

Gut Health, lifestyle and prostate cancer



Professor Robert Thomas

Bedford and Addenbrookes Cambridge University Hospitals
Biological & Exercise Scientist Bedford University



Bedfordshire Hospitals
NHS Foundation Trust



Cambridge University Hospitals
NHS Foundation Trust

Disclosures

Educational and travel grants - Astra Zeneca, Janssen Cilag, Novaritis, Roche, Pfizer, Ciba Naturemedical, Helsinn.

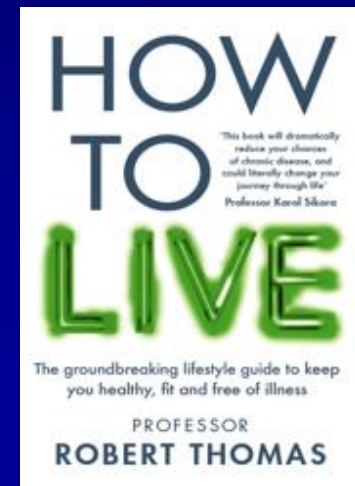
Medical Journalist for National News

Author of “How to Live” by Short books

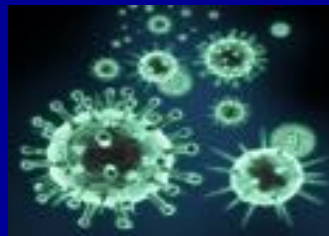
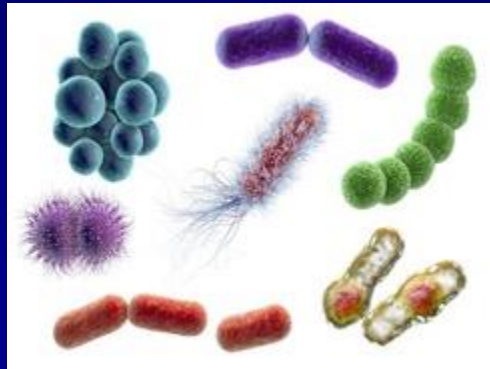
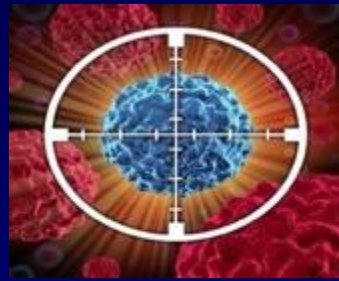
No financial connection with:

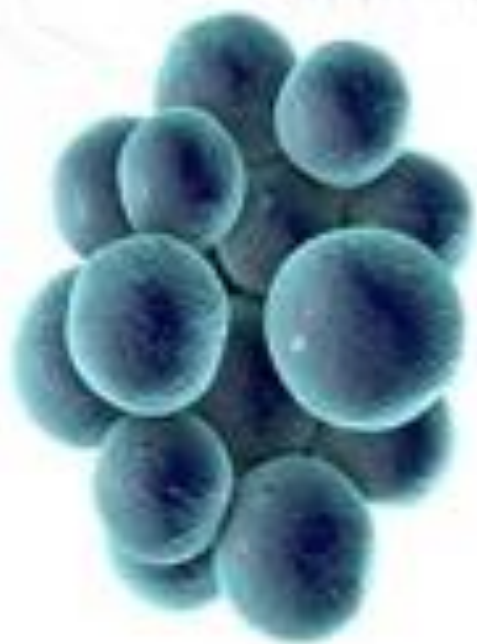
- YourPhyto study
- YourGut Plus

NationalWorld



Lifestyle Research Unit

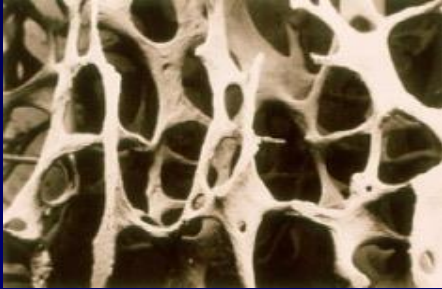




Poor gut health and wellbeing



Poor gut health and chronic disease



- MI
- Dementia
- Stroke
- Parkinson's
- Osteoporosis
- Ageing
- Cancer
- Cancer treatments

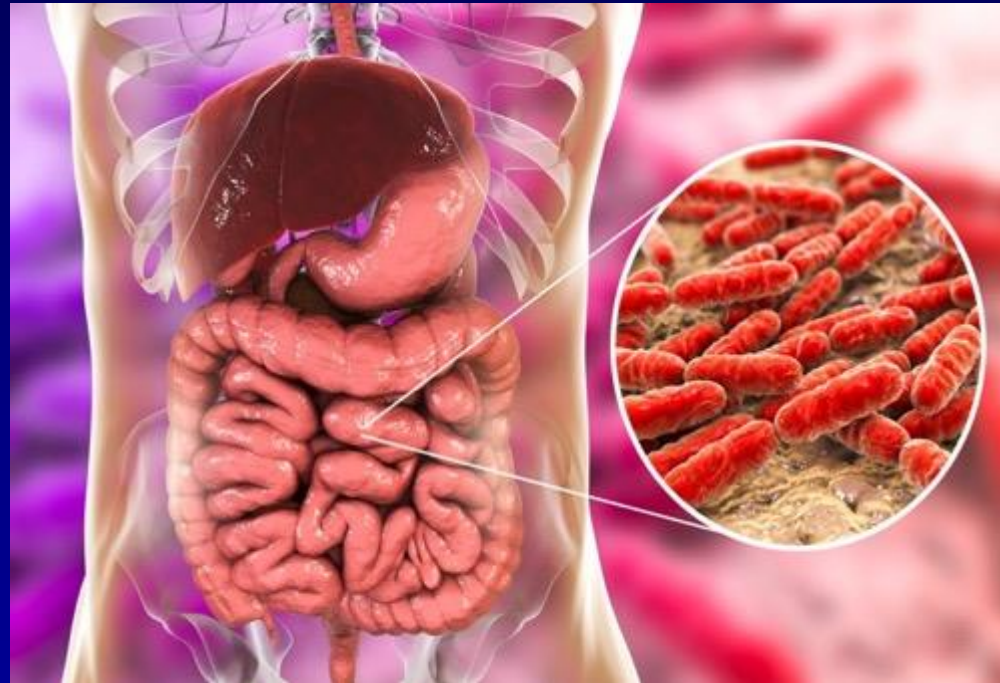
Better response to Immunotherapies

PDL1 inhibitors

40% Better response rates

- Better gut flora
- Metastatic melanoma

THE UNIVERSITY OF TEXAS
MD Anderson
Cancer Center

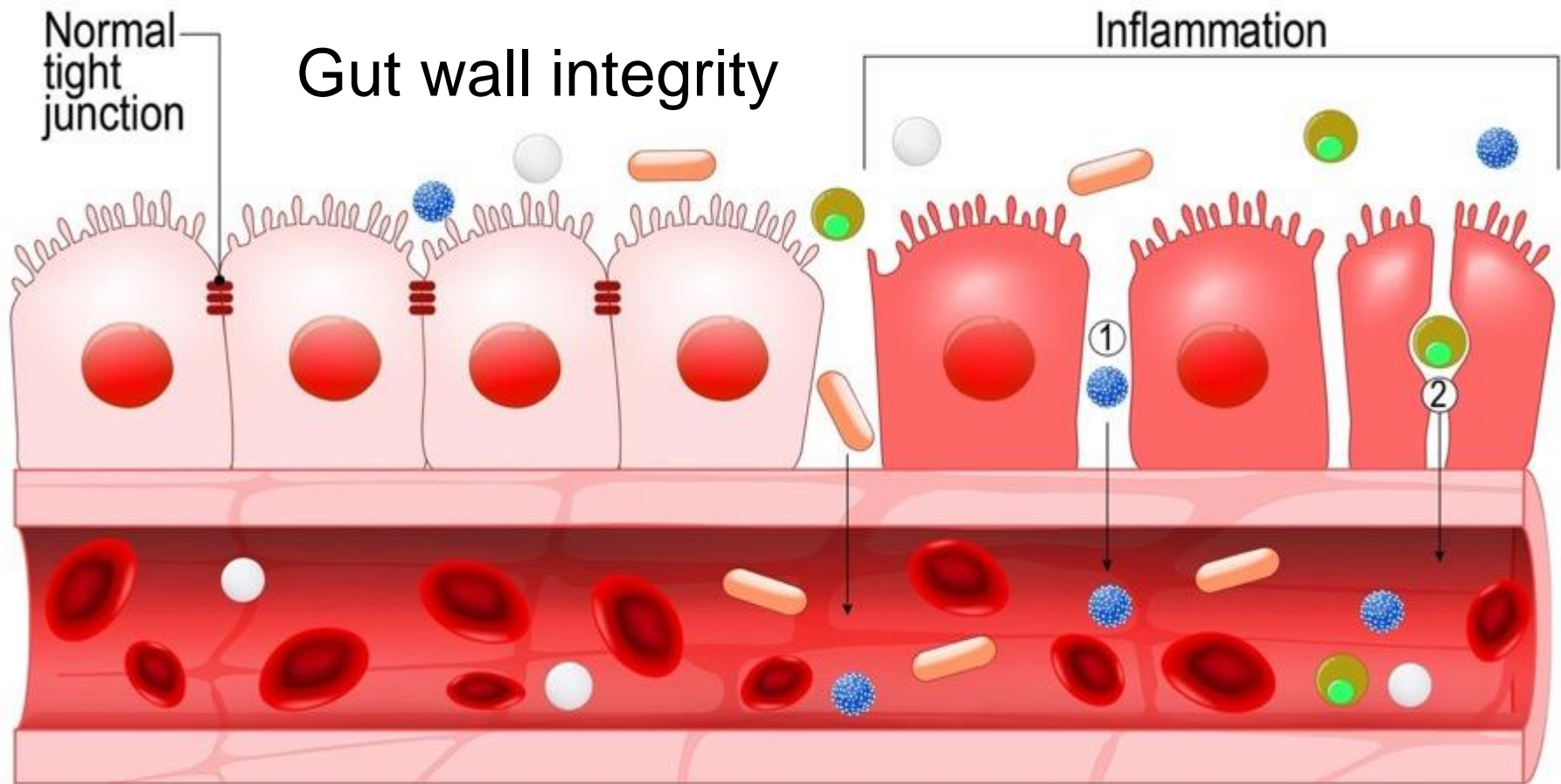


Mechanisms

- Breaks down soluble fibres (Inulin) into butyrate (SCFA)
 - Improve gut immune and integrity, mucous production
- Breaks down phytochemicals to bioactive units
 - Helps absorption and bioavailability
- Lessen impact from carcinogens
 - Convert food nitrates to nitric oxide not nitrosamines
- Improves vitamin D absorption

Shahanavaj K: Cancer and the microbiome: . Expert Rev Anticancer Ther 15:317-30, 2015.
Russo E et al. The microbiome and immune response. Therapy Adv Gastrol 9:594, 2016.
Pevsner-Fischer. Role of the microbiome in non-GI cancers. World J Clin Oncol 7:200-13, 2016


Breaks down complex carbohydrates and soluble fibres into butyrate (SCFA)



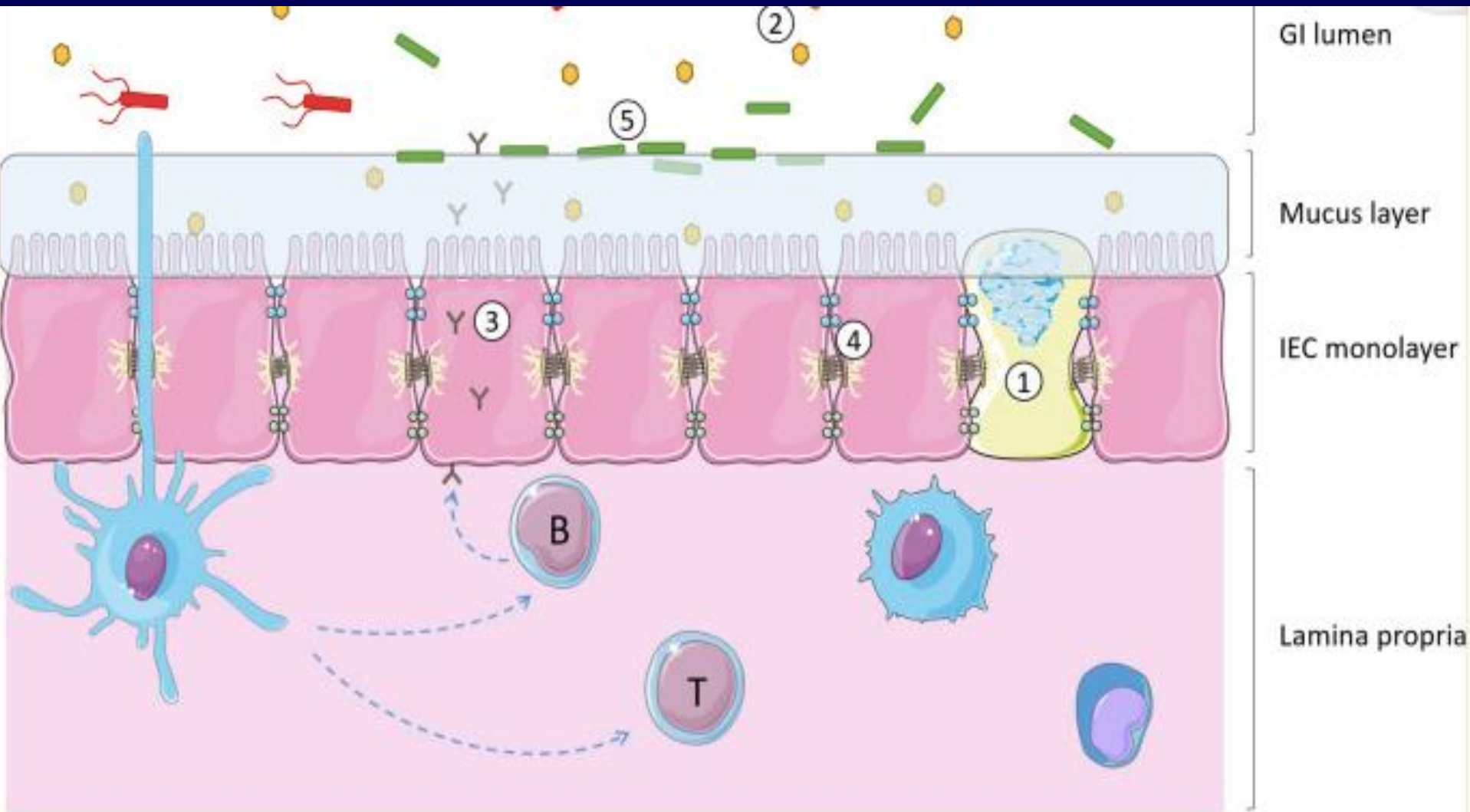
1. Paracellular

2. Transcellular

 Pathogens

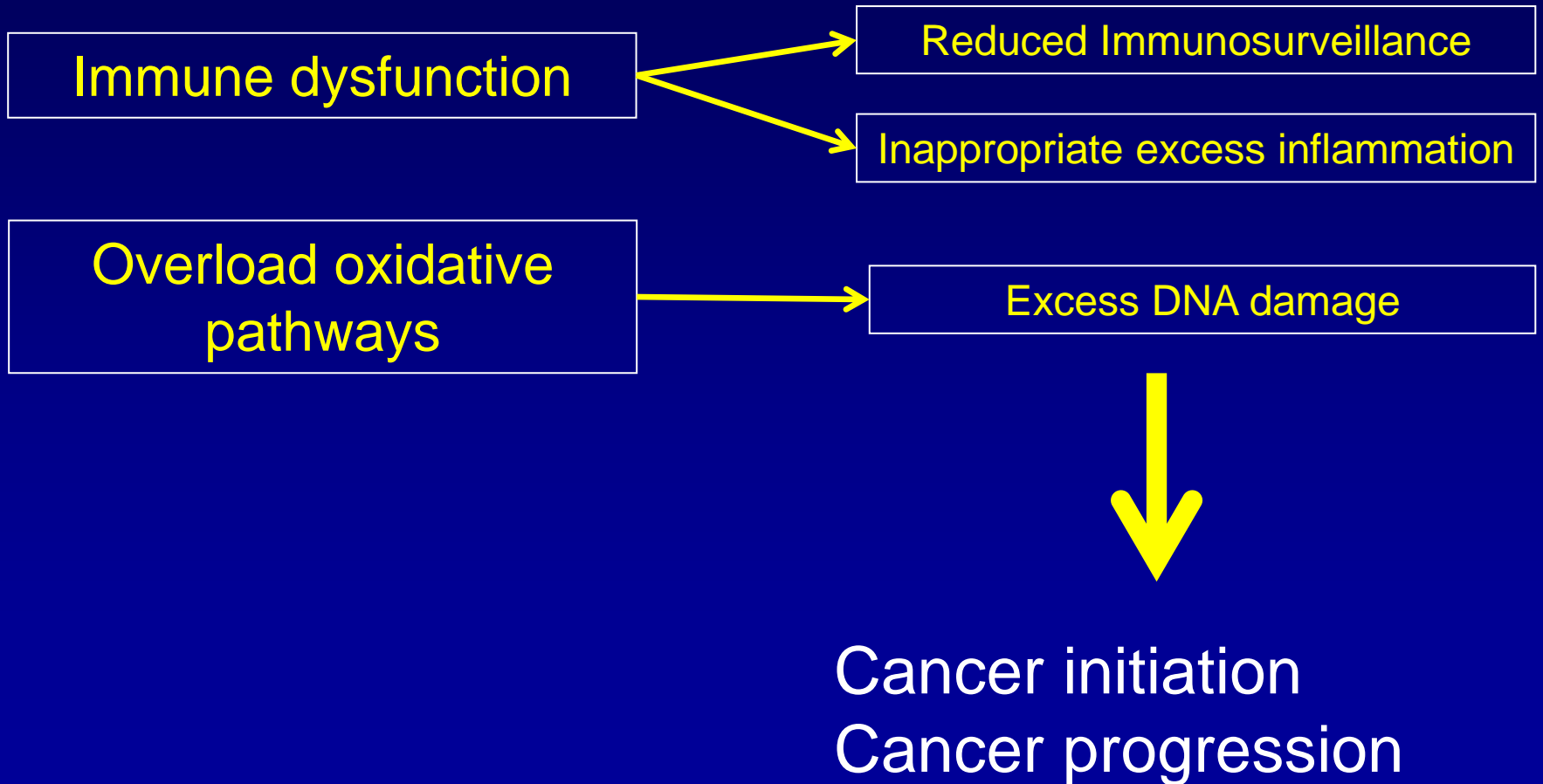
 Food allergen

Mucous production



Poor gut bacterial profile

Dysbiosis





Gut bacteria and phytochemicals

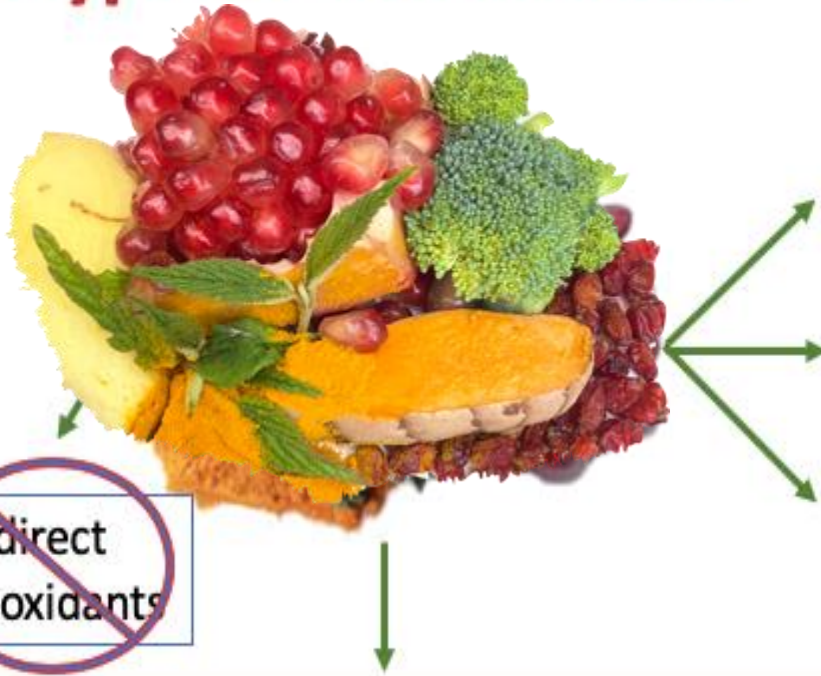
Phytochemicals act as pre-biotics
- promote healthy gut bacterial colonisation



Bacteria breaks down phytochemicals - bioactive units
- Helps absorption and bioavailability



Polyphenol rich foods



~~Not direct anti-oxidants~~

Enhance anti-oxidant enzyme capacity

via Nrf-2 efficiency and other cytoprotective phase 2 enzymes

- SOD
- Gluathione
- Catalase

Inflammatory regulation:

- Cox-2 and 5- Lox
- Nf-KappaB
 - Genetic transcription factor for innate immunity
 - Cytokines, chemokines, adhesion molecules

Epigenetic expression

- Promote tumour suppressor genes
- Inhibit cancer promotor genes

Improve gut health

- Pre-biotics
- Interfere with firmicute (inflammatory) growth

Diabetic protection

- Slow Glycaemic index
- Increase insulin sensitivity

Direct cancer proliferation inhibition

- HER2
- PARP
- BCL-s


Improve DNA repair

- Upregulate BRCa 1
- Upregulate p53

BMJ 2013;347:f1241

Polyphenols in cancer prevention & management?

Robert Thomas, Elizabeth Barber, Fabio Maggi and Melissa Williams

 Current Research in Complementary & Alternative Medicine

Review Article

Phytochemicals in Cancer Management

Robert Thomas¹, Elizabeth Barber², Fabio Maggi³, Melissa Williams⁴

Polyphenols rich foods Cancer



Fruit, tomatoes, rich herbs spices

HPFS – Giovannucci et al JN Can Instit, 2002



Soy

Meta-analysis - Hwang et al Nutr Cancer 2009



Carotenoid rich foods

National Health & Nutrition Exam Survey. Chaoyang 2011

Cruciferous and other vegetables,

Joseph et al Nutr Cancer 2004. Thomas et 2020 ASCO



Tea

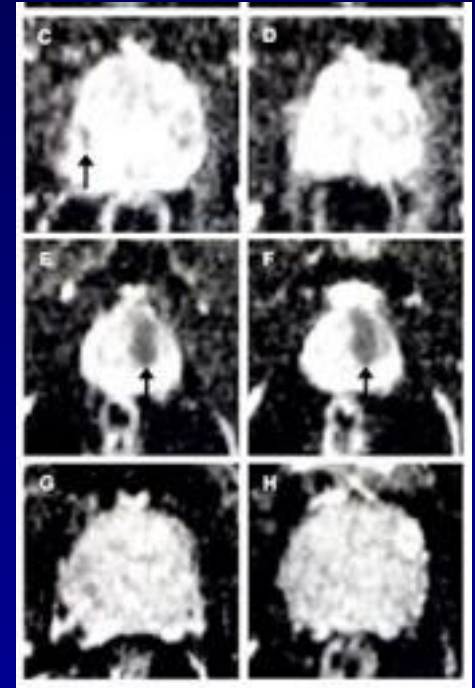
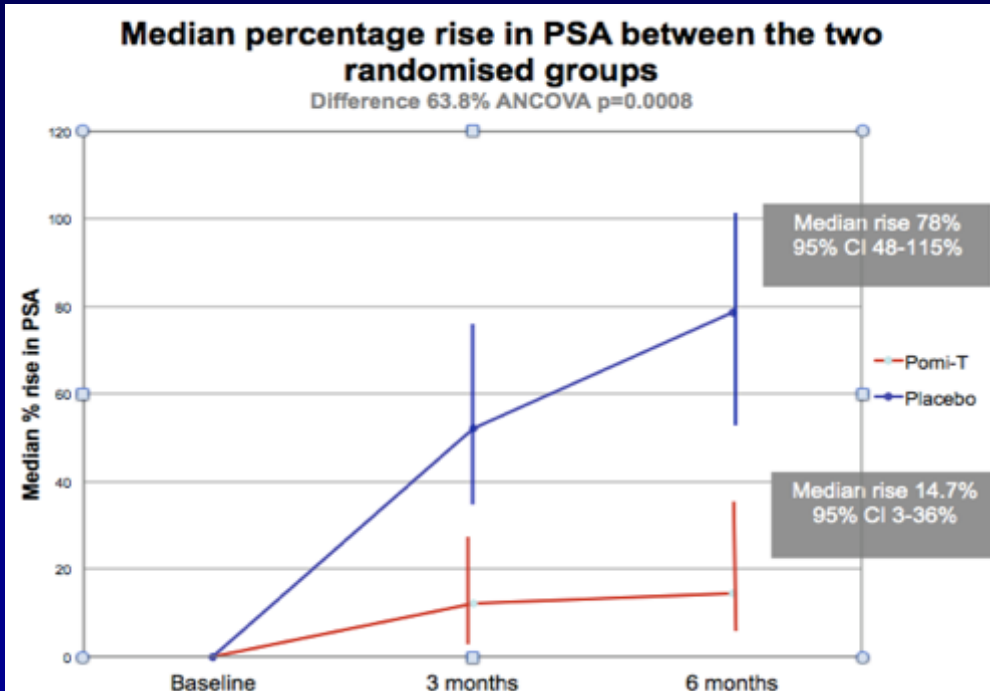
Singapore Health Study and PLCO Thomas et al 2020 ASCO

Strawberries

Slowed Barrett's oesophagus, Chen Ohio State 2011

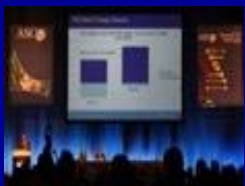


Polyphenols and CaP progression



Thomas et al The Pomi-T study Prostate cancer & Prostate diseases 2014 2014, (17)

Thomas et al. J Lifestyle Med. 2015 (1) 01







Carcinogenesis



Plant nitrates

Animal nitrates


Nitric Oxide
(NO)

- Healthy gut
- Polyphenols
- Vitamin C

- Unhealthy gut
- Few polyphenols
- Low vitamin C
- High haem iron

Healthy

- Tissue oxygenation
- Blood pressure
- Cognitive function
- Exercise performance

 + high temp
+ amino acids

Harmful

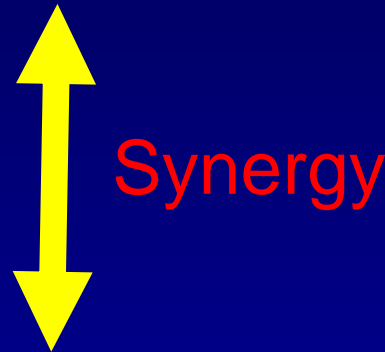
- Nitrosamines formation
- Inflammation
- DNA damage
- Higher risk of cancer

A close-up photograph of a person in a white lab coat holding a white rectangular sign. The sign has the words "Vitamin D" printed in a bold, blue, sans-serif font. The person's hands are visible, holding the sign from the sides. A blue stethoscope is draped around their neck, and a white button is visible on the lab coat. The background is slightly blurred, focusing attention on the sign and the person's hands.

**Vitamin
D**

Gut bacteria and Vitamin D

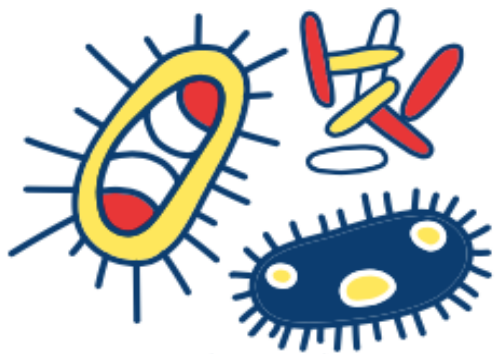
Vitamin D absorption is improved by co-administration with Lactobacillus probiotics



Vitamin D acts as a prebiotic helping healthy bacterial growth



Yoon et al (2011). Probiotic regulation of vitamin D receptor. *Gastroenterology* 140
Jones et al (2013). Lactobacillus & Vit D levels: a RCT. *J Clin End Metab*, 98, 294
Waterhouse et al. Vitamin D & gut microbiome *Eur. J. Nutr.* 58, 2895



reduced risk
of flu



protects memory



healthy pregnancy

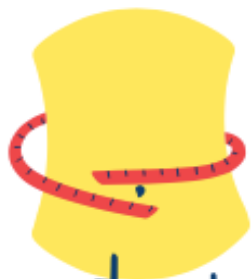
Vitamin D



cancer prevention



supports bone health



prevents obesity



avoids diabetes



boosts heart health

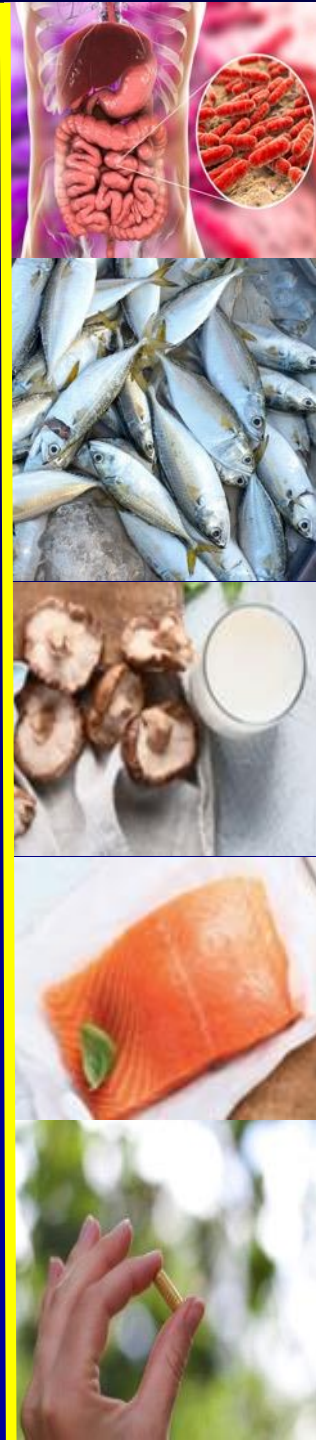
Vitamin D and Cancer

Low levels linked to great incidence of

- Breast, bowel cancer
- Gastric cancer and melanoma

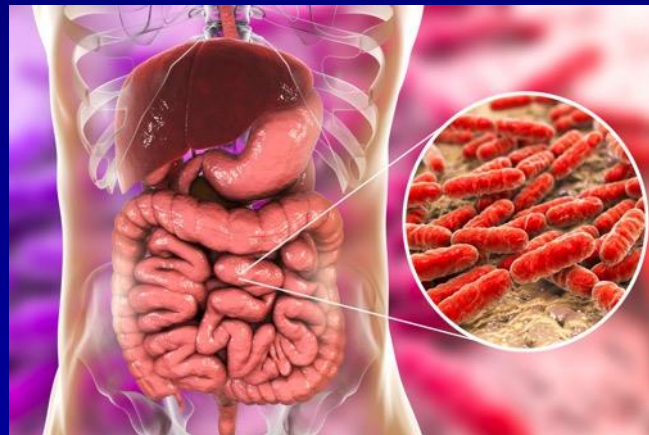
Every 20nmol/L increment, below normal, 10% increase:

- Prostate cancer-specific mortality
- All cause mortality



Sources of vitamin D

- Sunlight
- Oily fish
- Egg yolks
- Mushrooms
- Probiotics
- Gut Health



Gokhale, S., Provitamin D₃ modulation through prebiotics. *Sci Rep* **9**, 19267 (2019).

Jones ML, Probiotic lactobacillus increases Vit D a RCT . *J Clin Endocrin Meab*. 2013.

Prebiotics



Prebiotic polyphenols

Fermentable soluble fibres



Probiotics



Gut health Education

Verbal consultation

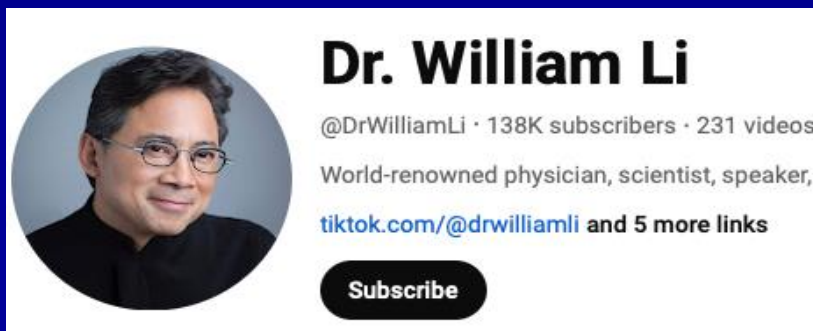
- 45 minute chemotherapy nurse

Signpost to online resources

- Keep-healthy.com
- Yourgutplus.com



Video links



Dr. William Li
@DrWilliamLi · 138K subscribers · 231 videos
World-renowned physician, scientist, speaker, and author of *Dr. Li's Prescription for Gut Health*
[tiktok.com/@drwilliamli](https://www.tiktok.com/@drwilliamli) and 5 more links

Subscribe

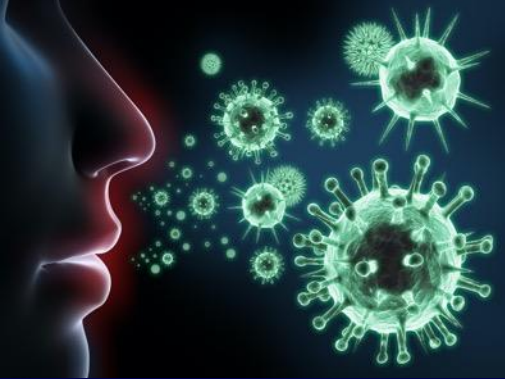


Role for pro/prebiotic supplements

- After anti-biotics
- Chemotherapy
- Radiotherapy
- NSAID
- Travelling
- Going into hospital
- Alcoholic binge
- Covid

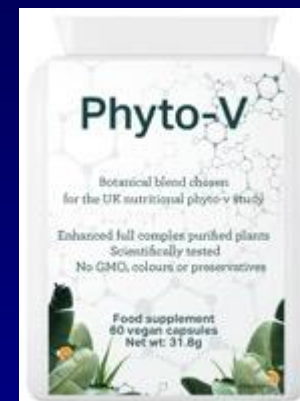
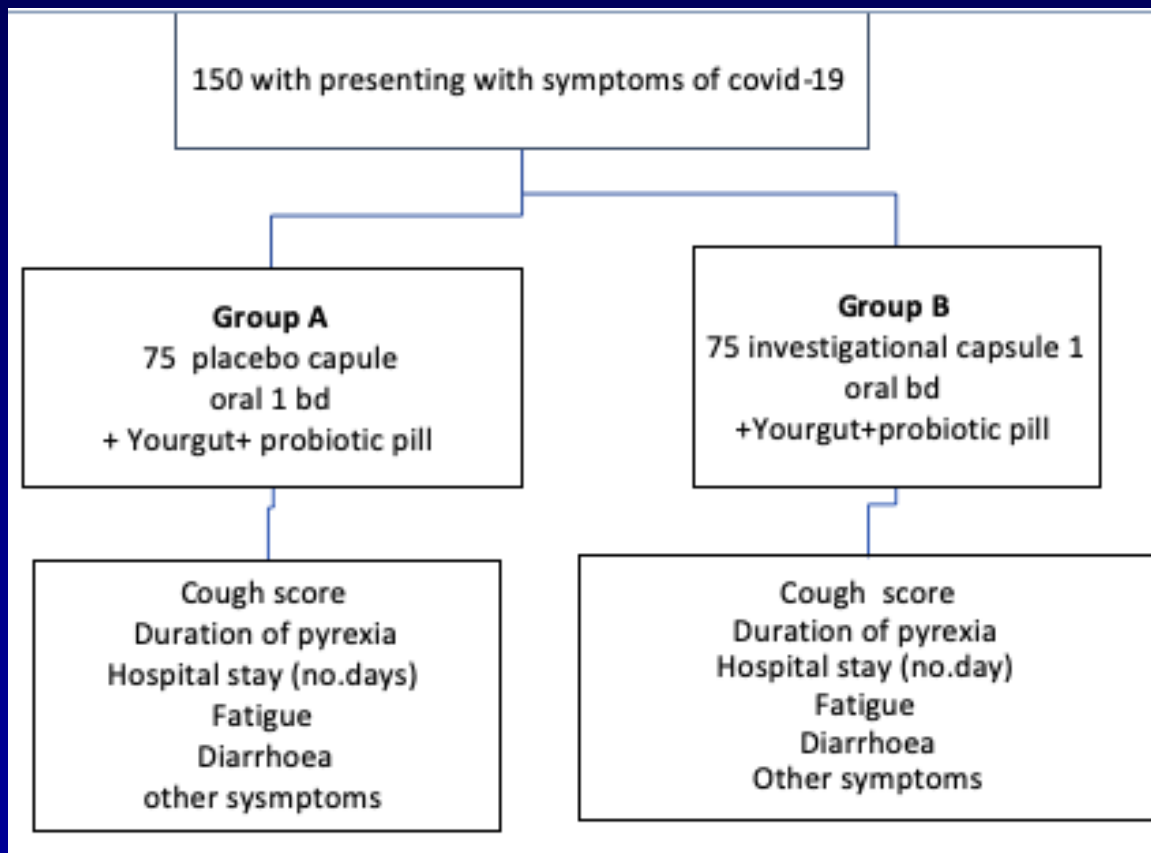


Kechagia M, Basoulis D, Konstantopoulou S, Dimitriadi D, Gyftopoulou K, Skarmoutsou N, Fakiri EM. Health benefits of probiotics: a review. ISRN Nutr. 2013

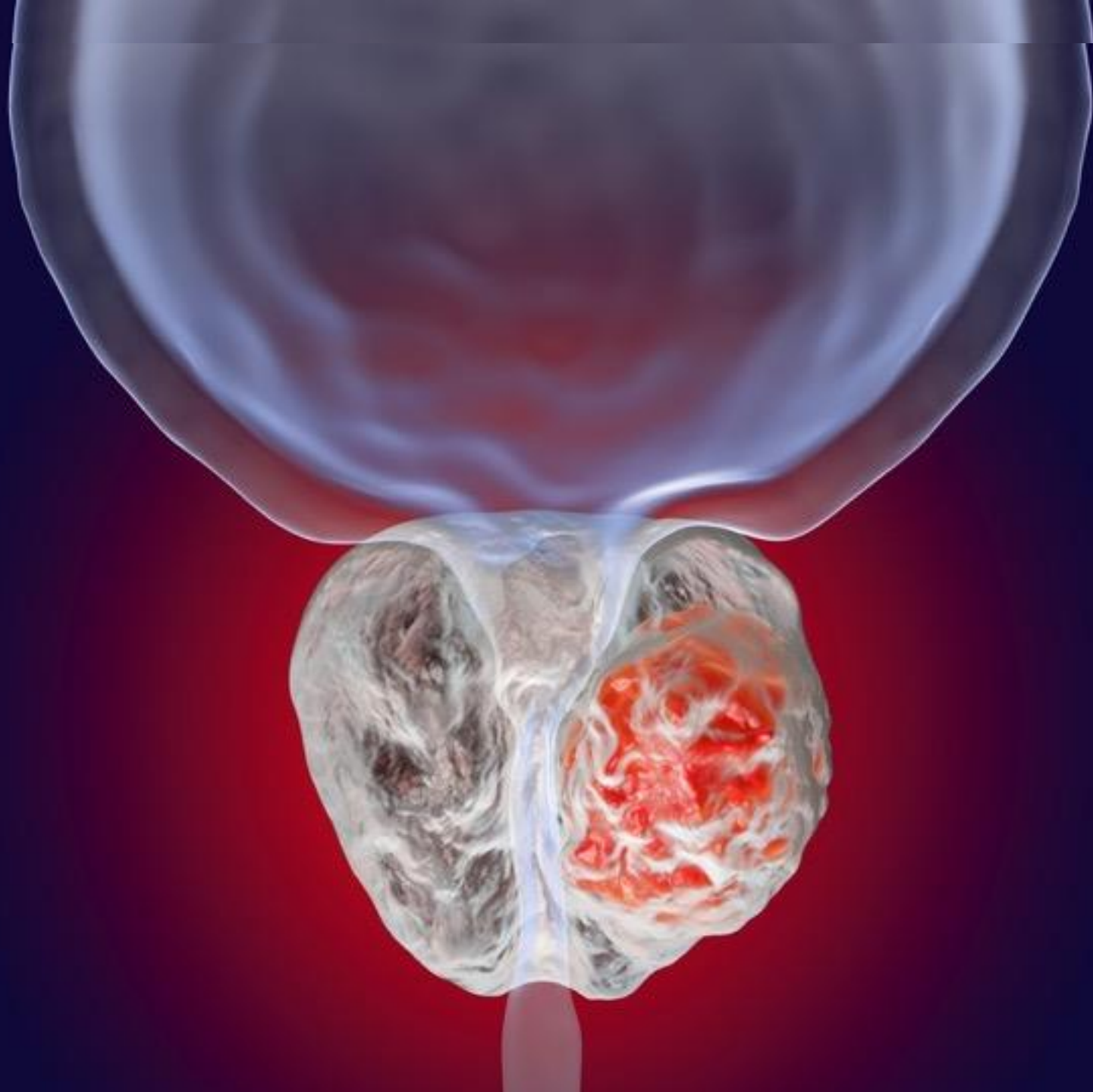


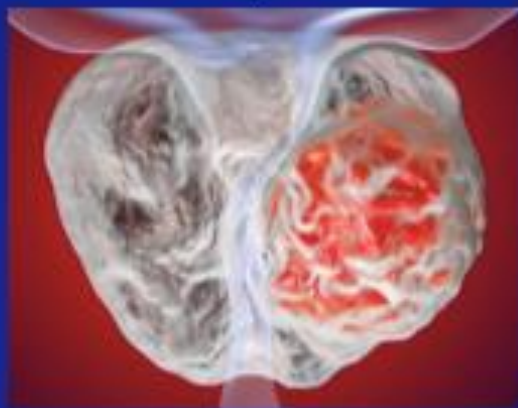
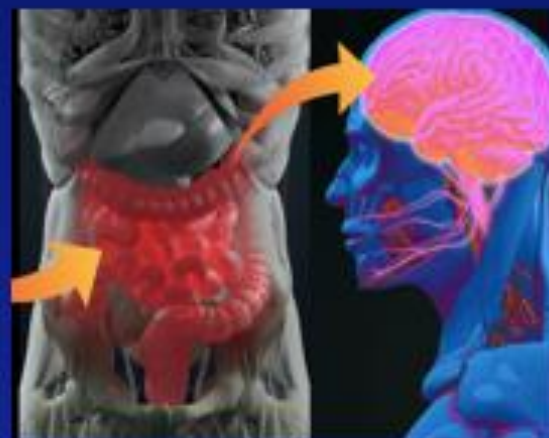
Covid nutritional intervention study

The UK Phyto-V study (phyto.v.com)

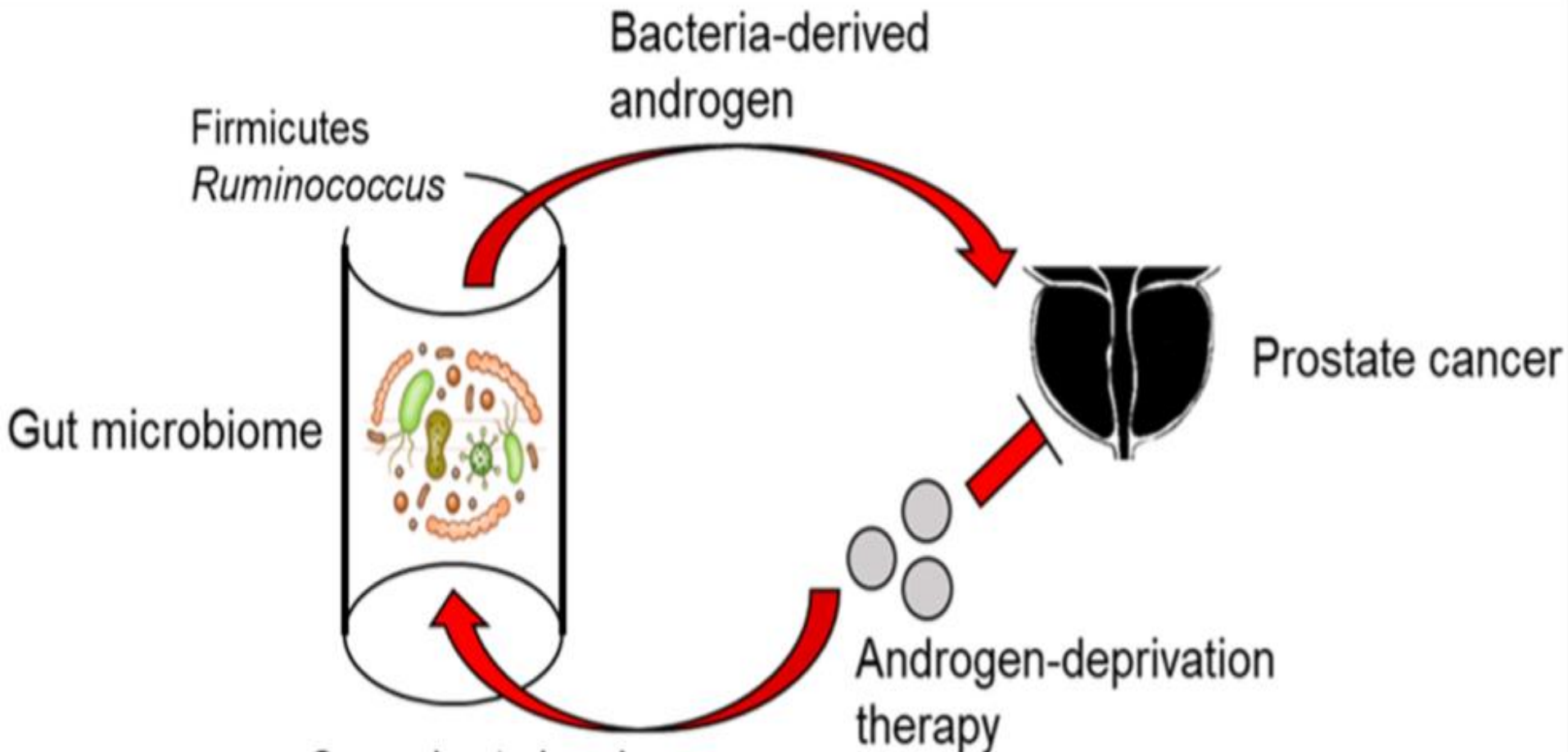


Thomas, R. Double-Blind, RCT Evaluating a Phytochemical-Rich Nutritional Capsule in Addition to a Probiotic Capsule among Individuals with COVID-19—The UK Phyto-V Study. *COVID* **2022**, 2, 433-449.



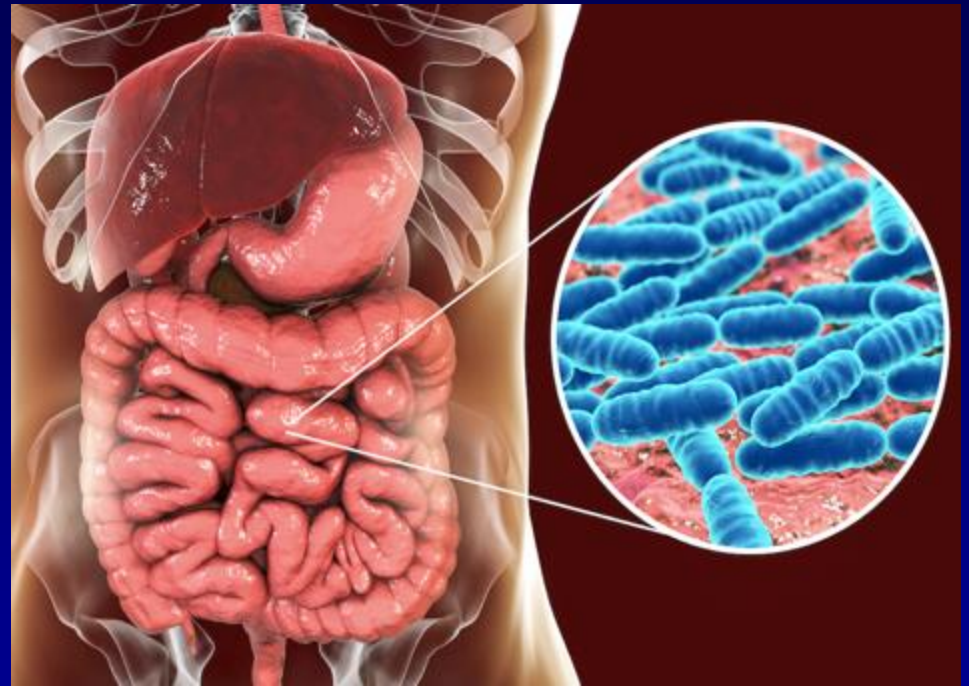


The gut – Prostate pathway



Hsiao et al Circulating androgen regulation by androgen-catabolizing gut bacteria
Gut Microbes. 2023, 15(1):

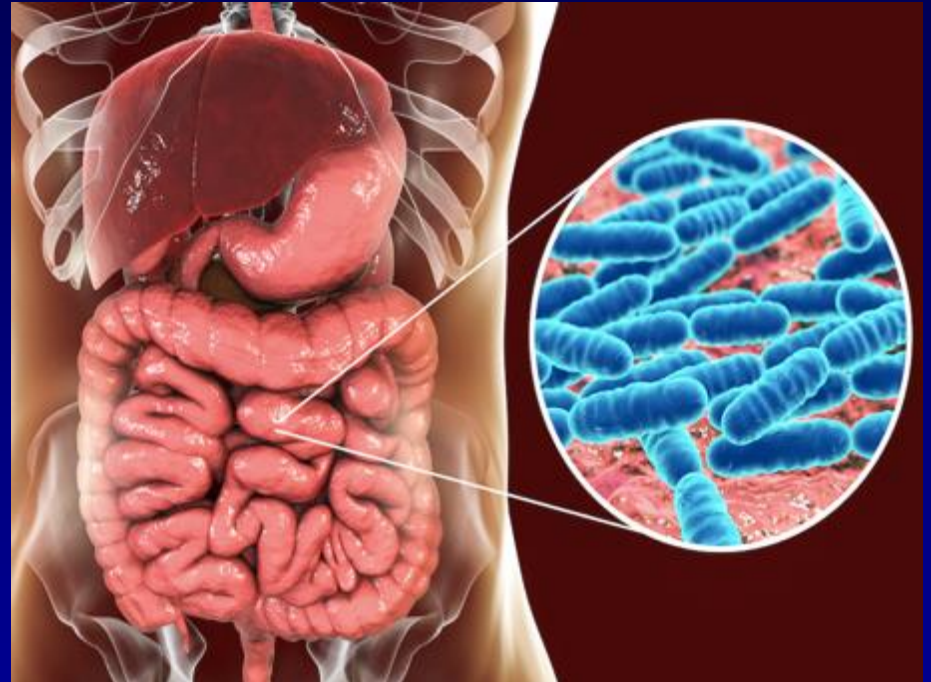
Dysbiosis is triggered by ADT



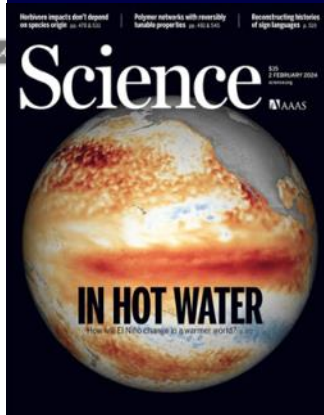
Kure A et al . Gut environment changes due ADT in patients with prostate cancer. *Prostate Cancer Prostatic Dis.* 2023;26(2):323-330.

Sfanos K et al. GI microbiota in prostate cancer patients treated with ADT. *Prostate Cancer Prostatic Dis.* 2018;21(4):539

Worse dysbiosis linked to CRPC



Terrisse S, et al. Immune system and intestinal microbiota determine efficacy of androgen deprivation therapy against prostate cancer. *J Immunother Cancer*. 2022 Mar;10(3):e004191.



Commensal bacteria promote endocrine resistance in prostate cancer through androgen biosynthesis

NICOLÒ PERNIGONI ^{ID}, ELENA ZAGATO ^{ID}, ARIANNA CALCINOTTO ^{ID}, MARTINA TROIANI, RICARDO PEREIRA MESTRE ^{ID}, BIANCA CALI ^{ID}, GIUSEPPE ATTANASIO, JA-

Faecal microbiota transplantation (FMT):

- From hormone-sensitive CaP patients converted CRPC to mice to hormone sensitive

Nicolò Pernigoni et al. Commensal bacteria promote endocrine resistance in prostate cancer through androgen biosynthesis. *Science*, 2021 DOI: [10.1126/science.abf8403](https://doi.org/10.1126/science.abf8403)

What do these findings mean for men?



“In the long-term, our aim would be to produce a bacteria rich product to prevent resistance to treatment, which could help men live longer”

Can an intervention to improve gut health improve Prostate Cancer Outcomes?



Chief and principle investigators: Mr Z Fazili Consultant Urologist, Robert Thomas Bedford & Addenbrookes Cambridge University Hospitals, Biological & Exercise Scientist Bedford University

Co-Collaborators: Stacey Kenfield, California, Rob Newton Australia, Simon Russel Cambridge, Anita Mehta UCLH

NHS

Bedfordshire Hospitals
NHS Foundation Trust



Cambridge University Hospitals
NHS Foundation Trust



What probiotic

Altering the ratio

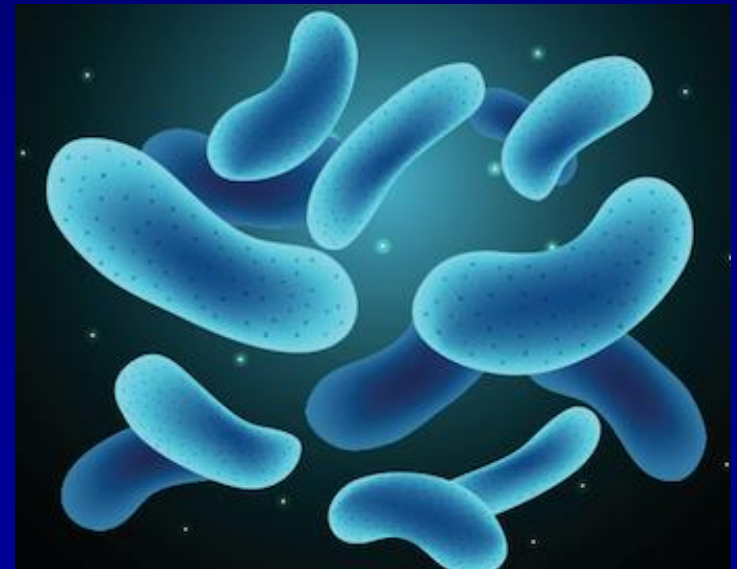
Pro-inflammatory



Anti-inflammatory

Lactobacillus:

- Lactic acid producing
- Improve PH of large bowel
- Direct antimicrobial properties
- Safe
- Survive gastric acid





Which Probiotic?

10 Billion CFU:

- 5 non-histamine lactobacillus

Built-in Prebiotic - Inulin (chicory)

Vitamin D - 800iu

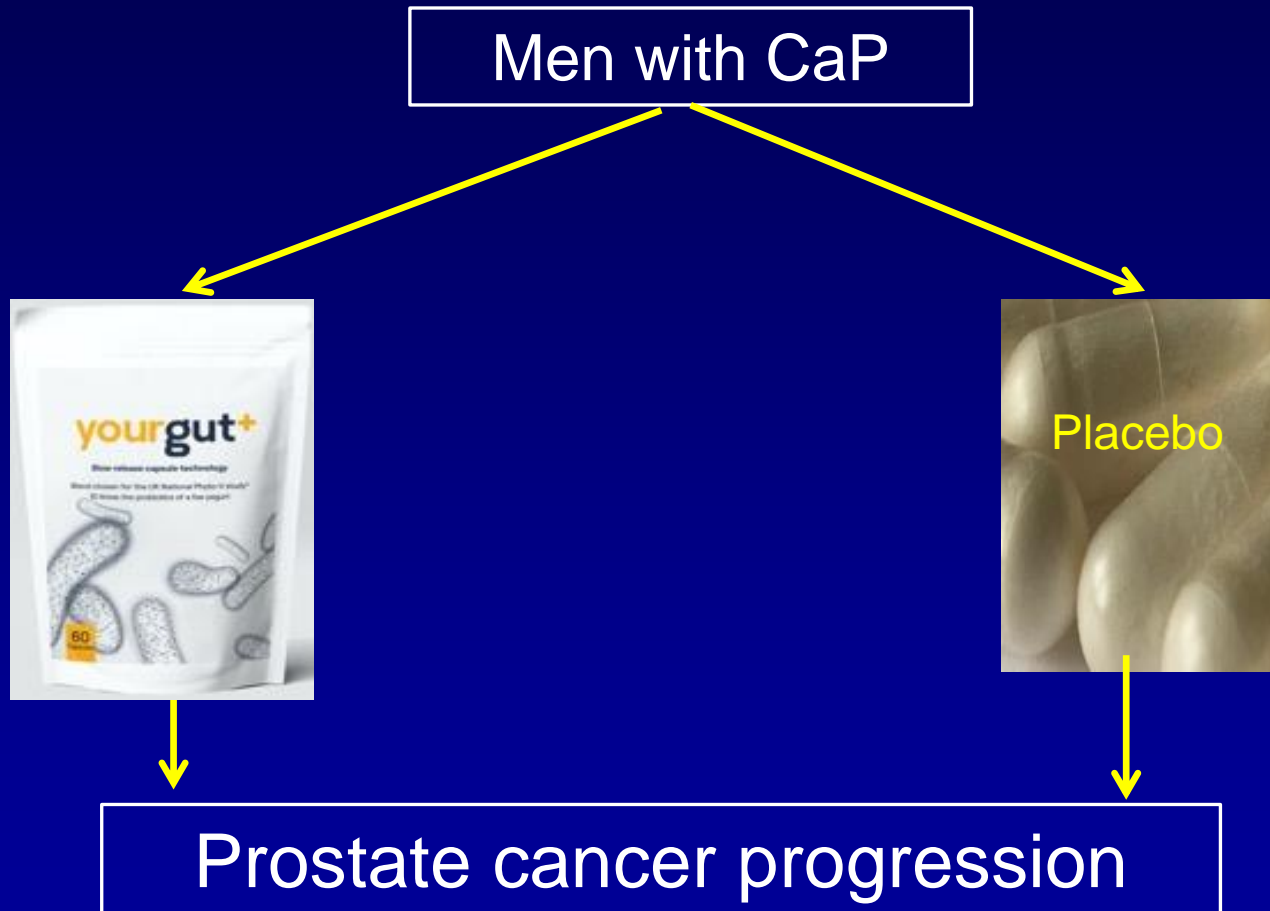
Delayed release vegan capsule

In previous studies:

- Vitamin D levels increased
- Showed clinical benefit
- Safe

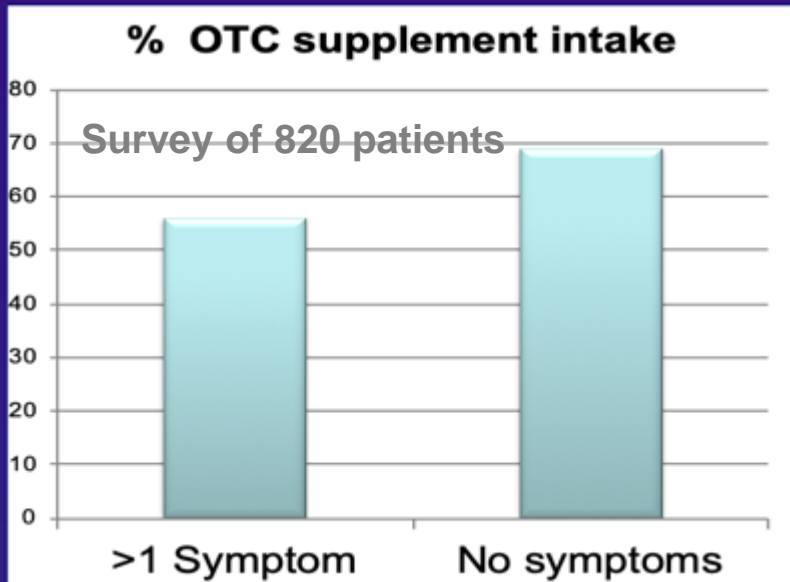


Potential design





Australia



The Bedford Real World Study
Thomas R, Williams M, Smith G, Ashdown G

880 oncology participants
Bedford and Cambridge

MASCC/ISCOO
ANNUAL MEETING ON
SUPPORTIVE CARE IN CANCER
Adelaide, Australia | 23-25 June, 2016





Patient input

- Melton Mowbray Support Group
- Bedford Prostate Support
- Cambridge Cancer Support

Happy

- To be randomised to probiotic

Not happy

- To stop other OTC unless we provide the best available phytochemical rich capsule
- To have a placebo only arm



Potential design

Men with CaP surveillance – no ADT

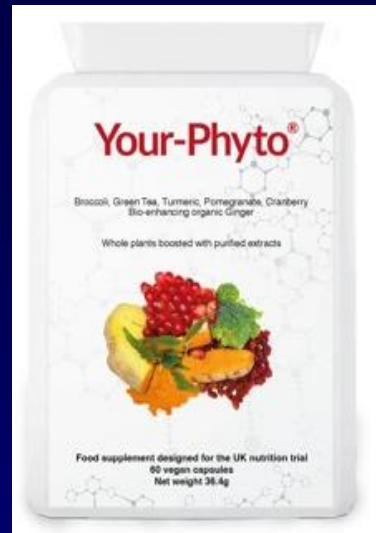




- Whole broccoli
- Whole turmeric
- Pomegranate
- Green tea



- Whole broccoli
- Whole turmeric
- Turmeric extract
- Whole pomegranate
- Pomegranate extract
- Green tea
- Whole organic ginger
- Cranberry extract



Bio-enhancing Ginger:

- Better tolerance
- Improved absorption
- Further trial data

Cranberry:

- Further trial data
- Potential symptoms

Standardised:

- Curcuminoid Ellagic Acid

Higher strength:

- Whole plant plus
- Targeted extracts



Can a probiotic & Vita D plus a phytochemical rich foods aid men with CaP? A double blind placebo RCT IRAS 321309

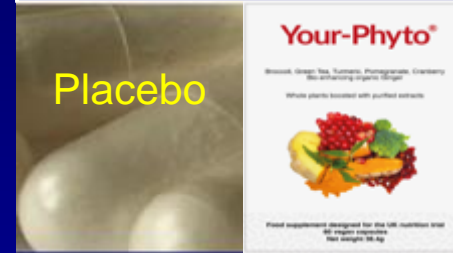
220 men with CaP surveillance – no ADT

1:1
randomisation

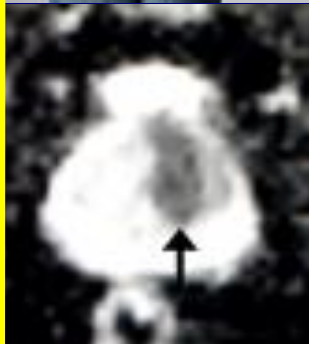
100 men



100 men

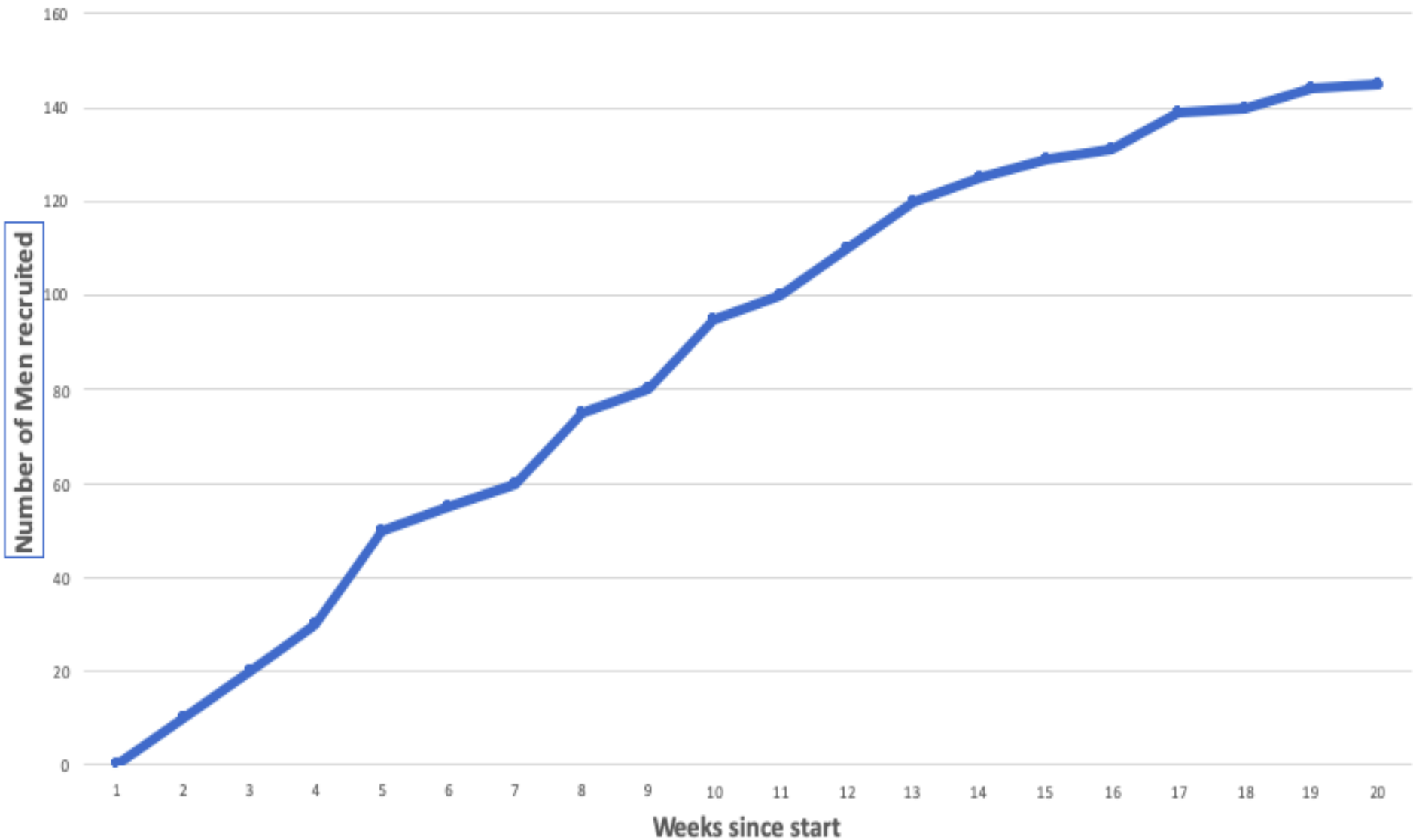


- Psadt (density) – pre and post trial between two groups
- MRI changes
- IPSS
- Erectile function (IIEF)
- Grip strength
- Testosterone and vitamin D levels

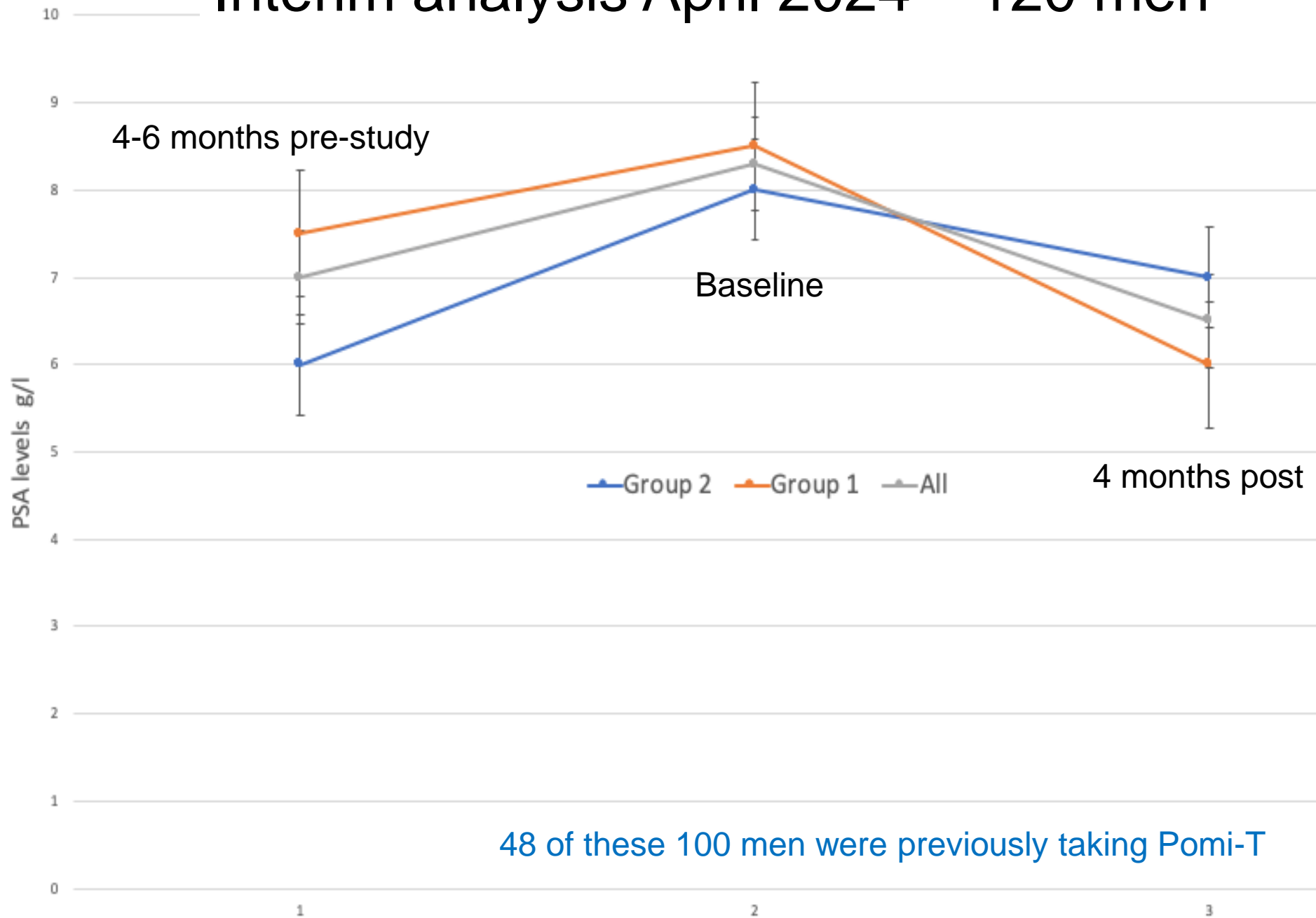


Recruitment figures since September 23

230 men recruited to May 2024



Interim analysis April 2024 – 120 men



48 of these 100 men were previously taking Pomi-T

Adverse and positive effects

Interim analysis April 2024 – 100 men

Serious – 3% (Stroke, gall stones, fall)

Skin rash – 1%

Bloating / wind 8%

Bowel symptoms improved – 14%

Urinary symptoms improved 30%

Erectile function improved 15%

Conclusions / summary

- Lifestyle and nutrition advice to improve gut health would be very sensible - on current data
- Interventions with pre and probiotics may have a role

Trial information

[Yourphyto.com/scientific-study](https://yourphyto.com/scientific-study)

