



WOMEN'S BRAIN PROJECT®

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# Sex and Gender Differences for Precision Medicine

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Dr Antonella Santucciono Chadha, Co-founder and CEO, Women's Brain Project, Switzerland

"Ensure healthy lives and promote well-being for all at all ages" – United Nations SDG goal # 3





## Faculty Disclosure

<input type="checkbox"/>	No, nothing to disclose
<input checked="" type="checkbox"/>	Yes, please specify:

Company Name	Honoraria/ Expenses	Consulting/ Advisory Board	Funded Research	Royalties/ Patent	Stock Options	Ownership/ Equity Position	Employee	Other (please specify)
Altoida							X	Chief Medical Officer
Women's Brain Project							Pro Bono	CSO and co-founder
Euresearch							Pro Bono	Vice President

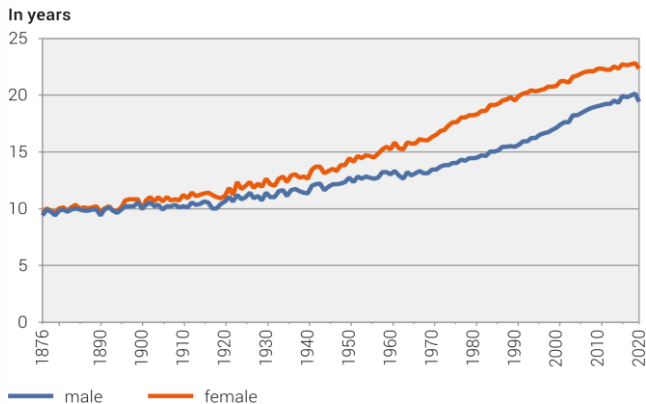
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<input checked="" type="checkbox"/>	No
<input type="checkbox"/>	Yes, please specify:

*This presentation represents Dr. Santuccione Chadha personal view only and not the position of any group or entity with which she is associated*

# Women live longer

## Life expectancy at age 65



Sources: FSO – ESPOP, BEVNAT, STATPOP

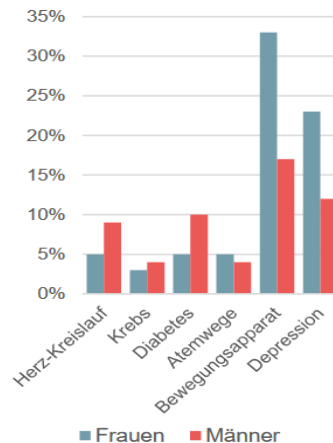
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Schweizerische Eidgenossenschaft  
Confédération suisse  
Confederazione Svizzera  
Confederaziun svizra

# Women suffer more with depression and disease related to motility

## Nicht-übertragbare Krankheiten bei Personen ab 55 Jahren



Prävalenzen der NCD bei Personen ab 55 Jahren, Quelle: SHARE 6 (2014), N=2569



# Women are the majority of the patients living with dementia

T1: Geschätzte Anzahl Personen mit Demenz in der Schweiz 2020 nach Altersgruppen und Geschlecht

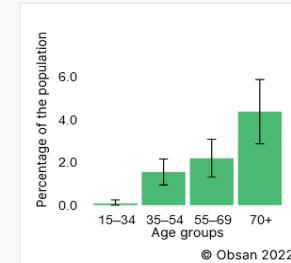
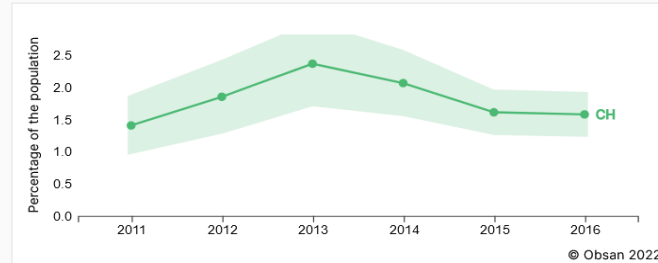
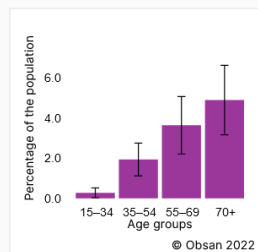
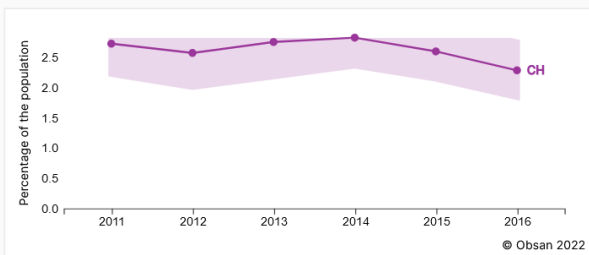
Altersgruppe	Männer		Frauen		Total	
	Anzahl Betroffene	Prävalenz-rate	Anzahl Betroffene	Prävalenz-rate	Anzahl Betroffene	Prävalenz-rate
30-59	3'000	0.2%	1'661	0.1%	4'661	0.1%
60-69	2'817	0.6%	5'673	1.2%	8'490	0.9%
70-79	16'111	4.8%	22'757	5.9%	38'868	5.4%
80-89	19'056	12.7%	39'647	17.9%	58'703	15.8%
90+	7'134	29.7%	26'371	44.8%	33'506	40.4%

Quelle: Alzheimer Europe 2020 (ab 65-Jährige), EuroCoDe 2009 (60-64-Jährige), EURODEM 1991 (<60-Jährige), BFS Statpop 2019

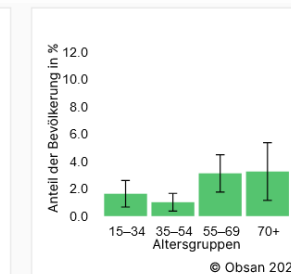
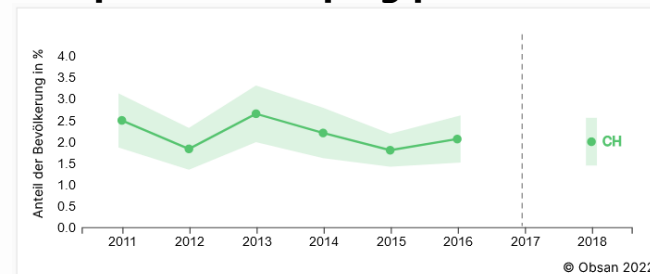
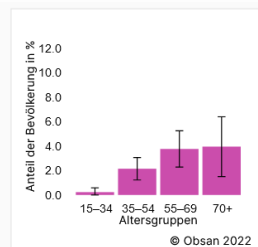
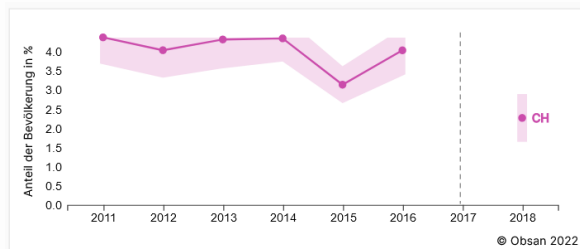


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## Percentage of the population with almost daily consumption of painkillers



## Percentage of the population with almost daily consumption of sleeping pills



<https://ind.obsan.admin.ch/indicator/monam/chronische-medikamenteneinnahme-alter-15>

# Biology or society?

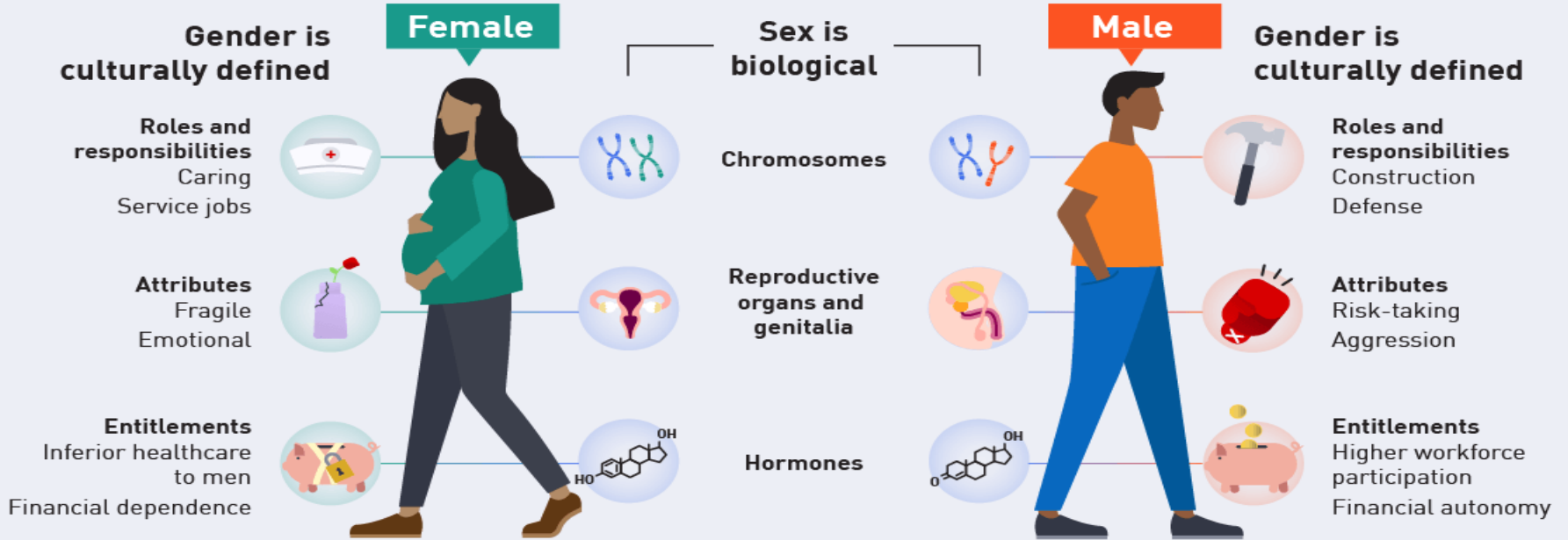


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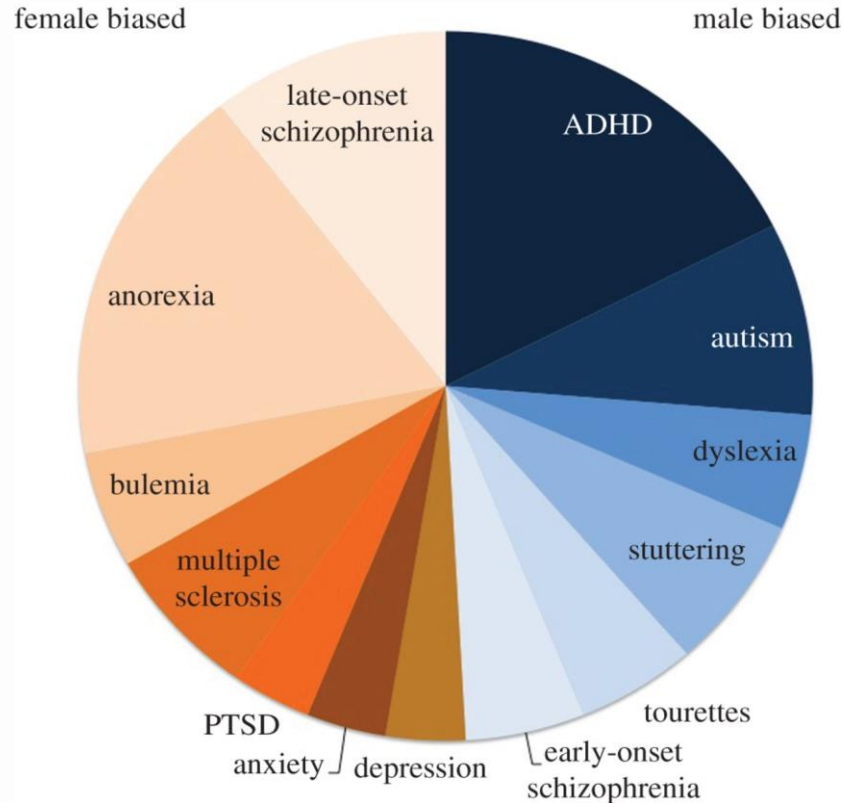
## Sex vs Gender



# Almost all brain and mental diseases present a sex bias



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## Female biased:

- Alzheimer's disease
- Depression
- Anxiety
- NMDA-R encephalitis
- Migraine
- Traumatic Brain Injury
- Long COVID
- Late stroke
- Meningiomas
- Dystonia

## Male biased:

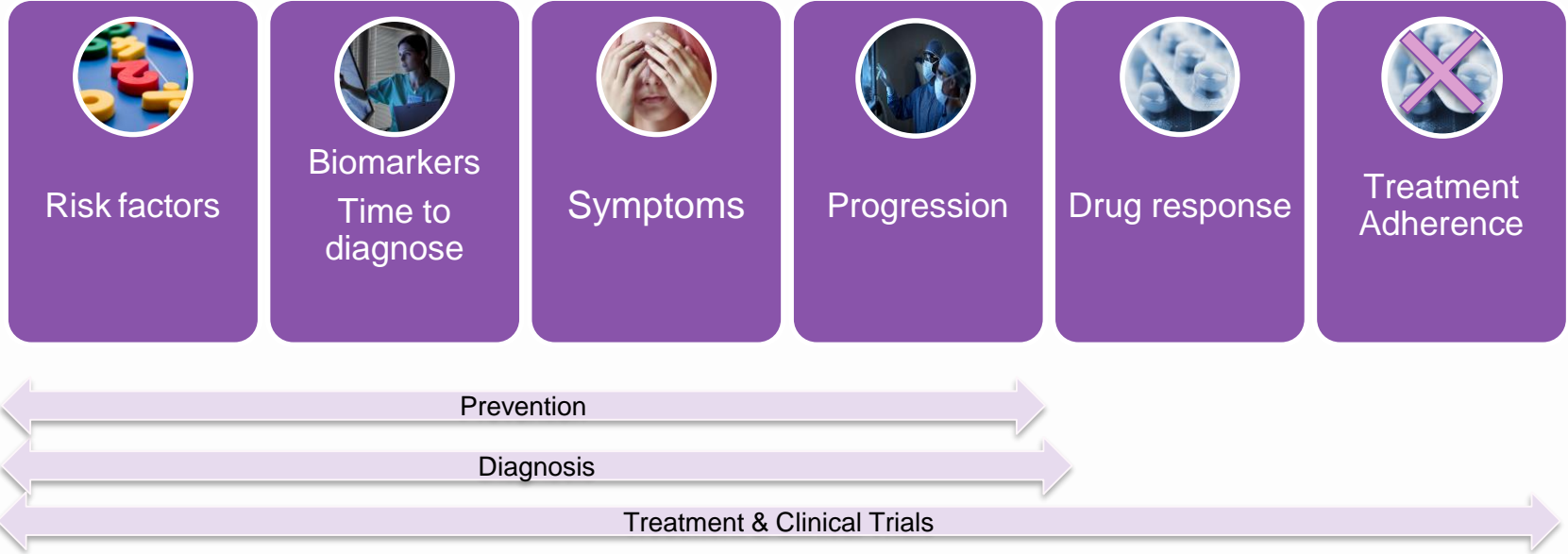
- Parkinson disease
- ALS
- Midlife stroke
- ...

Multifaceted origins of sex differences in the brain,  
Volume: 371, Issue: 1688, DOI: (10.1098/rstb.2015.0106)  
Clayton JA. *Dialogues Clin Neurosci.* 2016;18(4):357-360.  
doi:10.31887/DCNS.2016.18.4/jclayton



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# It is not only about Incidence and Prevalence



Multifaceted origins of sex differences in the brain, Volume: 371, Issue: 1688, DOI:  
(10.1098/rstb.2015.0106)

Clayton JA. *Dialogues Clin Neurosci.* 2016;18(4):357-360. doi:10.31887/DCNS.2016.18.4/jclayton

# Alzheimer's disease (AD) under the sex and gender lens

Women represent the majority of patients with AD and related dementias (68.2% and 62.1% of patients, on average, in Europe and US, respectively)<sup>1,2</sup>.

Sex differences occur in disease symptoms, progression, biomarkers<sup>3</sup>.

Sex differences occur in APOE4 genetic risk effect<sup>4</sup>.

1. Alzheimer Europe. Dementia in Europe Yearbook. Estimating the prevalence of dementia in Europe. 108 (2019).
2. .2020 Alzheimer's disease facts and figures. Alzheimer's Dement. 16, 391–460 (2020).
3. Ferretti, M. T. et al. Sex differences in Alzheimer disease—the gateway to precision medicine. Nat. Rev. Neurol. 14, 457–469 (2018).
4. Hohman, T. J. et al. Sex-specific association of apolipoprotein e with cerebrospinal fluid levels of tau. JAMA Neurol. 75, 989–998 (2018).

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HARE August 11, 2020 ARTICLE

Sex differences in CSF biomarkers vary by Alzheimer's disease stage and APOE ε4 genotype

Rosha Babapour Mofrad, Betty M Tijms, Philip Scheltens, Frederik Barkhof, Wiesje M van der Flier, Sietske AM Sikkes, Charlotte E Teunissen

First published August 11, 2020, DOI: <https://doi.org/10.1212/WNL.00000000000010629>



## The accumulation rate of tau aggregates is higher in females and younger amyloid-positive subjects

Ruben Smith,<sup>1,2</sup> Olof Strandberg,<sup>1</sup> Niklas Mattsson-Carlgren,<sup>1,2,3</sup> Antoine Leuzy,<sup>1</sup> Sebastian Palmqvist,<sup>1,4</sup> Michael J. Pontecorvo,<sup>5</sup> Michael D. Devous Sr,<sup>5</sup> Rik Ossenkoppele<sup>1,6</sup> and Oskar Hansson<sup>1,4</sup>

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October 09, 2019 ARTICLE

Sex-specific norms for verbal memory tests may improve diagnostic accuracy of amnesic MCI

Erin E. Sundermann, Pauline Maki, Anat Blegion, Richard B. Lipton, Michelle M. Melke, Mary Machulda, Mark W. Bondi, for the Alzheimer's Disease Neuroimaging Initiative

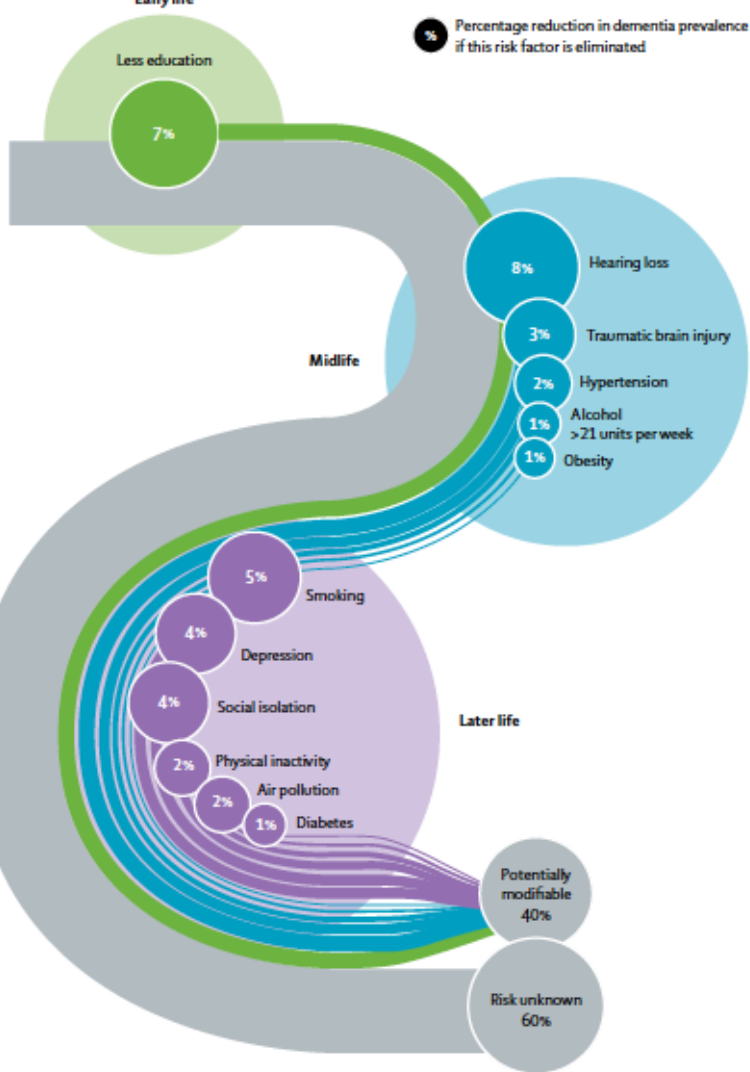
First published October 9, 2019, DOI: <https://doi.org/10.1212/WNL.00000000000008467>



# Dementia is preventable (by 40%)

Three gender medicine aspects relevant for individual-level risk prediction and prevention:

1. Epidemiology of known risk factors
2. Sex-specific risk factors
3. Risk factors with different 'weight' across sexes



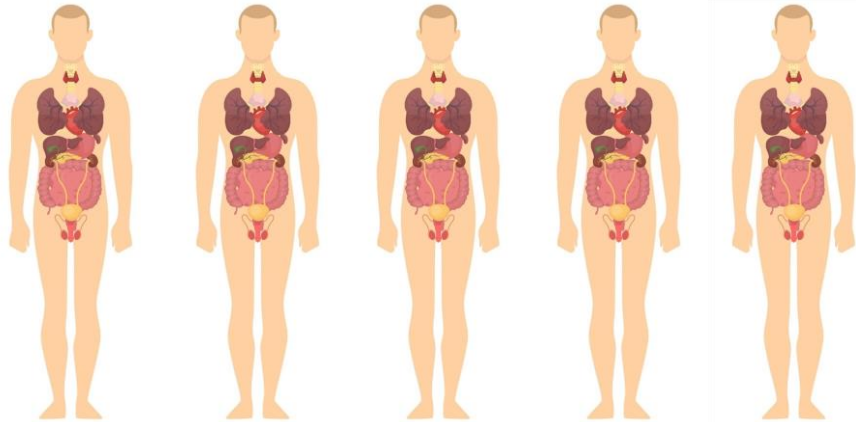
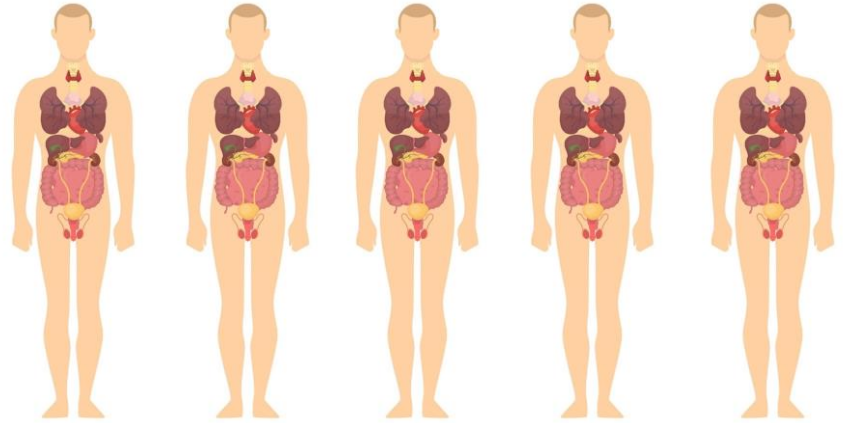
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**The problem:** Are sex and gender factors considered in medicine when we study disease and develop novel treatment solution?

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...NO. This is a problem

The male body is the default for biomedical research and care



In pre-clinical research and mice models findings are **heavily influenced by sex** but data are not stratified by sex and gender

In clinical development **women are less likely to be represented** particularly in Phase I and Phase II clinical trials

For new FDA approved drugs (2015-2016), **women enrolled are 40% on average**



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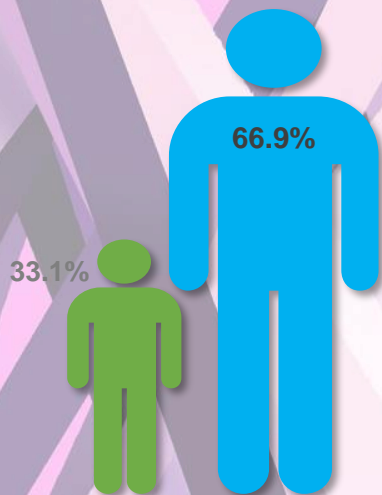
**The problem:** Is diversity considered when we study disease and develop novel treatment solution?

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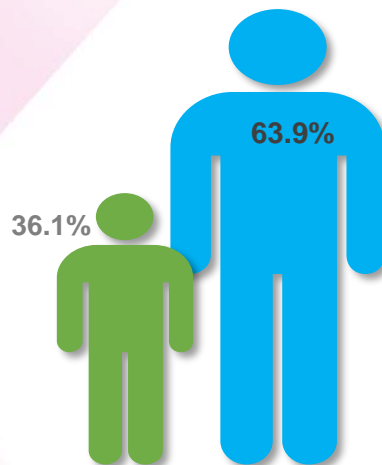


# Industry Clinical Trials not Representative of US Population

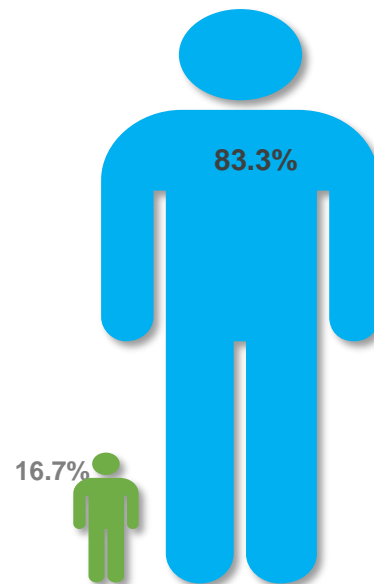
ALL MINORITIES  
WHITE



TOTAL U.S.  
POPULATION



NIH-FUNDED  
CLINICAL RESEARCH

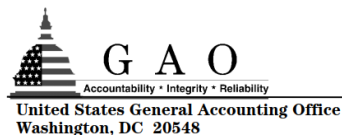


INDUSTRY-FUNDED  
CLINICAL TRIAL



# Example: Sex and Gender Differences in Drug development

In the USA **8/10** drugs withdrawn from the market posed a greater threat to women than to men



January 19, 2001

The Honorable Tom Harkin  
The Honorable Olympia J. Snowe  
The Honorable Barbara A. Mikulski  
United States Senate

The Honorable Henry A. Waxman  
House of Representatives

Subject: Drug Safety: Most Drugs Withdrawn in Recent Years Had Greater Health Risks for Women



Resulting in waste and increased healthcare system costs

Source: United States General Accounting Office, 2001



## Regulators are starting to pay attention

Although in this case it means women cannot benefit from drug development

### ***F.D.A. Approves New H.I.V. Prevention Drug, but Not for Women***

Citing a lack of evidence, the agency will require Gilead to conduct further trials in women.



Hot off the press: 4 Oct 2019

Drug was tested on men and transgender women only. FDA said there is no evidence the drug works in women, and has not approved it for women.

SUSTAINABLE DEVELOPMENT GOALS

5 GENDER EQUALITY



3 GOOD HEALTH AND WELL-BEING



Source: <https://www.nytimes.com/2019/10/04/health/fda-descovy-truvada-hiv.html>



# WBP promotes precision medicine leading to reduced side effects & risk of DDI

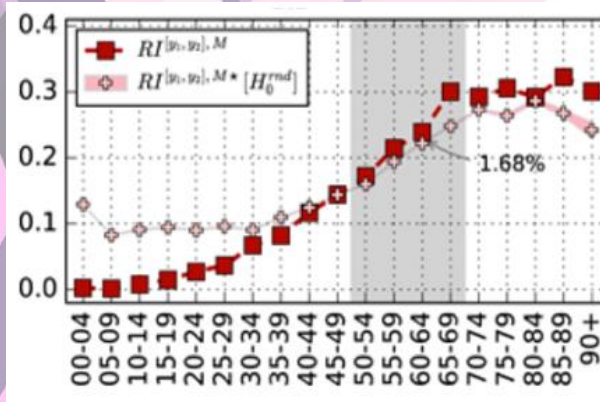


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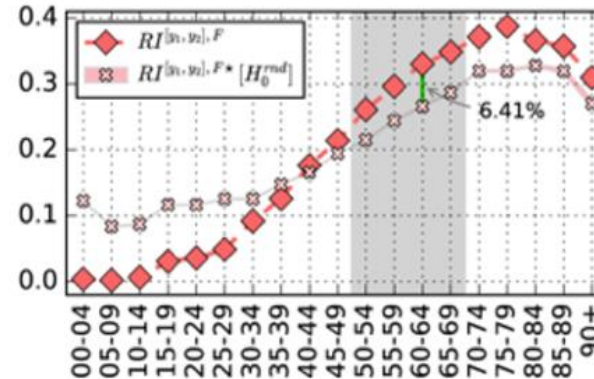
Sex related Drug-Drug interactions (DDI)

Women suffer from increased side effects with polytherapy

Risk interaction, men



Risk interaction, women



‘The large-scale analysis reveals that **women have a 60% increased risk of DDI** as compared to men; **the increase becomes 90%** when considering only DDI known to lead to major ADR’

Source: Blumenau pop. ≈340,000, Correio et al., Nature Digital Medicine 2019



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## **The solution: Women's Brain Project**

Build a Sex and Gender Precision Medicine Research  
Institute

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## WHO WE ARE



WOMEN'S BRAIN PROJECT®

# We achieve this vision through clear objectives and a strong culture

We are a group of scientists from various disciplines including medicine, neuroscience, psychology, pharmacy and communication who **WORK TOGETHER** with caregivers, patients and their relatives, policymakers and other stakeholders.

Improve the state of medical treatments and drug development for **BRAIN AND MENTAL HEALTH** through sex and gender factors analysis as a gateway to **PRECISION MEDICINE**

### EVIDENCE

WBP is an engine for data generation and interpretation and has the proof to support its conjectures

### EXPERTISE

WBP is *the* expert on sex and gender influences on health; when someone wants info on this, they come to WBP

### AWARENESS

WBP has effectively raised the profile of sex and gender factor impact among naïve audiences

## PRECISION MEDICINE INSTITUTE FOR BRAIN & MENTAL DISEASES

Our institute will focus on research and consulting to analyse existing data sets from clinical trials and private business to understand and advise on sex and gender factors on health outcomes

# What we do



## SCIENCE:

- >50 scientific papers
- 5 books
- 4 Policy Reports

## EVENTS:

- 3 International Forum on Women's Brain and Mental Health
- Emozioni Forum

## TEACHING AND OUTREACH:

- 200 plus lectures/talks
- 3 CME courses
- >40 international collaborations
- Regulatory Roundtable on Women's Health and Precision Medicine
- Education campaigns

## AWARDS

- World Sustainability Award
- Women in Business Award Switzerland
- Bold Women Award Switzerland
- Women for Innovation University Basel
- Premio Medicina Italia

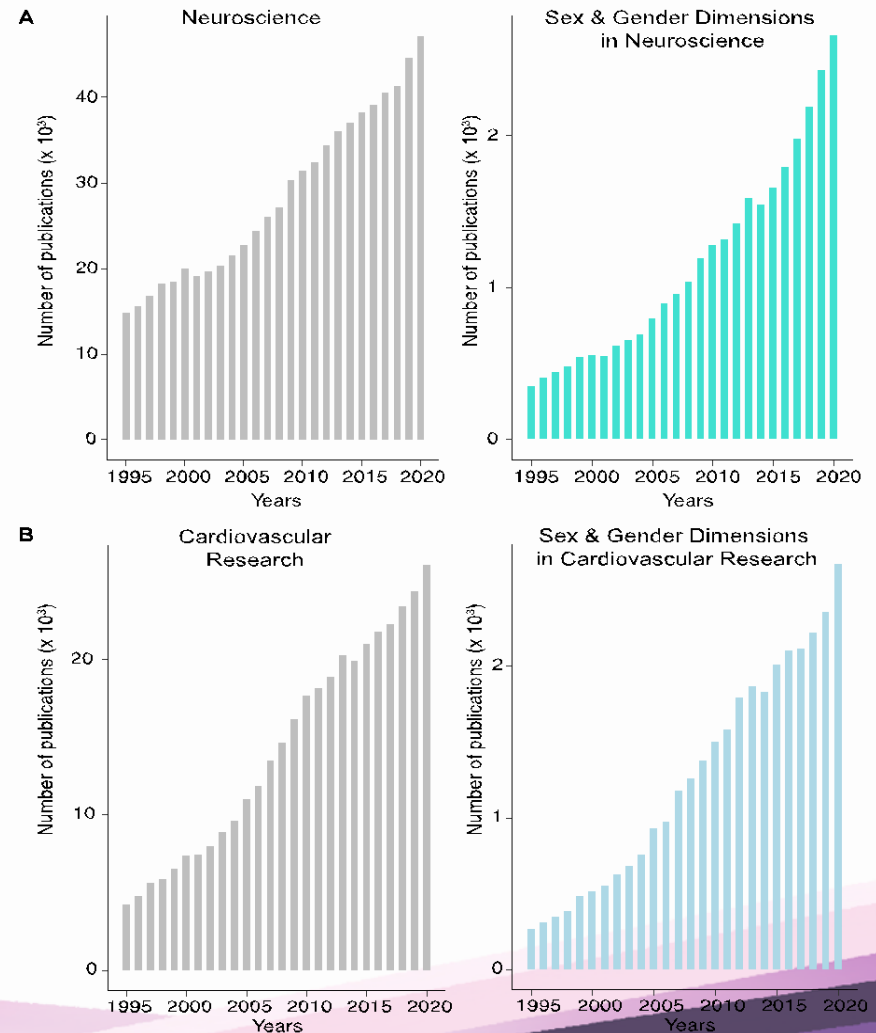


TOTAL NUMBER OF PUBLICATION IN NEUROSCIENCE AND  
CARDIOVASCULAR (GRAY)

TOTAL NUMEBR OF PUBLICATION ON SEX AND GENDER  
DIMENSION IN NEUROSCIENCE AND CARDIOVASCULAR  
(BLUE)

Mapping of European activities on the integration of sex and gender factors in  
neurology and neuroscience

Hentzen, et al. on behalf of the Gender and Diversity Task force of the EAN\*  
submitted

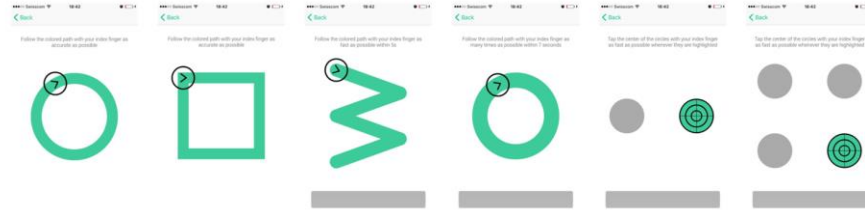




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# 2022 PROJECT 1 | WBP & The Economist

## Digital solution as possible solution for sex and gender differences in brain disorders



# altoida

*Creating the New*  
**Gold Standard  
in Brain Health**

SUSTAINABLE  
DEVELOPMENT  
GOALS

9 INDUSTRY, INNOVATION  
AND INFRASTRUCTURE



5 GENDER  
EQUALITY



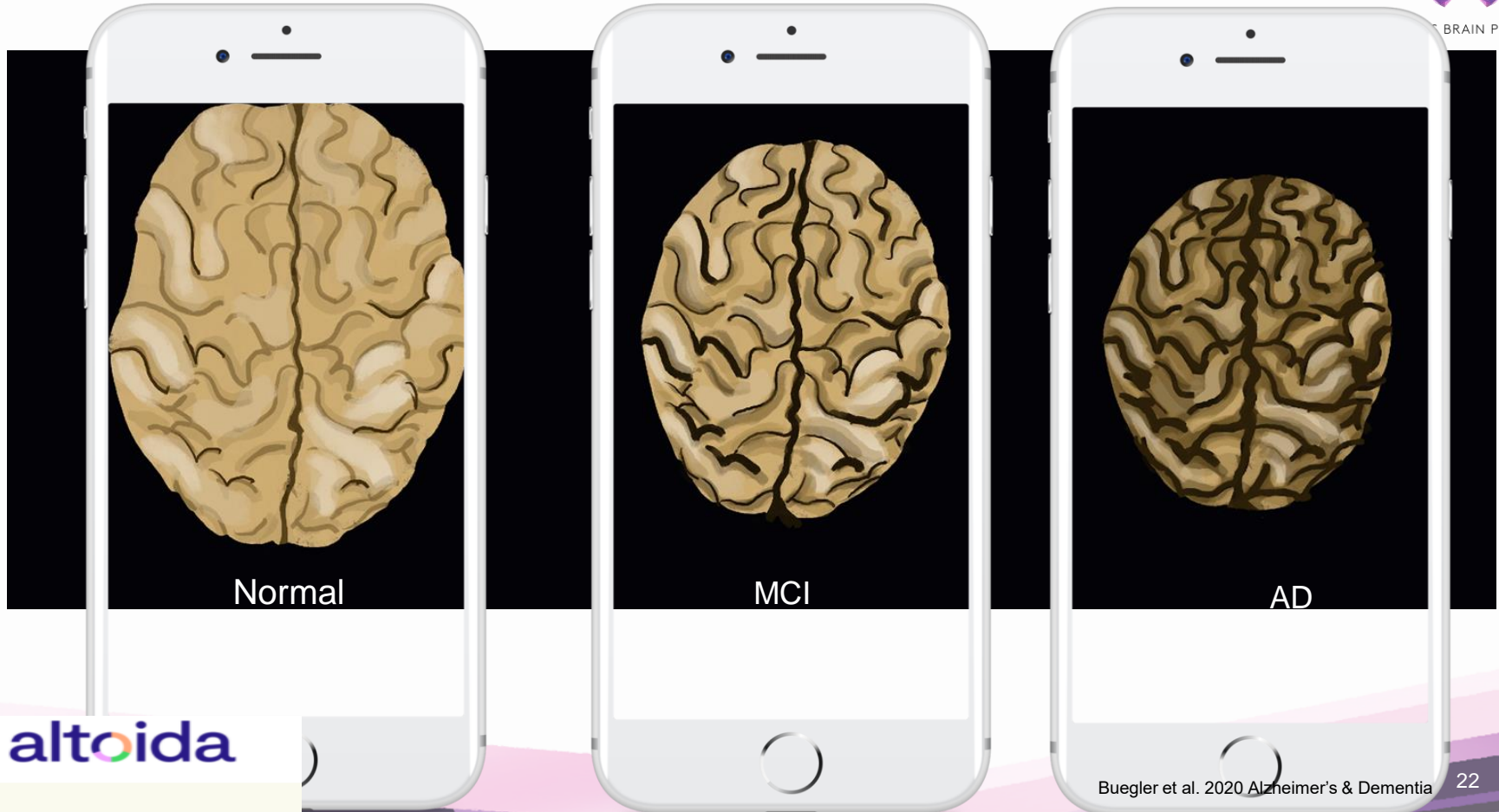
3 GOOD HEALTH  
AND WELL-BEING



# Digital solution to detect Alzheimer's and Mild cognitive Impairment



BRAIN PROJECT®



altoida



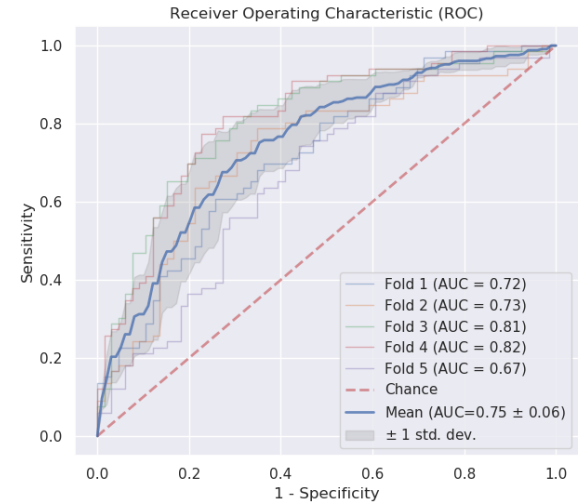
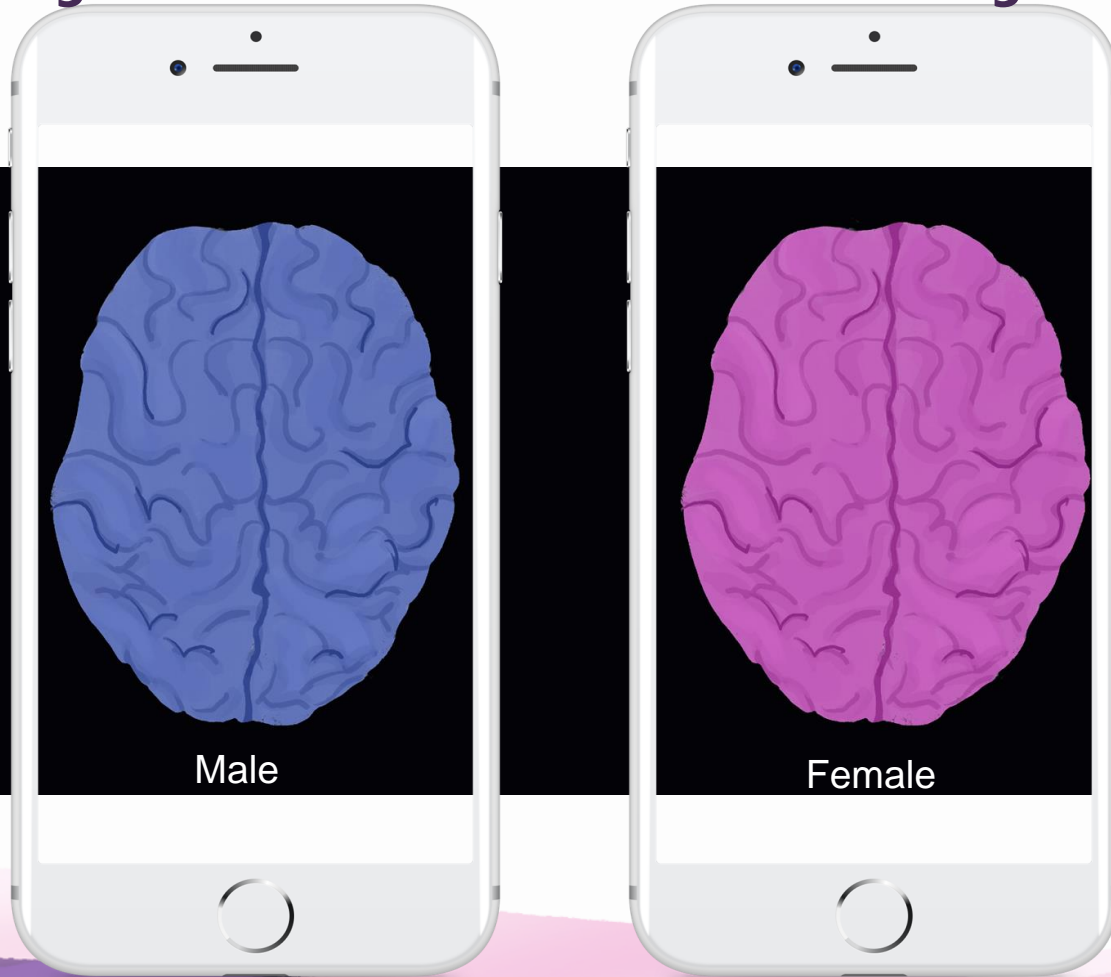


# Digital solution to characterize sex and gender

altoida



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*Receiver Operating Characteristic Curve (ROC) with five-fold cross-validation results for the digital biomarker sex classifier.*

# Case study: We surveyed 142 patients (or their caregivers) from US & Germany with MCI or mild-to-moderate Alzheimer's Disease

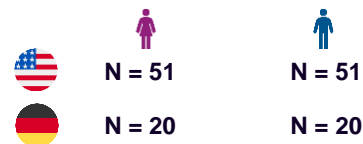
## Screening Criteria

- MCI & mild-to-moderate AD patients (or their caregivers) with the ability to speak about milestones they have experienced during journey
- Representative number of patients of both genders
- ~50% with confirmed A $\beta$  pathology; excluding familial AD
- Caregivers must be the primary caretaker with the ability to speak about milestones patients have experienced during journey

## Methodology

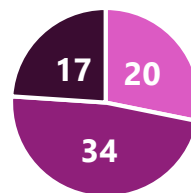
- 45 min quantitative online survey
- Pilot interviews to test logic, language and flow of survey before full fielding start
- Caregiver support encouraged for patients

## Sample Size

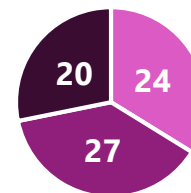


## Disease Severity of Patients

### Females



### Males

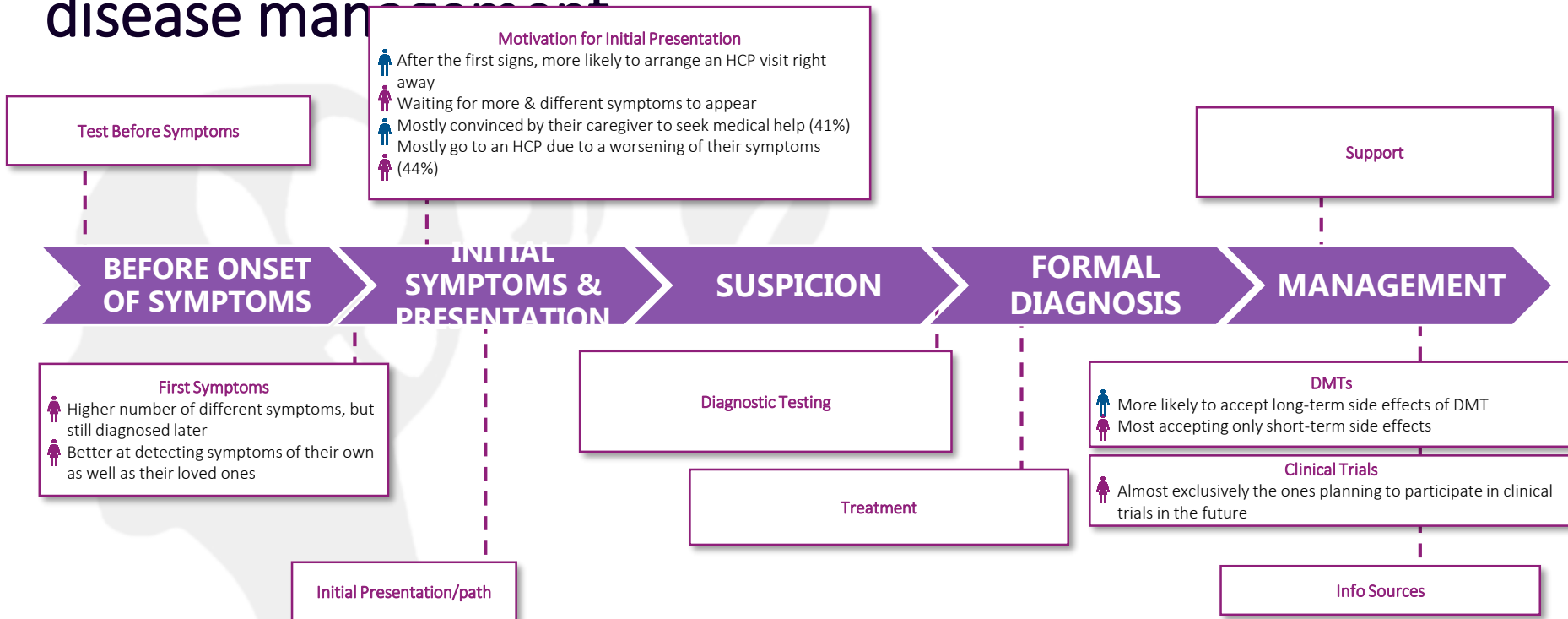


■ MCI/Prodromal AD ■ Mild AD ■ Moderate AD

38% of patients had a confirmed A $\beta$ + pathology



# Women & men had key differences in symptom detection, support attitude, treatment regimens and disease management



Support Us: Donate or be part of this Movement



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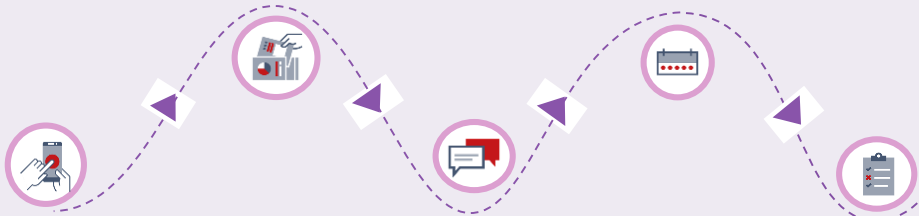
# Brain App

## A New User Journey

The Women's Brains Project app will provide individual assistance and support the patient along their **journey**.

Complete profile (sex, gender, disease type, status) to enable precision customization, track first routines & medical documents

Find verified information about treatments, research, clinical trials, cognitive trainings and events



Download the mobile app, create a profile, decide on data donation and perform digital diagnosis

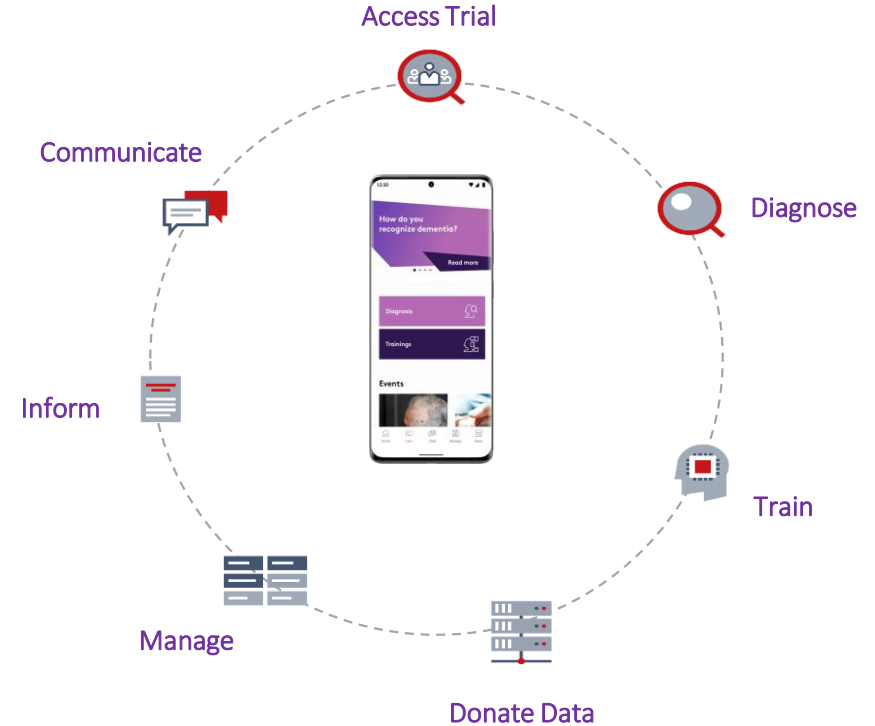
Chat with patient organizations, caregivers, or healthcare professionals in a data-secured environment

Manage and plan daily life and documents; and get updated about the latest research and treatment options

The user-centered Alzheimer app could start with few main functions for patients and caregivers. The app could function as a platform that integrates existing and new services of WBP partners. WBP partners could also benefit from the app's patient reach by donated data or promotion of clinical trials

## Solution

All-round services for patients and caregivers on one device:



A **mobile app** promises **benefits** for both, the end users as well as Women's Brain Project and its supporters.

**ECONOMIST  
IMPACT**



**WOMEN'S  
BRAIN  
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# Sex, gender and the brain: Towards an inclusive research agenda

Project Overview

October 6, 2022

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BRAIN  
PROJECT®**



# Introduction

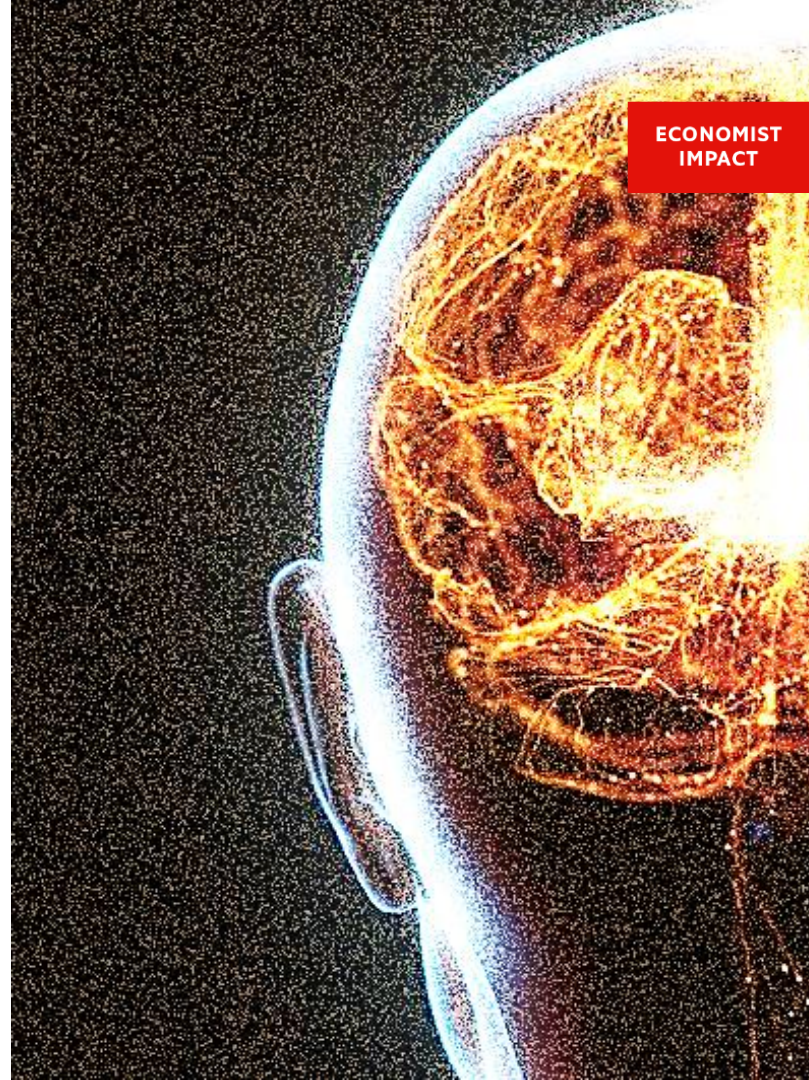
Economist Impact with support from the Women's Brain Project, has conducted a research programme bringing sex and gender differences in brain health to the centre of the scientific debate.

The 2-step research program examines the economic story for investing in sex and gender specific brain research

## SPECIFIC OBJECTIVES

Examine the role played by sex and gender differences in brain disorders and their outcomes

Examine the economic impact of investing in sex and gender differentiated brain research



# Approach

ECONOMIST  
IMPACT

## Phase 1: Evidence Review

Evidence review for key literature around sex and gender differences in 5 select brain disorders

With focus on:

**Multiple Sclerosis, Stroke, Parkinson's disease, Alzheimer's disease and Migraine**

## Phase 2: Expert Engagement

Global insights from 5 key interviews with leading experts in the field



## Phase 3: Conceptual modelling framework

Development of 5 disease-specific conceptual modelling frameworks demonstrating the economic impact of investing in sex and gender specific brain research

Current Phase

## Phase 4: Reporting

Defining the economic modelling protocol across 5 diseases  
Compilation of summative white paper

White paper launching October-November 2022





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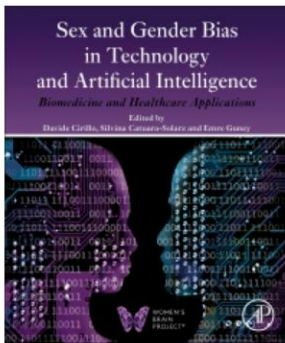


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# Sex and Gender Differences in Alzheimer's Disease

Edited by  
Maria Teresa Ferretti, Annemarie Schumacher Dimech,  
Antonella Santuccion Chadha



Preview

[View on ScienceDirect](#)

## Sex and Gender Bias in Technology and Artificial Intelligence

Biomedicine and Healthcare Application

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eBook ISBN: 9780128213933



ANTONELLA SANTUCCIONE CHADHA  
MARIA TERESA FERRETTI

# UNA BAMBINA SENZA TESTA

Storie di malattie del cervello  
e della mente e le differenze  
tra uomini e donne

PREFAZIONE DI  
VIVIANA  
KASAM





## Foundation / Stiftung (Basel)



Purpose: The Foundation researches and advocates for gender differences in brain and mental health disorders to enter the precision medicine. It operates an Institute for Precision Medicine to research gender differences in brain and mental health disorders. It may support the activities and commercialization of legal entities established as spin-offs of the Institute for Precision Medicine to research gender differences in brain and mental health disorders and manage intellectual property.

Founded by representatives of the University Basel and WBP



## Institute (Basel)

Purpose: Research Site and Philanthropic AND Governmental Activities.  
Affiliation to University and supported by Cantons BS & BL

# Support Us: Donate or be part of this Movement





# Who we are: WBP Team

We are a group of scientists from various disciplines including medicine, neuroscience, psychology, pharmacy and communication who work together with caregivers, patients and their relatives, policymakers and other stakeholders.



# Support Us: Donate or be part of this Movement



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## Donate and profit

When you make a gift to the Women's Brain Project you'll join us in our mission for better brain and mental health for all. Women's Brain Project is a not-for-profit charity formed in Switzerland.

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Just enter your email for a receipt of your donation.

[info@womensbrainproject.com](mailto:info@womensbrainproject.com)