

Cancer & the wound that does not heal Hypothesis as justification for maintaining life-long Maasai level of Vitamin D



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Sick note diagnosis as predictor of subsequent cause of death

(Head J et al BMJ 2008; 337:a1469)

	Cardio-vascular HR	Cancer HR	Other HR
No Sick notes	1.0 (n=36)	1.0 (n=64)	1.0 (n=27)
Circulatory Sick note	6.2 (n=5)	2.6 (n=3)	6.5 (n=4)
Psychiatric sick note	1.2 (n=3)	2.5 (n=12)	1.4 (n=4)
Other sick note	~2.2 (n=43)	~1.78 (n=66)	~1.7 (n=41)

The journey of discovery

McFarland Burnett and “immune” surveillance hypothesis

Exercise and prevention of cancer (Oliver Lancet 1993; 341: 1033)

Grant geography and sunshine hypothesis

Prostate cancer correlation with geography and “lack” of correlation with Vitamin D level and anaerobes

Clemens T.L et al. Lancet 1982 1:74-76

Cathelicidine & TB

Sir Michael Marmot and Civil Servants & Health inequalities studies

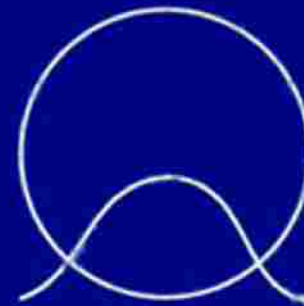
Sunshine and exercise as health benefit confounding variables

Index of fitness and Schools, Universities & over 50s Olympiad

STAGES OF CANCER GROWTH



AVASCULAR SPHEROID



VASCULARISATION



INVASION



METASTASIS

Immunotherapy of tumour infiltrating lymphocyte content and HLA class I/II expression in diffuse large cell non-Hodgkin lymphoma

(List et al 1991)

	No. of Cases	Proportion of TIL cells	Proportion with normal HLA class I/II
Tumours in immuno-compromised patients	18 *	2.8%	93%
Sporadic tumour	83	11.6% p = 0.001	26% p < 0.001

* n = 19 studied

20 year study of Sporting & regular walking activity verses total/site specific adjusted cancer risk

(Wannamethee SG et al B J Cancer 2001; 85: 1311-1316)

TOTAL PARTICIPANTS (n= 7735 men)	Sporting activity =<1 month (n=5508)	Sporting activity >1 month (n=2080)	Walking <40 mins/day (n=6514)	Walking 40-80 mins/day (n=786)	Walking >80 mins/day (n=288)
Total Cancer (n=969)	1.00	0.82	1.00	0.96	0.77
Lung Cancer (n=265)	1.00	0.82	1.00	1.04	0.77
Colorectal (n=135)	1.00	0.90	1.00	0.74	0.76
Prostate (n=120)	1.00	0.85	1.00	1.09	0.36

Comparison Breast, Cervix and PSA screening statistics

Numbers screened	Lives saved	Extra “cancers” treated	False alarms
2,000 breast screening 10 years	1	10	200
1410 PSA screening 10 years	1	48	252
1,000 cervix screening for 35 years	1	(53)	(152)

Factors influencing serum PSA in gold miners attending STD clinic in South Africa

(Oliver JC et al 2001)

Anti chlamydial antibody response	No. of cases	PSA > 0.8 ng/ml
Titre < 1/64	201	17%
Titre > 1/64	61	27% (P < 0.001)
Age at first sexual intercourse		
≤ 16	34	35%
> 16	49	18% (P = 0.08)

PSA in stored serum and later risk of prostate cancer

Prostate cancer verses matched control samples	OR for prostate cancer associated with raised PSA
Fang et al 2001 Age 40-49 (n=351)	3.75
Fang et al 2001 age 50-59 (n=445)	3.75
Lilja H et al 2007 age<50 (N=21,277, 462 PCa & 1222 Controls)	3.69

Infection/Inflammation and cancer

- Osteomyelitis and osteosarcoma
- Helicobacter and stomach cancer
- Ulcerative colitis and colon cancer
- Prostatitis and Prostate cancer
- Mastitis and breast cancer
- Bronchitis and lung cancer

Synchronised seasonal variation of Mammographic breast density and Vitamin D levels

(Brisson J et al Ca Epid Biom Prev 2007;16:929)

	Jan to April	Crossover May	Jun to Sept	Crossover October	Nov to Dec
Increased Breast density	43%	41.3%	39%	41.3%	44%
25(OH) Vit D (nmol/l)	56	67	75	67	58

Correlation of Circumcision Status and Prostate cancer occurrence

	No of controls	No of cases	OR
Rosenblatt et al	703	753	0.86
Ewings et al	325	159	0.62
Newell et al	167	94	1.89
Ross et al	284	311	0.55
Wynder et al	142	172	1.17
Total	1621	1499	0.87

Comparison of Circumcision Status and Cervix or Prostate cancer occurrence

	No of controls	No of cases	OR
Cervix cancer (Castellsague et al NEJM 2002)	936	977	0.72
Prostate cancer (Oliver in preparation)	1631	1550	0.86

Global Incidence and Mortality of Prostate Cancer (PC) & Cervix Cancer (CC) (GLOBOCAN 2008)

	Deaths PC per 10 ⁵	Incidence PC per 10 ⁵	Deaths CC per 10 ⁵	Incidence CC per 10 ⁵
Brazil c-	16.3	50.3	10.9	24.5
USA c+	9.7	83.8	1.7	5.7
Denmark c-	2.5	72.5	2.5	11
India c-	2.5	3.7	15.2	28.9
Bangladesh c+	1.2	1.9	17.9	27
Saudi Arabia c+	5.1	7.7	0.9	2.1
Israel c+	7.6	55	2.1	5.6
China c-	1.8	4.3	4.6	9.6
Japan c[-	5	22.7	2.6	9.8

Change in aerobic vs anaerobic colonisation of glans penis after circumcision

(Price, LB et al 2009)

	Statistical test	P value
All aerobic groups	$t = - 1.0294$	$p=0.3236$
All anaerobes	$t = 3.4765$	$p=0.0046$
Chlostridiales family	$t = 2.308$	$p=0.0210$
Prevotella family	$z = 2.469$	$p=0.0138$

Prostate cancer and use of condoms with commercial sex workers (Hayes RB et al 2000)

	No of cases	OR	95% CI
No access to sex industry	637	1.0	Referent
Usually used condoms	83	1.0	0.7-1.4
Usually didn't use condoms	155	1.4	1.1-1.8
p for trend		0.01	

Correlation of Serum Vitamin D and occurrence of Prostate cancer

	No of controls	No of cases	Incidence of PC (Low vs. High serum vit D)
Braun et al, 1995	122	61	P for trend = 0.6
Normura et al, 2008	136	136	P for trend = 0.68
Ahonen et al, 2000	566	149	P for trend = 0.01
Jacobs et al, 2004	166	83	P for trend = 0.51
Mikhak et al, 2007	692	684	OR = 0.62
Ahn et al, 2008	781	749	OR = 1.006

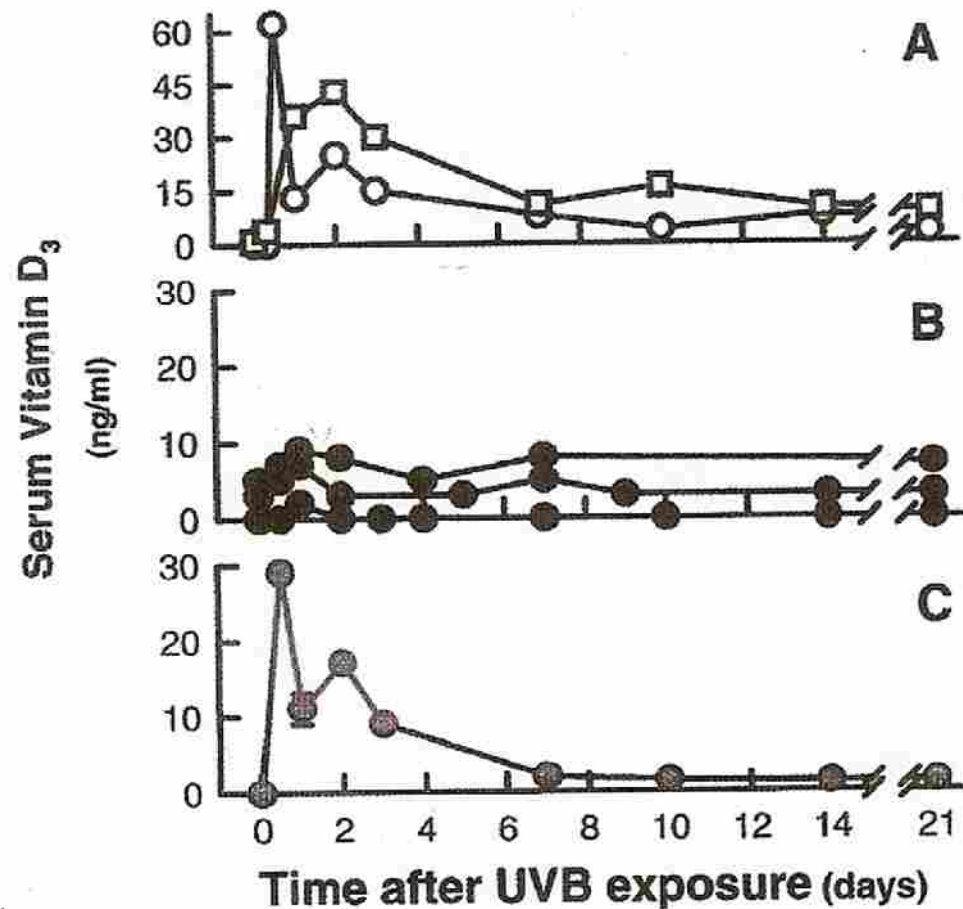
PC mortality in European countries of highest vs. lowest latitudes

(Source: GLOBOCAN 2002)

Country	Age Standardised mortality Rate (ASR)
Iceland	23
Finland	18
Norway	28.4
Mean	23.1
Italy	12.2
Spain	14.9
Greece	11.2
Mean	12.8

Life-time sun exposure and Prostate cancer incidence

	No of controls	No of cases	OR (High vs. Low long term sun exposure)
Luscombe CJ, 2001	155	210	0.75
Bodiwala D, 2003	135	212	0.75
John EM, 2007	3,367	160	0.59
Gilbert R, 2009	4884	986	0.87



Change in serum concentrations of vitamin D in:
 (A) two lightly pigmented white (skin type 2); (B) three heavily pigmented black subjects (skin type 5) after total-body exposure to 54mJ/cm² of UVB radiation; (C) Serial change in circulation vitamin D after re-exposure of one black subject in panel B to a 320mJ/cm² dose of UVB radiation.

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Clemens T.L et al. Lancet
 1982 1:74-76

Prostate Cancer incidence per 100,000 in East London's
different ethnic populations
(Chinegwundoh F et al 2006)

	European (N/n=45,432/248)	African Caribbean (N/n=7616/91)	Asian (N/n8207/20)
< 65	40	250	65
65-75	353	862	260
>75	758	2174	685

Macrophage induction of anti-Micobacterium toxic peptide, *Cathelicidin* mRNA, by high and low vitamin D containing serum

Liu PT et al Science 2006; 311: 1770-3

Source of serum	Median concentration of 25(OH)D ₃	Cathelicidin mRNA response (higher better)
African American (n=19)	~25 nmol/l	~98%
Caucasian (n=14)	~78 nmol/l	~240%

Therefore: Vitamin D stimulates macrophages to produce micobacteriocidal toxic peptide

The Olympic Legacy

- This part of my presentation summarises attempts to develop a stronger scientific evidence base for both the health and academic performance benefits of sun and exercise using the Sports Search fitness index .
- It also demonstrates the potential of using internet based population medians of this index to provide the basis of a 2012 legacy event, a Schools, Universities and over 50s Olympiads, to foster world wide participation in schools fitness awareness but also awareness in their parents and grandparents

Fluctuation of strength with seasons (Hettinger T, Muller

EA Int Z Angew Physiol 1956:16: 90-94)



FIGURE 4—Average trainability of forearm wrist flexors during the course of the year in seven subjects who trained every day in a uniform

Effect of 30 days regular exercise on ability of mice to learn mental tasks & DNA synthesis in critical hippocampal region of the brain (van Praag H et al 1999)

	Time to perform task	No of DNA synthesising Hippocampal cells
Controls (n=17)	27 secs	1,409
Runners (n=17)	18 secs	3,746
	$p < 0.04$	$P, < 0.002$

Materials & Methods

- **Sport Search** is an interactive computer-based programme recording sports performance in a series of short exercise tests that can be entered on line into a data-base using hybrid CD-ROM and internet technology. The median of MSF was the primary indicator used to assess group performance.
- The Multistage fitness (MSF) test is made up of 23 levels where each level lasts approximately one minute. Each level comprises of a series of 20m shuttles where the starting speed is 8.5km/hr and increases by 0.5km/hr at each level..
- The maximum oxygen uptake (VO₂ max) is derived from the [MSF Table](#) using the Level and Shuttle achieved.
- The pupils tested were from two consecutive year 7 classes. 773 boys and 973 girls from 16 schools

Boy's Results

School	Number of pupils		MSF		VO2 Max	
	06-07	07-08	06-07	07-08	06-07	07-08
School J	59	67	45.37	46	34.23	34.76
School B	33	42	44	42	33.8	33.2
School C	158	126	36	32.17	31.2	29.7
School D	N/A	23	N/A	52	N/A	36.67
School E	68	14	67	78	39.9	45.6
School F	21	31	44	59	33.1	39
School G	N/A	27	N/A	27	N/A	28.05
School H	43	61	45	63.9	34.5	40.3

Interaction between fitness as measured by MSF test and year 7 academic performance as measured by CAT test

	Boys	Girls
Median CAT in those ≥ 6 in MSFT	98 (n=60)	95 (n=55)
Median CAT in those < 6 in MSFT	89 (n=27)	95 (n=51)
Median MSFT in Academic sets 1-3	7.3	6.2
Median MSFT in Academic sets 4-6	6.6	5.5

Correlation of Median SAS scores with Beep Test (BT) and improvement 2009-10

Mean SAS score	Number of year 7 boys	Beep test July 2010	BT score improvement 2009/10
>107	4	10.2	9.3%
96-107	10	8.8	5.0%
<96	3	7.7	-11.8%

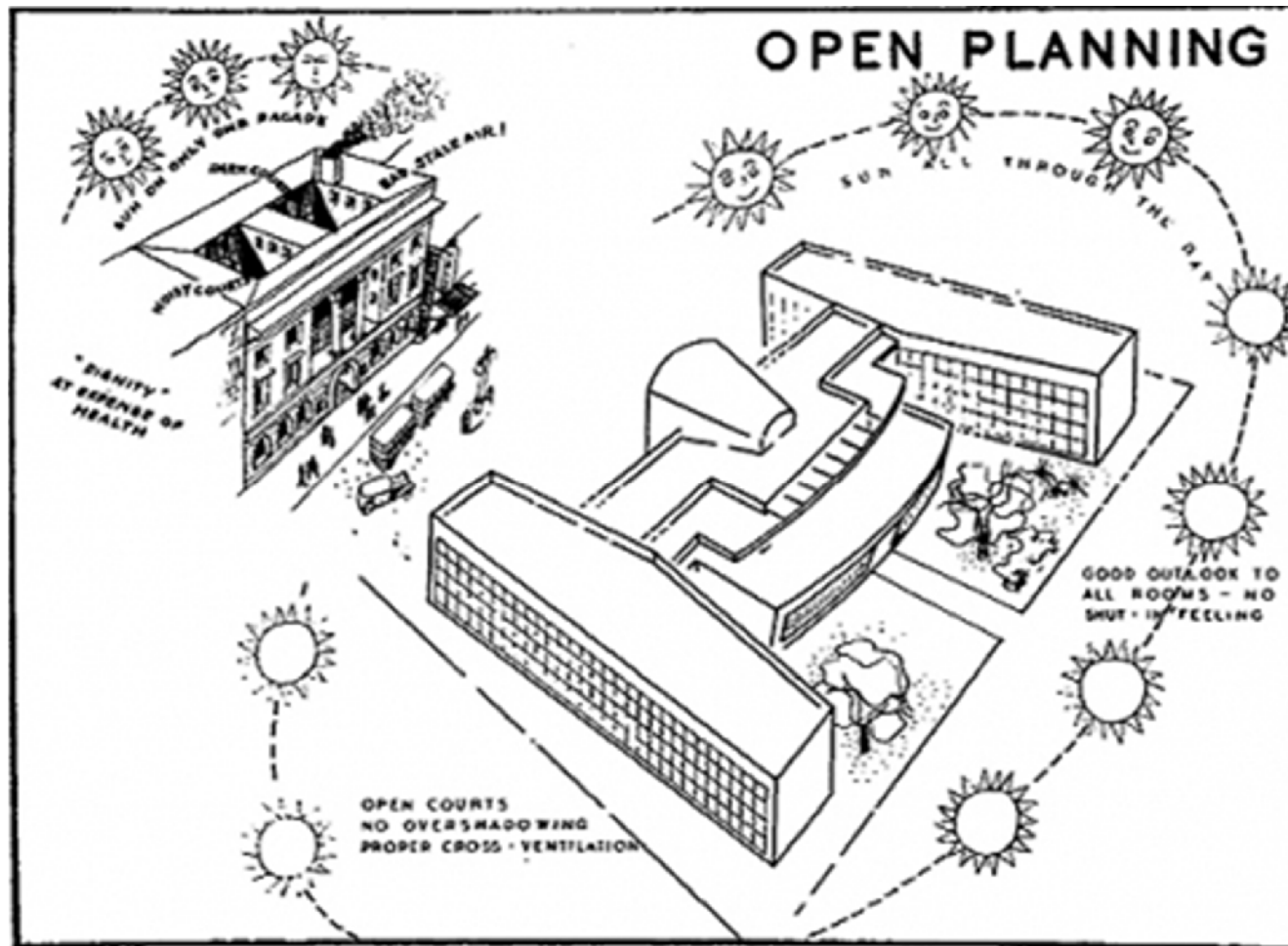
CONCLUSIONS

- All causes of cancer take from 10-50 years to act
- The concept of anaerobe colonisation of poorly vascular scar tissue creating a wound that does not heal in a setting of sustained or intermittent Vitamin D deficiency provides a rational explanation for how cancers in most organs could develop
- Population based interventions to ensure lifelong safe intermittent sun exposure and exercise as a general approach to reducing health inequalities is clearly justified by data on low cancer rates of farmers, builders and golfers
- GPs, as the “Gatekeepers” to the NHS, should be encouraged to maintain Maasai levels of Vitamin D in all their patients.
- The data presented suggesting that fitness in schools correlates with academic performance justifies more curriculum time for outdoor sport.
- The internet based indices of fitness of populations could provide the opportunity for four yearly Schools, Universities and over 50s Olympiads.

Finsbury Health Centre Now



The sun and Berthold Lubetkin's Finsbury Health Centre



Recreational physical activity and risk of prostate cancer: 29,110 men followed 17 years

Nilson TI et al Int J Ca 2006; 119:2943-2947

	No. Prostate Ca deaths/ ObsPersYear	RR (adjust)
No activity(ref)	64/ 57,712	1.00
Frequency =<1/wk	130/ 243,362	~0.73
Frequency 2-3/wk	64/101,736	0.67
Frequency >3/wk	96/ 54,127	0.85
Duration Episode <30 minutes	121/ 114,612	~0.81
Duration Episode 30-60 minutes	82/125,237	0.73
Duration Episode >60 minutes	55/ 78,003	0.68

**Nurses health study(n=121,700) breast cancer cases (n=2967)
exercise habit post diagnosis and survival**

(Holmes MD et al JAMA 2005;293:2479-86)

TOTAL (N=2967)	<3 MET/wk (n=969)	3-9 MET/wk (n=862)	9-15 MET/wk (n=335)	>15 MET/wk (n=831)
Total deaths (n=463)	1.0	0.69	0.59	0.61
Breast ca deaths (n=280)	1.0	0.79	0.47	0.62
Recurrence (n=370)	1.0	0.82	0.53	0.70

Exercise and colon cancer survivorship

Meyerhardt JA et al JCO 2006;24:3535-43

TOTAL (N=832)	<3 MET/wk (n=273)	3-9 MET/wk (n=187)	9-18 MET/wk (n=137)	>18 MET/wk (n=235)
Total deaths (n=84)	1.0	0.85	0.71	0.54
Colon ca recurrence (n=159)	1.0	0.86	0.89	0.55
Recurrence or any death (n=166)	1.0	0.87	0.90	0.53

Randomised controlled trial of 3 months resistance exercise (RE)
after anti-androgen therapy for prostate cancer

Segal RJ et al J Clin Oncol 2003; 21: 1653-1659

	Control before(n=82)	Control after(n=82)	RE Group before(n=73)	RE Group after(n=73)	P <
Fatigue scores	42.5	40.3	40.8	41.6	0.002
Quality of life (FACT- P)	120.9	117.6	118.2	120.2	0.001
Chest presses	32.3	29.5	32.0	43.1	0.009
Leg presses	38.4	36.8	36.4	48.2	0.001

Correlation of latitude and UV index with PC mortality

Author (yr)	Correlation coefficient PC mortality: <u>Latitude</u>	P	Correlation coefficient PC mortality: <u>UV index</u>	P
Colli & Colli; 2006	0.33	0.003	-0.38	0.001
Grant, WB; 2002	NA	NA	White Americans = - 0.32	<0.001
			Black Americans = -0.44	0.061
Hanchette & Schwartz; 2006	0.19	<0.01	-0.15	<0.01
Mizoue; 2004			-0.07	
Schwartz & Hanchette; 2006	0.27	<0.0001	-0.16	<0.0001
Mean values	0.26		-0.25	

Impact of years since achieved UK Sports Academy status on
academic performance improvement 2005-2007

	Designation 5-10 years	Designation <5 years
Number of UK Sports Colleges	155	189
Improvement in last 2 years in GCSE index	13.2%	6.0%

Average Results

	Total number tested		MSF (mean)		VO2 Max (mean)	
	06-07	07-08	06-07	07-08	06-07	07-08
GIRLS	564	409	33.8	33.2	30.1	30.0
BOYS	382	391	46.9	50.0	34.5	35.9