Why do doctors prescribe treatments that don’t work?

Andreas Makris

Mount Vernon Cancer Centre

Disclosures (Conflicts of Interest)

- Advisory Boards

  Lilly, Roche, Pfizer, Novartis, Astra Zeneca, Aventis, Seagen

- Lecture Honorariums

  Lilly, Roche, Pfizer, Novartis, Veracyte

George Washington’s death

- Died aged 67, on 14.12.1799 at home at Mount Vernon
- Suffered from a throat infection probably acute epiglottitis
- His physicians advised blood letting on four occasions
- Lost 40% of his blood volume

Why do doctors prescribe treatments that don't work?

Most of the time, doctors prescribe the appropriate treatment for the right patient at the right time

But, on occasions they may prescribe

- Ineffective treatments
- Treatments with marginal benefits
- Treatments where toxicity out-weighs the benefit
- Treatments where the cost does not justify the expenditure
- More treatment than is necessary

Why do doctors prescribe treatments that don't work?

- Patient expectations (real or perceived)
- Need to do something
- Over-reliance on clinical experience rather than evidence
- Natural history of the disease
- Arrogance
- Greed

Doctors may prescribe ineffective treatments that are:

- Evidence-based
  - The evidence at the time was wrong
  - The data on which the evidence was produced was either falsified or selectively published
- Non evidence-based

Evidence-based medicine

- Term first used by Gordon Guyatt, Professor of Epidemiology at MacMaster University, in a 1992 JAMA paper
- He wanted to use the term scientific medicine but others in his department resisted this as ‘scientific medicine is what basic scientists did’

Evidence-based medicine – an oral history
Richard Smith
BMJ 2014; 348: g371

Doing what we have always done

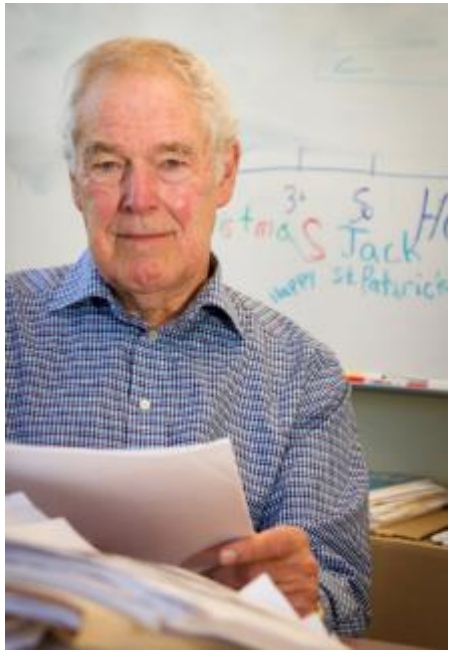
- George Washington – blood letting
- Iron supplements – standard dose 200mg TDS, now shown optimal dose is between 200mg OD or every other day
- Tonsillectomies
- Appendicectomies
- Ear grommets
- Frontal lobotomy
- Insulin for schizophrenia

Tonsillectomies

- 1960s Vermont, noticed that in two towns
  - 70% of children had tonsillectomies in one town
  - 20% had tonsillectomies in another town

- No difference in children's health in the two towns before or after tonsillectomies

Dr John Wennberg
American epidemiologist
1935-2024



Dartmouth Atlas Project

Home Data + Interactive Apps + Publications + About + Contact

The Dartmouth Atlas of Health Care

For more than 20 years, The Dartmouth Atlas Project has documented glaring variations in how medical resources are distributed and used in the United States. The project uses Medicare and Medicaid data to provide information and analysis about national, regional, and local markets, as well as hospitals and their affiliated physicians.

What's New?

- **News:** Atlas rates now available in dataverse
- **News:** John E. Wennberg, founder of Dartmouth Atlas, dies at 89
- **News:** Mapping out a new Dartmouth Atlas of Health Care: An interview with TDI Director Amber Barnato
- **News:** Atlas collection now available at the National Library of Medicine
- **Report:** Variations in Spending and Utilization Across Payer Types

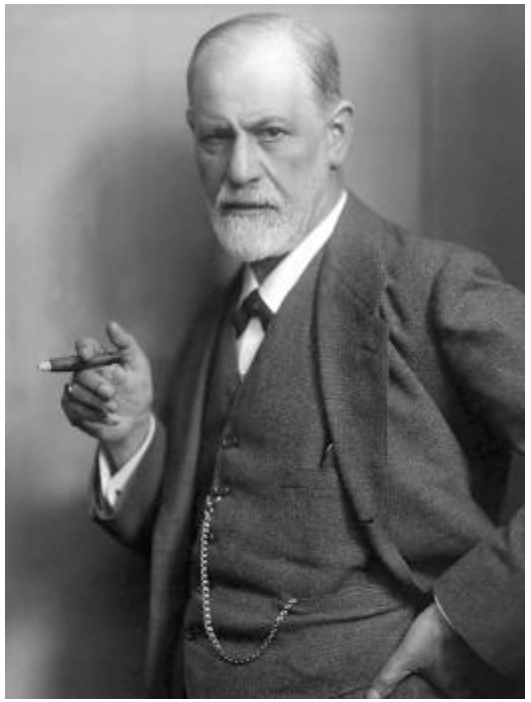
High-dose chemotherapy for EBC and MBC

- Started to be widely used in USA in 1980s and 90s, prior to the randomized controlled trials
- Based on
  - logical/plausible case (higher doses kill more cancer cells)
  - comparisons with historical controls
  - benefit based on surrogate end-points of tumor response
  - enthusiasts who hyped the benefit
- In 1990s USA, breast cancer was the commonest cancer for which patients received HD chemotherapy
- In 2000s, MBC was the commonest cancer for which anti-angiogenic therapies (esp. avastin) was used

‘Expert-based medicine’

- Princess Anne, Prince Philip’s mother, started behaving strangely, and having ‘religious delusions’ after her husband the King of Greece was deposed and court-marshalled
- She was diagnosed with schizophrenia

- Sigmund Freud’s opinion sought
- Freud believed her delusions were due to sexual frustrations recommended radiation of her ovaries



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REVIEW ARTICLE

Why Do Patients Choose Chemotherapy Near the End of Life? A Review of the Perspective of Those Facing Death From Cancer

Robin Matsuyama, Sashidhar Reddy, and Thomas J. Smith

- In all of the studies spanning multiple countries and two decades, patients would choose chemotherapy for a small benefit
- In many cases, patients would choose chemotherapy for a smaller expected benefit compared to the choices their healthcare providers would make for themselves
- Adverse effects appeared to be less of a concern for terminally ill patients than their well healthcare providers
- Patients attitudes and wishes vary widely when faced with a life-threatening or terminal illness, however, with some patients unwilling to undergo any treatment and others willing to undergo almost any treatment for any small chance of benefit

- 22% of all Medicare patients start a new chemotherapy regimen in the last month of life
- Within 2 weeks of death treatment started was 18.5%

Earle CC et al. JCO 2024; 22: 315-321

Prescribing more than is necessary

3 versus 6 months of adjuvant oxaliplatin-fluoropyrimidine combination therapy for colorectal cancer (SCOT): an international, randomised, phase 3, non-inferiority trial

Timothy J Iveson*, Rachel S Kerr*, Mark P Saunders, Jim Cassidy, Niels Henrik Hollander, Josep Tabernero, Andrew Haydon, Bengt Glimelius, Andrea Harkin, Karen Allan, John McQueen, Claire Scudder, Kathleen Anne Boyd, Andrew Briggs, Ashita Waterston, Louise Medley, Charles Wilson, Richard Ellis, Sharadah Essapen, Amandeep S Dhadda, Mark Harrison, Stephen Falk, Sherif Raouf, Charlotte Rees, Rene K Oleson, David Propper, John Bridgewater, Ashraf Azzabi, David Farrugia, Andrew Webb, David Cunningham, Tomas Hickish, Andrew Weaver, Simon Gollins, Harpreet S Wasan, James Paul

Lancet Oncol 2018; 19: 562–78
See Comment page 442
*Joint first authors

Summary

Background 6 months of oxaliplatin-containing chemotherapy is usually given as adjuvant treatment for stage 3 colorectal cancer. We investigated whether 3 months of oxaliplatin-containing chemotherapy would be non-inferior to the usual 6 months of treatment.

Interpretation In the whole study population, 3 months of oxaliplatin-containing adjuvant chemotherapy was non-inferior to 6 months of the same therapy for patients with high-risk stage II and stage III colorectal cancer and was associated with reduced toxicity and improved quality of life. Despite the fact the study was underpowered, these data suggest that a shorter duration leads to similar survival outcomes with better quality of life and thus might represent a new standard of care.

6 versus 12 months of adjuvant trastuzumab for HER2-positive early breast cancer (PERSEPHONE): 4-year disease-free survival results of a randomised phase 3 non-inferiority trial

Helena M Earl, Louise Hiller, Anne-Laure Vallier, Shrushma Loi, Karen McAdam, Luke Hughes-Davies, Adrian N Harnett, Mei-Lin Ah-See, Richard Simcock, Daniel Rea, Sanjay Raj, Pamela Woodings, Mark Hamies, Donna Howe, Kerry Raynes, Helen B Higgins, Maggie Wilcox, Chris Plummer, Janine Mansi, Ioannis Gounaris, Betania Mahler-Araujo, Elena Provenzano, Anita Chhabra, Jean E Abraham, Carlos Caldas, Peter S Hall, Christopher McCabe, Claire Hulme, David Miles, Andrew M Wardley, David A Cameron, Janet A Dunn on behalf of PERSEPHONE Steering Committee and Trial Investigators*

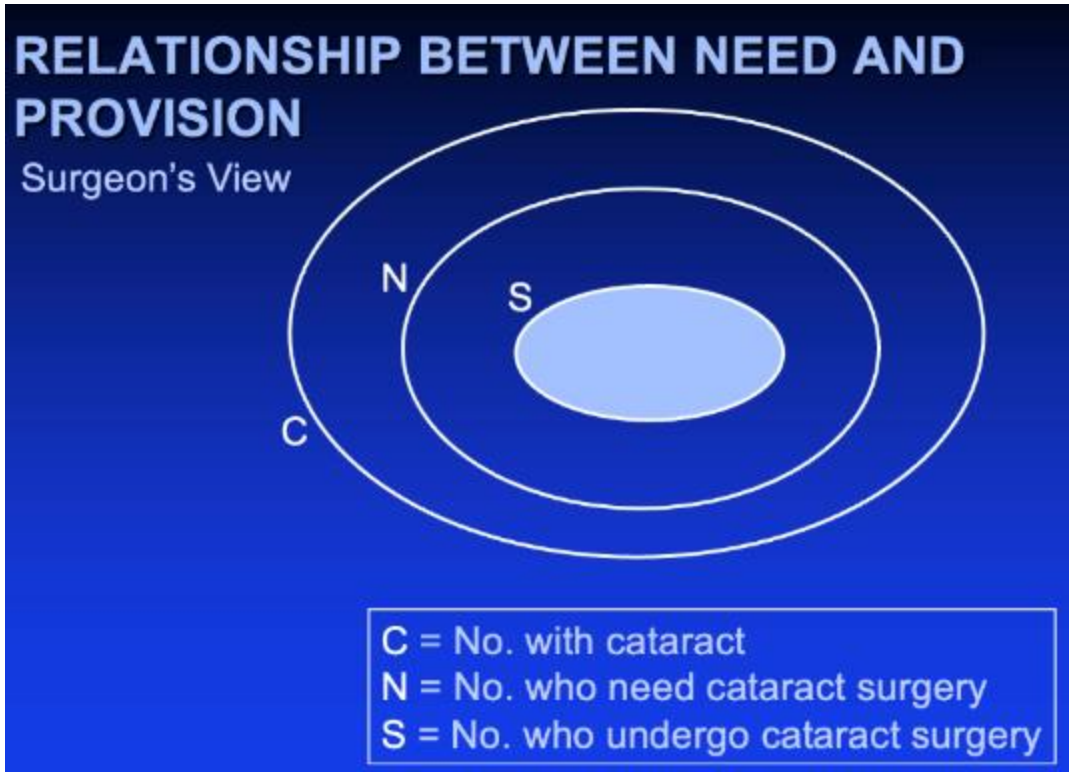
Lancet 2019; 393: 2599–612
Published Online
June 6, 2019
http://dx.doi.org/10.1016/
S0140-6736(19)30650-6

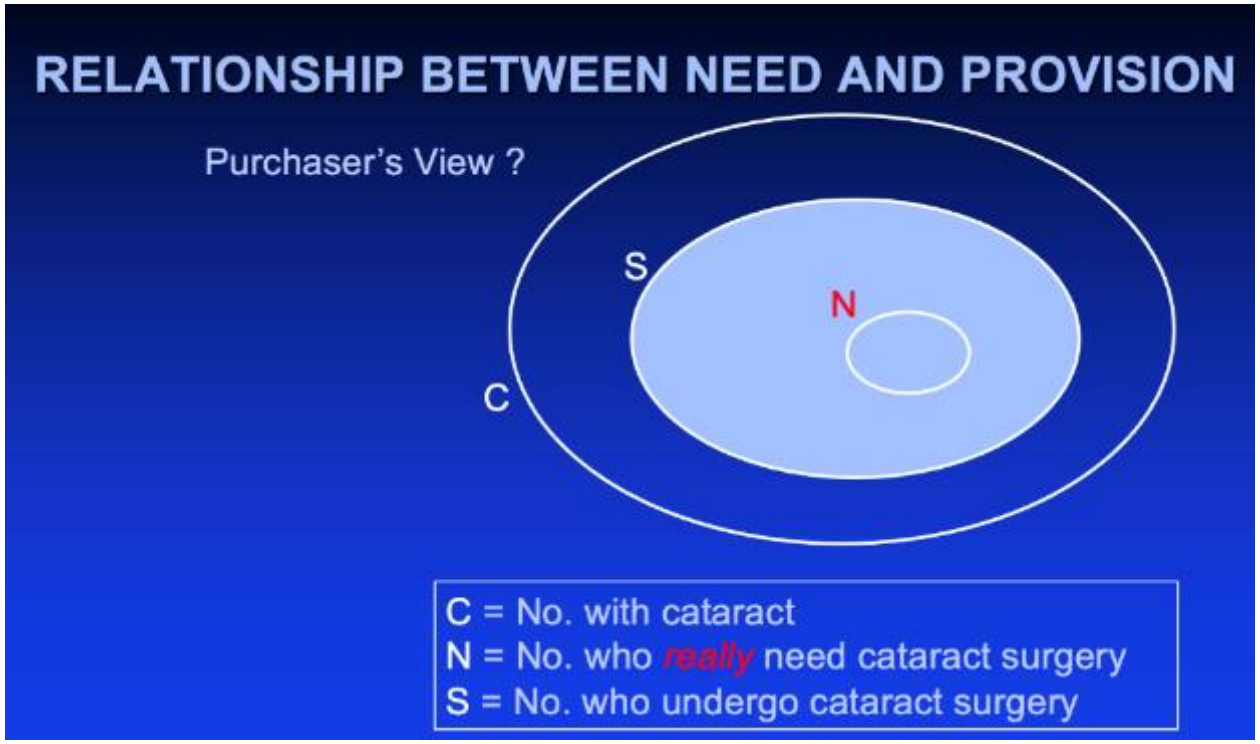
Summary

Background Adjuvant trastuzumab significantly improves outcomes for patients with HER2-positive early breast cancer. The standard treatment duration is 12 months but shorter treatment could provide similar efficacy while reducing toxicities and cost. We aimed to investigate whether 6-month adjuvant trastuzumab treatment is non-inferior to the standard 12-month treatment regarding disease-free survival.

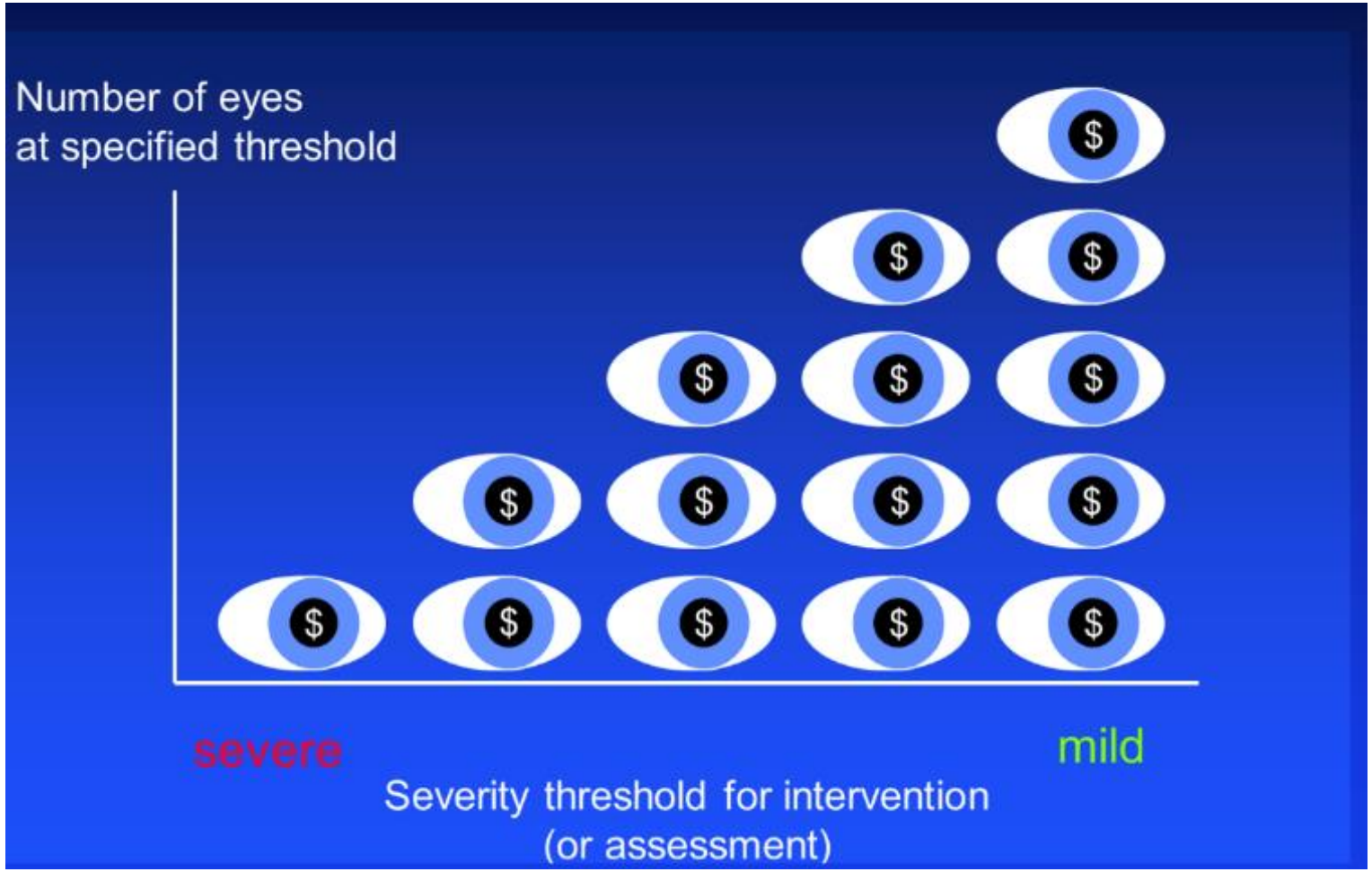
Interpretation We have shown that 6-month trastuzumab treatment is non-inferior to 12-month treatment in patients with HER2-positive early breast cancer, with less cardiotoxicity and fewer severe adverse events. These results support consideration of reduced duration trastuzumab for women at similar risk of recurrence as to those included in the trial.

Does everyone who has cataract surgery need it?



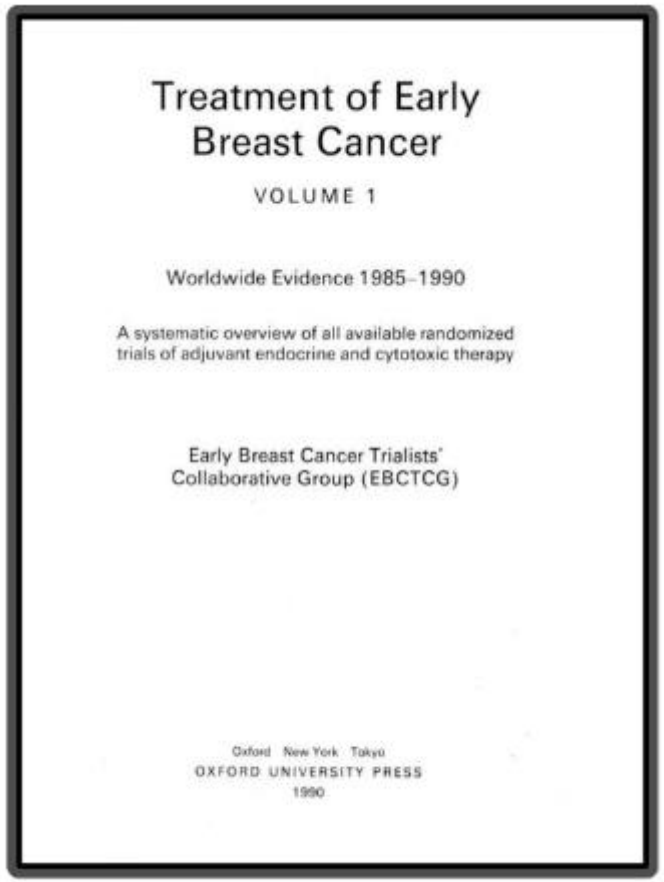


The golden triangle of ophthalmology!!




I WANT TO
BELIEVE
FBI

Sometimes evidence and guidance is wrong



'Benefit of tamoxifen irrespective of ER status'

SPECIAL ARTICLE

National Institutes of Health Consensus Development Conference Statement: Adjuvant Therapy for Breast Cancer, November 1–3, 2000

*National Institutes of Health Consensus Development Panel**

'Because adjuvant polychemotherapy improves survival, it should be recommended to the majority of women with localized breast cancer regardless of lymph node, menopausal, or hormone receptor status'

JNCI 2001; 93: 979-989

Falsification of research data

- Examples
  - Oncology
    - Werner Bezwoda, South Africa, High-dose chemotherapy in EBC and MBC
  - Obstectrics
    - Dr Malcolm Pearce, UK, ectopic pregnancy extracted successfully reimplanted in patient’s uterus
  - COVID
    - Didier Raoult, France, benefit with hydroxychloroquine in COVID
    - Sapun Desai, US, no benefit with hydroxychloroquine in COVID but increased deaths and heart disease, led WHO to close multiple trials
  - Surgery
    - Paolo Macchiarini, Sweden, transplantation of synthetic tracheas

High-dose chemotherapy in MBC
Falsified data published

Dr Werner Bezwoda

- ASCO on site audit of the South African high-dose chemotherapy for MBC
- 90 patients involved and records searched
  - 61 could not be found
  - Only 27 had sufficient records to verify eligibility
  - 18/27 did not meet at least one eligibility criteria
  - Only 25 appeared to have received the assigned treatment, temporarily associated with their enrollment date
  - 22/25 had received HD chemotherapy

Raymond B et al. JCO 2001; 19

Pharmaceutical industry

- Relationship between pharma and doctors may not be in patients' best interest
- Pharma may support doctors by
  - Consultancy fees
  - Lecture honorariums
  - Research grants
  - Hospitality
  - Attendance of meetings
- Doctors may
  - Prescribe expensive drugs when benefits are unclear
  - Be involved in producing guidelines that influence others

Pfizer Gabapentin scandal

- Pfizer pleaded guilty pleaded guilty to numerous civil and criminal charges for illegally promoting the off-label use of gabapentin
- Pfizer was charged under the Racketeer Influenced and Corrupt Organisations Act
- Agreed to pay $240m criminal fine and $152m to state and federal healthcare programs

- Dr David Franklin, Harvard microbiologist filed a whistleblower suit in 2002 under the 1996 False Claims Act
- Claimed that Pfizer used ‘fraudulent scientific evidence’ to promote off-label use
- Claimed the company suppressed study results, planted people in medical audiences to ask questions, perks to doctors, used ghostwriters, gave consultation fees to thought leaders etc
- Company trained staff for at least 11 off-label uses
- Claimed off-label use accounted for >90%

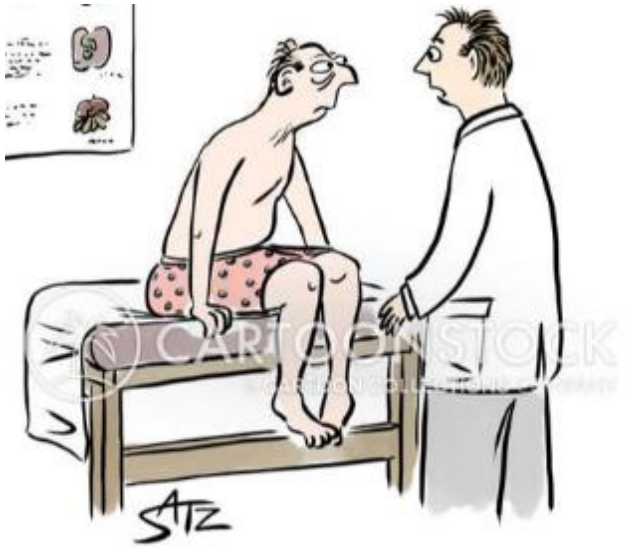
Dr David Franklin, received $24.6m as part of the settlement

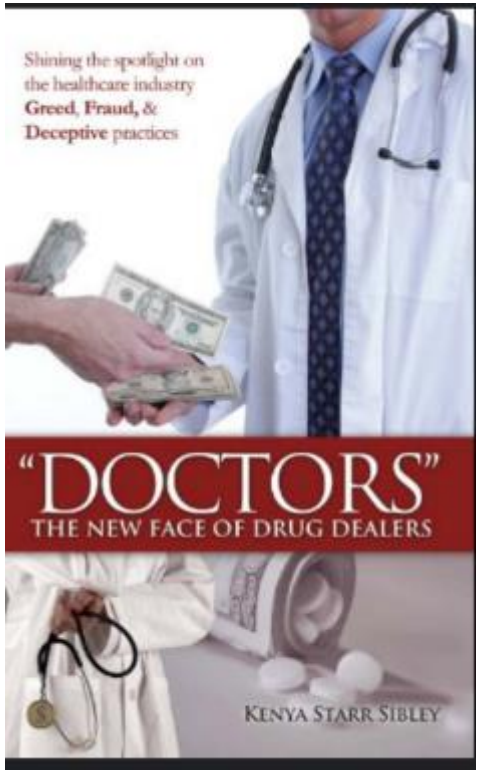
BMJ 2004; 238: 1217

Greed and the medical profession

‘With an ethic of greed doctors cease to base their decisions on compassion and caring to become merchants selling medical services to the highest bidder’

BMJ 1993; 306:151. Ralph Crawshaw, Professor of Psychiatry in Portland, Oregon





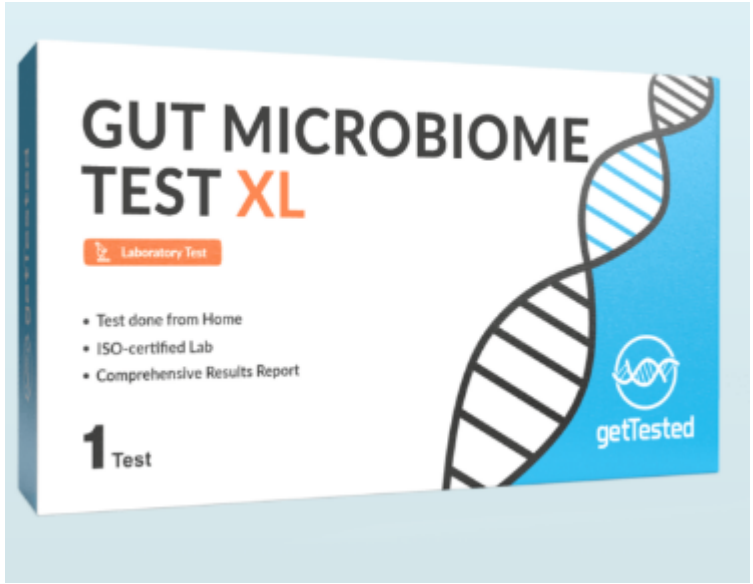
Ian Patterson

Breast surgeon, Birmingham 1997-2011

Sentenced to prison for 20 yrs in 2017

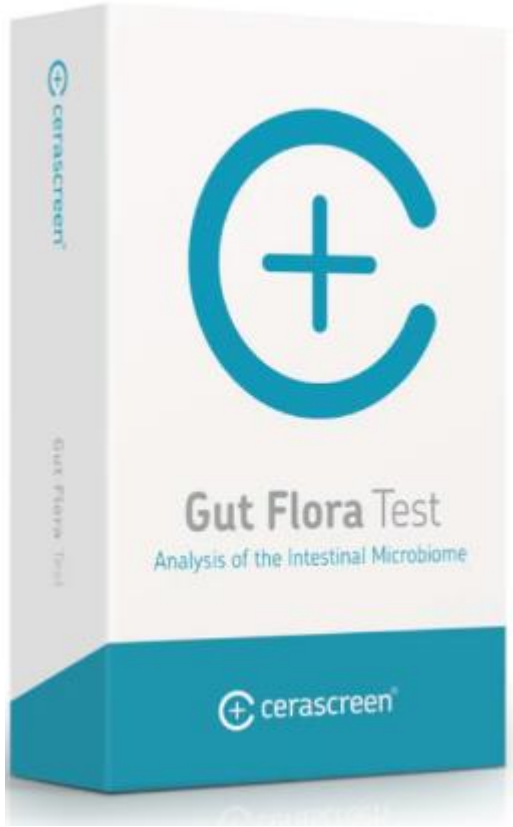
- Cleavage sparing mastectomies
  - >800, mainly in NHS, some in private sector
  - Motivating factors: **ARROGANCE, BULLY, 'GOD COMPLEX'**
- Unnecessary surgery
  - Mainly in private sector
  - Motivating factor: **GREED**

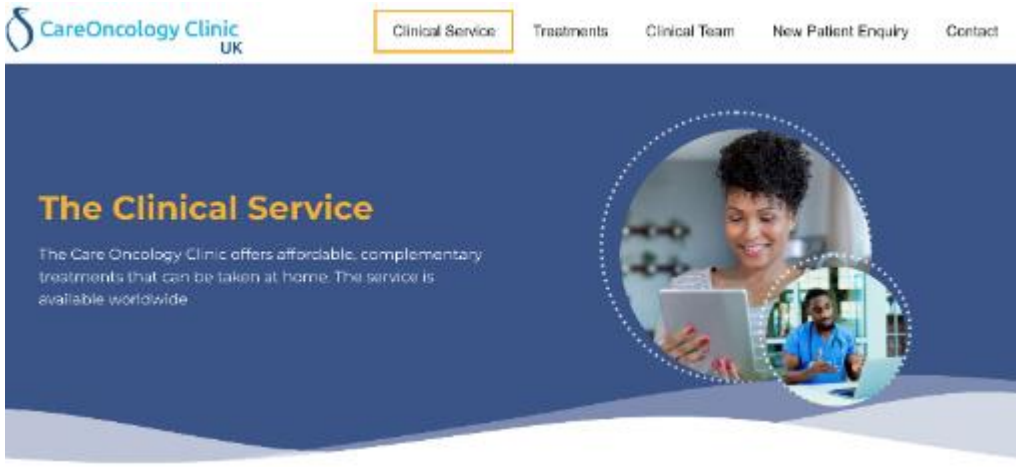
Microbiome Home Test kits



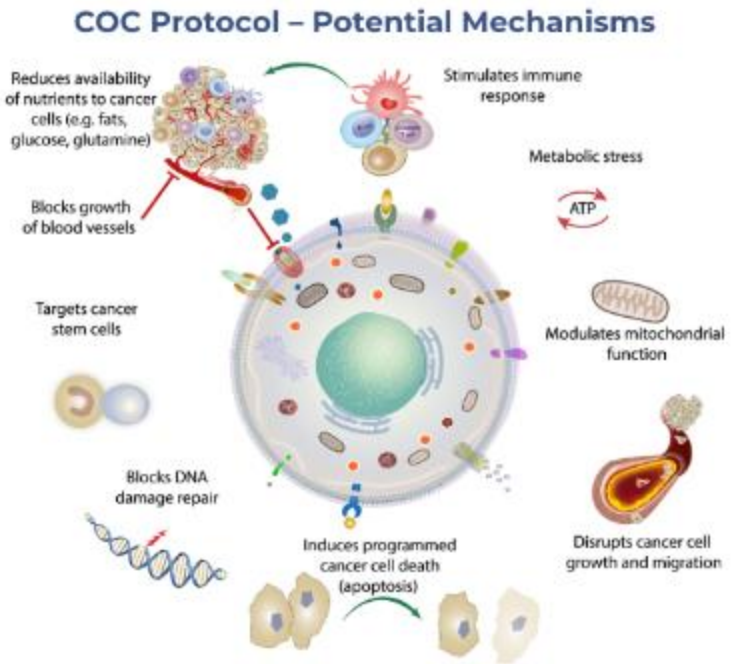
£ 279,00

The Gut Microbiome Test XL is for those who really want to understand their health. Whether you have IBS/IBD, stomach issues like Crohn's disease or ulcerative colitis, weight problems, diseases such as Parkinson's or Alzheimer's, depression, or other diffuse problems with no apparent cause, this test can provide answers to any gut imbalances you may have. It is our most comprehensive and best-selling gut health test.





Metformin, statin, doxycycline, mebendazole



Who is the COC Protocol for?

By targeting the altered metabolic mechanisms which are common to most cancers (but not usually healthy cells), we believe the COC Protocol can be used in patients with any cancer regardless of specific type, stage, or location.

Patients **aged 18 and over** may engage with Care Oncology Clinic at different points in their cancer journey. You could be someone who has:

- a new diagnosis and is about to begin systemic treatment for a type of cancer which carries a risk of progression or recurrence
- completed a course of cancer treatment and is on active surveillance
- no evidence of disease (NED) but is at risk of recurrence
- disease progression and commencing further lines of therapy
- commenced palliative care

What are the costs associated with the Care Oncology Clinic?

Cost Overview

Initial consultation (40-45 mins)	£510 (**Option to split the cost into three instalments using PayPal Pay in 3**)
Follow-up consultations (20-25 mins)	£250 (first review appointment 6 weeks from commencement of treatment; 12 week reviews thereafter)

Inspected and rated

Good

CareQuality Commission

https://careoncologyclinic.com

Discussion

- Most prescriptions by most doctors are appropriate
- On occasions doctors may prescribe treatments that are ineffective, have marginal benefits, toxicity or expense do not justify the treatment, and may prescribe more than is necessary
- The reasons for inappropriate prescribing are complex but seeking to understand them can lead to more appropriate prescribing and better outcomes for our patients