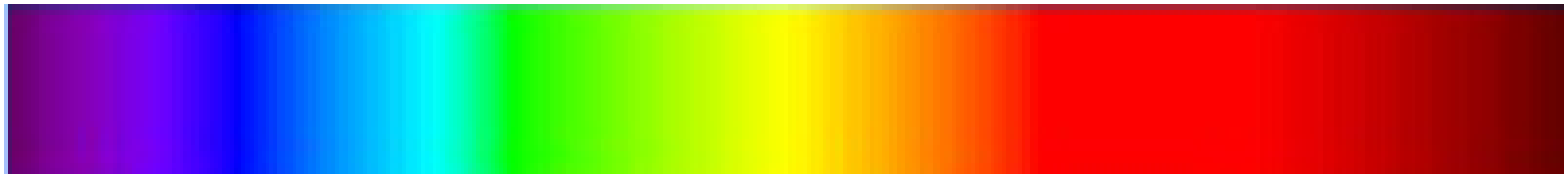
Diagnosis and Treatment of Vitamin D Deficiency Workshop



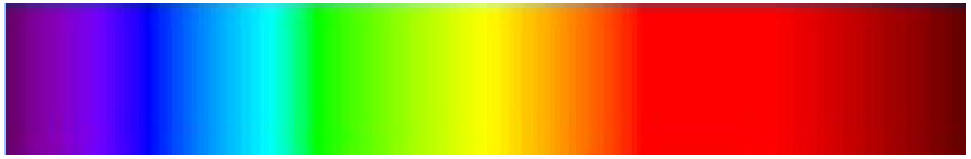
UV: The original Source! How to use it

April 9, 2010

Edward D. Gorham, Ph.D., Cedric F. Garland, Dr.P.H., and Sharif B. Mohr, M.P.H., Frank C. Garland, Ph.D.

UCSD Department of Family and Preventive Medicine

DISCLOSURES



The following personal financial relationships with commercial interests relevant to this presentation existed during the past 12 months:

No relationships to disclose

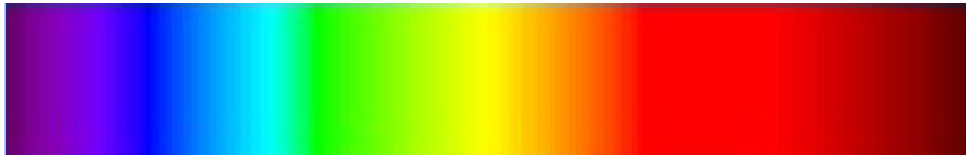
Edward D. Gorham, Ph.D.

Cedric F. Garland, Dr.P.H.

Sharif B. Mohr, M.P.H.

Frank C. Garland, Ph.D.

OBJECTIVES



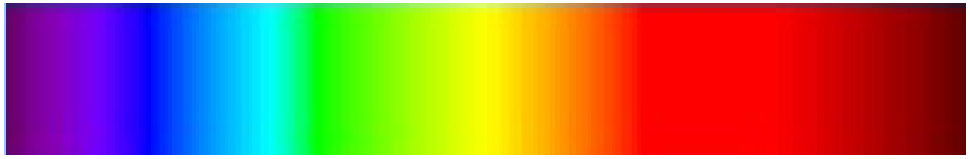
Identify environmental, behavioral, and constitutive risk factors for vitamin D deficiency syndrome

Describe cutaneous evolutionary adaptations for use of UVB for vitamin D synthesis

Identify the portion of the UVB spectrum available and effective in Vitamin D Photosynthesis

Make recommendations for optimal serum levels of 25 (OH) D for any patient whether from sun exposure or oral intake

Vitamin D Deficiency as a Syndrome



Marfan's Syndrome

Affects connective tissue leading to a myriad of disease consequences, including skeletal and coronary vascular disorders

Vitamin D Deficiency Syndrome

Affects intercellular communications (tight junctions) and calcium regulation also with a myriad of health consequences.

These include skeletal and coronary heart disease effects and increased risk of :

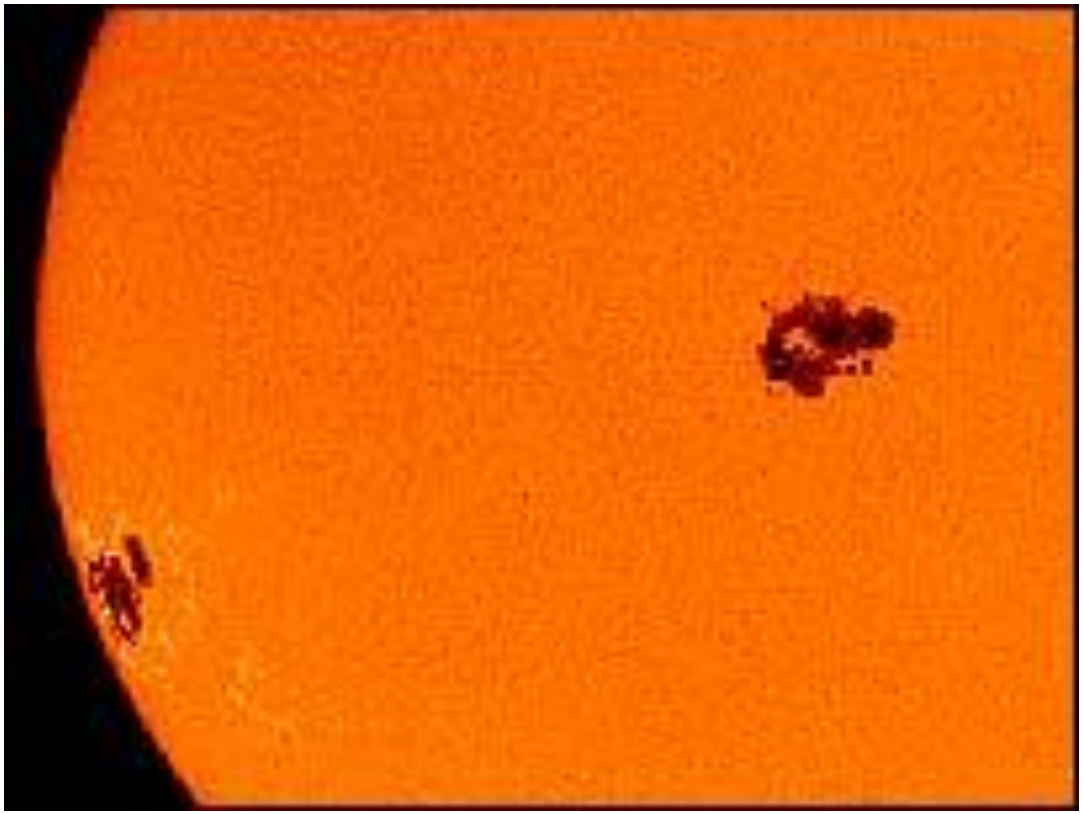
Cancers (17 sites*) Multiple sclerosis Seasonal influenza

Diabetes (Types 1 & 2) Muscle pain and weakness

Pregnancy complications Impaired wound healing

*Sources: Grant WB, Mohr SB. Ecological studies of ultraviolet B, vitamin D and cancer since 2000. Ann Epidemiol. 2009;19:446-54. ///Grant WB. An ecologic study of cancer mortality rates in Spain with respect to indices of solar UVB irradiance and smoking. Int J Cancer. 2007;120:1123-8

UVB Photons and Vitamin D Synthesis

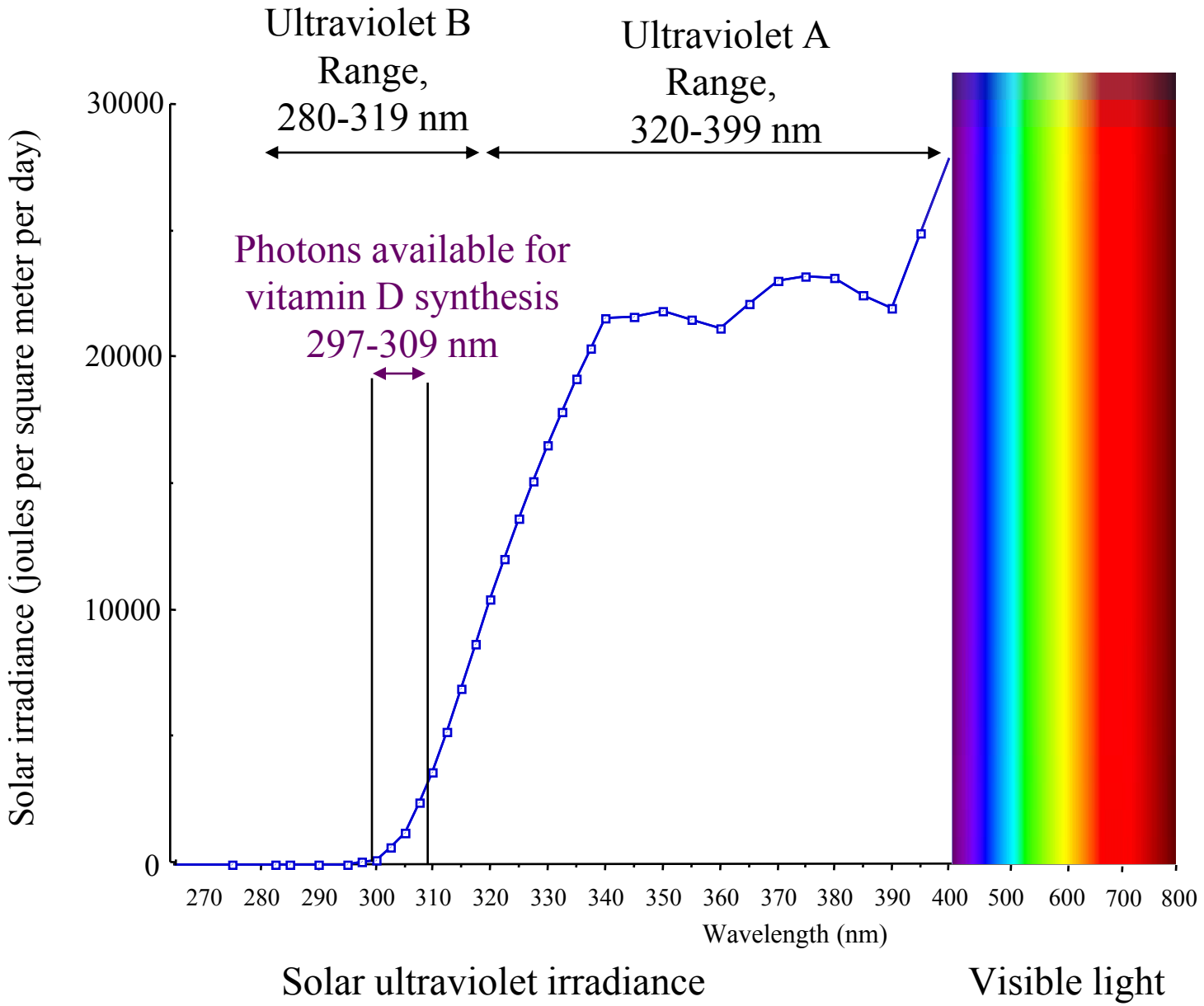


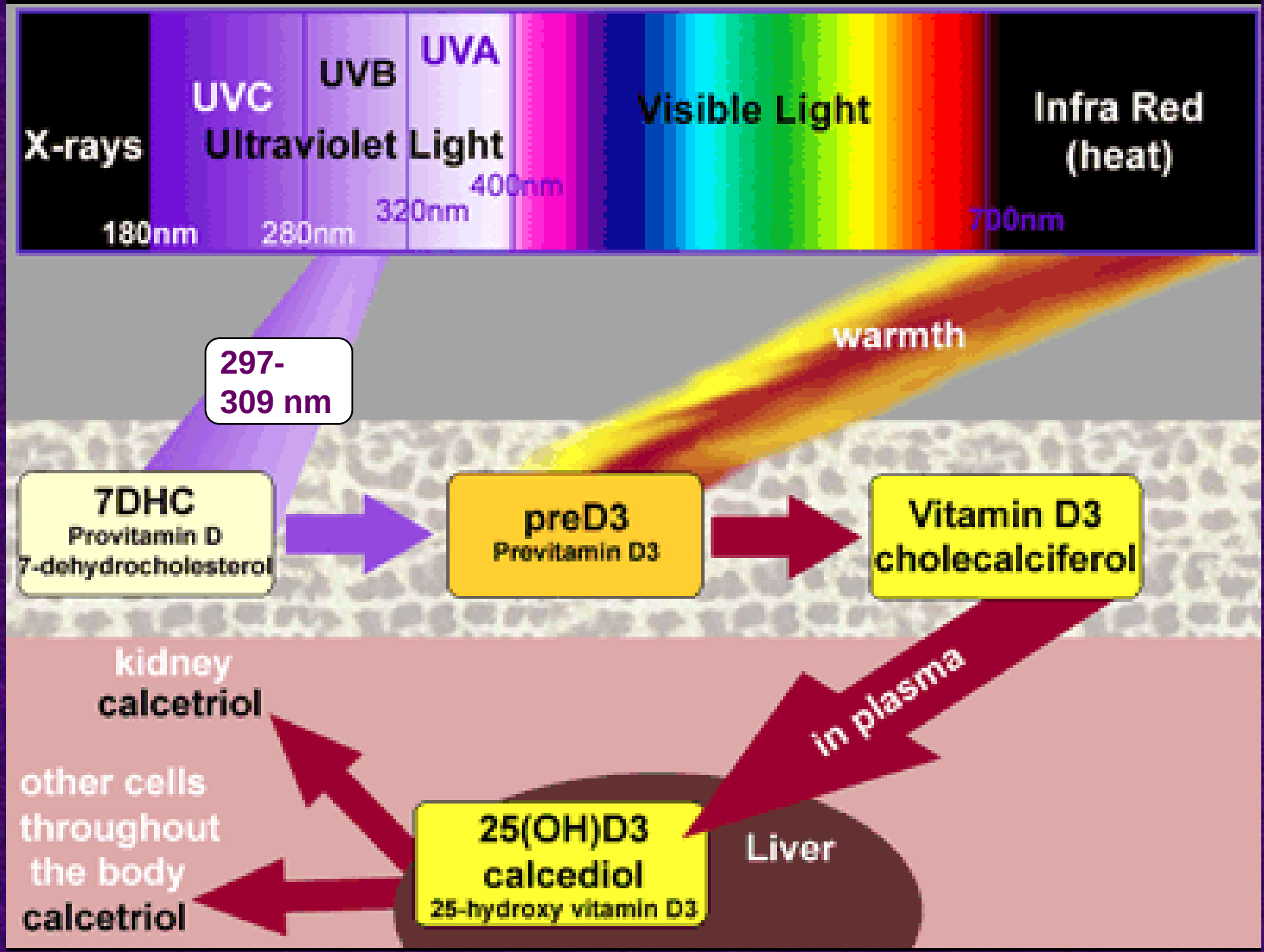
(Photo: Stanford Univ)

The sun is the source of UVB photons used to make vitamin D

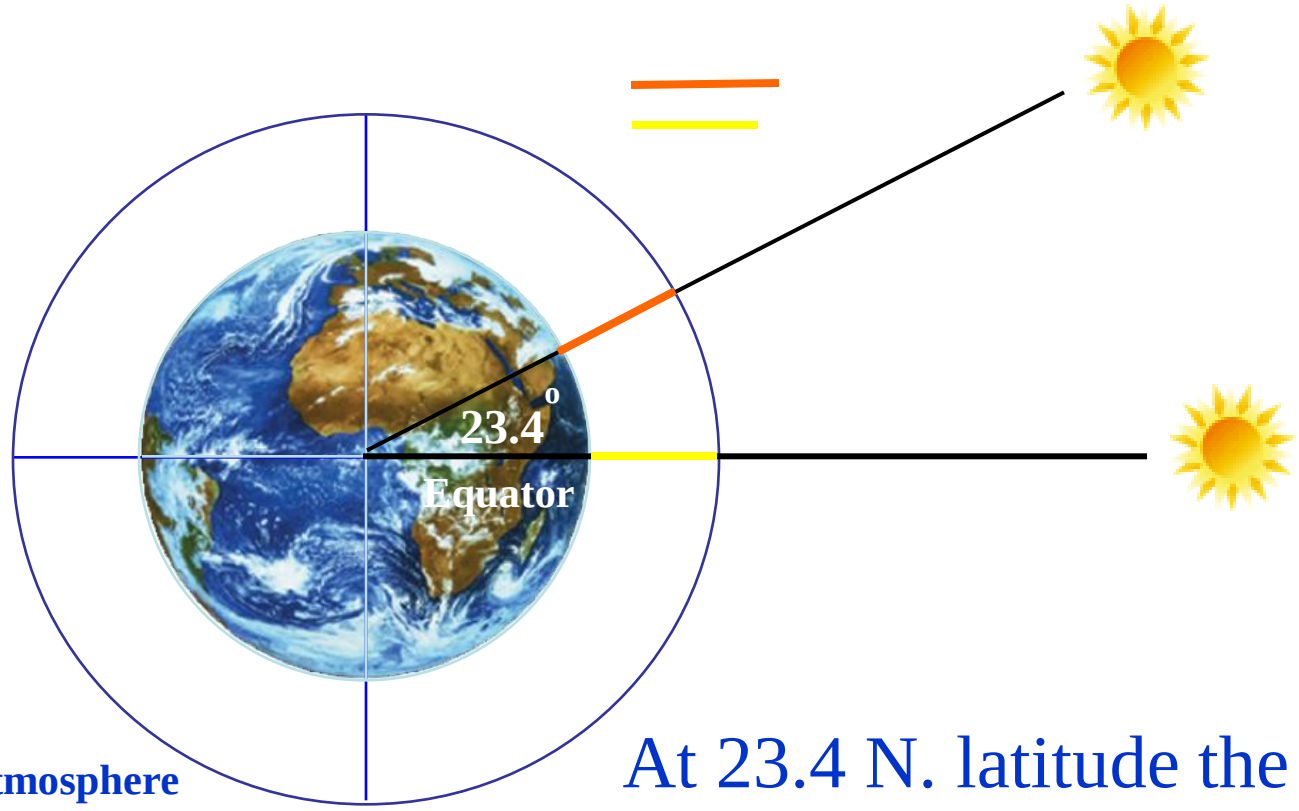
Of all solar photons available at noon at ground level, fewer then 0.5% are useful in vitamin D synthesis (297-309 nm wavelength)

Photons Available for Vitamin D Photosynthesis: 297-309 nm



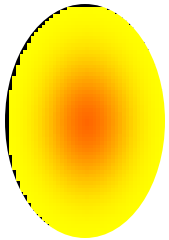

X-rays
UVC
UVB
UVA
Ultraviolet Light
Visible Light
Infra Red
(heat)
180nm
280nm
320nm
400nm
700nm
297-
309 nm
warmth
7DHC
Provitamin D
7-dehydrocholesterol
preD3
Previtamin D3
Vitamin D3
cholecalciferol
kidney
calcetriol
in plasma
other cells
throughout
the body
calcetriol
25(OH)D3
calcediol
25-hydroxy vitamin D3
Liver

Photons for UVB photosynthesis vary by Solar Angle which changes with Season, Latitude, and Time of Day

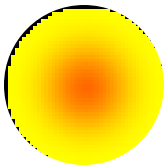


Atmosphere not to scale

The flashlight beam model



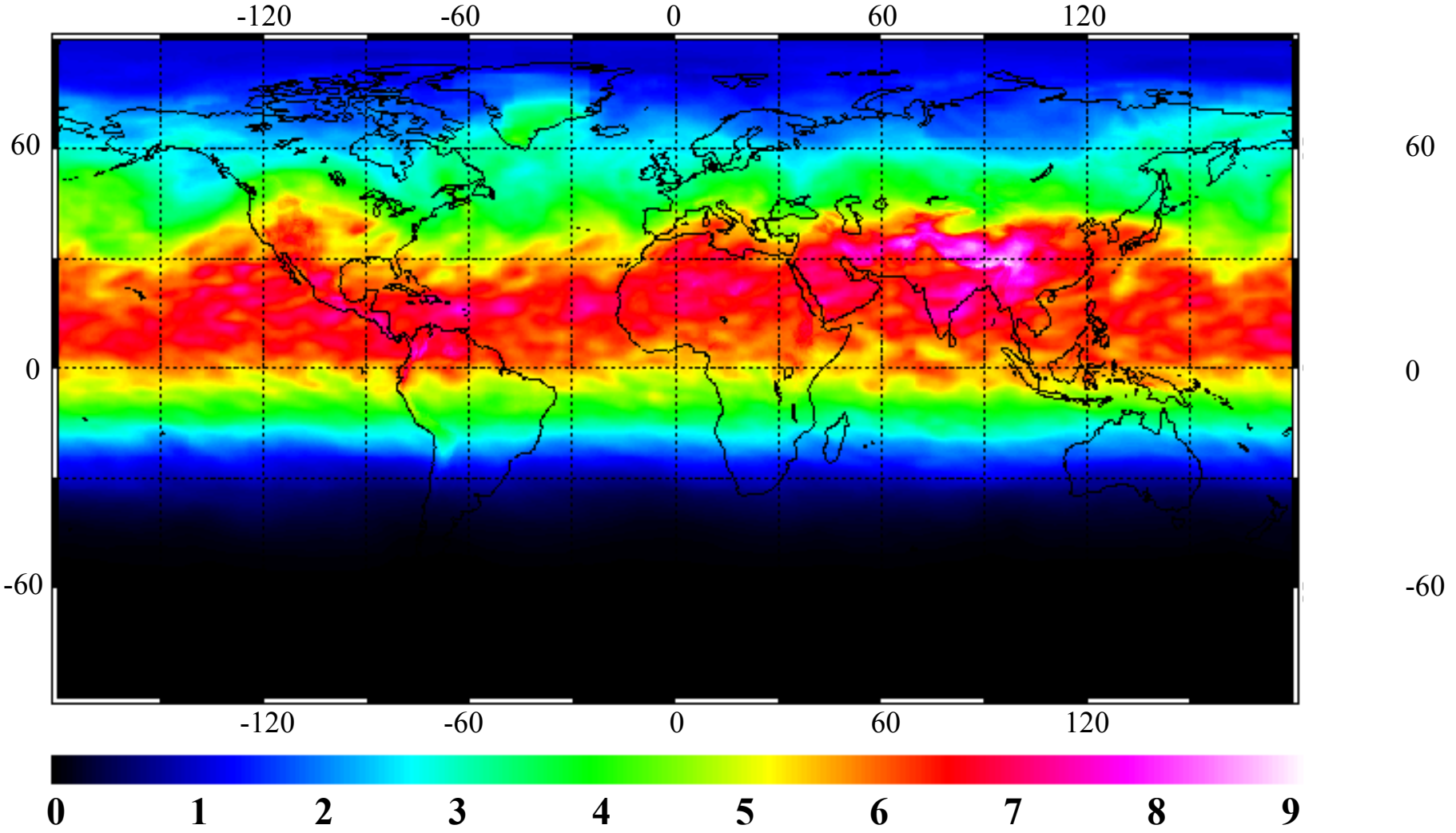
Oblique Rays



Perpendicular Rays

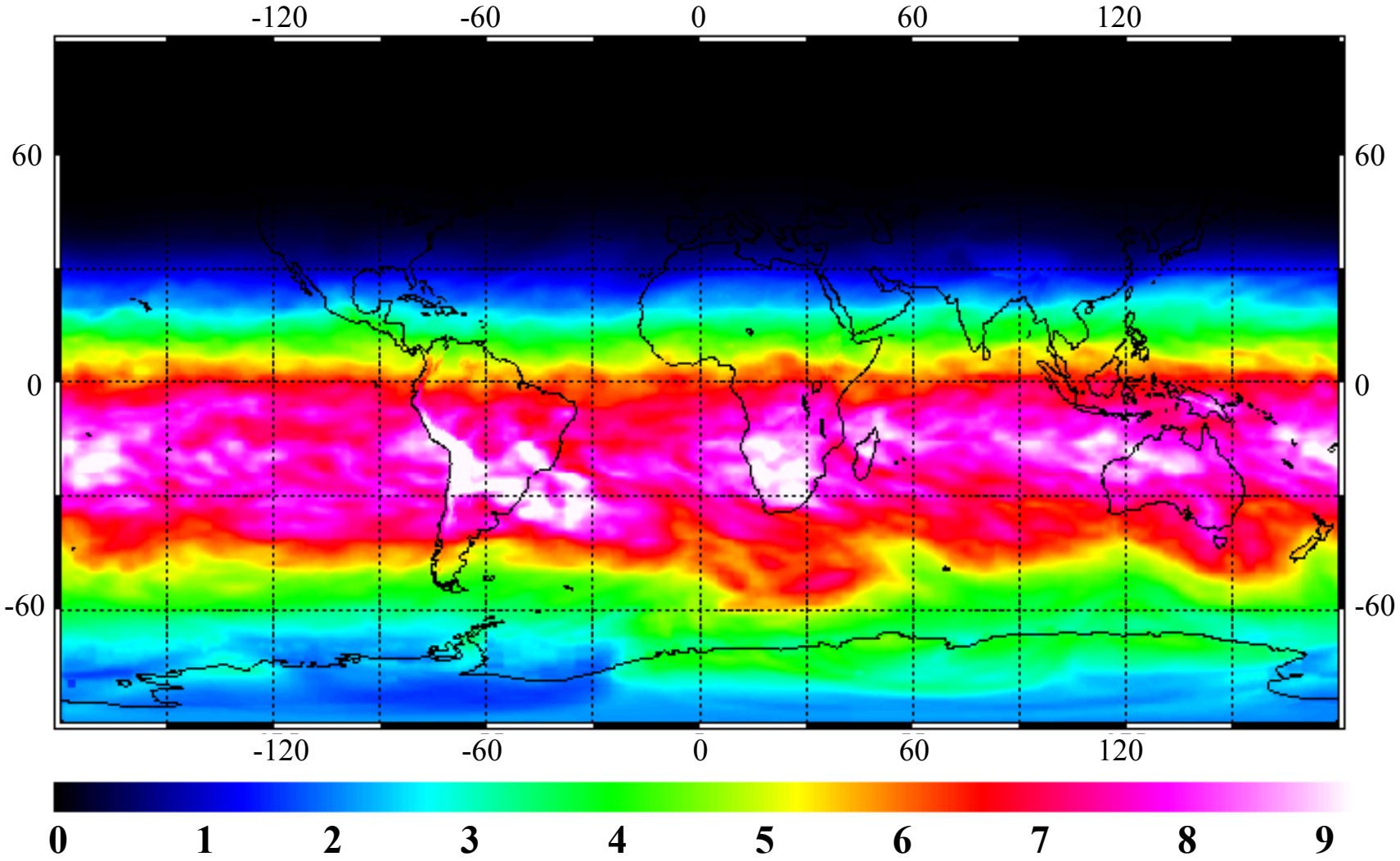
At 23.4 N. latitude the optical path length of sunlight through the atmosphere is longer at the equator

Erythemal UVB dose (kiloJoules/square meter) on a globally clear day at world-wide solar noon on the Summer Solstice, 21 June 2007



Source: http://www.temis.nl/uvradiation/UVindex.html acessed 4/5/2010. Model described in: J. van Geffen, R. van der A, M. van Weele, M. Allaart and H. Eskes, Surface UV radiation monitoring. Proceedings of the ENVISAT & ERS Symposium, 6-10 September 2004, Salzburg, Austria, European Space Agency publication SP-572, 2005

Erythemal UVB dose (kiloJoules/square meter) on a globally clear day at world-wide solar noon on the Winter Solstice, 21 December 2007.



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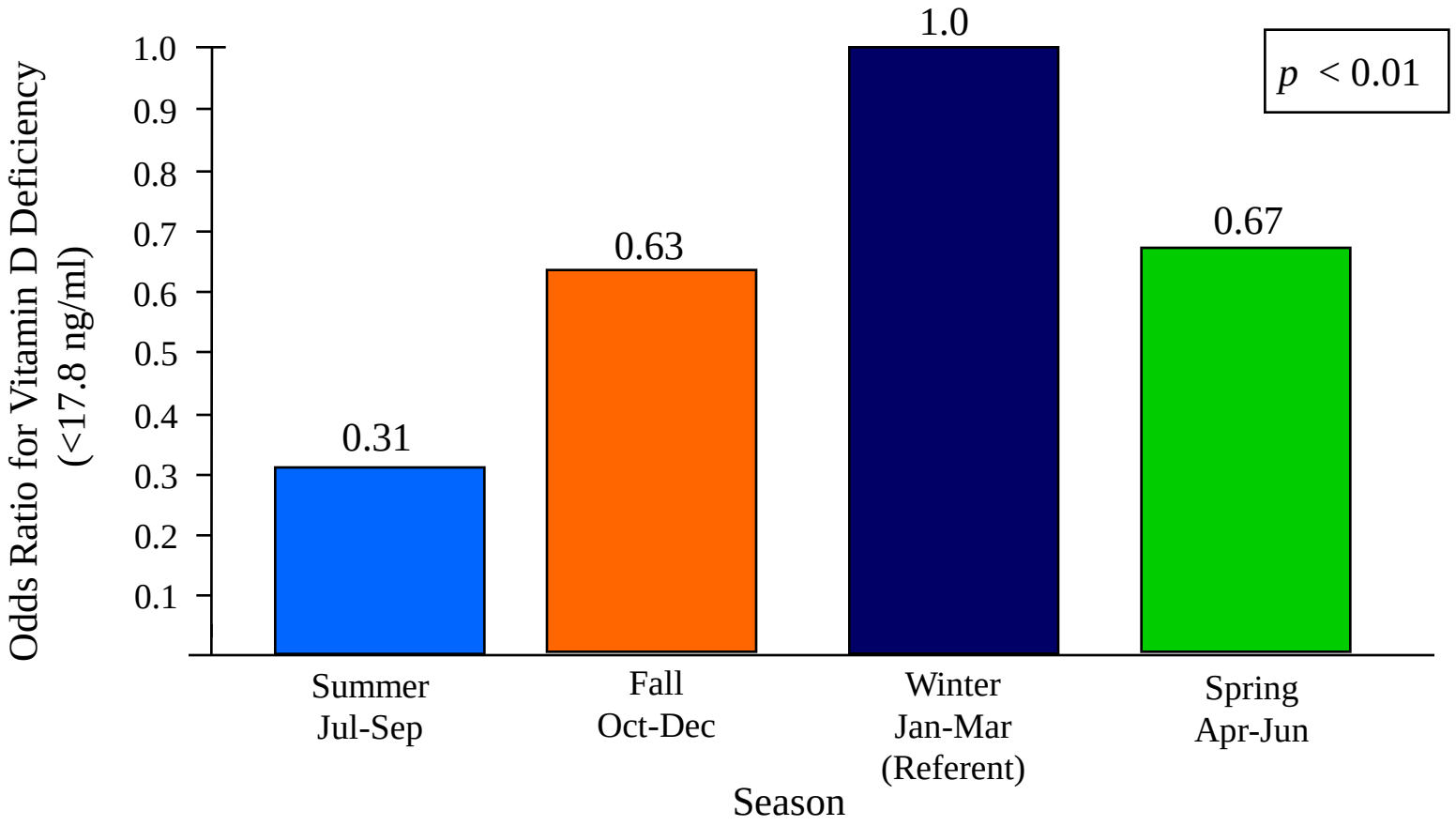
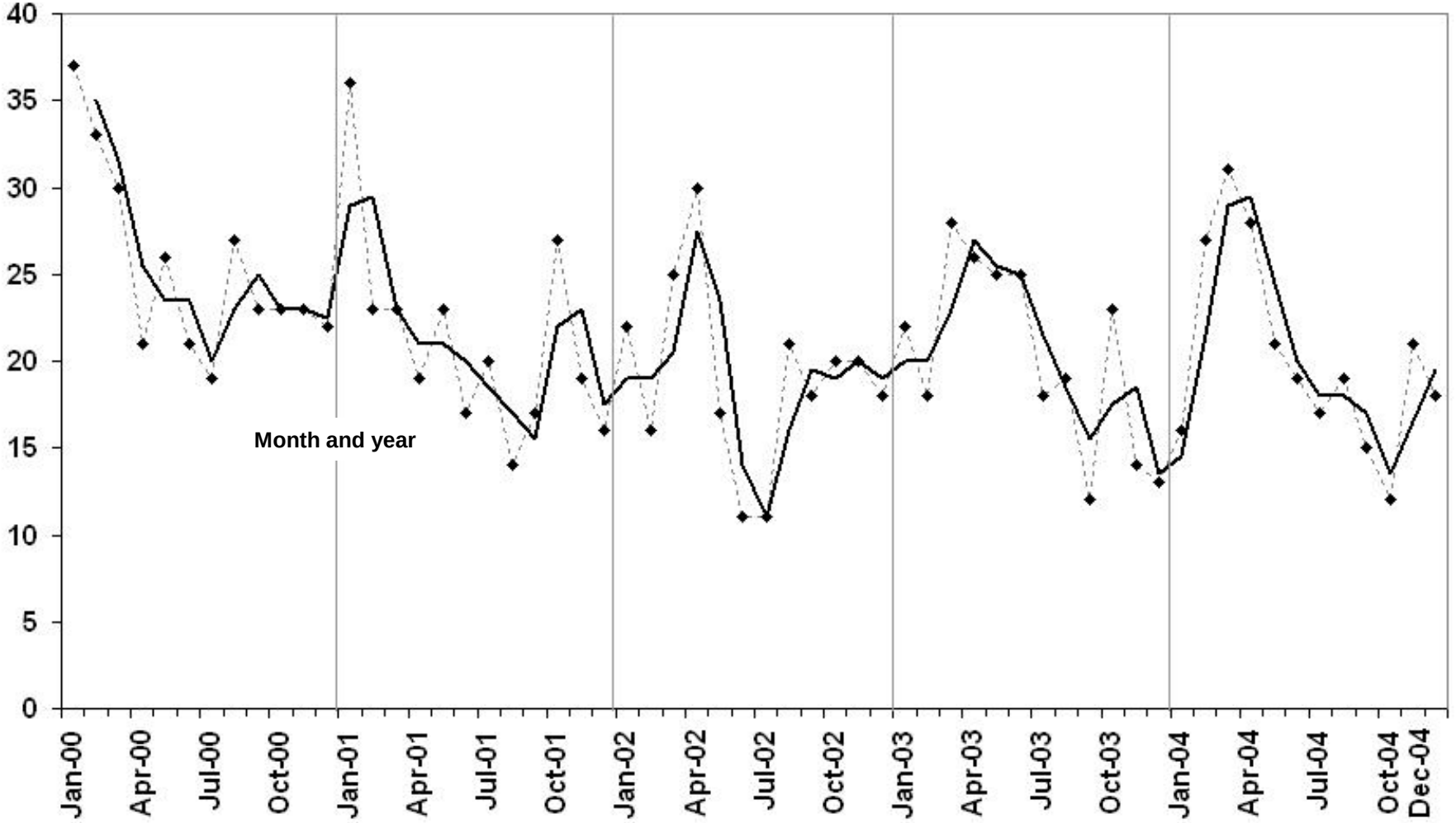


Odds Ratios of 25-hydroxyvitamin D deficiency below 17.8 ng/ml (lowest quartile) by Season of blood draw, National Health and Nutrition Examination Survey III, N=13,331 Participants

Source: Melamed ML, Michos ED, Post W, Astor B. 25-hydroxyvitamin D levels and the risk of mortality in the general population. Arch Intern Med. 2008;168:1631.

Type 1 Diabetes Incidence Peaks Annually in the Winter-Spring Season (Odds Ratio = 1.46, $p < 0.01$)

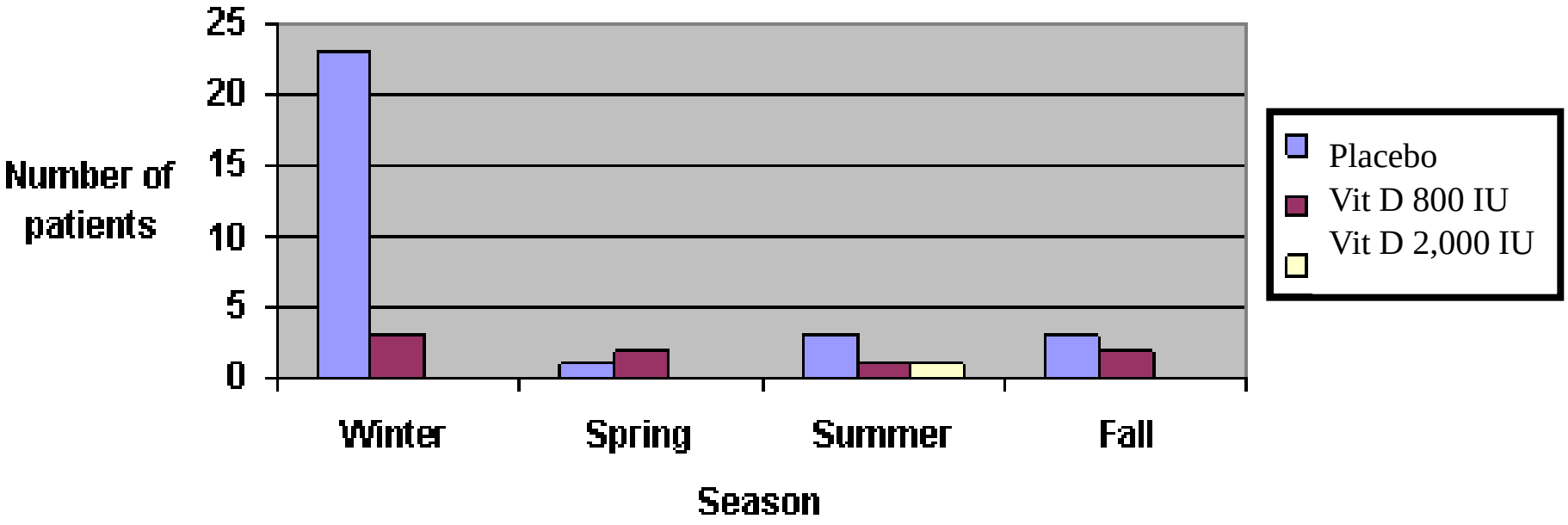


Incidence of Type 1 diabetes by month and year, active-duty DoD, 2000-2004, N = 2,918 new cases,18-44 years (median age 28 years)

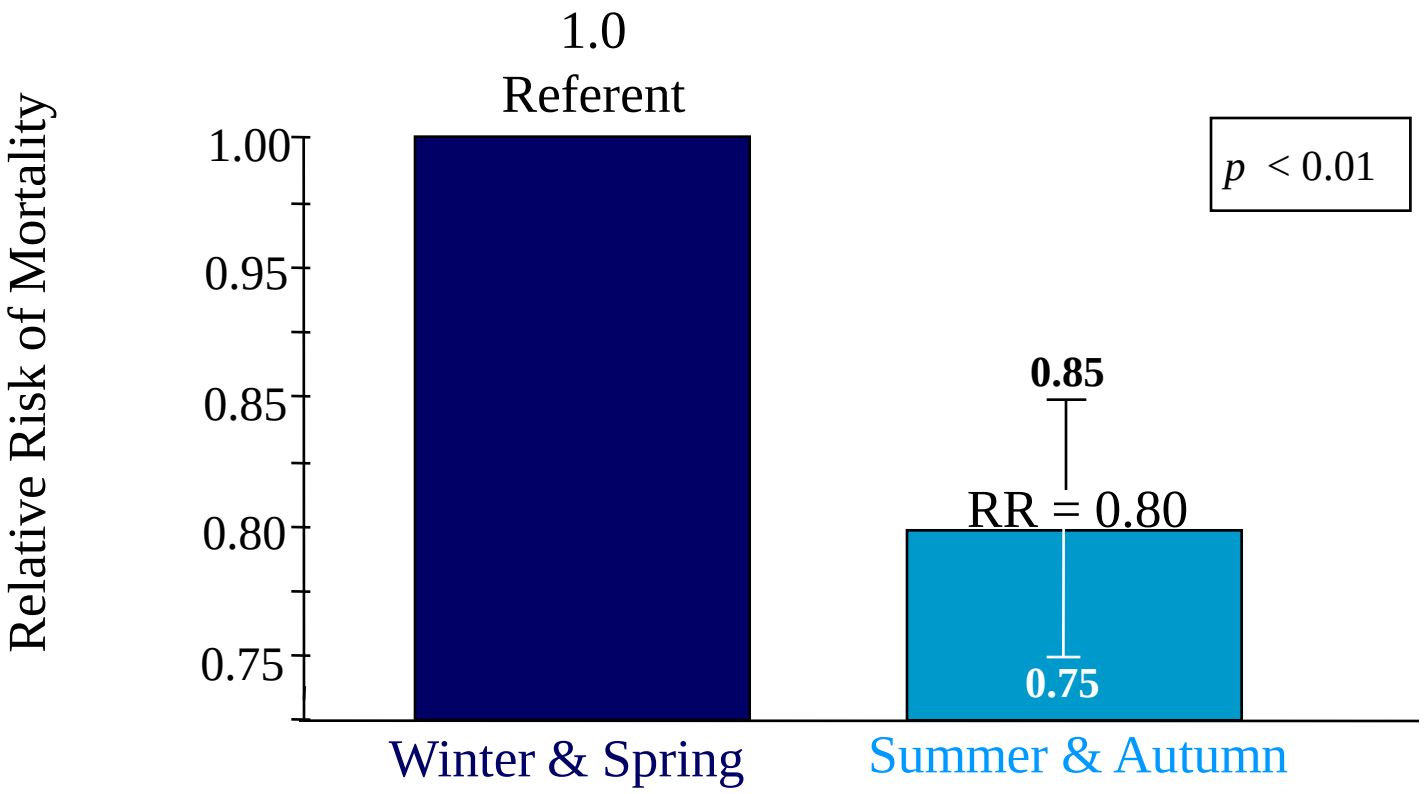
Gorham ED, Barrett-Connor E, Highfill-McRoy RM, Mohr SB, Garland CF, Garland FC, Ricordi C. Incidence of insulin-requiring diabetes in the US military. Diabetologia. 2009;52:2087-91

Randomized Controlled Trial of Vitamin D and Bone Loss in Postmenopausal Women

Follow-up every 6 months for self-reported flu symptoms



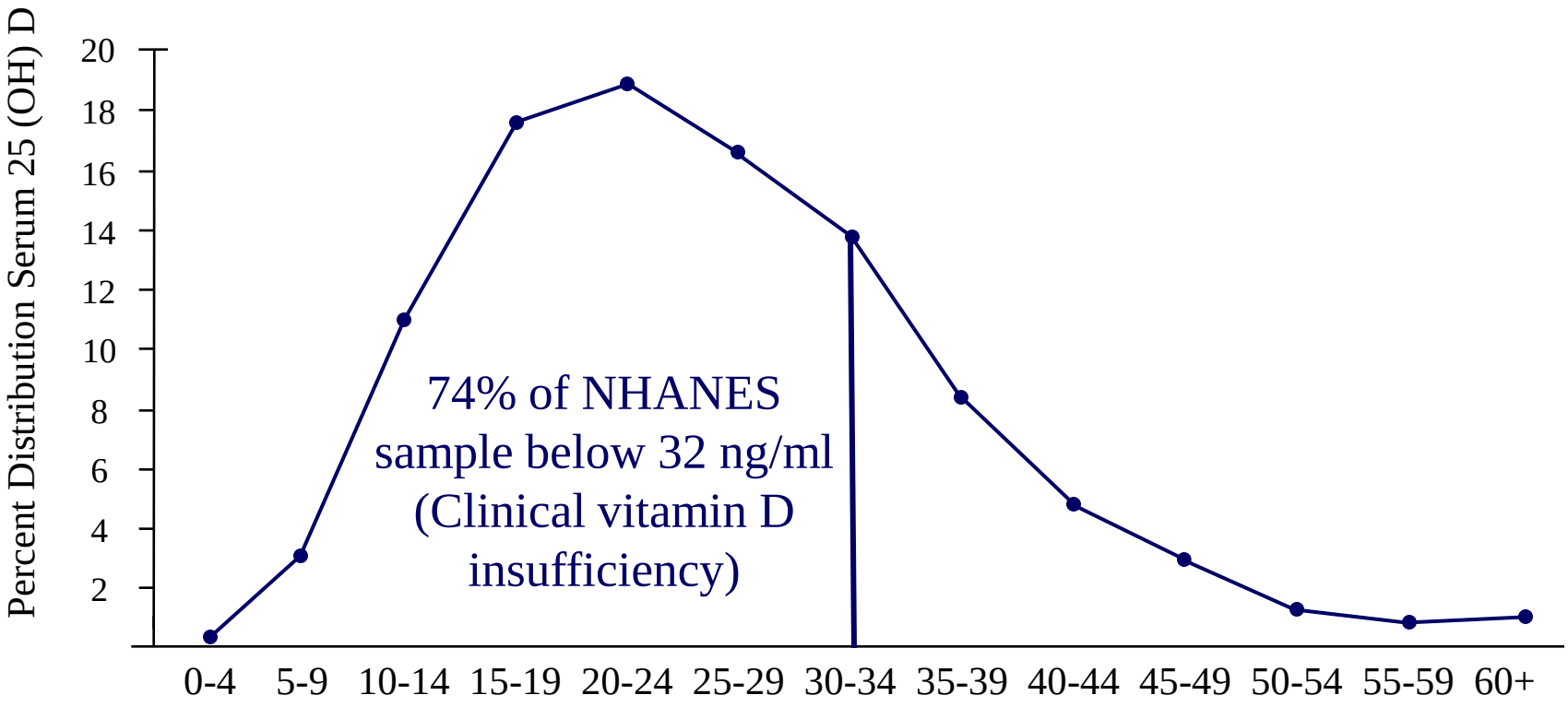
Aloia JF, Li-Ng M. Re: epidemic influenza and vitamin D. Epidemiol Infect. 2007;135:1095-6



Prostate Cancer Survival by Season of Diagnosis,
N = 46,205 Cases, 1964-1992, Norway

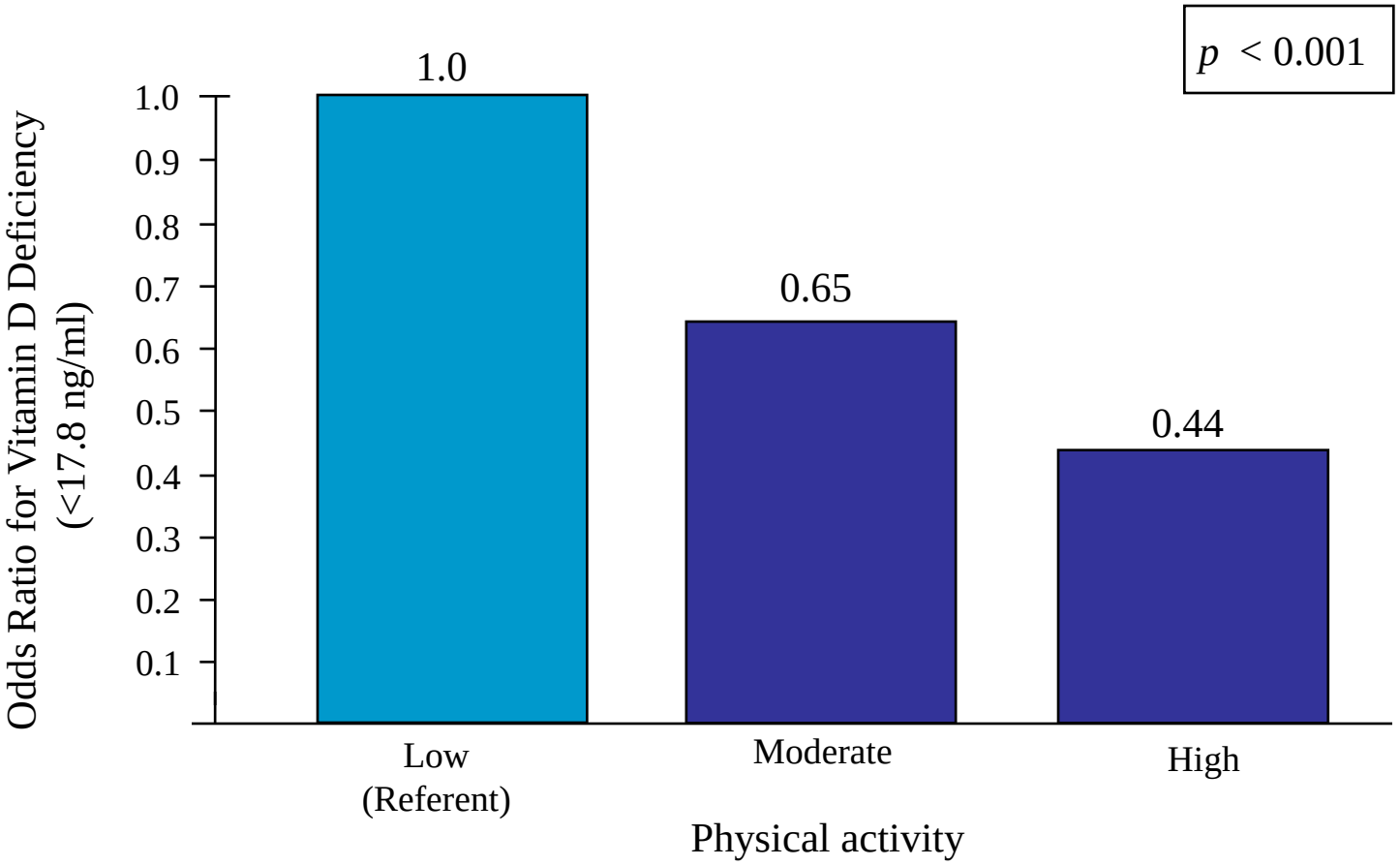
Source: Lagunova Z, Porojnicu AC, Dahlback A, Berg JP, Beer TM, Moan J. Prostate cancer survival is dependent on season of diagnosis. Prostate. 2007;67:1362-70.

Serum 25(OH)D levels from NHANES III



25-Hydroxyvitamin D Serum Levels, 15,536 participants
National Health and Nutrition Examination Survey III, Seasonal Sampling

Low Physical Activity is Associated with Lower Plasma 25-hydroxyvitamin D Concentration



Odds Ratios of 25-hydroxyvitamin D deficiency below 17.8 ng/ml (lowest quartile) by Physical Activity, National Health and Nutrition Examination Survey III, N=13,331 Participants

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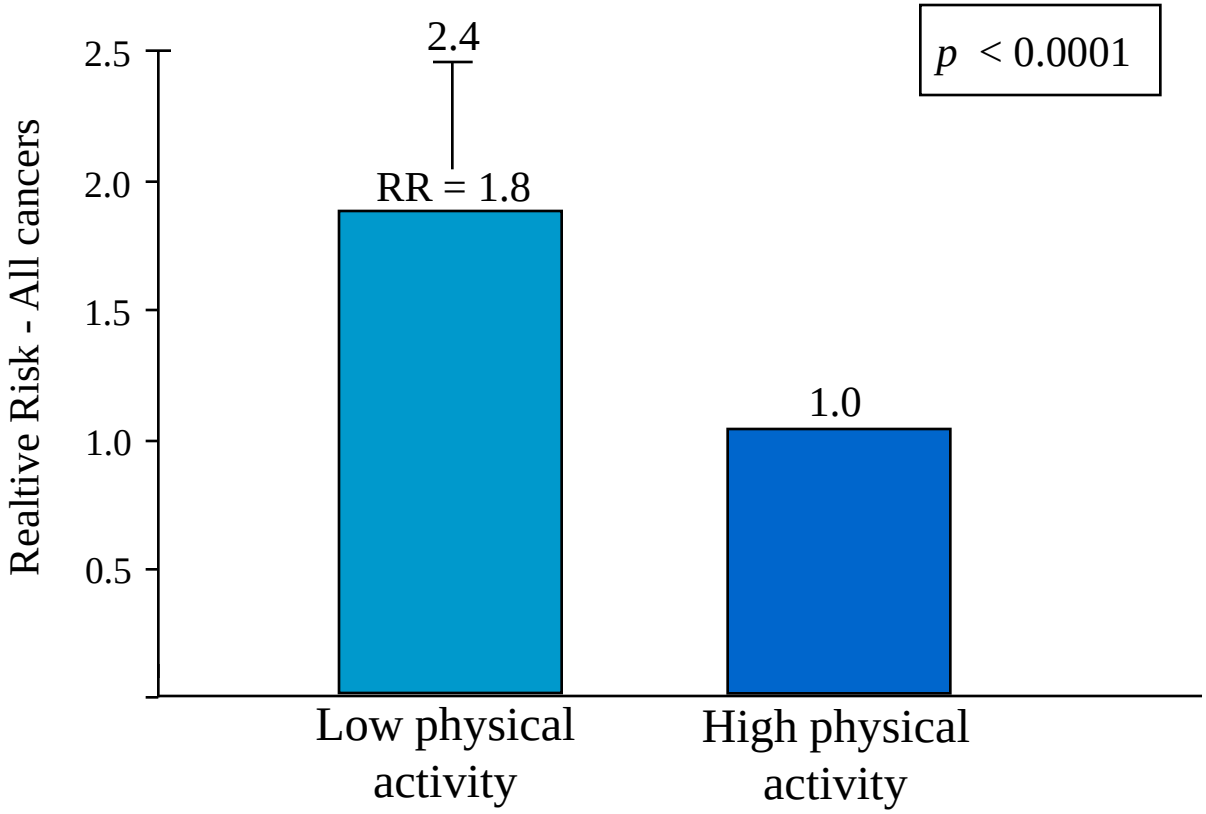
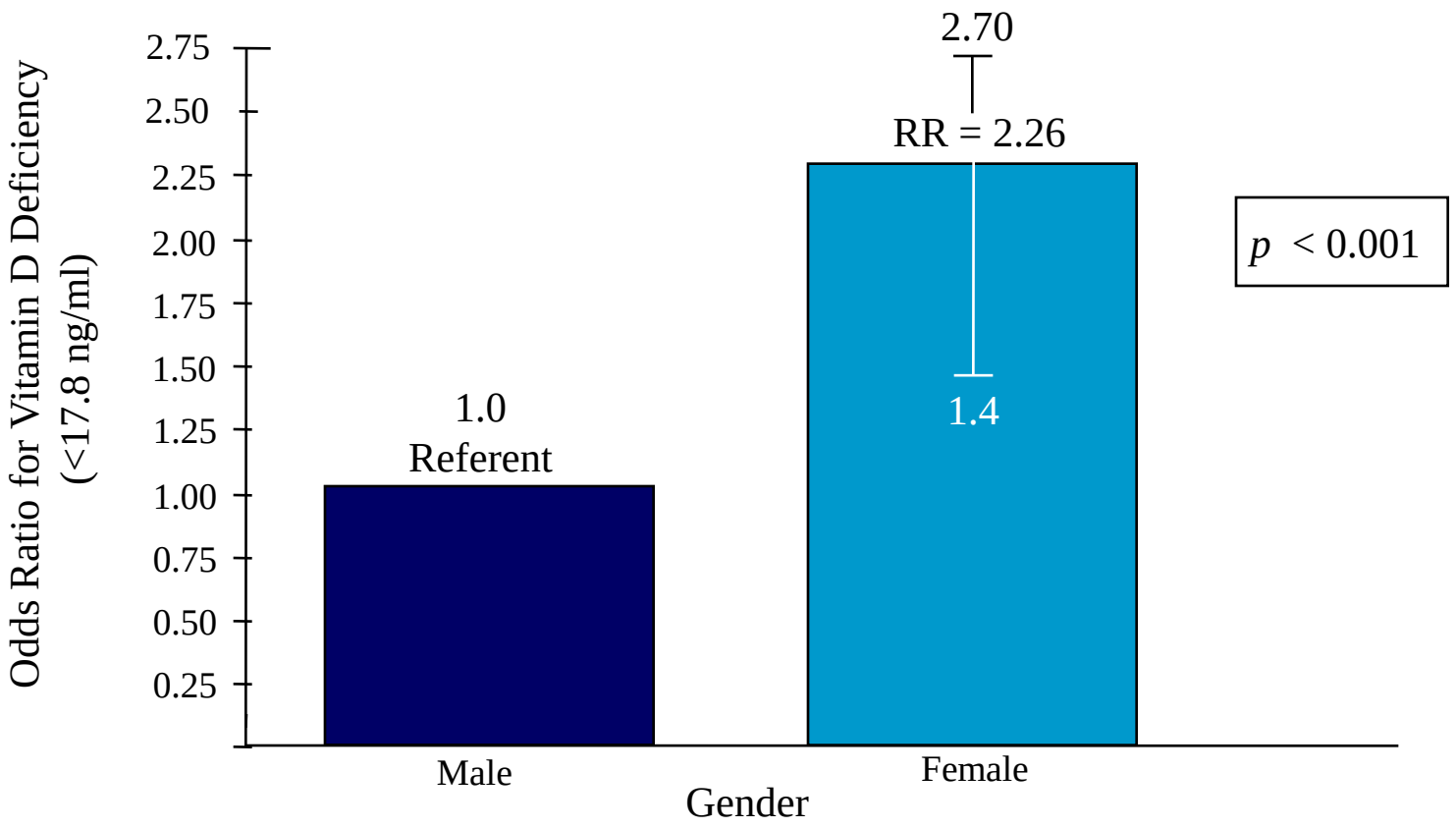


Physical Activity and Cancer Incidence Among 5,138 men 25-74 years of age, 1982-84, NHANES 1

D Albanes, A Blair, and P R Taylor

Physical activity and risk of cancer in the NHANES I population. ***Am J Public Health.*** **1989; 79: 744–750**

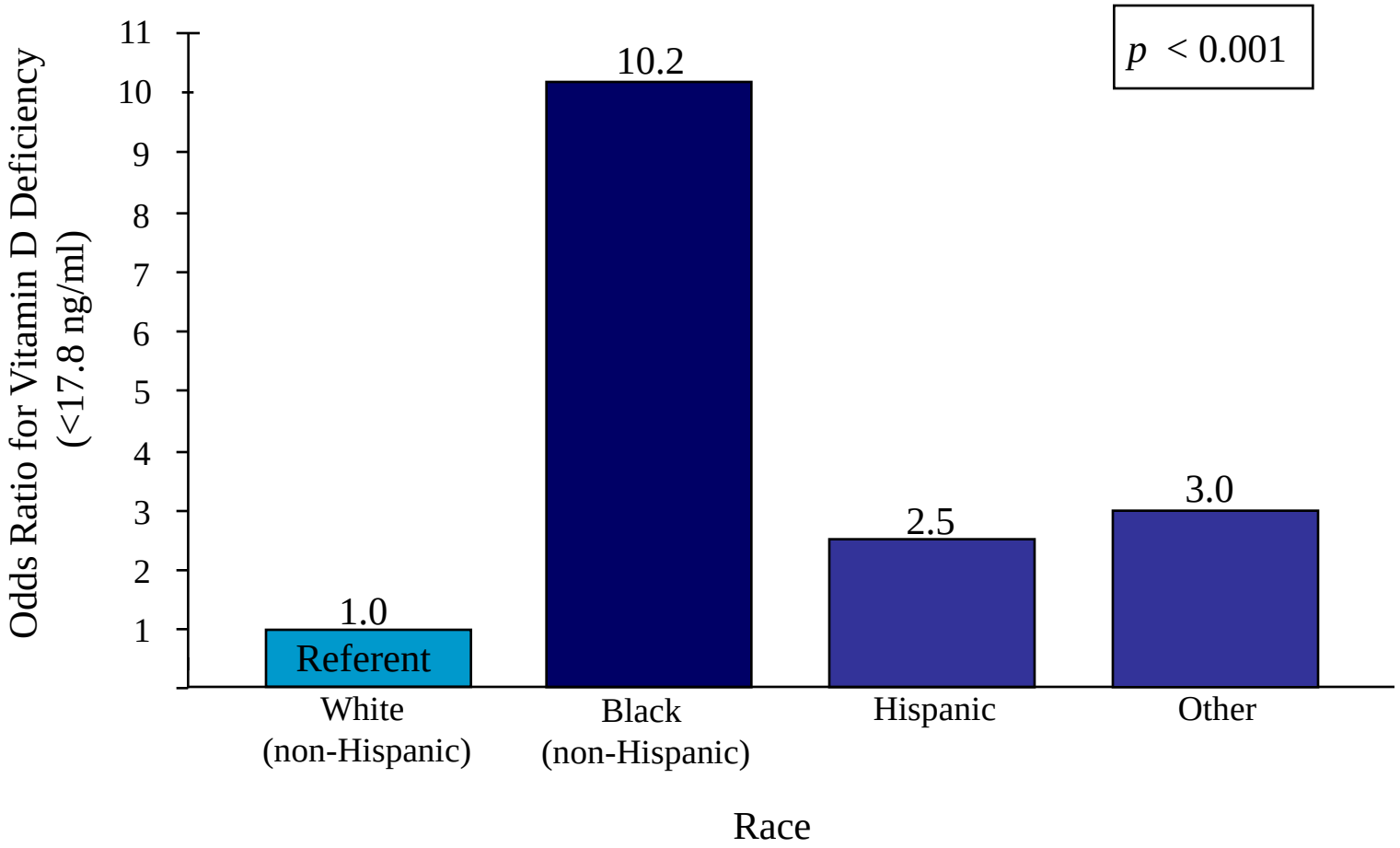
Women are at Elevated Risk for Vitamin D Deficiency



Odds Ratios of 25-hydroxyvitamin D deficiency below 17.8 ng/ml (lowest quartile) by Gender, National Health and Nutrition Examination Survey III, N=13,331 Participants

Source: Melamed ML, Michos ED, Post W, Astor B. 25-hydroxyvitamin D levels and the risk of mortality in the general population. Arch Intern Med. 2008;168:1631.

Constitutive Pigmentation is a Risk Factor for Vitamin D Deficiency



Odds Ratios of 25-hydroxyvitamin D deficiency below 17.8 ng/ml (lowest quartile) by Race, National Health and Nutrition Examination Survey III, N=13,331 Participants

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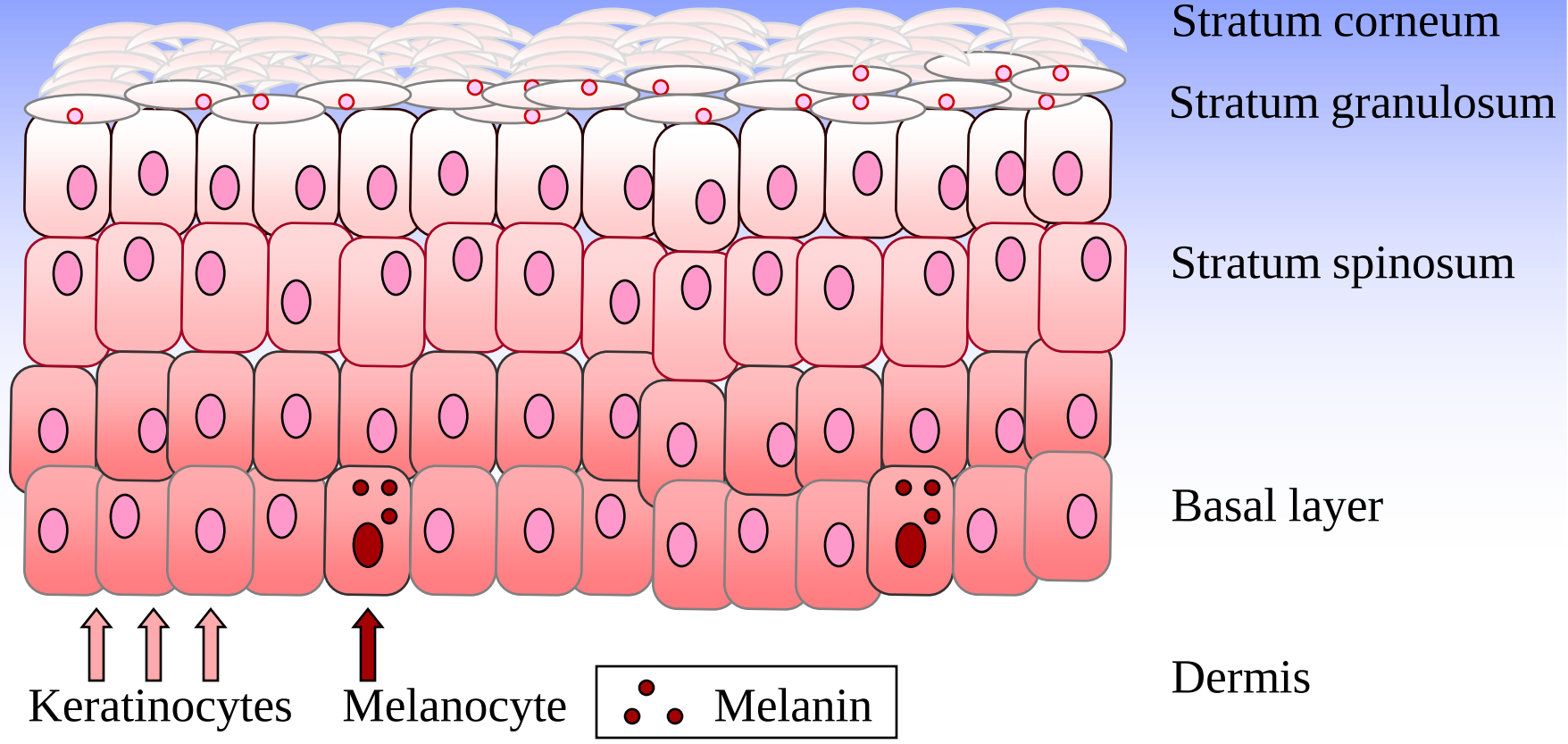
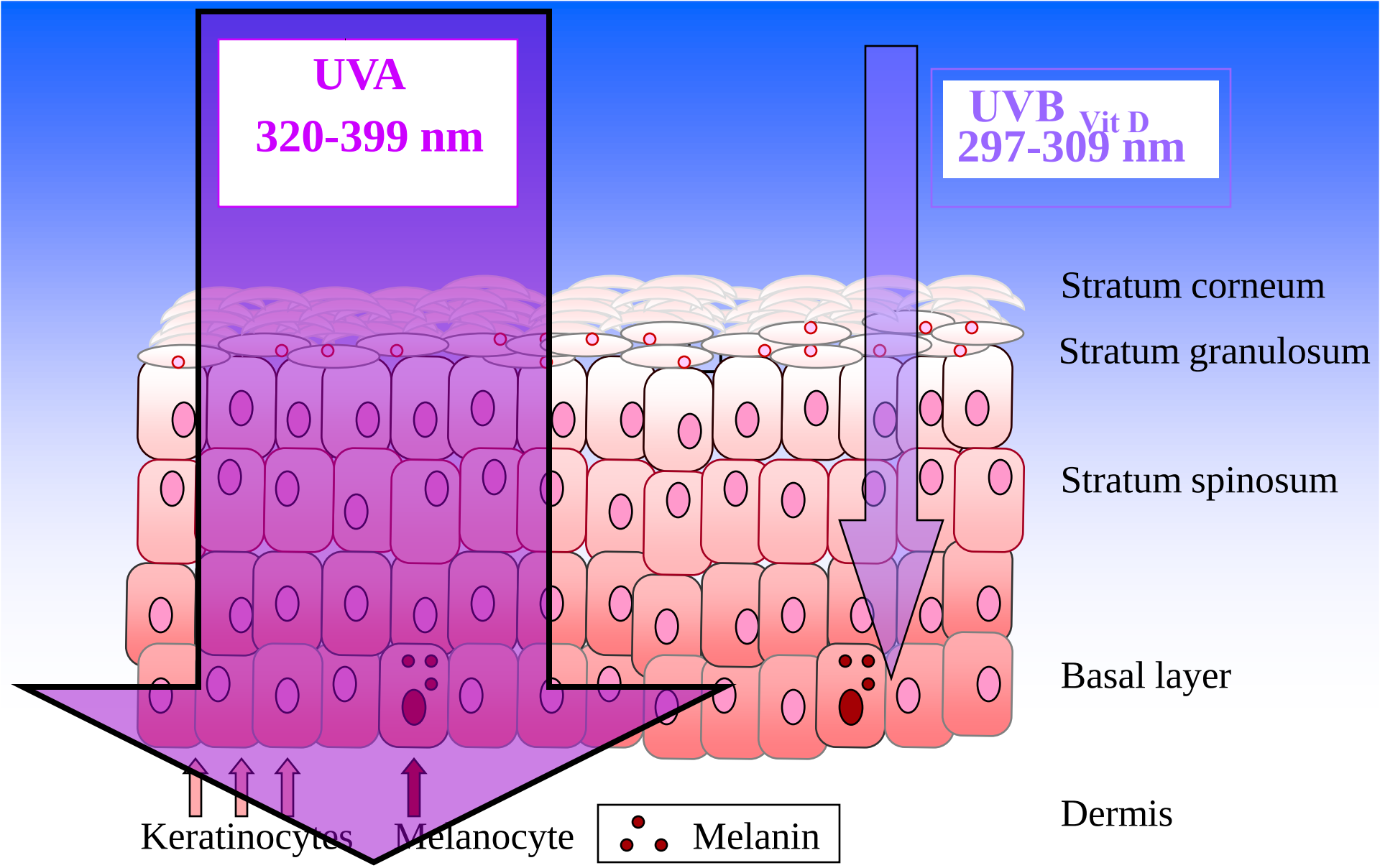


Human Photoprotective Response



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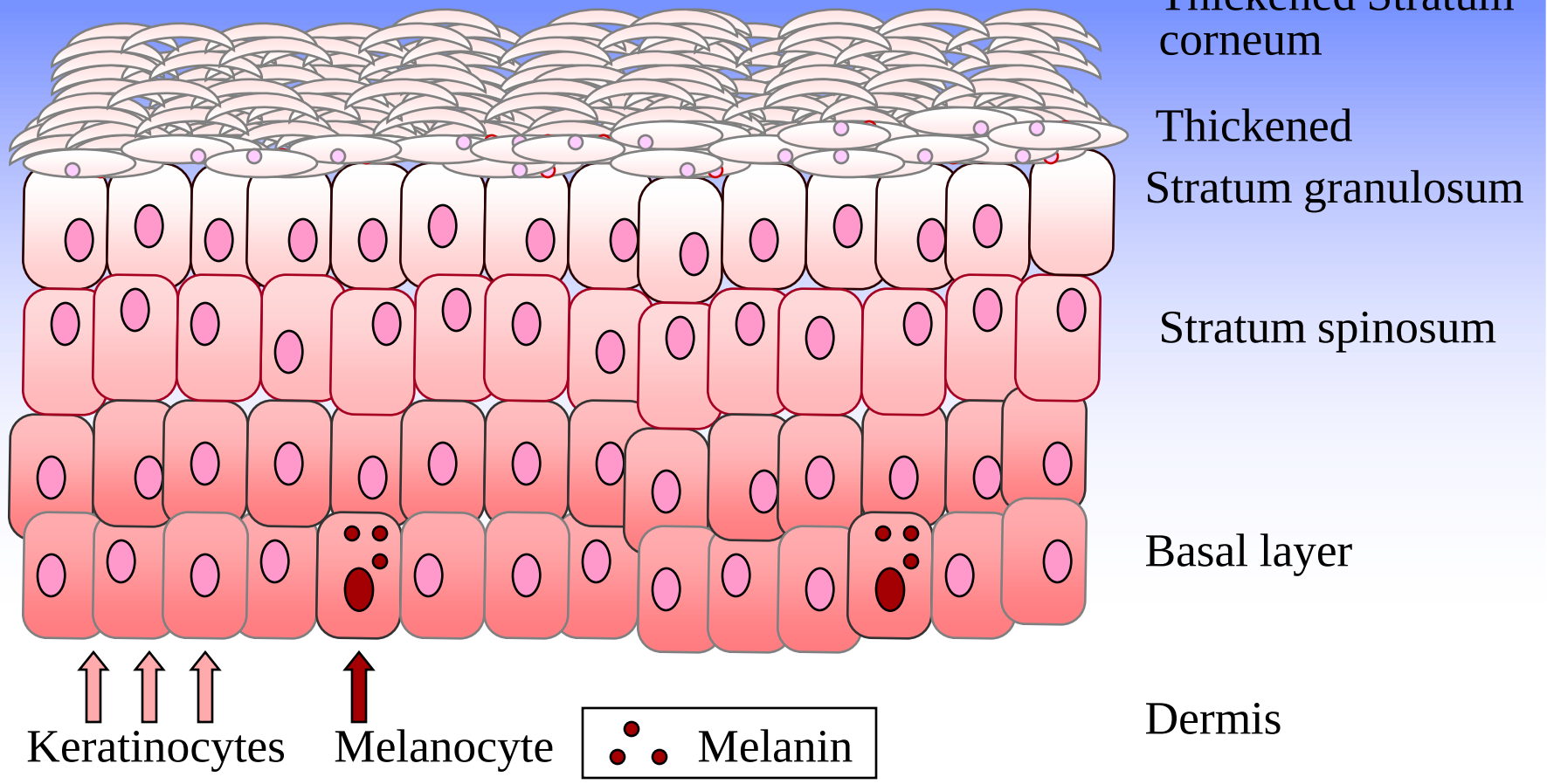

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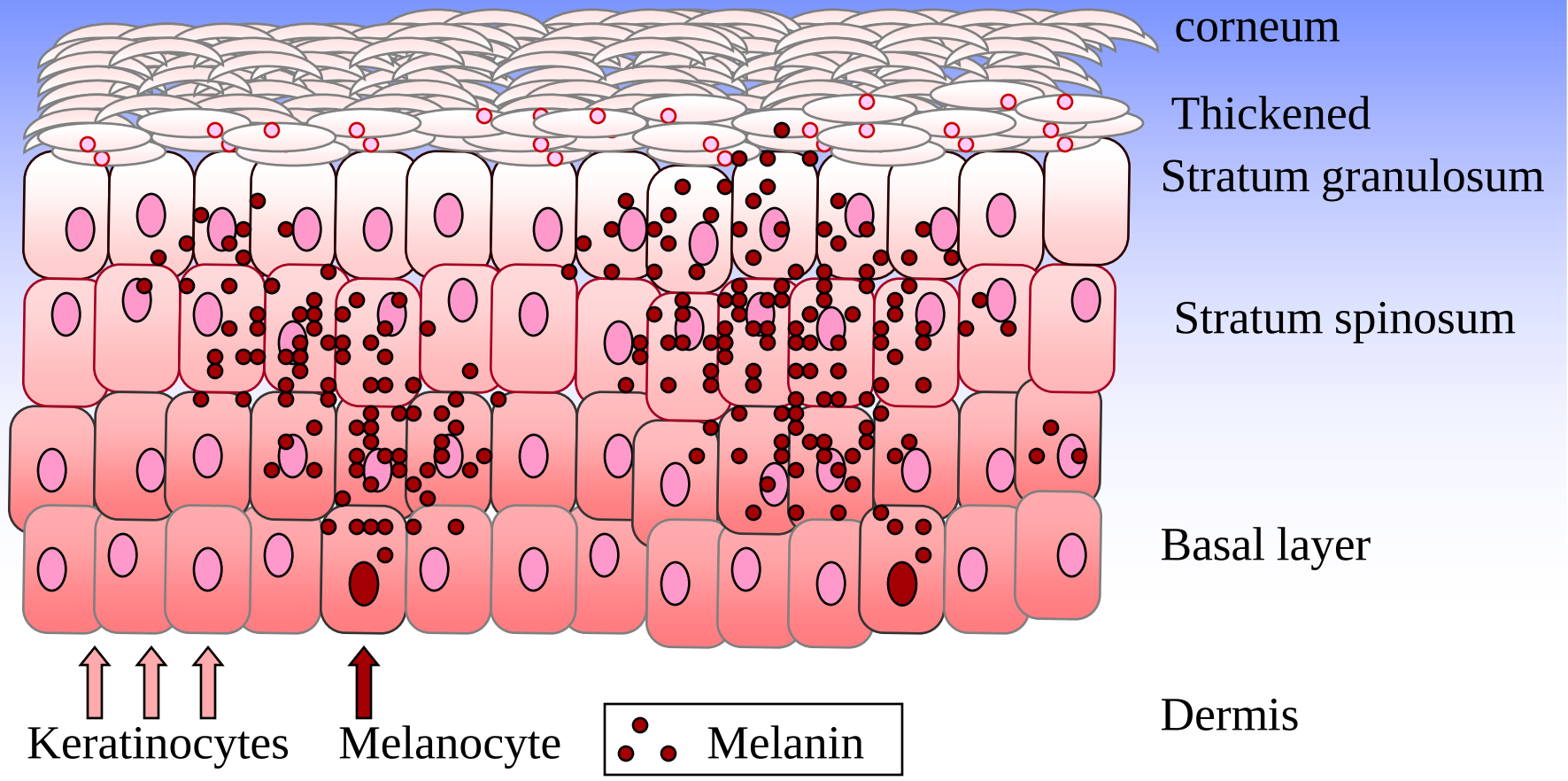

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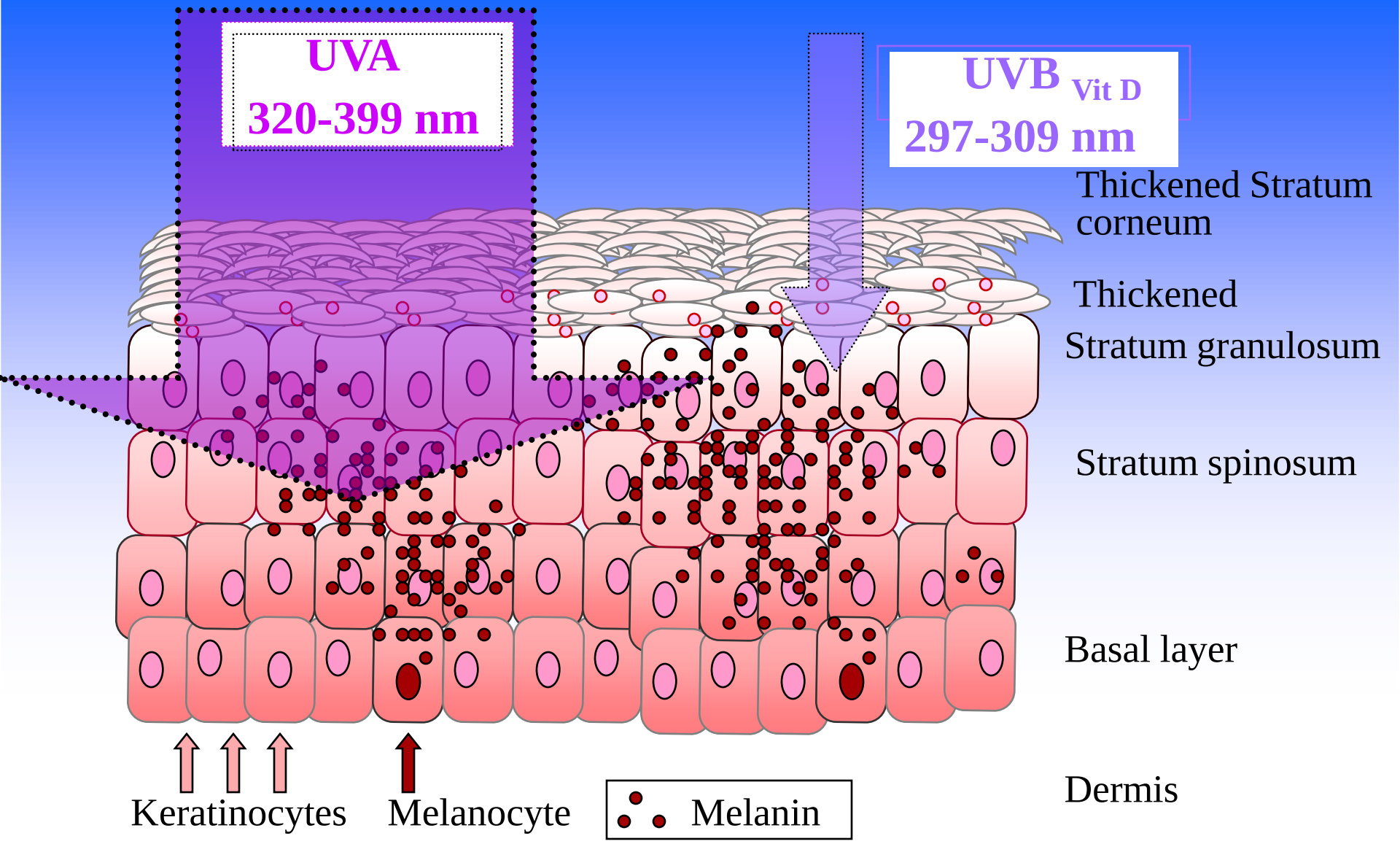

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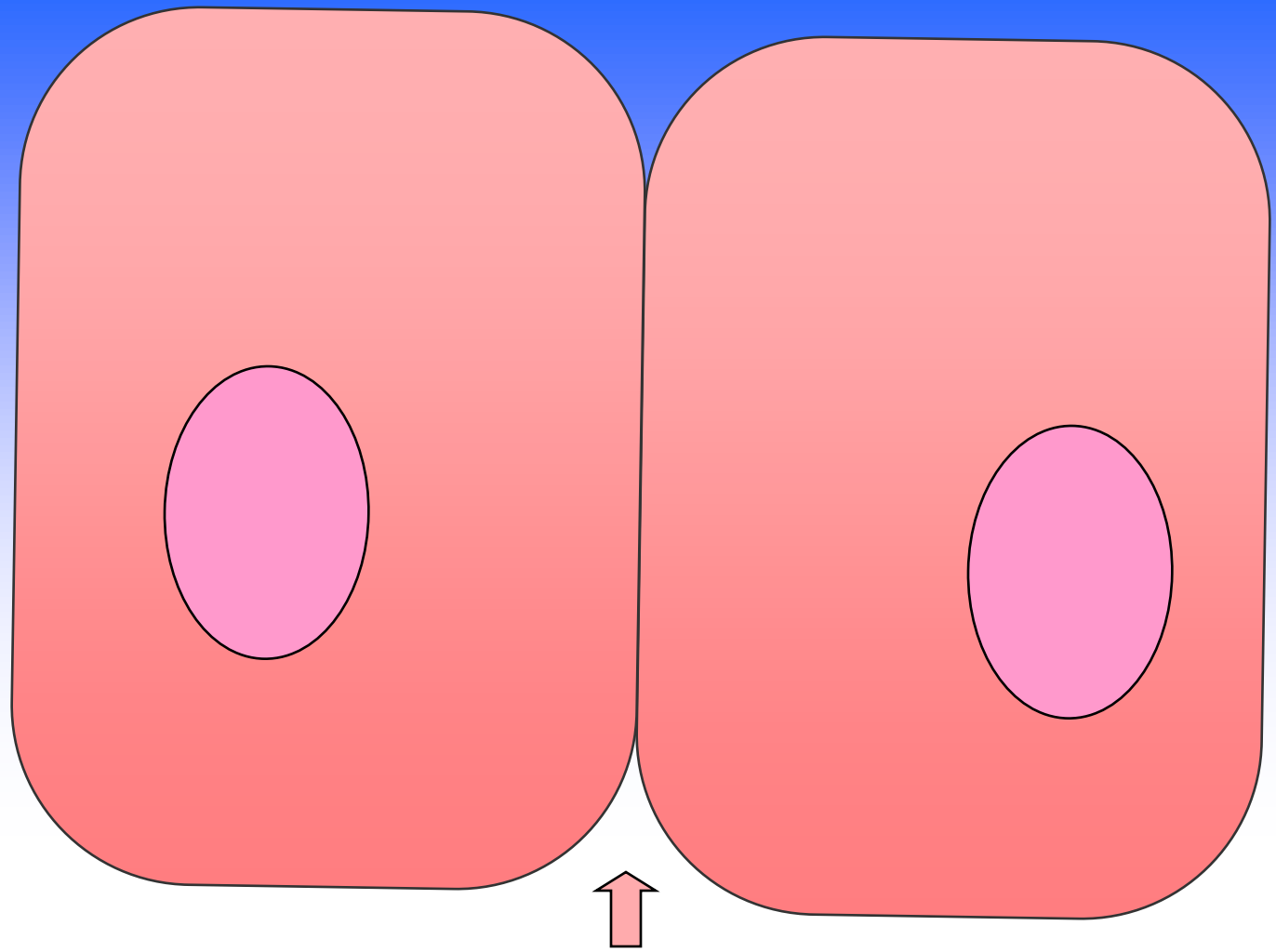
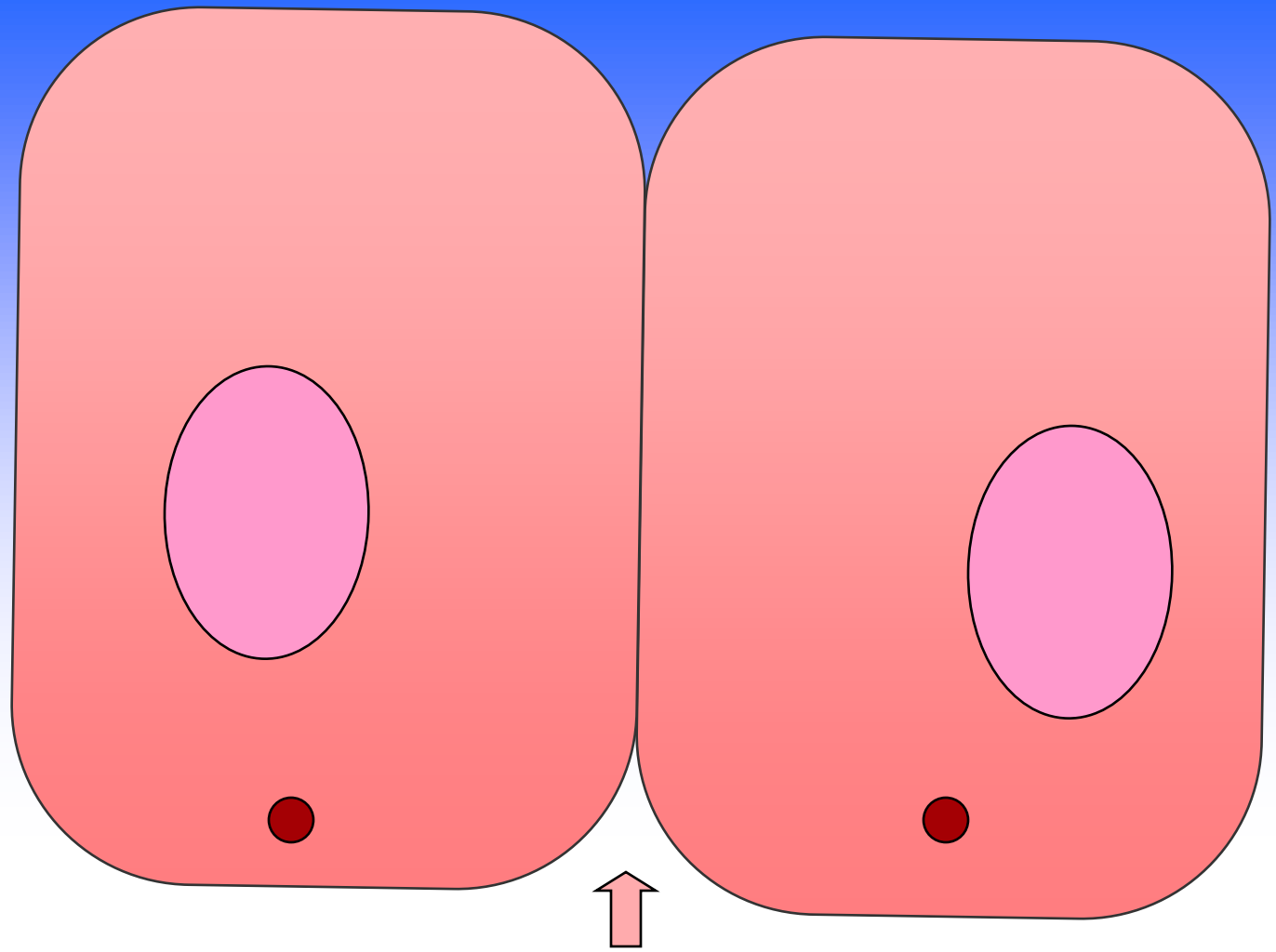


Melanosome

Keratinocytes

Melanosome migration in response to UV



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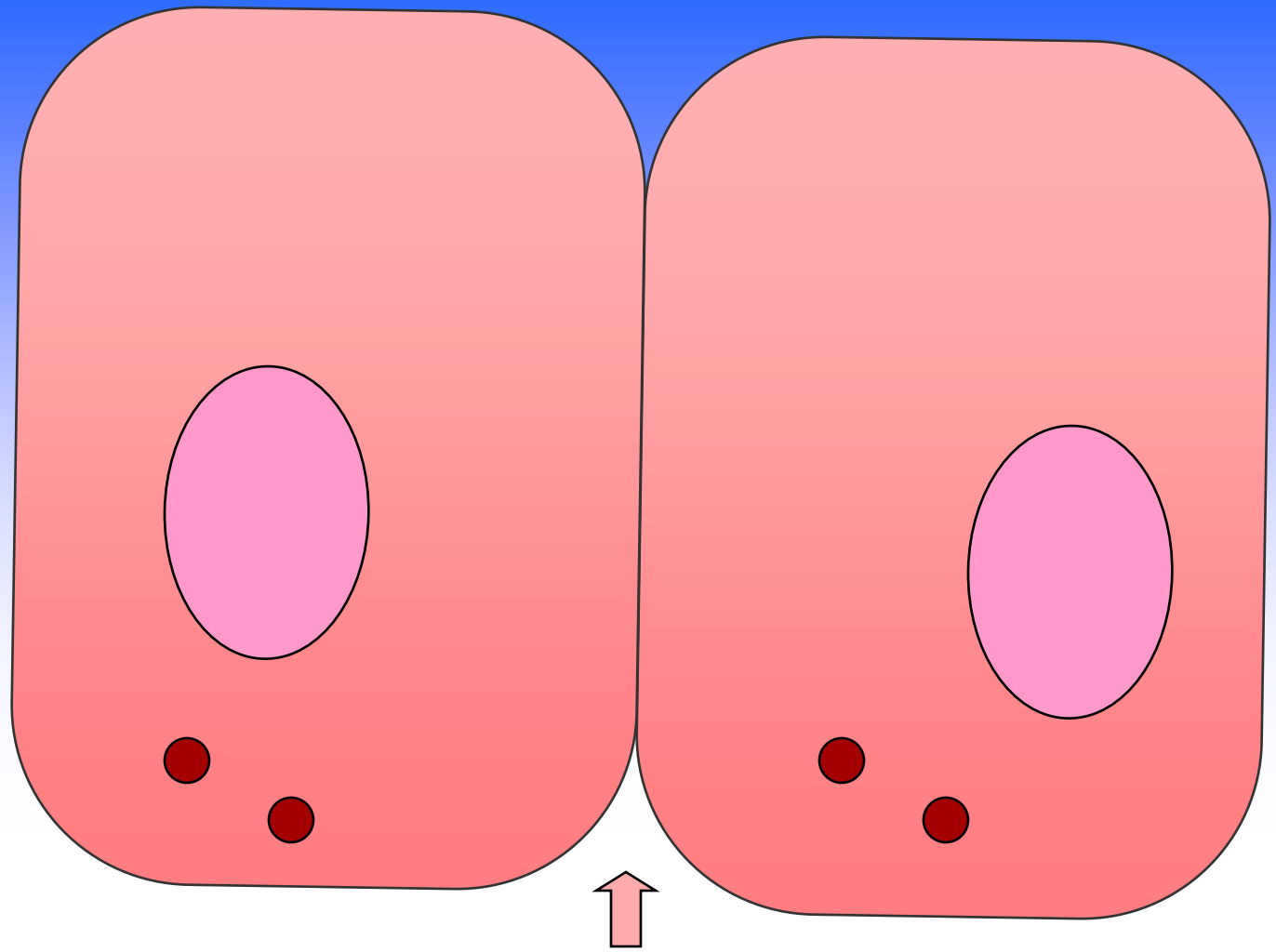

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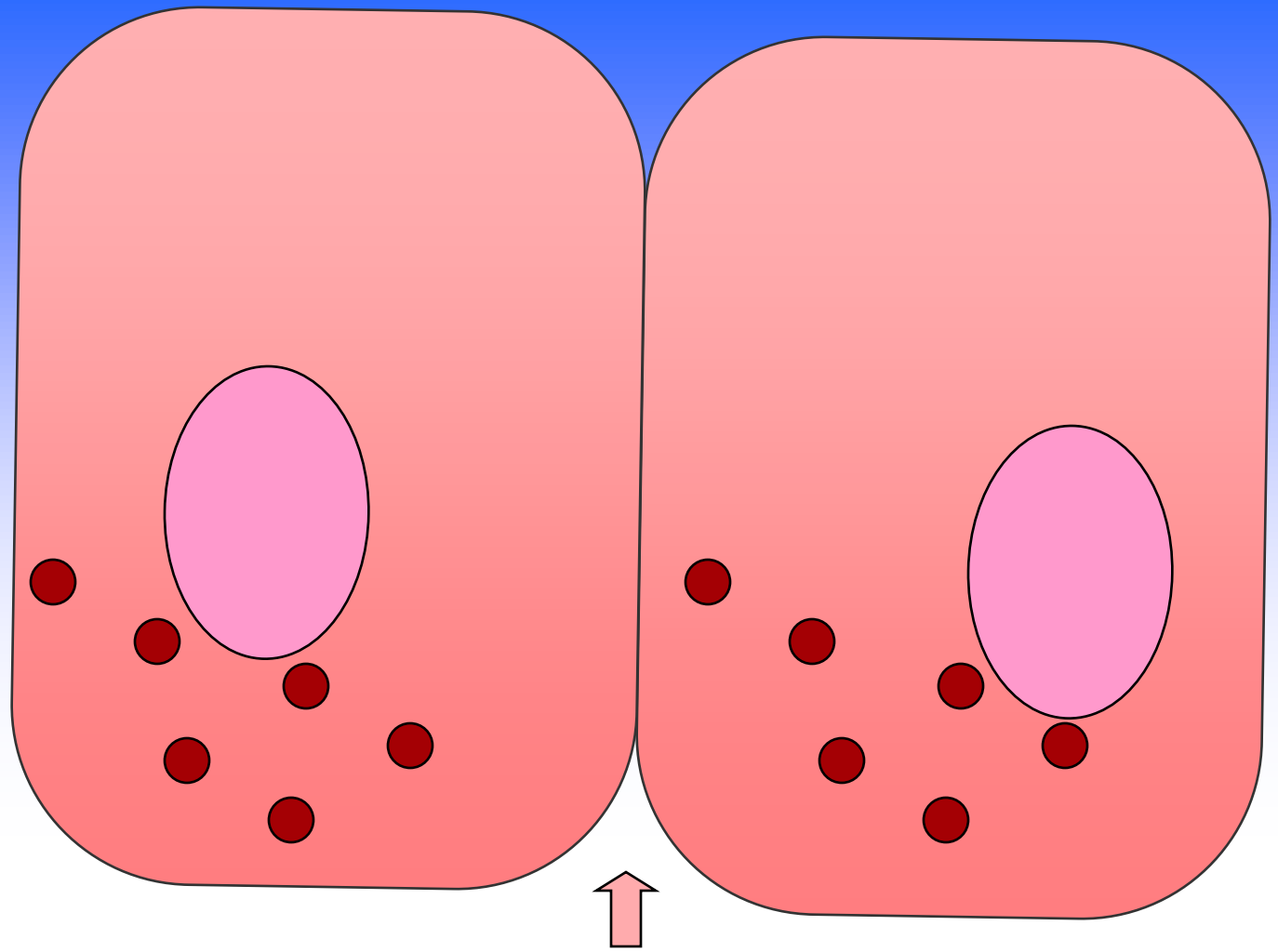

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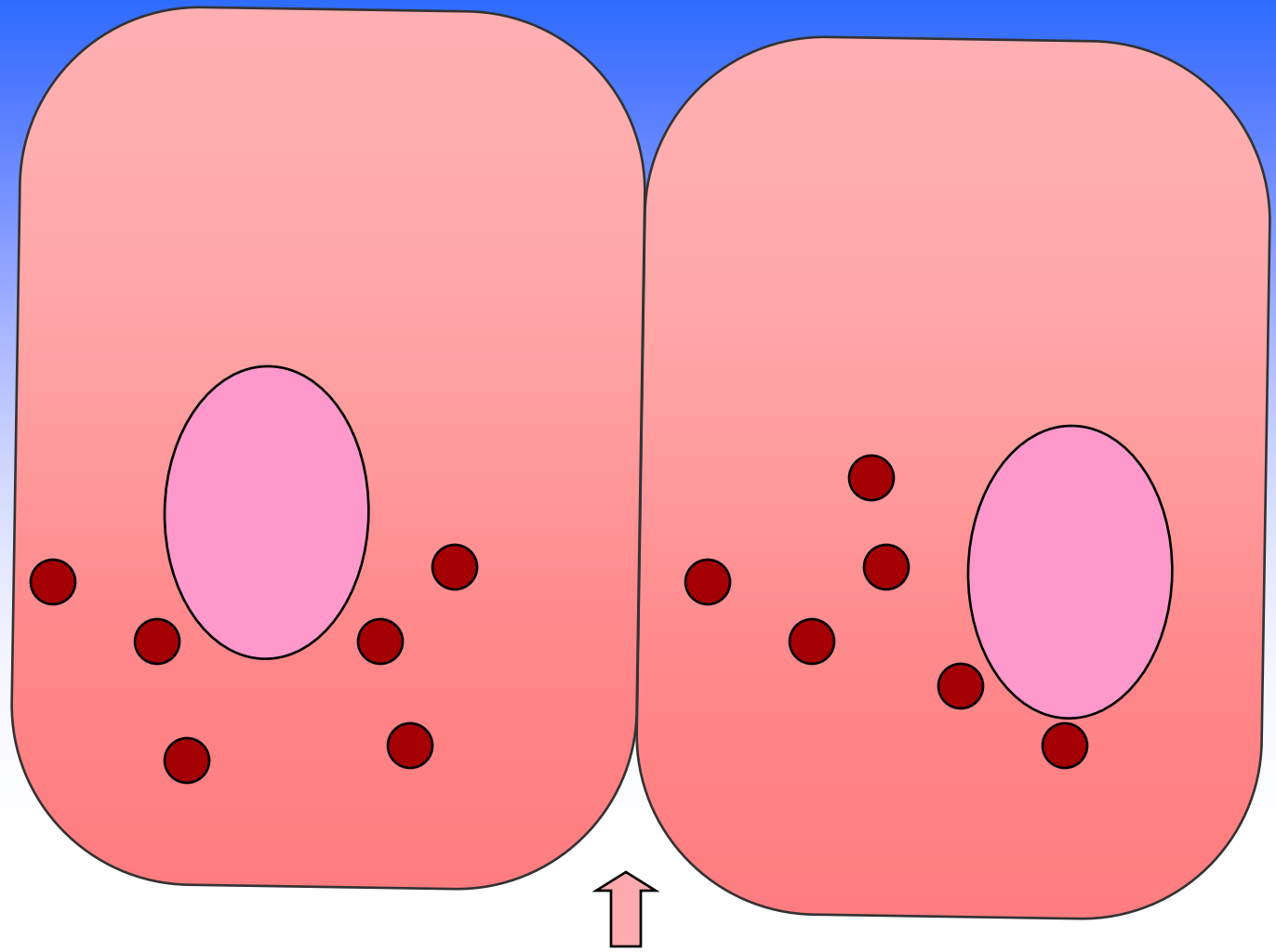

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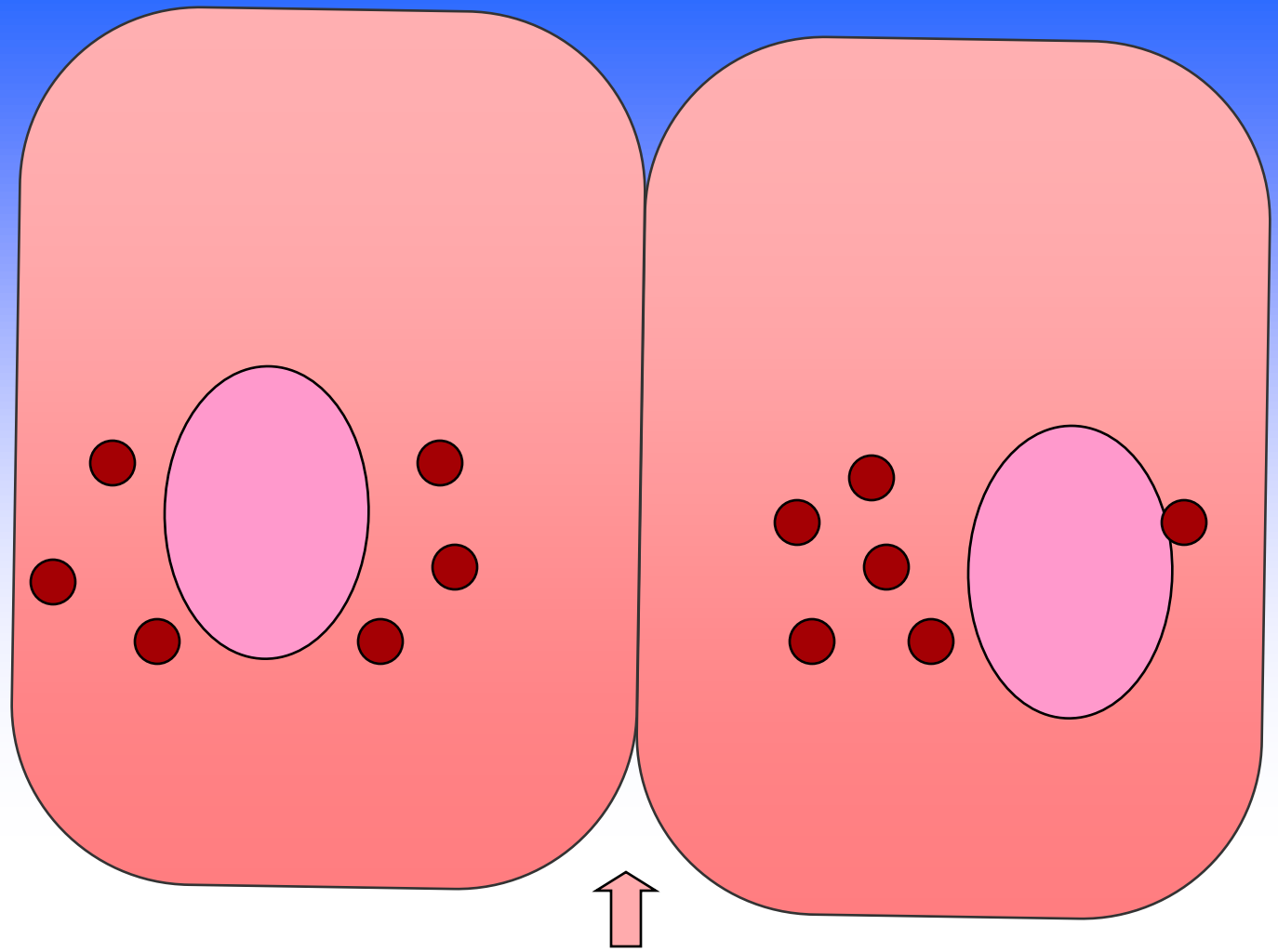

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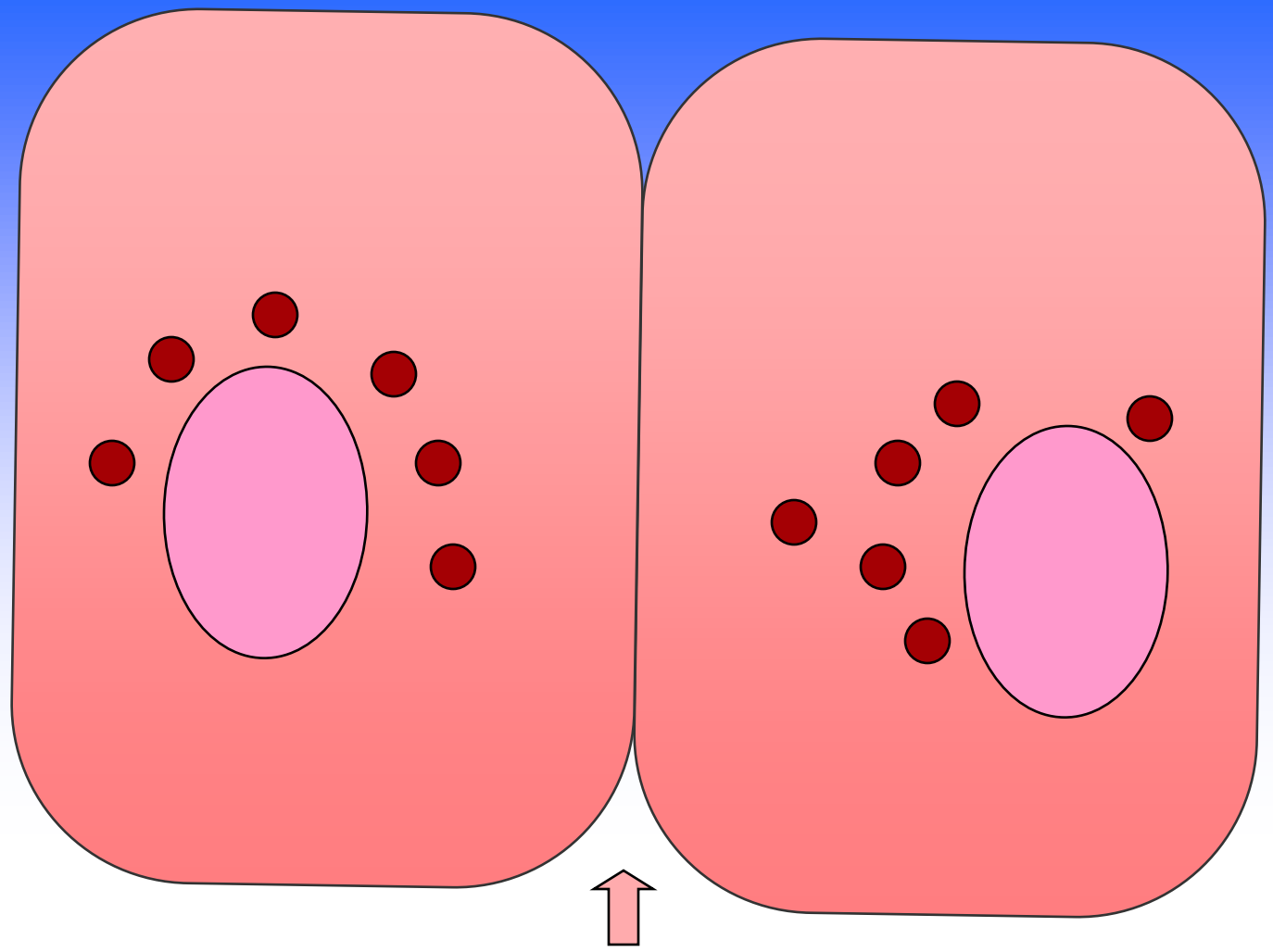

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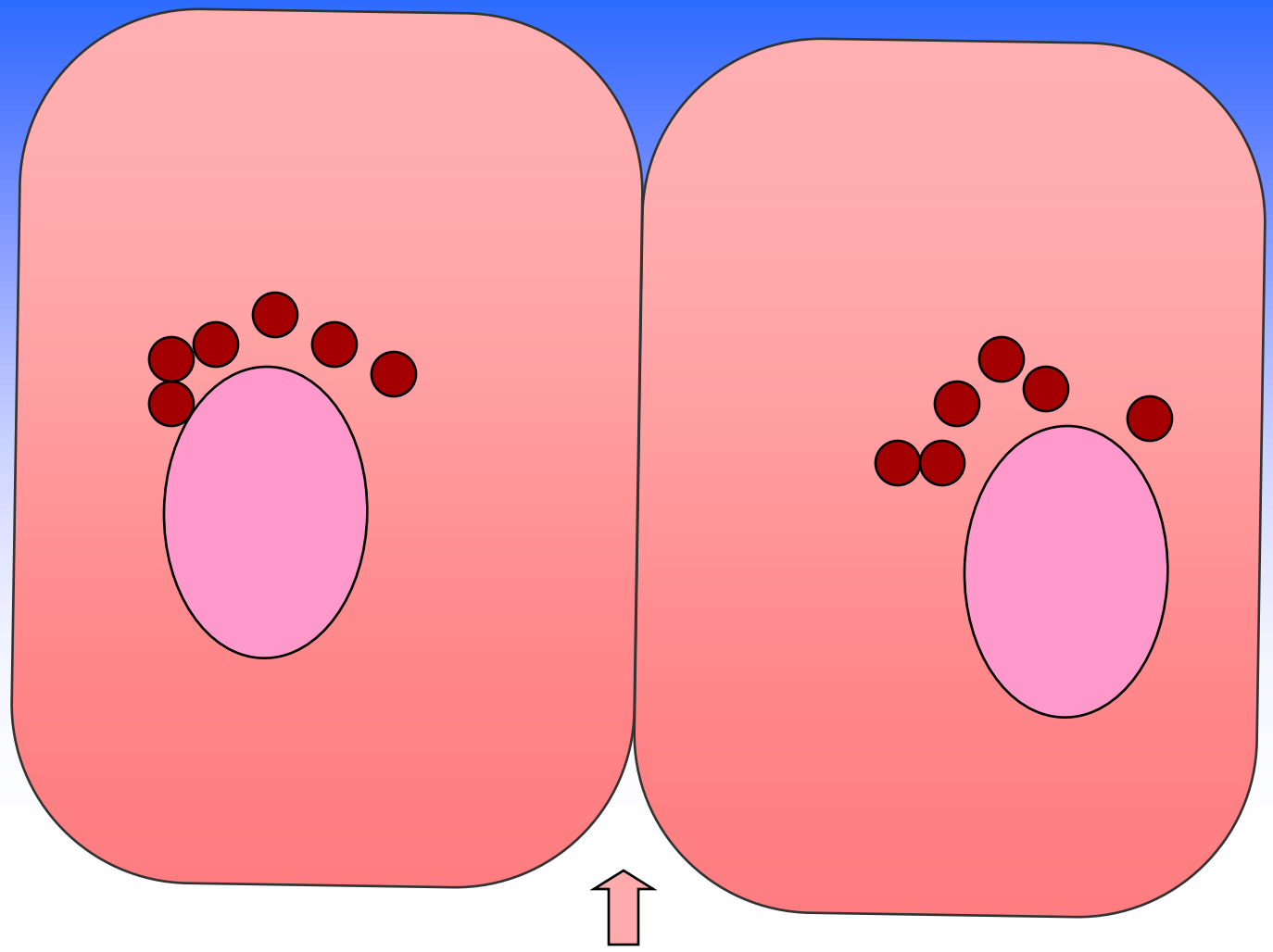

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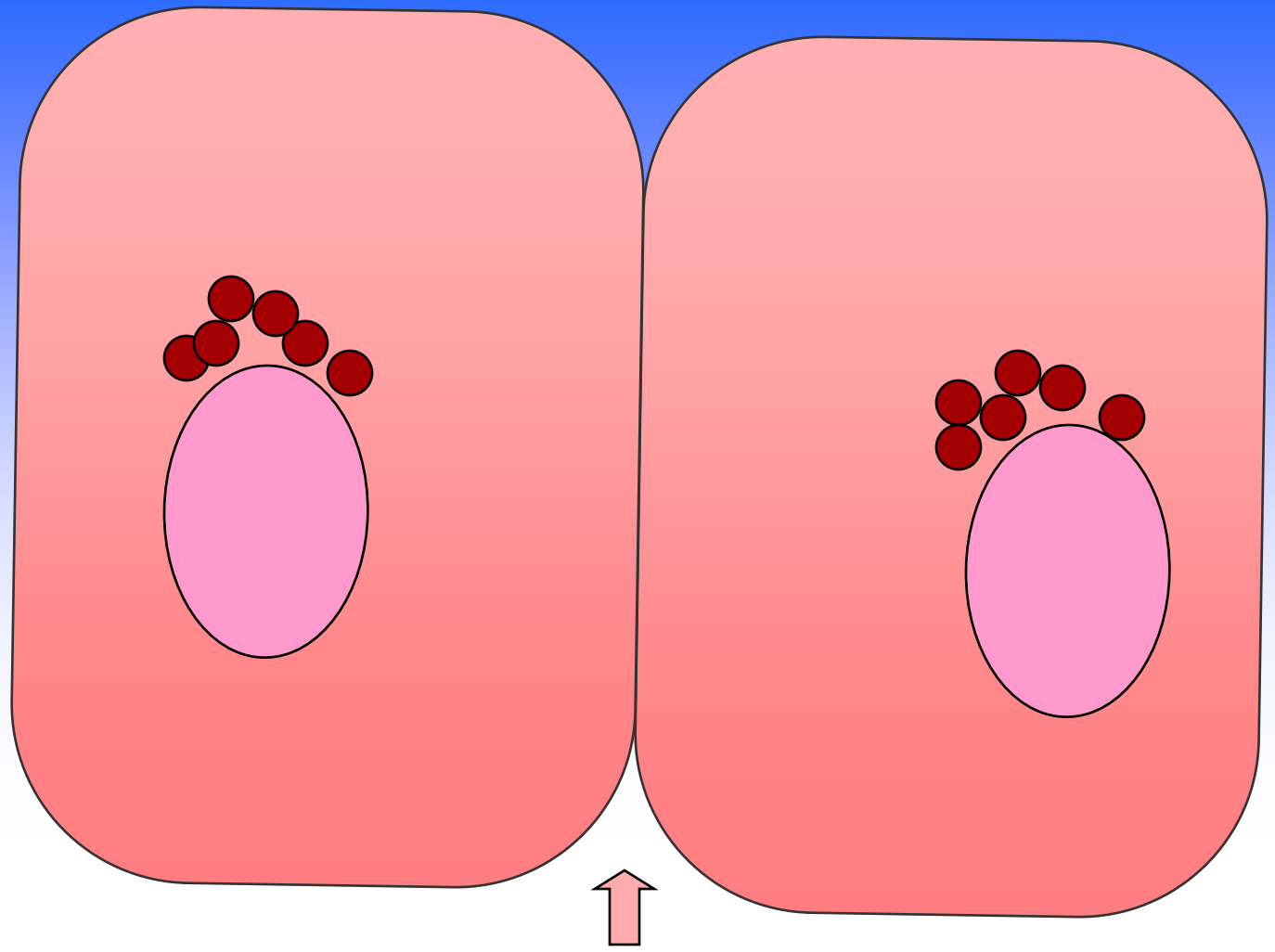
Keratinocytes

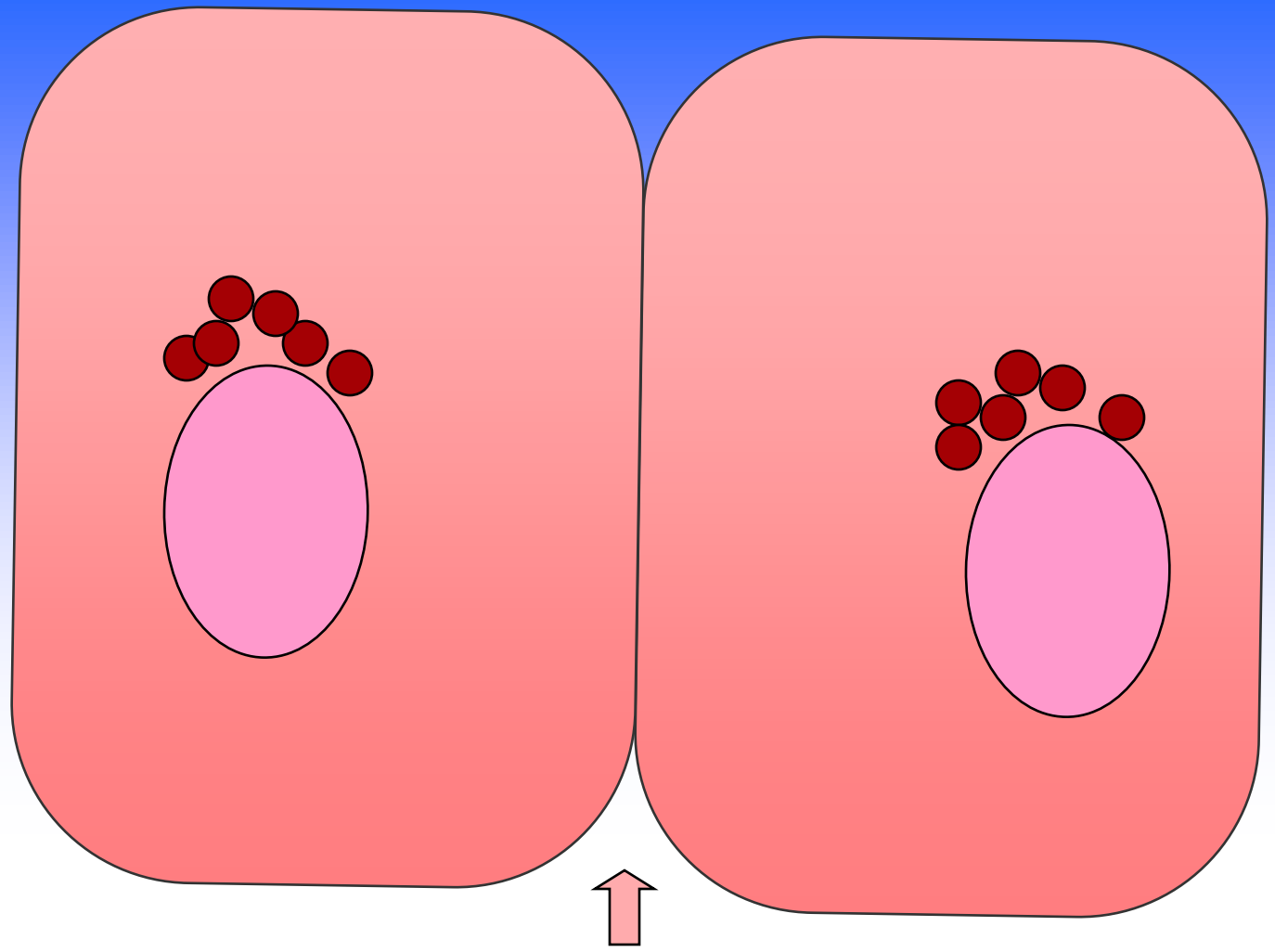
Melanosome migration in response to UV



Melanosome

Keratinocytes

Melanosome migration in response to UV



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Keratinocytes

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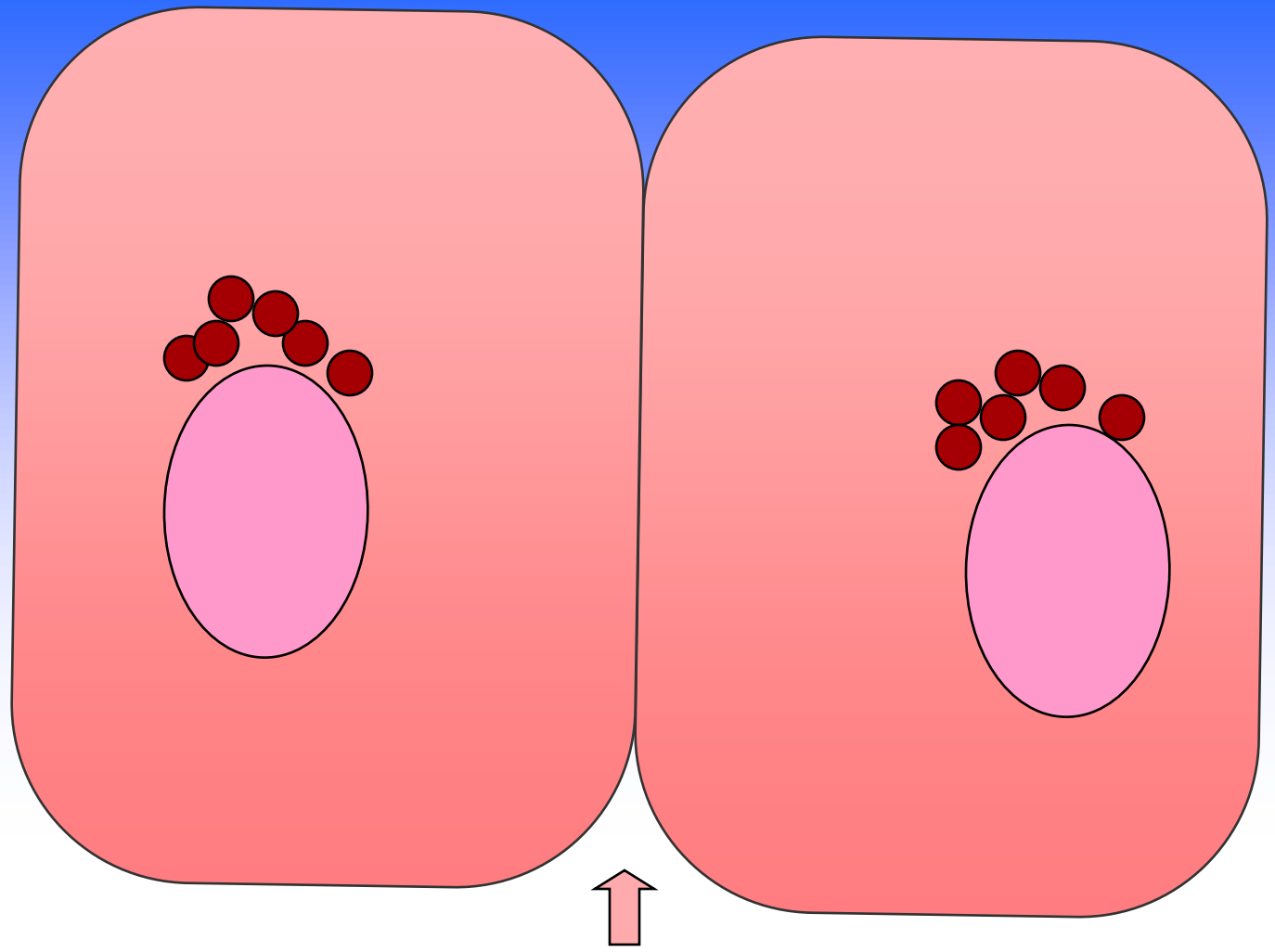


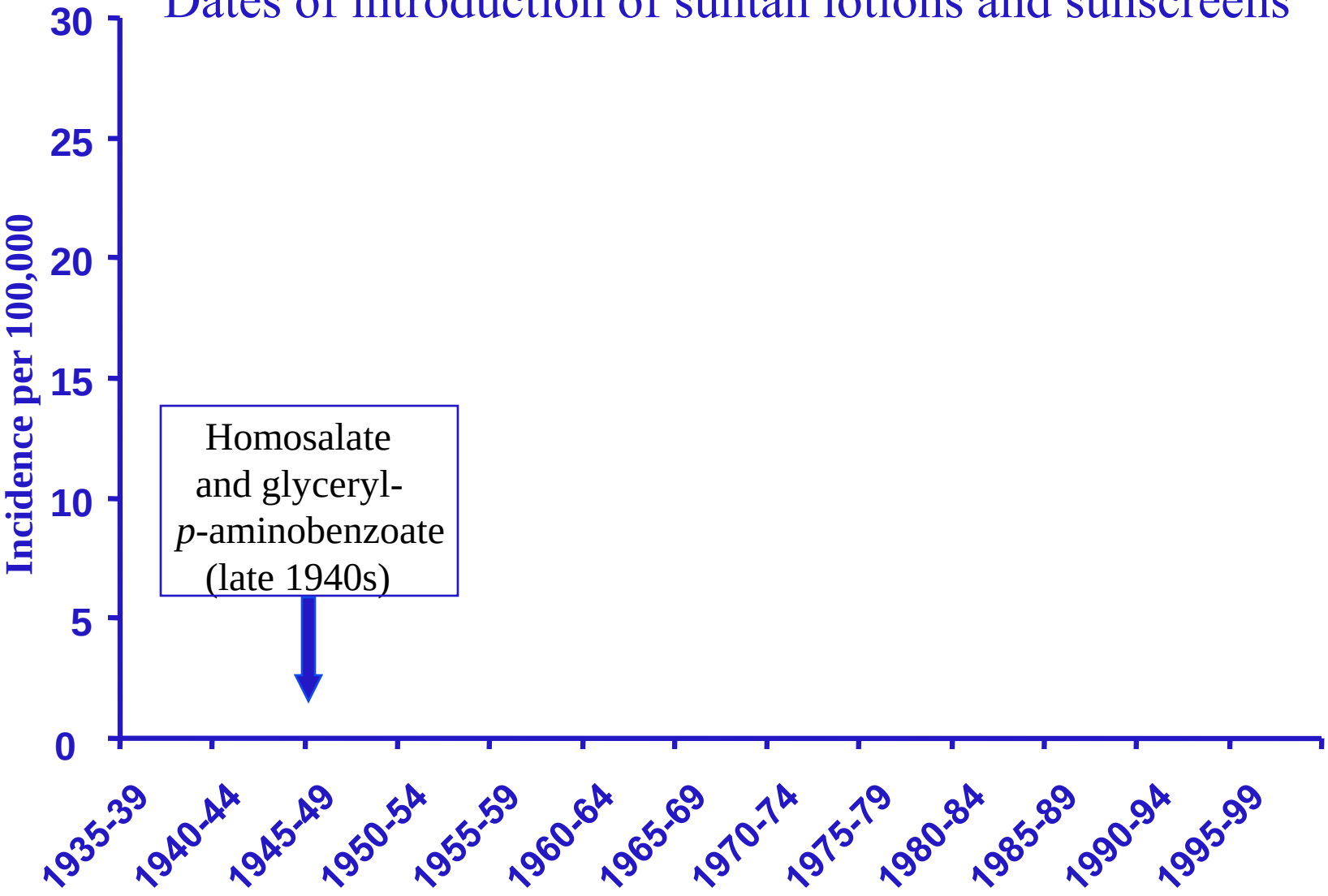
Melanosome

Keratinocytes

Melanosome migration in response to UV


INSTANT
Waterproof Protection
Coppertone
Water
BABIES
UVA/UVB SUNBLOCK LOTION
45
SPF
#1 Pediatrician
Recommended
Brand
8 FL OZ (237 mL)

Dates of introduction of suntan lotions and sunscreens



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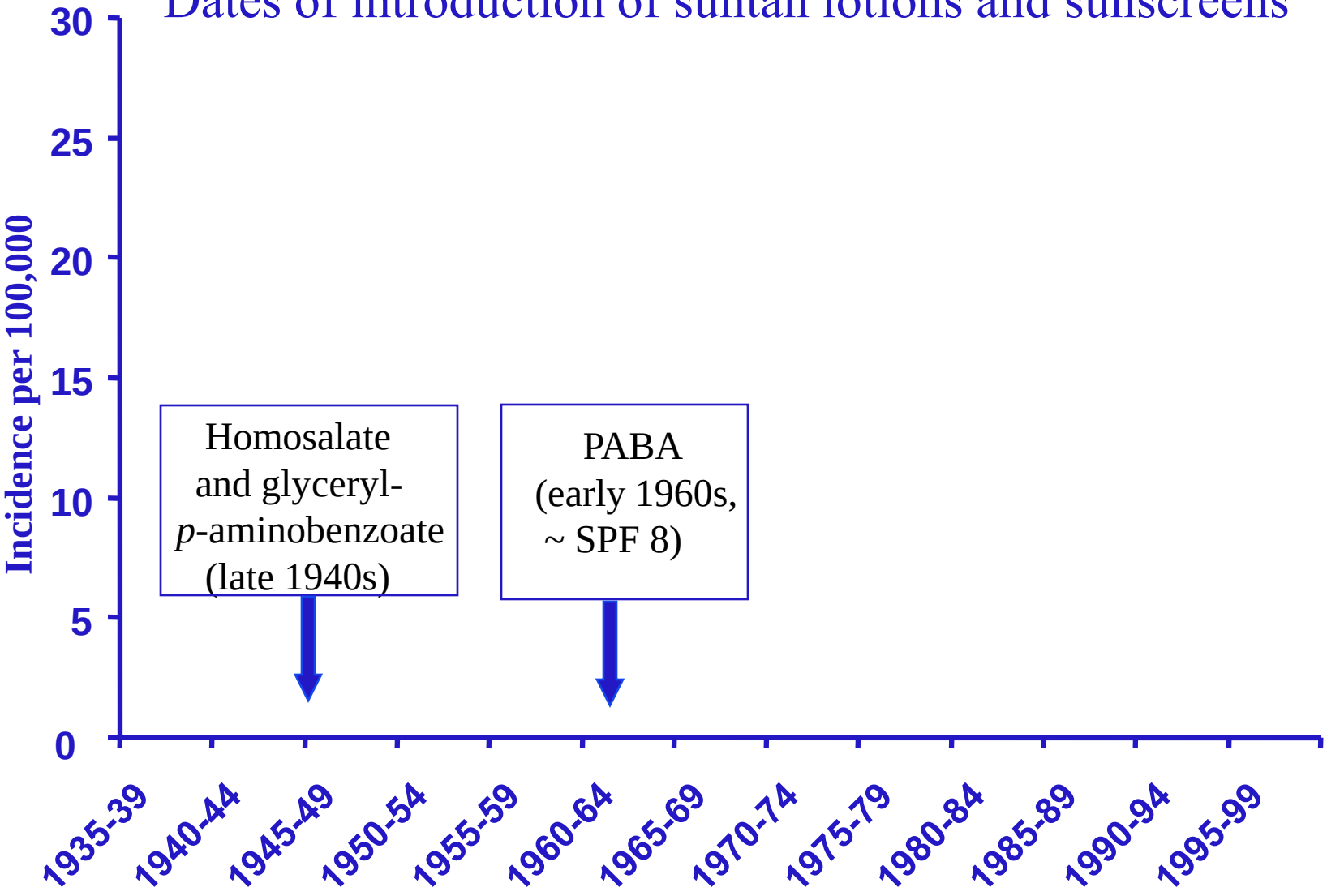
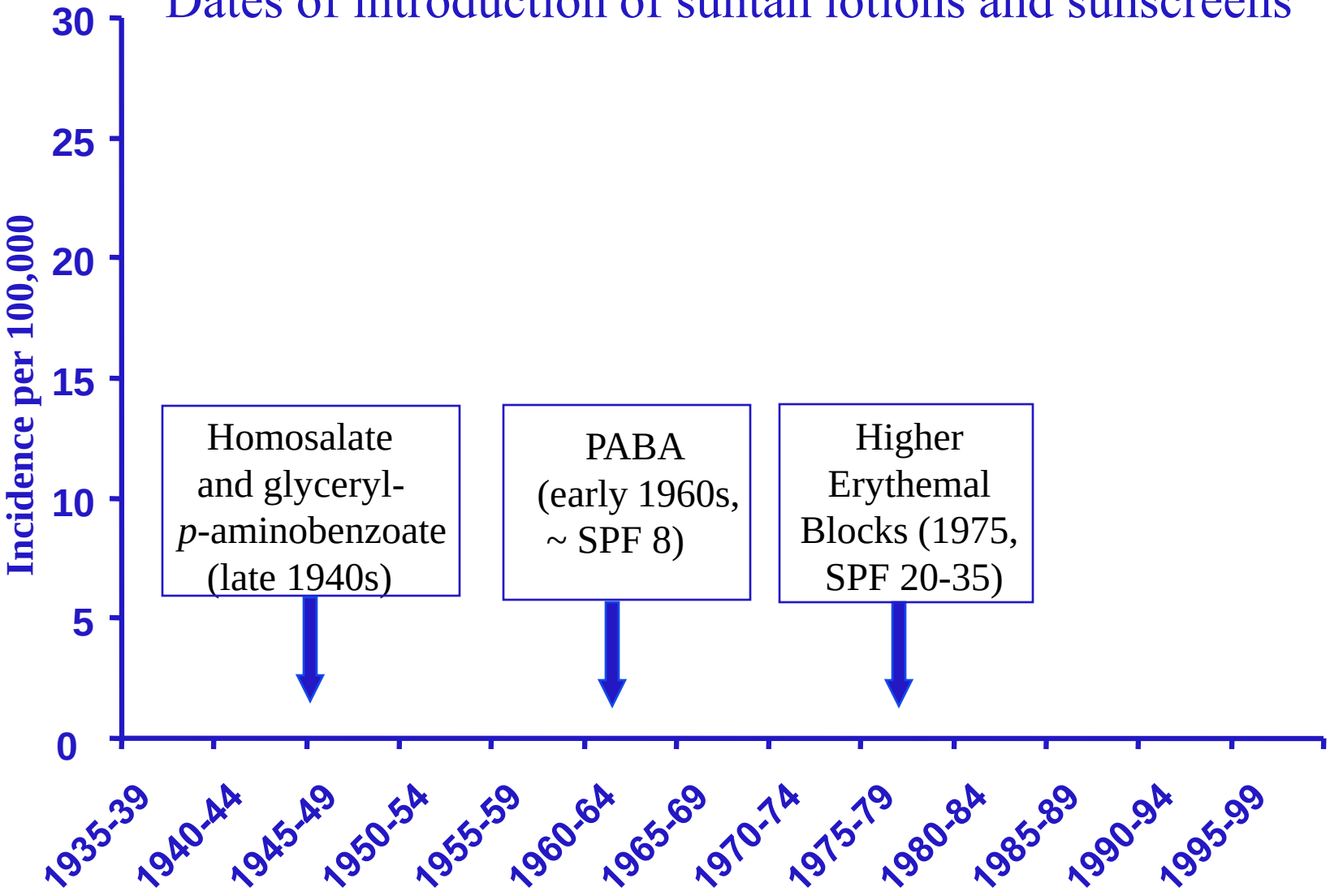
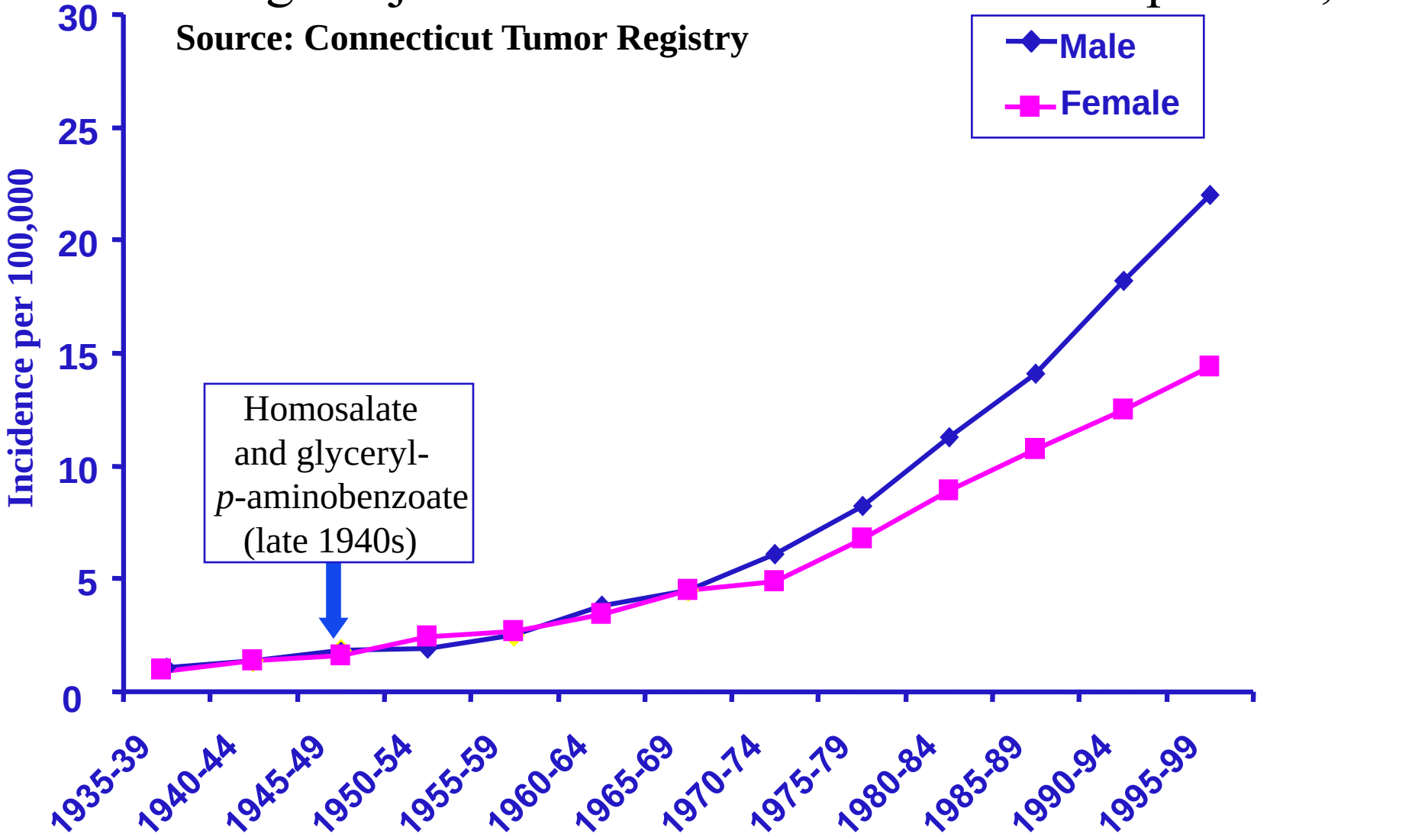


Dates of introduction of suntan lotions and sunscreens



Dates of introduction of suntan lotions and sunscreens and age-adjusted melanoma incidence rates per 100,000



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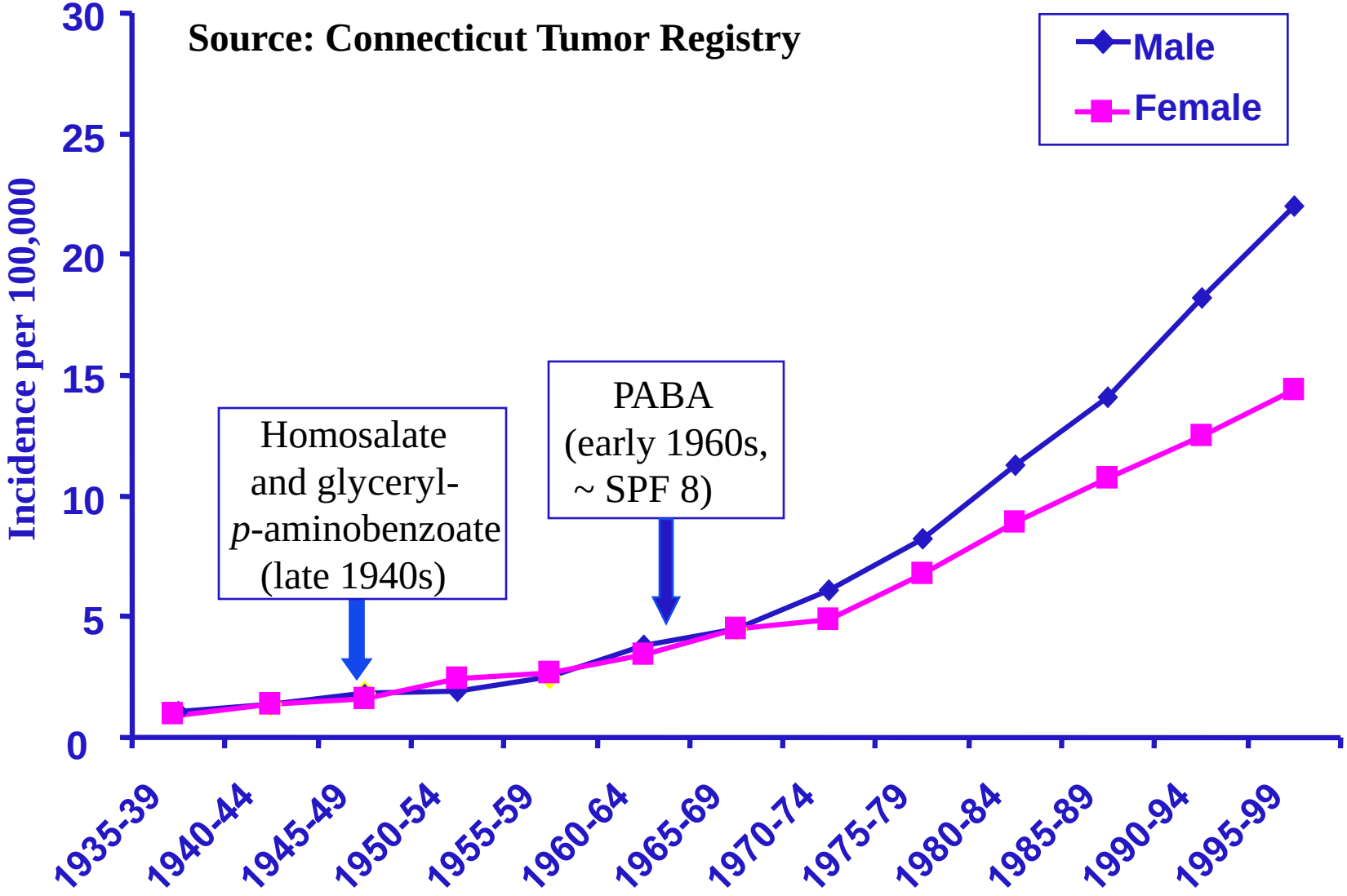

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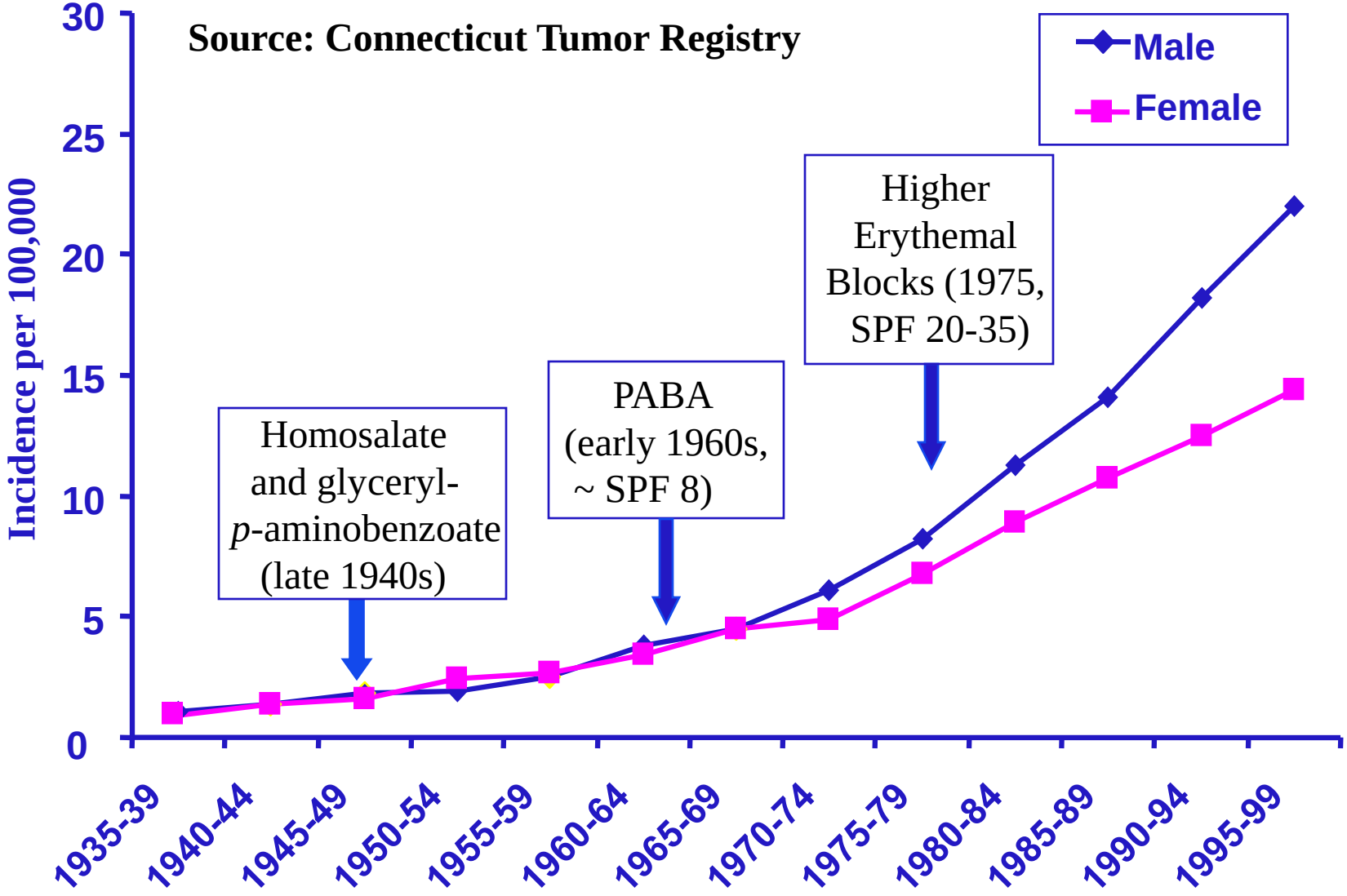
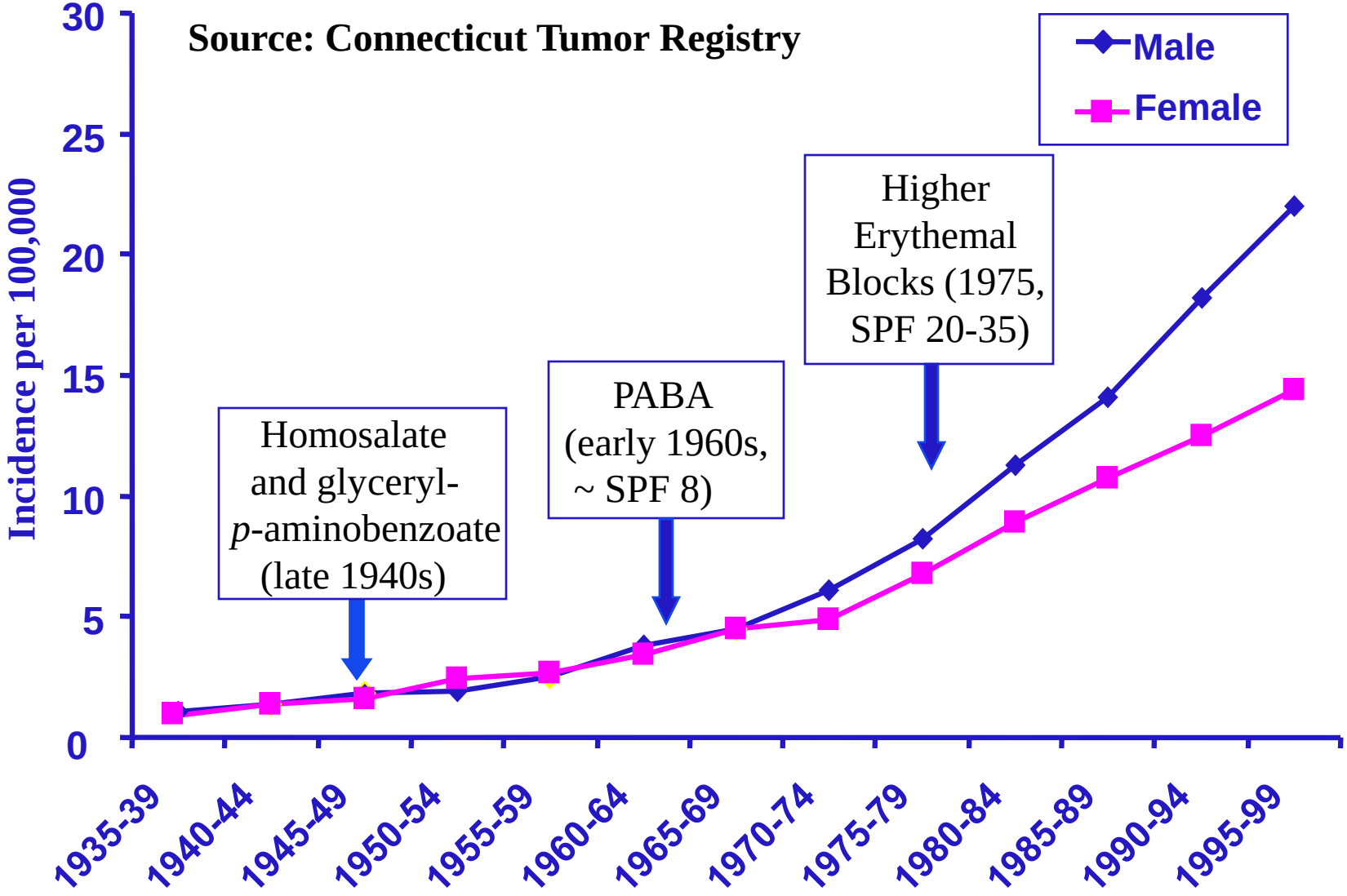
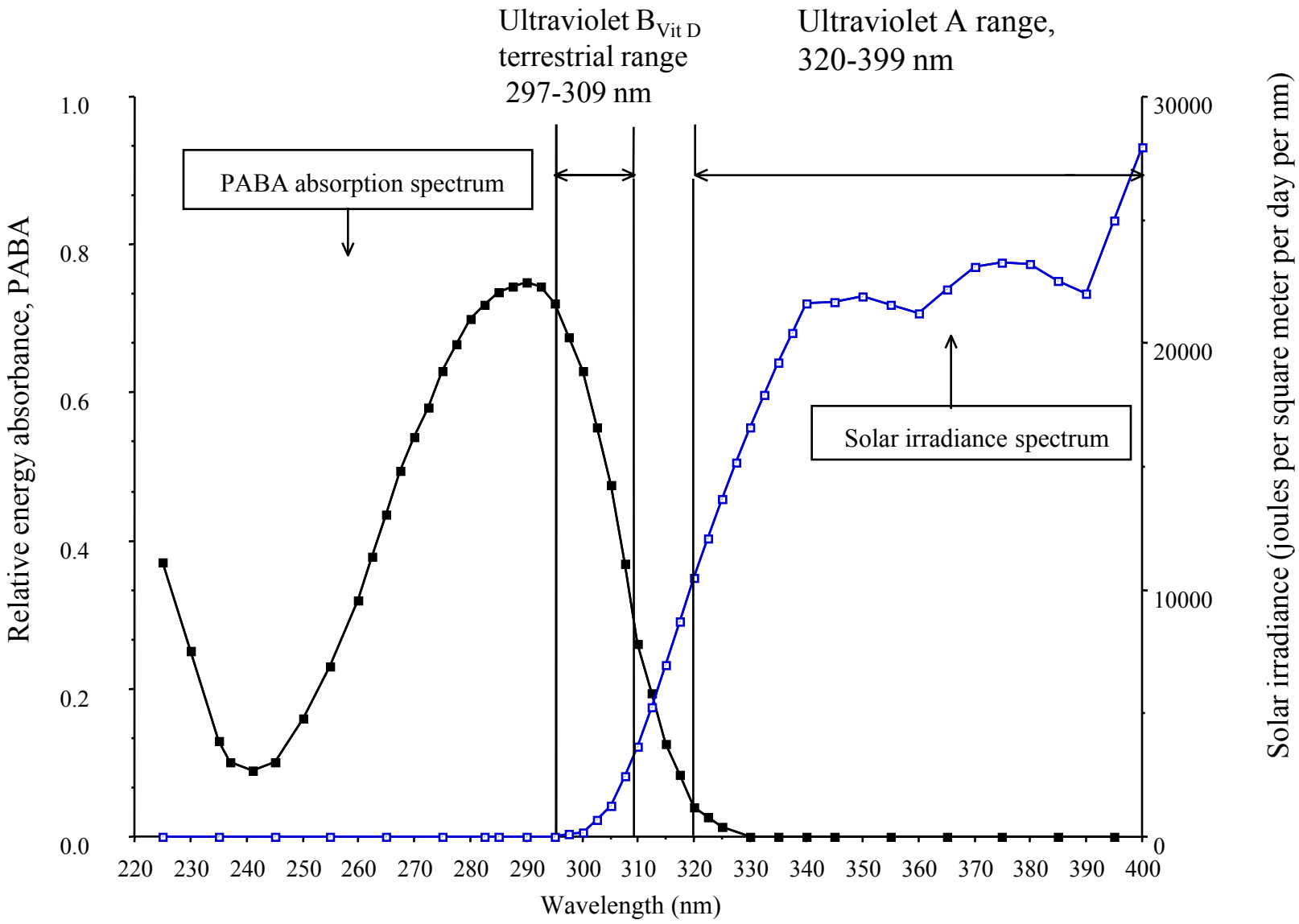
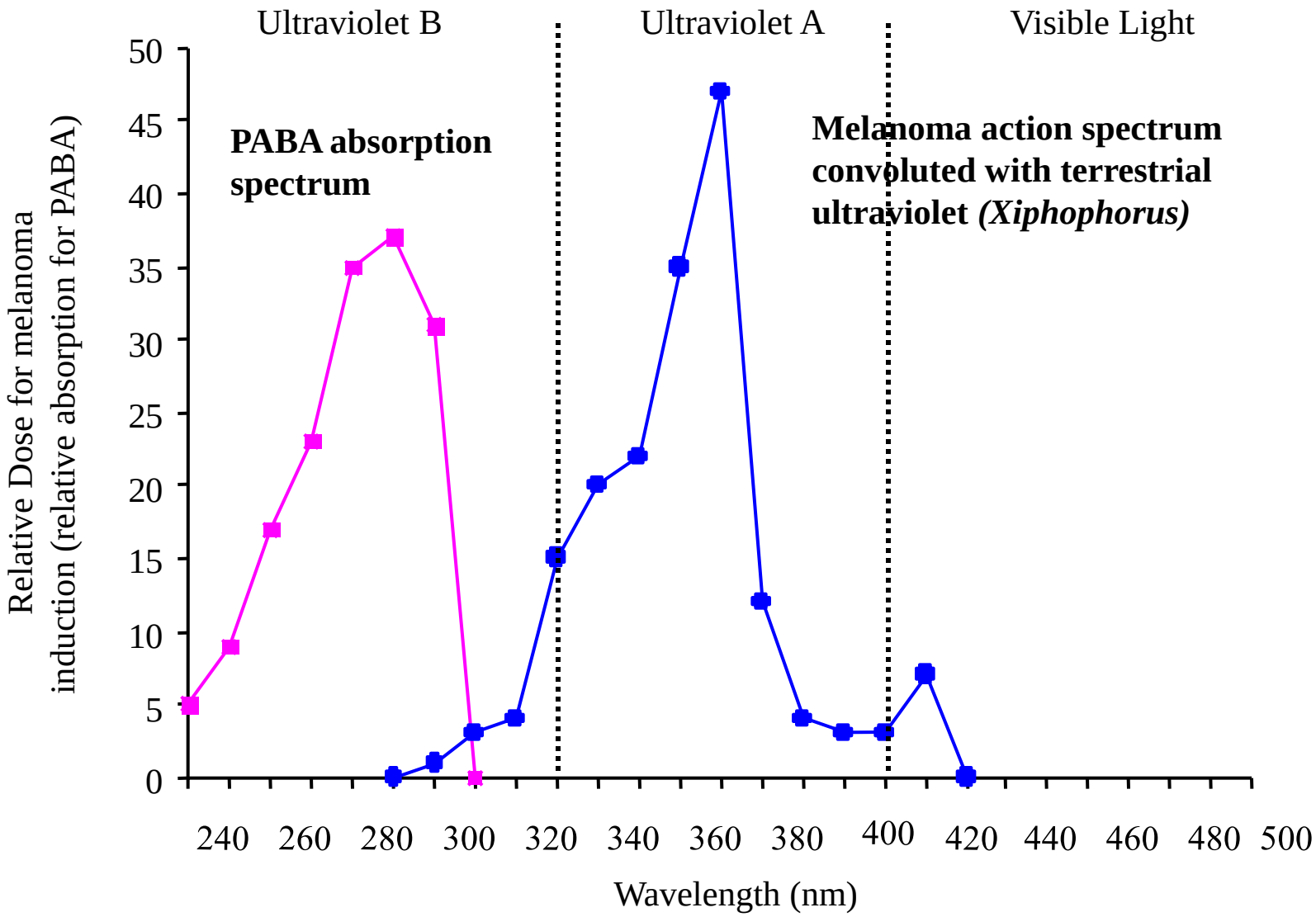


Dates of introduction of suntan lotions and sunscreens and age-adjusted melanoma incidence rates per 100,000



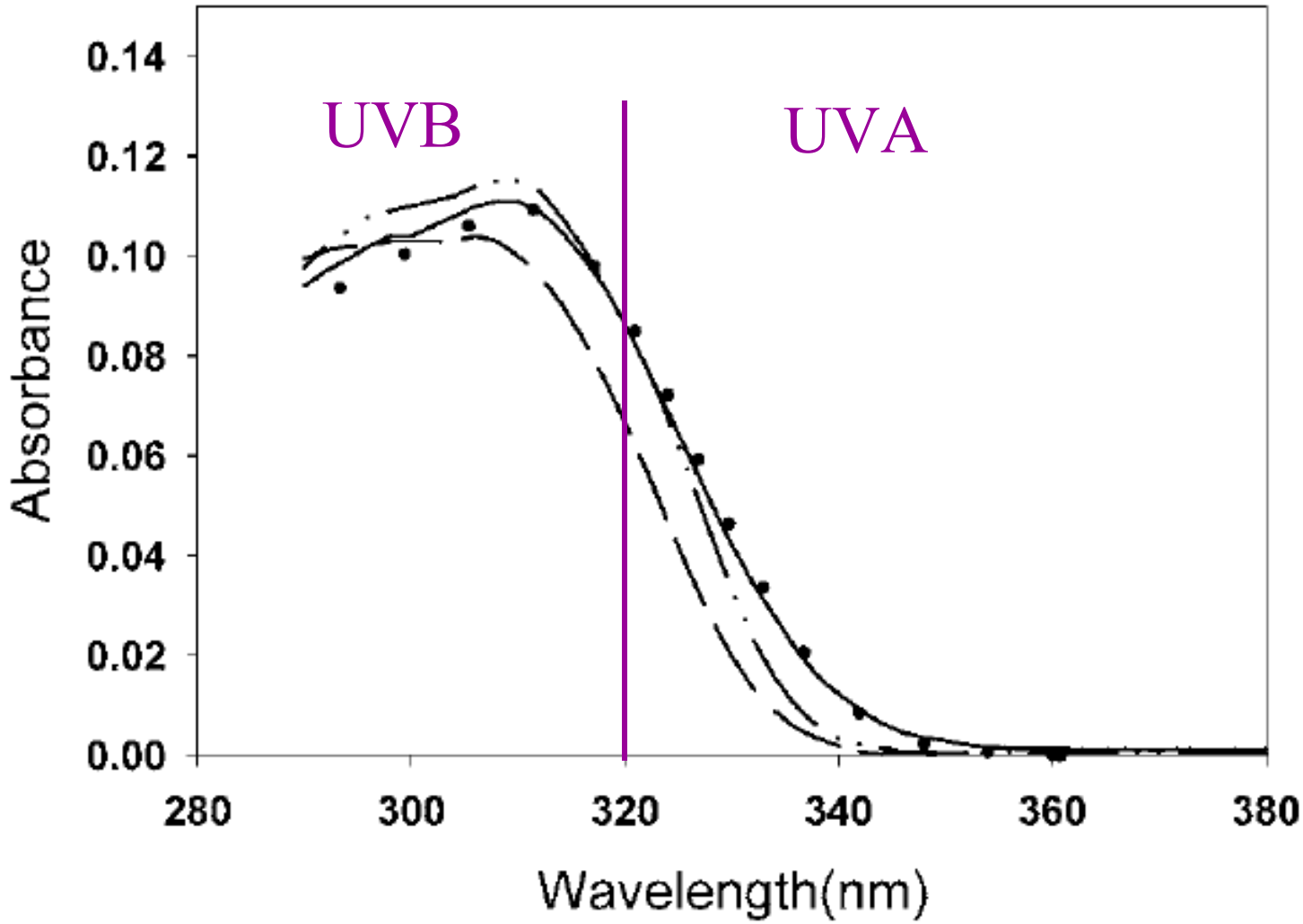


Solar ultraviolet irradiance and relative energy absorbance by para-aminobenzoic acid



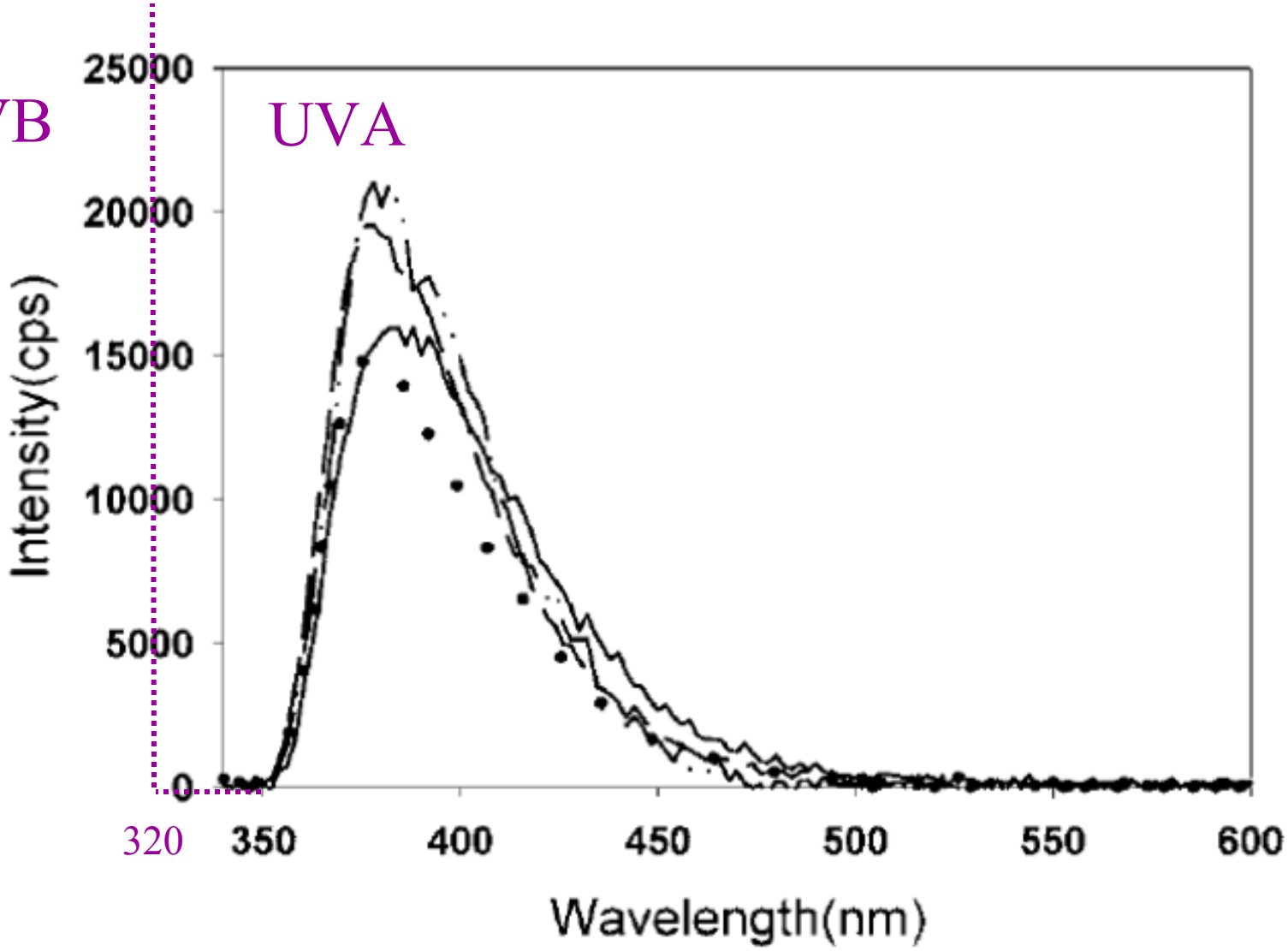
Relative absorption spectrum of PABA sunscreen agent and fish melanoma action spectrum

Source: Setlow RB, Woodhead AD. Temporal Changes in the incidence of melanoma: explanation from an action spectrum. Mutation Res 1994; 307: 365-74.



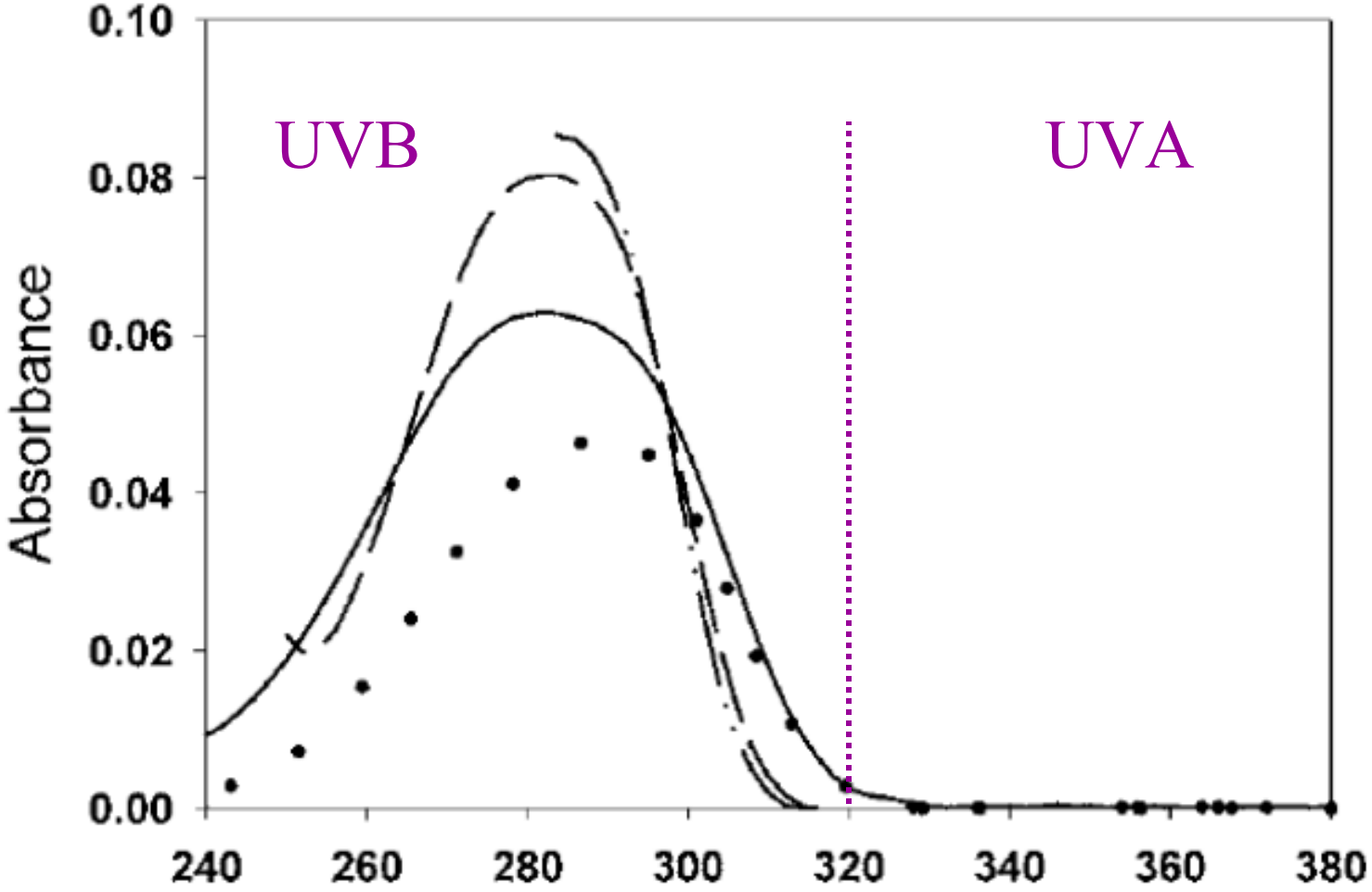
Absorption spectrum of octyl methoxycinnamate in toulene (— --); ethyl acetate (– –); 1 propanol (---); and methanol (—)

Source: Krishnan R, Carr A, Blair E, Nordlund TM. Optical spectroscopy of hydrophobic sunscreen molecules adsorbed to dielectric nanospheres.Photochem Photobiol. 2004 Jun;79(6):531-9



Emission spectrum of octyl methoxycinnamate
in toulene (— --); ethyl acetate (– –); 1 propanol (---); and methanol (—)

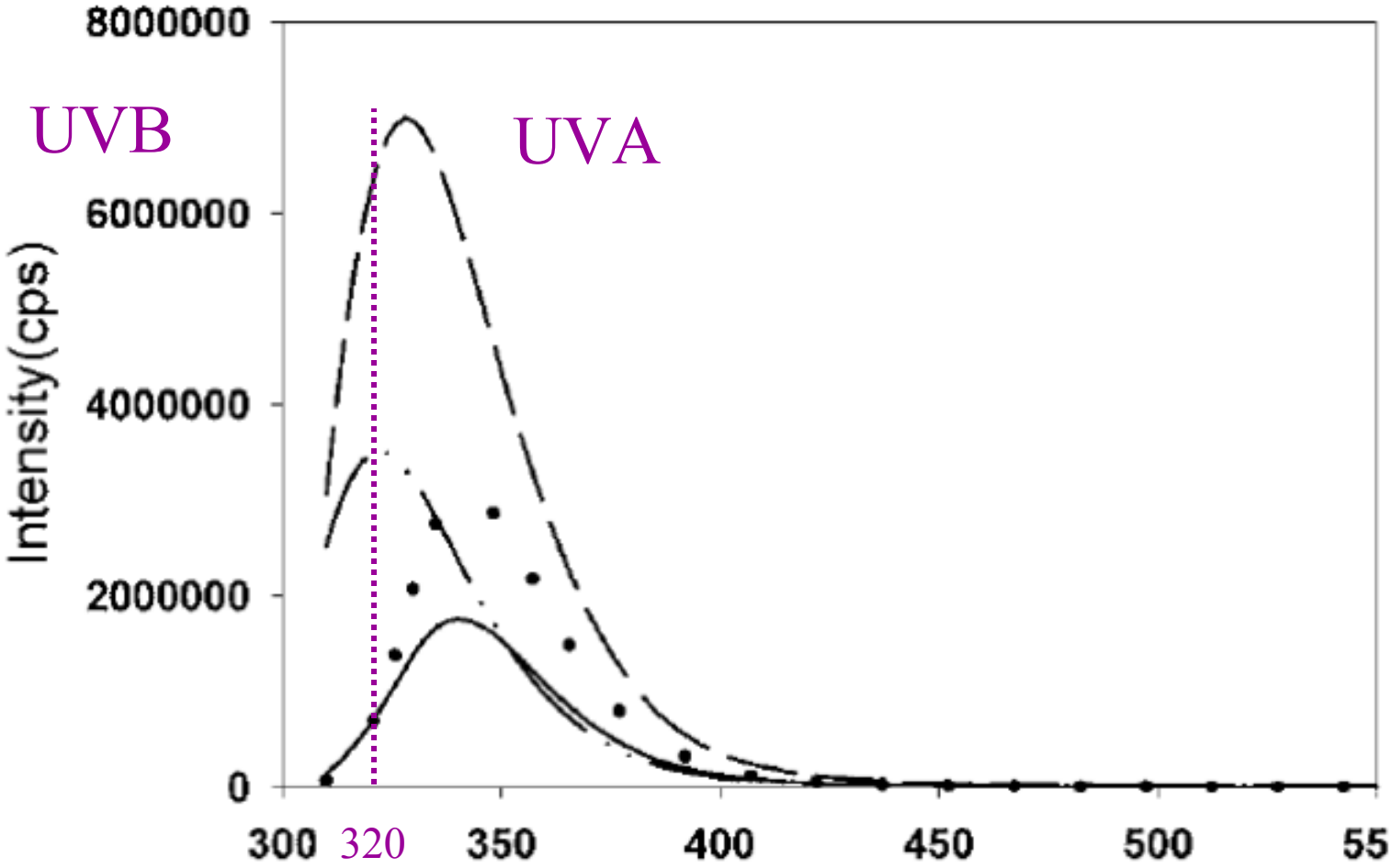
Source: Krishnan R, Carr A, Blair E, Nordlund TM. Optical spectroscopy of hydrophobic sunscreen molecules adsorbed to dielectric nanospheres.Photochem Photobiol. 2004 Jun;79(6):531-9



Absorption spectrum of PABA

in toulene (— --); ethyl acetate (- -); 1 propanol (---); and methanol (—)

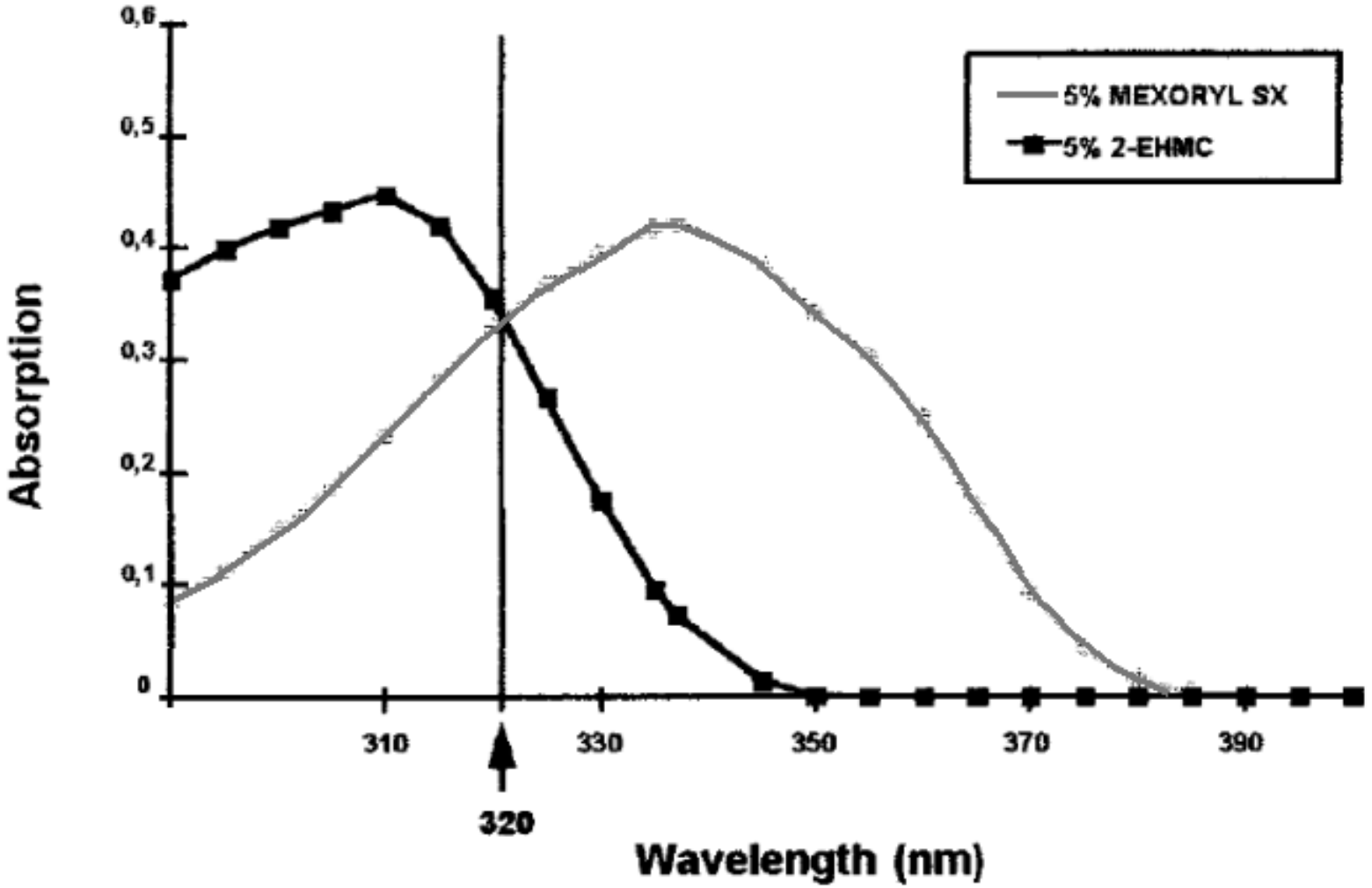
Source: Krishnan R, Carr A, Blair E, Nordlund TM. Optical spectroscopy of hydrophobic sunscreen molecules adsorbed to dielectric nanospheres.Photochem Photobiol. 2004 Jun;79(6):531-9



Emission spectrum of PABA

in toulene (— --); ethyl acetate (- -); 1 propanol (---); and methanol (—)

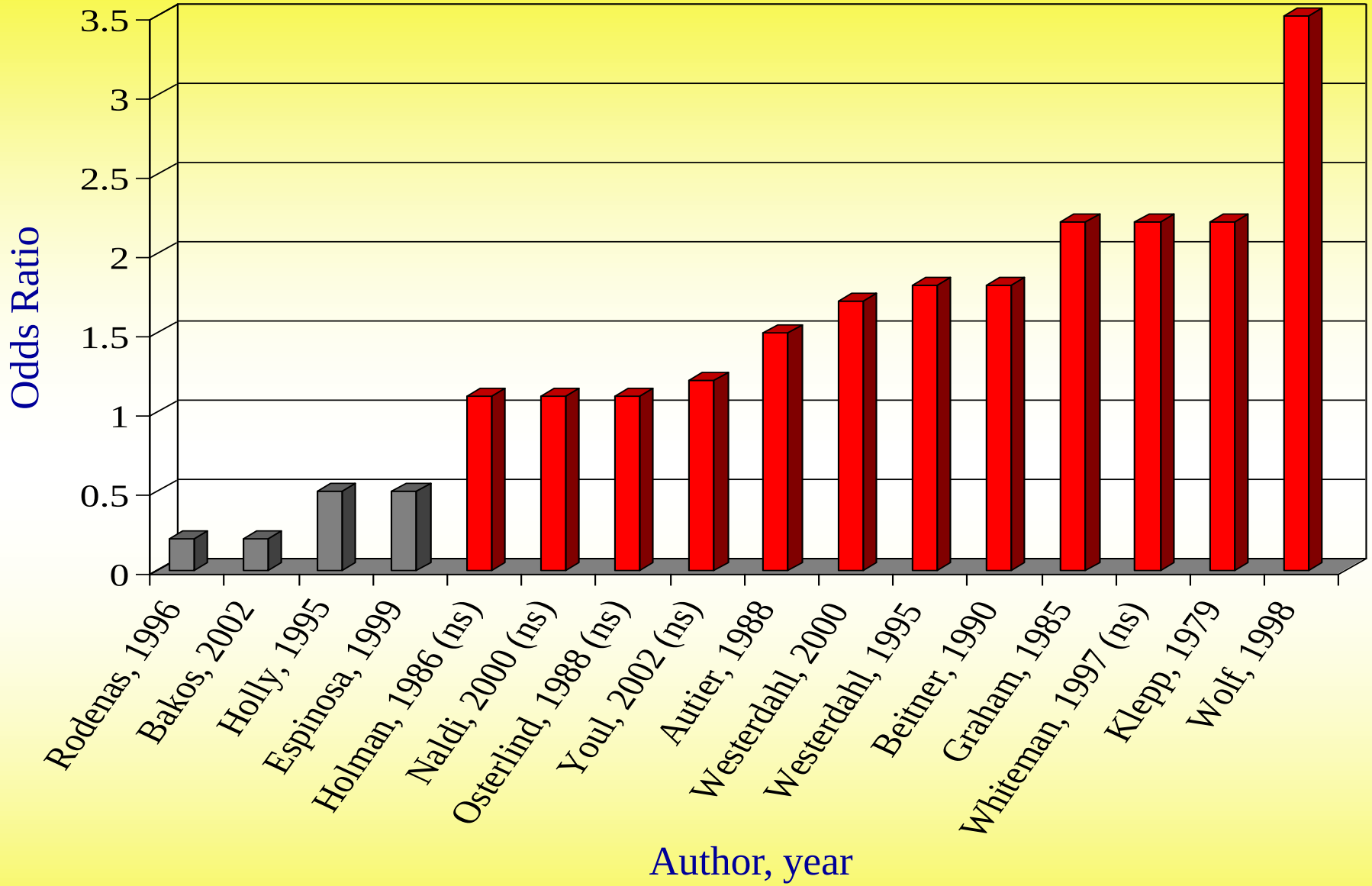
Source: Krishnan R, Carr A, Blair E, Nordlund TM. Optical spectroscopy of hydrophobic sunscreen molecules adsorbed to dielectric nanospheres.Photochem Photobiol. 2004 Jun;79(6):531-9



Absorption spectrum of 5 % Mexoryl SX and 5%2-EHMC

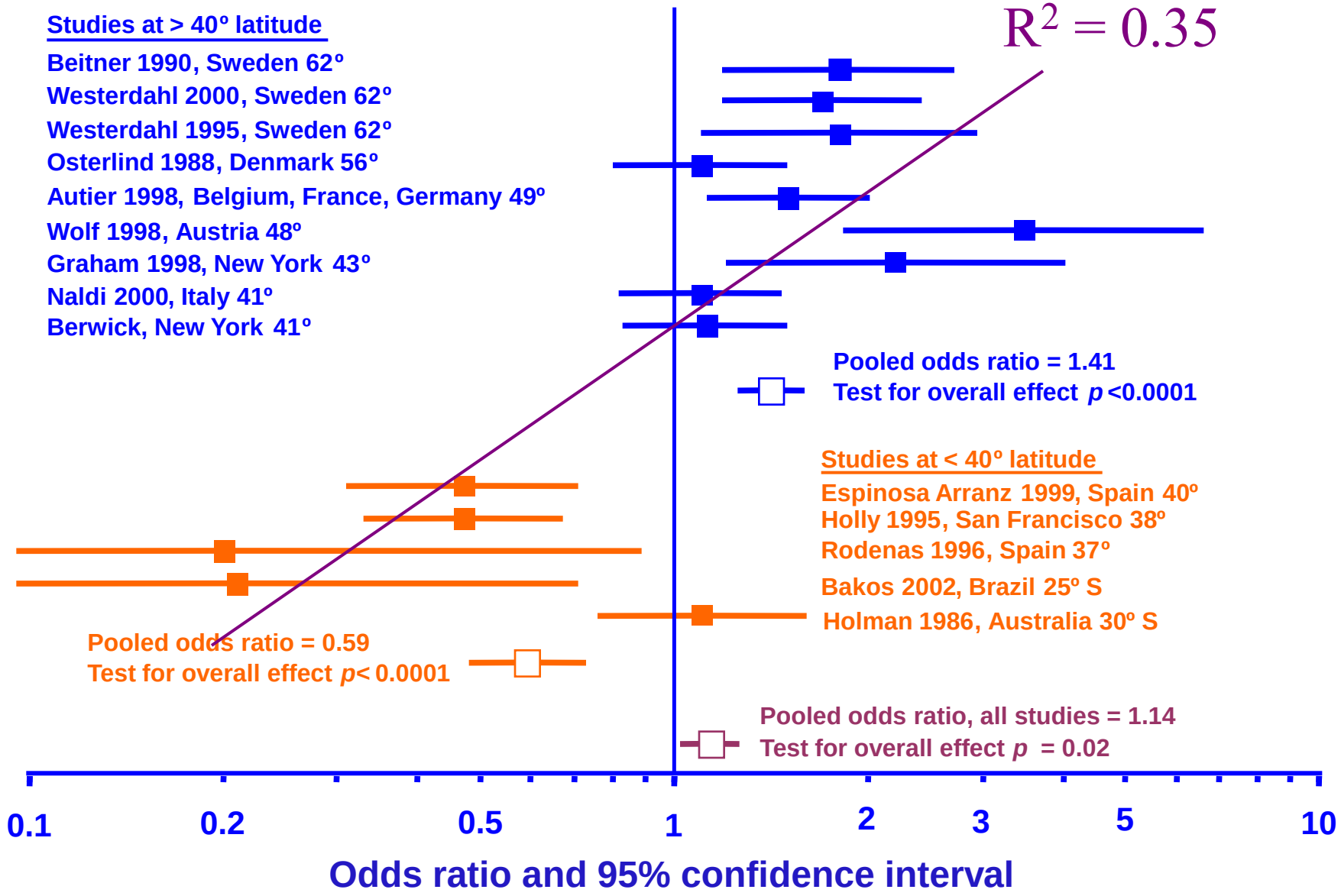
Source: Bernerd F, Vioux C, Asselineau D. Evaluation of the protective effect of sunscreens on in vitro reconstructed human skin exposed to UVB or UVA irradiation. Photochem Photobiol. 2000 Mar;71(3):314-20.

16 Case-Control Studies of Sunscreen Use and Melanoma

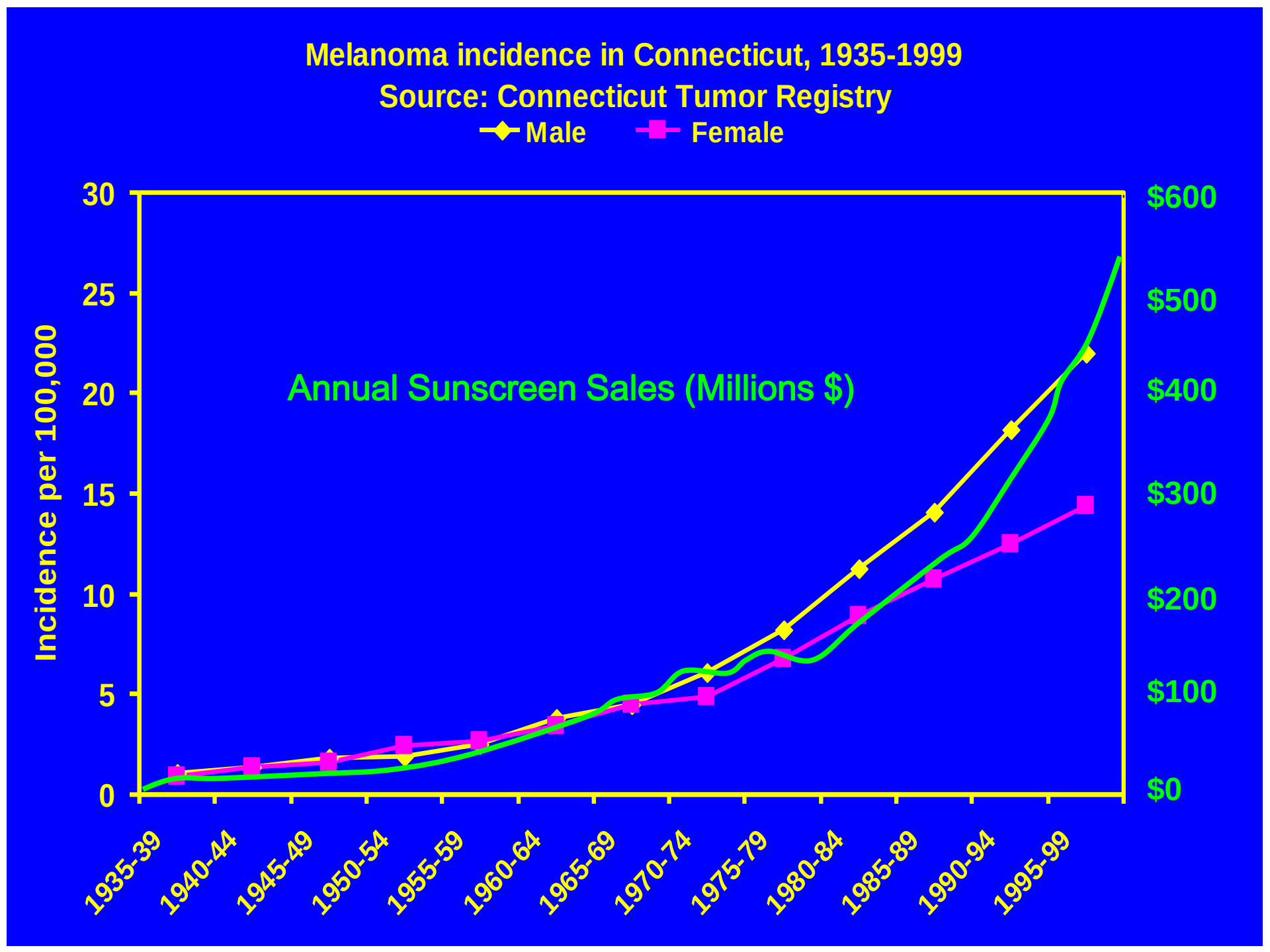


Odds Ratios for malignant melanoma associated with sunscreen use

(4 lower, 5 not statistically significant, 7 elevated)



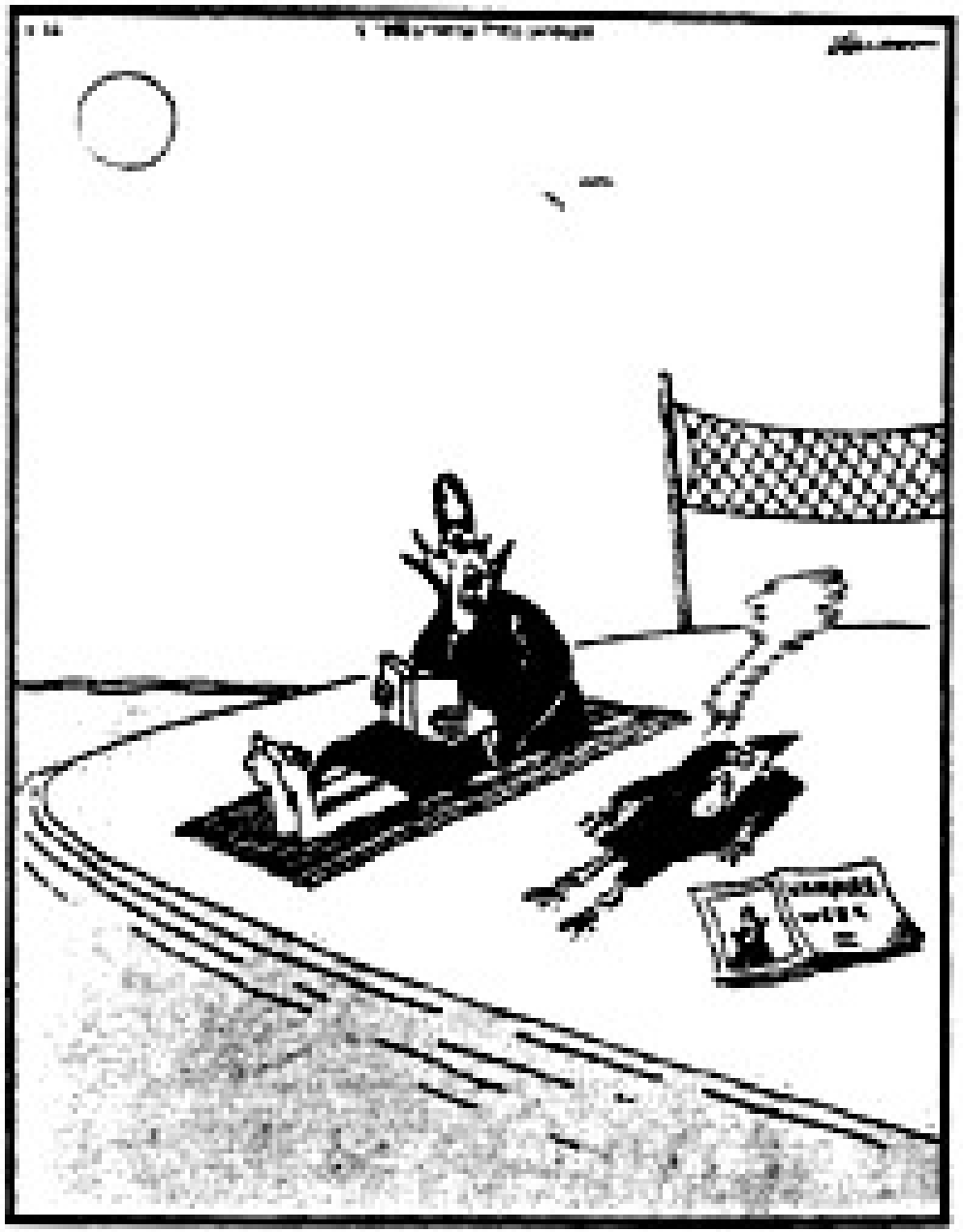
Source: Gorham ED, Mohr SB, Garland CF, Chaplin G, Garland FC. Do sunscreens increase risk of melanoma in populations residing at higher latitudes? Ann Epidemiol. 2007;17:956-63.


Melanoma incidence in Connecticut, 1935-1999
Source: Connecticut Tumor Registry
Male
Female
Annual Sunscreen Sales (Millions $)
Incidence per 100,000
30
25
20
15
10
5
0
$600
$500
$400
$300
$200
$100
$0
1935-39
1940-44
1945-49
1950-54
1955-59
1960-64
1965-69
1970-74
1975-79
1980-84
1985-89
1990-94
1995-99

Sunscreens and Free Speech

- “Whether consumers are told that a product has an S.P.F. rating at a specific level above 30, or that a product containing sunscreen helps prevent skin aging,— it is difficult to see how the transmission of such information results in real harm…”

- Mr. John G. Roberts, Cosmetics Industry Lawyer in a letter to F.D.A., 2001



“Well, Donald – forgot your sun block, I see.”

Recommendations for Vitamin D Photosynthesis

Guiding Principal: Minimize UVA exposure while allowing beneficial UVB exposure

- If skin type allows, advise 10-15 minutes per day in the sun more for heavily pigmented individuals
- Expose $\geq$ 40% of skin area without application of chemical sunscreen
- Advise sun exposure between 10:00 AM and 2:00 PM on clear days
- Control SO_2 and particulate air pollution that blocks or scatters UVB photons

But when season, latitude, skin type or atmospheric conditions preclude sun exposure:

- Use oral supplementation with vitamin D_3 to achieve circulating levels of 25 (OH)D between 40-60 ng/ml or 100-150 nMols/L

Gauging Vitamin D Status

What is the best serum 25 (OH) Vitamin D concentration?

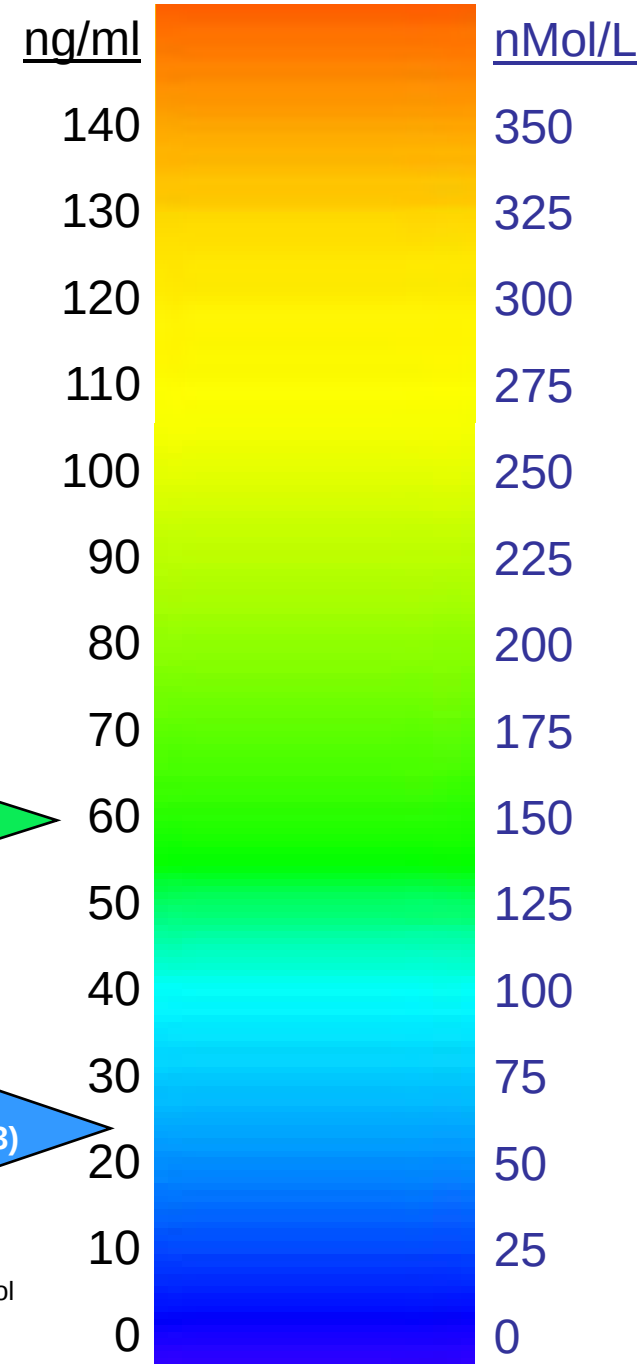
People living in sunny places with minimal clothing that doesn't limit vitamin D photosynthesis have serum 25(OH)D levels of 54 to 90 ng/ml (1).

A good target is:

40-60 ng/ml good target

A useful rule of thumb is that for every 100 IU of vitamin D_3 ingested, there is a gain of 1 ng/mL in serum 25 (OH)D (2).

25 ng/ml US median (NHANES 3)



1. Hollis BW. Circulating 25-hydroxyvitamin D levels indicative of vitamin D sufficiency: implications for establishing a new effective dietary intake recommendation for vitamin D. J Nutr. 2005;135:317-22

2. Heaney RP, Davies KM, Chen TC, Holick MF, Barger-Lux MJ. Human serum 25-hydroxycholecalciferol response to extended oral dosing with cholecalciferol. Am J Clin Nutr. 2003;77:204-10.