Sun, Death and Dermatologists

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University of Edinburgh Centre for Inflammation Research
& Dept of Dermatology

Dr Richard Weller

Disclosure of Relevant Financial Relationships

I have the following financial relationships to disclose:

Consultant for: Novartis, AOBiome
Speaker's Bureau for: Johnson and Johnson. Almirall S.A.
Grant/Research support from:
Stockholder in: Relaxsol Ltd
Honoraria from: Johnson and Johnson, Novartis.
Employee of: Relaxsol Ltd

Disclosure of Off-Label and/or investigative Uses

I will not discuss off label use and/or investigational use in my presentation.

Event Programme

The International Year of Light will consist of coordinated activities on national, regional and international levels. Activities will be planned so that people of all ages and all backgrounds can gain an appreciation for the central role of light in science and culture, and as a cross-cutting scientific discipline that can advance sustainable development.

SUBMIT AN EVENT

Event Form

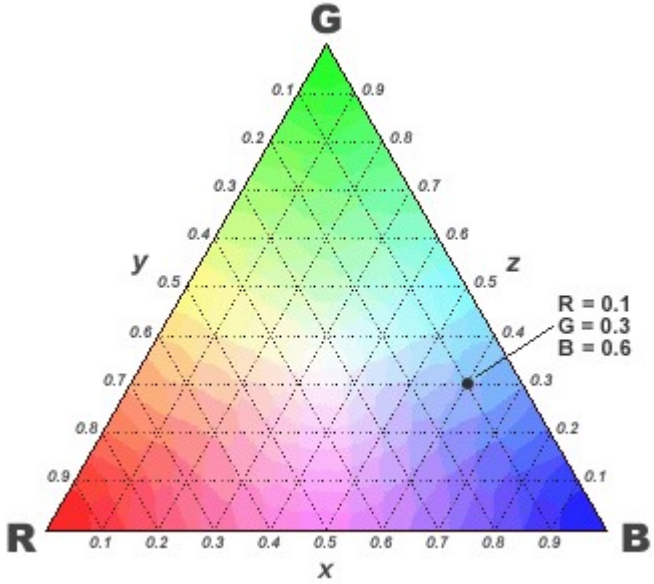
CONTACT THE SECRETARY

Light2015.org

Email: Light2015@ictp.it

Opening Ceremony of the International Year of Light

James Clerk Maxwell

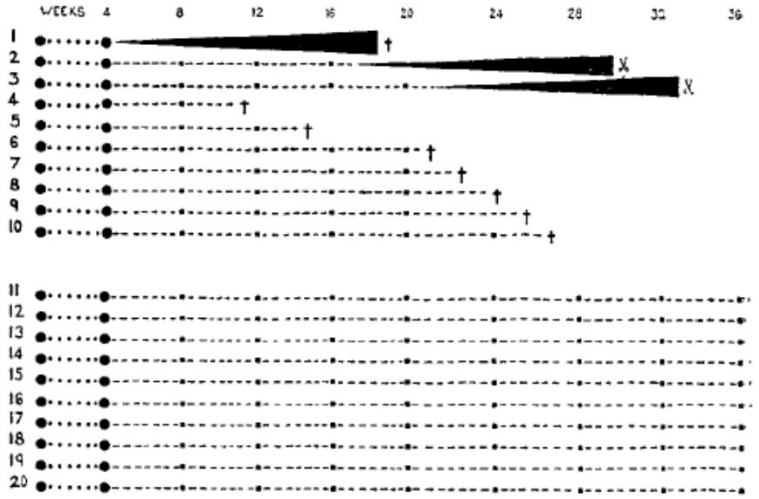


ULTRA-VIOLET LIGHT AND SKIN CANCER.

BY G. M. FINDLAY, O.B.E., M.D., SC.D.EDIN.

(From the Laboratories of the Imperial Cancer Research Fund, London.)

CHART 2.

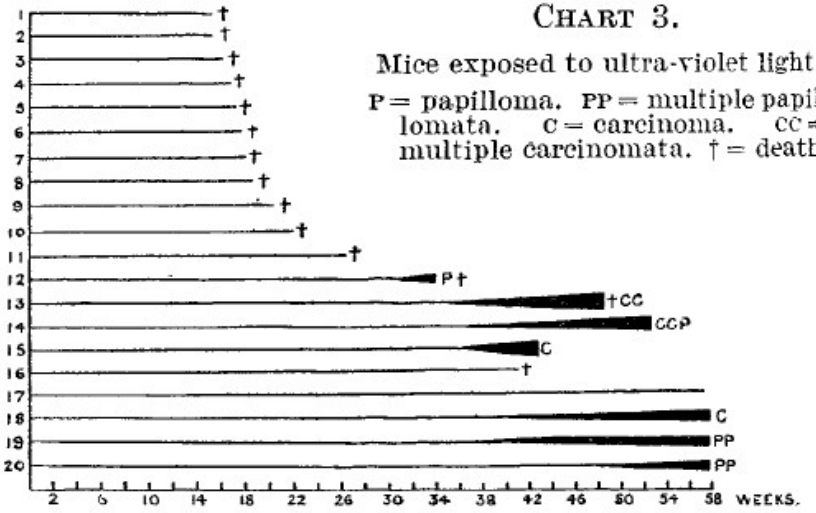


1–10 = Mice tarred twice weekly and exposed to the mercury-vapour lamp for one month.
11–20 = Mice tarred twice weekly for one month.

CHART 3.

Mice exposed to ultra-violet light.

P = papilloma. PP = multiple papillomata. C = carcinoma. CC = multiple carcinomata. † = death.



SunSmart - Skin Cancer Information and Sun Protection Advice

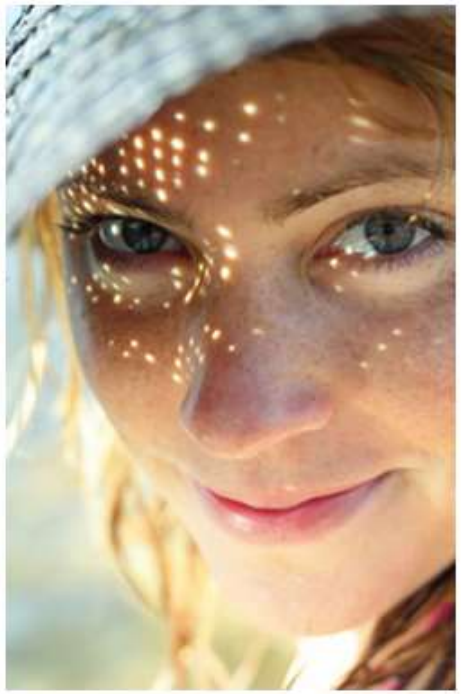
Most skin cancers are caused by overexposure to ultraviolet (UV) radiation from the sun or sunbeds

Enjoy the sun safely. Whether you're at home or abroad, use shade, clothing and at least SPF15 sunscreen to protect yourself.

Find out more about...

- UV, the sun and skin cancer
- Sunscreen
- Sunburn
- Vitamin D
- Sunbeds

Enjoy the sun safely



Highlights

Moles and skin cancer

Learn to spot the signs of skin cancer early; it could save your life

How the sun and UV cause skin cancer

Get the latest information and statistics on skin cancer

The truth about sunbeds

Using a sunbed can make you look old before your time. Get the facts

Skin types and UV index

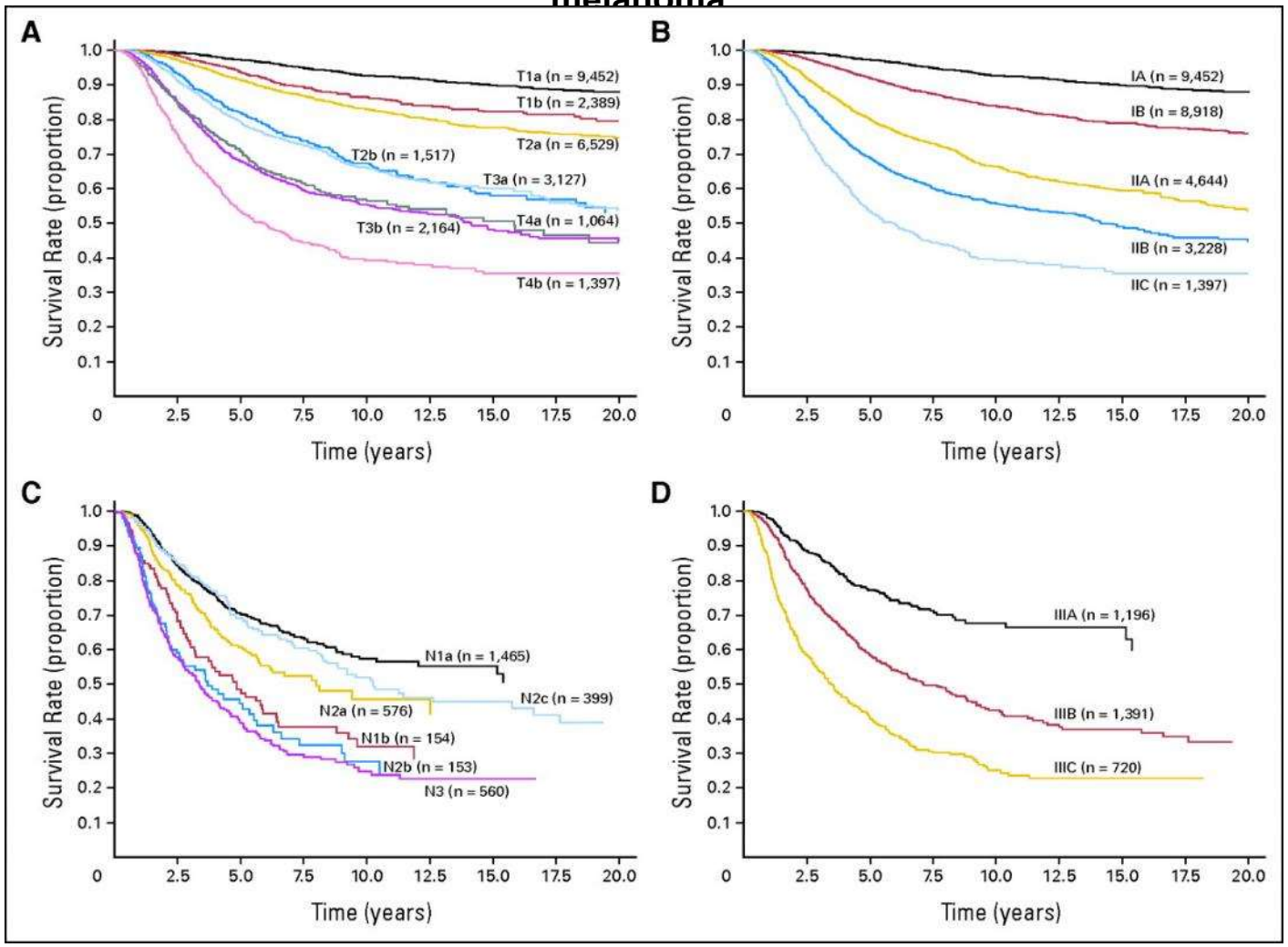
Use our graph to check out your skin type

SunSmart resources

Posters and leaflets from the SunSmart campaign

Melanoma

Survival curves from the American Joint Committee on Cancer Melanoma Staging Database comparing (A) the different T categories and (B) the stage groupings for stages I and II melanoma



Charles M. Balch et al. JCO 2009;27:6199-6206

Melanoma

Risk factor	OR (95% CI)[a] $n = 12,387$	N
Hair color		
Brown/black	1	7,704
Red	1.76 (1.41–2.16)	3,608
Blond	1.41 (1.19–1.67)	942
Skin type		
III+IV	1	7,508
I+II	1.66 (1.36–2.01)	3,666
Freckling		
No	1	5,129
Yes	1.58 (1.25–2.01)	5,050
Family history of melanoma		
No	1	9,054
Yes	1.74 (1.21–2.46)	614
Total body nevus count distribution[b]		
0%–50%	1	1,354
50%–75%	1.64 (1.12–2.30)	638
75%–90%	2.72 (1.89–3.81)	794
>90%	5.50 (3.73–7.89)	701
Large nevi on body (≥5 mm)		
None	1	1,851
1–2	2.26 (1.29–3.68)	1,041
≥3	4.10 (2.19–7.08)	712
Sunburn[c]		
No	1	3,080
Yes	1.28 (1.05–1.27)	6,070

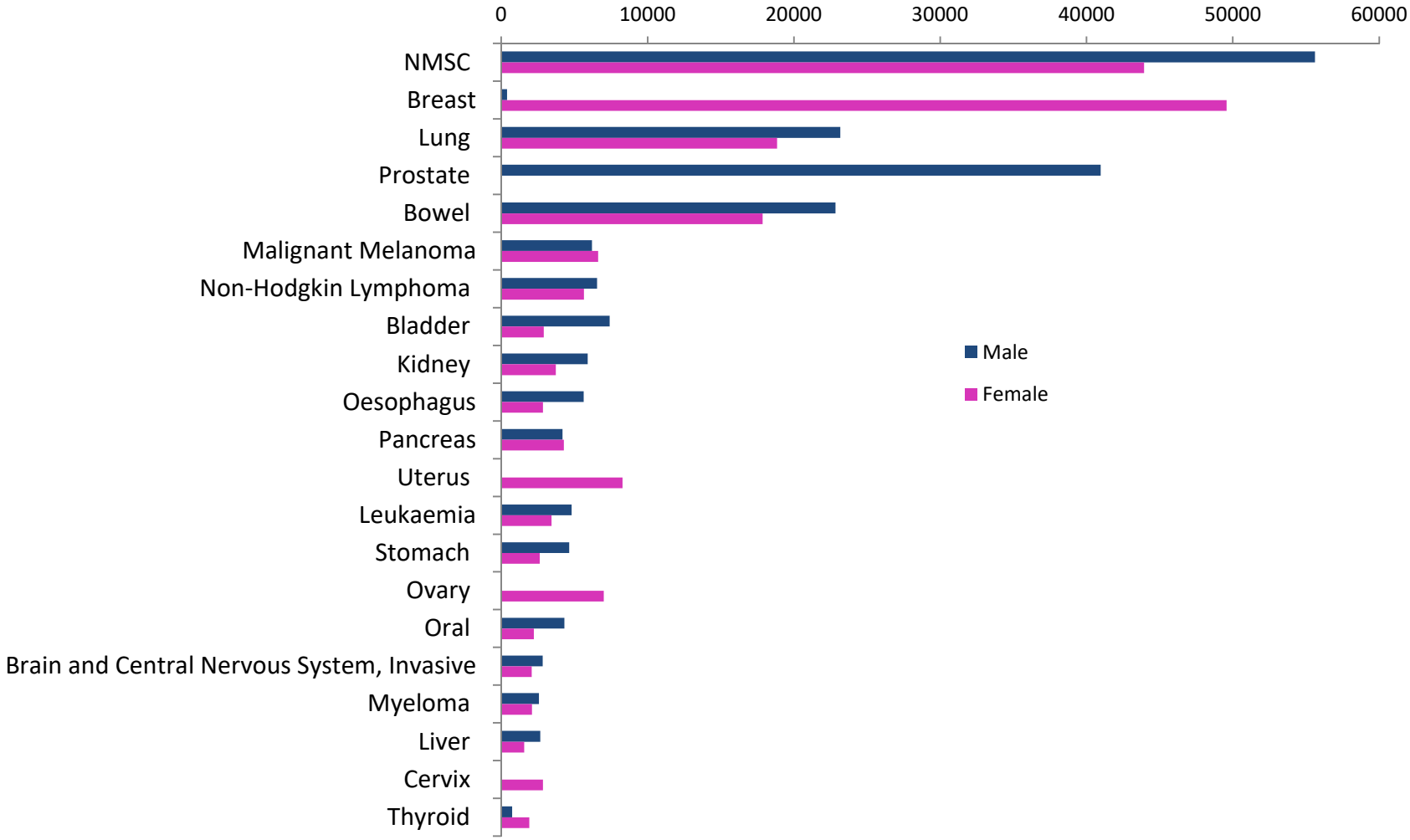
Davies et al. 2015. Cancer Epidemiol Biomarkers Prev

Non-Melanoma Skin Cancer

Squamous Cell Cancer

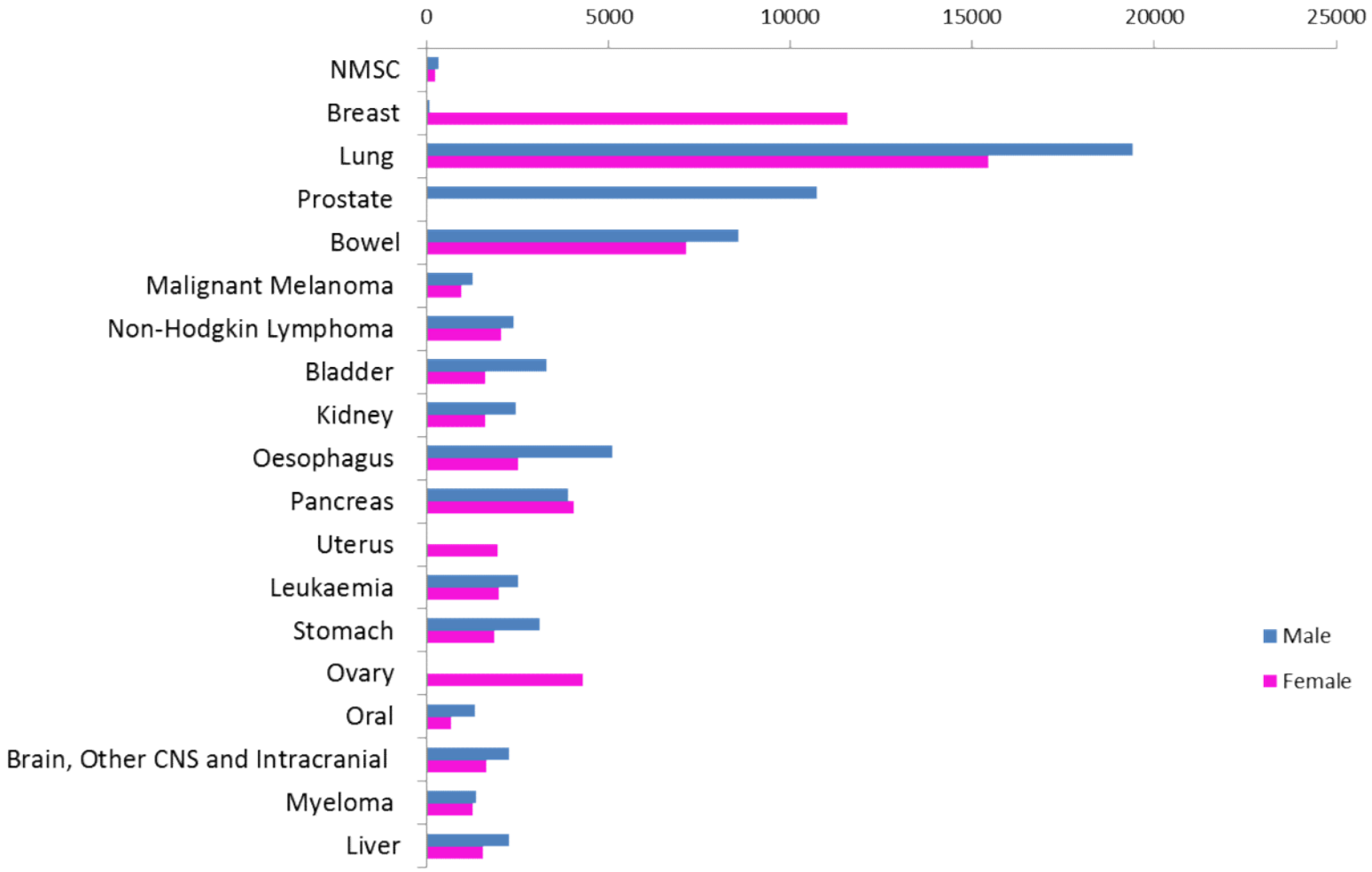
Basal Cell Cancer (Rodent ulcer)

UK Cancer incidence 2010



Cancer Research UK. http://www.cancerresearchuk.org

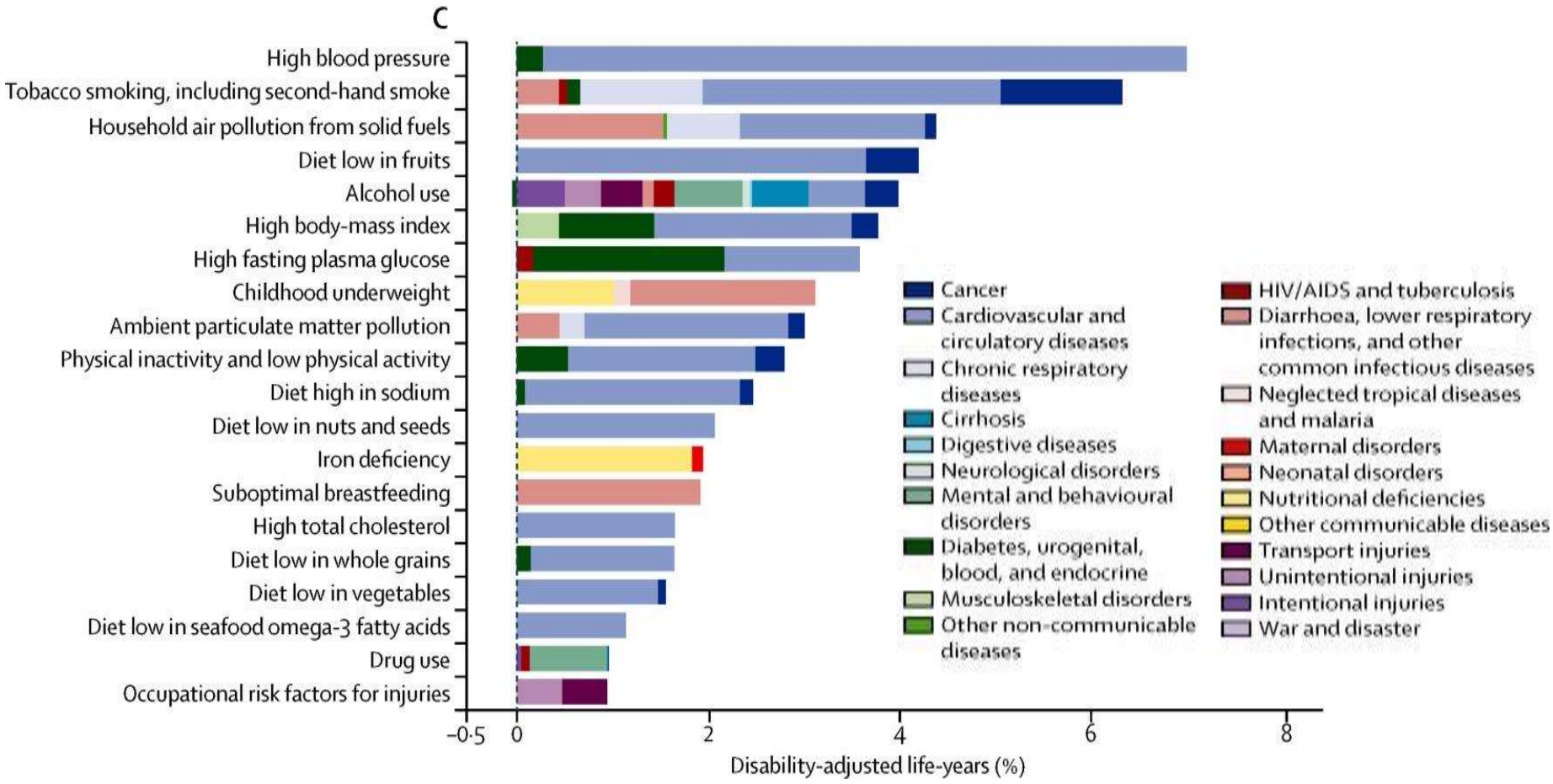
UK Cancer mortality 2010



Cancer Research UK. http://www.cancerresearchuk.org

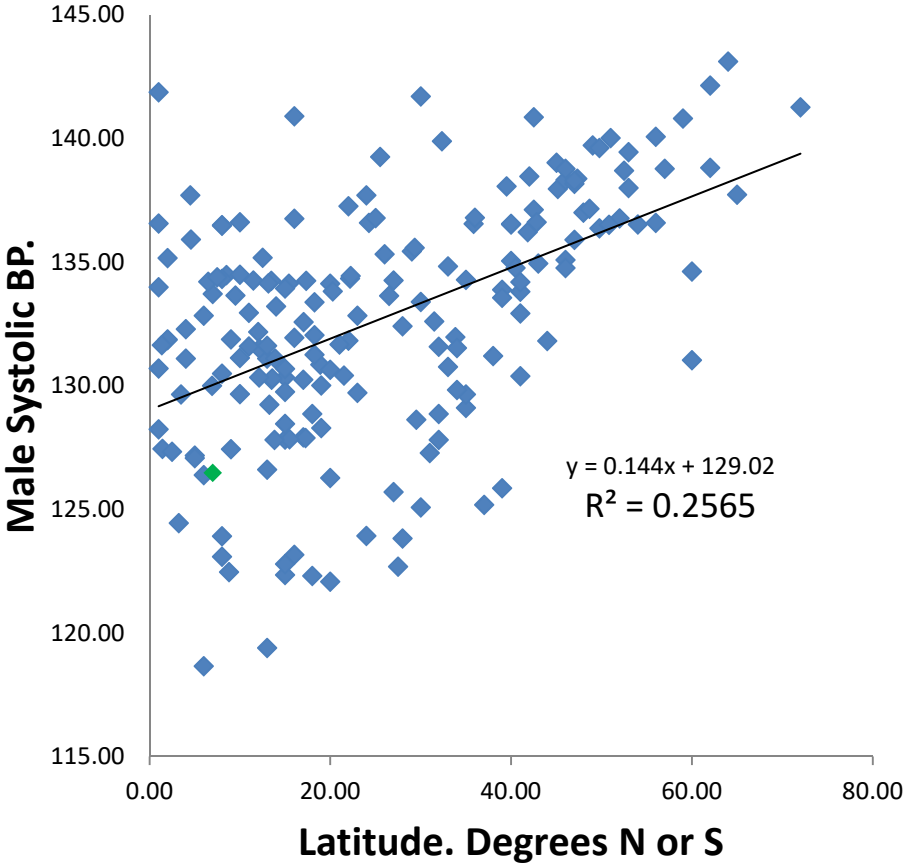
"Slim has a dry scaly patch on his neck! Ride to town and bring the dermatologist."

Global burden of disease
Top 20 risk factors in 2010

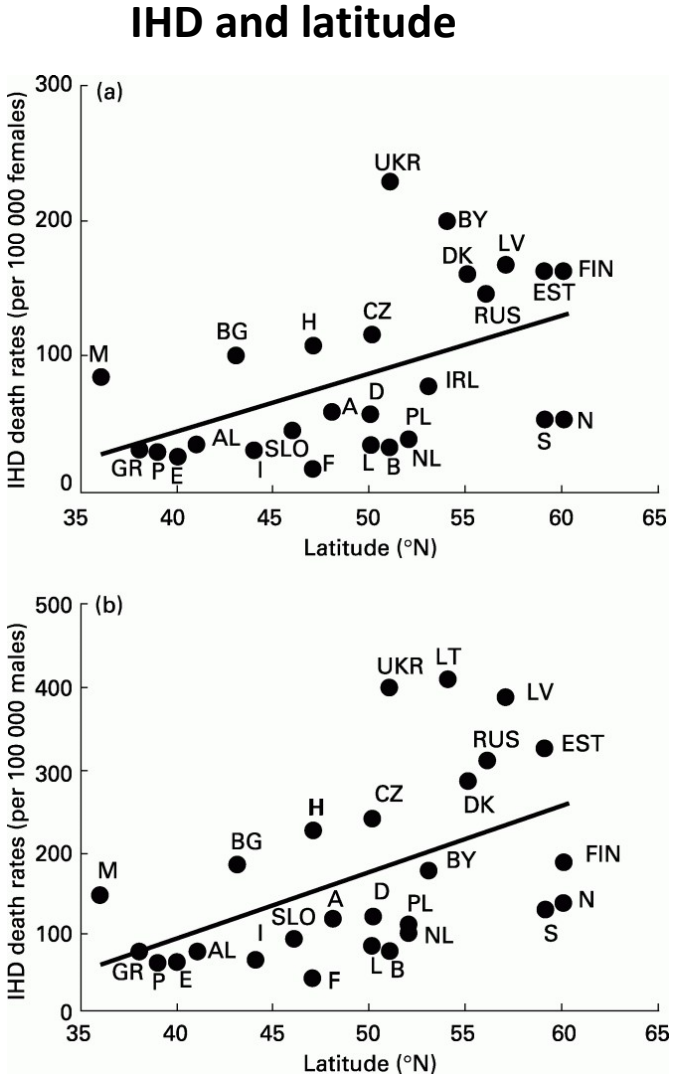


The Lancet **2013** 380, 2224 - 2260

BP and IHD correlate with latitude



MRC-HPA Centre for Environment and Health (1980 data)



Zitterman. Progress in Molecular Biophysics 2006

BP is lower in summer

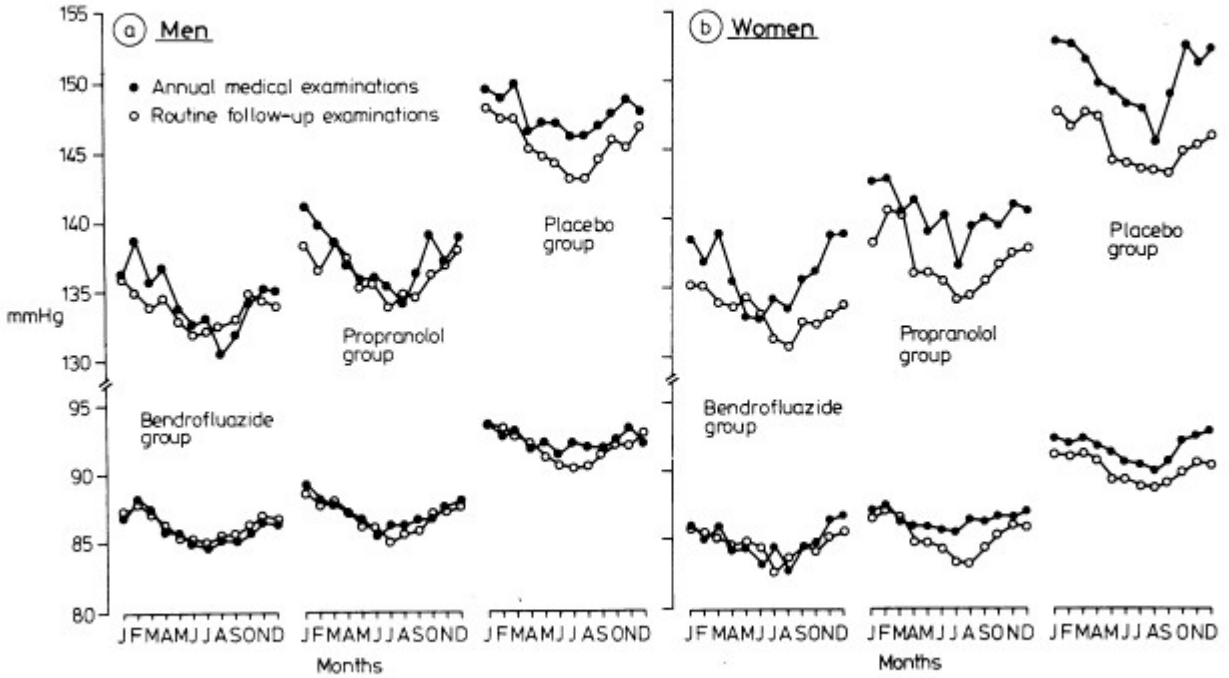


FIG 2—MRC treatment trial for mild hypertension: seasonal trends in blood pressure in (a) men and (b) women by treatment regimen and type of examination.

Serum vitamin D levels inversely correlate with BP and CVD

Annals of Internal Medicine | REVIEW

Systematic Review: Vitamin D and Cardiometabolic Outcomes

Anastassios G. Pittas, MD, MS; Mei Chung, MPH; Thomas Trikalinos, MD; Joanna Mitri, MD; Michael Brendel, BA; Kamal Patel, MPH; Alice H. Lichtenstein, DSc; Joseph Lau, MD; and Ethan M. Balk, MD, MPH

Ann Intern Med. 2010;152(5):307-314

Heatherbank Museum of Social Work

Figure 1. Association between vitamin D status and incident hypertension or cardiovascular disease in longitudinal observational cohorts.

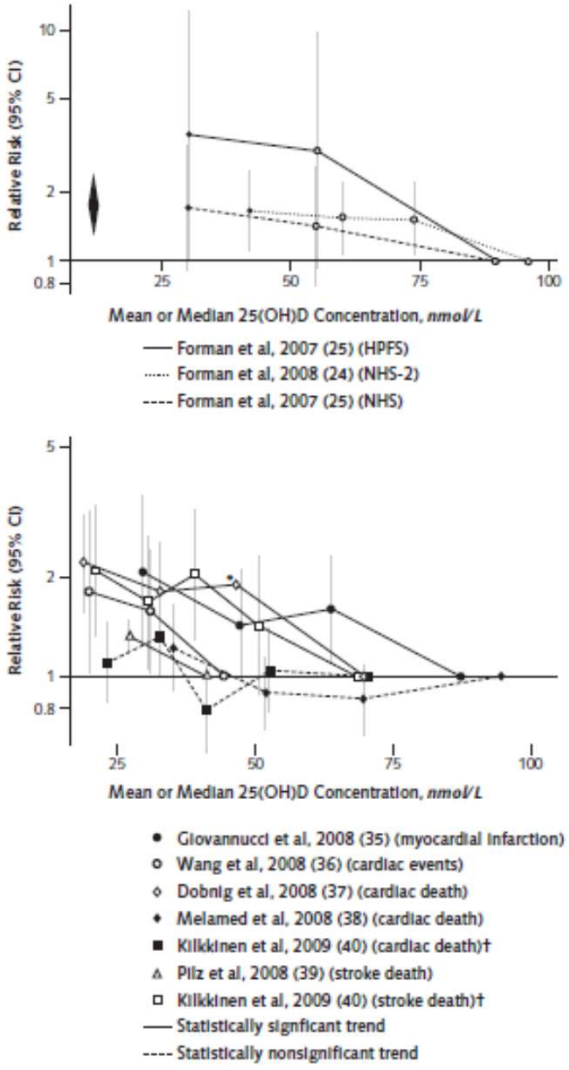
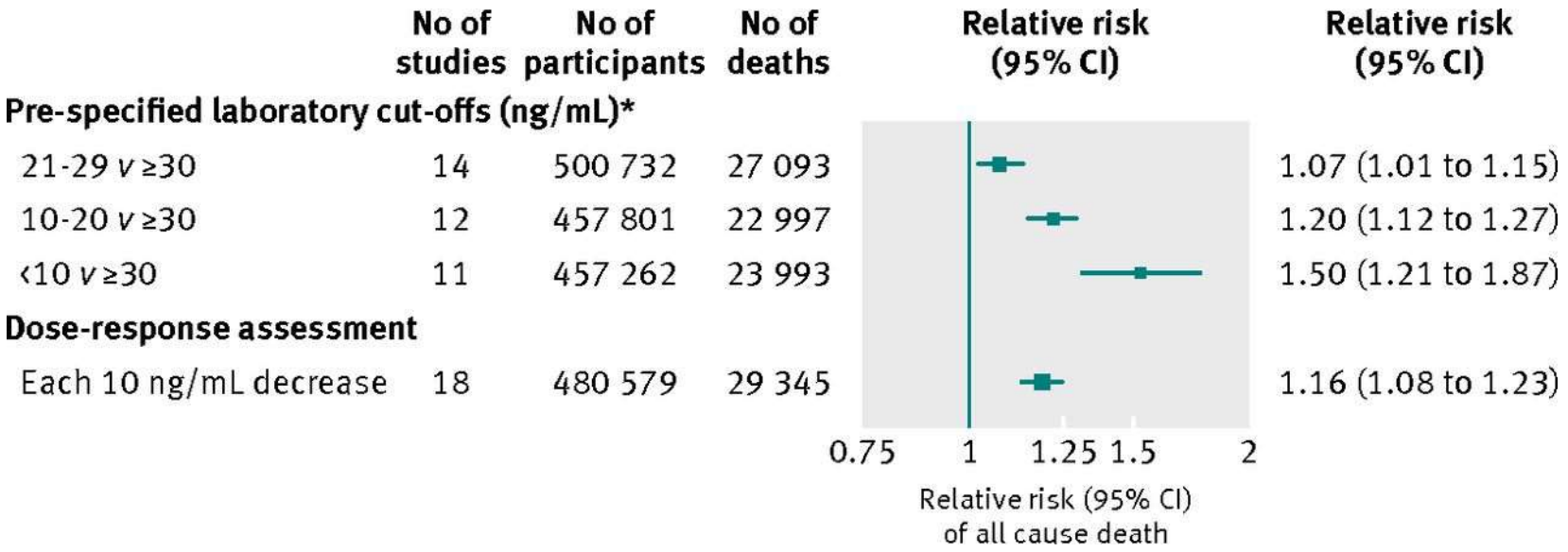


Fig 2 Association of circulating 25-hydroxyvitamin D concentrations with all cause mortality, based on primary prevention cohorts. *Indirect comparisons based on available studies with relevant information in each category; summary estimates presented were calculated using random effects models.



Chowdhury R et al. BMJ 2014;348:bmj.g1903

Oral Vitamin D supplementation has no effect on BP

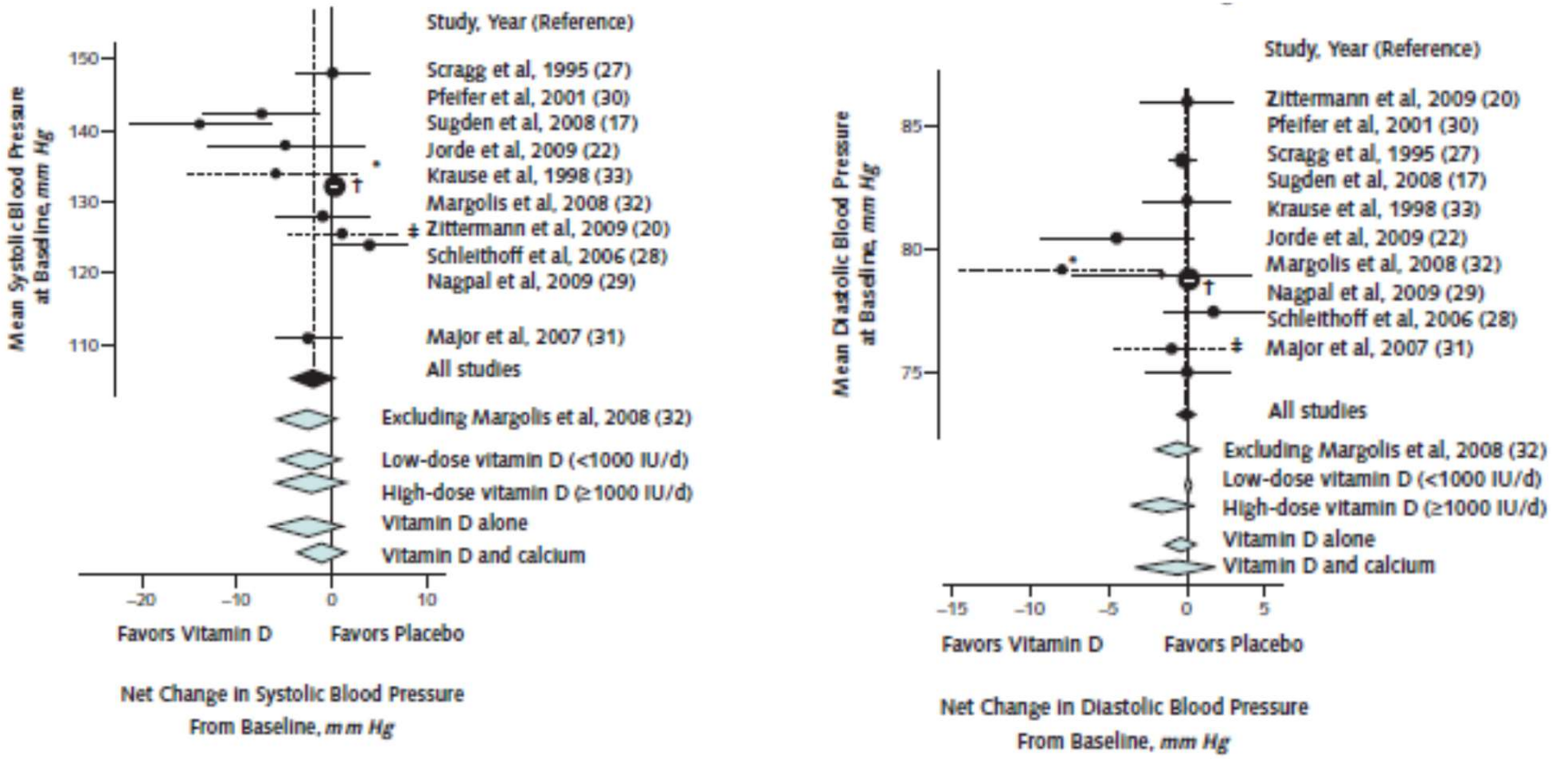
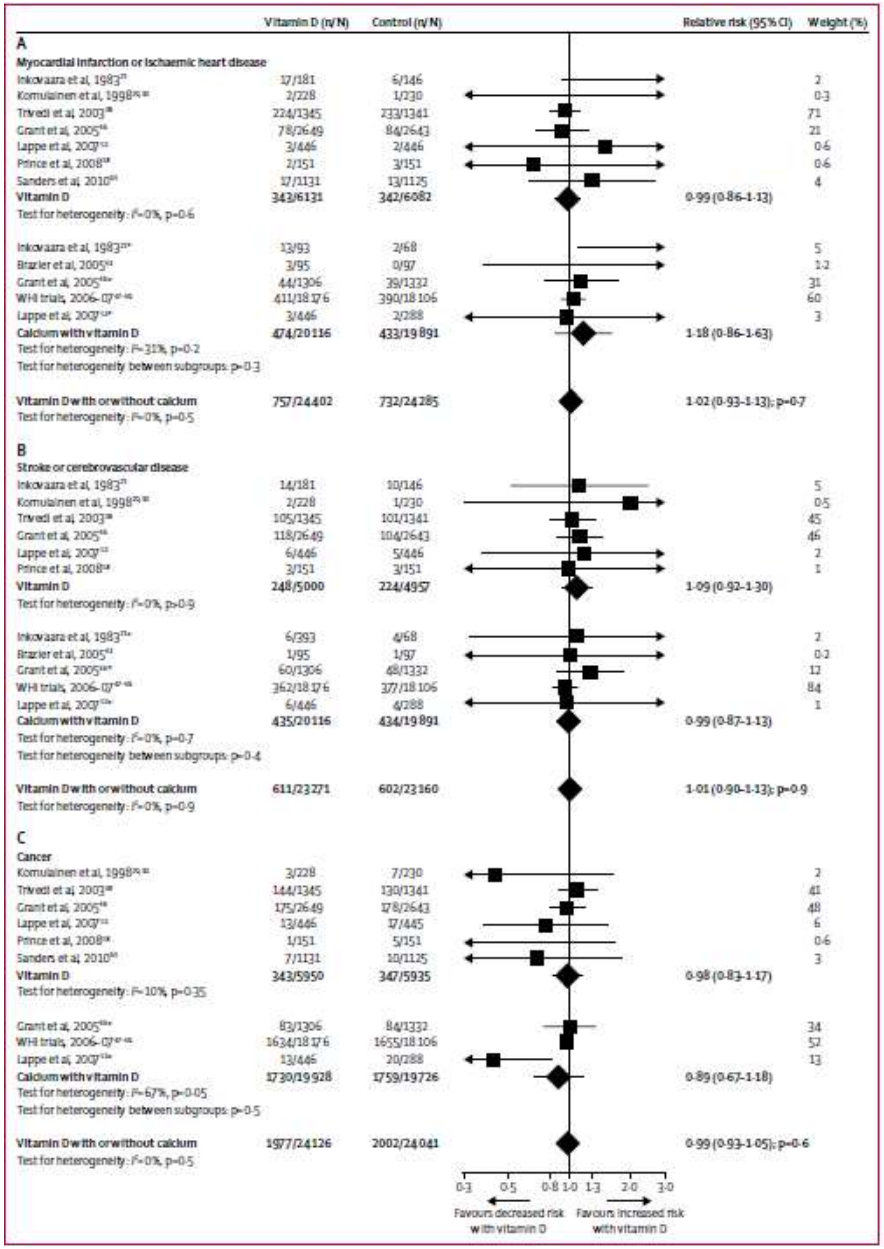
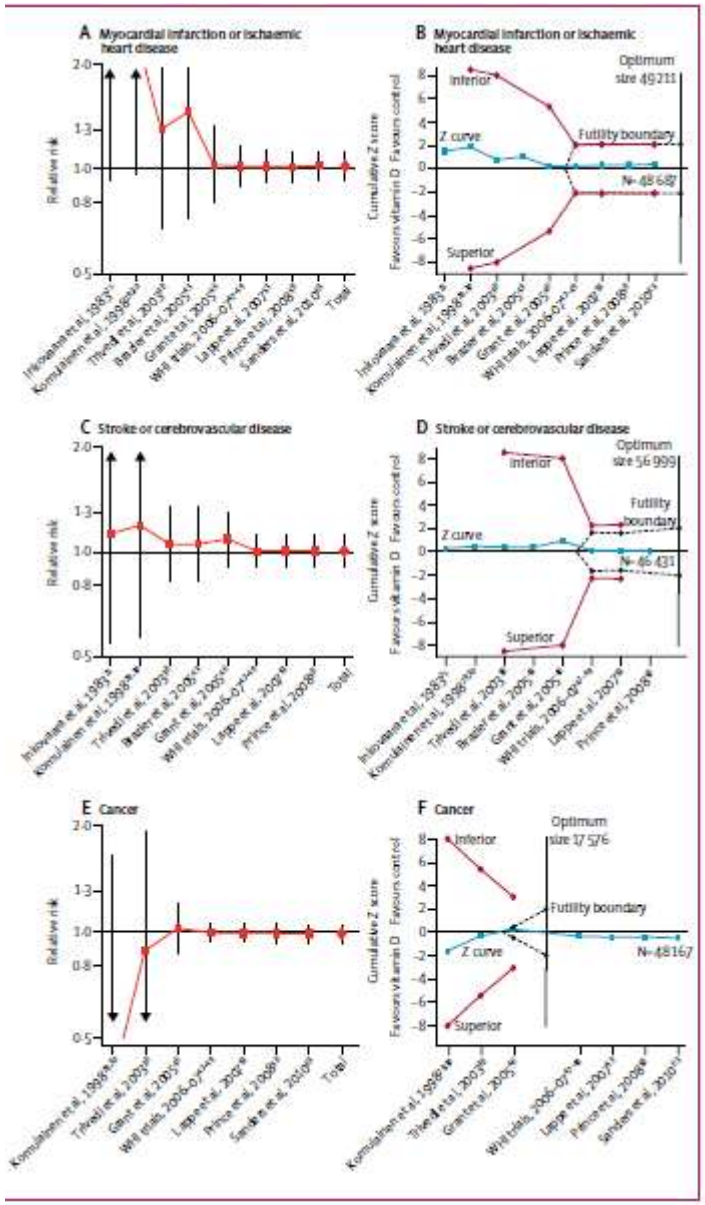


Figure 2. Meta-analyses of the effect of vitamin D supplementation on net change in blood pressure.

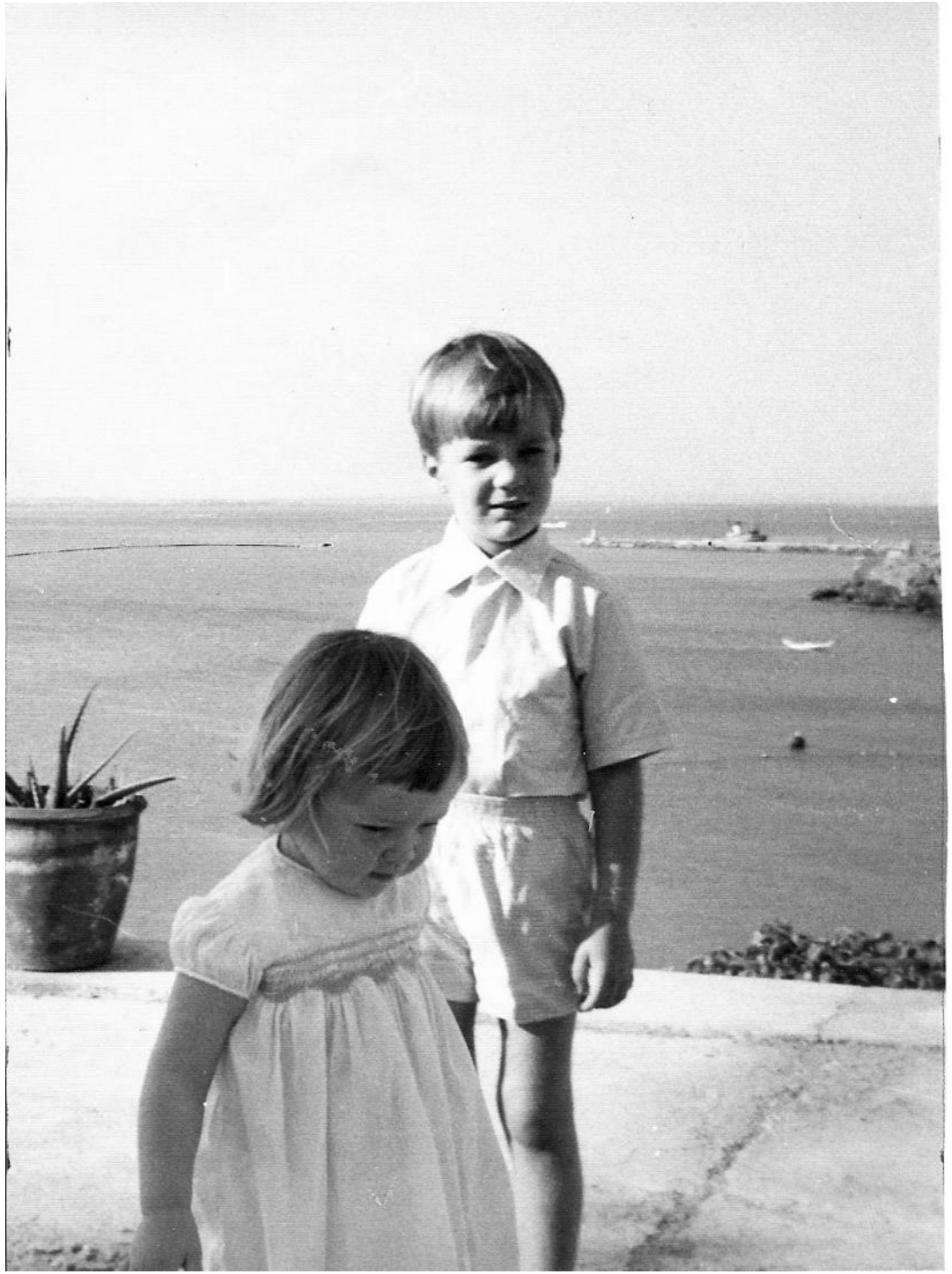
Pittas et al. *Ann Intern Med*. 2010;152(5):307-314

….or IHD, Stroke or Cancer





Bolland et al. Lancet Diabetes Endocrinol. 2014



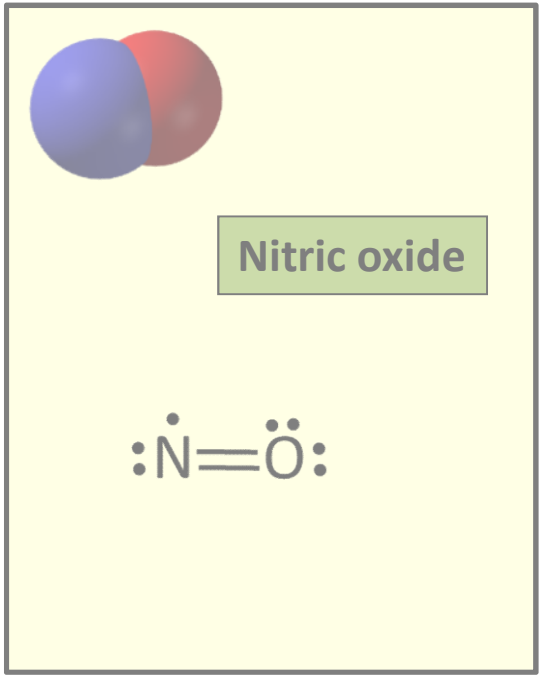
From NO to Nitrite and Nitrate….and Back Again:
Role in Mammalian Biology

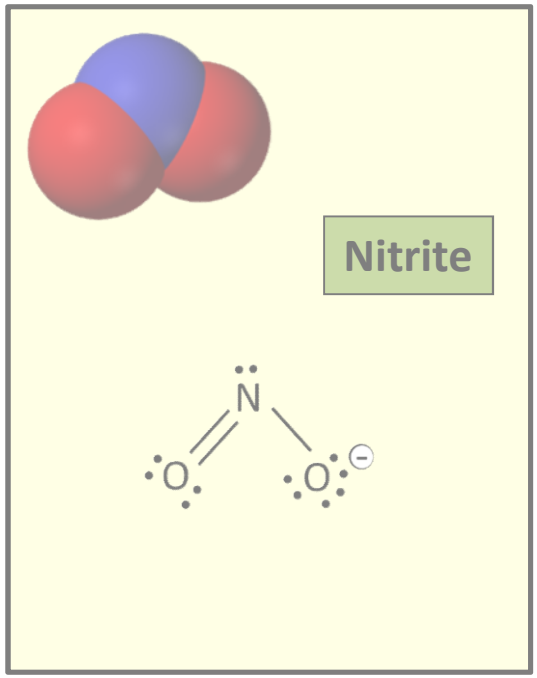
L-arginine

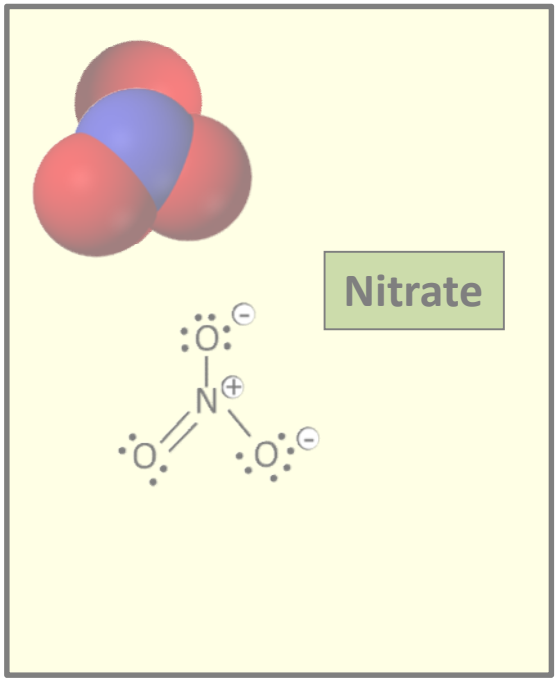
Nitric oxide synthases

Nitric oxide

Vasodilation
Neurotransmission
Cell signalling
Immune regulation
Inflammation
Apoptosis







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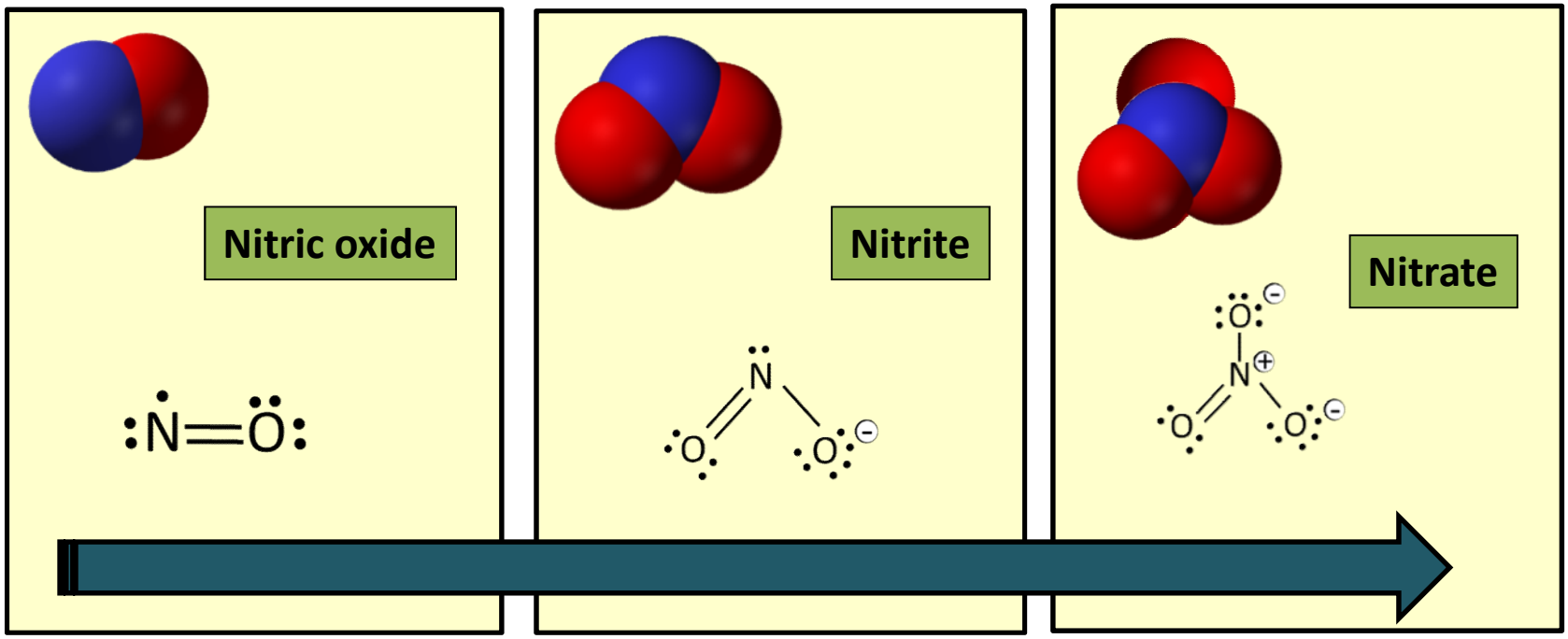

Weller *et al* JID 1998

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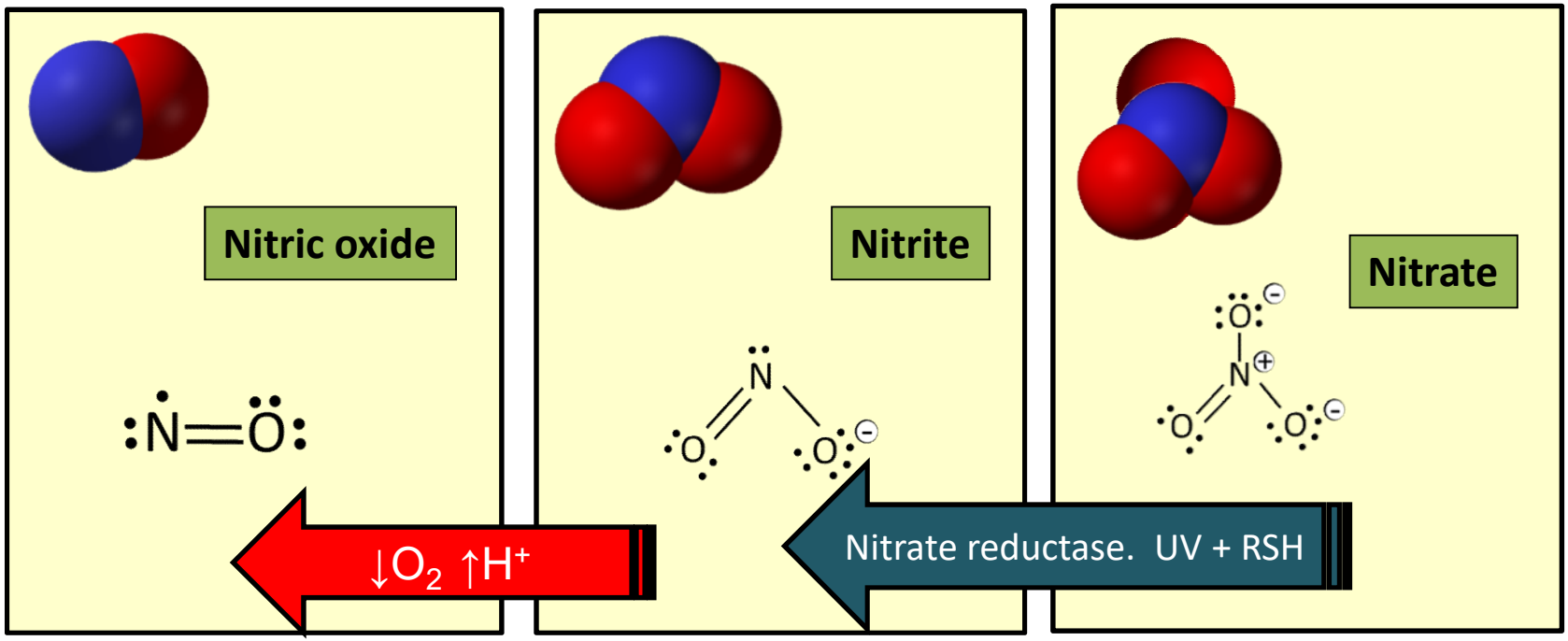
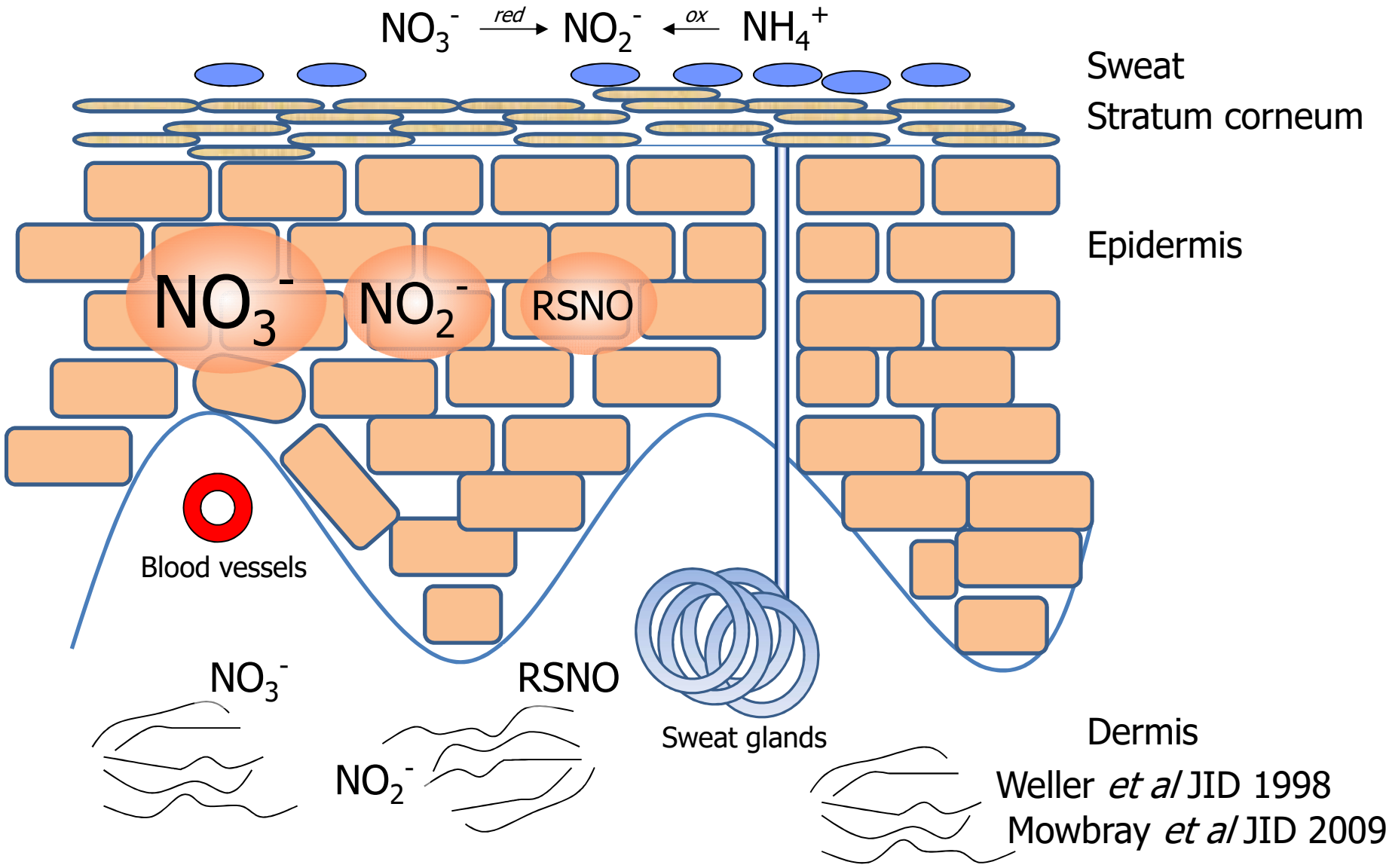


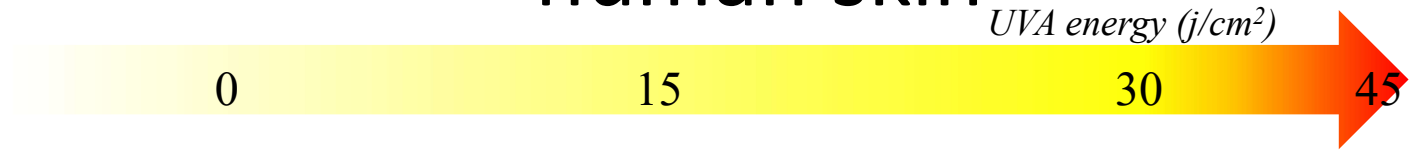
Weller *et al* JID 1998

The skin contains significant stores of bound NO species

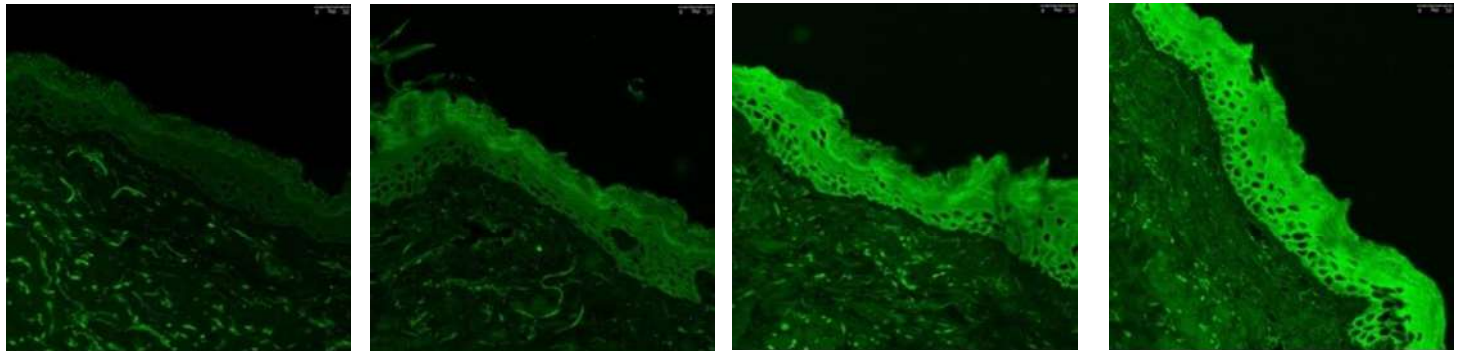


Weller *et al* JID 1998
Mowbray *et al* JID 2009

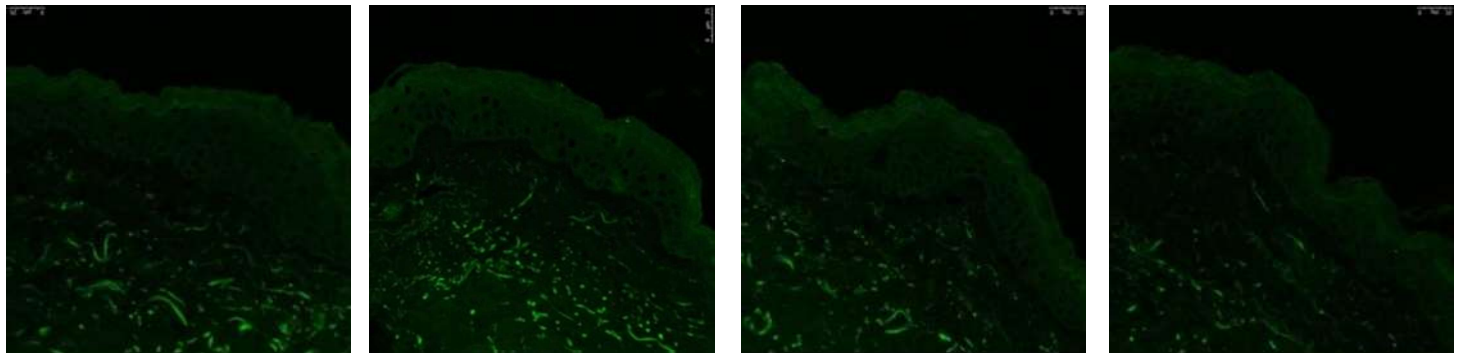
UVA dose dependently releases NO from human skin



Irradiated group

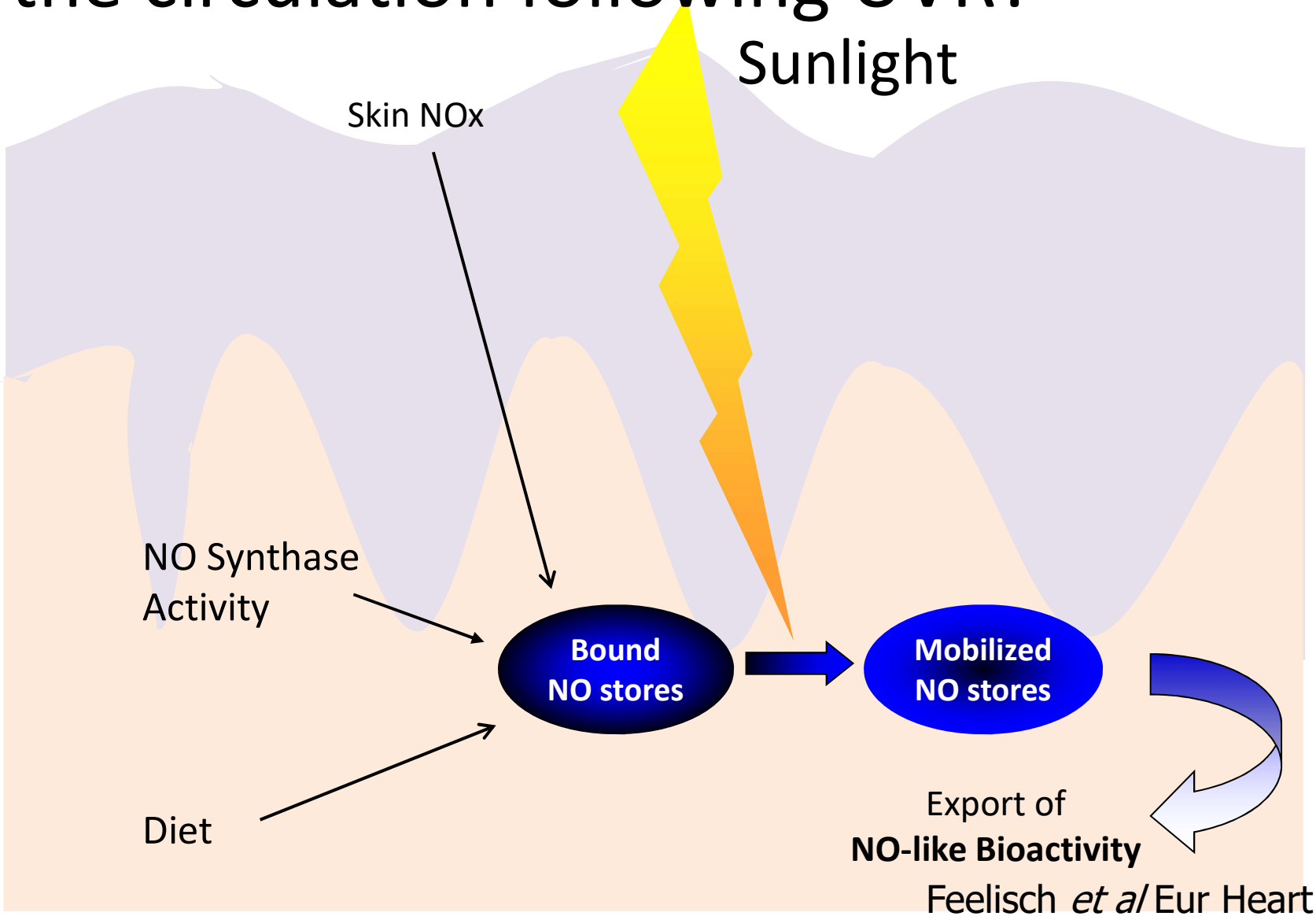


Sham-irradiated group



Liu *et al* JID 2014

Can cutaneous NO can be exported to the circulation following UVR?

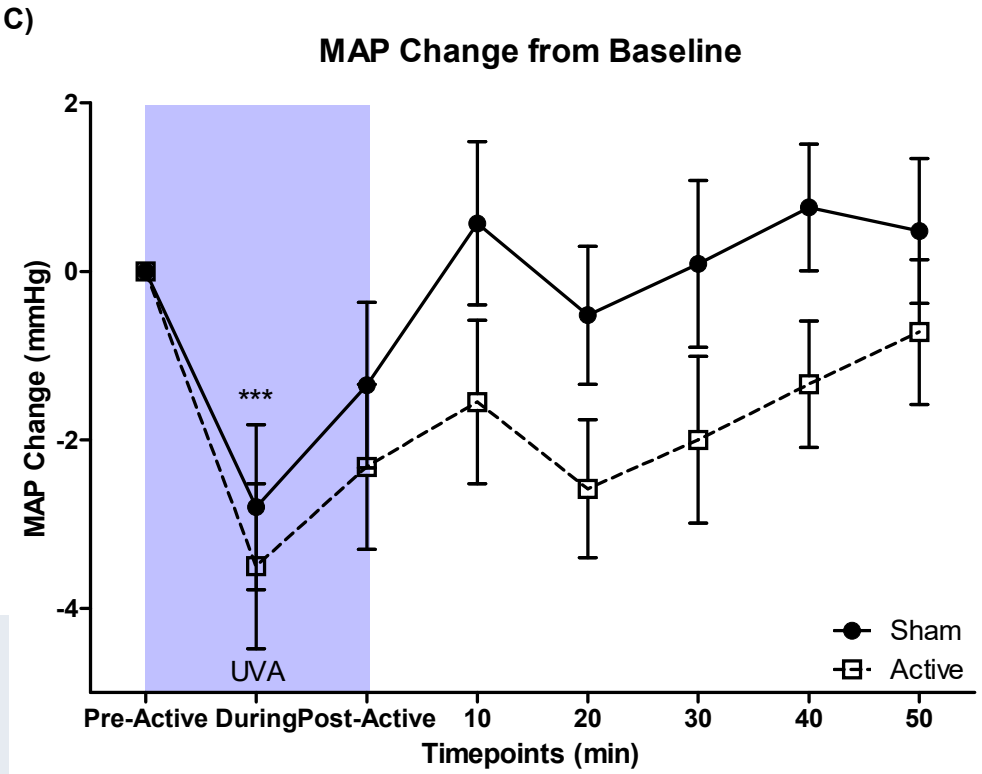


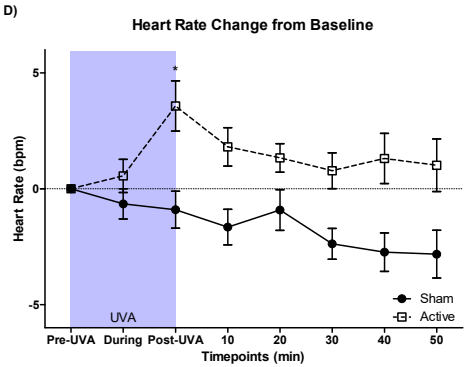
Feelisch *et al* Eur Heart J 2010

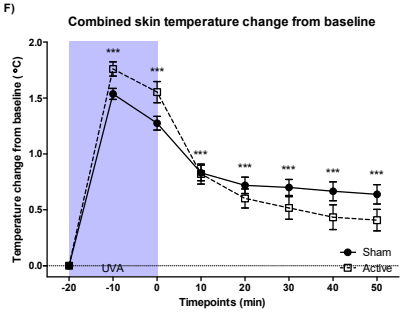
UVA lowers BP

20J/cm^2 UVA

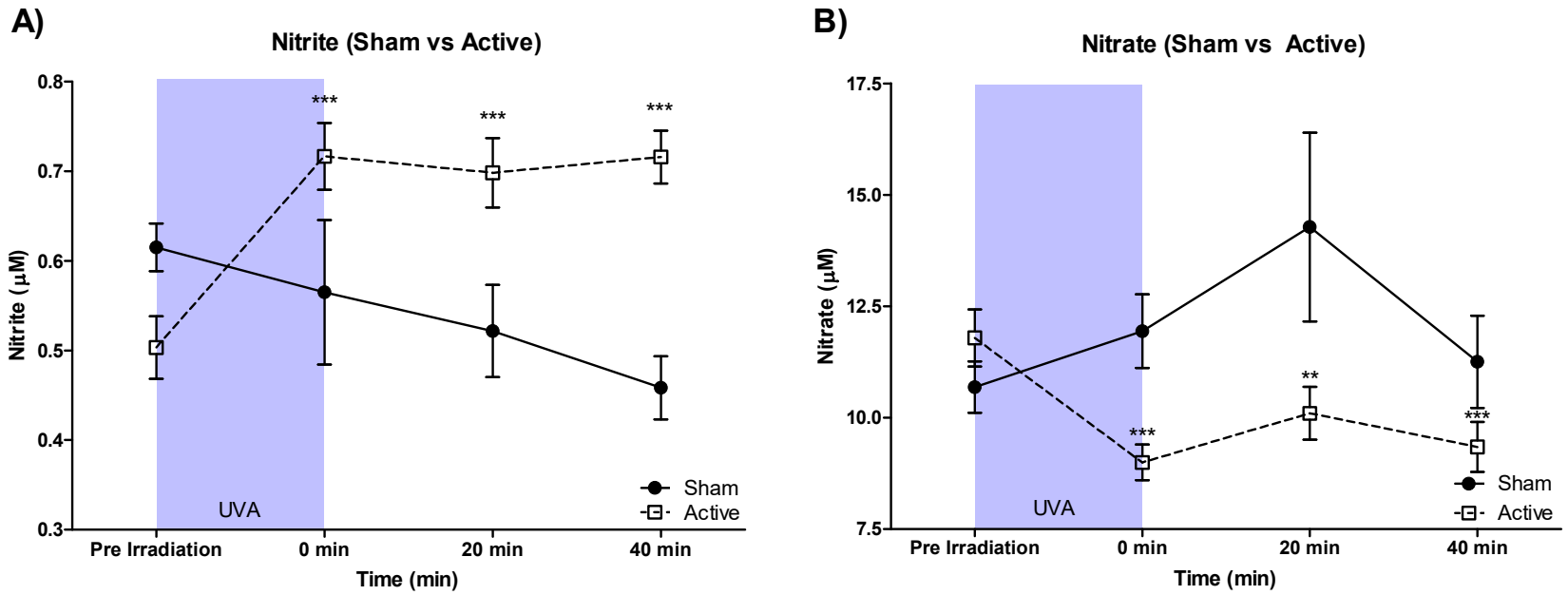
Liu *et al* JID 2014





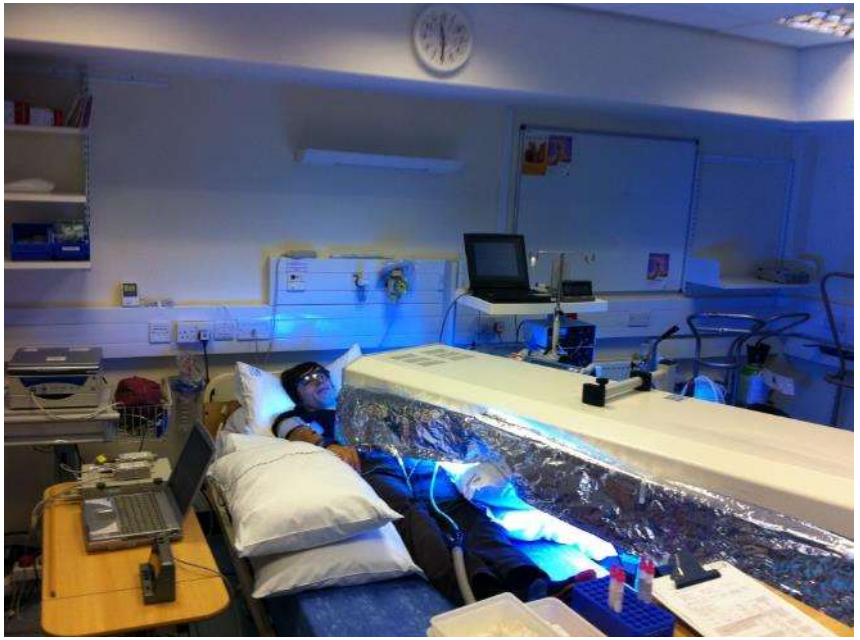


UVA lowers circulating NO_3 and increases NO_2



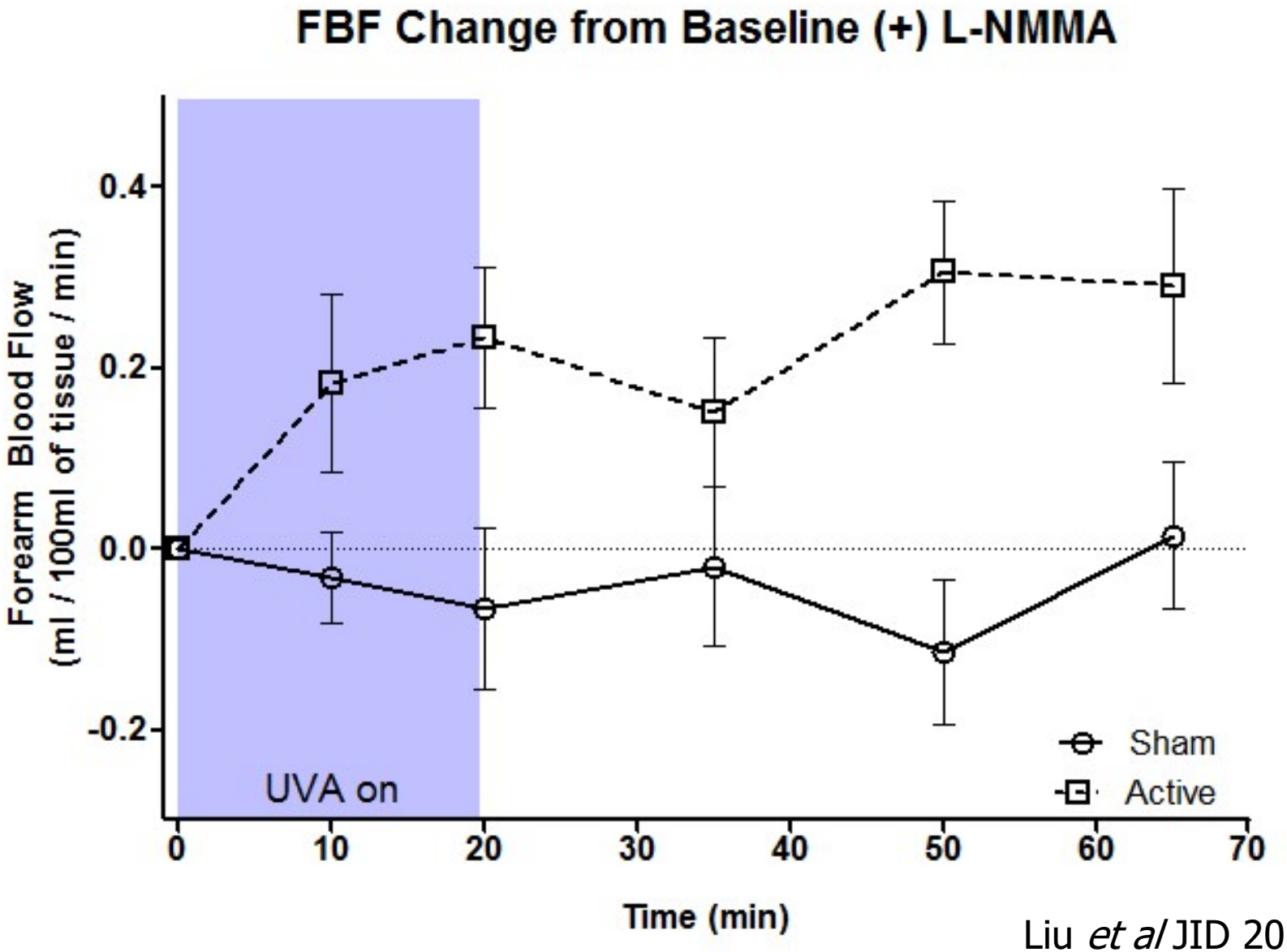
Liu *et al* JID 2014

Forearm Plethysmography

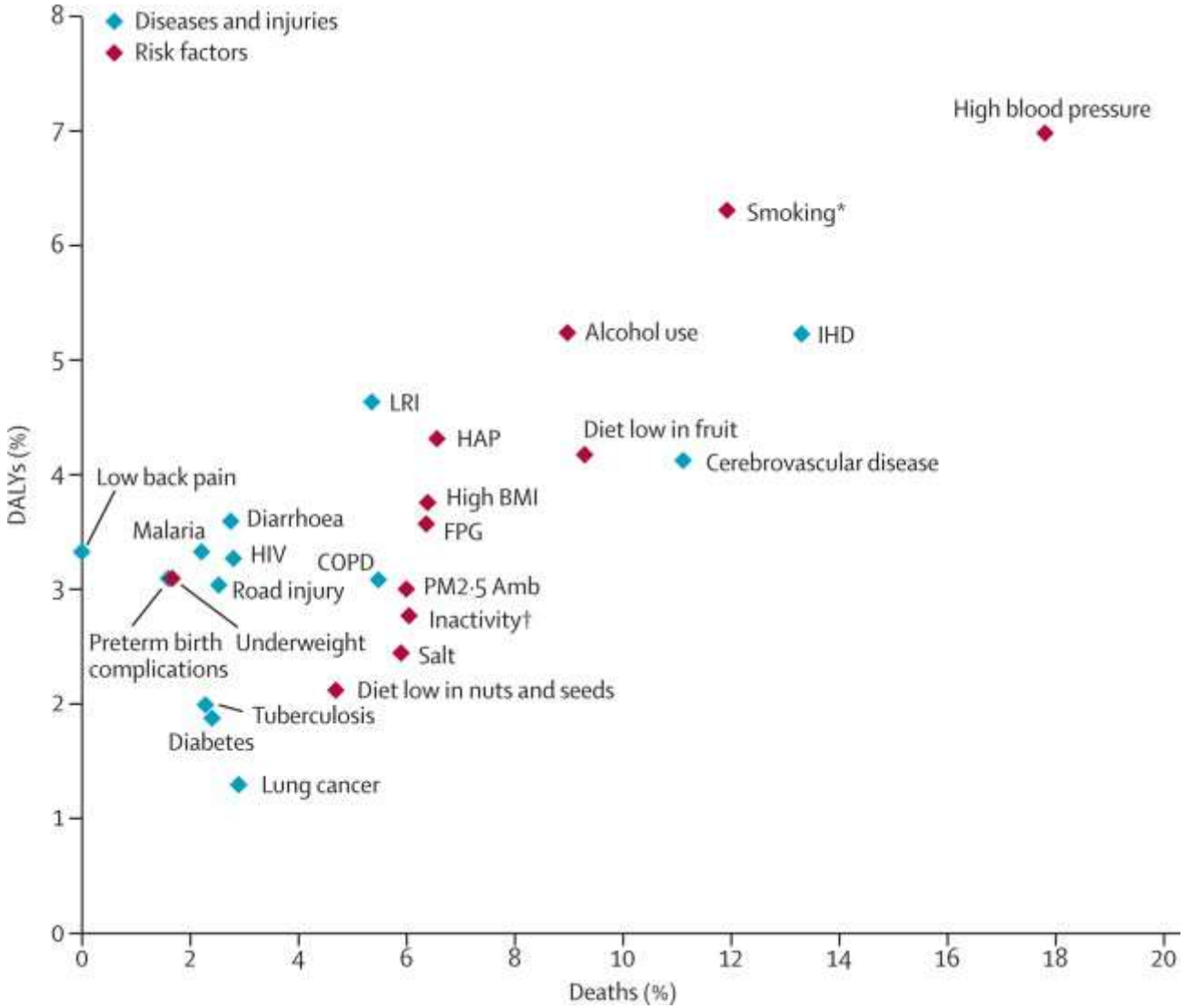


NOS antagonist (L-NMMA) infused to brachial artery
Arm irradiated (or sham)

UVA vasodilates arterial vasculature



Liu *et al* JID 2014



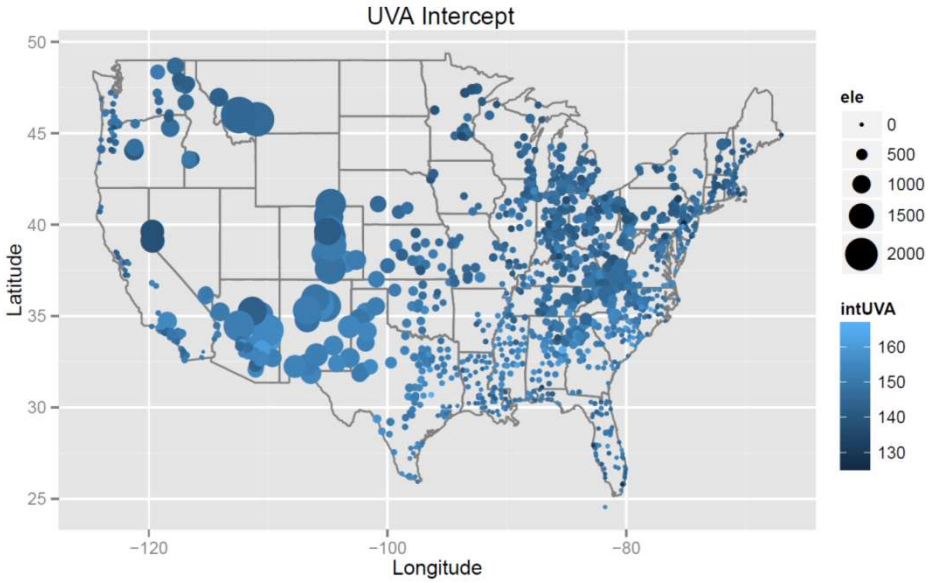
Christopher JL Murray , Majid Ezzati , Abraham D Flaxman , Stephen Lim , Rafael Lozano , Catherine Michaud , Mohse...

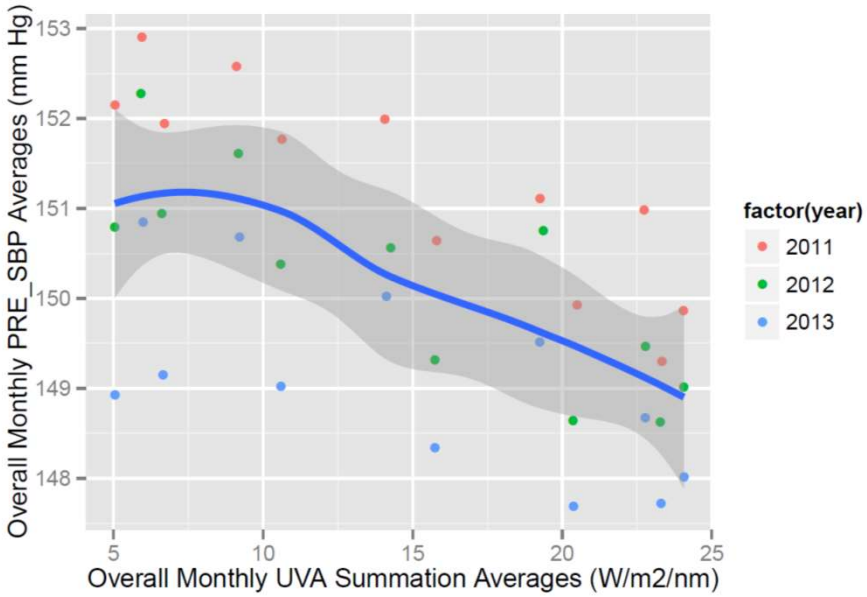
GBD 2010: design, definitions, and metrics

The Lancet Volume 380, Issue 9859 2012 2013 2063 - 2066

http://dx.doi.org/10.1016/S0140-6736(12)61899-6

UVA inversely correlates with pre-dialysis BP





355,831 patients
2178 dialysis units
Thrice weekly for 3 years

UVA Irradiation of Human Skin Vasodilates Arterial Vasculature and Lowers Blood Pressure Independently of Nitric Oxide Synthase

Donald Liu[1], Bernadette O. Fernandez[2], Alistair Hamilton[3], Ninian N. Lang[4], Julie M.C. Gallagher[5], David E. Newby[4], Martin Feelisch[2] and Richard B. Weller[1,3]

Journal of Investigative Dermatology advance online publication, 20 February 2014; doi:10.1038/jid.2014.27

American Diabetes Association. diabetes

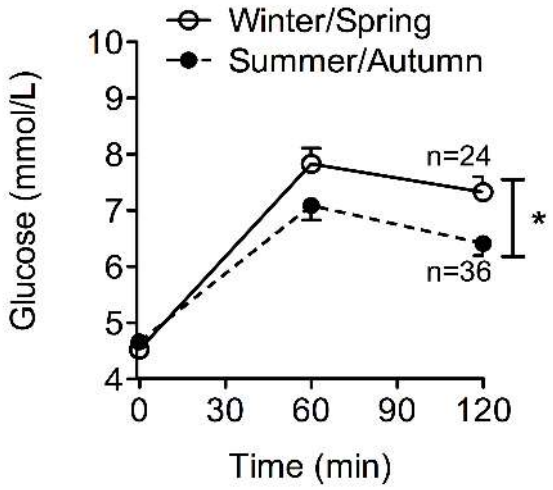
Diabetes Volume 63, ■■■ 2014

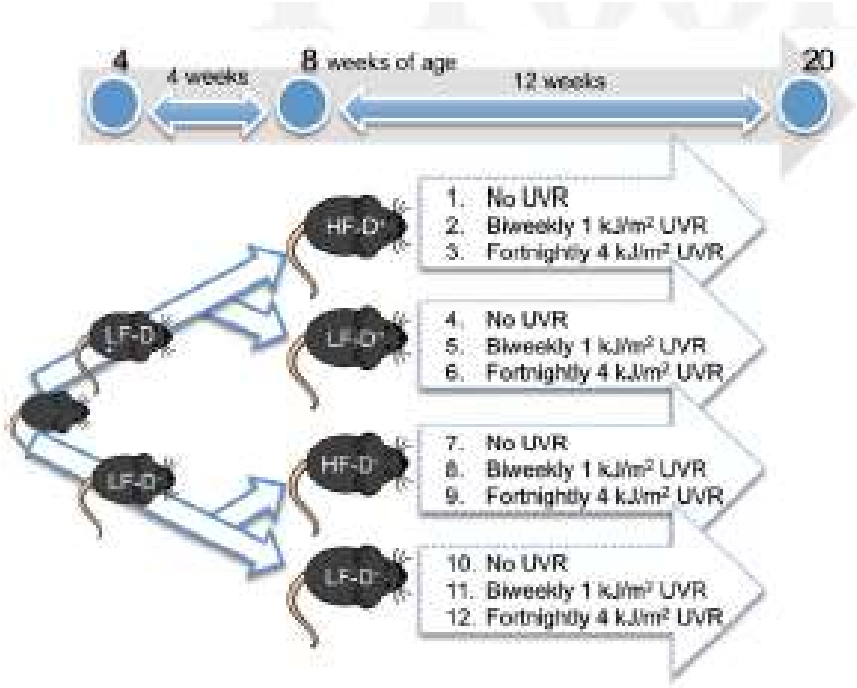
Sian Geldenhuys,[1] Prue H. Hart,[1] Raelene Endersby,[1] Peter Jacoby,[1] Martin Feelisch,[2] Richard B. Weller,[3] Vance Matthews,[4] and Shelley Gorman[1]

Ultraviolet Radiation Suppresses Obesity and Symptoms of Metabolic Syndrome Independently of Vitamin D in Mice Fed a High-Fat Diet

Diabetes 2014;63:1–11 | DOI: 10.2337/db13-1675

UV and metabolic syndrome

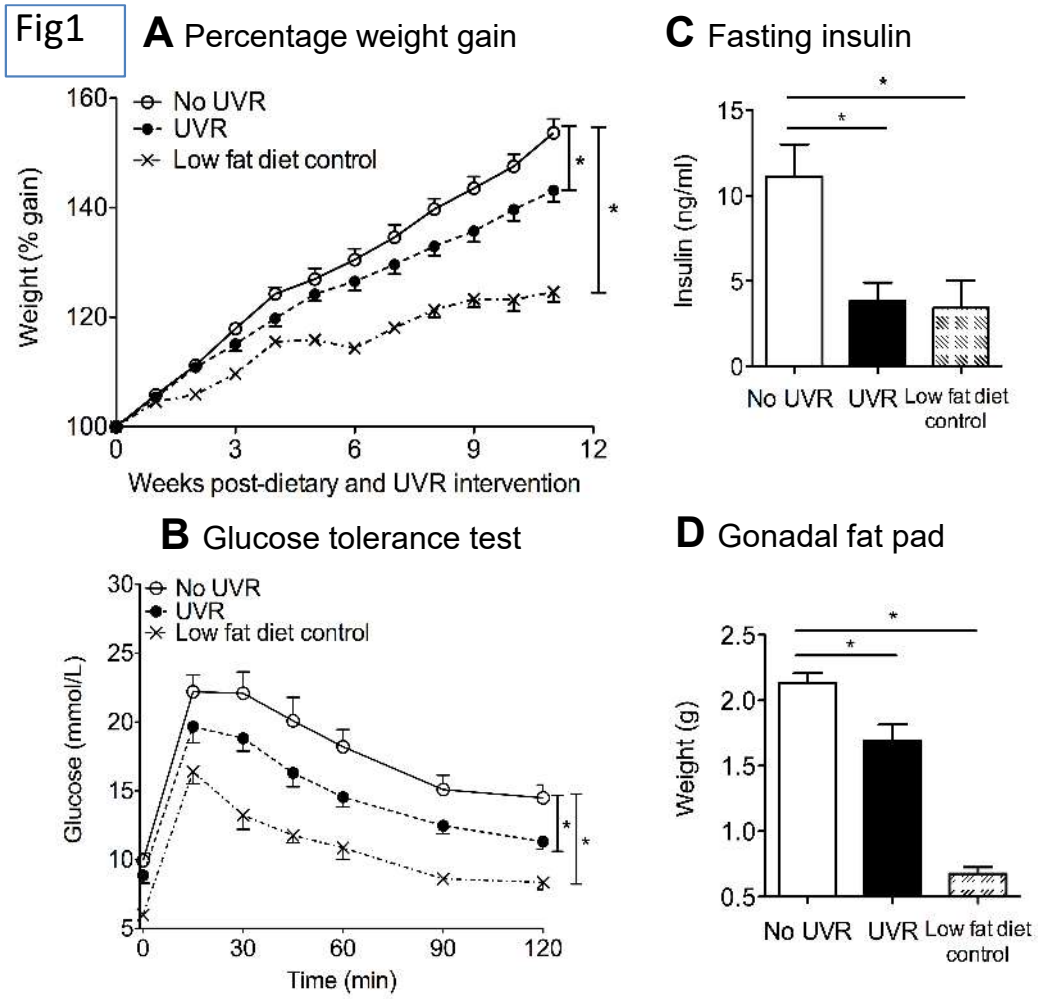




Shelley Gorman
Telethon Institute of Child Health
West Australia

Geldenhuys et al. Diabetes. 2014

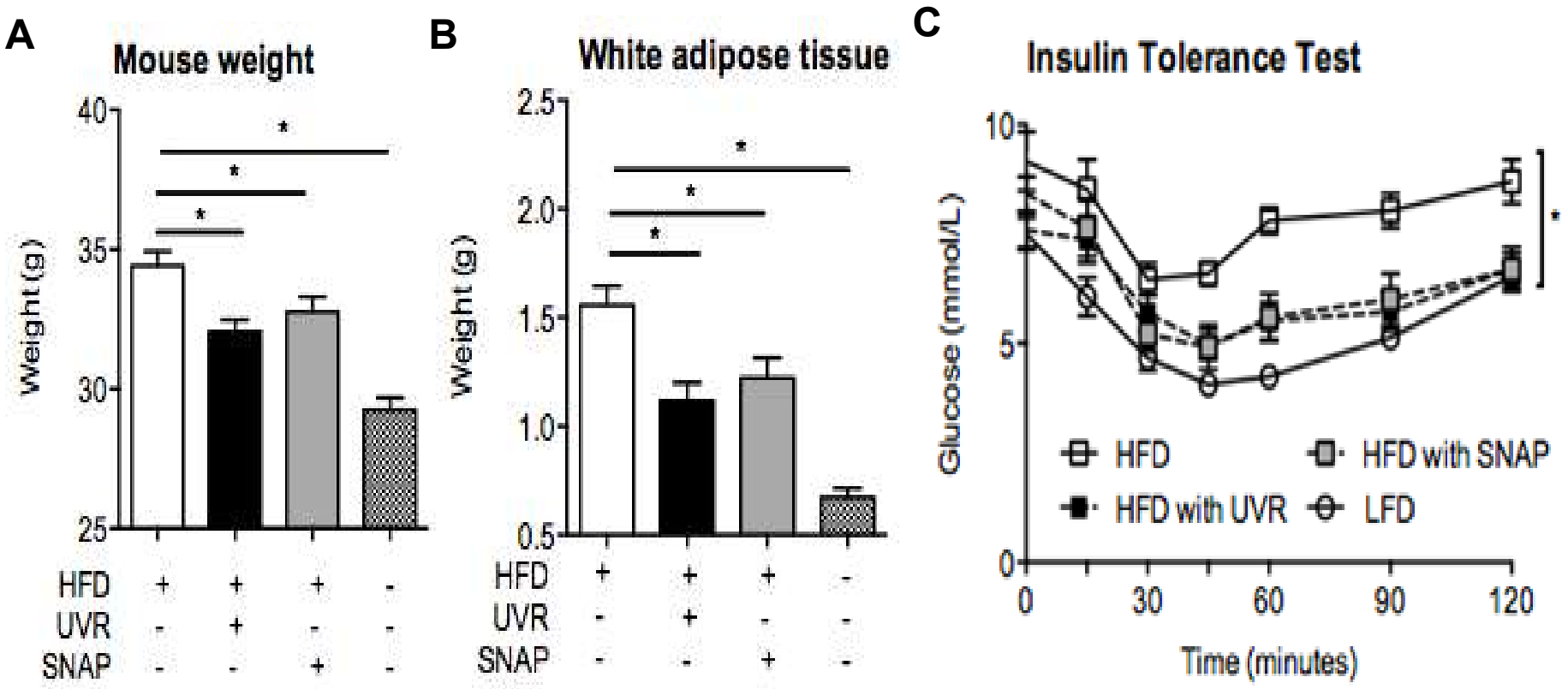
UV and metabolic syndrome



- UV (erythemal or sub-erythemal) reduces metabolic syndrome
- Vitamin D independent.

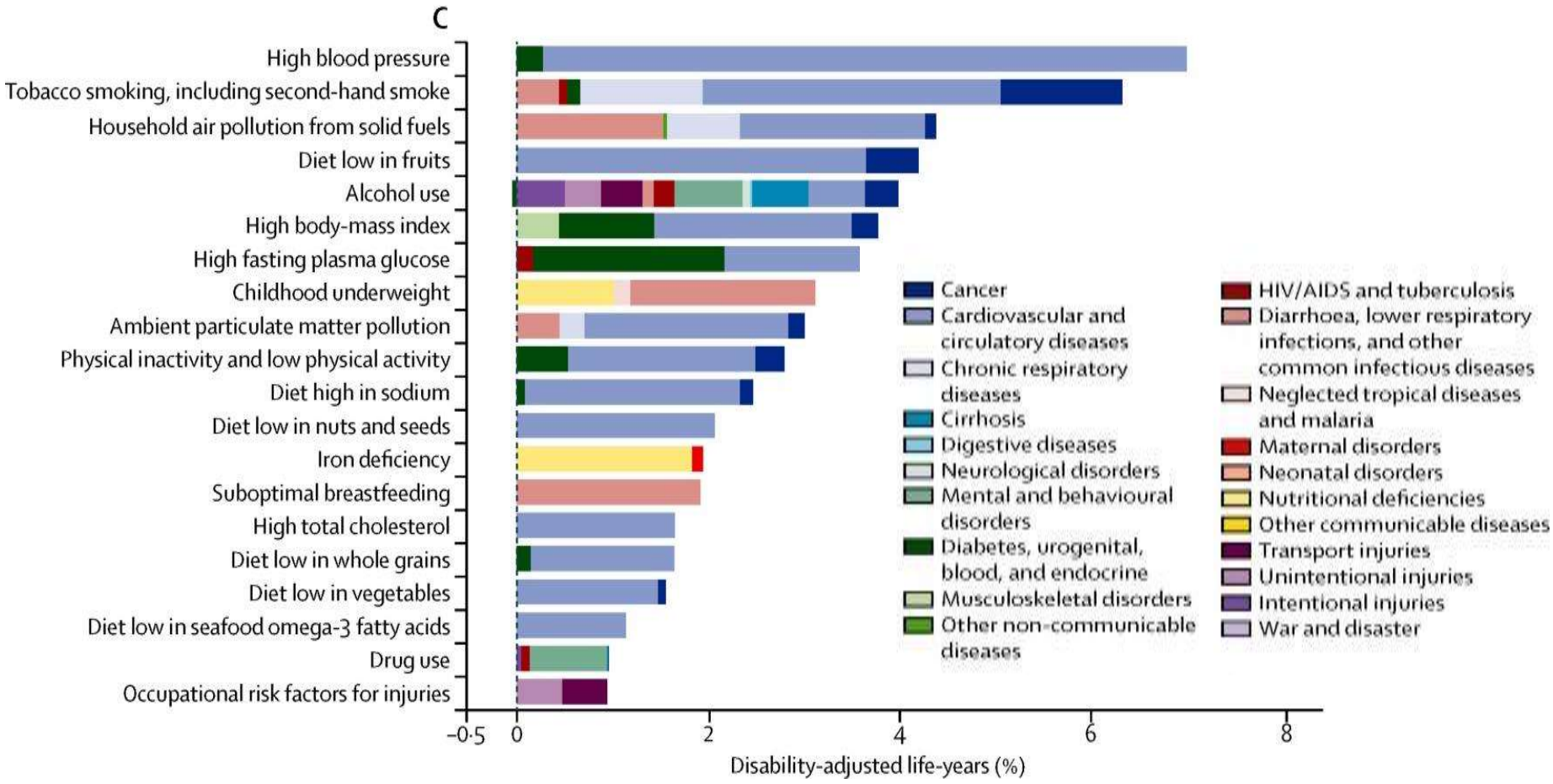
Geldenhuys et al. Diabetes. 2014

UVR or topical NO limit weight gain and ITT impairment



Geldenhuys et al. Diabetes. 2014

Global burden of disease
Top 20 risk factors in 2010



The Lancet **2013** 380, 2224 - 2260

…but what about skin cancer?

Skin cancer as a marker of sun exposure associates with myocardial infarction, hip fracture and death from any cause

Peter Brøndum-Jacobsen,[1,3] Børge G Nordestgaard,[1,3] Sune F Nielsen[1] and Marianne Benn[2,3]*

- Entire Danish population aged > 40
- 1990-2006.
- 4.4 million individuals
- Confounders
  - Occupation
  - Education
- Exposures
  - NMSC
  - MM
- Outcomes
  - MI
  - Hip fracture
  - Death

ol. 2013 Oct;42(5):1486-96

…but what about skin cancer?

Skin cancer as a marker of sun exposure associates with myocardial infarction, hip fracture and death from any cause

Peter Brøndum-Jacobsen,[1,3] Børge G Nordestgaard,[1,3] Sune F Nielsen[1] and Marianne Benn[2,3]*

Non-melanoma skin cancer.

OR all cause death.	0.96 (0.95-0.97)
OR MI	0.87 (0.85-0.9)

Original Article | Journal of INTERNAL MEDICINE

Click here to view the Editorial Comment by N. G. Jablonski

doi: 10.1111/joim.12251

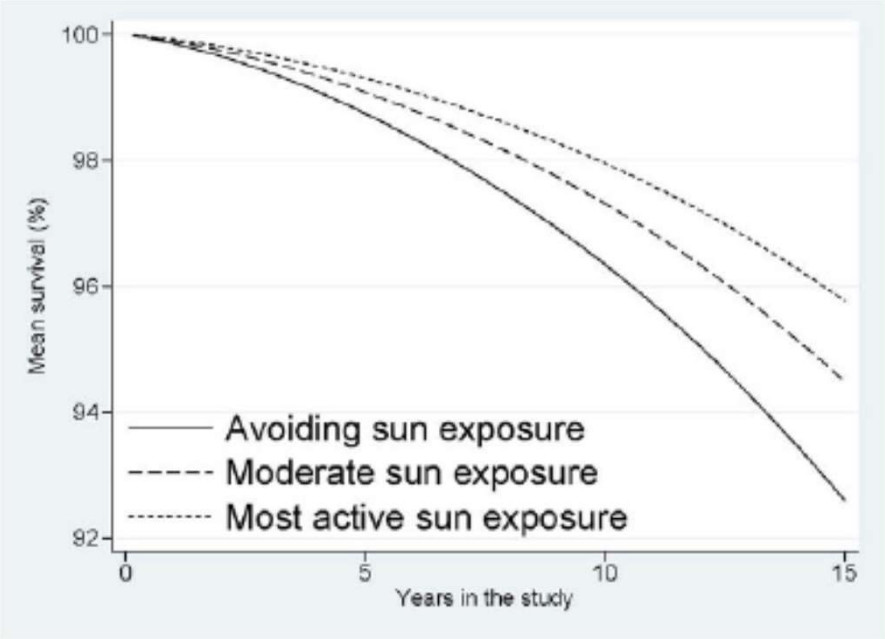
Avoidance of sun exposure is a risk factor for all-cause mortality: results from the Melanoma in Southern Sweden cohort

P. G. Lindqvist[1], E. Epstein[2], M. Landin-Olsson[3], C. Ingvar[4], K. Nielsen[5], M. Stenbeck[6] & H. Olsson[7]

- 30,000 Swedish Women
- 20 years follow up
- Sun habits
  - Sun bed use
  - Summer sunbathing
  - Winter sunbathing
  - Foreign hols
- Confounders
  - Marital status
  - Education
  - Income
  - Smoking
  - Alcohol
  - Pregnancies
  - Comorbidity
    - DM/Anticoag/CVS
  - BMI
  - Exercise

Sun exposure	Alive	Dead	HR	95%CI
0	1352	364	1	Ref
1	6229	771	0.8	0.7-0.9
2	8384	782	0.71	0.6-0.8
3	8081	508	0.61	0.5-0.7
4	2927	115	0.53	0.4-0.7

	Women alive	Women dead	Model 1 HR	95% CI
Use of sunbeds?*				
No	11,117	1,825	1.0	ref
Yes	12,856	720	0.77	0.7–0.8



Lindqvist et al. J Internal Med. 2014
Lindqvist et al. J Internal Med. 2016

VOLUME 29 · NUMBER 3 · JANUARY 20 2011

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Reduced Melanoma After Regular Sunscreen Use: Randomized Trial Follow-Up

Adèle C. Green, Gail M. Williams, Valerie Logan, and Geoffrey M. Strutton

See accompanying editorial on page 249

INTRODUCTION

The need for more effective prevention of melanoma is recognized around the world as climbing incidence and high mortality in white populations persist.[1-3] In the United States, approximately 68,700 new melanoma occurrences and more than 8,600 deaths were expected to occur in 2009.[4] Exposure to solar ultraviolet (UV) radiation is the only established modifiable cause of melanoma.[5,6]

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See accompanying editorial on page 249

Results

Ten years after trial cessation, 11 new primary melanomas had been identified in the daily sunscreen group, and 22 had been identified in the discretionary group, which represented a reduction of the observed rate in those randomly assigned to daily sunscreen use (hazard ratio [HR], 0.50; 95% CI, 0.24 to 1.02; $P = .051$). The reduction in invasive melanomas was substantial (n = 3 in active *v* 11 in control group; HR, 0.27; 95% CI, 0.08 to 0.97) compared with that for preinvasive melanomas (HR, 0.73; 95% CI, 0.29 to 1.81).

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…**an ambitious and unique study**: it was conducted in a region with the highest rate of skin cancer in the world, had a follow-up period of 10 years after the trial, and achieved relatively high rates of compliance among the participants assigned to the group using sunscreen.[4]

Gimotty and Glanz JCO 2010.

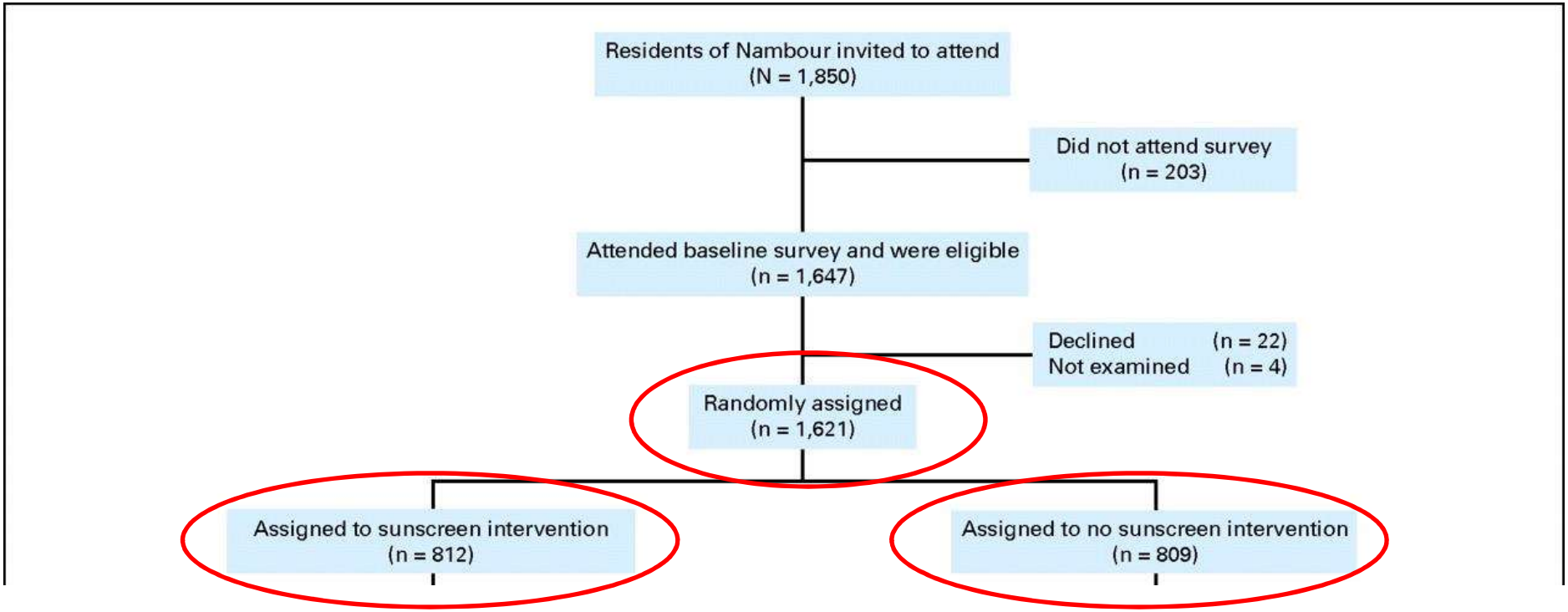
……this **carefully executed** and **ambitious** study is **commendable**……

Hensin Tsao. NEJM Journal Watch 2011

unprecedented and is **not likely to be replicated** given the magnitude of the study, the long-term follow-up, and the high rate of compliance of participants.

Bigby and Kim. Arch Derm. 2011

Nambour Skin Cancer Prevention Trial follow-up profile.



Green A C et al. JCO 2011;29:257-263

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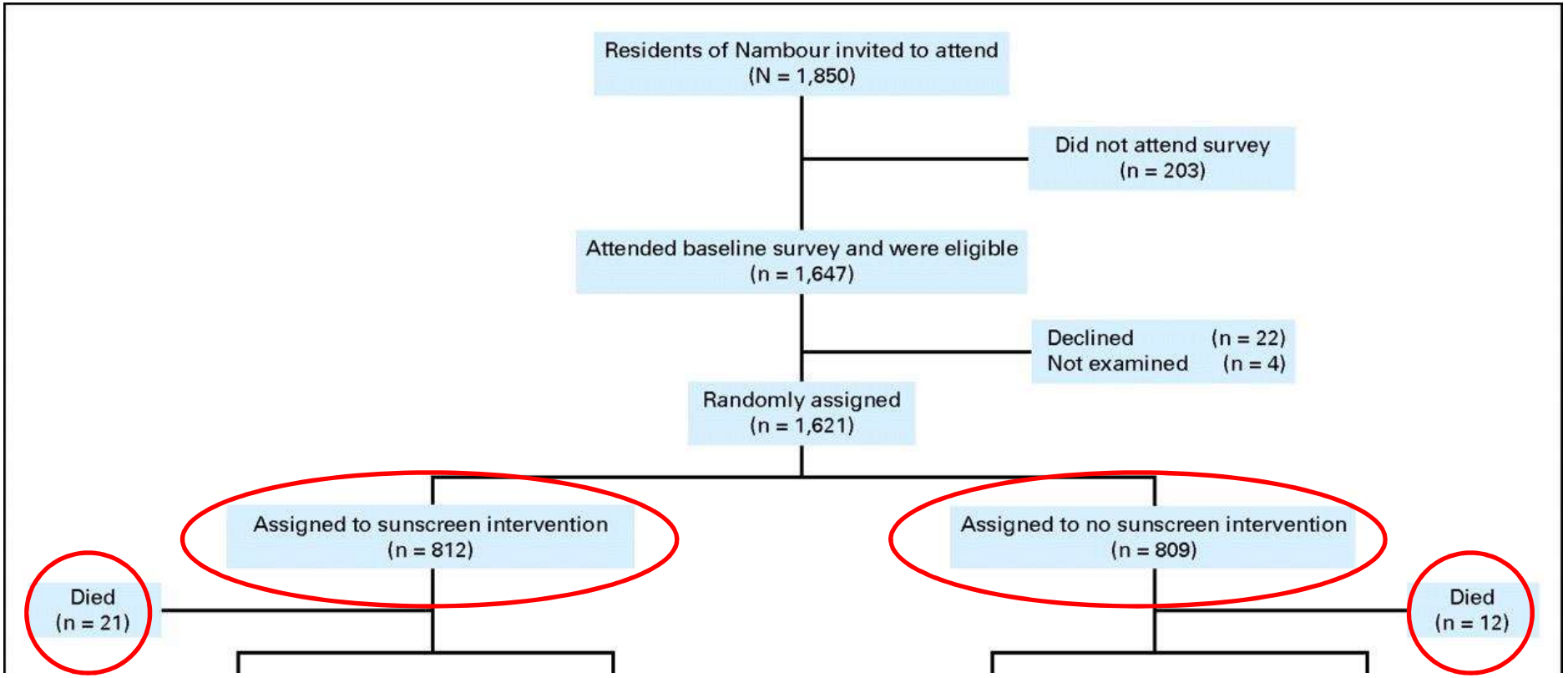

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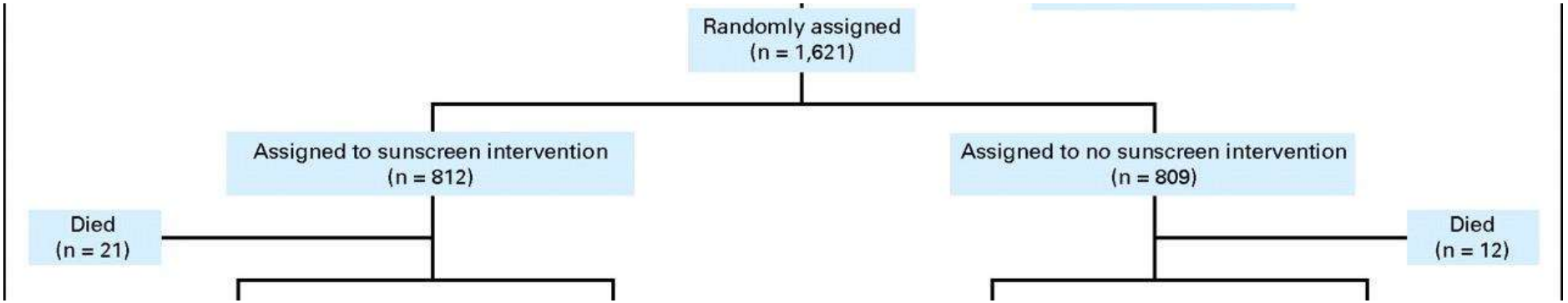
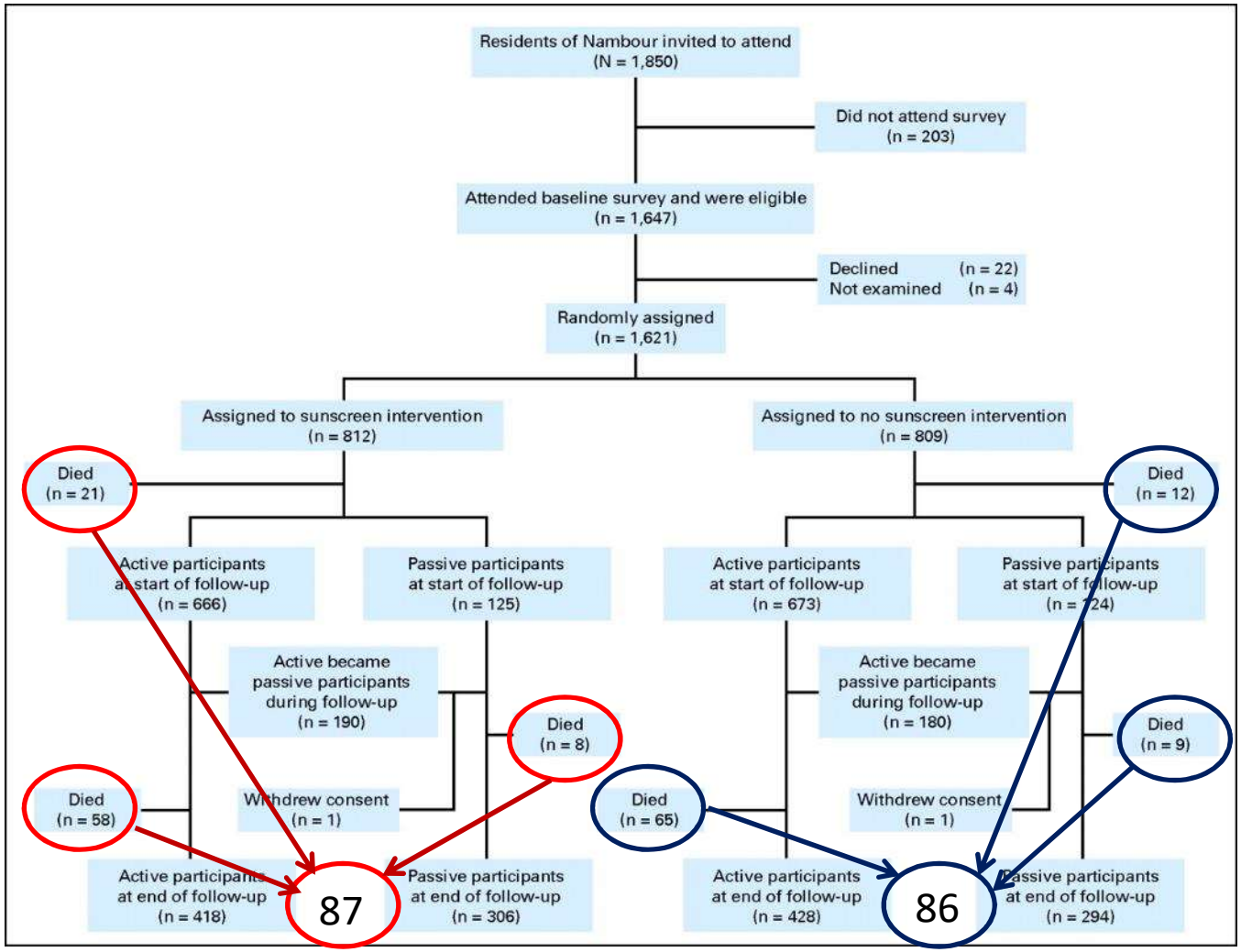


	Sunblock	Control	
Dead	21	12	
Alive	791	797	p=.116

Green A C et al. JCO 2011;29:257-263

Nambour Skin Cancer Prevention Trial follow-up profile.



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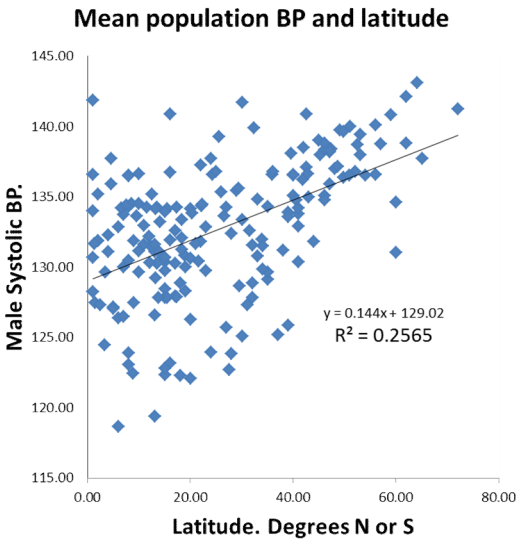
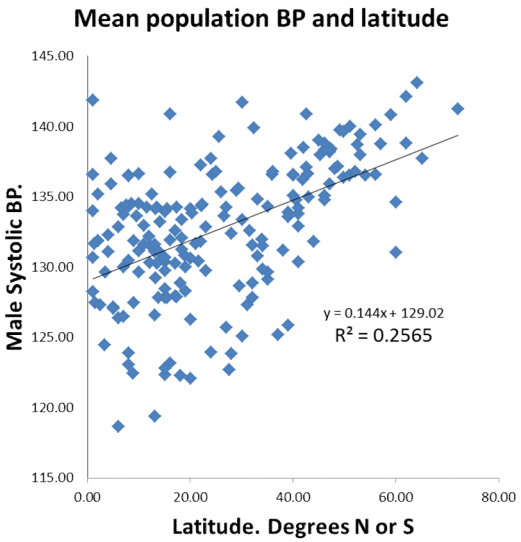
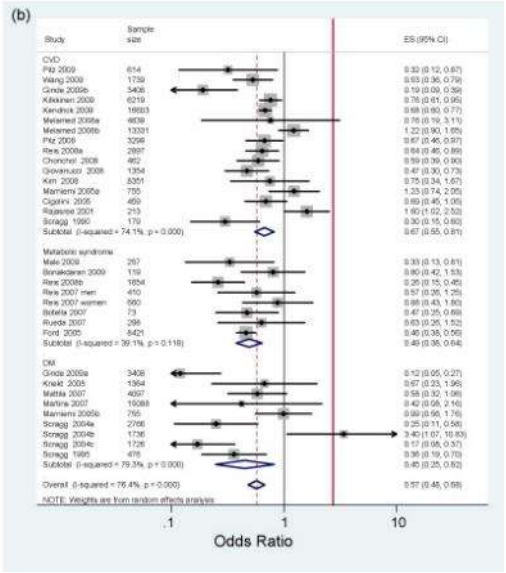
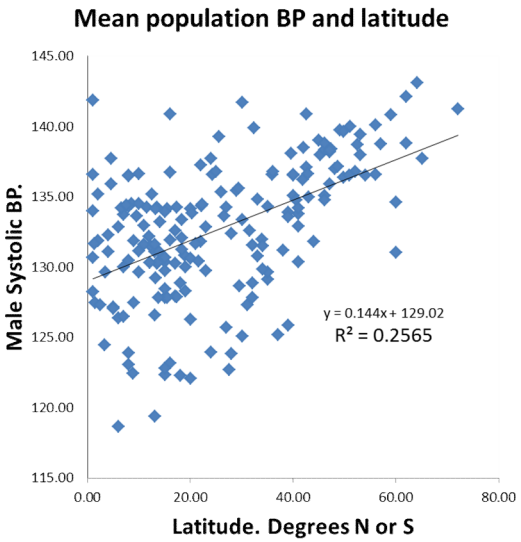
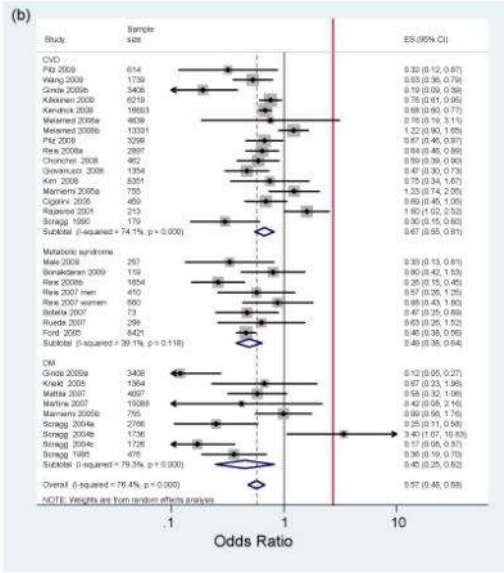

Mean population BP and latitude
Male Systolic BP.
145.00
140.00
135.00
130.00
125.00
120.00
115.00
0.00
20.00
40.00
60.00
80.00
Latitude. Degrees N or S
y = 0.144x + 129.02
R² = 0.2565



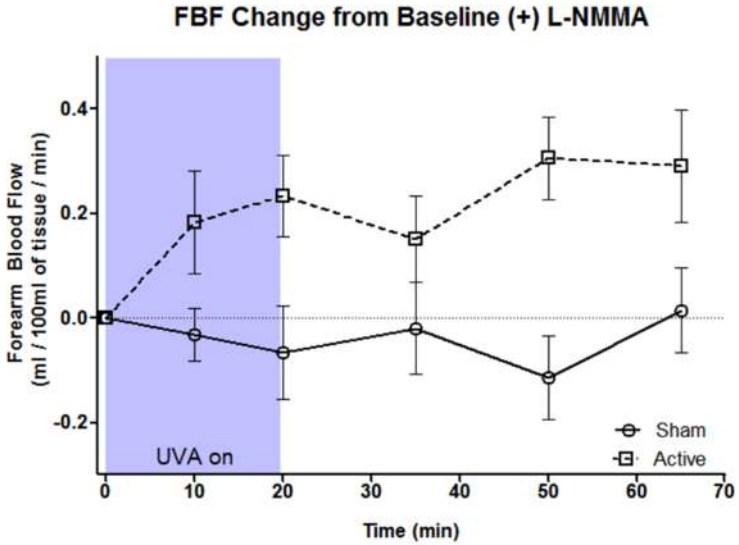


Pittas et al. *Ann Intern Med*. 2010

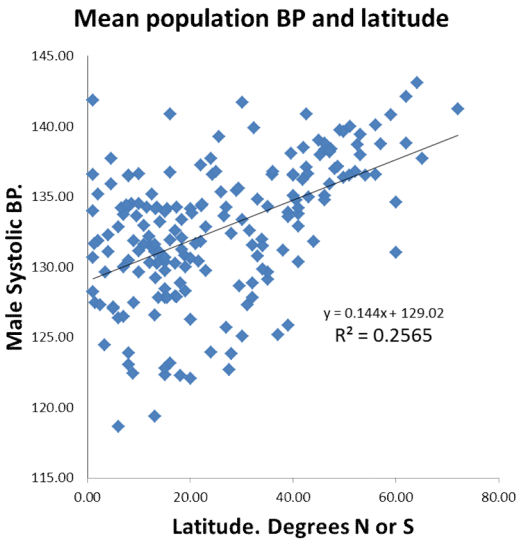


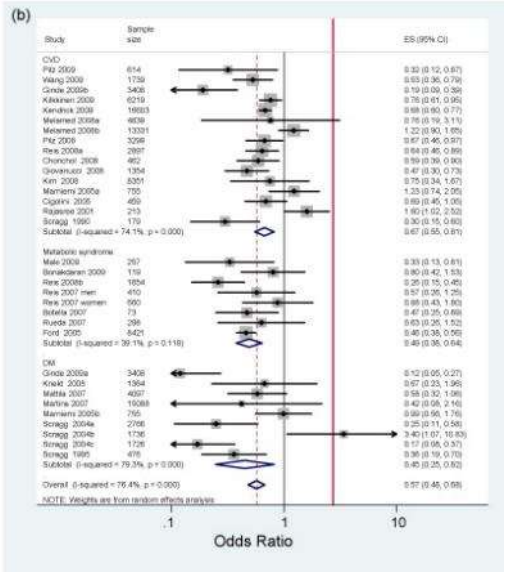


Pittas et al. *Ann Intern Med*. 2010



Liu et al. JID. 2014





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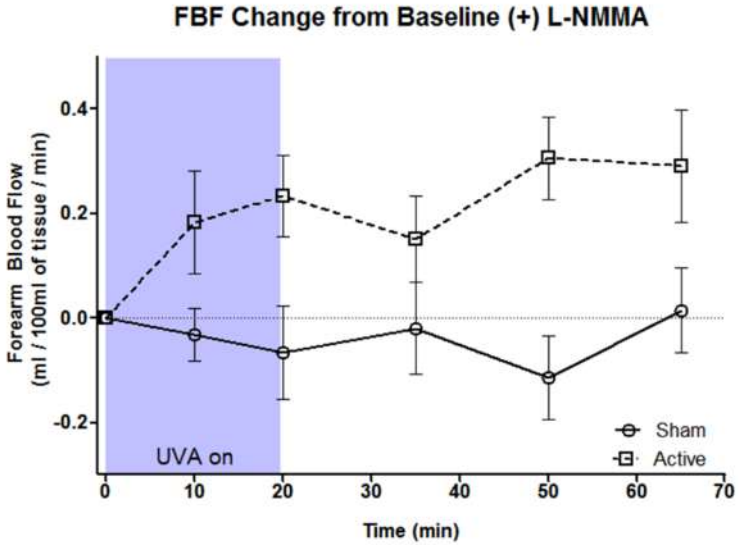

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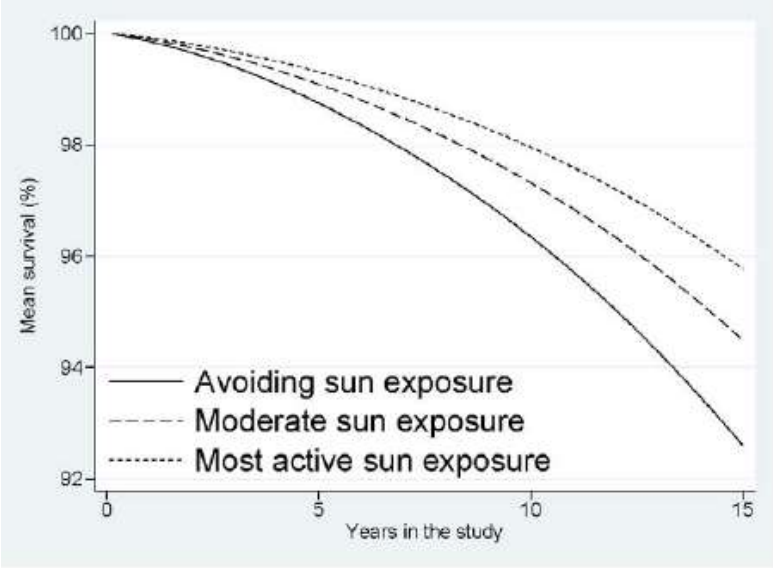

Lindqvist et al. J Int Med 2014

The Edinburgh message

"….when you have eliminated the impossible, whatever remains, *however improbable*, must be the truth."

(Sherlock Holmes: The Sign of Four)

The Edinburgh message

- Sunlight has health benefits.
- Vitamin D only accounts for some of these.
- ‘All cause mortality’ trumps skin cancer

Thanks-Funds

Collaborators
University of Warwick
Martin Feelisch
University of Edinburgh
David Newby
Telethon Child Health Institute
Shelley Gorman

Research Fellows
Donald Liu
Sharnika Abeyakirthi
Megan Mowbray
Julie Gallagher
Ninian Lang
Alistair Hamilton

Funding

medical research scotland
FUNDING A HEALTHIER FUTURE

Chest Heart & Stroke Scotland

50 years of COMMONWEALTH SCHOLARSHIPS

BRITISH SKIN FOUNDATION
The charity for skin disease research

Foundation for Skin Research

…..and most of all - my subjects!