STRESS and EPIGENETICS: how stress-related work impact health?

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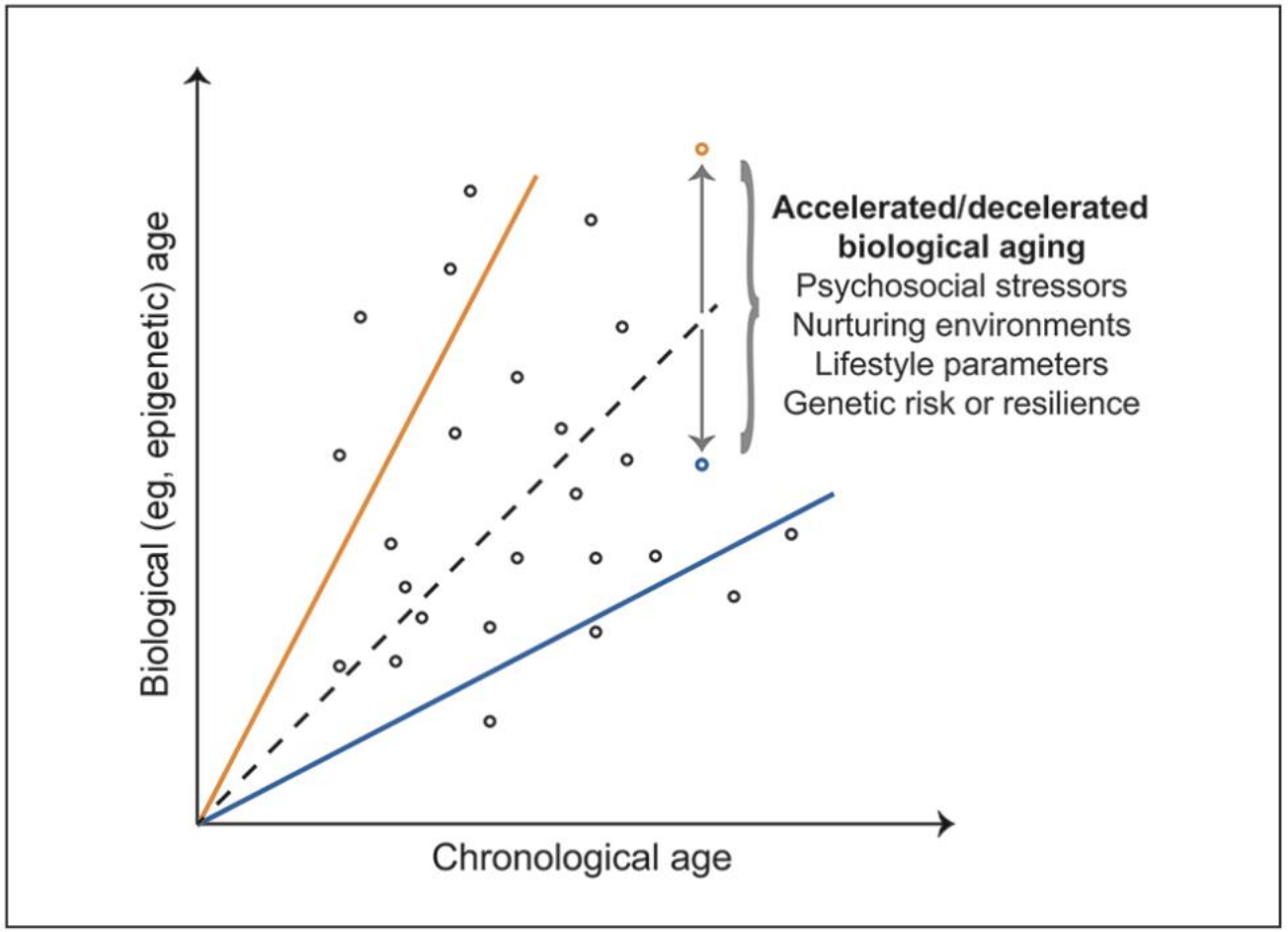
Quinta conferenza nazionale ANAAO- Firenze 8-9 novembre 2024

Stress and acceleration of biological age



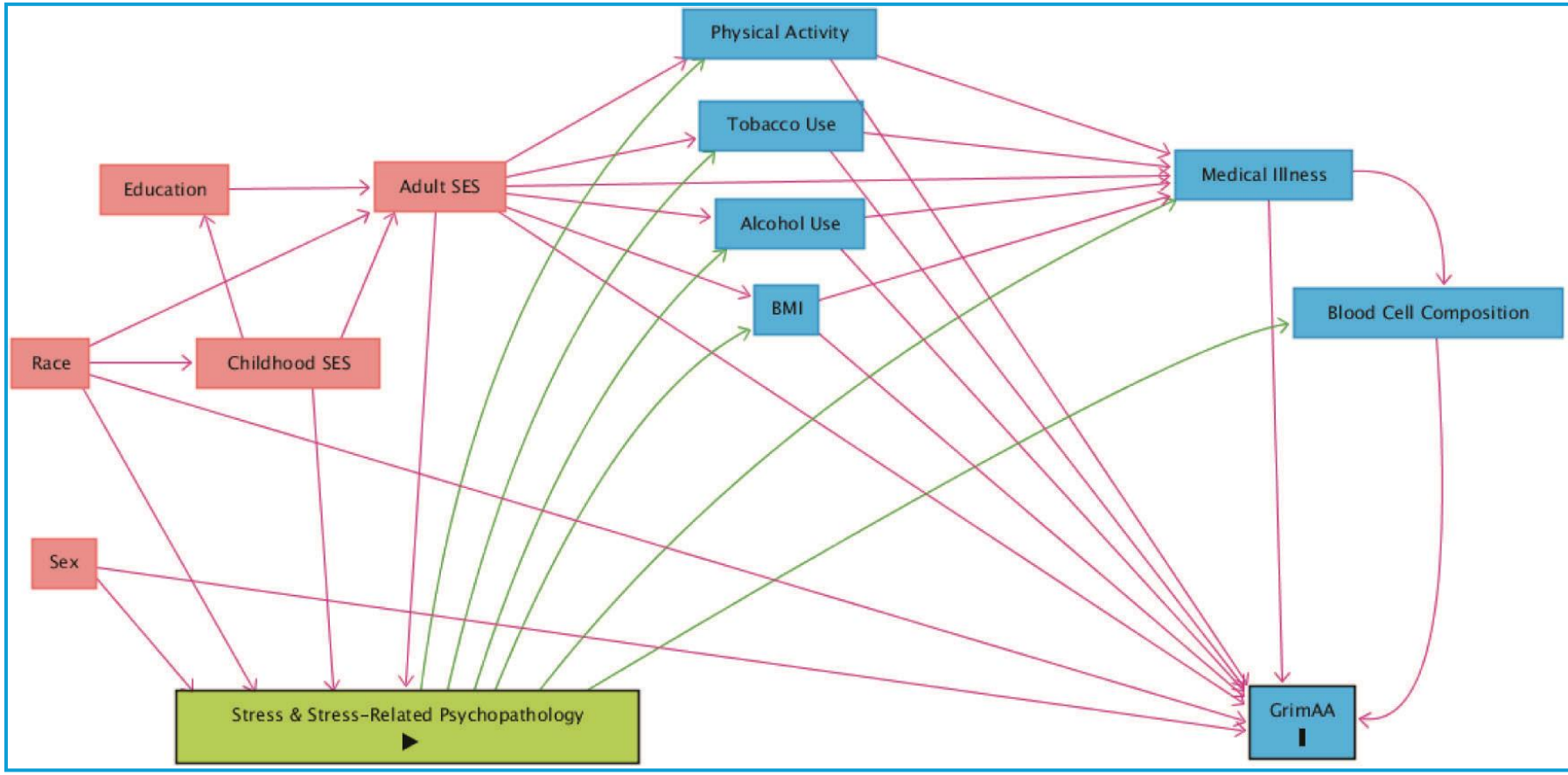
Gabbianelli Rosita, 2024

Translational Psychiatry www.nature.com/tp

REVIEW ARTICLE OPEN

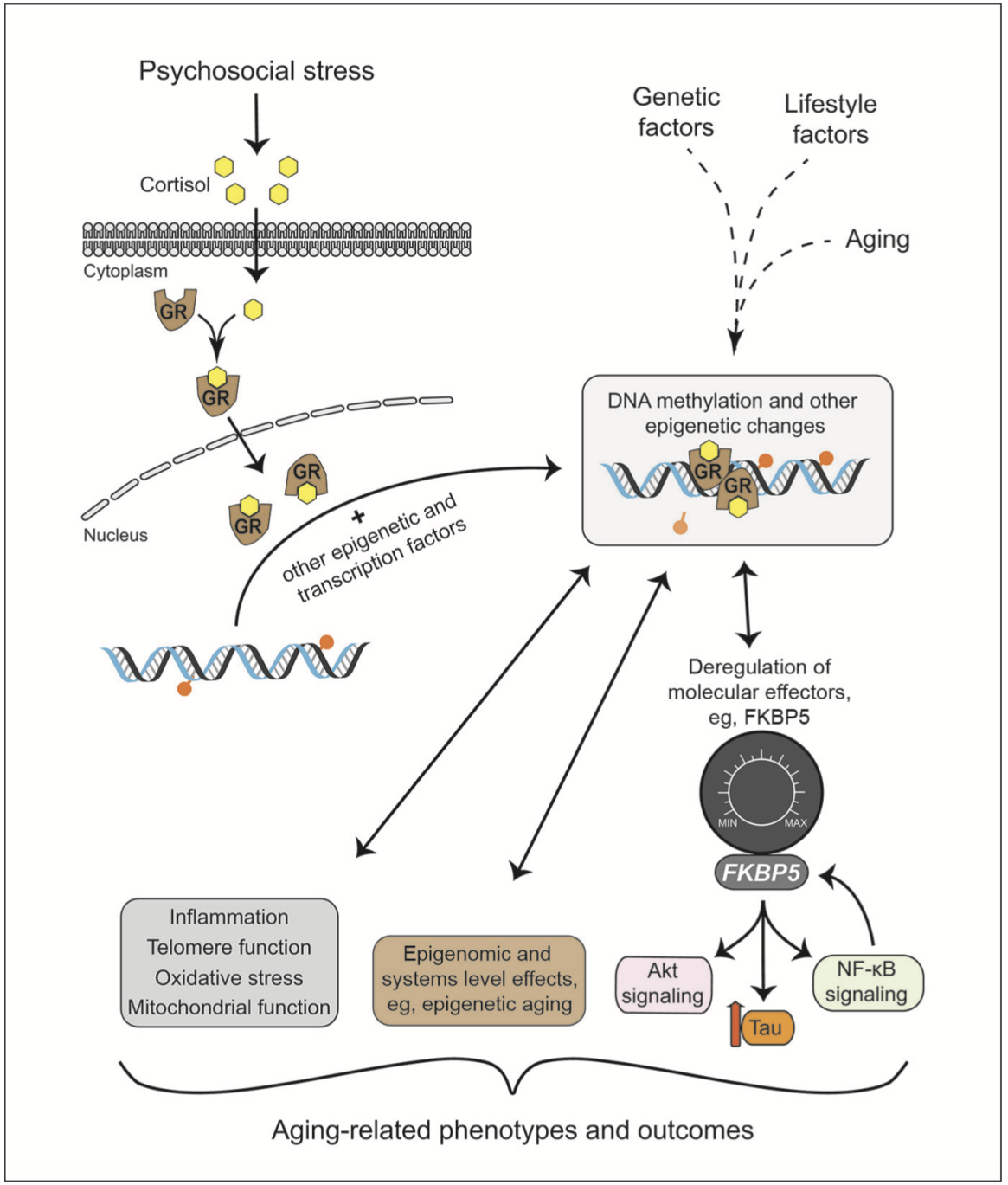
Associations of stress and stress-related psychiatric disorders with GrimAge acceleration: review and suggestions for future work

Ekaterina Protsenko[1,2✉], Owen M. Wolkowitz[3] and Kristine Yaffe[2,3,4]



Directed acyclic graph depicting the relationships between stress and stress-related psychopathology and GrimAA. **Green lines indicate causal or mediating paths**. **Pink lines indicate confounding paths.** Minimally sufficient adjustment set (MSAS) for direct effect of stress and stress-related psychopathology on GrimAA = Tobacco Use + Alcohol Use + BMI + Physical Activity + Medical Illness + Blood Cell Composition + Sex + Race + Adult SES. MSAS for Total Effect = Adult SES + Race + Sex. Generated with daggity.net, modified for clarity. Supplementary Materials include code to reconstruct this DAG at dagitty.net.

Gabbianelli Rosita, 2024



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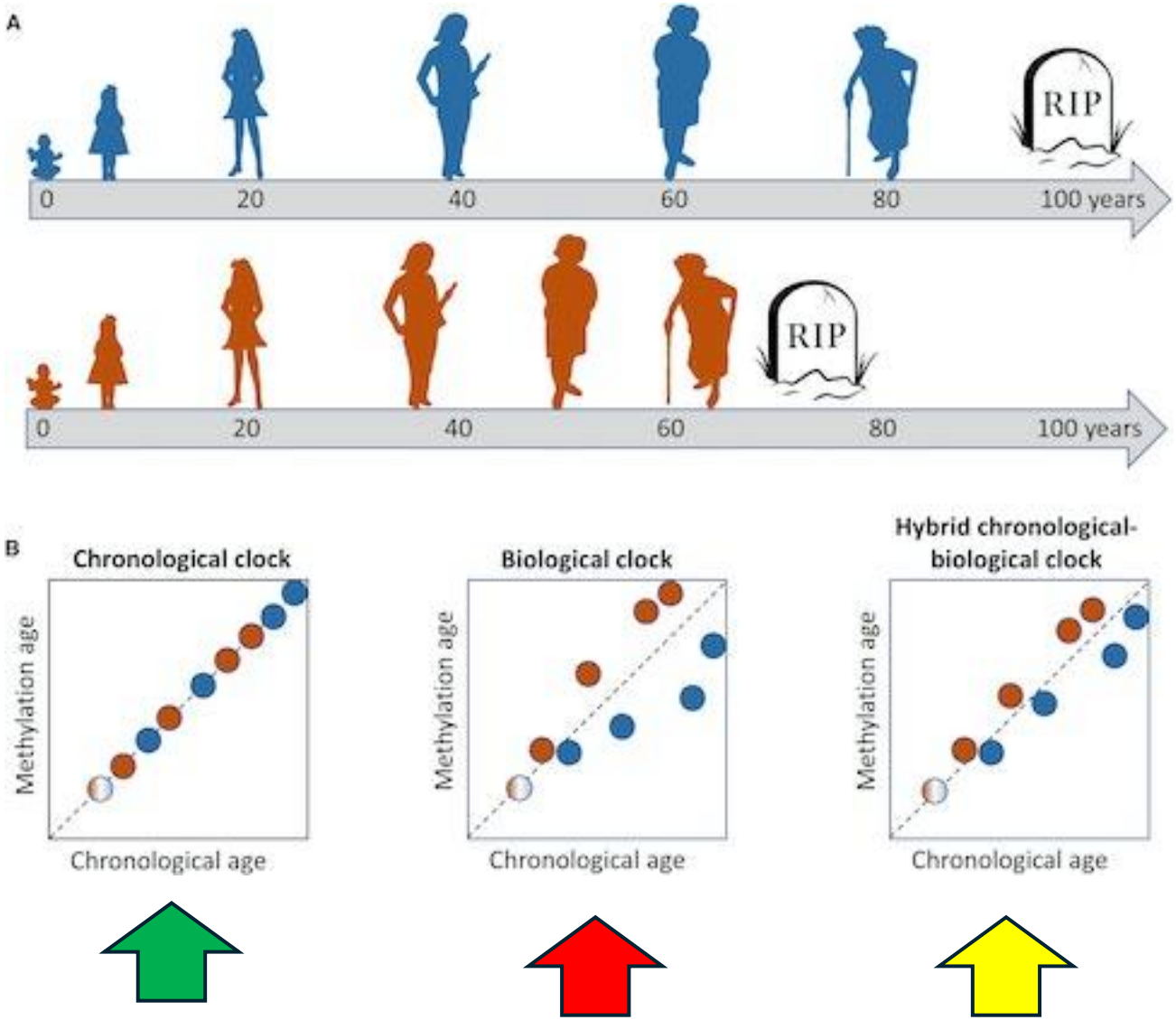
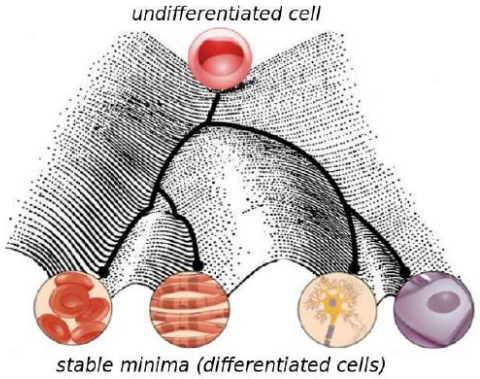
The same chronological age ……..different biological age



https://doi.org/10.1111/joim.13533

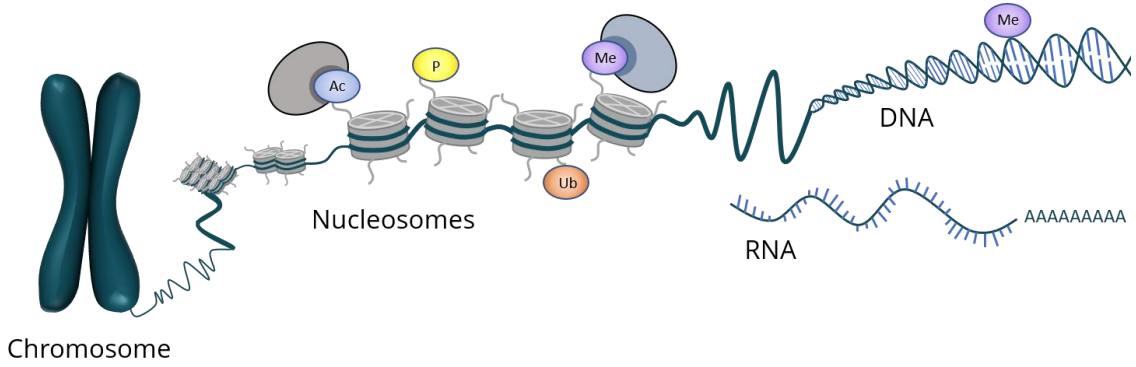
Gabbianelli Rosita, 2024

Epigenetic mechanisms

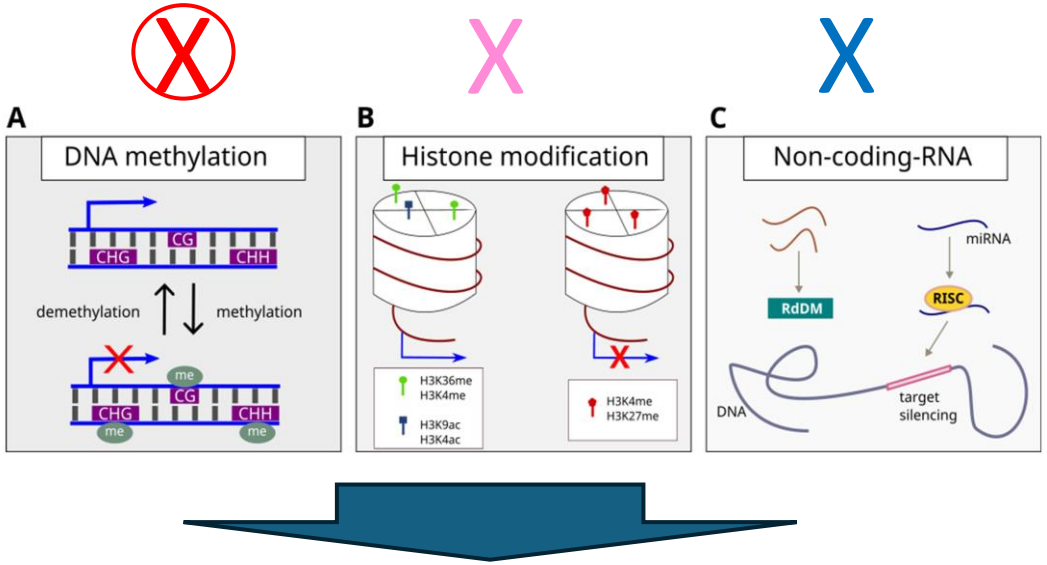


~ 30 x 10^{12} cells
~ 300 cell types

Multiple Epigenomes



Cell differentiation



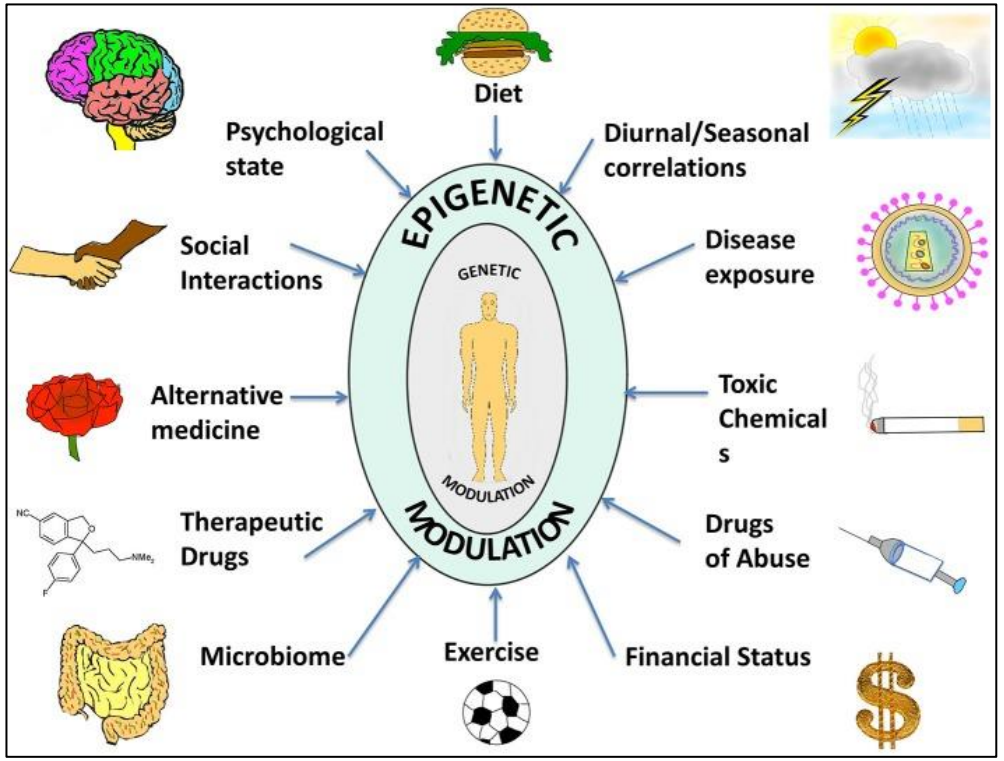
Protein synthesis (how much is espressed)

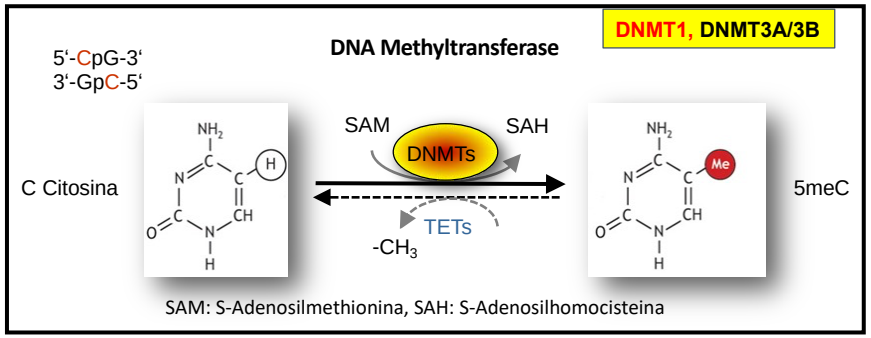
Epigenetics vs Genetics

How strong or long-lasting does the stimulus need to induce an epigenetic change?

The presence of a stressful event per se, i.e., the objective stress, and subjective stress, i.e., how stressful this event is perceived?

EXPOSOME

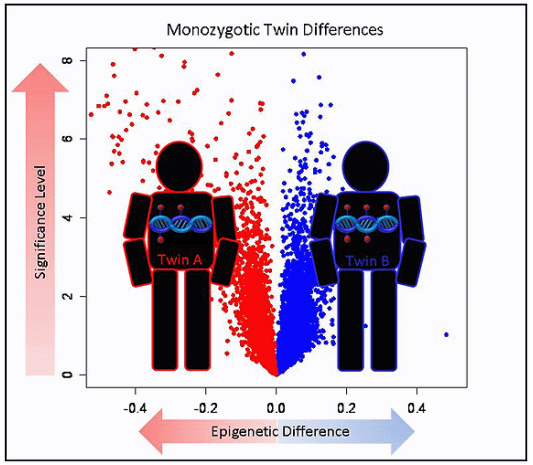




Genetically identical…

https://medicinaonline.co/2017/03/06/e-vero-che-il-gemello-partorito-per-primo-e-quello-minore/

…phenotypically different



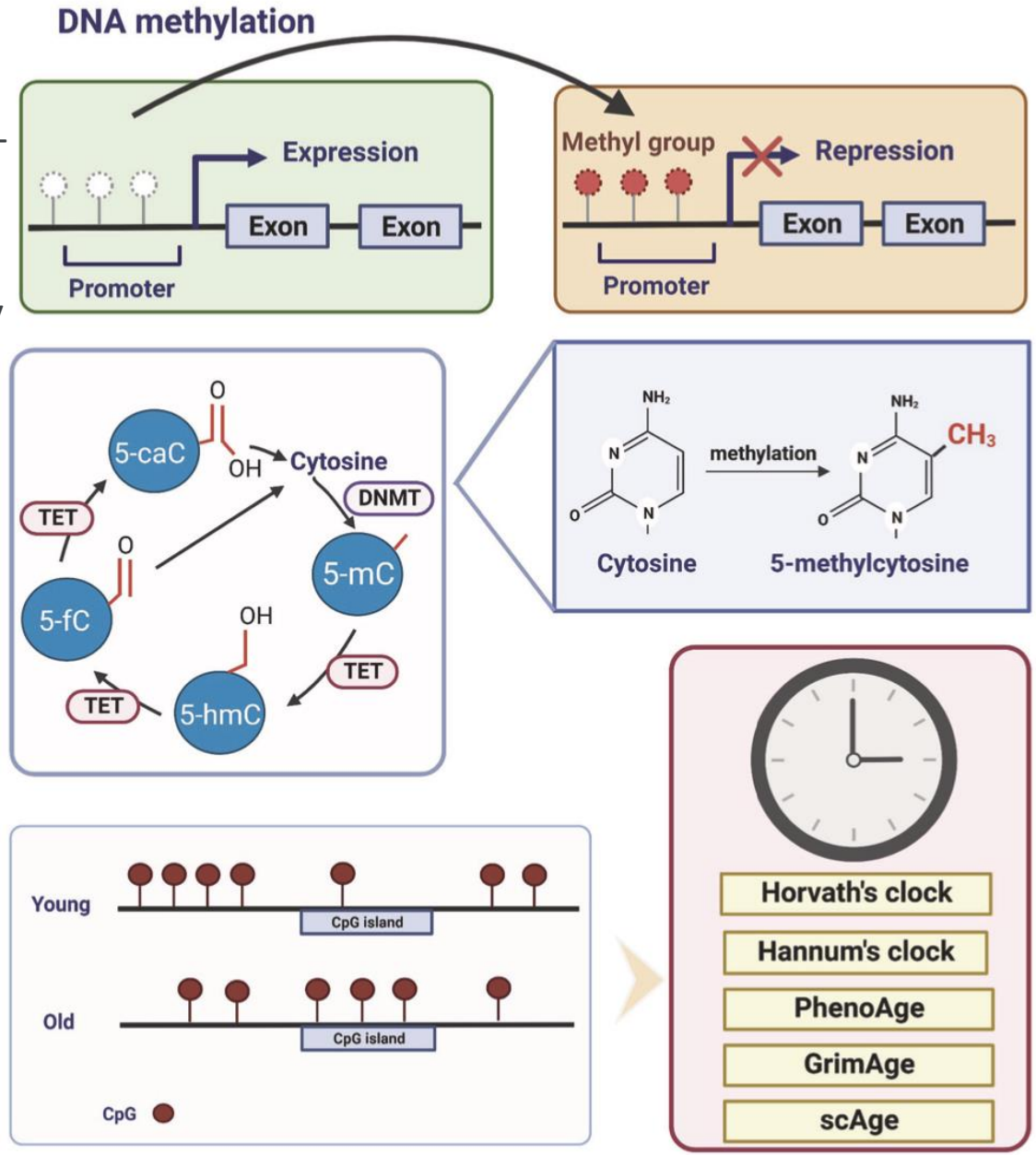
Kaminsky, ZA, et al., NAT GENET, 41 (2): 240-245 FEB 2009

40% CpGs with GREATEST methylation variability with age (Age-associated variably methylated positions)

+

60% CpGs with DECREASED methylation with age (Differentially methylated positions associated with age)

Evaluation of epigenetic age



about ¼ of the CpG DNAmAge (85/353) are at the elements that respond to glucocorticoids, showing a correlation between stress and acceleration of aging

Signal Transduction and Targeted Therapy (2022)7:374

www.aging-us.com AGING 2022, Vol. 14, No. 3

Research Paper

Work-related stress and well-being in association with epigenetic age acceleration: A Northern Finland Birth Cohort 1966 Study

Anna Freni-Sterrantino[1], Giovanni Fiorito[1,2], Angelo D'Errico[3], Oliver Robinson[1], Marianna Virtanen[4,5], Leena Ala-Mursula[6], Marjo-Riitta Järvelin[1,6], Justiina Ronkainen[6], Paolo Vineis [1,7,8]

Long working hours (>55hours/week) and shift work have been associated with **increased risk of chronic conditions** like **stroke or breast cancer and** working long hours is a risk factor for **shortened sleeping hours and difficulty falling asleep**

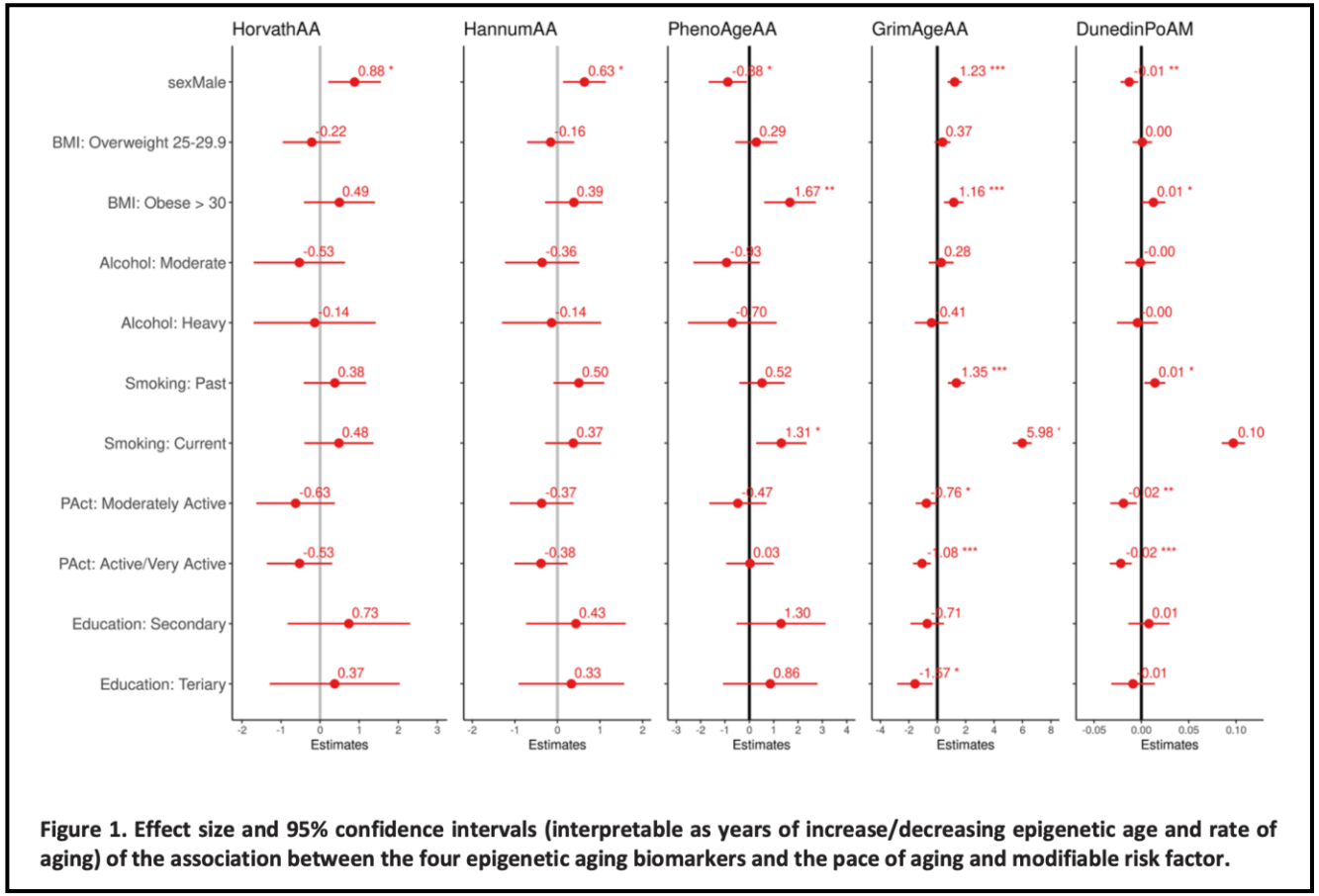


Figure 1. Effect size and 95% confidence intervals (interpretable as years of increase/decreasing epigenetic age and rate of aging) of the association between the four epigenetic aging biomarkers and the pace of aging and modifiable risk factor.

- Significant associations between **work stress** indicators and epigenetic age acceleration, limited to a range of **±2 years**
- Association was found for **working for more than 40 hours per week** that increased the aging over **1.5 years,** (HorvathAA β =2.058 95%CI 0.517,3.599, HannumAA β=1.567, 95%CI 0.415,2.719).

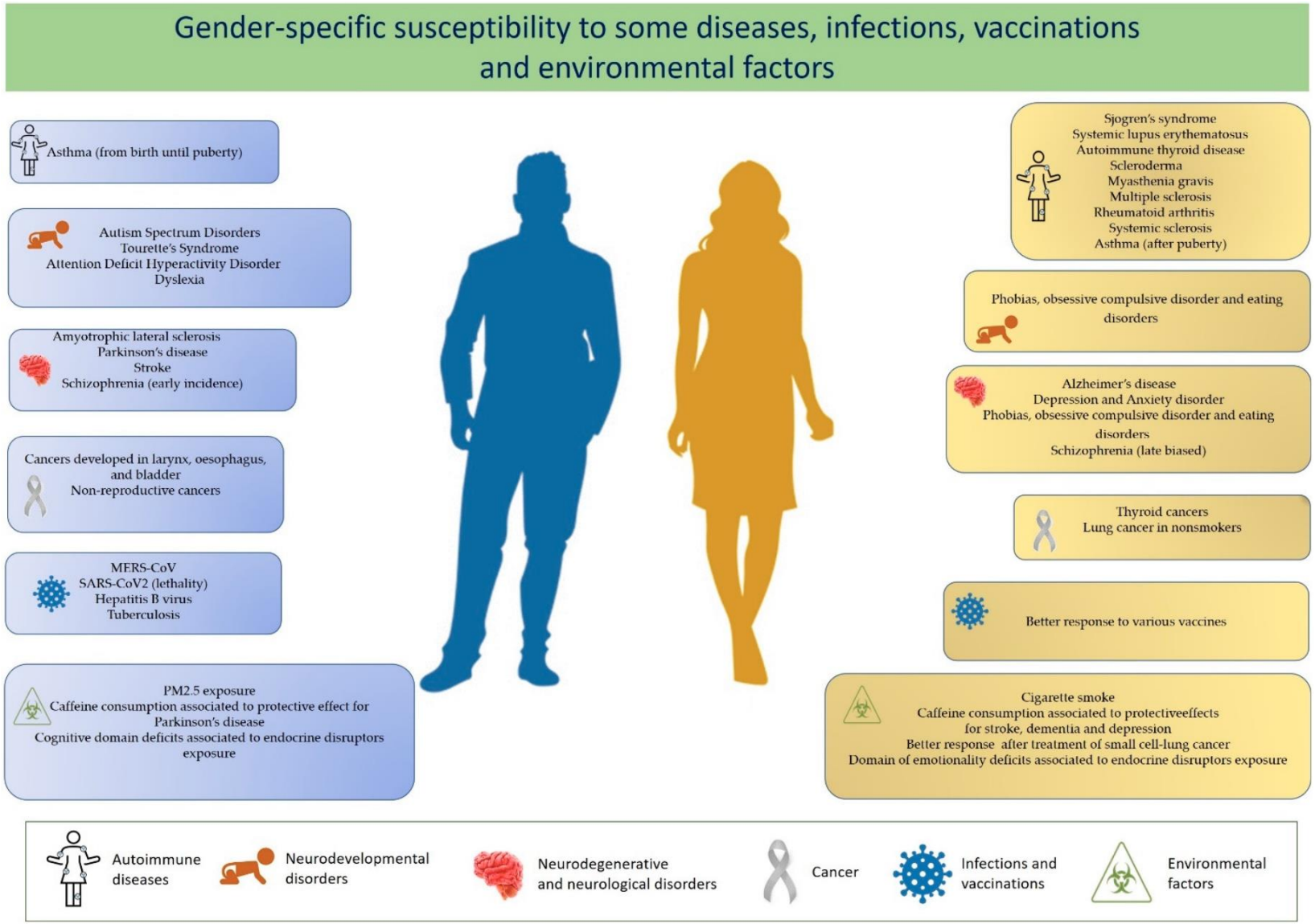


Figure 1. Increased susceptibility to some diseases and infections and to the effects of vaccinations and environmental factors in males (left panels) and females (right panels).

Iannuzzi et al. Genus (2023) 79:1
https://doi.org/10.1186/s41118-023-00181-1

Genus

ORIGINAL ARTICLE Open Access

The role of genetics and epigenetics in sex differences in human survival

Vincenzo Iannuzzi[1], Maria Giulia Bacalini[2], Claudio Franceschi[3] and Cristina Giuliani[1*]

” Innate” mechanisms (both genetic and epigenetic) common to all males and to all females play a major role in sex differences in lifespan, but solely on their own are not sufficient to explain the magnitude of this gap between sexes

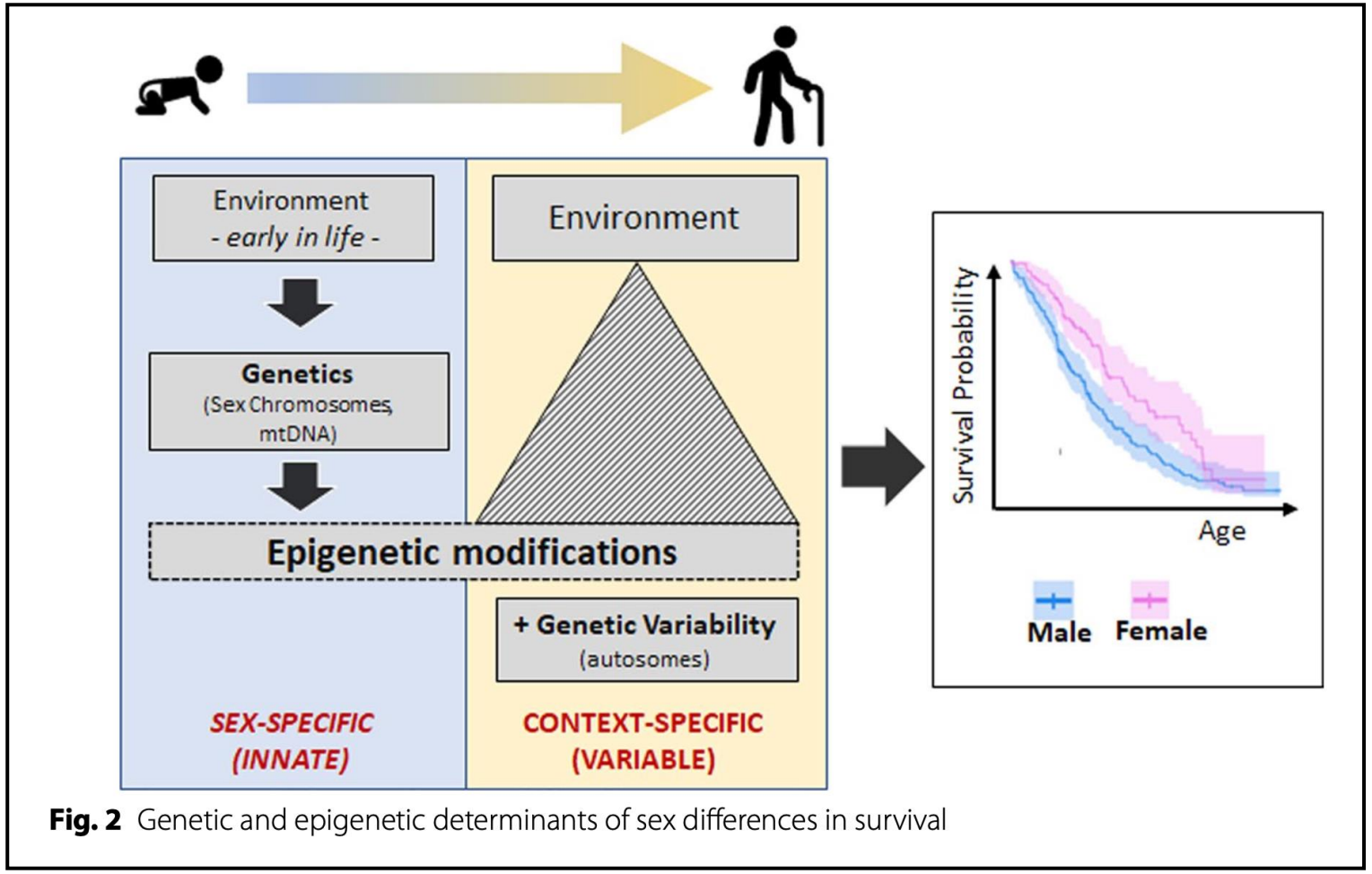


Fig. 2 Genetic and epigenetic determinants of sex differences in survival

Brain, Behavior, and Immunity 88 (2020) 901–907

Contents lists available at ScienceDirect

Brain, Behavior, and Immunity

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

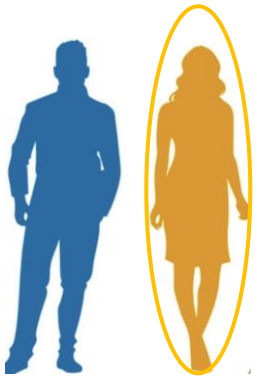
Prevalence of depression, anxiety, and insomnia among healthcare workers during the COVID-19 pandemic: A systematic review and meta-analysis

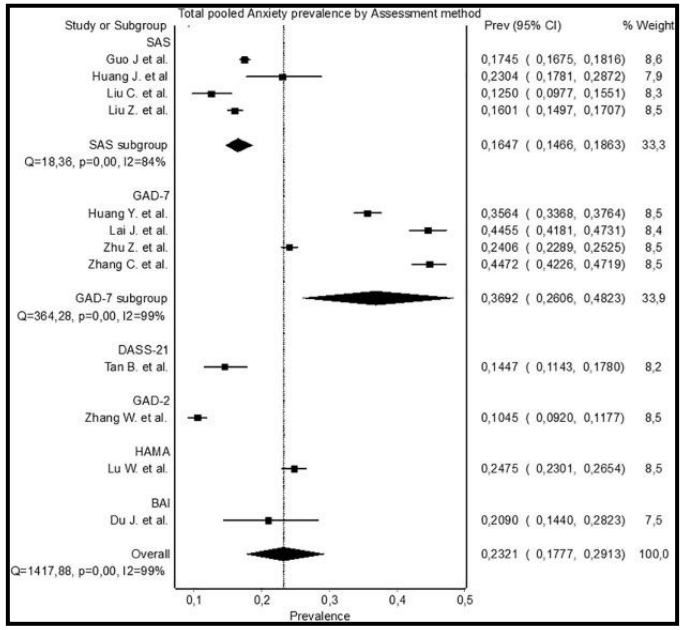
Sofia Pappa[a,b,*,1], Vasiliki Ntella[c,1], Timoleon Giannakas[c], Vassilis G. Giannakoulis[c], Eleni Papoutsi[c], Paraskevi Katsaounou[c,d]

Median number of individuals per study was 1563 (range 134, 11118) with a median male representation of 18% (281·5/1563) and a median questionnaire participation rate of 85·3% (range 43·2%, 94·88%).

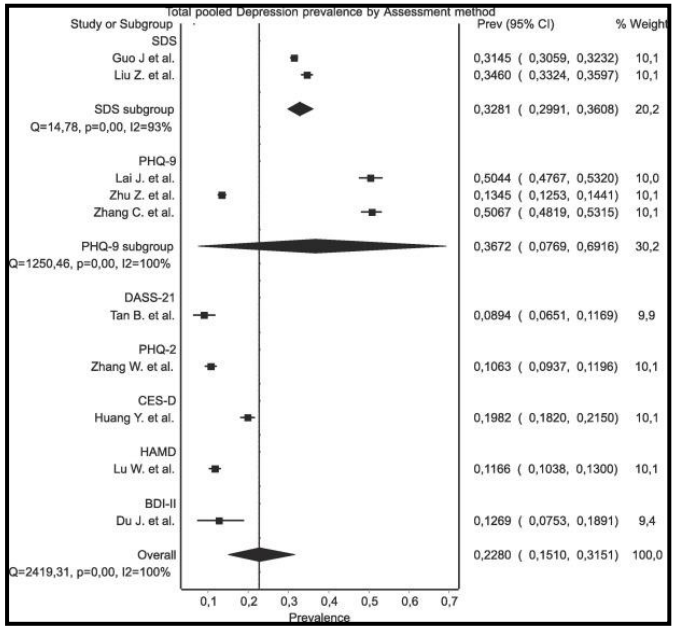
Highlights

- At least **one in five healthcare** professionals report symptoms of **depression and anxiety.**
- Almost **four in ten healthcare workers** experience **sleeping difficulties and/or insomnia.**
- **Rates of anxiety and depression were higher for FEMALES healthcare workers and nursing staff.**
- Milder mood symptoms are common and screening should aim to identify mild and sub-threshold syndromes.





Anxiety was estimated in 12 studies; the pooled prevalence was 23%



Depression was assessed in 10 out of 13 studies, with a calculated pooled prevalence of 22%

Table 3
Subgroup analysis of Anxiety and Depression Prevalence.

		Anxiety	Depression
Gender	Female	**29·06%** 95% CI 20·21-38·78 I^2 = 99%	**26·87%** 95% CI 15·39-40·09 I^2 = 99·56%
	Male	**20·92%** 95% CI 11·86-31·65 I^2 = 98%	**20·34%** 95% CI 11·57-30·75 I^2 = 98%
Severity	Mild	**17·93%** 95% CI 11·33-25·62 I^2 = 99%	**24·60%** 95% CI 16·65 – 33·51 I^2 = 99%
	Moderate/ severe	**6·88%** 95% CI 4·39-9·87 I^2 = 97%	**16·18%** 95% CI 12·80-19·87 I^2 = 97%
HCW group	Doctors	**21·73%** 95% CI 15·27-28·96 I^2 = 97%	**25.37%** 95% CI 16·63-35.20 I^2 = 98%
	Nurses	**25·80%** 95% CI 19·20-33·00, I^2 = 98%	**30.30%** 95% CI 18·24-43.84 I^2 = 99·52%

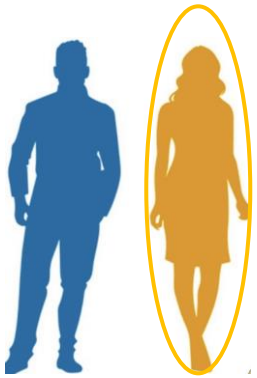
International Journal of
Environmental Research and Public Health

MDPI

Article

Investigating the Psychological Impact of COVID-19 among Healthcare Workers: A Meta-Analysis

Kavita Batra [1,2,*], Tejinder Pal Singh [3], Manoj Sharma [1], Ravi Batra [4] and Nena Schvaneveldt [5]



Sixty-five studies met the inclusion criteria and the total sample constituted 79,437 participants.

The pooled prevalence of **anxiety, depression, stress, post-traumatic stress syndrome, insomnia, psychological distress, and burnout** was 34.4%, 31.8%, 40.3%, 11.4%, 27.8%, 46.1%, and 37.4% respectively.

The subgroup analysis indicated **higher anxiety and depression prevalence among FEMALES**, nurses, and frontline responders than males, doctors, and second-line healthcare workers.

This study highlights the need for designing a targeted intervention to improve resilience and foster post-traumatic growth among frontline responders.

Gabbianelli Rosita, 2024

Received: 30 November 2020 | Revised: 11 February 2021 | Accepted: 12 March 2021
DOI: 10.1111/jan.14839

REVIEW

JAN WILEY

Nurses' burnout and associated risk factors during the COVID-19 pandemic: A systematic review and meta-analysis

Petros Galanis[1] | Irene Vraka[2] | Despoina Fragkou[1] | Angeliki Bilali[3] | Daphne Kaitelidou[1]

from January 1 to November 15, 2020 18,935 nurses

The overall prevalence in nurses of:
FEMALE: emotional exhaustion was 34.1%,
Male: depersonalization was 12.6% and of lack of personal accomplishment was 15.2%.

Studies	Estimate (95% C.I.)	Cases/sample size
Chen et al. 2020	0.215 (0.208, 0.222)	2709/12596
Aydin Sayilan et al. 2020	0.337 (0.282, 0.395)	90/267
Cortina-Rodrvguez et al. 2020	0.696 (0.497, 0.862)	16/23
Hu et al. 2020	0.397 (0.377, 0.418)	835/2101
Jalili et al. 2020	0.530 (0.473, 0.586)	159/300
Zhang et al. 2020	0.056 (0.021, 0.107)	6/107
Overall (I^2=98.92 % , P< 0.001)	0.341 (0.225, 0.466)	3815/15394

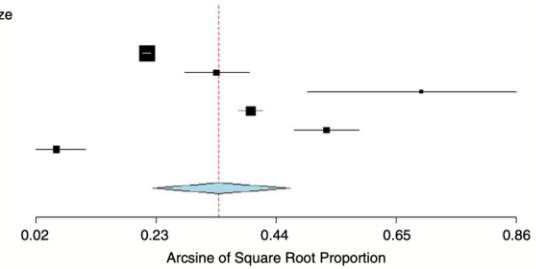
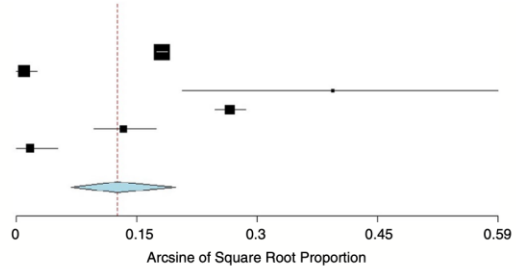
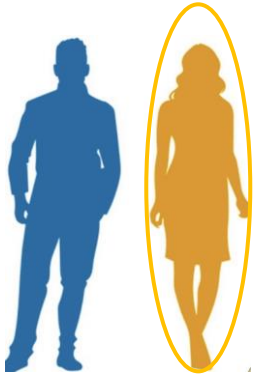


FIGURE 2 Forest plot of the prevalence of emotional exhaustion among nurses according to the Maslach Burnout Inventory.

Studies	Estimate (95% C.I.)	Cases/sample size
Chan et al. 2020	0.181 (0.174, 0.188)	2279/12596
Aydin Sayilan et al. 2020	0.011 (0.002, 0.027)	3/267
Cortina-Rodrvguez et al. 2020	0.391 (0.206, 0.594)	9/23
Hu et al. 2020	0.265 (0.246, 0.284)	556/2101
Jalili et al. 2020	0.133 (0.097, 0.174)	40/300
Zhang et al. 2020	0.019 (0.002, 0.053)	2/107
Overall (I^2=98.02 % , P< 0.001)	0.126 (0.069, 0.197)	2889/15394





Studies	Estimate (95% C.I.)	Cases/sample size
Chen et al. 2020	0.012 (0.010, 0.013)	145/12596
Aydin Sayilan et al. 2020	0.002 (0.000, 0.011)	0/267
Cortina-Rodriguez et al. 2020	0.522 (0.321, 0.718)	12/23
Hu et al. 2020	0.367 (0.346, 0.388)	771/2101
Jalili et al. 2020	0.003 (0.000, 0.013)	1/300
Zhang et al. 2020	0.486 (0.392, 0.580)	52/107
Overall (I^2=99.79 % , P< 0.001)	0.152 (0.014, 0.398)	981/15394

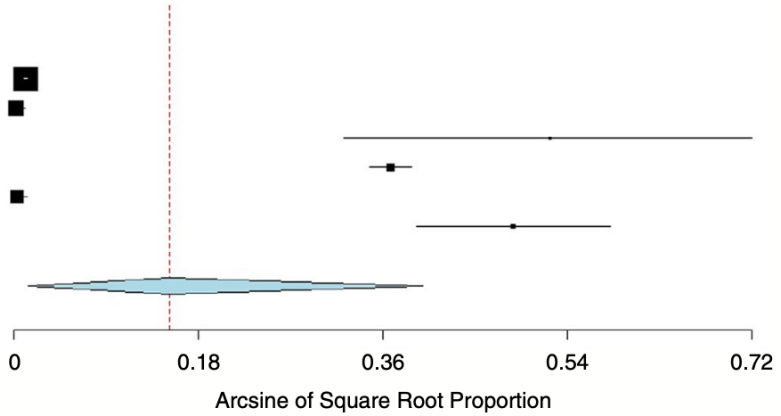


FIGURE 4 Forest plot of the prevalence of lack of personal accomplishment among nurses according to the Maslach Burnout Inventory.

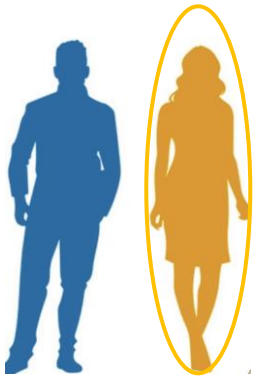
Received: 21 May 2020 | Revised: 28 July 2020 | Accepted: 3 August 2020
DOI: 10.1111/jonm.13124

ORIGINAL ARTICLE

WILEY

Acute stress disorder, coping self-efficacy and subsequent psychological distress among nurses amid COVID-19

Ghada Shahrour PhD, PMHCNS, RN, Assistant Professor[1] |
Latefa Ali Dardas PhD, PMHN, Assistant Professor[2]



A total of 448 Jordanian nurses **(73% females**).

The majority of nurses (64%) are experiencing ASD due to the COVID-19 pandemic and thus are at risk for PTSD predisposition. **More than one-third of nurses (41%) are also suffering significant psychological distress.**

Among our sample, age, ASD and coping self-efficacy significantly predicted psychological distress.

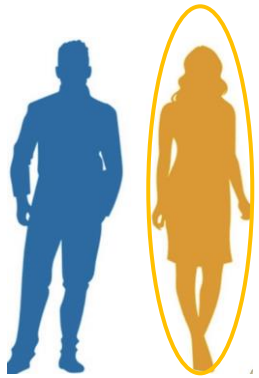
More specifically, **younger nurses** are more prone to experience psychological distress than older ones. While higher scores on ASD showed more resultant psychological distress, coping self-efficacy was a protective factor.

Original article

Arch Argent Pediatr 2021;119(5):317-324 / 317

Prevalence of stress, burnout syndrome, anxiety, and depression among physicians of a teaching hospital during the COVID-19 pandemic

Prof. Francisco J. Appiani, M.D.[a], Federico Rodríguez Cairoli, M.D.[a], Prof. Luis Sarotto Jr., M.D.[b], Claudio Yaryour, M.D.[c], María E. Basile, M.D.[a] and Juan M. Duarte, M.D.[a]



Observational, cross-sectional study conducted 2 months after the lockdown was established in Argentina in physicians

- The **prevalence of stress was 93.7 %** (95 % confidence interval [CI]: 90.33-96.2), **burnout syndrome 73.5 %** (95 % CI: 68.2-78.4), **anxiety 44 %** (95 % CI: 38.4-49.8), and **depression 21.9 %** (95 % CI: 17.3-26.9).

- **The frequency of burnout syndrome, anxiety, and depression was significantly higher among residents and physicians working in the emergency department**

- **The prevalence rate of anxiety and depression appeared to be higher in FEMALES,**
- **Less trained FEMALE workers had a higher prevalence of anxiety, depression, and post-traumatic stress disorder**

- **No association was observed between the frequency and medical specialty.**

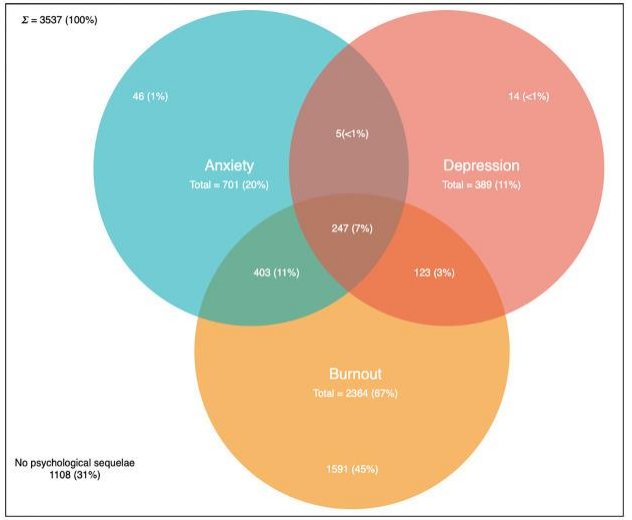
PLOS ONE

RESEARCH ARTICLE

Determinants of burnout and other aspects of psychological well-being in healthcare workers during the Covid-19 pandemic: A multinational cross-sectional study

Max Denning[1], Ee Teng Goh[1], Benjamin Tan[2], Abhiram Kanneganti[3], Melanie Almonte[1], Alasdair Scott[1], Guy Martin[1], Jonathan Clarke[1], Viknesh Sounderajah[1], Sheraz Markar[1], Jan Przybylowicz[1], Yiong Huak Chan[4], Ching-Hui Sia[2,5], Ying Xian Chua[6], Kang Sim[7,8], Lucas Lim[9], Lifeng Tan[10], Melanie Tan[11], Vijay Sharma[2], Shirley Ooi[12,13], Jasmine Winter Beatty[1], Kelsey Flott[1], Sam Mason[1], Swathikan Chidambaram[1], Seema Yalamanchili[1], Gabriela Zbikowska[1], Jaroslaw Fedorowski[14], Grazyna Dykowska[15], Mary Wells[1], Sanjay Purkayastha[1]*, James Kinross[1]

- clinical roles confer a higher burnout risk compared with non-clinical roles
- adapting to a new method of working,
- increased service demands,
- prolonged periods wearing personal protective equipment,
- feeling “powerless” to manage patients’ conditions,
- fear of becoming infected or infecting others
- Staff who were redeployed to new clinical areas had a higher risk of burnout
- **FEMALE gender was predictive of anxiety** (OR 1.47), which is in keeping with previous findings during Covid-19
- However **FEMALE gender was also found to be inversely correlated with depression**, which contrasts from previous research



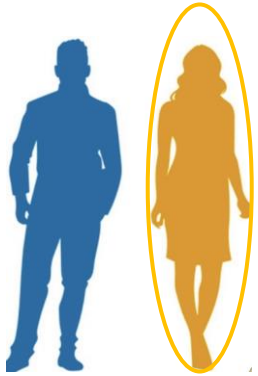


Fig 2. Radar plot demonstrating SAQ subscale by psychological state. This figure demonstrates the SAQ subscale scores by psychological outcome. Distance from the centre represents proportion of a subscale answered positively. A greater distance represents a more positive score. § patients may be represented in more than one series. §§ Not all subscales are weighted equally in calculating overall SAQ score, the area of the radar plot will therefore not represent the overall SAQ score.

Intensive & Critical Care Nursing 62 (2021) 102966

Contents lists available at ScienceDirect

Intensive & Critical Care Nursing

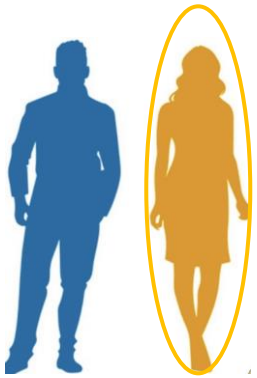
journal homepage: www.elsevier.com/iccn

Research article

Nurses' perceptions and demands regarding COVID-19 care delivery in critical care units and hospital emergency services

María Teresa González-Gil *, Cristina González-Blázquez, Ana Isabel Parro-Moreno, Azucena Pedraz-Marcos, Ana Palmar-Santos, Laura Otero-García, María Victoria Navarta-Sánchez, María Teresa Alcolea-Cosín, María Teresa Argüello-López, Coro Canalejas-Pérez, María Elena Carrillo-Camacho, María Lourdes Casillas-Santana, María Luisa Díaz-Martínez, Asunción García-González, Eva García-Perea, Mercedes Martínez-Marcos, María Luisa Martínez-Martín, María del Pilar Palazuelos-Puerta, Carmen Sellán-Soto, Cristina Oter-Quintana

This is a cross-sectional study (the first phase of a mixed methods study) with critical care and emergency nurses from **26 public hospitals in Madrid** using an online questionnaire.



87% female nurses

The response rate was 557, **with:**

- **37.5% reporting working with the fear of becoming infected** and its consequences,
- **28.2% reported elevated workloads**,
- high patient-nurse ratios and shifts that did not allow them to disconnect or rest, while taking on **more responsibilities** when managing patients with COVID-19 (**23.9%).**

They also reported:

- **deficiencies in communication with middle management (21.2%),**
- **inability to provide psycho-social care to patients and families**
- **being emotionally exhausted (53.5%),**
- **difficulty in venting emotions (44.9%).**

Received: 25 June 2020 | Revised: 23 July 2020 | Accepted: 3 August 2020
DOI: 10.1111/jonm.13121

ORIGINAL ARTICLE

WILEY

COVID-19 anxiety among front-line nurses: Predictive role of organisational support, personal resilience and social support

Leodoro J. Labrague RN, DM, PhD, Lecturer[1] |
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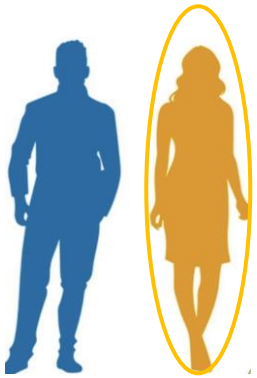
325 registered nurses from the Philippines using four standardized scales.



Results: Of the **325 nurses** in the study, **123 (37.8%)** were found to have dysfunctional levels of **anxiety.**

Using multiple linear regression analyses, social support (β = −0.142, p = .011), personal resilience (β = −0.151, p = .008) and **organisational support** (β = −0.127, p = .023) predicted COVID-19 anxiety. Nurse characteristics were not associated with COVID-19 anxiety.

Conclusions: RESILIENT NURSES and those **who perceived higher organisation and social support** were more likely to report lower anxiety related to COVID-19.

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ORIGINAL ARTICLE

Journal of Clinical Nursing WILEY

Work-related stress among health professionals in Swiss acute care and rehabilitation hospitals—A cross-sectional study

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293 Swiss hospitals: In total, 3,398 health professionals working in acute care or rehabilitation hospitals took part in the study.

66% nurses, 2% midwives, 11% physicians, 9% medical-technical professionals and 9% medical-therapeutic profes- sionals. Participants were mostly highly educated (academic level) (79%), female (81%), with a mean age of 40 years.

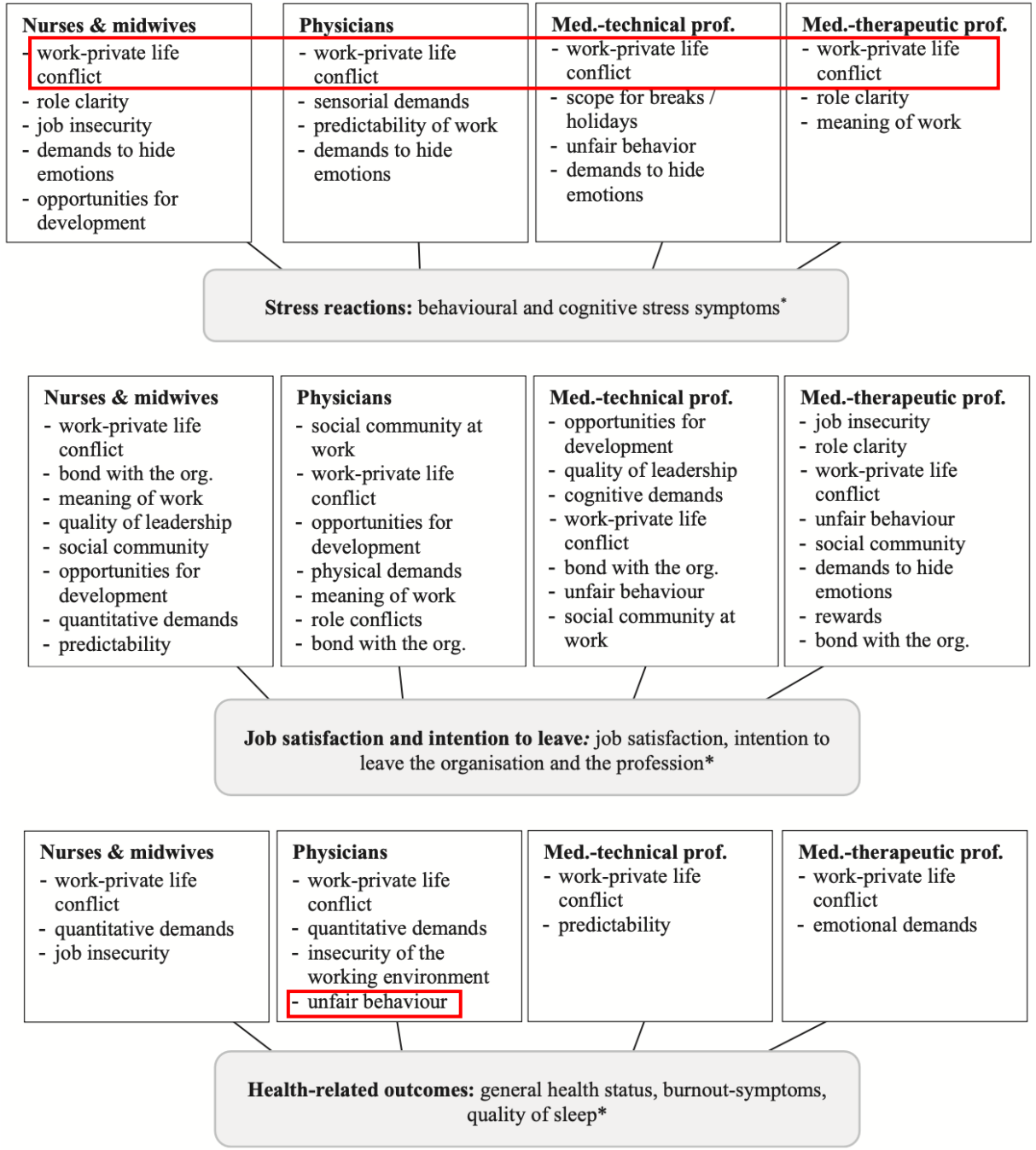
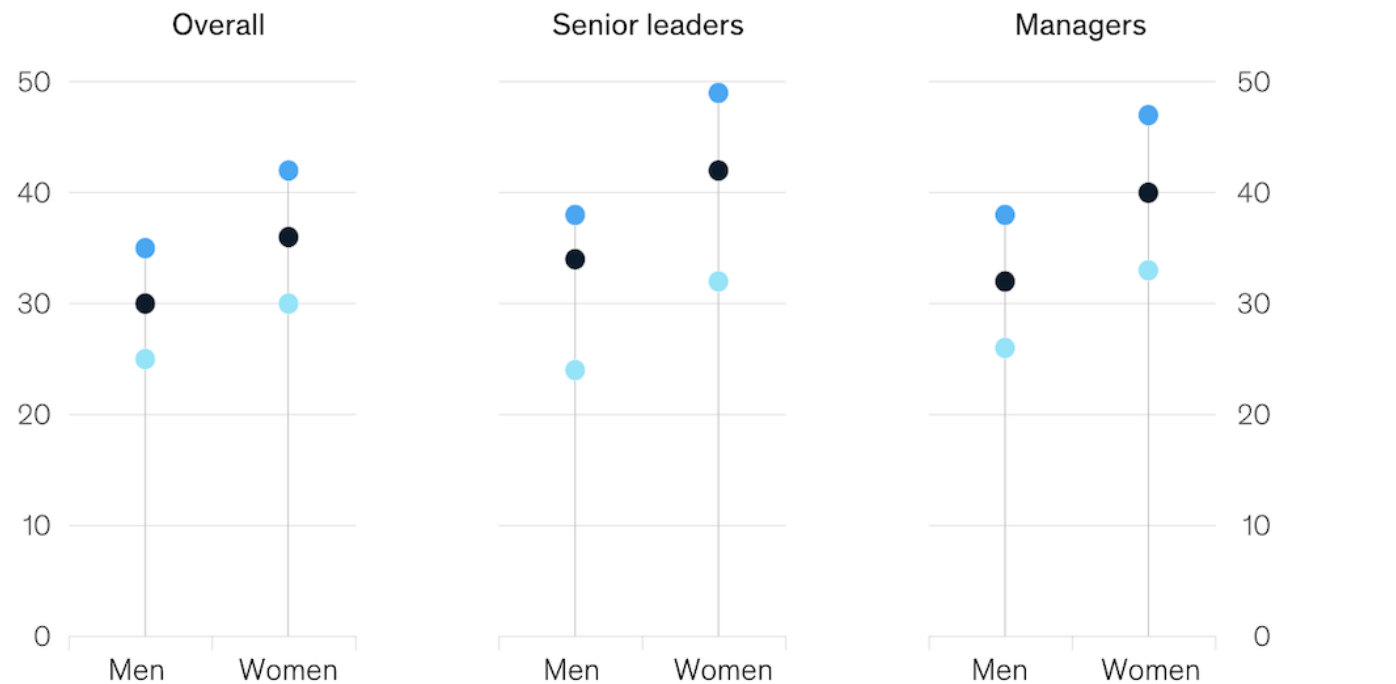


FIGURE 2 Relevant profession-specific stressors at work associated with stress symptoms, job satisfaction, intention to leave and health-related outcomes. *significant work stressors for stress reactions, job satisfaction and intention to leave and health-related outcomes (Beta>0.1)

Burnout, stress, and exhaustion continue to affect women more than men.

Respondents experiencing burnout, stress, or exhaustion, by gender,[1] %



Curr Cardiol Rep (2015) 17: 74
DOI 10.1007/s11886-015-0630-8

PSYCHOLOGICAL ASPECTS OF CARDIOVASCULAR DISEASES (A STEPTOE, SECTION EDITOR)

Work Stress as a Risk Factor for Cardiovascular Disease

Mika Kivimäki[1] · Ichiro Kawachi[2]

600,000 men and women from 27 cohort studies in Europe, the USA and Japan suggests that work stressors, such as job strain and long working hours, are associated with a **moderately elevated risk of incident coronary heart disease and stroke.**

The excess risk for exposed individuals is **10–40 % compared** with those free of such stressors.

ORIGINAL ARTICLES

Work-Related Stress and Occurrence of Cardiovascular Disease

A 13-Year Prospective Study

Feng, Meng-Yao BM; Wang, Hui-Xin PhD; Zhuo, Lai-Bao MPH; Yao, Wu PhD; Hao, Chang-Fu PhD; Pei, Jin-Jing PhD

Author Information

Journal of Occupational and Environmental Medicine 64(11):p 927-933, November 2022. | ***DOI:*** 10.1097/JOM.0000000000002645

A total of **5651 CVD-free participants older than 50 years** from the Survey of Health, Ageing and Retirement in Europe were followed up for 13 years to detect incident CVD.

Results

High physical demands (hazard ratio [HR], 1.30) and low reward (HR, 1.19) compared with their counterparts, as well as active physical jobs (HR, **1.41**) **and high physical strain** (HR**, 1.45**) in comparison with low physical strain were associated with **higher risk of incident CVD after adjusting for confounders**.

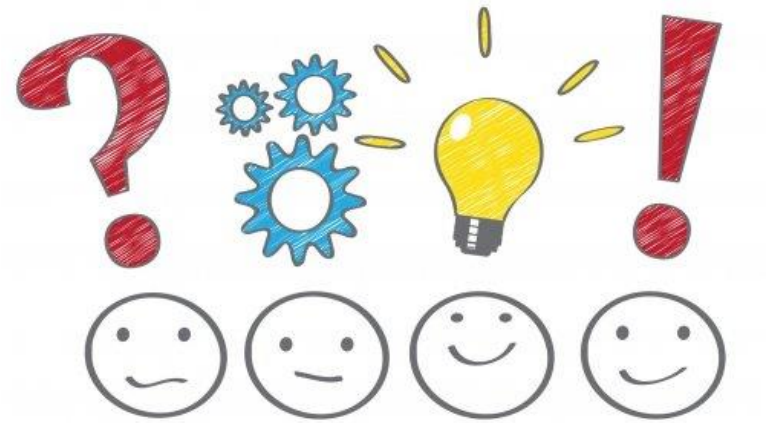
Conclusions

Avoiding physically stressful jobs or providing appropriate reward may reduce the occurrence of CVD.

Conclusions

- Long working hours (>55hours/week) increased risk of chronic conditions like stroke or breast cancer and shortened sleeping hours and difficulty falling a sleep;
- Individual respose to stress; Female and male have a different response;
- Data from COVID-19 period highlighted significant stress related consequence in female and young health care professionals;
- Measures to provide maximum exposure period (i.e. four hours), facilitating breaks for basic needs and venting emotions can contribute to improving the physical and emotional wellbeing;
- Training and clinical practice guidelines with clear and precise instructions (for nurses);
- Interventions aimed at providing higher organization and social support can help the management of stress (i.e. mindfulness, aerobic exercise and bibliotherapy may also be successful)

- **Can gender difference and related stress response be partially related to a different approach to work and/or "a very meticulous and precise person" "hard on oneself aiming for perfection" from female?**



GRAZIE DELL'ATTENZIONE

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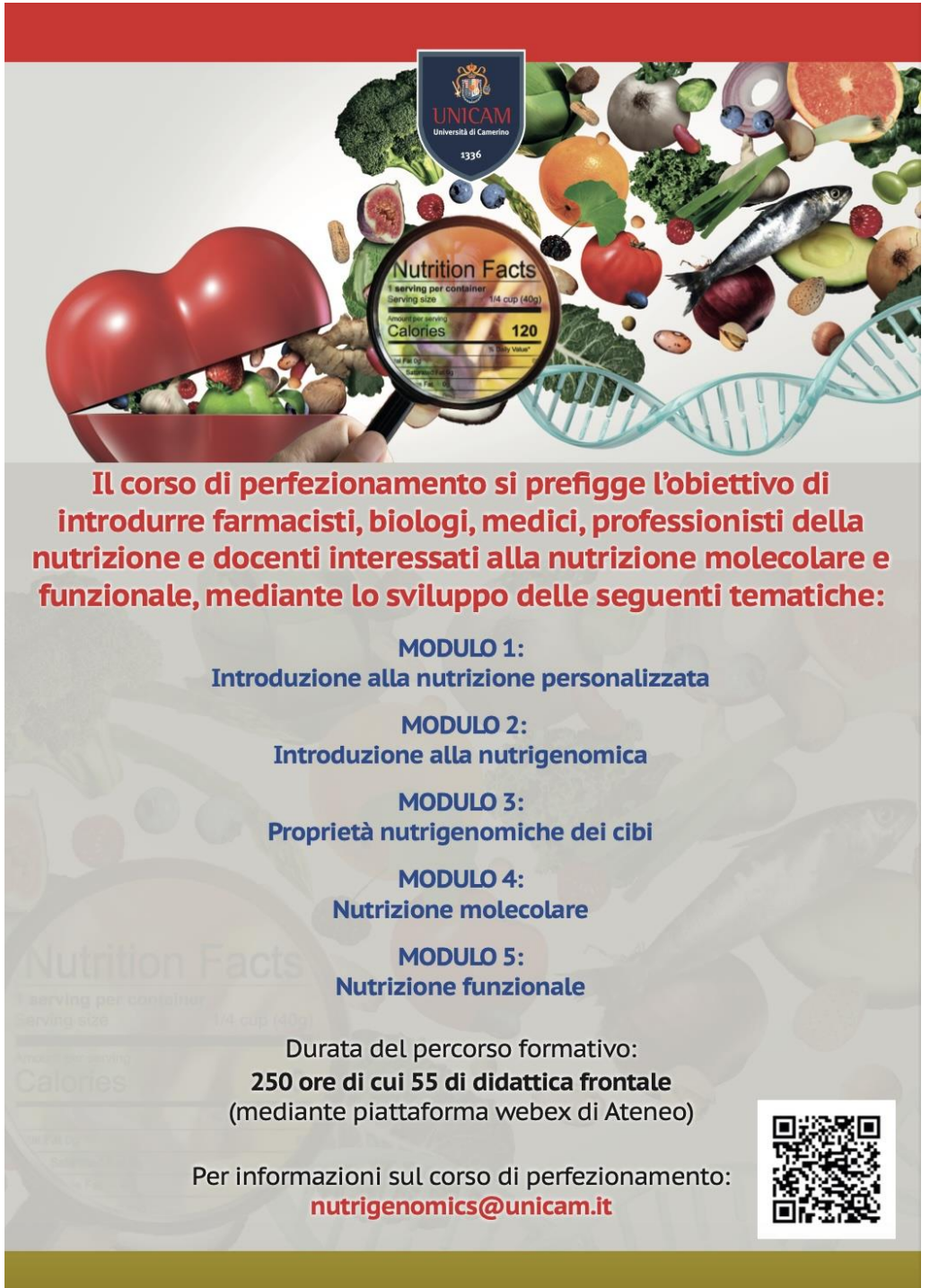

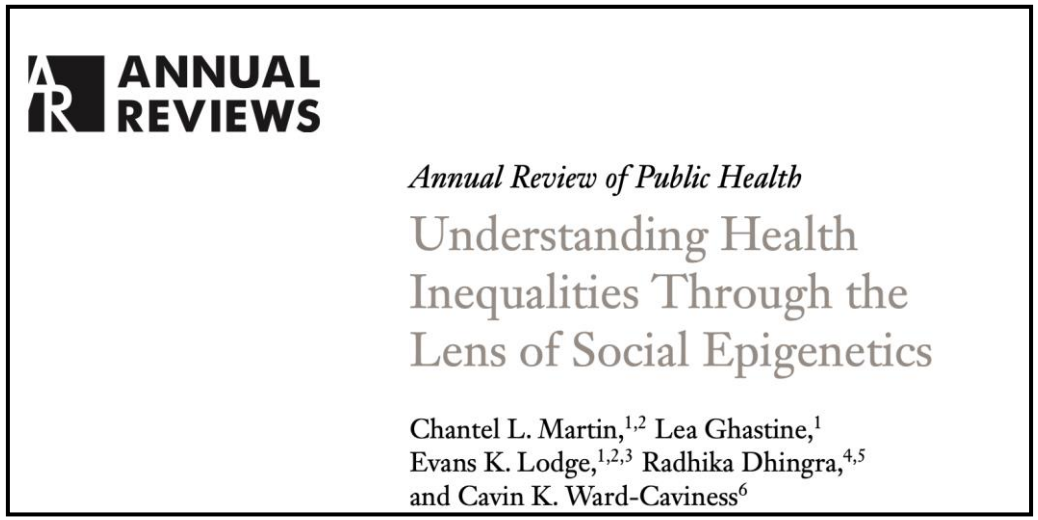

Although maternal stress was not associated with preterm birth in their study, they found that higher prenatal stress was associated with increased offspring methylation in the *MEST* DMR, and the associations differed for male and female offspring.

PNAS RESEARCH ARTICLE | ANTHROPOLOGY OPEN ACCESS

Pregnancy is linked to faster epigenetic aging in young women

Calen P. Ryan[a,1], Nanette R. Lee[b], Delia B. Carba[b], Julie L. MacIsaac[c], David T. S. Lin[c], Parmida Atashzay[c], Daniel W. Belsky[a,d,e], Michael S. Kobor[c,e,f,g], and Christopher W. Kuzawa[h]

Edited by Peter Ellison, Harvard University, Cambridge, MA; received October 5, 2023; accepted February 13, 2024

Table 2. Relationship between pregnancy (ever pregnant vs. never pregnant) and cross-sectional epigenetic age for six epigenetic clock measures of biological aging in 825 young women in the Philippines

	Horvath		PhenoAge		DunedinPACE	
Predictors	Estimates	*P*	Estimates	*P*	Estimates	*P*
Ever pregnant (yes)	0.26 (0.12–0.39)	**<0.001**	0.27 (0.12–0.41)	**<0.001**	0.28 (0.14–0.42)	**<0.001**
Observations	825		825		825	
R^2/R^2 adjusted	0.054/0.036		0.156/0.139		0.196/0.180	
	Hannum		GrimAge		DNAmTL	
Predictors	Estimates	*P*	Estimates	*P*	Estimates	*P*
Ever pregnant (yes)	0.17 (0.02–0.32)	**0.023**	0.14 (−0.01–0.29)	0.062	−0.19 (−0.34– −0.04)	**0.012**
Observations	825		825		825	
R^2/R^2 adjusted	0.107/0.090		0.168/0.152		0.106/0.089	

Estimates and 95% CI are in SD, equivalent to Cohen's d, and *P*-values below alpha of 0.05 are bolded.