gender in mind and are often not gender balanced

- Sex or gender of subjects are not reported

- If sex or gender of subjects are reported, outcome data are rarely disaggregated by sex

- Analysis ignores potential sex and gender dimensions, and findings are presented as if of general applicability: *Overgeneralization*



* Modified based on "Nieuwenhoven and Klinge, Scientific Excellence in Applying Sex- and Gender-Sensitive Methods in Biomedical and Health Research Journal of Women's Health 2010" (Modified)

The SAGER guidelines (2016)

#SAGERguidelines

Heidari *et al. Research Integrity and Peer Review* (2016) 1:2
DOI 10.1186/s41073-016-0007-6

Research Integrity and Peer Review

REVIEW Open Access

Sex and Gender Equity in Research: rationale for the SAGER guidelines and recommended use

Shirin Heidari[1], Thomas F. Babor[2*], Paola De Castro[3], Sera Tort[4] and Mirjam Curno[5]

Abstract

Background: Sex and gender differences are often overlooked in research design, study implementation and scientific reporting, as well as in general science communication. This oversight limits the generalizability of research findings and their applicability to clinical practice, in particular for women but also for men. This article describes the rationale for an international set of guidelines to encourage a more systematic approach to the reporting of sex and gender in research across disciplines.

Methods: A panel of 13 experts representing nine countries developed the guidelines through a series of teleconferences, conference presentations and a 2-day workshop. An internet survey of 716 journal editors, scientists and other members of the international publishing community was conducted as well as a literature search on sex and gender policies in scientific publishing.

Results: The Sex and Gender Equity in Research (SAGER) guidelines are a comprehensive procedure for reporting of sex and gender information in study design, data analyses, results and interpretation of findings.

Conclusions: The SAGER guidelines are designed primarily to guide authors in preparing their manuscripts, but they are also useful for editors, as gatekeepers of science, to integrate assessment of sex and gender into all manuscripts as an integral part of the editorial process.

Keywords: Sex, Gender, Guidelines, SAGER, Scientific research, Scientific publishing, Gender bias, Equity

Not WHO Normative Guidelines

- SAGER guidelines (2016) were developed to address sex and gender biases in research and data analysis, bridging the gender evidence gap.
- Encourage systematic reporting of sex and gender dimensions in publications.
- Applicable across the research cycle, from design and protocol development to analysis and reporting.

Heidari S, Heidari S, Babor TF, De Castro P, Tort S, Curno M. Sex and gender equity in research: rationale for the SAGER guidelines and recommended use. Res Integr Peer Rev. 2016;1:2. doi: 10.1186/s41073-016-0007-6.

World Health Organization

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

General principles

- Authors should use the terms *sex* and *gender* 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.

Heidari S, Heidari S, Babor TF, De Castro P, Tort S, Curno M. Sex and gender equity in research: rationale for the SAGER guidelines and recommended use. Res Integr Peer Rev. 2016;1:2. doi: 10.1186/s41073-016-0007-6.

SAGER Recommendation # 1
Title and Abstract

If only one sex is included in the study, the title as well as the abstract should specify the sex of animals or any cells, tissues, and other material derived from these, and the sex/gender of human participants.

SAGER Recommendation # 2
Introduction

Authors should report, where relevant, whether sex and/or gender differences may be expected.

Heidari S, Babor TF, De Castro P, Tort S, Curno M. Sex and gender equity in research: rationale for the SAGER guidelines and recommended use. Res Integr Peer Rev. 2016;1:2. doi: 10.1186/s41073-016-0007-6.

The safety and immunogenicity of two novel live attenuated monovalent (serotype 2) oral poliovirus vaccines in healthy adults: a double-blind, single-centre phase 1 study

	Candidate 1 (n=15)	Candidate 2 (n=15)	Total (n=30)
Sex, n (%)			
Male	13 (87%)	12 (80%)	25 (83%)
Female	2 (13%)	3 (20%)	5 (17%)

Summary

Between May 22 and Aug 22, 2017, 48 volunteers were screened, of whom 15 (31%) volunteers were excluded for reasons relating to the inclusion or exclusion criteria, three (6%) volunteers were not treated because of restrictions to the number of participants in each group, and 30 (63%) volunteers were sequentially allocated to groups (15 participants per group). Both novel OPV2 candidates were immunogenic and increased the median blood titre of serum neutralising antibodies; all participants were seroprotected after vaccination. Both candidates had acceptable tolerability, and no serious adverse events occurred during the study. However, severe events were reported in six (40%) participants receiving candidate 1 (eight events) and nine (60%) participants receiving candidate 2 (12 events); most of these events were increased blood creatinine phosphokinase but were not accompanied by clinical signs or symptoms. Vaccine virus was detected in the stools of 15 (100%) participants receiving vaccine candidate 1 and 13 (87%) participants receiving vaccine candidate 2. Vaccine poliovirus shedding stopped at a median of 23 days (IQR 15–36) after candidate 1 administration and 12 days (1–23) after candidate 2 administration. Total shedding, described by the estimated median shedding index (50% cell culture infective dose/g), was observed to be greater with candidate 1 than candidate 2 across all participants (2·8 [95% CI 1·8–3·5] *vs* 1·0 [0·7–1·6]). Reversion to neurovirulence, assessed as paralysis of transgenic mice, was low in isolates from those vaccinated with both candidates, and sequencing of shed virus indicated that there was no loss of attenuation in domain V of the 5′-untranslated region, the primary site of reversion in Sabin OPV.

EXAMPLE

SAGER Recommendation # 3
Methods

How sex and gender were taken into account in the *design* of the study, whether adequate representation were ensured, and the *reasons for any exclusion* justified.

In vivo and in vitro studies using primary cultures of cells, or cell lines from humans or animals, or ex vivo studies with tissues from humans or animals must state the sex of the subjects or source donors

The safety and immunogenicity of two novel live attenuated monovalent (serotype 2) oral poliovirus vaccines in healthy adults: a double-blind, single-centre phase 1 study

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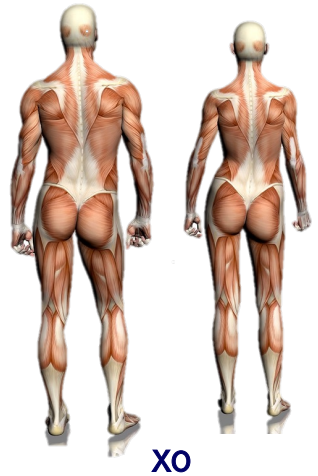
Eligible volunteers were **healthy men or women** (aged 18–50 years), with complete IPV-only polio vaccination histories. Inclusion criteria included a willingness to adhere to all prohibitions and restrictions necessary for full containment for the study duration, …, and no professional food handling activity or household or professional contact with immunosuppressed individuals or people without a full poliovirus vaccination (such as infants under 6 months of age). … **Women of childbearing age** were required to have a negative urine pregnancy test on day 0, not to be breastfeeding, and to use an approved contraceptive method until 3 months after vaccine administration.

EXAMPLE

 Lancet 2019; 394: 148–58

SAGER Recommendation # 3
Methods

Transparent, **clear** and **comprehensive** reporting of the sources of data and methods used to collect data on sex and/or gender, and the purpose of a particular study/analysis to enhances accuracy, minimizes confusion, improves reliability and allows for meaningful interpretation.



How is data on sex collected? Genotyping? Examination of reproductive anatomy? Legally recognised sex? Self-reported sex assigned at birth?*

How is data on gender collected? Self-reported gender? Researcher/provider-reported gender? Legal documents?

*In some countries, individual can change their sex listed on some legal documents to reflect their gender identity.

Collection of other sex/gender relevant data

Unexpected vaginal bleeding and COVID-19 vaccination in nonmenstruating women

KRISTINE BLIX, IDA LAAKE, LENE JUVET, ANNA HAYMAN ROBERTSON, IDA HENRIETTE CASPERSEN, SIRI MJAALAND, SIRI N. SKODVIN, PER MAGNUS, BERIT FEIRING, AND LILL TROGSTAD Authors Info & Affiliations

SCIENCE ADVANCES • 22 Sep 2023 • Vol 9, Issue 38 • DOI: 10.1126/sciadv.adg1391

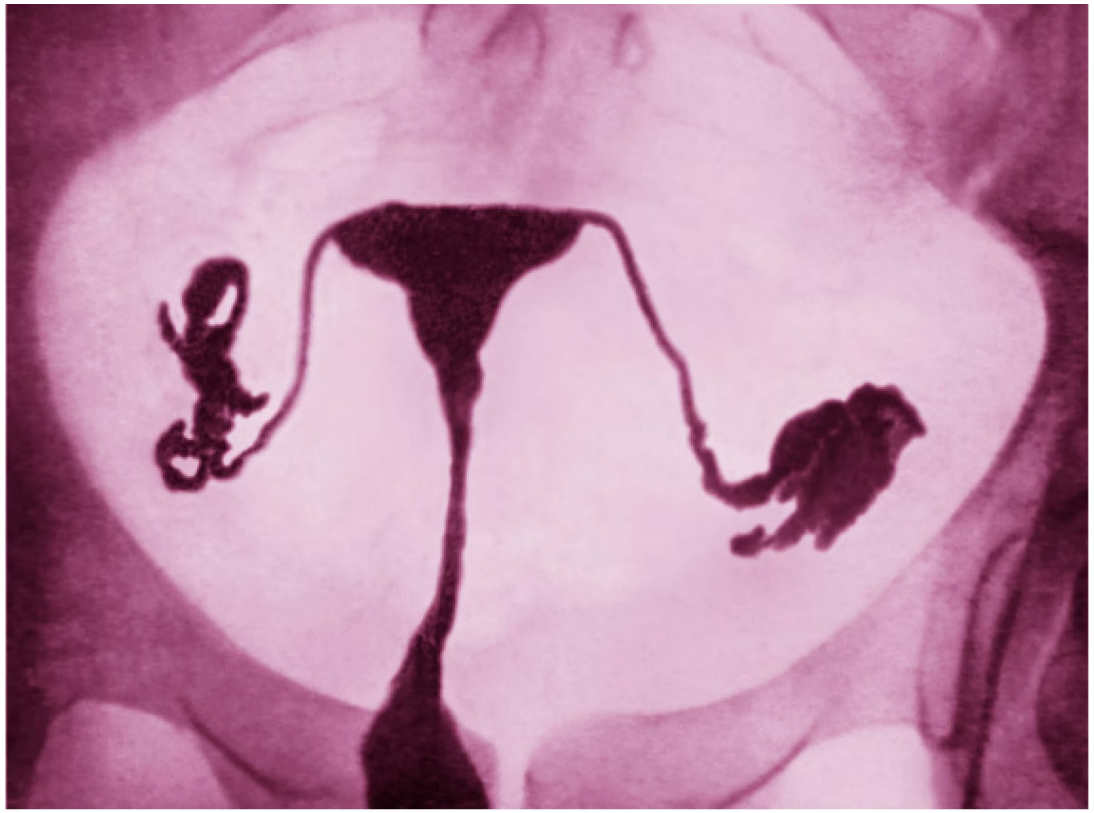
COVID-19 can interfere with your period in many ways. I

There could be temporary disruptions to your cycle a issues after a severe bout of COVID-19.

By Meryl Davids Landau

November 15, 2023 • 7 min read

"One important lesson is that the effects of medical interventions on menstruation should not be an afterthought in future research," she concludes.



This color enhanced hysterosalpingogram shows a female reproductive system, with fallopian tubes and a healthy uterus.

PHOTOGRAPH BY JAMES CAVALLINI, SCIENCE SOURCE NATIONAL GEOGRAPHIC

World Health Organization

SAGER Recommendation # 4
Results

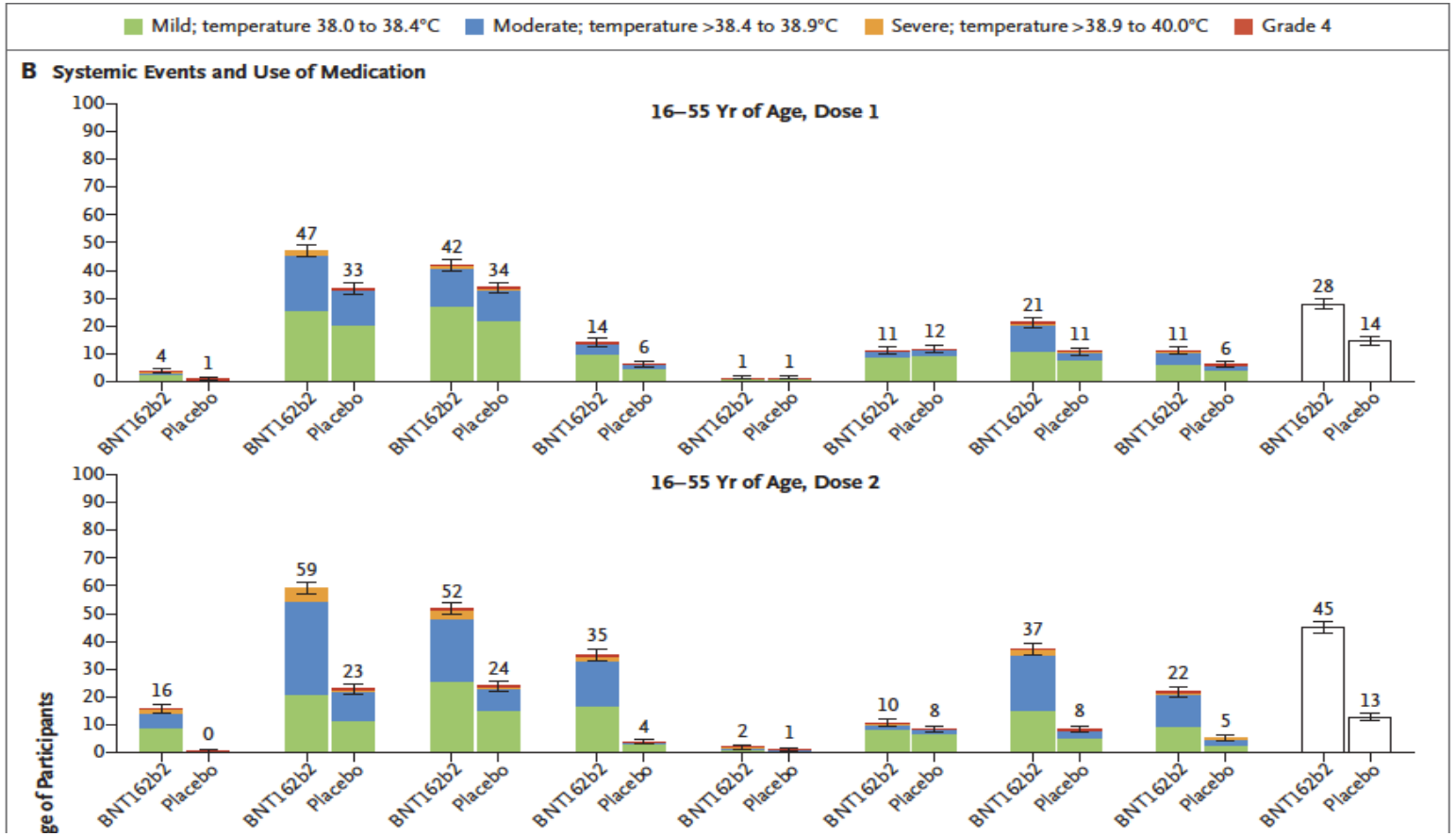
- Data should be routinely presented disaggregated by sex.
- Where appropriate, meaningful sex- and gender-based analyses should be reported regardless of outcome. The reasons for lack of such analysis should be justified.
- Raw data should be published disaggregated by sex and gender for future pooling and meta-analysis.
- In clinical trials, data on withdrawals, dropouts and adverse events should also be reported disaggregated by sex.

Heidari S, Babor TF, De Castro P, Tort S, Curno M. Sex and gender equity in research: rationale for the SAGER guidelines and recommended use. Res Integr Peer Rev. 2016;1:2. doi: 10.1186/s41073-016-0007-6.

Target group	Vaccine	difference in acceptance	Sex difference in immune response	difference in adverse reactions	Age (years)
Children	Hepatitis B	Not defined	Greater in females	Not defined	<12
	Diphtheria	Not defined	Greater in females	Not defined	<2
	Pertussis	Not defined	Greater in females	Not defined	<2
	Pneumococcal	Not defined	Greater in females	Not defined	6–9
	Rabies	Not defined	Greater in females	Not defined	6–9
	Measles	Not defined	Greater in females or equivalent in both sexes	Increased in females	<3
	Malaria (RTS,S)	Not defined	Greater in females	Increased in females	<2
	Human papillomavirus	Less in males	Greater in females	Increased in females	5–17
Adults	Influenza	Less in females	Greater in females	Increased in females	18–49
	Hepatitis B	Not defined	Greater in females	Increased in females	18+
	Herpes virus	Not defined	Greater in females	Not defined	18+
	Yellow fever	Not defined	Greater in females	Increased in females	18+
	Rabies	Not defined	Greater in females	Not defined	18+
	Smallpox	Not defined	Greater in females	Not defined	18+
Aged adults	Influenza	Less in females	Greater in females	Increased in females	65+
	Td/Tdap	Less in females	Greater in males	Increased in females	65+
	Pneumococcal	Less in females	Greater in males	Increased in females	65+
	Shingles	Not defined	Not defined	Increased in females	65+

Source: Flanagan et al. Sex and Gender Differences in the Outcomes of Vaccination over the Life Course. Annu Rev Cell Dev Biol. 2017

Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine



EXAMPLE

 Polack et al (2020) Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine. NEJM

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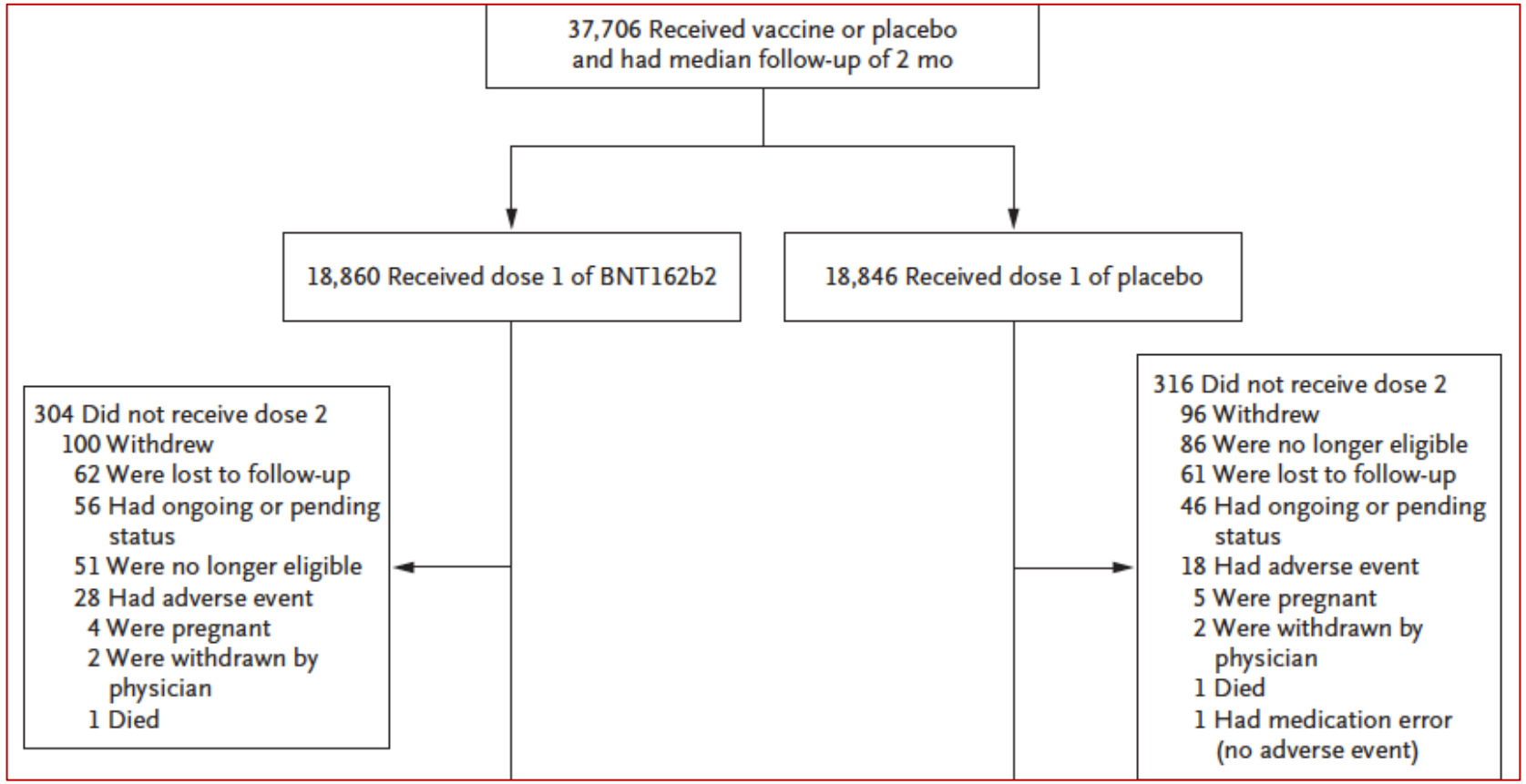
Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine



EXAMPLE

DOI: 10.1056/NEJMoa2034577

World Health Organization

Recommendation # 5
Discussion

- The implications of sex/gender analyses, or lack thereof, should be discussed.
- It should be indicated whether lack of such analyses could have affected the results.

The safety and immunogenicity of two novel live attenuated monovalent (serotype 2) oral poliovirus vaccines in healthy adults: a double-blind, single-centre phase 1 study *Lancet* 2019; 394: 148–58

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EXAMPLE

The results from our phase 1 trial indicate that both candidates are safe and immunogenic in adults. There were no serious adverse events but severe adverse events that were considered possibly to be related to the vaccines were increased blood enzyme concentrations (predominantly creatine kinase, but also alanine transaminase and aspartate transaminase), which were observed in about half the participants 1 week after vaccine administration. These increases were transient and without any abdominal symptoms or other indicators of liver damage; γ-glutamyltransferase and bilirubin concentrations were unaffected.

SAGER checklists!

Table 2 Authors' checklist for gender-sensitive reporting

Research approaches ✓

- ✓ Are the concepts of gender and/or sex used in your research project?
- ✓ If yes, have you explicitly defined the concepts of gender and/or sex? Is it clear what aspects of gender and/or sex are being examined in your study?
- ✓ If no, do you consider this to be a significant limitation? Given existing knowledge in the relevant literature, are there plausible gender and/or sex factors that should have been considered? If you consider sex and/or gender to be highly relevant to your proposed research, the research design should reflect this

Research questions and hypotheses

- ✓ Does your research question(s) or hypothesis/es make reference to gender and/or sex, or relevant groups or phenomena? (e.g., differences between males and females, differences among women, seeking to understand a gendered phenomenon such as masculinity)

Heidari *et al. Research Integrity and Peer Review* (2016)

Van Epps H et al. European Science Editing (2022)

Heidari S, Babor TF, De Castro P, Tort S, Curno M. Sex and gender equity in research: rationale for the SAGER guidelines and recommended use. Res Integr Peer Rev. 2016;1:2. doi: 10.1186/s41073-016-0007-6.

World Health Organization

#SAGERguidelines in other languages

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Article Accesses

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Citation

Equidade de sexo e gênero na pesquisa: fundamentação das diretrizes SAGER e uso recomendado*

研究中的性和性别平等：SAGER 指南和建议使用的理由

Bình đẳng giới và giới tính trong nghiên cứu (SAGER): Sự cần thiết của Bộ hướng dẫn SAGER và cách sử dụng

Equidad según sexo y de género en la investigación: justificación de las guías SAGER y recomendaciones para su uso

ARAŞTIRMALARDA CİNSİYET VE TOPLUMSAL CİNSİYET EŞİTLİĞİ: SAGER YÖNERGELERİNİN GEREKÇESİ VE KULLANIM ÖNERİSİ#

연구에서의 성별과 젠더 형평성: SAGER 지침의 근거 및 이용방법

equator network

Enhancing the QUAlity and Transparency Of health Research

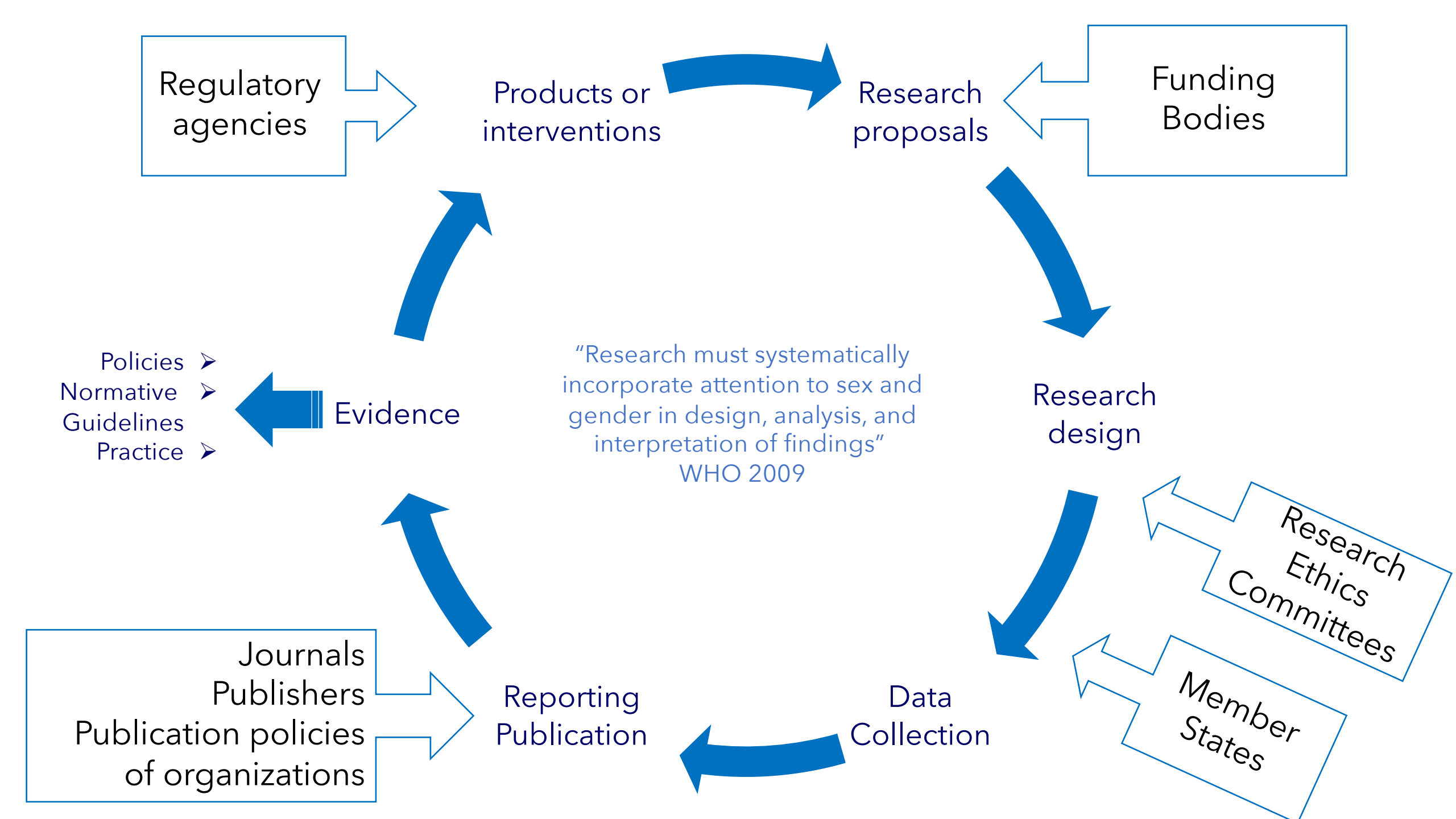
World Health Organization

WHO adopted the SAGER guidelines in Dec 2023

- Introduced in the WHO eManual
- Apply to all research and data-driven publications and technical products by and in collaboration with WHO.
- Apply to WHO workforce, collaborating partners and anyone engaged with WHO in using and producing evidence.
- The aspiration is to instigate change across the evidence generation cycle: to be applied in research design, development of protocol, ethical evaluations, data collection, analysis, reporting, and informing policy and operational decisions.

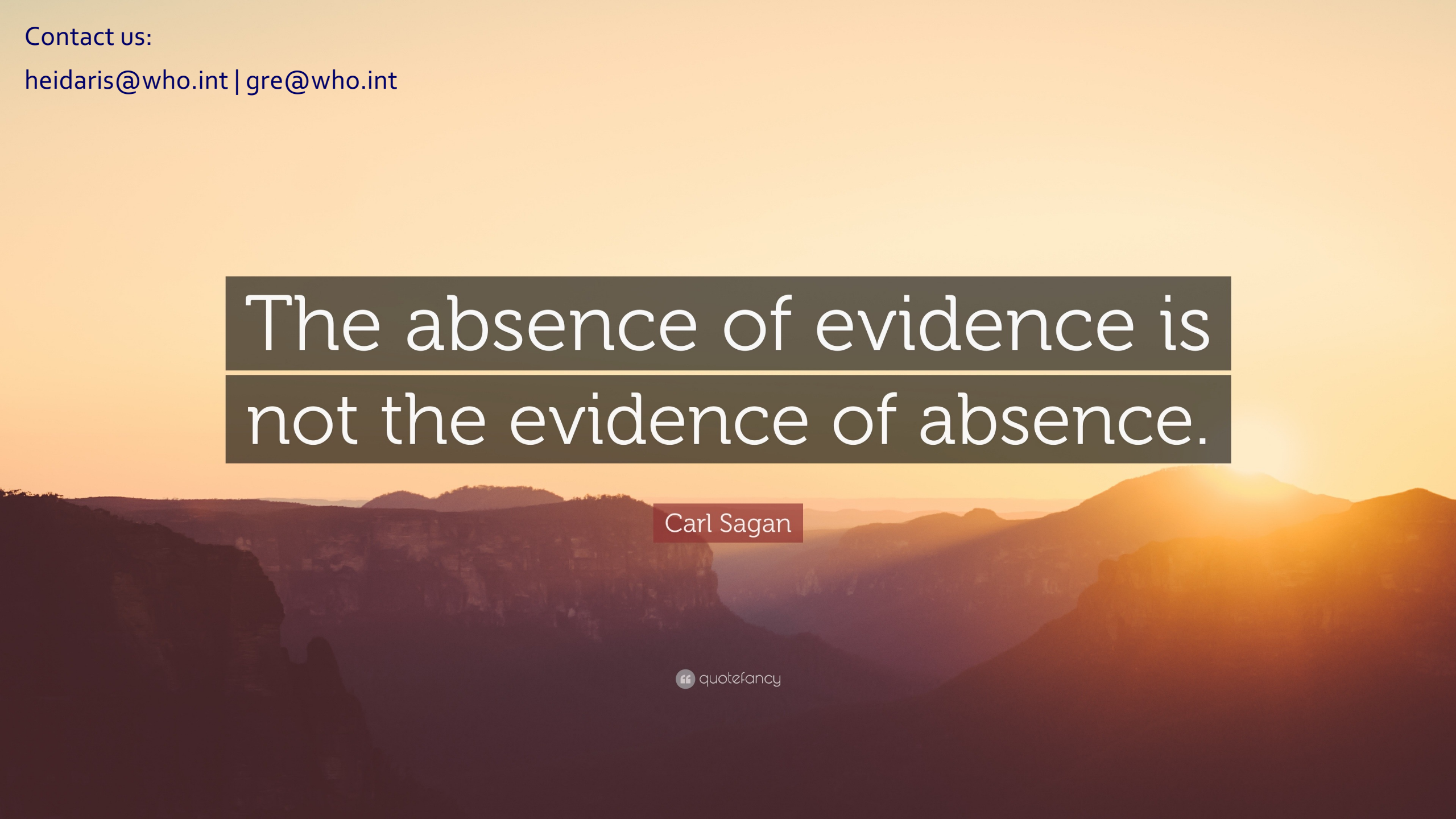
https://doi.org/10.1016/S0140-6736(23)02807-6

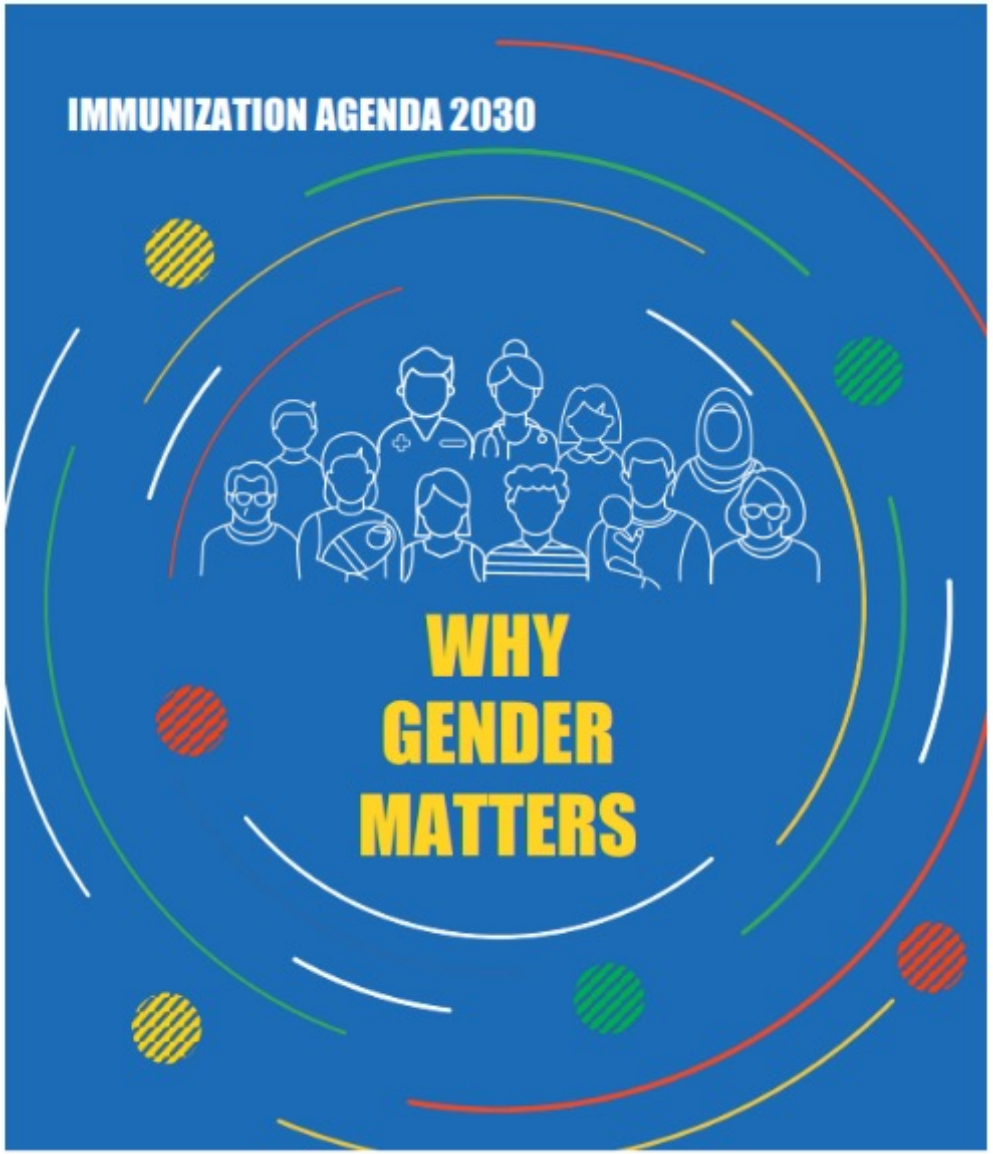
World Health Organization


Regulatory agencies
Products or interventions
Research proposals
Funding Bodies
Policies
Normative Guidelines
Practice
Evidence
"Research must systematically incorporate attention to sex and gender in design, analysis, and interpretation of findings"
WHO 2009
Research design
Research Ethics Committees
Member States
Data Collection
Reporting Publication
Journals
Publishers
Publication policies of organizations

Contact us:

heidaris@who.int | gre@who.int





World Health Organization

unicef for every child

Gavi The Vaccine Alliance

Q and A

All materials and recordings from this and previous webinars available here: https://www.technet-21.org/en/hot-topics-items/429-programme-management/15449-gender-and-immunization

For more info, visit: https://www.who.int/teams/immunization-vaccines-and-biologicals/gender