

CANCER – Introduction and clinical challenges

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Format of talk

- Introduction to Cancer – cancer biology
- Introduction to Cancer treatment
- Current and projected cancer burden
- Clinical challenges – opportunities for ML

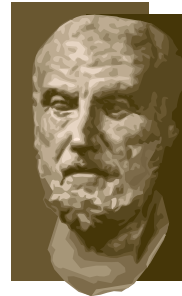
What is cancer?

Uncontrolled growth of abnormal cells in a tissue, invasive and spreading

Egyptian papyrus 3000-1500 BC - description of breast cancer



Hippocrates 400 BC - recognition of difference between malignant and benign tumours



Origins of cancer - tumours arise from normal tissues

Majority of tumours originate from epithelial tissues

Benign and malignant tumours

Squamous cell carcinomas and adenocarcinomas

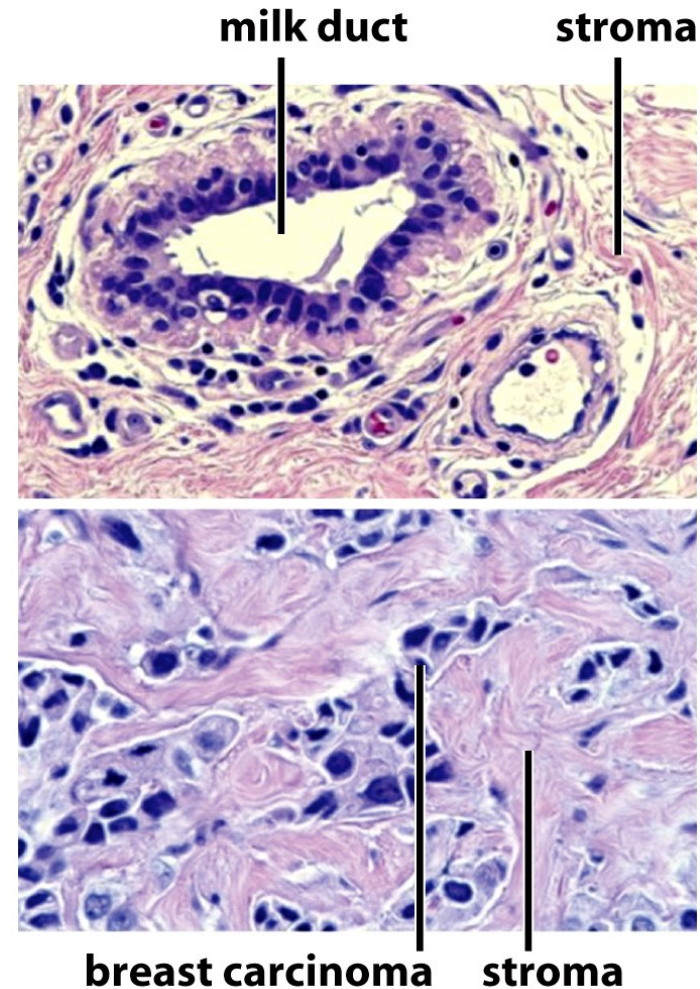


Figure 2.1b *The Biology of Cancer* (© Garland Science 2007)

Origins of
cancer –
tumours arise
from normal
tissues

Other tumours
arise from
non-epithelial
cells

Sarcomas - from
mesenchymal
cells

Neuroectodermal tumours - cells from
central and peripheral nervous
system

Brain tumours (eg gliomas,
neuroblastoma)

Leukaemias and
lymphoid and
myeloid tumours -
from
haematopoietic
tissue and cells of
immune system

Complexity of
disease

"Microevolution"
process leading to
accumulation of
5-10 critical
mutations requires
many years.

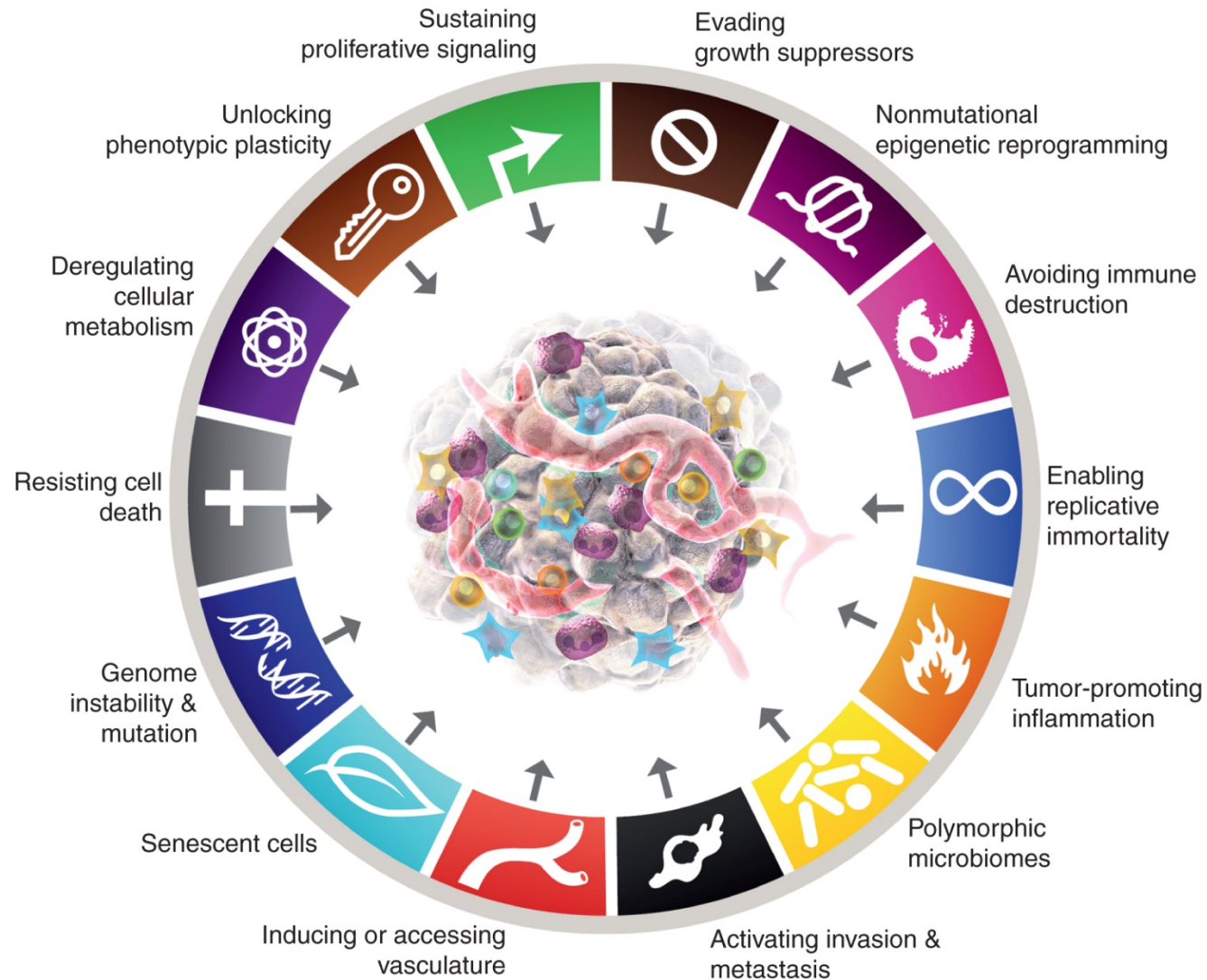
Cancer is a
genetic disease

Mutations causing
cancer occur

- ❑ in germline
and
- ❑ in somatic cells

Mutations in different types of genes may initiate cancer

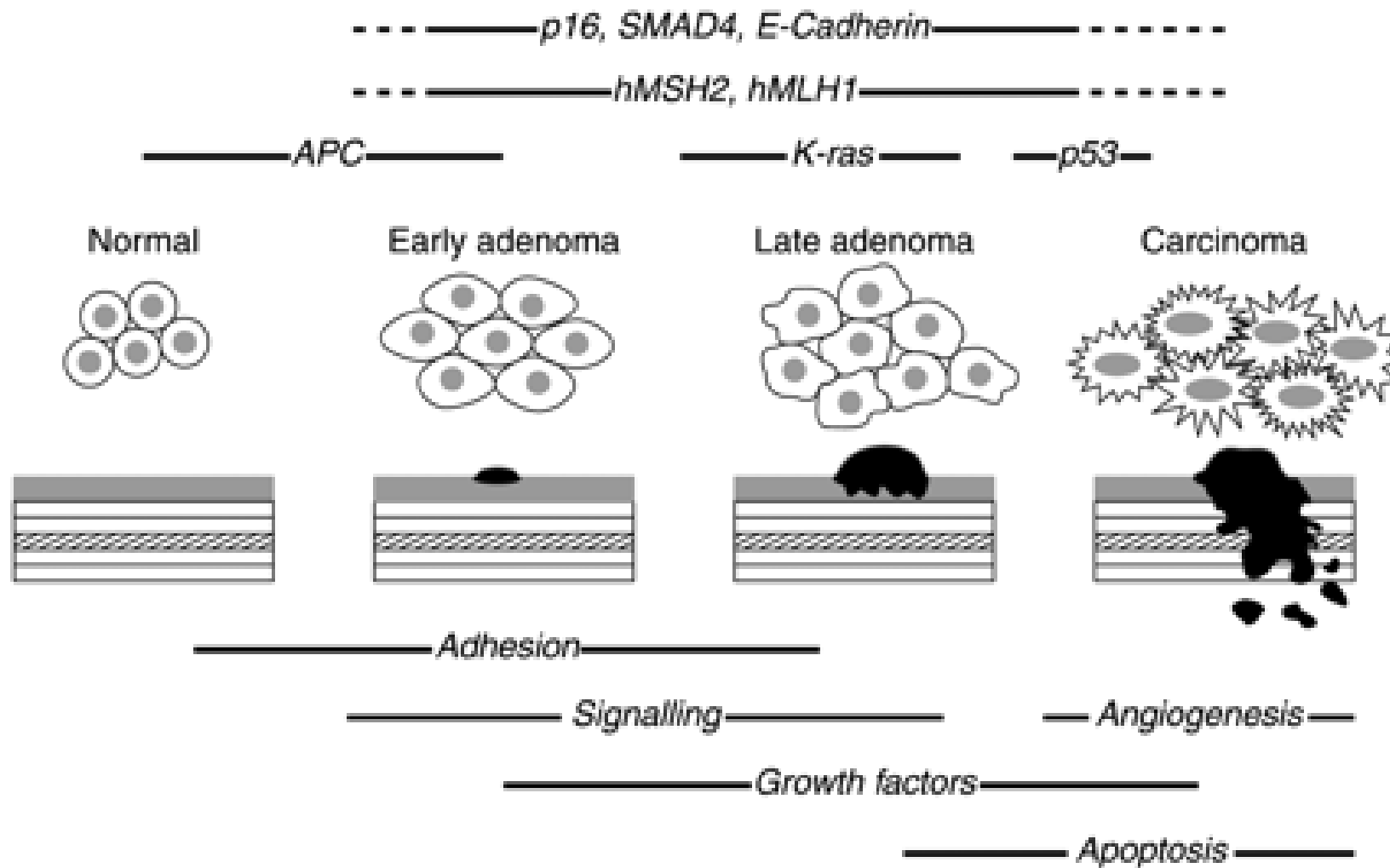
- **Genes that normally control:**
 - Growth
 - Passing on of signals from outside the cell
 - (receptors) across the cytoplasm to the nucleus
 - Programmed cell death (apoptosis)
 - The cell cycle
 - Stemness
 - The integrity of the genome- DNA repair



How do mutations arise?

- **Copying errors during DNA replication – ageing**
- **Spontaneous depurination**
- **Exposure to different agents - carcinogens**
 - **e.g. background ionising radiation**
 - **UV light**
 - **Tobacco products**
 - **Human papilloma virus**
 - **Obesity**

Cancer is a progressive multistep disorder



Fearnhead et al, Br.Med. Bull. 64: 27-43 (2002)

<http://bmb.oxfordjournals.org/content/64/1/27.full.pdf+html>

Cancer can originate from any tissue

Cancer is a genetic disease driven by mutations in genes controlling vital cellular processes

Cancer is a progressive disorder resulting from multiple genetic steps

Cancer – fundamentals of treatment

Cancer characteristics

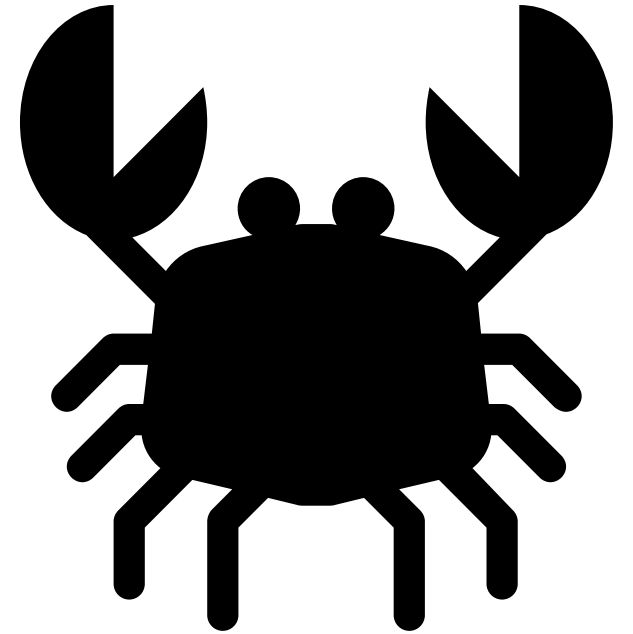
- Tissue of origin
Stage
Aggressiveness(grade)

Cancer tests

- Biopsy
Imaging
Fitness of patient

Treatments

- Surgery
Radiotherapy
Chemotherapy



Cancer outcomes

- Survival – cure
- Survival – living with cancer
- Progression to Death

- Priorities of cancer treatment are
 - Treat cancer adequately
 - minimizing side effects of treatment
 - Monitoring patient so can pick up recurrence early

Summary of cancer care

- Rule of 3!



Cancer – Burden

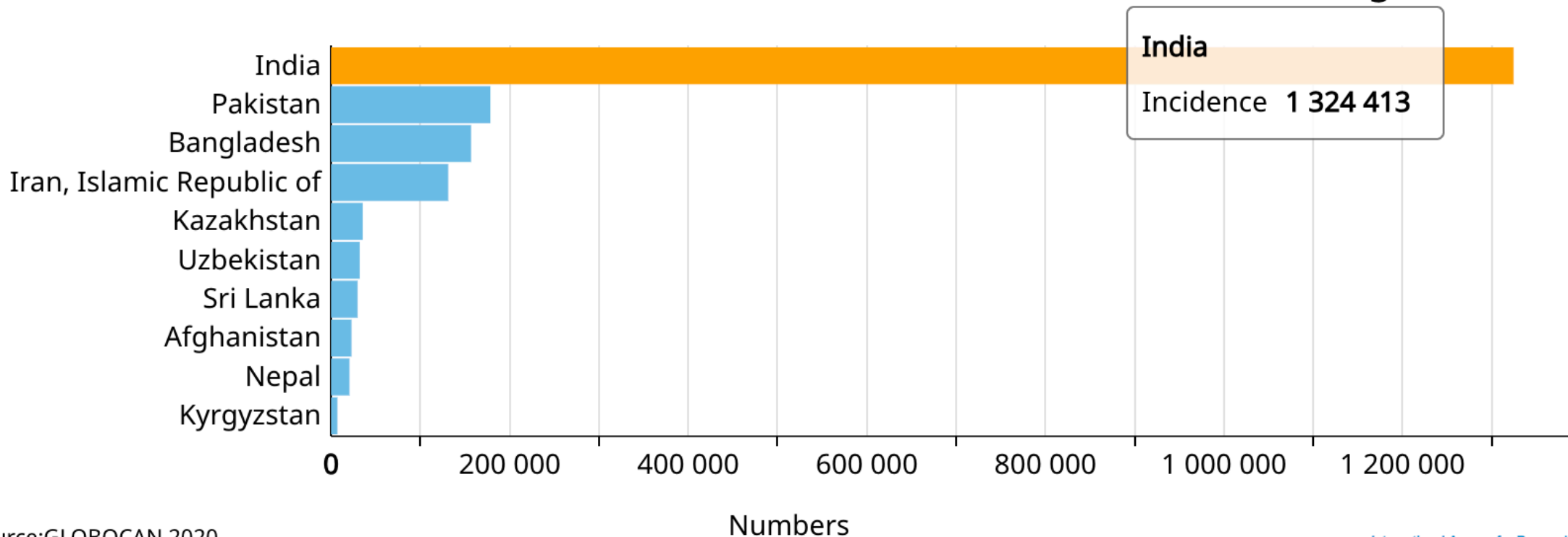


Cancer India Burden – Globocan 2023

Home / Explore / Bar chart

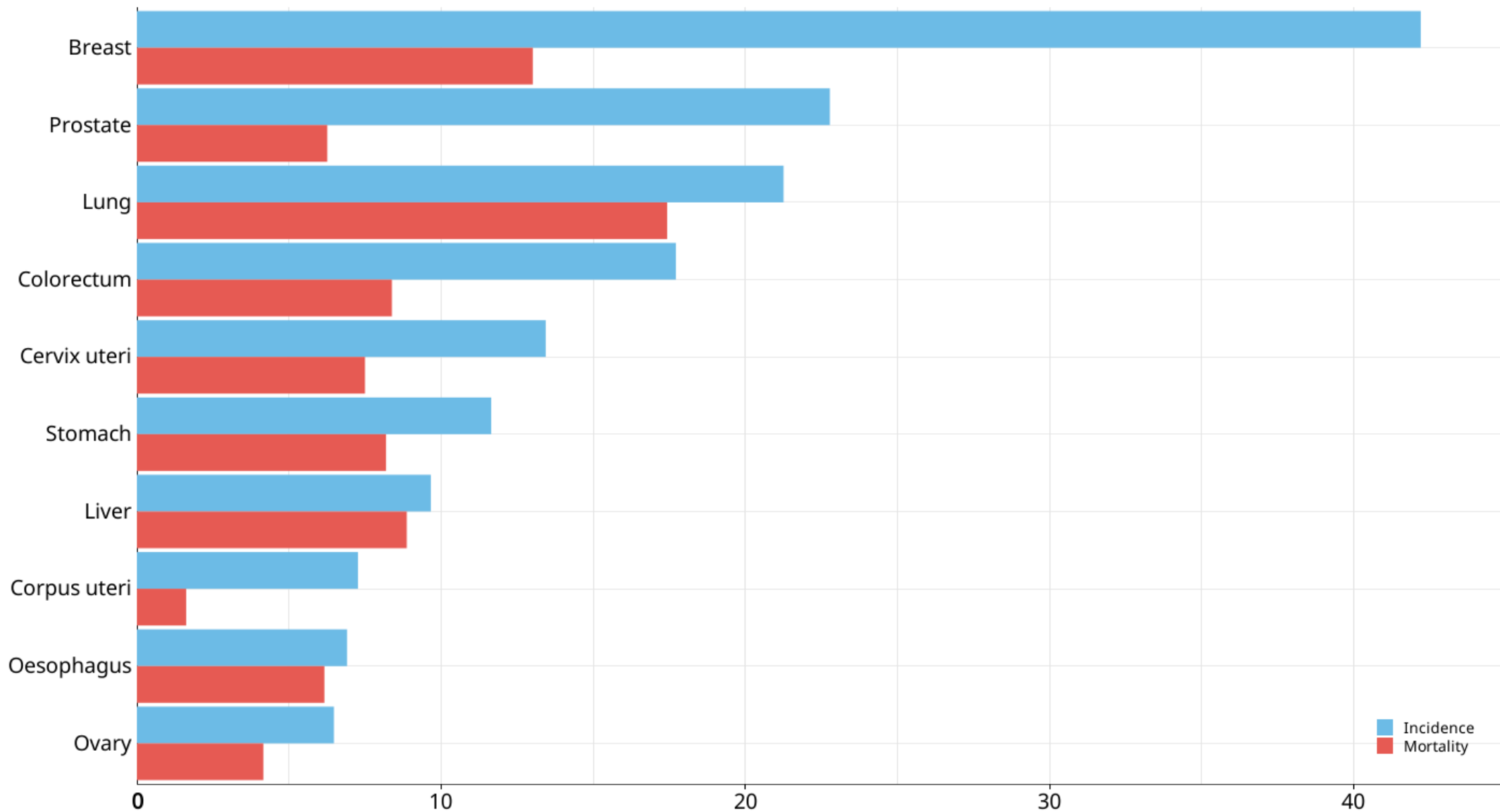
GRAPHIC TABLE

Estimated number of incident cases all cancers, both sexes, all ages



Data source: GLOBOCAN 2020
Graph production: Global Cancer Observatory (<http://gco.iarc.fr/>)
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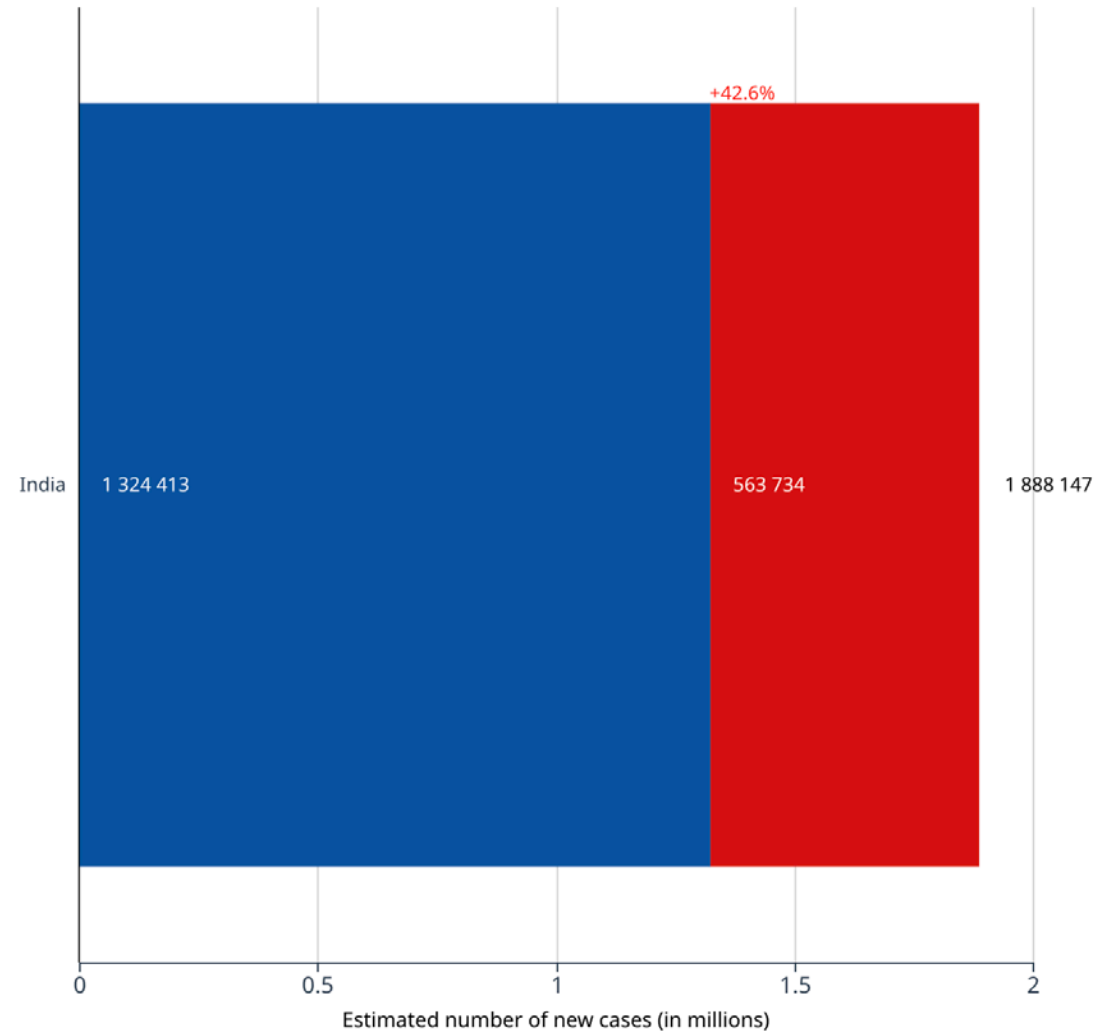
Estimated age-standardized incidence and mortality rates (World) in 2020, Asia, World, India, both sexes, all ages (excl. NMSC)



Cancer burden India 2035 – 42% increase – Globocan

Most common
Breast,
Oral,
Cervical,
Gastric,
Lung cancers

Estimated number of new cases from 2020 to 2035, Both sexes, age [0-85+]
All cancers



Types of cancers, 1990	Types of cancers, 2016	Mean percentage change in number of DALYs, 1990–2016 (95% UI)	Mean percentage change in crude DALY rate, 1990–2016 (95% UI)	Mean percentage change in age-standardised DALY rate, 1990–2016 (95% UI)
1 Stomach cancer	1 Stomach cancer	36.2% (25.0 to 51.8)	-10.6% (-18.0 to -0.4)	-31.4% (-37.3 to -23.7)
2 Cervical cancer	2 Breast cancer	114.9% (56.1 to 174.6)	41.1% (2.7 to 80.2)	8.6% (-20.6 to 36.4)
3 Leukaemia	3 Lung cancer	136.0% (106.5 to 157.8)	54.9% (35.6 to 69.2)	15.3% (1.1 to 26.2)
4 Breast cancer	4 Lip and oral cavity cancer	102.9% (75.3 to 122.0)	33.2% (15.0 to 45.7)	-0.1% (-13.3 to 8.7)
5 Lip and oral cavity cancer	5 Pharynx cancer other than nasopharynx	106.1% (60.5 to 139.2)	35.3% (5.3 to 57.0)	1.9% (-20.6 to 18.3)
6 Pharynx cancer other than nasopharynx	6 Colon and rectum cancer	109.6% (66.1 to 138.0)	37.5% (9.3 to 56.2)	5.8% (-15.6 to 20.9)
7 Lung cancer	7 Leukaemia	35.0% (16.2 to 63.5)	-11.4% (-23.7 to 7.3)	-9.2% (-20.0 to 7.0)
8 Colon and rectum cancer	8 Cervical cancer	21.6% (13.2 to 52.5)	-20.2% (-48.5 to 0.1)	-38.7% (-56.3 to -23.0)
9 Oesophageal cancer	9 Oesophageal cancer	59.3% (48.5 to 70.9)	4.6% (-2.7 to 12.2)	-21.6% (-27.2 to -15.9)
10 Larynx cancer	10 Brain and nervous system cancer	85.2% (48.8 to 239.9)	21.6% (-2.5 to 123.1)	14.0% (-7.6 to 112.2)
11 Brain and nervous system cancer	11 Liver cancer	206.1% (153.1 to 235.5)	100.9% (66.1 to 120.2)	51.2% (24.0 to 65.9)
12 Non-Hodgkin lymphoma	12 Non-Hodgkin lymphoma	133.9% (108.8 to 157.3)	53.5% (37.1 to 68.9)	35.4% (20.7 to 48.8)
13 Hodgkin's lymphoma	13 Gallbladder and biliary tract cancer	169.4% (83.0 to 219.0)	76.8% (20.1 to 109.4)	31.0% (-10.7 to 54.2)
14 Gallbladder and biliary tract cancer	14 Larynx cancer	40.5% (30.2 to 52.2)	-7.8% (-14.5 to -0.1)	-31.6% (-36.7 to -25.7)
15 Liver cancer	15 Pancreatic cancer	122.6% (109.0 to 137.7)	46.1% (37.2 to 56.0)	6.7% (-0.1 to 14.7)
16 Pancreatic cancer	16 Ovarian cancer	157.2% (131.1 to 190.3)	68.8% (51.7 to 90.5)	28.1% (15.1 to 44.3)
17 Ovarian cancer	17 Prostate cancer	140.3% (93.5 to 195.3)	57.7% (27.0 to 93.8)	9.4% (-10.7 to 32.3)
18 Nasopharynx cancer	18 Bladder cancer	104.0% (79.1 to 122.9)	33.9% (18.0 to 46.3)	-1.5% (-12.6 to 7.4)
19 Thyroid cancer	19 Nasopharynx cancer	29.1% (4.8 to 55.5)	-15.2% (-31.2 to 2.1)	-33.5% (-46.1 to -19.8)
20 Prostate cancer	20 Thyroid cancer	36.8% (21.6 to 67.9)	-10.2% (-20.2 to 10.2)	-28.5% (-36.0 to -13.2)
21 Uterine cancer	21 Myeloma	158.5% (113.3 to 225.9)	69.7% (40.0 to 113.9)	28.2% (5.6 to 63.1)
22 Bladder cancer	22 Hodgkin's lymphoma	-30.3% (-42.9 to -4.8)	-54.3% (-62.5 to -37.5)	-54.8% (-62.5 to -39.6)
23 Myeloma	23 Uterine cancer	37.5% (20.6 to 65.7)	-9.8% (-20.8 to 8.8)	-31.5% (-40.0 to -17.8)
24 Testicular cancer	24 Kidney cancer	124.0% (100.4 to 158.9)	47.0% (31.5 to 69.9)	20.0% (6.6 to 38.1)
25 Kidney cancer	25 Mesothelioma	126.6% (77.1 to 183.3)	48.7% (16.3 to 86.0)	13.8% (-11.5 to 43.9)
26 Mesothelioma	26 Malignant skin melanoma	110.7% (71.6 to 209.7)	38.3% (12.6 to 103.3)	10.2% (-8.9 to 58.7)
27 Malignant skin melanoma	27 Testicular cancer	-29.8% (-40.2 to -20.3)	-53.9% (-60.7 to -47.7)	-59.2% (-65.4 to -53.8)
28 Non-melanoma skin cancer	28 Non-melanoma skin cancer	90.2% (73.2 to 112.1)	24.9% (13.7 to 39.2)	-7.4% (-15.3 to 2.2)

[Lancet Oncol. 2018 Oct; 19\(10\): 1289–1306.](https://doi.org/10.1016/S1470-2045(18)30447-9)
doi: [10.1016/S1470-2045\(18\)30447-9](https://doi.org/10.1016/S1470-2045(18)30447-9)

The burden of cancers and their variations across the states of India: the Global Burden of Disease Study 1990–2016

India State-Level Disease Burden Initiative Cancer Collaborators[†]

Figure 4

Change in DALYs for different types of cancers in India, 1990–2016

Cancer

- Suffering
- Loss of life for patient
- Loss of income
- Side effects of treatment
- Financial toxicity for family
- Impact on carers
- Impact on society – economic productivity

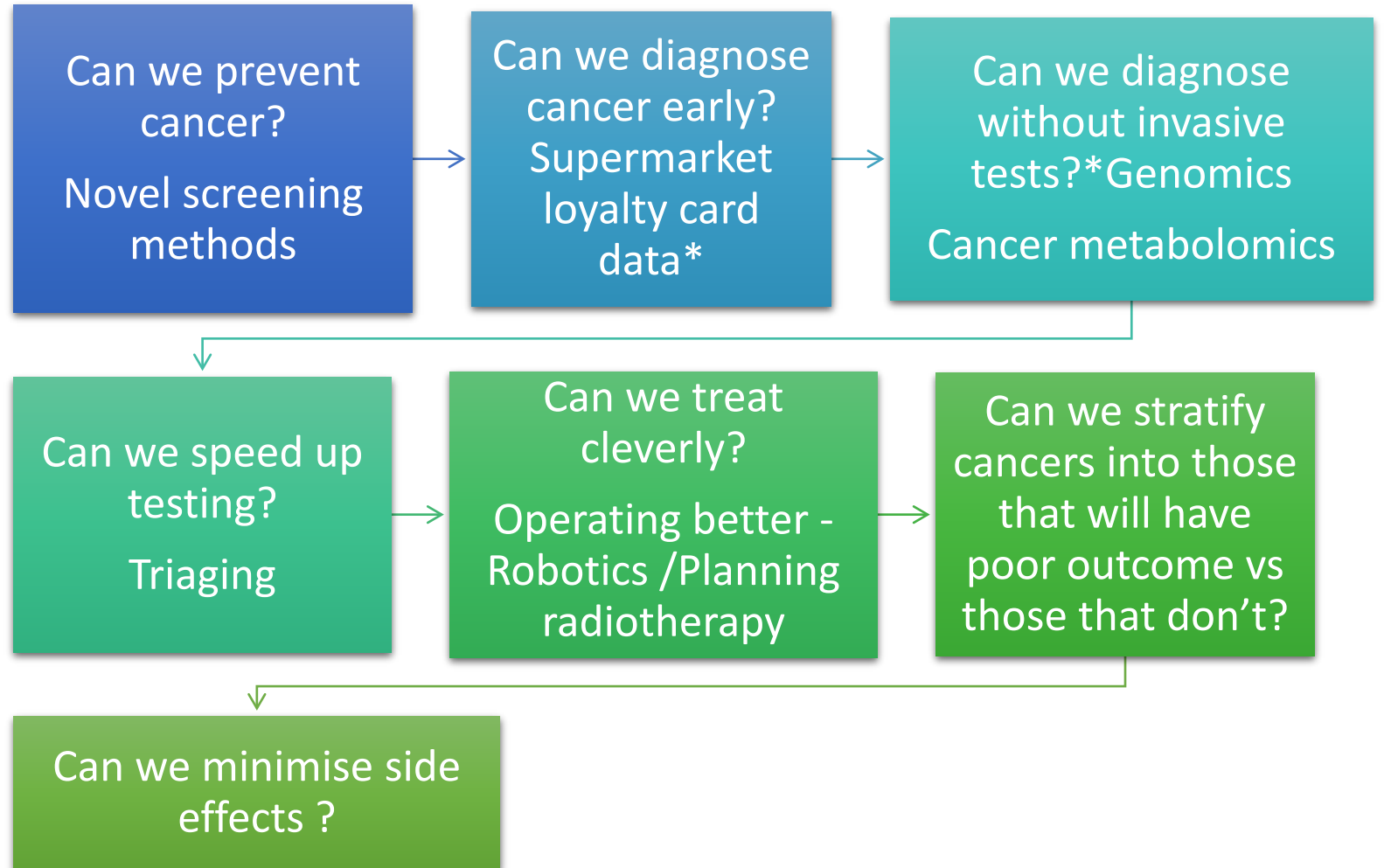
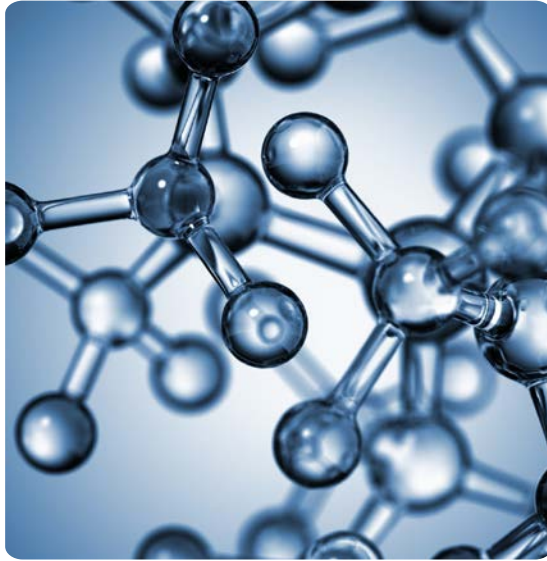
Current cancer paradigm – a numbers game!

- Patient with symptoms goes to doctor
- Investigations – usually painful-invasive
- Biopsy – histology of a piece of tissue for definitive diagnosis
- Staging investigations – CT scan/imaging
- Determine site of tumour/stage/histology and aggressiveness of tumour
- Treatment options – surgery/chemotherapy/radiotherapy
- Outcome – relapse – further treatments - death or survival (usually with side effects of treatment)

Current cancer research

- Majority of research in HIC
 - Majority of research in patients of Caucasian ethnicity
 - Majority in drug discovery in advanced cancer
 - Majority driven by pharma
-
- Analysis of benefit from FDA approved new cancer drugs : Novel pharmaceuticals increased patient survival by a median of 2.80 months (IQR, 1.97-4.60 months) for OS and 3.30 months (IQR, 1.50-5.58 months) for PFS. (Michaeli et al, JCO 2022)

Opportunities for Machine learning



Shopping can save your life!

[Original Paper](#)

Association Between Purchase of Over-the-Counter Medications and Ovarian Cancer Diagnosis in the Cancer Loyalty Card Study (CLOCS): Observational Case-Control Study

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Lifestyle + Health & Families

Ovarian cancer could be spotted with loyalty cards

Ovarian cancer is known as the 'silent killer' because it is often caught too late - once the tumour has already spread

Mark Waghorn SWNS • Friday 27 • Comments



There is a difference in purchases of pain and indigestion medications among women with and without ovarian cancer up to 8 months before diagnosis. Facilitating earlier presentation among those who self-care for symptoms using this novel data source could improve ovarian cancer patients' options for treatment and improve survival.

Imperial – PI - Dr James Flanagan, Imperial, Dr Hannah Brewer
UCL/UCLAN – Dr Yasemin Hirst

Brewer HR, ...Sundar S, .. Hirst Y.
Cancer Loyalty Card Study (CLOCS): feasibility outcomes for an observational case-control study focusing on the patient interval in ovarian cancer. *BMJ Open*. 2023 :

Genomics and metabolomics as diagnostic tests

- ROCKeTS GEN investigates ctDNA
Joint PI – Prof James Brenton, Cambridge,
- Collaborators - Prof Nitzan Rosenfield, Cambridge, Prof Sue Mallett, UCL
- STEMOVA investigates urinary metabolomics in mucinous ovarian cancer
- Collaborators, Prof Weibke Arlt, UoB/MRC, Dr Paul Foster, Dr Alice Stitch, UoB
- PhD Dr David Jeevan completed



**BWCH Global
Research fund**

Summary

- Many opportunities for ML research in cancer
- Transformative research is desperately needed
- Balancing cancer research towards prevention and diagnosis/
research in LMIC/research across different ethnicities

Thank you!

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Patient with symptoms visits Dr



Undergoes investigations



Undergoes biopsy



Cancer treatment

Outcome - relapse or survival