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Molecular studies of sunscreen in humans

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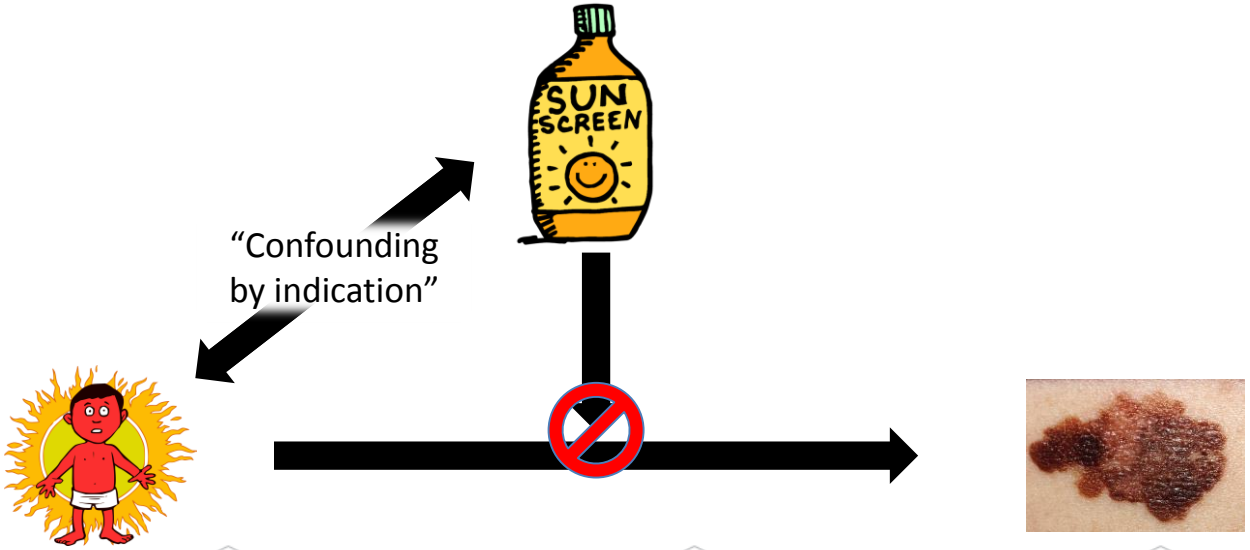
Overview

1. Sunscreen & skin cancer: epidemiologic challenges
2. DNA damage in skin cancer
3. An experiment
4. Systematic review
5. Summary and conclusions

Sunscreen for skin cancer prevention?

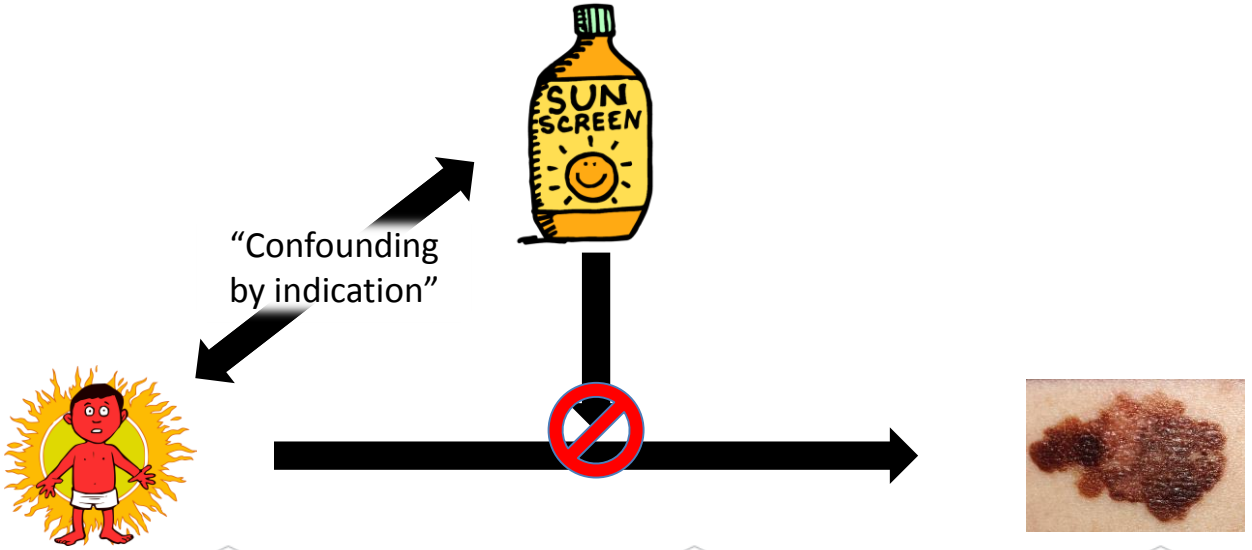
Epidemiologic data

- Observational studies → intractable confounding



Sunscreen for skin cancer prevention?

Epidemiologic data
- Randomized trials → only one



Sunscreen for melanoma prevention?

First author (publication year)	Location	Study design	Cases/controls (Cohort size)	Exposure assessment
Green et al. 2011	Australia	RCT	33/1621	Assigned
Cho et al. 2005*	USA	Cohort	535/178,155 (F:152,949; M:25,206)	Self-report
Lazovich et al. 2011	USA	Case-control	1167/1101	Self-report
Youl et al. 2002*	Australia	Case-control	201/205	Self-report
Westerdahl et al. 2000	Sweden	Case-control	571/913	Self-report
Whiteman et al. 1997*	Australia	Case-control	52/156	Self-report
Autier et al. 1995*	Germany, Belgium, France	Case-control	418/438	Self-report
Westerdahl et al. 1995	Sweden	Case-control	400/640	Self-report
Holly et al. 1995	USA	Case-control	452/930	Self-report
Herzfeld et al. 1993*	USA	Case-control	324/415	Self-report
Beitner et al. 1990*	Sweden	Case-control	523/505	Self-report
Osterlind et al. 1988	Denmark	Case-control	474/926	Self-report
Holman et al. 1986*	Australia	Case-control	507/507	Self-report

Sunscreen for melanoma prevention?

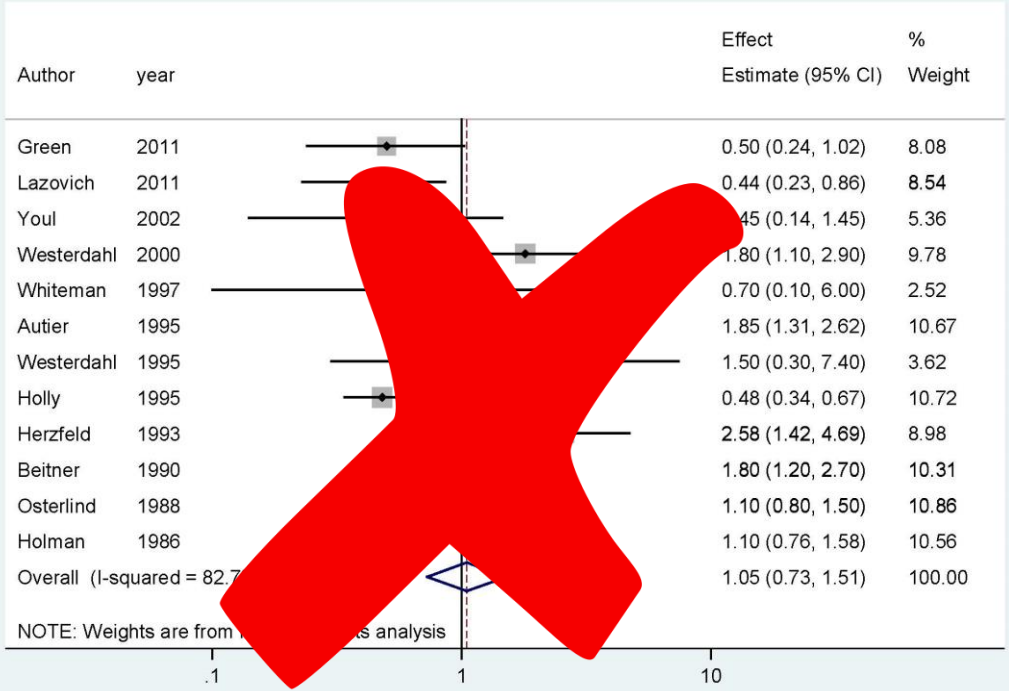
RCT →

Source: Olsen et al. *submitted* (2017)

Sunscreen for melanoma prevention?

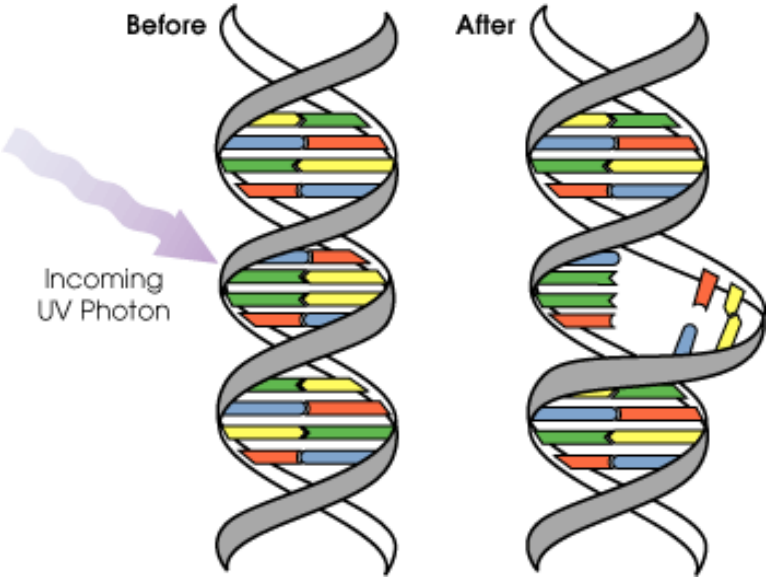
RCT →

Observational



Source: Olsen et al. *unpublished*

UV damage in skin cells



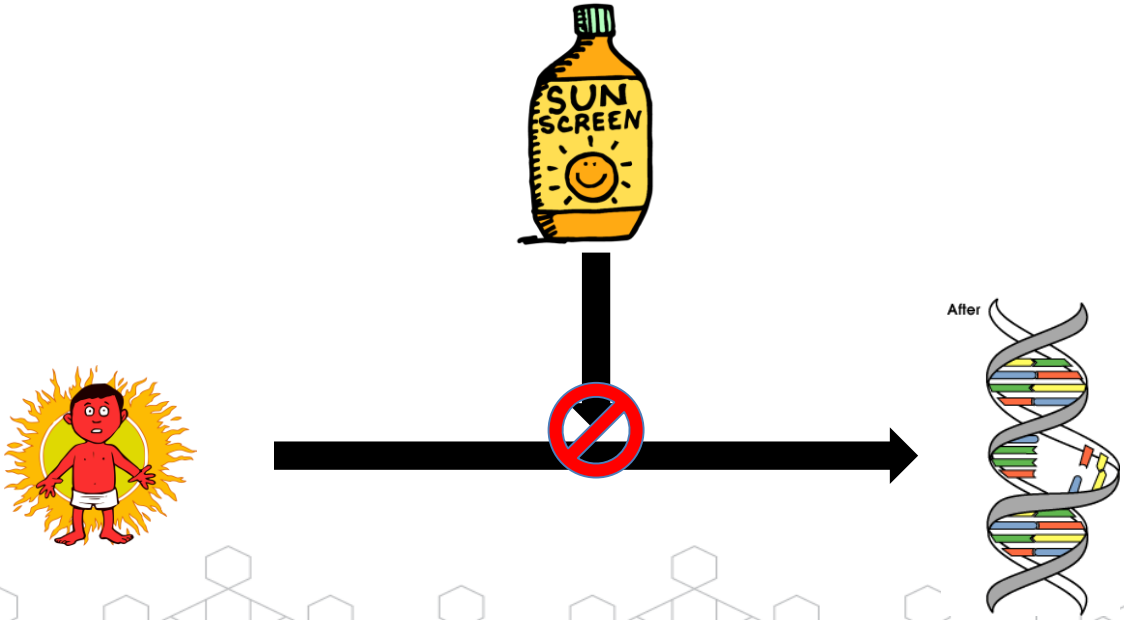
Cyclobutane pyrimidine dimers (CPD = TT, CT, TC)

Pyrimidine (6-4) pyrimidone photoproducts (6-4TT)

If photolesions not repaired…
→ fixed mutation in daughter cells

Biomarkers as an intermediate endpoint

Experimental data
- Biomarker / mutation studies



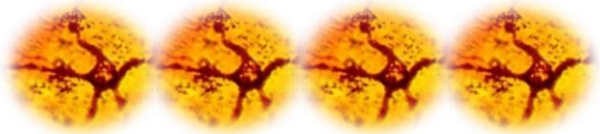
Effect of sunscreen on molecular & cellular markers

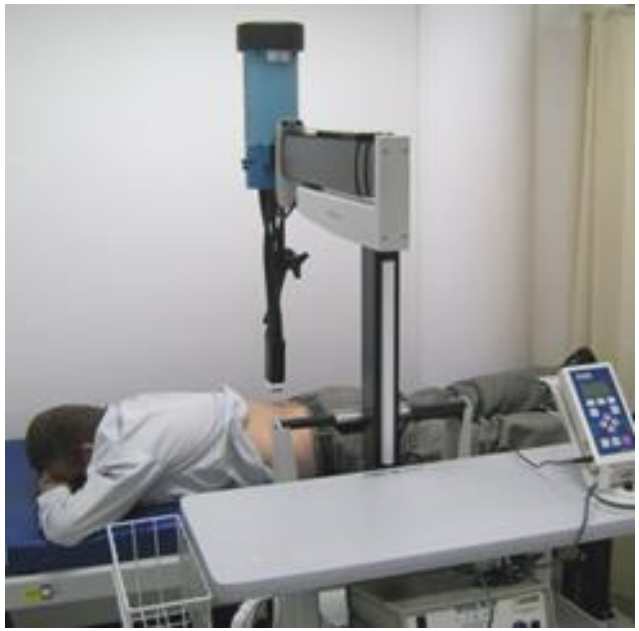
Pigment Cell Melanoma Res. **26**; 835–844

ORIGINAL ARTICLE

The effect of *MC1R* variants and sunscreen on the response of human melanocytes in vivo to ultraviolet radiation and implications for melanoma

Elke Hacker[1,2], Zachary Boyce[1], Michael G. Kimlin[1], Leesa Wockner[3], Thomas Pollak[2], Sam A. Vaartjes[1,2], Nicholas K. Hayward[2] and David C. Whiteman[1,2]

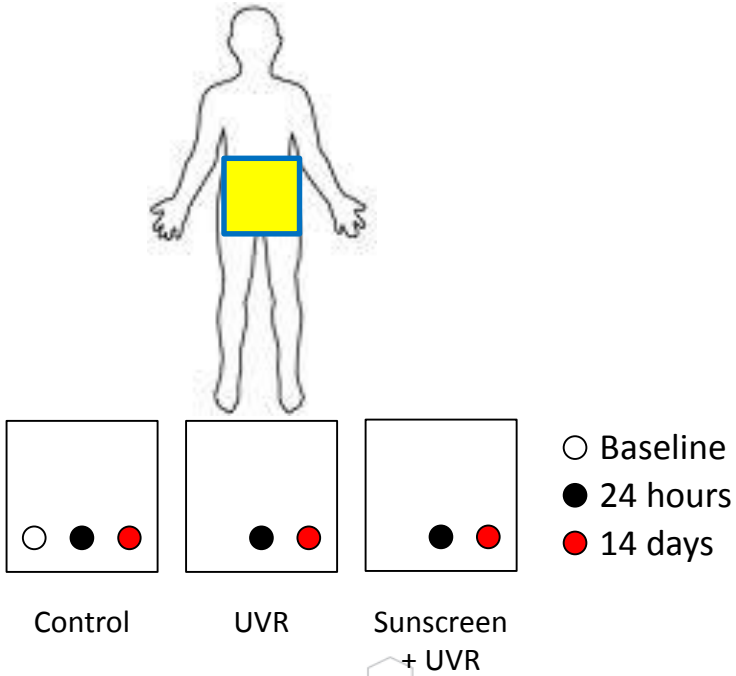




Objectives

1. Assess *DNA damage* in human skin *in vivo* before and after UVR exposure (2 MED)
2. Assess *melanocyte proliferation* in human skin *in vivo* before and after UVR exposure (2 MED)
3. Determine whether biomarkers affected by *sunscreen*

Design of study



SCREEN for eligibility / pigmentation

Baseline biopsy control skin **(Day 1)**
UV exposure - 2 MED at 2 sites

3 biopsies at 24 hr **(Day 2)**
-Control, UV, **UV + sunscreen**

3 biopsies at 14 days **(Day 14)**
-Control, UV, **UV + sunscreen**

Participants

57 healthy Caucasian volunteers

Mean age 25 years (range 18-34 yrs).

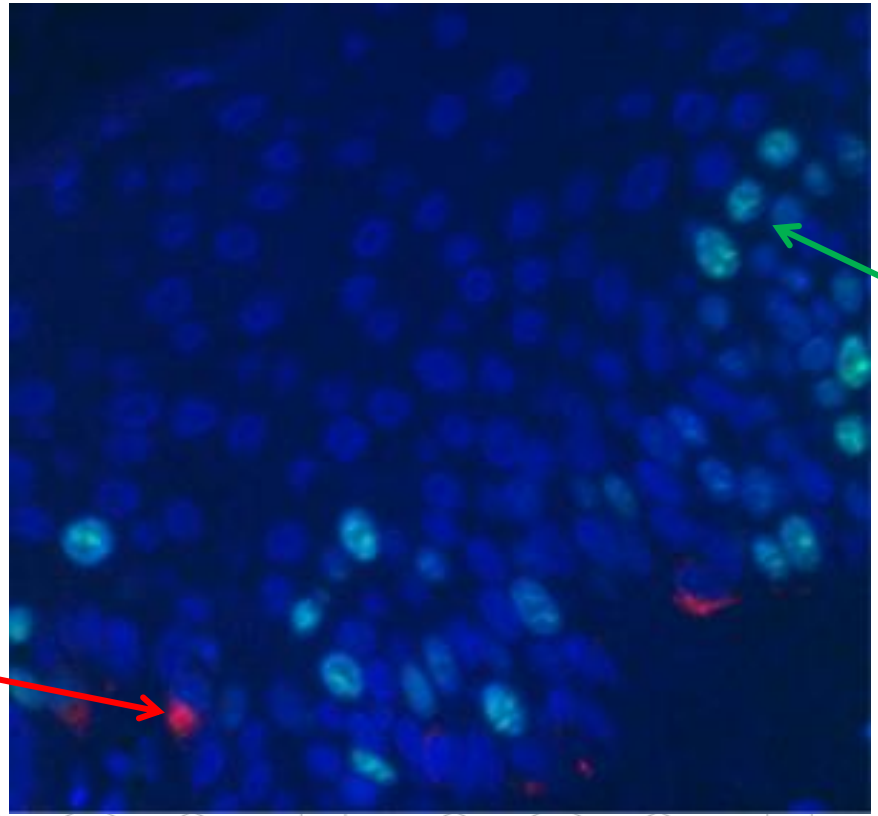
Fitzpatrick skin type

9% skin type 1
54% skin type 2
37% skin type 3

Biomarkers measured

Biomarker	Biological interpretation
Erythema	Acute inflammation
CPD	UV-specific damage to DNA sequence
ki67	Marker of cell proliferation
p53	**Over**expression indicates DNA damage
Melanocyte counts	Melanocyte proliferation

Dual staining to observe effects



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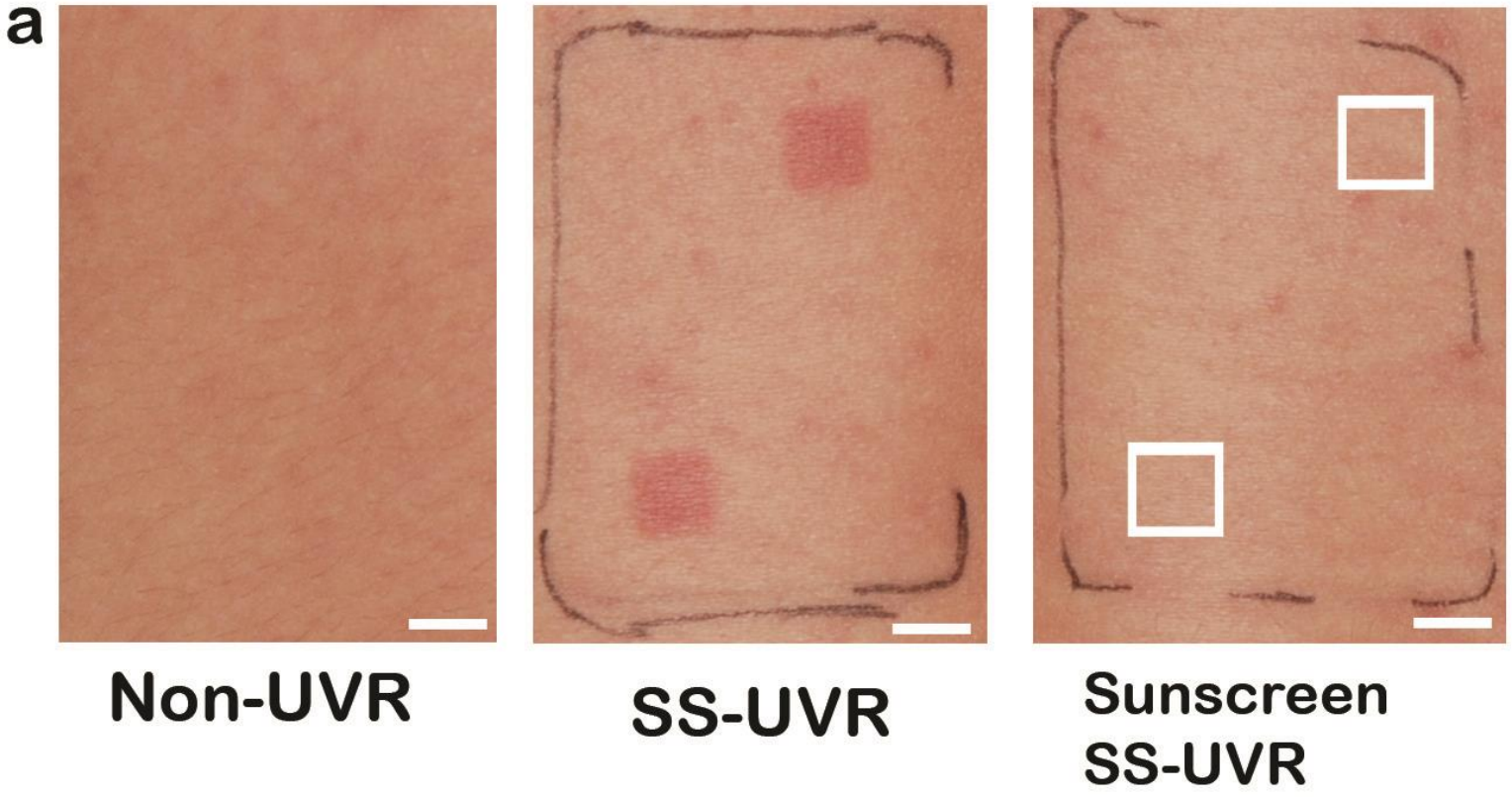
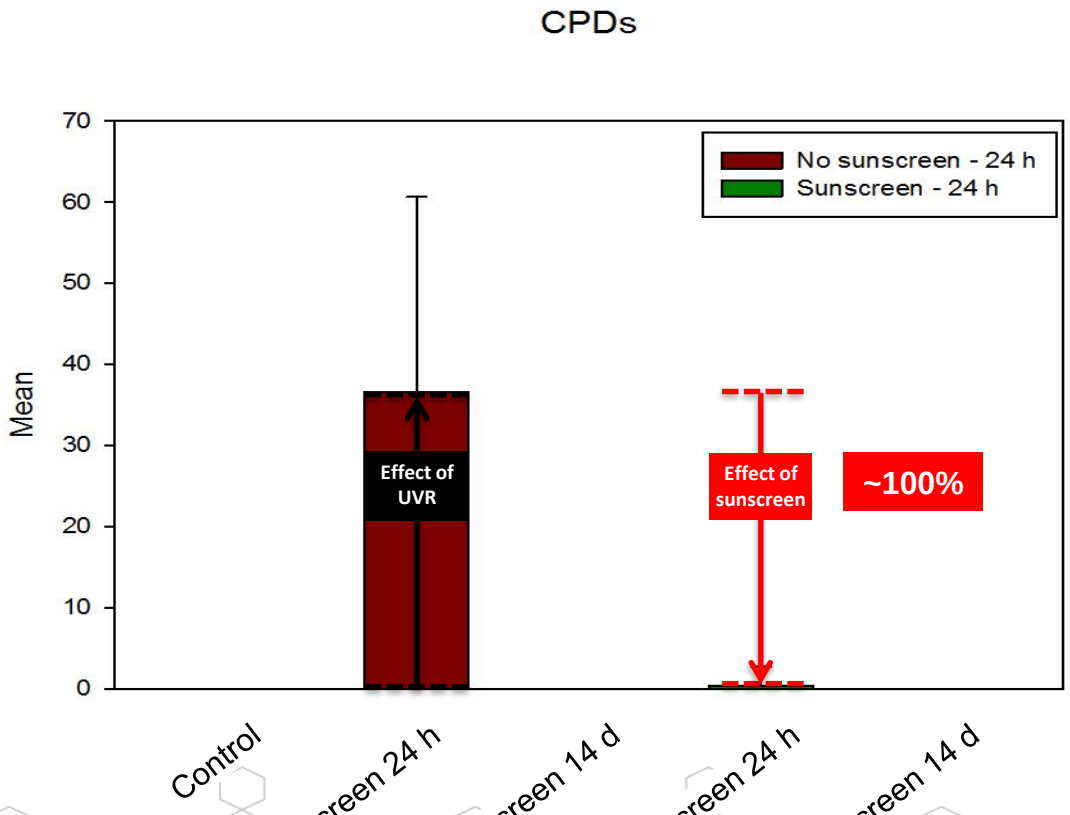
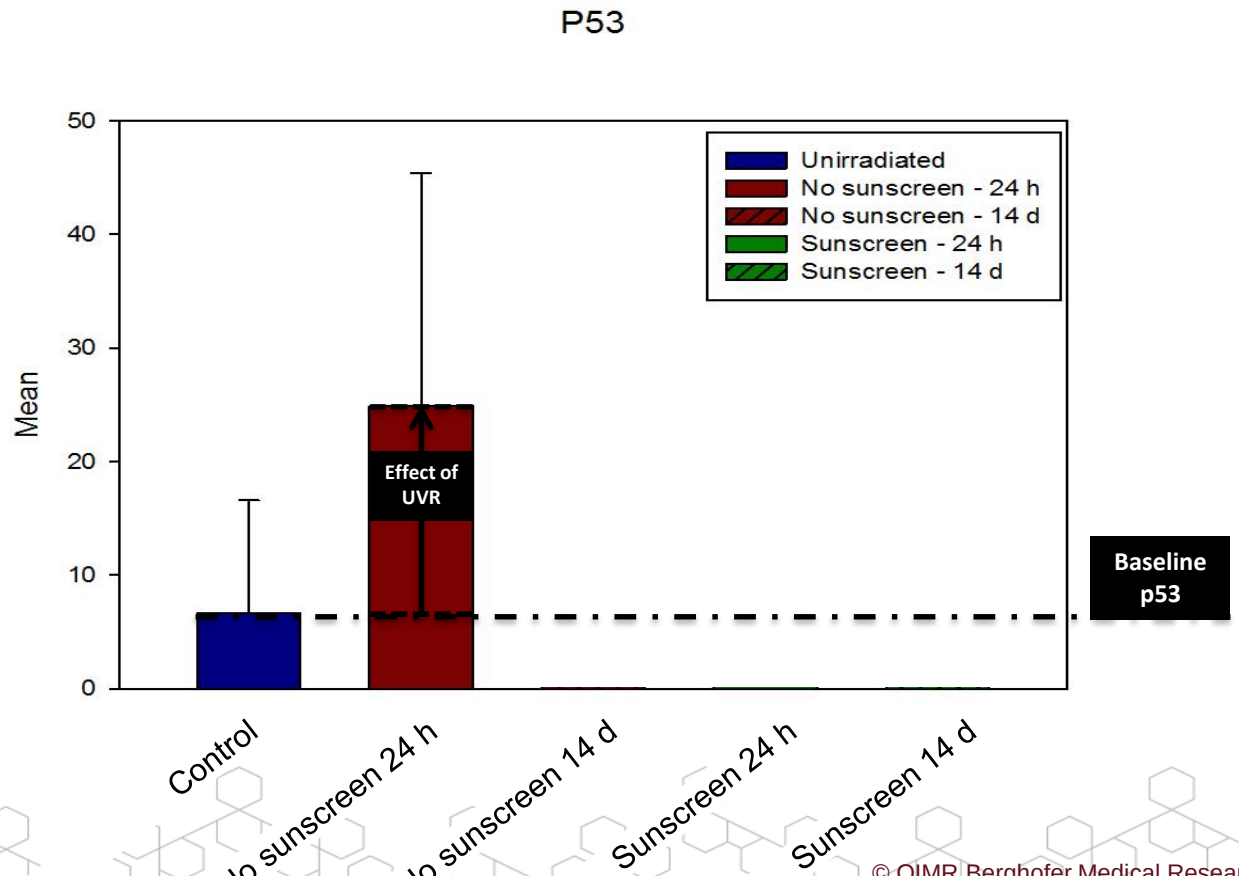
Effect of sunscreen on erythema



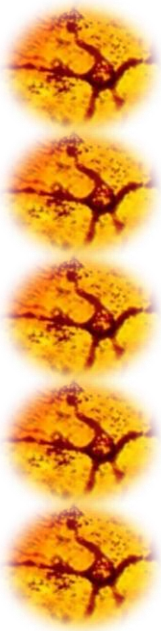
Effect of sunscreen on CPDs

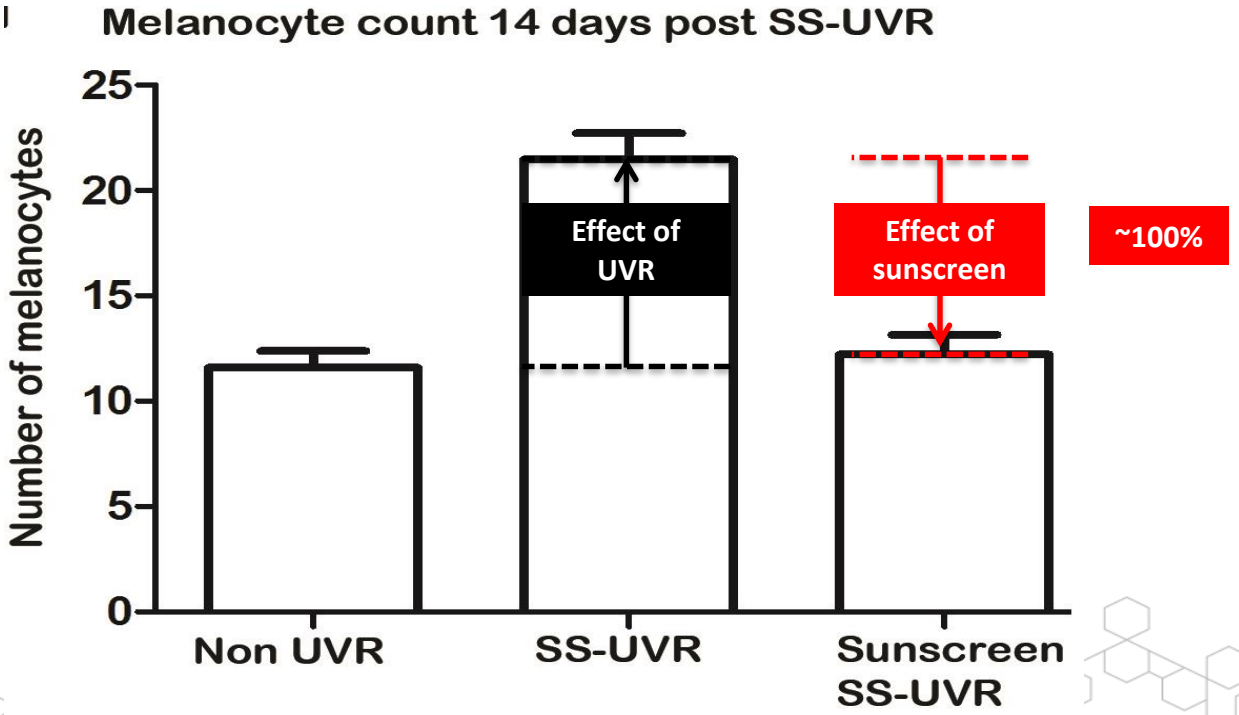


Effect of sunscreen on p53



Effect on melanocyte counts





Summary of findings

- **SPF 30+ sunscreen blocked virtually all UV-induced parameters measured:**
  - **Erythema**
  - **P53**
  - **CPD**
  - **Melanocyte proliferation**

Sunscreen and biomarkers – systematic review

Photodermatology, Photoimmunology & Photomedicine

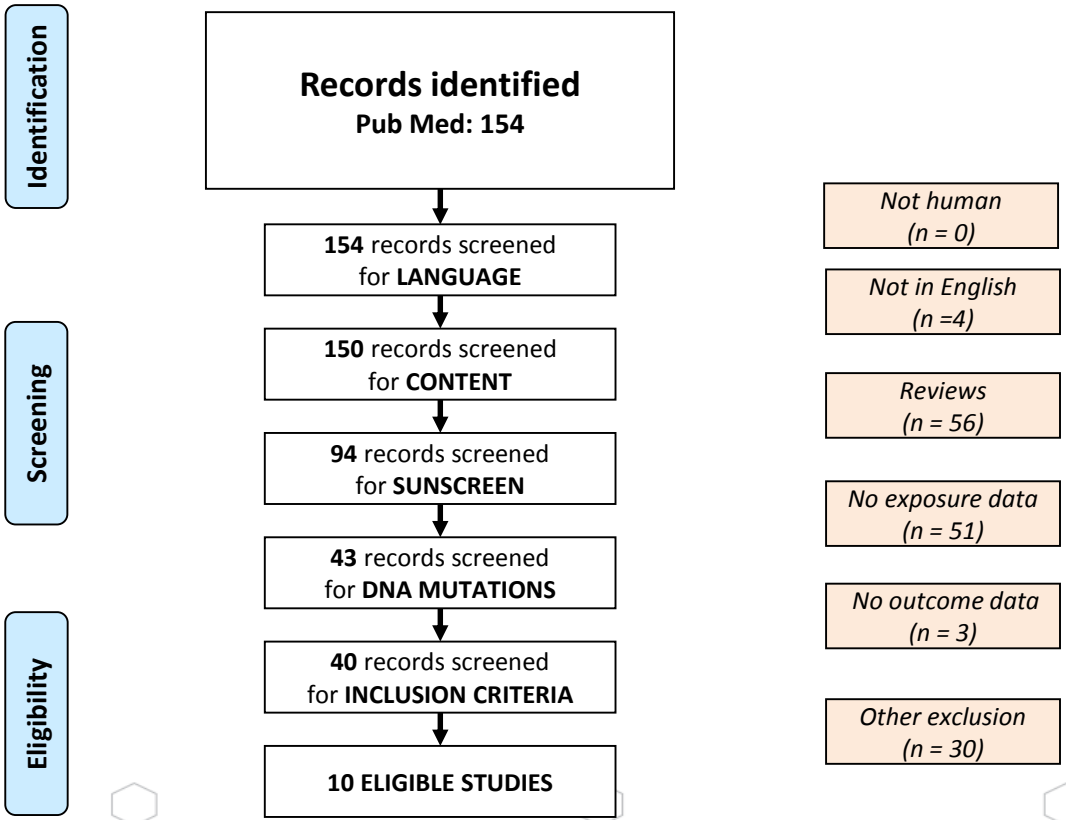
ORIGINAL ARTICLE

Prevention of DNA damage in human skin by topical sunscreens

Catherine M. Olsen[1,2], Louise F. Wilson[1], Adèle C. Green[1,2,3], Neela Biswas[1], Juhi Loyalka[1] & David C. Whiteman[1,2]

Source: Olsen et al. *Photoderm Photoimmunol Photomed* (2017)

Sunscreen and biomarkers – systematic review



Source: Olsen et al. *Photoderm Photoimmunol Photomed* (2017)

Sunscreen and biomarkers – systematic review

10 ELIGIBLE STUDIES

Natural UVR (n = 2) Observational	**UVB** (n = 2) Experimental	**SSUVR** (n = 6) Experimental

Source: Olsen et al. *Photoderm Photoimmunol Photomed* (2017)

Sunscreen and biomarkers – systematic review

First author (year)	DNA markers	Sample size	Sunscreen regimen
Young 1991	Unscheduled DNA synthesis	18	UVB sunscreen +/- 5-MOP
Van Praag 1993	TT dimer	10	SPF 10 30 mins prior
Bykov 1998	TT dimer	14	SPF 10
Young 2000	TT dimer, (6-4)PP	8	SPF 4 *(UVB vs UVA filters)* 20 mins prior
Ling 2001	TT dimer, P53	4	SPF 15 sunscreen 15 mins prior
Liardet 2001	CPD, p53, 8OHDG	8	SPF 15 15 mins prior
Mahroos 2002	TT dimer	18	SPF 15 30 mins prior
Hacker 2013	CPD, p53, Ki67, cell counts	57	SPF 30+ 20 mins prior

Source: Olsen et al. *Photoderm Photoimmunol Photomed* (2017)

Sunscreen and biomarkers – systematic review

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Hacker 2013	CPD, p53, Ki67, cell counts	57	SPF 30+ 20 mins prior	↓↓↓↓

Source: Olsen et al. *Photoderm Photoimmunol Photomed* (2017)

Summary of findings

- **Literature not extensive**
- **Sunscreen (SPF 15+) attenuates short- (24 hrs) and medium-term (14 d) biologic effects of UVR in human skin**
- **Higher SPF appears to confer higher attenuation than lower SPF**

Conclusions

- **Modern sunscreens prevent biological damage to human skin when applied before UVR exposure**

