

### The exposome of ageing

Food Forum 2024

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G3: Glasgow Geroscience Group



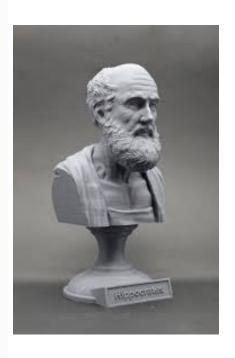




### Disclosures

- Consultancy on Geroscience for Revalesio (US), Eolas (UK).
- Scientific Reviewer Mars (UK),

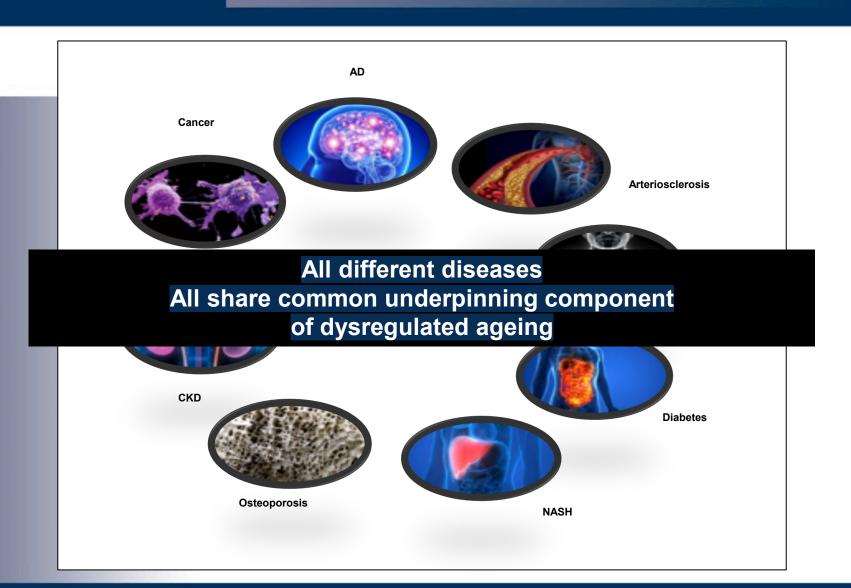




- More people in the world are over 60 than at any time in history
- This demographic is growing
- Years of healthy living have not kept apace with increase in lifespan



### Global Ageing





### Diseasome of ageing

- Common features
- All affected by a changing environment
- Diminished stress defenses (Nrf2)
- Loss of diversity in gut microbes
- Inflammatory burden
- Loss of physiological resilience

Peter Stenvinkel<sup>1</sup>, Paul G. Shiels<sup>2</sup>, Johanna Painer<sup>3</sup>, J. Jaime Miranda<sup>4</sup>, Barbara Natterson-Horowitz<sup>5,6,7</sup> and Richard J. Johnson<sup>8</sup> www.kidney-international.org

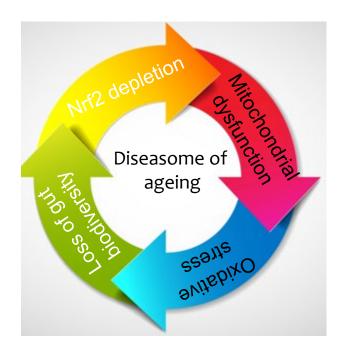
### A planetary health perspective for kidney disease

Check for updates

editorial

Kidney International (2020) 98, 261-265; https://doi.org/10.1016/j.kint.2020.03.024

KEYWORDS: biomimetics; burden of lifestyle disease; chronic kidney disease; heat stress; planet health; pollution Copyright © 2020, International Society of Nephrology. Published by Elsevier Inc. All rights reserved.



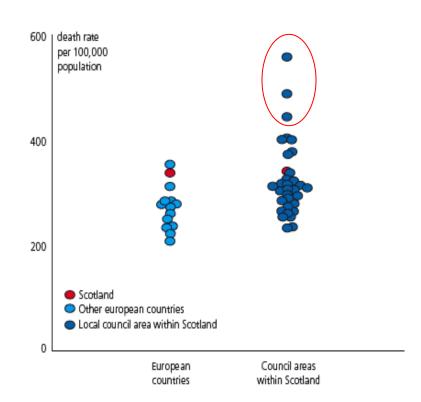


Scotland is 'sick man' of Europe

Glasgow is 'sick man' of Scotland

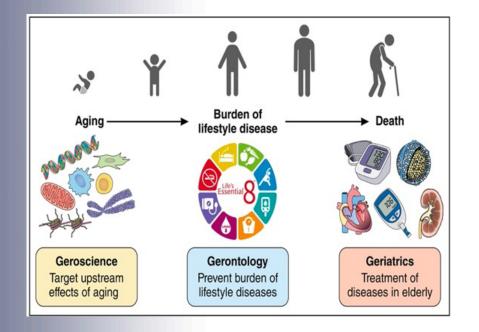
#### Why?

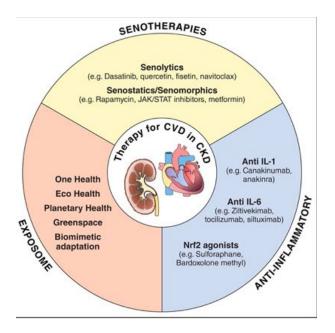
- III health tied to steep SE gradient
- May impact upon age related health





### Geroscience: 'bolting the door before the horse has gone'.

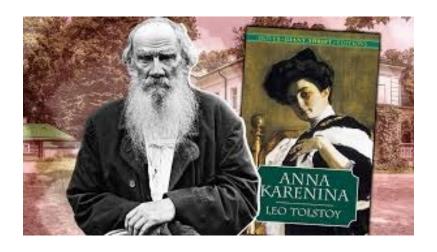




Hobson et al. Circulation Research. 2023;132:950-969



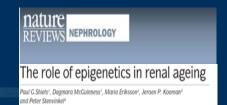
### Ageing is highly individual



"All happy families are alike; each unhappy family is unhappy in its own way."

Tolstoy- Ana Karenina





Tomar, A. et al. Nature https://doi.org/10.1038/s41586-024-07472-3 (2024).

nature > news > article

**NEWS** | 05 June 2024

## A dad's diet affects his sperm — and his sons' health

Mouse fathers who ate high-fat foods and human fathers with high body-mass index have male offspring with metabolic disorders.



### Hallmarks of ageing common across taxa

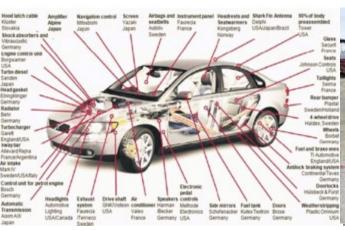
 It has been calculated that the impact on health span of curing both cancer and heart disease would add no more than 2-3 years to healthy life expectancy to a hypothetical 50-year-old woman, whereas slowing the ageing process would add an extra 25 years of healthy life

Burch et al J Gerontol A Biol Sci Med Sci. 2014 Jun; 69(Suppl 1): S1-S3.

The economic value of delayed aging is estimated to be \$7.1 trillion over 50 years.

Goldman Cold Spring Harb Perspect Med. 2016 Feb; 6(2): a025072.









### The exposome

Biochemical Journal (2021) 478 2889-2898 https://doi.org/10.1042/BCJ20200958



#### Review Article

#### Manipulating the exposome to enable better ageing

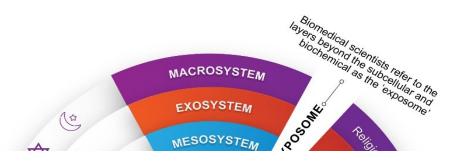
<sup>©</sup> Paul G. Shiels<sup>1</sup>, Johanna Painer<sup>2</sup>, Barbara Natterson-Horowitz<sup>3</sup>, Richard J. Johnson<sup>4</sup>, Jaime J. Miranda<sup>5</sup> and <sup>©</sup> Peter Stenvinkel<sup>6</sup>

The exposome comprises the totality of human environmental exposures (both biotic and abiotic) pre-conception to death.

Wild CP. Cancer Epidemiol Biomarkers Prev 2005;14:1847-50.



### The exposome





 Three simple exposome factors, namely air pollution, tobacco smoke and diet, account for ~50% of mortality globally

Lim SS, Vos T, Flaxman AD, et al Lancet 2012;380:2224-60.



Minnis; et al and Paul G Shiels Nature mental health: 132-140 (2024).



### The Glasgow exposome

Specific exposome factors influencing ageing and health in general population

OPEN BACCESS Freely available cells

PLOS OF

Accelerated Telomere Attrition Is Associated with Relative Household Income, Diet and Inflammation in the pSoBid Cohort

Paul G. Shiels<sup>1</sup>\*, Liane M. McGlyon<sup>1</sup>, Alan Macintyre<sup>3</sup>, Paul C. D. Johnson<sup>1</sup>, G. David Batty<sup>1,1</sup>, Harry Barras<sup>3</sup>, Janathan Cavanagh<sup>3</sup>, Ravin A. Deans<sup>1,2</sup>, Ian Forel<sup>2</sup>, Ales McConnachle<sup>2</sup>, Agnes McGinty<sup>3</sup>, Barras<sup>3</sup>, McLean<sup>1,2</sup>, Soith Miller<sup>2</sup>, Naveed Sattar<sup>1,2</sup>, Carol Tannabill<sup>1,2</sup>, Yoga N. Velugillal<sup>1,2</sup>, Chris J. Package<sup>1</sup>

scientific reports

www.impactaging.com

AGING, May 2016, Vol 8 No 5

Research Paper

Accelerated ageing and renal dysfunction links lower socioeconomic status and dietary phosphate intake

Ruth McClelland<sup>1</sup>, Kelly Christensen<sup>1</sup>, Suhaib Mohammed<sup>1</sup>, Dagmara McGuinness<sup>1</sup>, Josephine Cooney<sup>2</sup>, Andisheh Bakshi<sup>3</sup>, Evangelia Demou<sup>3</sup>, Ewan MacDonald<sup>3</sup>, Muriel Caslake<sup>2</sup>, Peter Stenvinkel<sup>4</sup>, and Paul G. Shiels<sup>1</sup>

- Microbial dysbiosis
  - Bacterial DNA signatures in the circulation

International Journal of
Environmental Researce
and Public Health

MDPI

Article

Perceived Neighbourhood Problems over Time and Associations with Adiposity

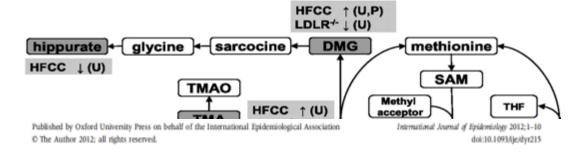
Anne Ellaway 1, \* 0, Ruth Dundas 1 0, Jonathan R. Olsen 1 0 and Paul G. Shiels 2



### The microbial exposome is a potential mediator of the methylome

#### **Glasgow population**

- Telomere attrition
- Increased PO4
- Inflammation
- Imbalanced diet
- Poor renal function among deprived



### Socio-economic status is associated with epigenetic differences in the pSoBid cohort

Dagmara McGuinness,<sup>1</sup> Liane M McGlynn,<sup>1</sup> Paul CD Johnson,<sup>2</sup> Alan MacIntyre,<sup>1</sup> G David Batty,<sup>3</sup> Harry Burns,<sup>4</sup> Jonathan Cavanagh,<sup>5</sup> Kevin A Deans,<sup>6</sup> Ian Ford,<sup>2</sup> Alex McConnachie,<sup>2</sup> Agnes McGinty,<sup>7</sup> Jennifer S McLean,<sup>8</sup> Keith Millar,<sup>5</sup> Chris J Packard,<sup>7</sup> Naveed A Sattar,<sup>9</sup> Carol Tannahill,<sup>8,10</sup> Yoga N Velupillai<sup>8,11</sup> and Paul G Shiels<sup>1\*</sup>





### Unfriendly gut bacteria linked to early ageing



Eating unhealthily is associated with a higher risk of disease

Bacteria that live in the <u>human gut</u> and thrive on an unhealthy diet have been linked to premature ageing among Scotland's poor.

nces

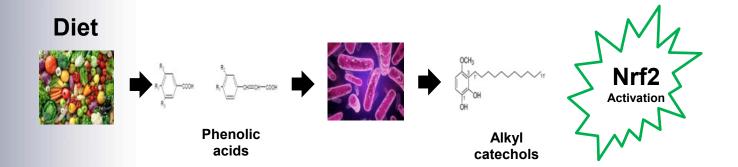
 Oral pathobionts and loss of salutobionts linked to faster ageing and poorer health



### Activation of the Nrf2 Cell Defense Pathway by Ancient Foods: Disease Prevention by Important Molecules and Microbes Lost from the Modern Western Diet

Donald R. Senger ☑, Dan Li, Shou-Ching Jaminet, Shugeng Cao

Published: February 17, 2016 • https://doi.org/10.1371/journal.pone.0148042





### Can we manipulate the exposome of ageing?

### nature food



**Brief Communication** 

https://doi.org/10.1038/s43016-023-00868-w

# Life expectancy can increase by up to 10 years following sustained shifts towards healthier diets in the United Kingdom

Received: 22 March 2023

Accepted: 29 September 2023

Published online: 20 November 2023

Lars T. Fadnes <sup>1,2</sup> ∠, Carlos Celis-Morales <sup>3,4</sup>, Jan-Magnus Økland <sup>1,5</sup>, Solange Parra-Soto<sup>3,6</sup>, Katherine M. Livingstone <sup>7</sup>, Frederick K. Ho <sup>8</sup>, Jill P. Pell <sup>8</sup>, Rajiv Balakrishna<sup>1</sup>, Elaheh Javadi Arjmand <sup>1,2</sup>, Kiell Arne Johansson<sup>1,2,5</sup>, Øystein A. Haaland <sup>1,5</sup> & John C. Mathers



### The Spring of Hope

- Resistant starch type-2 (RS2), a prebiotic, can mitigate inflammation and oxidative stress in patients with chronic kidney disease (CKD) on hemodialysis (HD).
- Generates Short Chain Fatty Acids via activity of saccharolytic bacteria in the gut
- Four weeks intervention for HD patients
- Analysis of changes in renal function and microbiota



#### F-Microbiota analysis



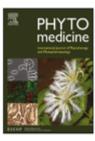
Phytomedicine 114 (2023) 154731



Contents lists available at ScienceDirect

#### Phytomedicine

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



Original Article



The effect of Brazilian Green Propolis extract on inflammation in patients with chronic kidney disease on peritoneal dialysis: A randomised double-blind controlled clinical trial

Beatriz Germer Baptista <sup>a</sup>, Susane Fanton <sup>b</sup>, Márcia Ribeiro <sup>c</sup>, Ludmila FMF Cardozo <sup>b</sup>, Bruna Regis <sup>b</sup>, Livia Alvarenga <sup>a,c</sup>, Marcelo Ribeiro-Alves <sup>d</sup>, Andresa A. Berretta <sup>e</sup>, Paul G. Shiels <sup>f</sup>, Denise Mafra <sup>a,c,\*</sup>

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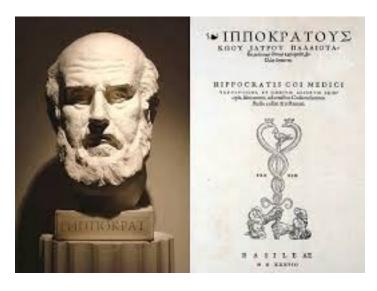


### Conclusions

- The exposome is a powerful mediator of ageing and health
- Amenable to simple interventions
- Tools now available to assess these in real time

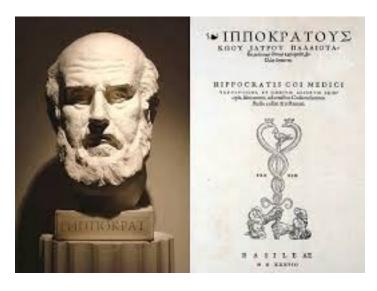


 "If we could give every individual the right amount of nourishment and exercise, not too little and not too much, we would have found the safest way to health." — Hippocrates.





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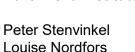


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U. Maastricht

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Denver Richard Johnson



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Harvard/UCLA Barbara Natterson Horowitz



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**Fluminense** Denise Mafra

