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COVID-19 pandemic is expected to cause a delayed increase in cancer rates due to its effect on lifestyles

Aleksey V. Belikov, Dr.rer.nat.

Cancer causes

ENVIRONMENTAL EXPOSURES

- air pollution
- secondhand smoke
- occupational exposure
- UV
- ionizing radiation
- viruses

POOR LIFESTYLE CHOICES

- smoking
- alcohol intake
- poor diet
- excess body weight
- insufficient physical activity
- insufficient breastfeeding
- postmenopausal hormone therapy
- oral contraceptives

DNA replication errors during stem cell divisions are the major cause of cancer ?

CANCER ETIOLOGY

Variation in cancer risk among tissues can be explained by the number of stem cell divisions

Cristian Tomasetti[1]* and Bert Vogelstein[2]*

Some tissue types give rise to human cancers millions of times more often than other tissue types. Although this has been recognized for more than a century, it has never been explained. Here, we show that the lifetime risk of cancers of many different types is strongly correlated (0.81) with the total number of divisions of the normal self-renewing cells maintaining that tissue's homeostasis. These results suggest that only a third of the variation in cancer risk among tissues is attributable to environmental factors or inherited predispositions. The majority is due to "bad luck," that is, random mutations arising during DNA replication in normal, noncancerous stem cells. This is important not only for understanding the disease but also for designing strategies to limit the mortality it causes.

DNA replication errors during stem cell divisions are the major cause of cancer ?

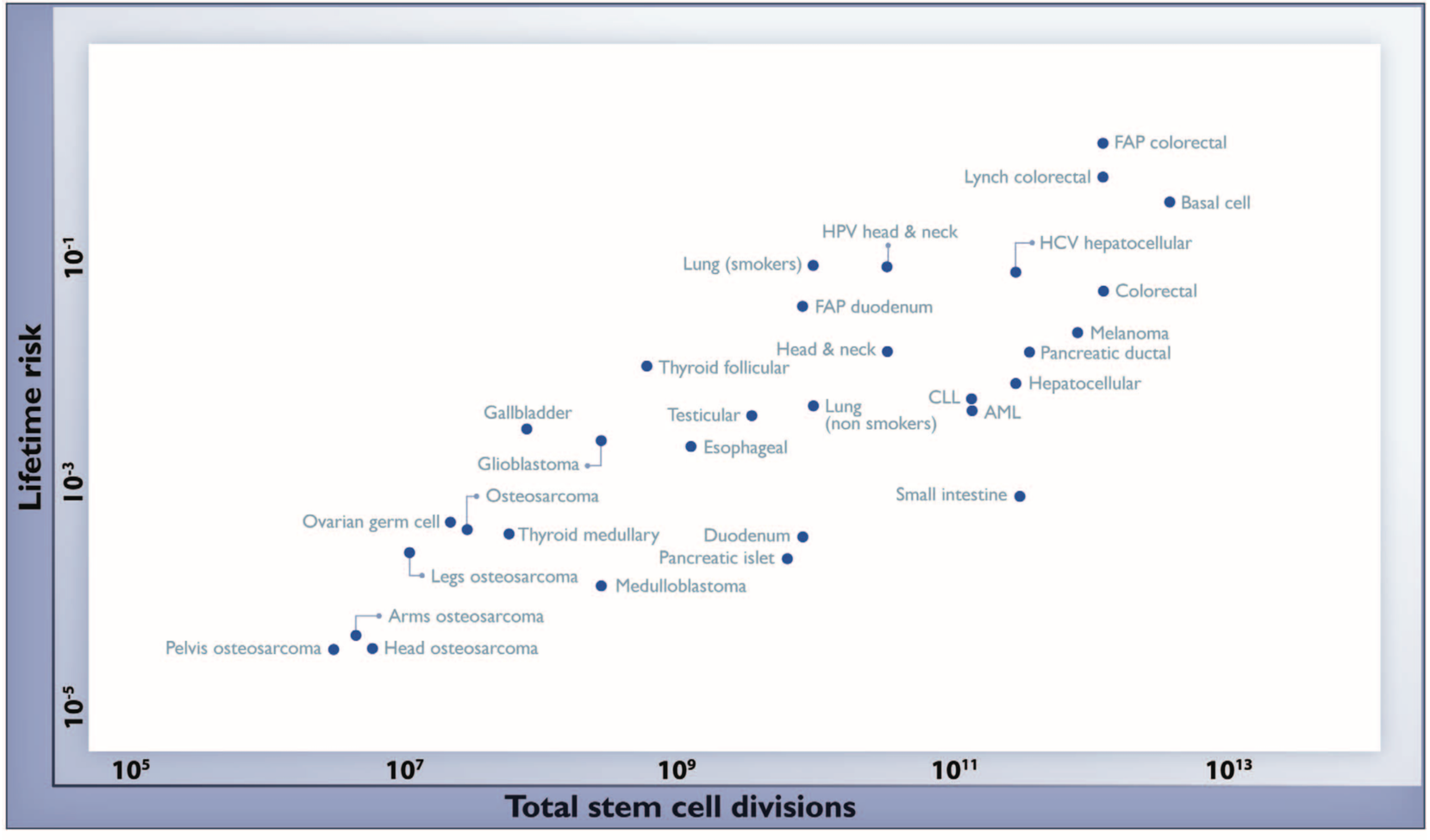
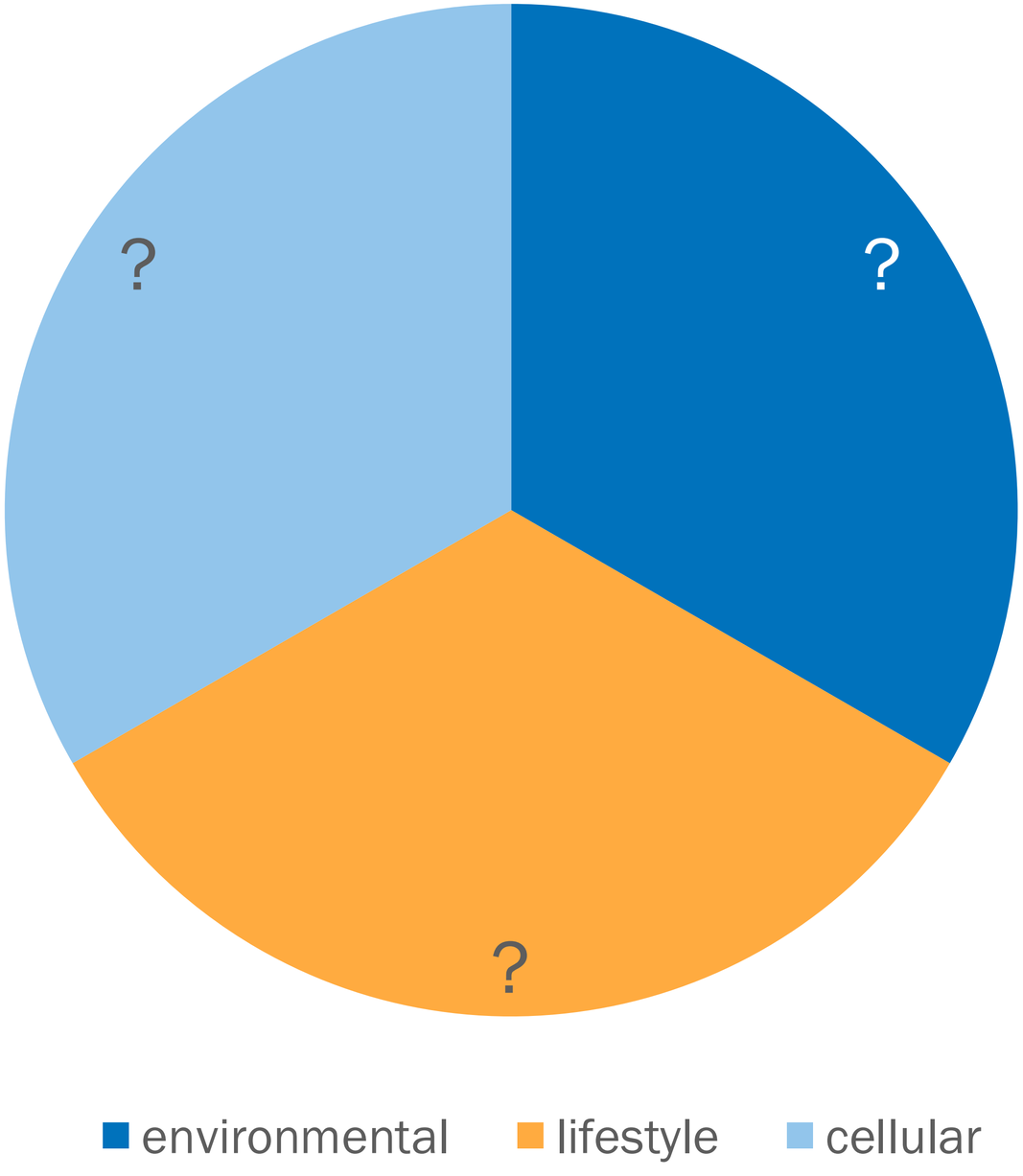


Fig. 1. The relationship between the number of stem cell divisions in the lifetime of a given tissue and the lifetime risk of cancer in that tissue. Values are from table S1, the derivation of which is discussed in the supplementary materials.

What is the relative contribution of environmental, lifestyle and cellular causes to carcinogenesis?



A novel statistical methodology to estimate the number of events driving cancer progression from the age distribution of cancer incidence

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The number of key carcinogenic events can be predicted from cancer incidence

Aleksey V. Belikov

The widely accepted multiple-hit hypothesis of carcinogenesis states that cancers arise after several successive events. However, no consensus has been reached on the quantity and nature of these events, although "driver" mutations or epimutations are considered the most probable candidates. By using the largest publicly available cancer incidence statistics (20 million cases), I show that incidence of 20 most prevalent cancer types in relation to patients' age closely follows the Erlang probability distribution ($R^2 = 0.9734–0.9999$). The Erlang distribution describes the probability y of k independent random events occurring by the time x, but not earlier or later, with events happening on average every b time intervals. This fits well with the multiple-hit hypothesis and potentially allows to predict the number k of key carcinogenic events and the average time interval b between them, for each cancer type. Moreover, the amplitude parameter A likely predicts the maximal populational susceptibility to a given type of cancer. These parameters are estimated for 20 most common cancer types and provide numerical reference points for experimental research on cancer development.

A novel statistical methodology to estimate the number of events driving cancer progression from the age distribution of cancer incidence

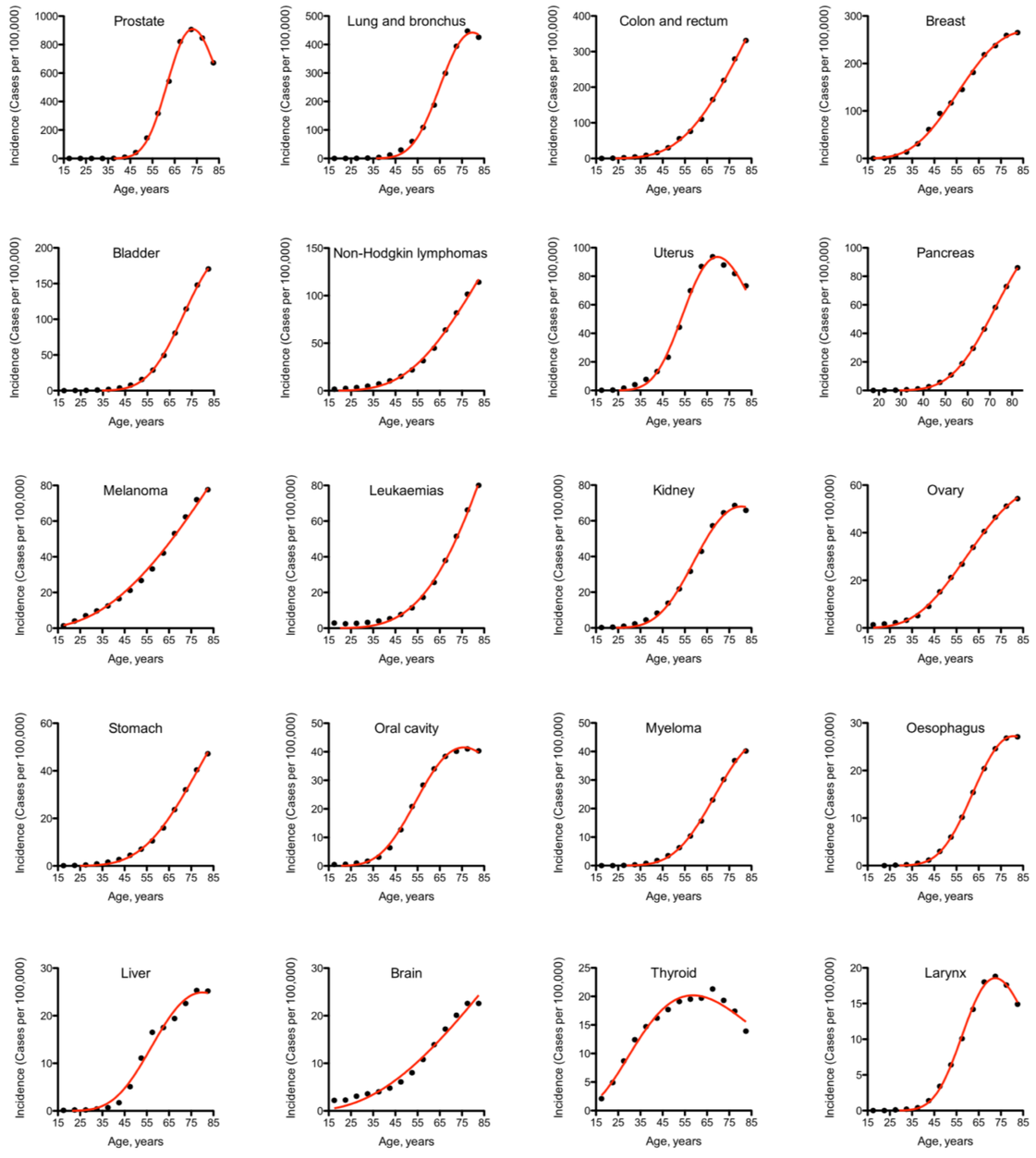

Figure 2. The Erlang distribution approximates cancer incidence by age for 20 most prevalent cancer types. Dots indicate actual data for 5-year age intervals, curves indicate the PDF of the Erlang distribution fitted to the data (see Table 1 for R^2 and estimated parameters). The middle age of each age group is plotted. Cancer types are arranged in the order of decreasing incidence.

A novel statistical methodology to estimate the number of events driving cancer progression from the age distribution of cancer incidence

Cancer type	*k* Number of carcinogenic events ± s.e.m.	*b* Average time between events, years ± s.e.m.	*A/1000* Maximal populational susceptibility, % ± s.e.m.	R^2 Goodness of fit
Prostate	41 ± 1	1.83 ± 0.00	26.40 ± 0.18	0.9992
Lung and bronchus	30 ± 2	2.75 ± 0.01	16.44 ± 0.24	0.9981
Colon and rectum	10 ± 1	13.75 ± 0.17	66.93 ± 3.80	0.9991
Breast	9 ± 1	10.71 ± 0.09	20.44 ± 0.46	0.9981
Bladder	21 ± 1	4.59 ± 0.02	9.93 ± 0.17	0.9995
Non-Hodgkin lymphomas	8 ± 1	19.26 ± 0.58	31.21 ± 3.90	0.9964
Uterus	20 ± 1	3.67 ± 0.02	3.77 ± 0.05	0.9954
Pancreas	15 ± 1	7.07 ± 0.01	7.15 ± 0.06	0.9999
Melanoma	4 ± 1	81.01 ± 7.38	100	0.9954
Leukaemias	8 ± 2	23.56 ± 1.09	49.57 ± 10.93	0.9957
Kidney	15 ± 1	5.75 ± 0.04	3.69 ± 0.07	0.9971
Ovary	8 ± 1	13.66 ± 0.12	5.40 ± 0.13	0.9989
Stomach	11 ± 1	11.51 ± 0.15	7.25 ± 0.42	0.9986
Oral cavity	13 ± 1	6.32 ± 0.03	2.29 ± 0.03	0.9983
Myeloma	16 ± 1	6.14 ± 0.03	2.67 ± 0.06	0.9992
Oesophagus	20 ± 0	4.25 ± 0.00	1.27 ± 0.00	0.9999
Liver	13 ± 2	6.67 ± 0.11	1.45 ± 0.07	0.9863
Brain	4 ± 1	76.69 ± 13.77	26.34 ± 14.52	0.9777
Thyroid	5 ± 0	14.67 ± 0.24	1.52 ± 0.04	0.9734
Larynx	24 ± 1	3.15 ± 0.01	0.71 ± 0.01	0.9989

Table 1. Estimated carcinogenesis parameters for 20 most prevalent cancer types. The parameters are determined for the Erlang distribution fitted to actual cancer incidence data (see Fig. 2). Cancer types are listed in the order of decreasing incidence.

How do these predictions relate to established risk factors?

Cancer type	*k* Number of carcinogenic events ± s.e.m.	*b* Average time between events, years ± s.e.m.	*A/1000* Maximal populational susceptibility, % ± s.e.m.	R^2 Goodness of fit
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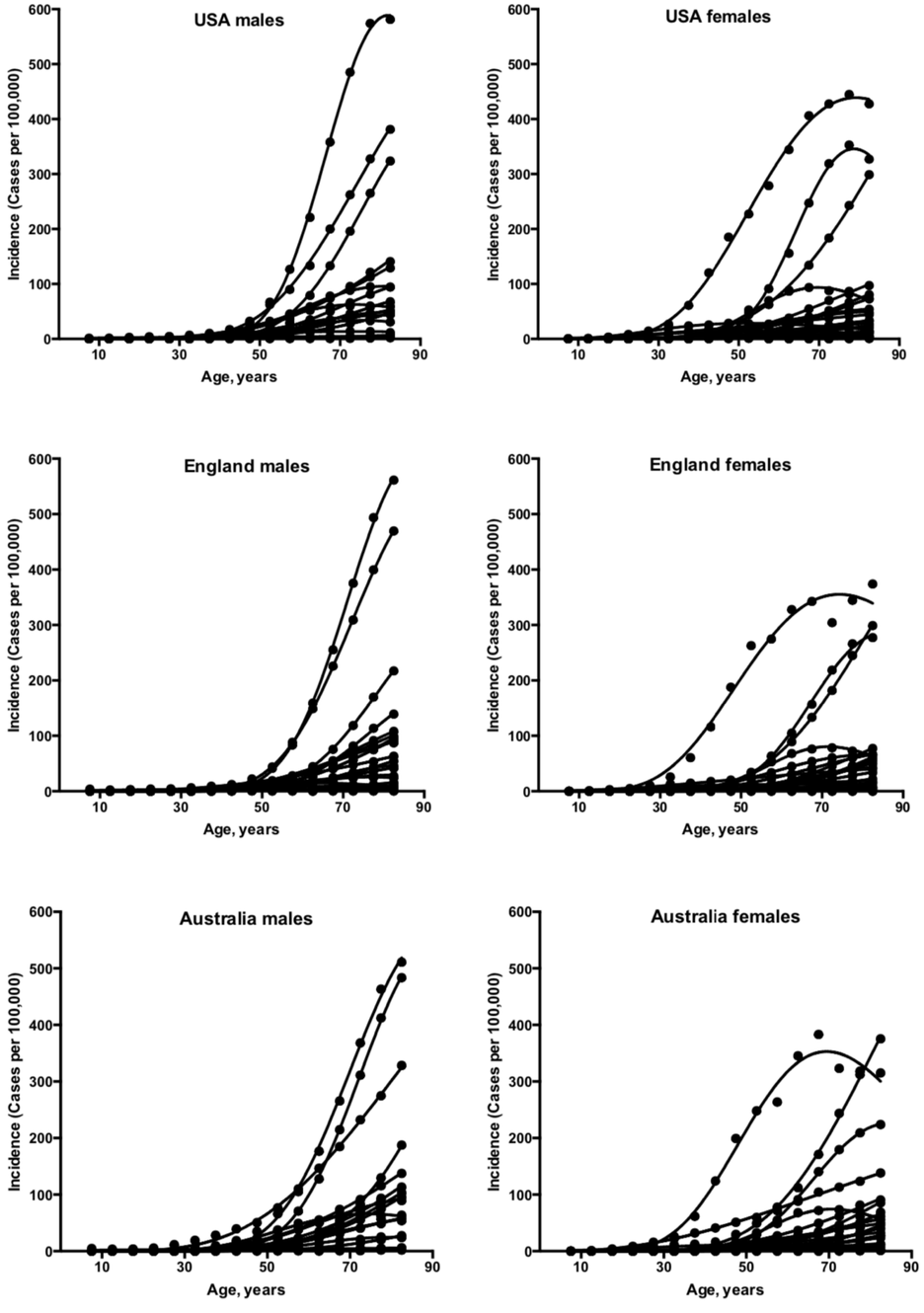
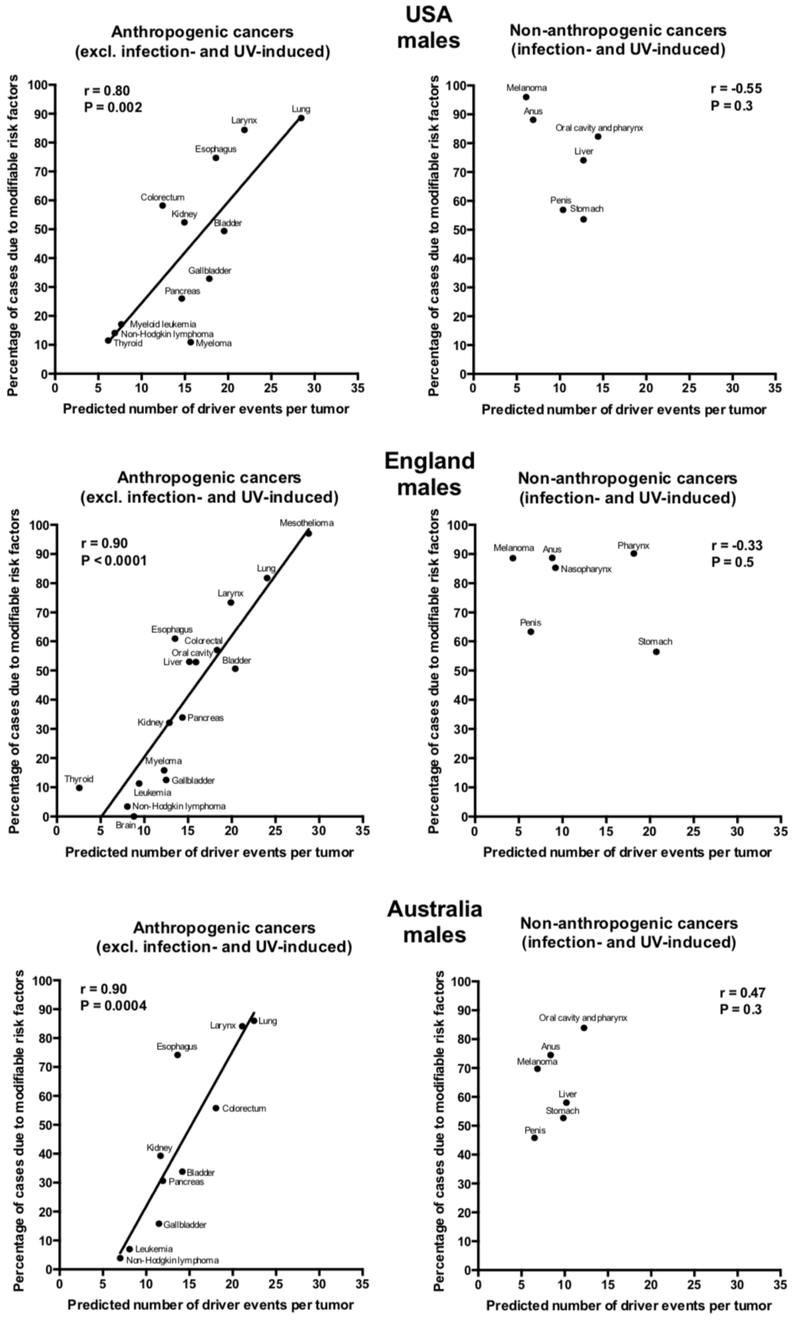
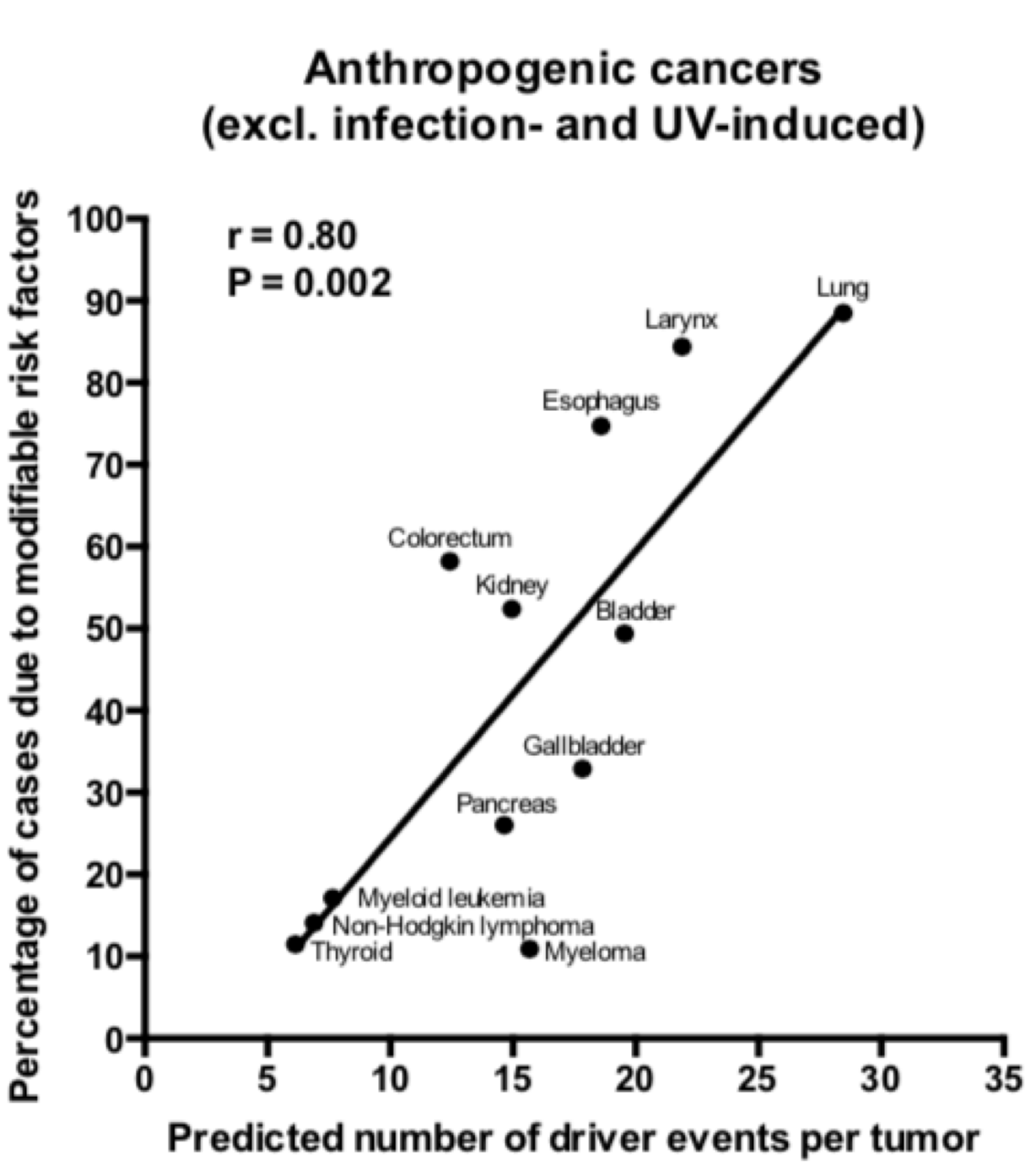
Model verified on three countries, three incidence databases, as well as on both sexes

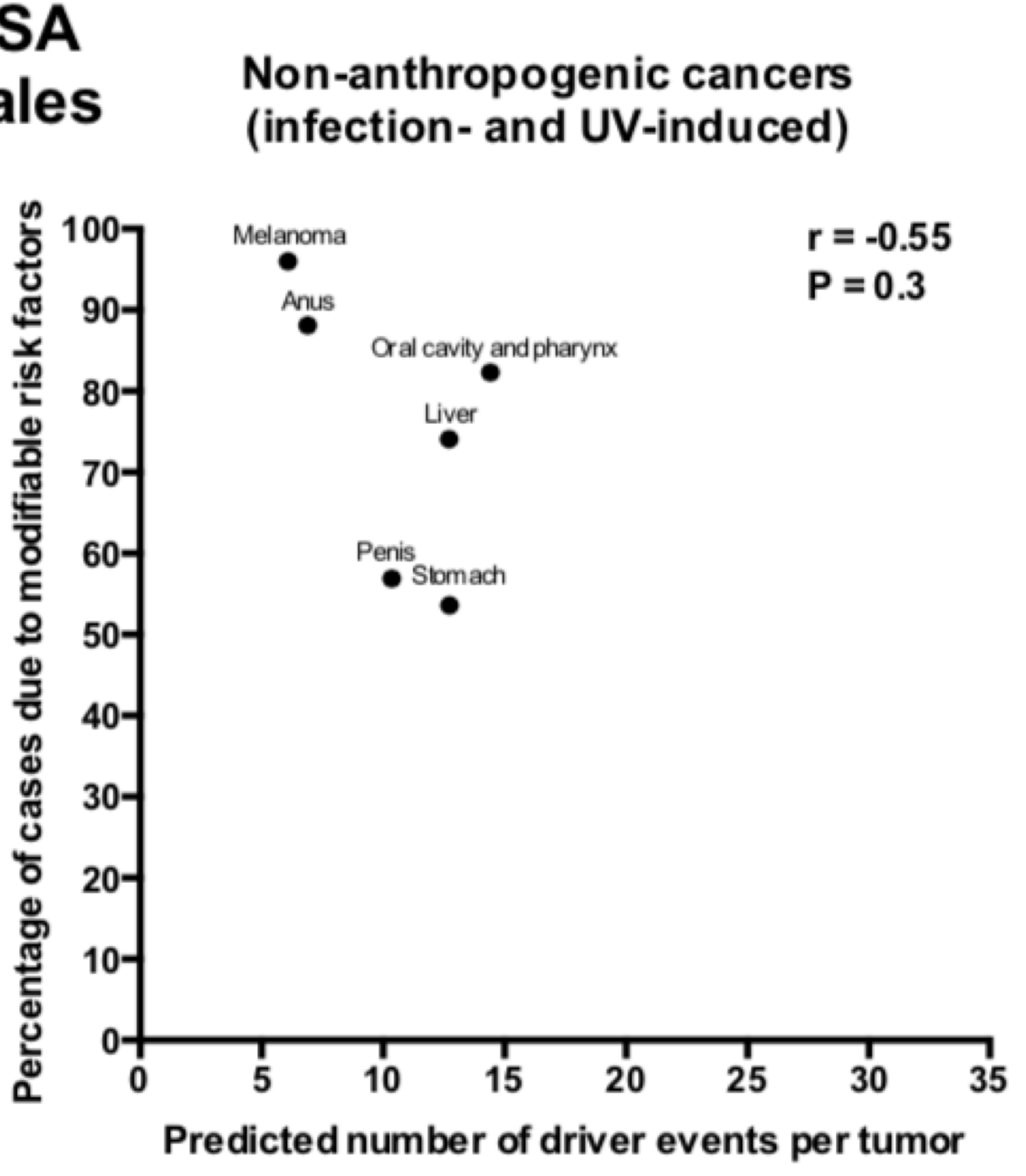


The predicted number of driver events per tumor strongly correlates with the proportion of cancer cases attributable to environmental and lifestyle risk factors for all cancers except those induced by infection or ultraviolet radiation

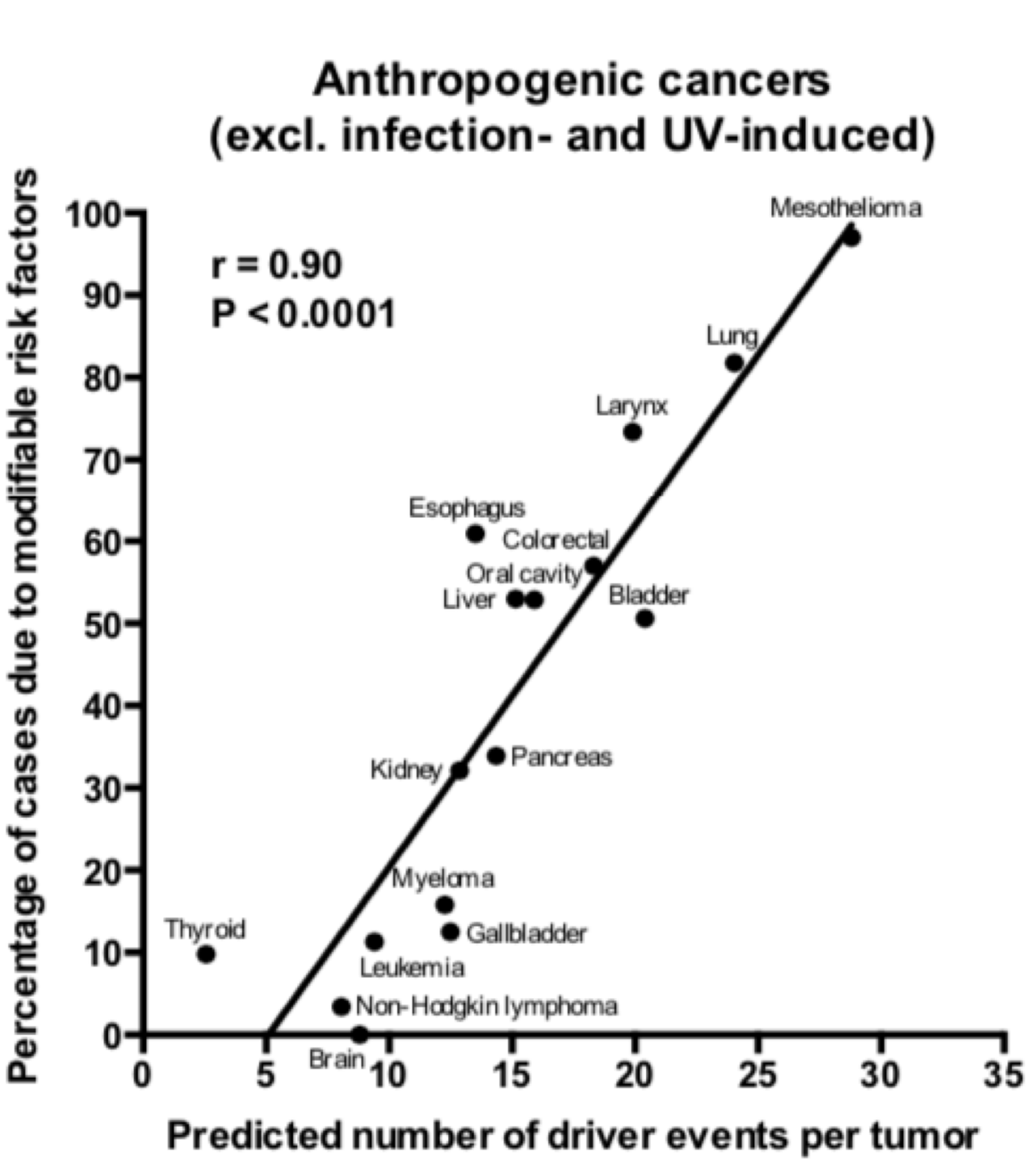


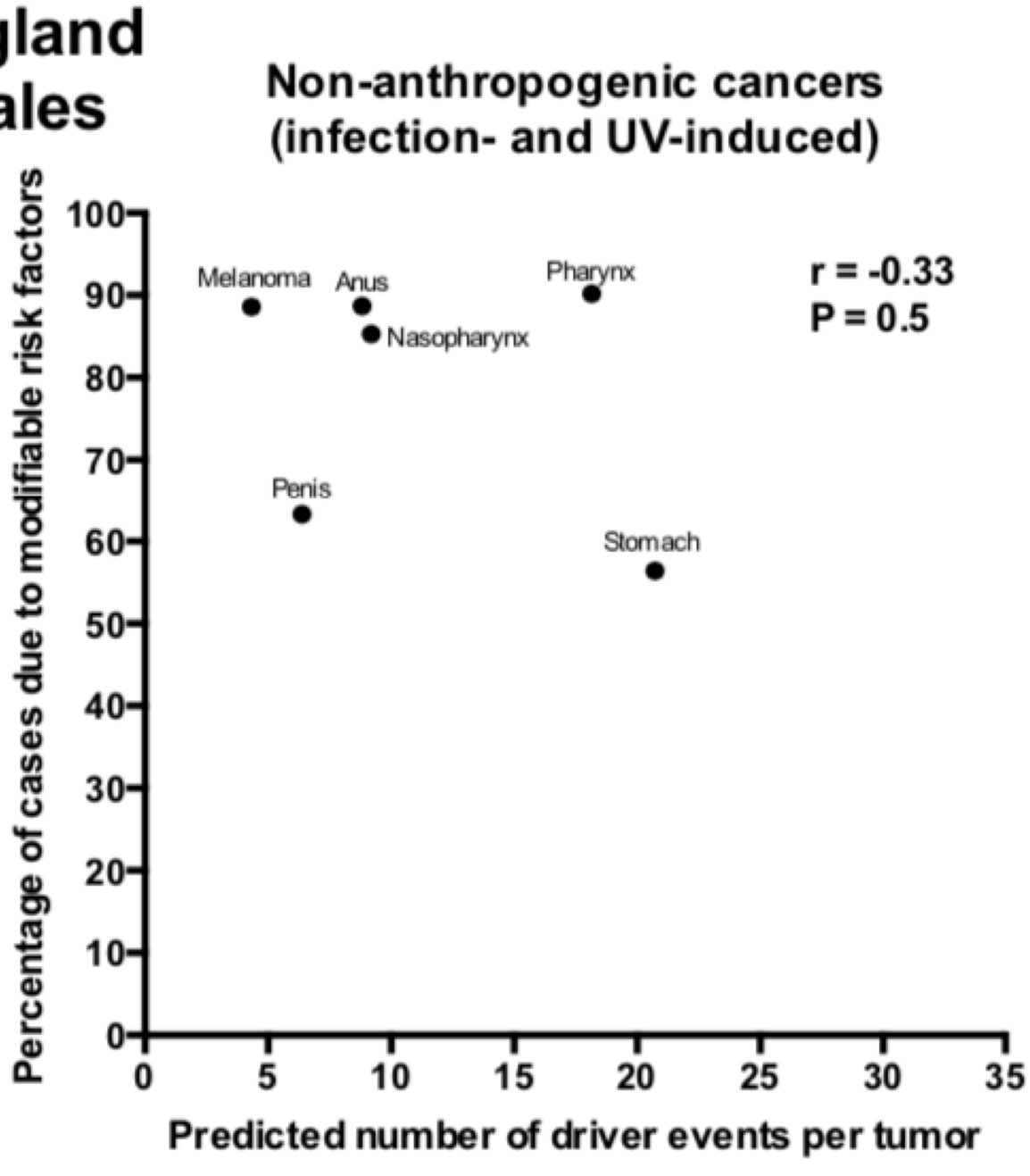
USA males


Anthropogenic cancers
(excl. infection- and UV-induced)
r = 0.80
P = 0.002
Lung
Larynx
Esophagus
Colorectum
Kidney
Bladder
Gallbladder
Pancreas
Myeloid leukemia
Non-Hodgkin lymphoma
Thyroid
Myeloma
Percentage of cases due to modifiable risk factors
Predicted number of driver events per tumor
0
10
20
30
40
50
60
70
80
90
100
0
5
10
15
20
25
30
35


Non-anthropogenic cancers
(infection- and UV-induced)
r = -0.55
P = 0.3
Melanoma
Anus
Oral cavity and pharynx
Liver
Penis
Stomach
Percentage of cases due to modifiable risk factors
Predicted number of driver events per tumor
0
10
20
30
40
50
60
70
80
90
100
0
5
10
15
20
25
30
35

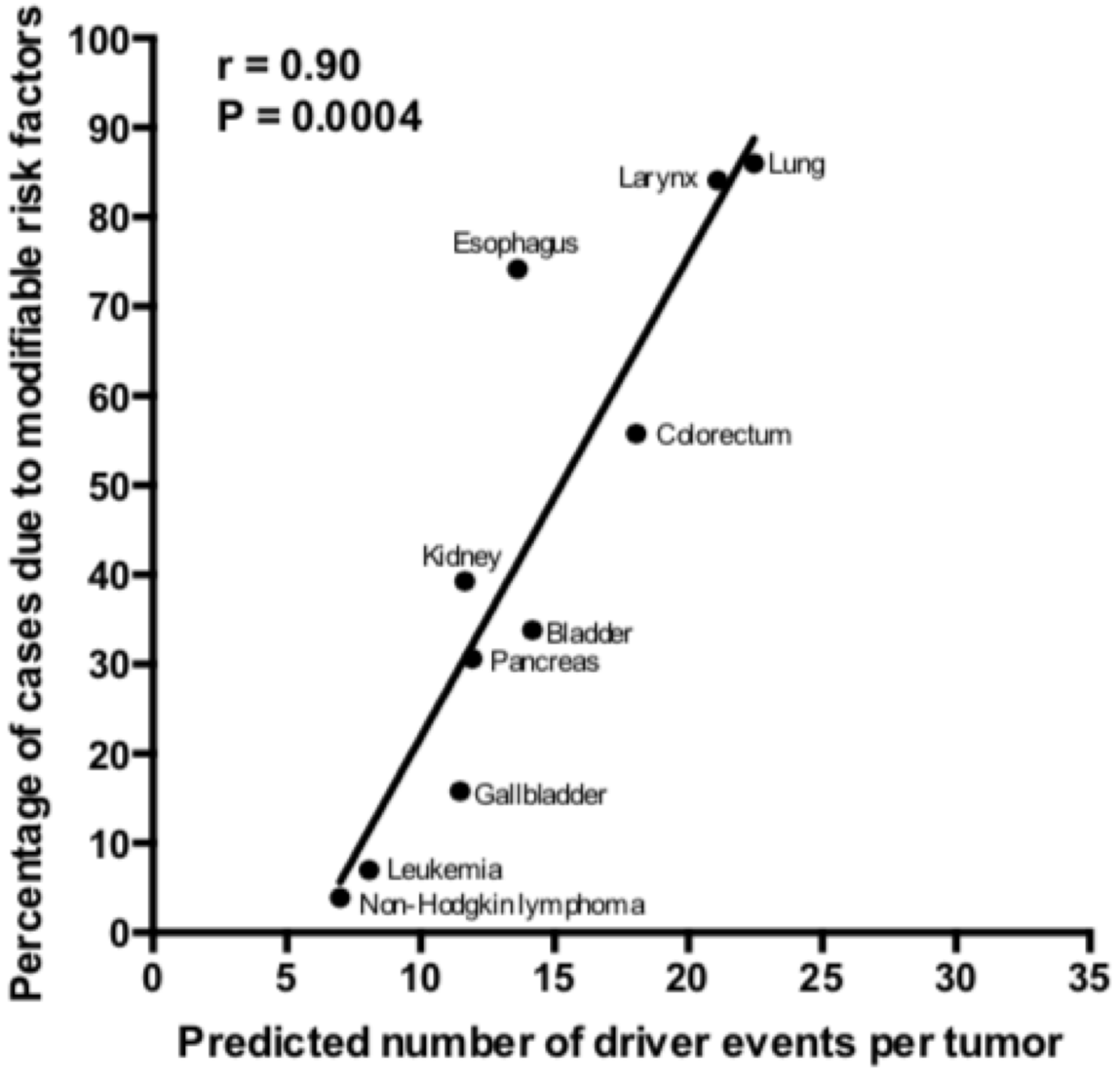
England males



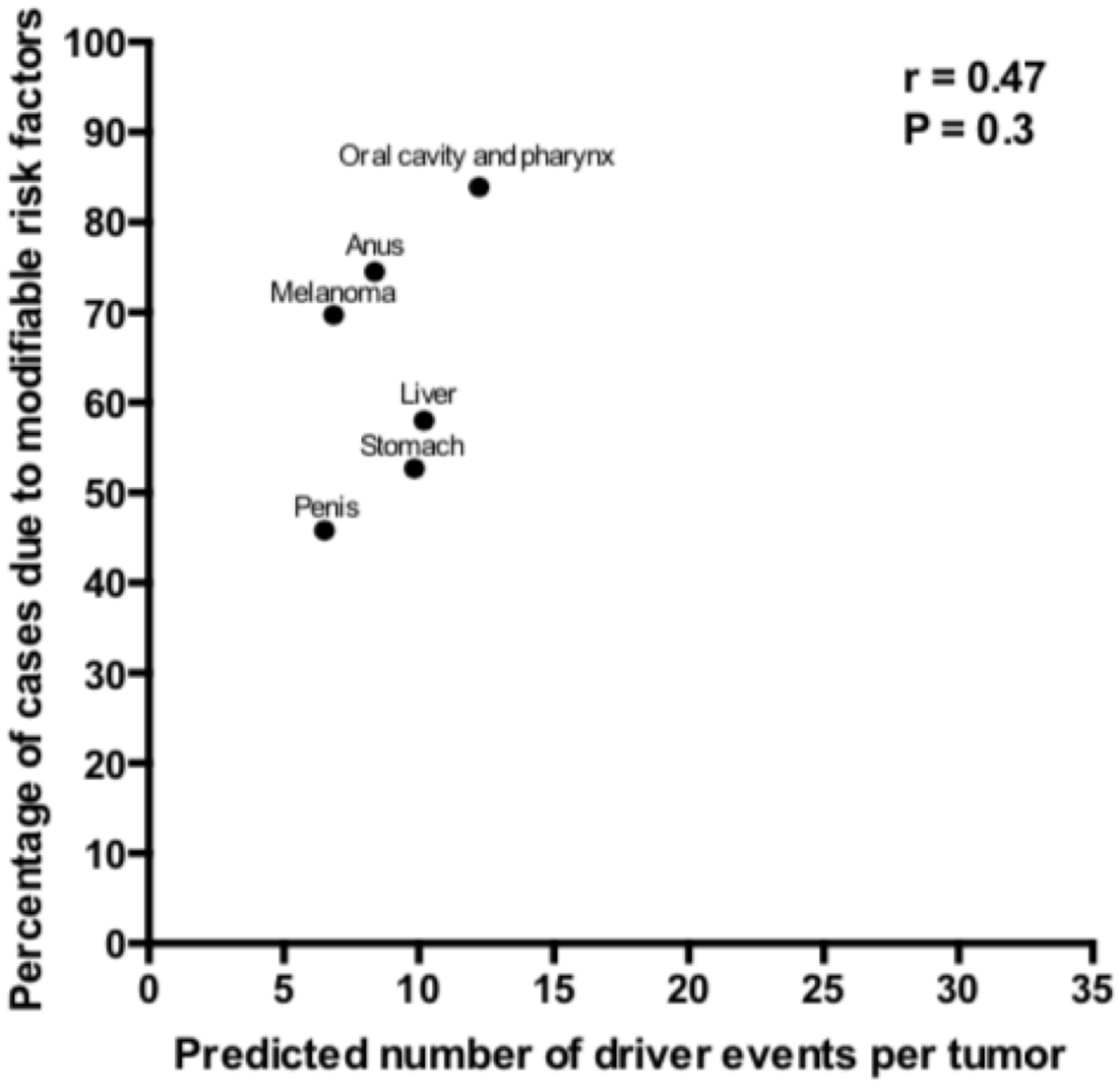


Australia males

Anthropogenic cancers (excl. infection- and UV-induced)



Non-anthropogenic cancers (infection- and UV-induced)



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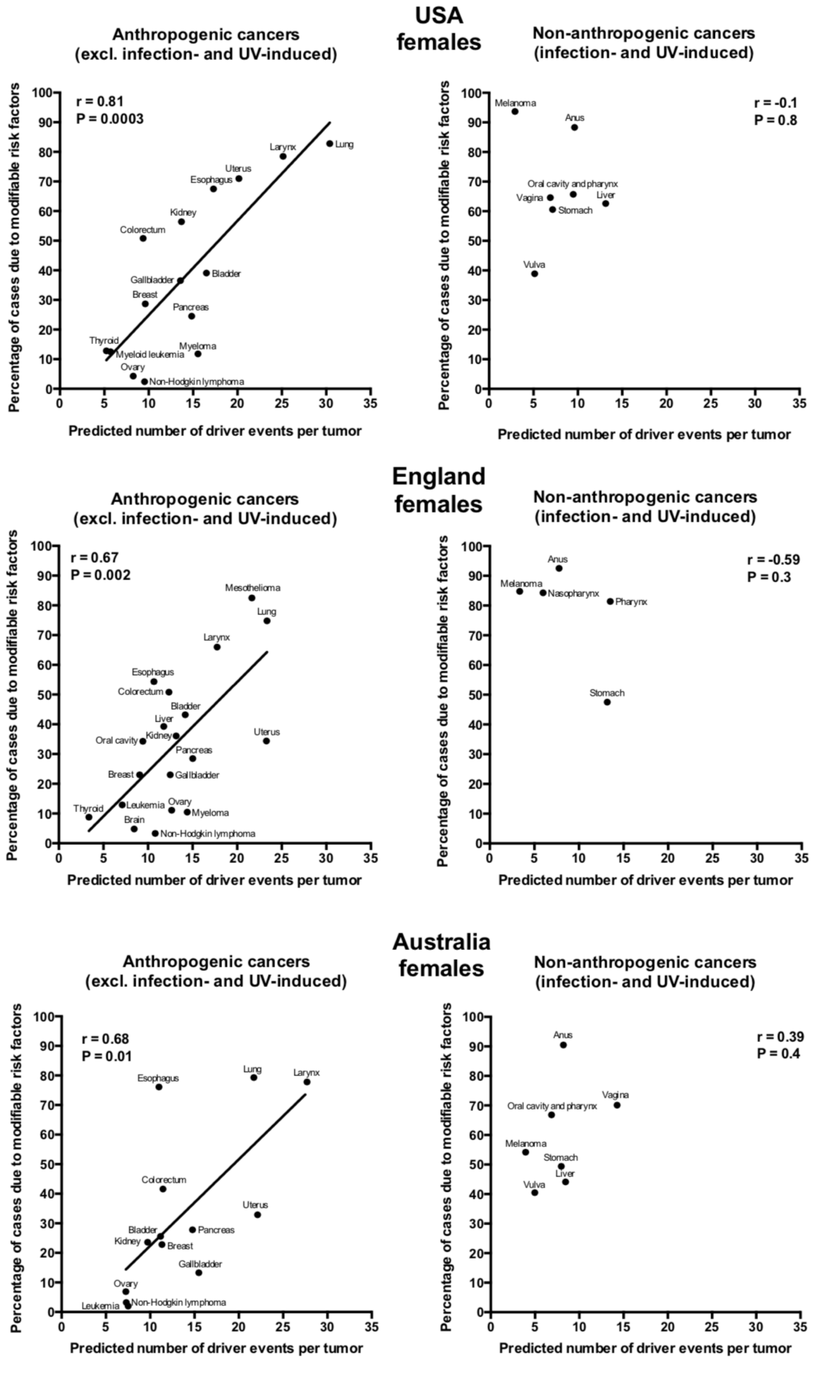
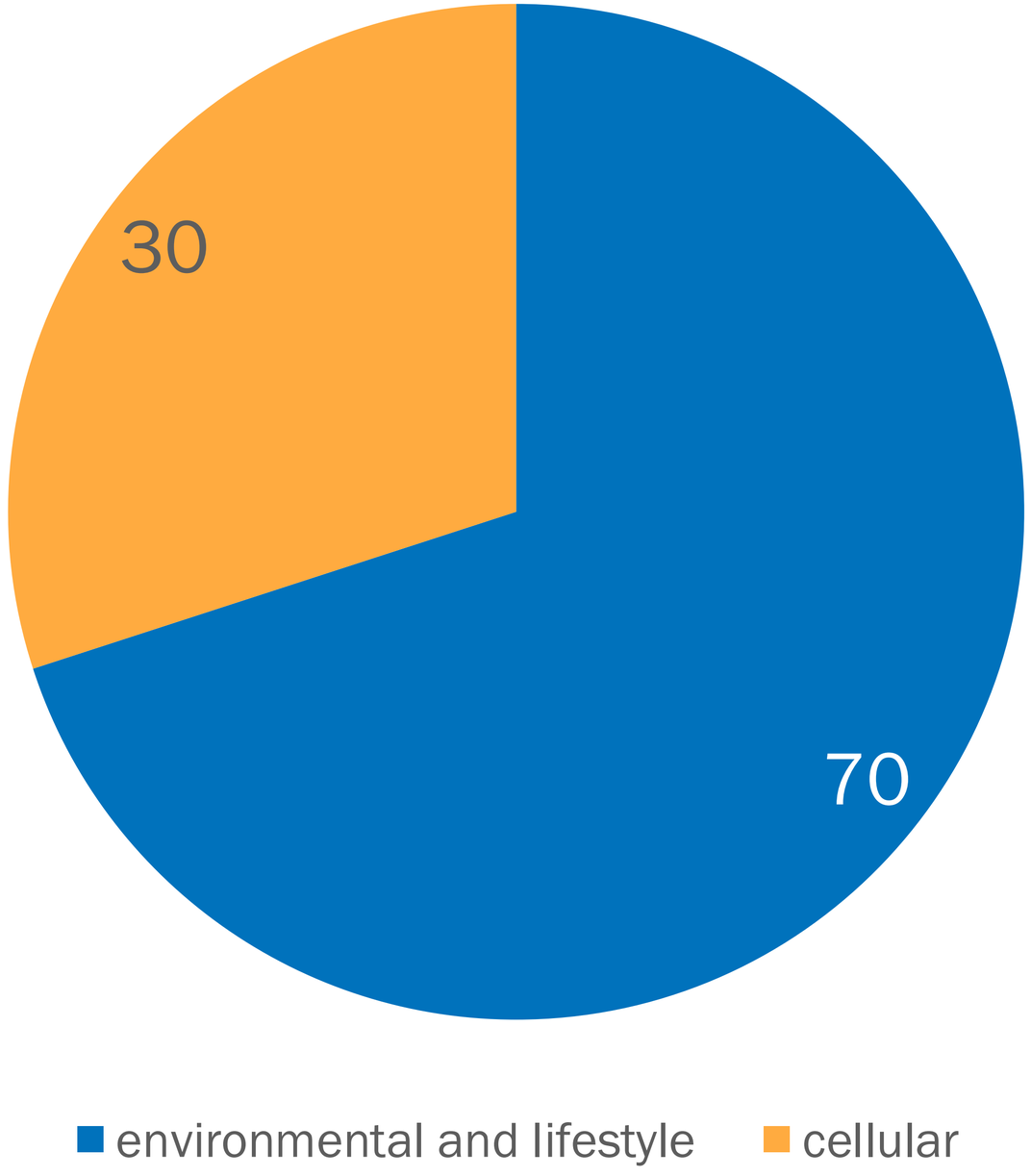
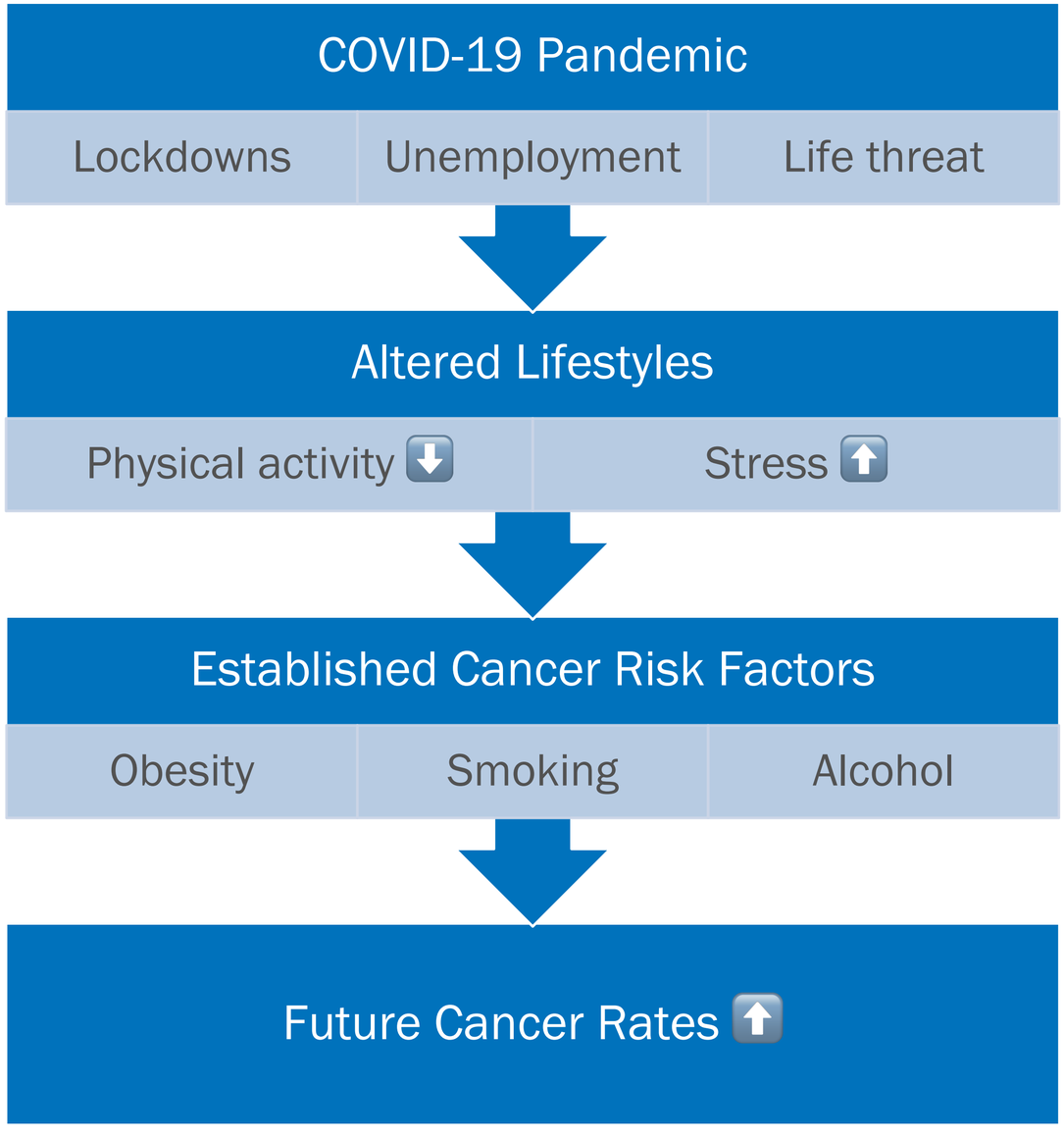


The majority of driver events are induced by environmental carcinogens and poor lifestyle choices and not by DNA replication errors or other internal processes



As COVID-19 pandemic has strong influence on people's lifestyles, it is expected to have a strong delayed impact on the rates of cancer in the future



THANK YOU
FOR YOUR ATTENTION!