FONDAZIONE ONDA ETS

23 - 24 settembre 2026

Evento in modalità virtuale

Politerapie e interazioni: nuova frontiera della farmacologia di genere

Luigia Trabace
Università degli Studi di Foggia
Coordinatrice GdL Farmacologia e Tossicologia di Genere
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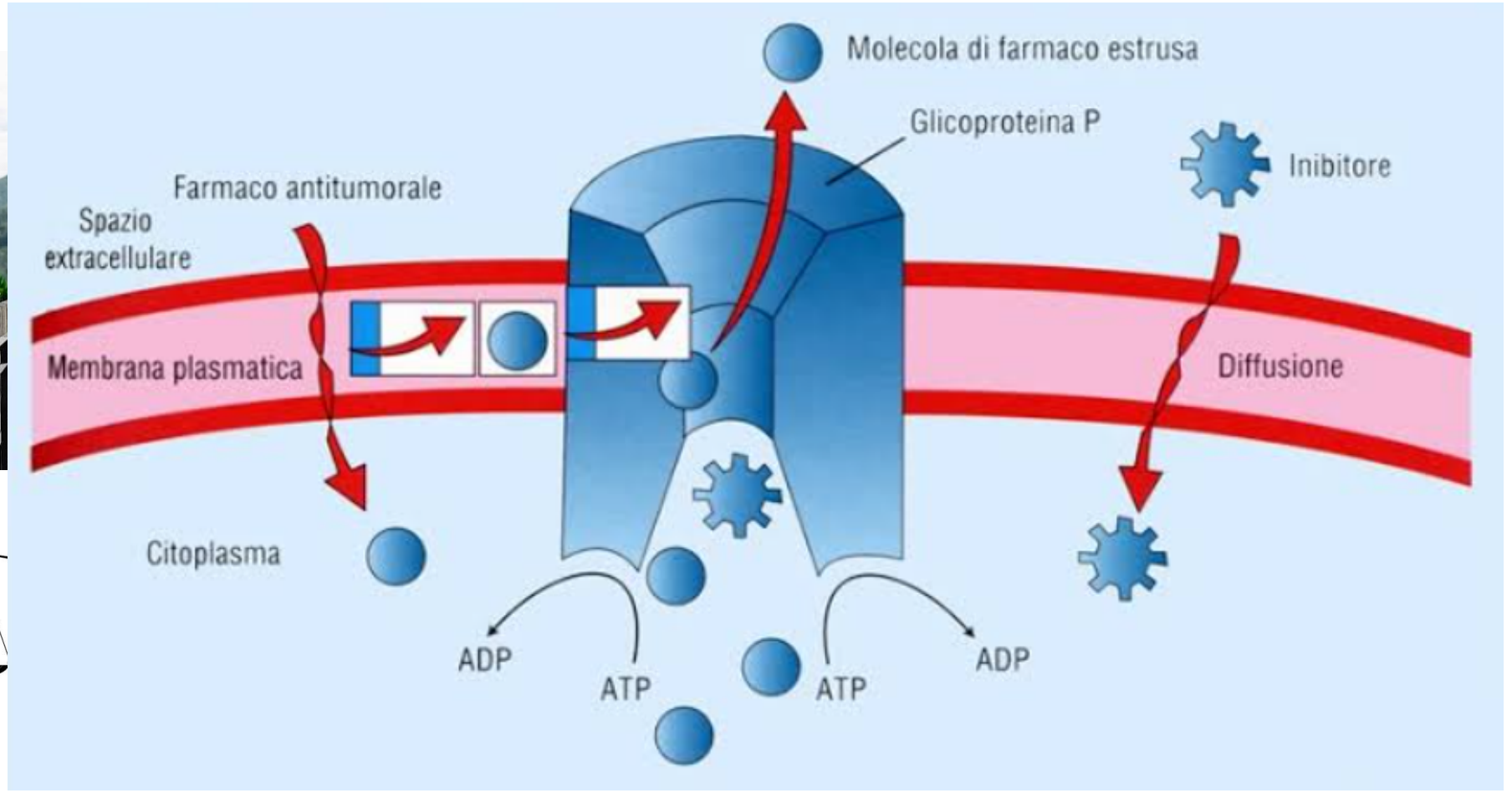
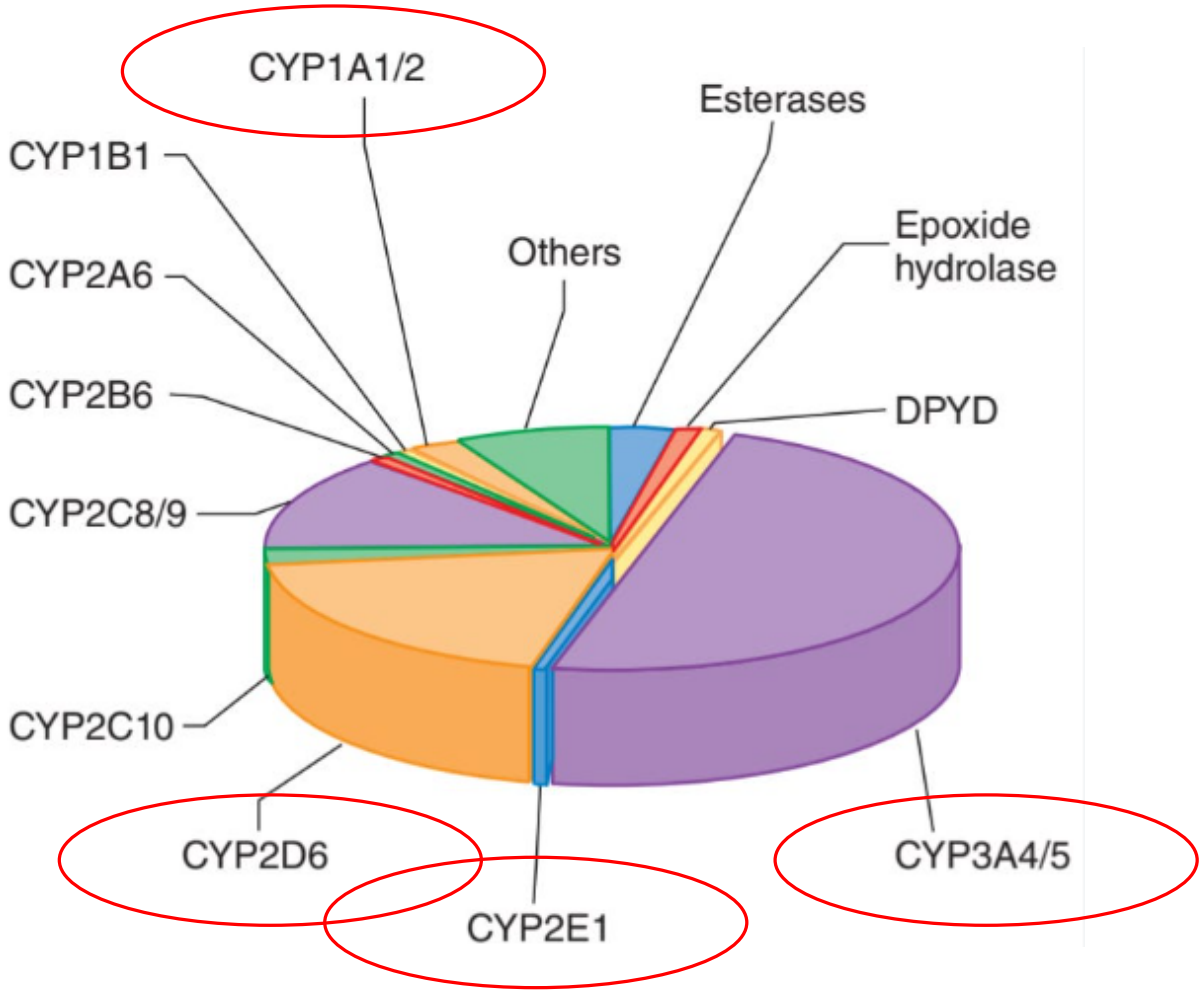
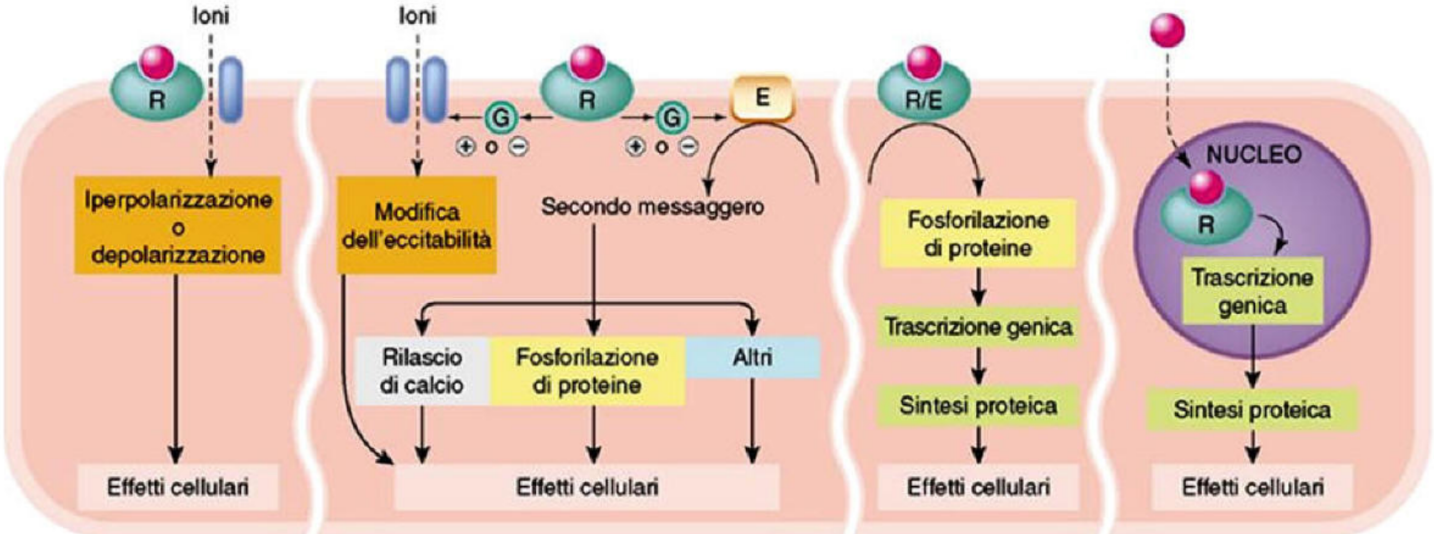

Molecola di farmaco estrusa
Glicoproteina P
Inibitore
Farmaco antitumorale
Spazio
extracellulare
Membrana plasmatica
Diffusione
Citoplasma
ADP
ATP
ATP
ADP


CYP1A1/2
CYP1B1
CYP2A6
CYP2B6
CYP2C8/9
CYP2C10
CYP2D6
CYP2E1
Others
Esterases
Epoxide hydrolase
DPYD
CYP3A4/5


Ioni
R
Iperpolarizzazione
o
depolarizzazione
Effetti cellulari
Ioni
R
G
G
E
Modifica
dell'eccitabilità
Secondo messaggero
Rilascio
di calcio
Fosforilazione
di proteine
Altri
Effetti cellulari
R/E
Fosforilazione
di proteine
Trascrizione genica
Sintesi proteica
Effetti cellulari
NUCLEO
R
Trascrizione
genica
Sintesi proteica
Effetti cellulari

Cosa succede quando le differenze
sesso-specifiche
della farmacocinetica e della
farmacodinamica entrano in una rete di
interazioni farmacologiche?

Archives of Gerontology and Geriatrics 78 (2018) 213–220

Contents lists available at ScienceDirect

Archives of Gerontology and Geriatrics

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

Polypharmacy prevalence among older adults based on the survey of health, ageing and retirement in Europe

Luís Midão[a], Anna Giardini[b], Enrica Menditto[c], Przemyslaw Kardas[d], Elísio Costa[a,*]

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[b] Psychology Unit, Instituti Clinici Scientifici Maugeri Spa – Società Benefit, Care and Research Institute, IRCCS Montescano (PV), Italy
[c] School of Pharmacy, CIRFF/Center of Pharmacoeconomics, University of Naples Federico II, Naples, Italy
[d] Department of Family Medicine, Medical University of Lodz, Lodz, Poland

collected data from 68,231 individuals, with ages between 24 and 106 years.

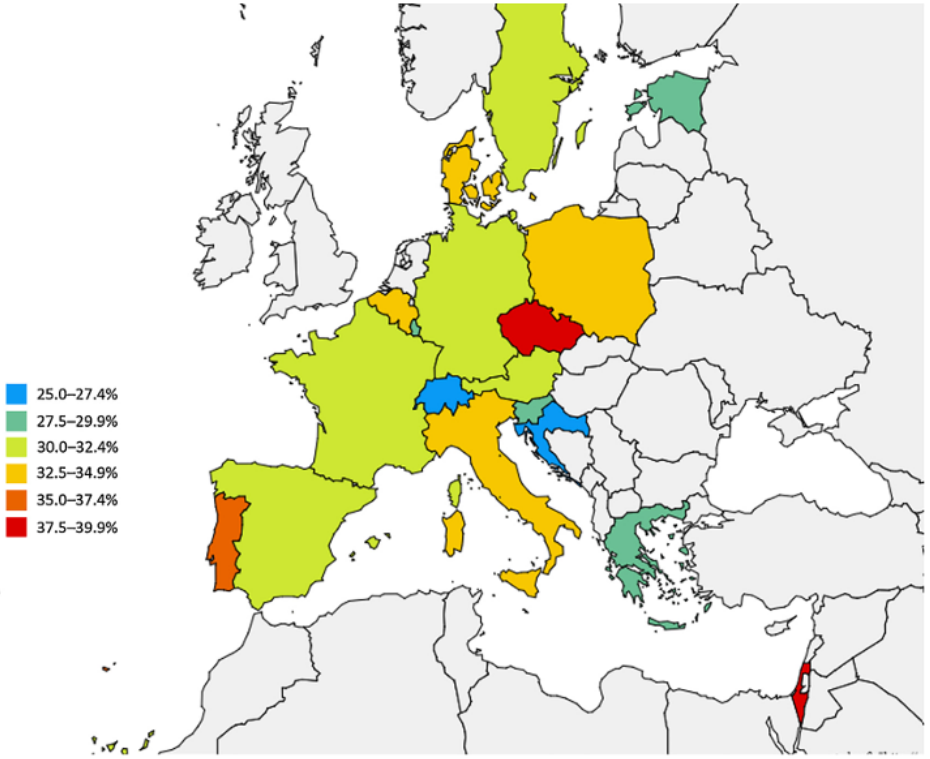


Fig. 2. Prevalence of polypharmacy in elderly (65 years or older) among 17 European countries and Israel.

"Globally, the prevalence of polypharmacy increases with age, being higher for women"

Received: 20 June 2024 | Revised: 24 October 2024 | Accepted: 27 October 2024

DOI: 10.1111/jgs.19282

CLINICAL INVESTIGATION

Journal of the
American Geriatrics Society

The impact of age, sex, and gender on polypharmacy and potential prescribing cascades: Lessons from five databases

The prevalence of polypharmacy and hyperpolypharmacy was generally higher among men.

Vasily Giannakeas PhD[1,2] | Altea Kthupi MPH[1] | Kieran Dalton PhD[11] |
Lisa M. McCarthy PharmD, MSc[12,13,14] | Robin Mason PhD[1] |
Amanda Giancola MSc[1] | Parya Borhani MPH[1] | Antonio Cherubini MD, PhD[15,16]

Polypharmacy, inappropriate prescribing, and deprescribing in older people: through a sex and gender lens

Paula A Rochon, Mirko Petrovic, Antonio Cherubini, Graziano Onder, Denis O'Mahony, Shelley A Sternberg, Nathan M Stall, Jerry H Gurwitz

Polypharmacy is very common in older adults and increases the risk of inappropriate and unsafe prescribing for older adults. Older adults, particularly women (who make up the majority of this age group), are at the greatest risk for drug-related harm. Therefore, optimising drug prescribing for older people is very important. Identifying potentially inappropriate medications and opportunities for judicious deprescribing processes are intrinsically linked, complementary, and essential for optimising medication safety. This Review focuses on optimising prescribing for older adults by reducing doses or stopping drugs that are potentially harmful or that are no longer needed. We explore how sex (biological) and gender (sociocultural) factors are important considerations in safe drug prescribing. We conclude by providing a practical approach to optimising medication safety that clinicians can routinely apply to the care of their older patients, highlighting how sex and gender considerations inform medication decision making.

Lancet Healthy Longev 2021; 2: e290–300

Women's College Research Institute, Women's College Hospital, Toronto, ON, Canada (P A Rochon MD, N M Stall MD); Department of Medicine and Institute of Health Policy, Management, and Evaluation, University of Toronto, Toronto, ON, Canada (P A Rochon, N M Stall); Section

A + B

≠

effetto del sesso + effetto dell'interazione

=

amplificazione dell'esposizione

"interazione sesso-modulata"

Review > Curr Drug Metab. 2019;20(2):114-123. doi: 10.2174/1389200220666181128160813.

Progress in the Consideration of Possible Sex Differences in Drug Interaction Studies

Panjasaram Naidoo [1], Manoranjenni Chetty [1]

Conclusion: This review has shown that only limited progress had been made with the inclusion of both sexes in DDI studies.


METOPROLOL
METOPROLOL A BETA-BLOCKER USED TO TREAT HIGH BLOOD PRESSURE, ANGINA, AND HEART FAILURE.
METOPROLOL
METOPROLOL A BETA-BLOCKER USED TO TREAT HIGH BLOOD PRESSURE, ANGINA, AND HEART FAILURE.

Clinical Pharmacology & Therapeutics

Pharmacokinetics and Drug Disposition

Gender-related effects on metoprolol pharmacokinetics and pharmacodynamics in healthy volunteers

Aileen Bown Luzier PharmD, Aaron Killian PharmD, John H. Wilton PhD, Michael F. Wilson MD, Alan Forrest PharmD, David J. Kazierad PharmD

First published: 19 December 1999 | https://doi.org/10.1053/cp.1999.v66.103400001 |

It is primarily metabolized by **CYP2D6** enzyme to α-hydroxymetoprolol and *O*-demethylmetoprolol

Received: 10 November 2022 | Revised: 29 January 2023 | Accepted: 31 January 2023

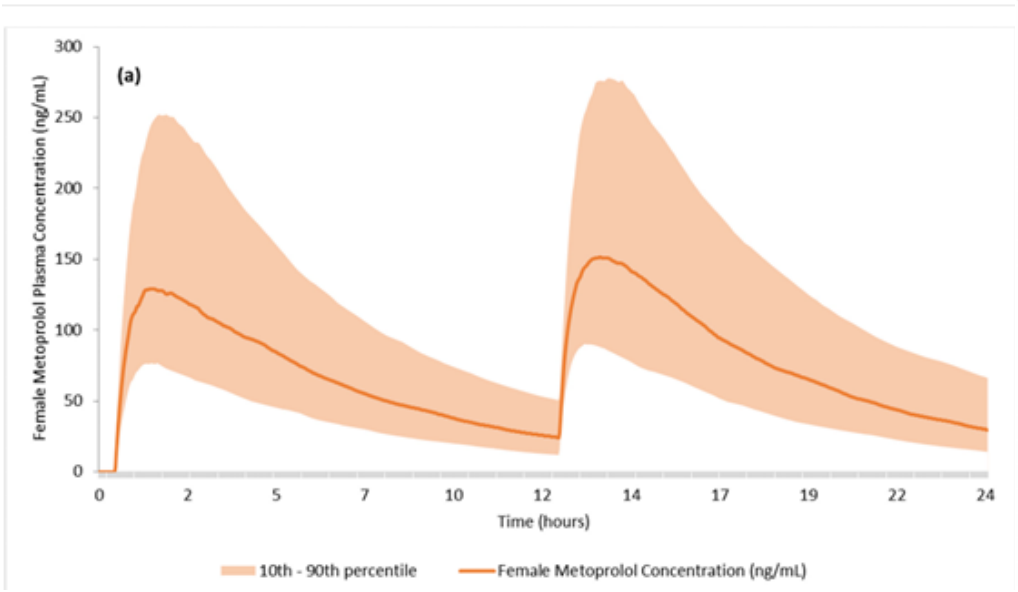
DOI: 10.1111/cts.13497

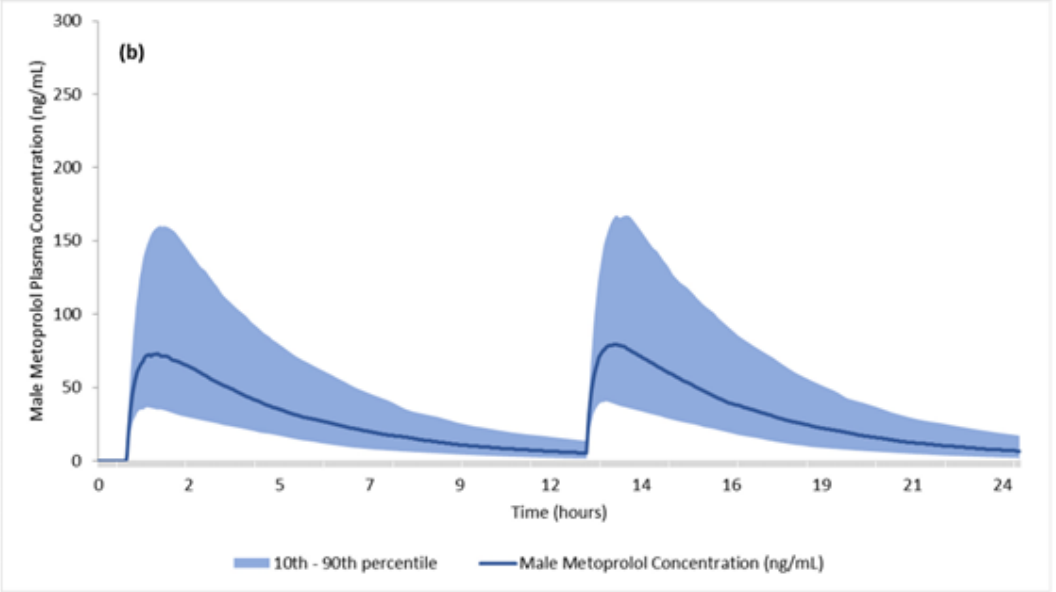
ARTICLE

Females present higher dose-adjusted drug concentrations of metoprolol and allopurinol/oxypurinol than males

Jessica Hindi[1,2,3] | Marc-Olivier Pilon[1,2,3] | Maxime Meloche[1,2,3] | Grégoire Leclair[1] | Essaïd Oussaïd[2,3] | Isabelle St-Jean[1] | Martin Jutras[1] | Marie-Josée Gaulin[2,3] | Ian Mongrain[2,3] | David Busseuil[2,3] | Jean Lucien Rouleau[2,4] | Jean-Claude Tardif[2,3,4] | Marie-Pierre Dubé[2,3,4] | Simon de Denus[1,2,3]

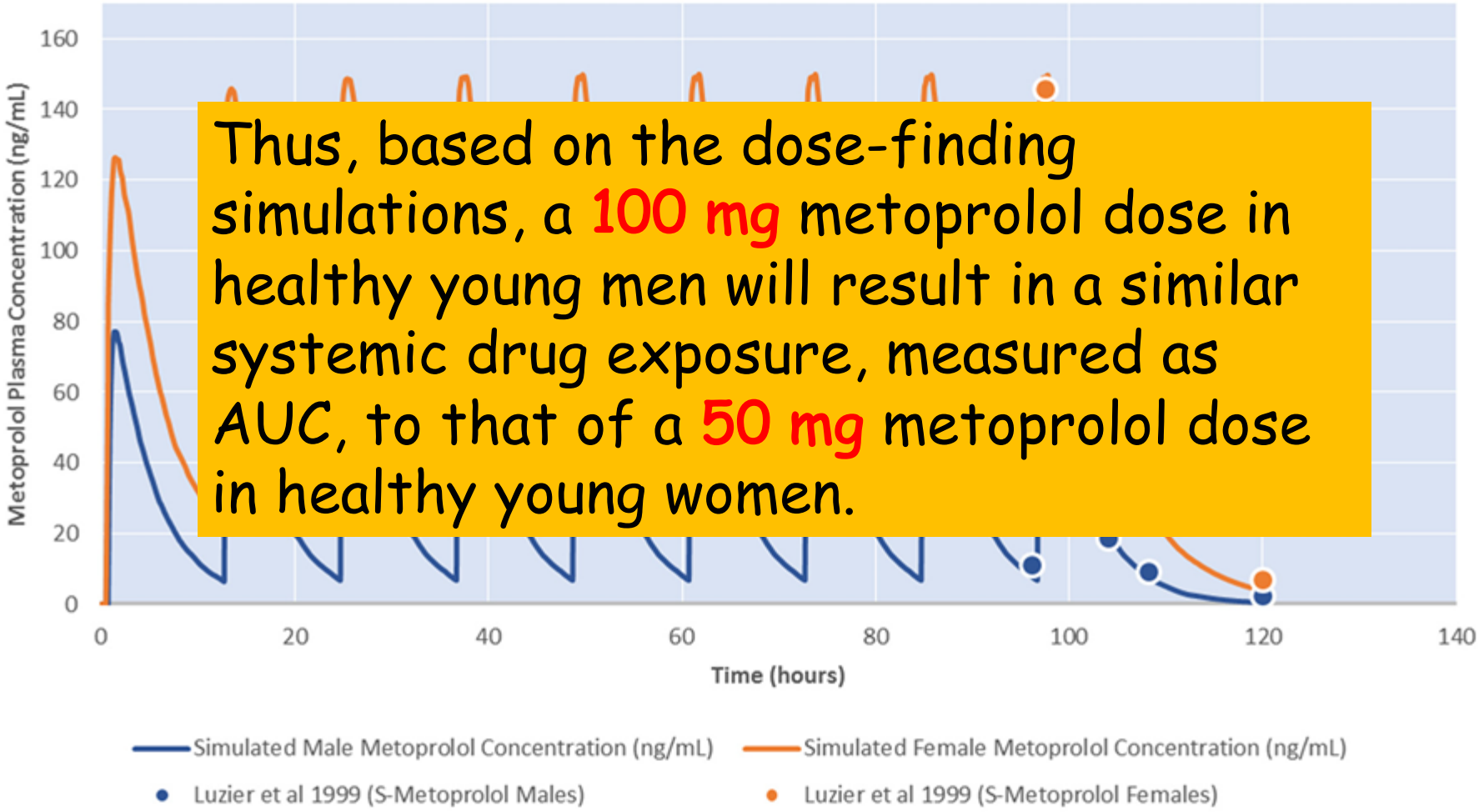
Metoprolol population		
Male ($N = 734$) (72.89%)	Female ($N = 273$) (27.11%)	All ($N = 1007$) (100.0%)





women:CL=101L/h;men:CL=253L/h

Med. Sci. 2016, 4, 18; doi:10.3390/medsci4040018



Thus, based on the dose-finding simulations, a 100 mg metoprolol dose in healthy young men will result in a similar systemic drug exposure, measured as AUC, to that of a 50 mg metoprolol dose in healthy young women.

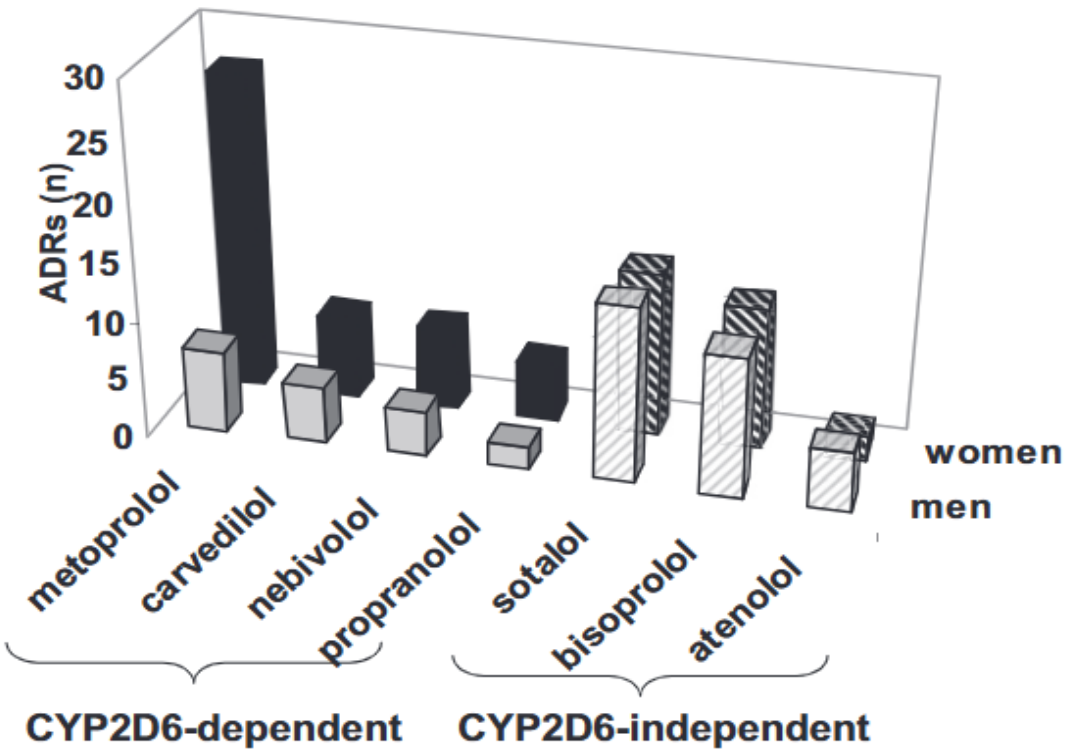


Fig 1. Sex-specific frequency of drug-related hospitalizations (adverse drug reactions [ADRs]) associated with different β-blockers grouped according to their metabolism via CYP2D6.

CLINICAL PHARMACOLOGY & THERAPEUTICS2006;80(5):549-60

Published in final edited form as:
Int J Clin Pharmacol Toxicol. 2016 May ; 5(3): 209–215.

Gender based Dosing of Metoprolol in the Elderly using Population Pharmacokinetic Modeling and Simulations

Andy R. Eugene, MD[1,2]

[1]Division of Clinical Pharmacology, Department of Molecular Pharmacology and Experimental Therapeutics, Gonda 19, Mayo Clinic, 200 First Street SW, Rochester, MN 55905, USA

[2]Joyner Lab: Integrative Human Physiology and Pharmacology Lab, Department of Anesthesiology, Rochester, MN, USA

Based from the findings, gender stratified doses for metoprolol yielding relatively similar systemic drug exposures were calculated to be **15mg for geriatric women** and **25mg for geriatric men** resulting in that found in healthy **young males administered a 50mg dose**

Gender differences in metoprolol exists in geriatric patients

sesso femminile +
età avanzata +
CYP2D6 a bassa attività +
metoprololo +

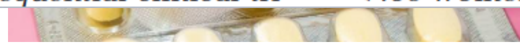
inibitore del CYP2D6 = ?

Toward Optimal Treatment in Women: The Effect of Sex on Metoprolol-Diphenhydramine Interaction

Ashish Sharma, RPEBC, PhD, DPMP, Philippe Pibarot, DVM, PhD, Sylvie Pilote, MSc, Jean G. Dumesnil, MD, FACC, Marie Arsenault, MD, Pierre Maxime Bélanger, PhD, Bernd Meibohm, PhD, FCP, and Bettina A. Hamelin, PharmD

The objective of this study was to determine if sex influences the pharmacokinetics and hemodynamics of the CYP2D6 substrate metoprolol and its interaction with diphenhydramine (CYP2D6 inhibitor) in healthy young participants with high (extensive metabolizer [EM]) or low (poor metabolizer [PM]) CYP2D6 activities. A prespecified comparative analysis of data from 2 sequential clinical tri-

*women compared to men). Diphenhydramine coadministration increased S-metoprolol AUC by 84% in EM women and 45% in EM men (*P *< .009 women compared to men). In the diphenhydramine arm, sex differences in pharmacokinetics persisted even after WT correction, resulting in greater negative chronotropic effects in women (all* Ps *< .05 women compared to men). Metoprolol dose should*



• . J Clinical Pharmacol. 2010 Feb;50(2):214-25.


FONDAZIONE
onda
ETS
L'integrazione del sesso come variabile fondamentale, tanto nella ricerca farmacologica quanto nella pratica clinica, è un
imperativo etico e scientifico
per una medicina veramente equa e personalizzata.
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