THE CONCEPT OF HARM REDUCTION IN THE CONTEXT OF CANCER

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RIGOROUS FIGHTER AGAINST SMOKING

In France:

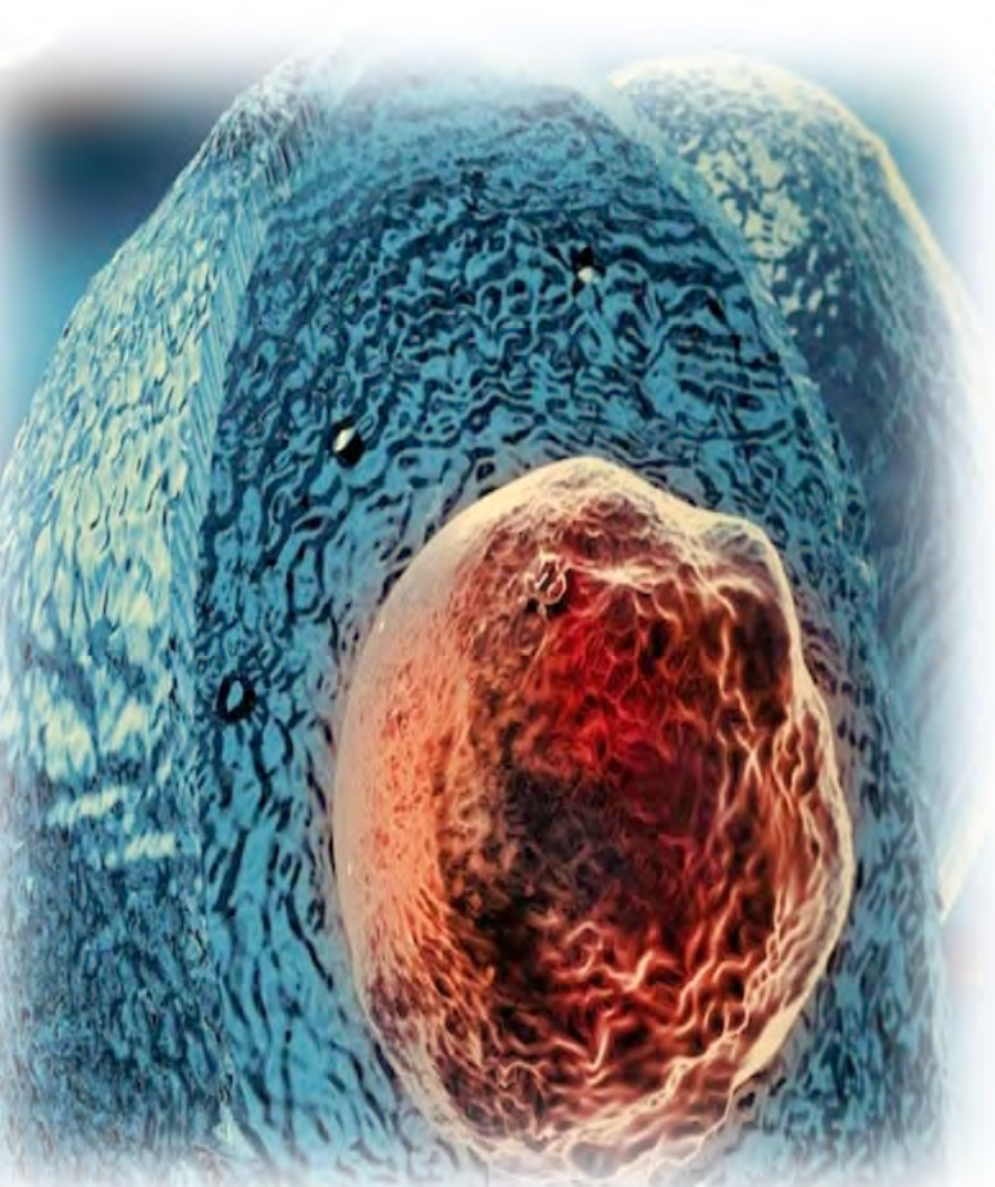
- 2002 to 2006 National Cancer Control Plan

Accomplishments

- Increased cost of a pack of cigarettes from 3 to 5 € within 2 years
- Decrease of 1.8 million smokers
- Decrease of in cigarette sales (from 80 to 55 billion sticks/year)
- Law on Ban on smoking in public place

THE CONCEPT OF HARM REDUCTION IN THE CONTEXT OF CANCER

WHAT DO WE KNOW ?



https://medi-paper.com/asco-2020-asco20-virtual-meeting-lung-cancer-breast-cancer-hepatocellular-cancer-colorectal-cancer/

WHAT IS A CANCER?

- It is an unlimited and uncontrolled proliferation of mutated cells
- These unrepaired mutations are usually related to the effect of exposure to carcinogens

CANCER IS A MAJOR PUBLIC HEALTH ISSUE

THE BURDEN OF NON-COMMUNICABLE DISEASES (NCDS) & CANCER

Global Burden of NCDs 2016

NCDs such as Cardiovascular, Respiratory Disease and Cancer cause:

- 56.9 Million Deaths
- 40.5 Million Deaths from NCDs (71%)
- 9 Million NCD Deaths from Cancer

Source: https://www.who.int/gho/ncd/mortality_morbidity/en/ (September 7th, 2020)

BURDEN OF NON-COMMUNICABLE DISEASES (NCDS) IN RUSSIA

2016 Russian Burden of NCDs

NCDs such as Cardiovascular, Respiratory Disease & Cancer cause:

- 1.9 Million Deaths
- 1.6 Million NCD Deaths (87%)
- ~310,000 Cancer Deaths

Behaviors leading to NCDs

- 37% of Adults use tobacco
- 18% are physically inactive
- Average daily salt intake is double the recommended levels
- Average alcohol consumption is higher than the European average (12 ℓ pure alcohol/year)

Source: https://www.who.int/nmh/countries/rus_en.pdf?ua=1 (September 7th, 2020)

WHAT ARE THE CONDITIONS FOR A CANCER TO HAPPEN ?

WHAT ARE THE CONDITIONS FOR A CANCER TO HAPPEN ?

EXPOSURE TO A CARCINOGEN

DOSE-RESPONSE

CANCER DEVELOPMENT - A MATTER OF DOSE RESPONSE

The greater amount of carcinogens you are exposed to

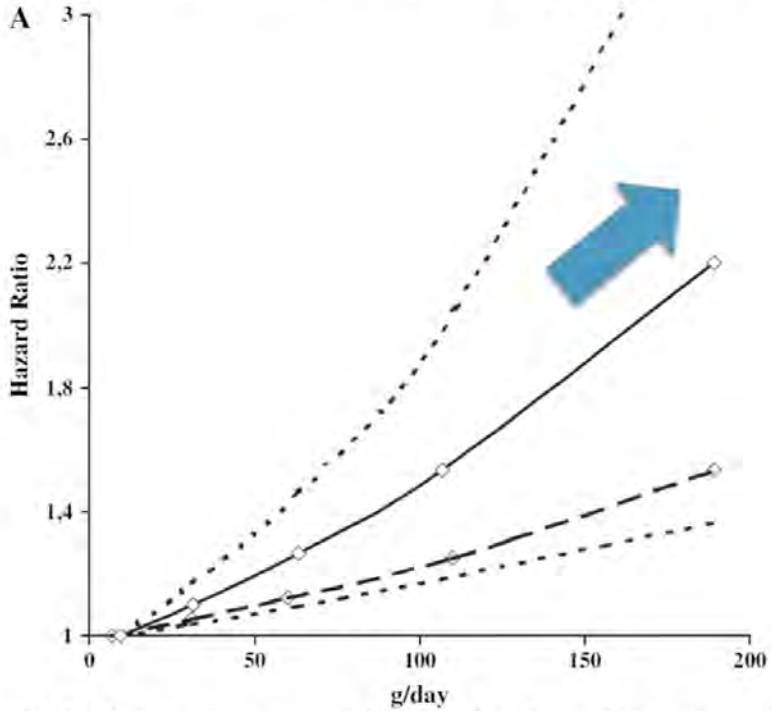
the higher the risk of cancer

IMPORTANCE OF THE EXPOSURE IS RELATED TO:

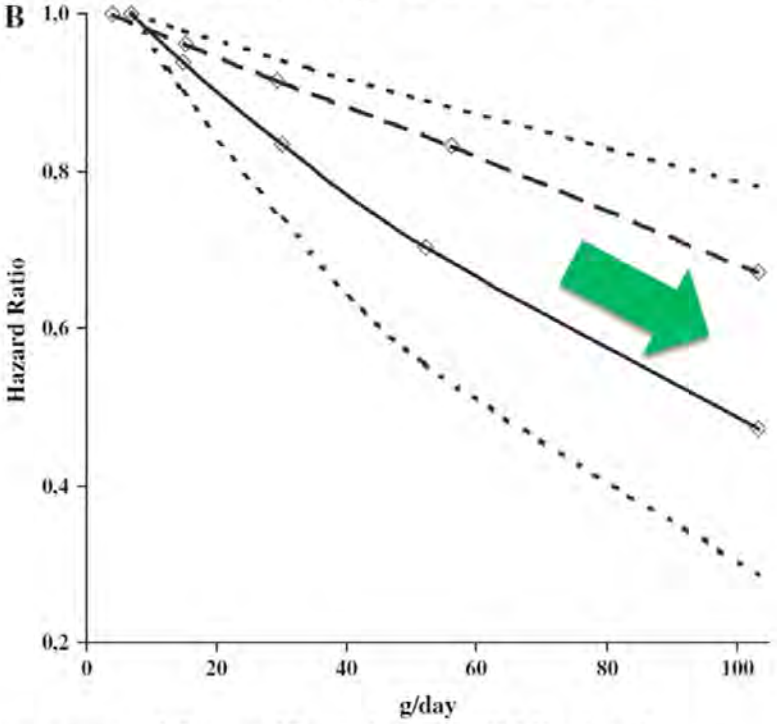
- Dose
- Duration
- Genomic succeptibility

DOSE:
FOOD - COLORECTAL CANCER RISK (CRC)

CRC Risk through intake of red and processed meat



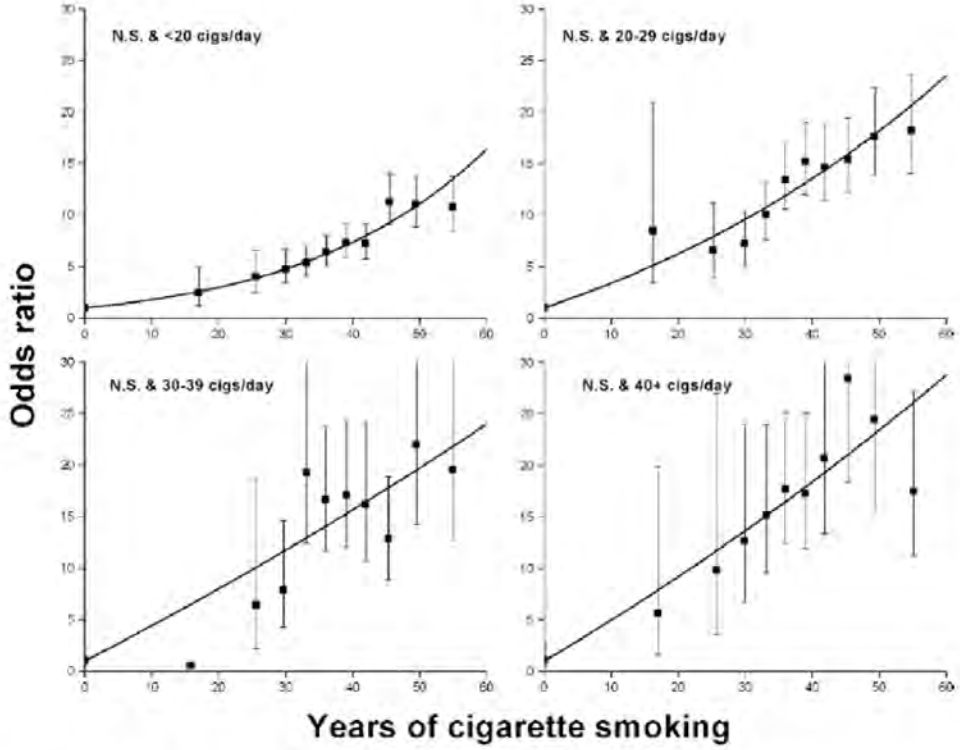
CRC risk through intake of Fish



Points in the figure represent median intakes in each category of consumption. Curves generated from calibrated data (**solid line**) and uncalibrated data (**hatched line**) and upper and lower confidence intervals for calibrated data (**dotted lines**) are shown.

Source: Norat, T; Meat, Fish, and Colorectal Cancer Risk: The European Prospective Investigation into Cancer and Nutrition DOI: 10.1093/jnci/dji164 *Journal of the National Cancer Institute*, Vol. 97, No. 12.

DURATION:
SMOKING - LUNG CANCER



Cigarette Smoking and Lung Cancer: Modeling Total Exposure and Intensity; Jay H. Lubin and Neil E. Caporaso; Cancer Epidemiol Biomarkers Prev March 1 2006 (15) (3) 517-523; **DOI:** 10.1158/1055-9965.EPI-05-0863

GENOMIC SUCCEPTIBILITY: SMOKING – LUNG CANCER

- Although 80% of all lung cancers occur in smokers

BUT

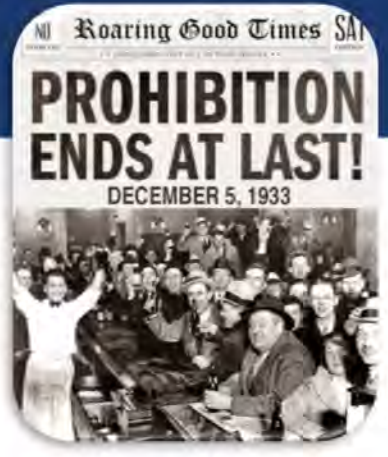
- Only 8% all smokers will develop lung cancer


WHAT
WE DO?

WHAT CAN WE DO ?

- Elimination of carcinogens
- Usage of anti-carcinogens
- Reduction in exposure to carcinogens
- Detection of susceptibilities

ELIMINATION OF CARCINOGENS



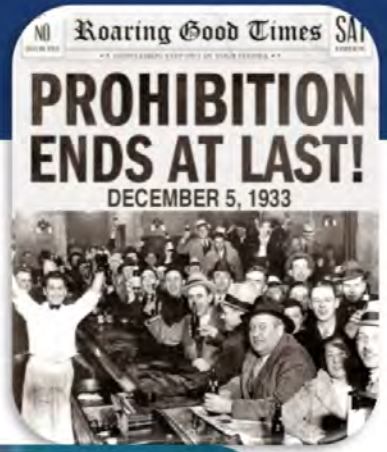
https://insidethecask.com/2017/12/05/an-end-to-prohibition-84-years-ago/

- 1920-1930's – Alcohol Prohibition
- Tobacco Control - aims to influence behavior related to smoking.
  - Policies vary by country
  - Global Convention entered into force 27 February 2005 (currently there are 181 Parties to the Convention).

FCTC
WHO FRAMEWORK CONVENTION ON TOBACCO CONTROL

ELIMINATION OF CARCINOGENS

- 1920-1930's – Alcohol Prohibition

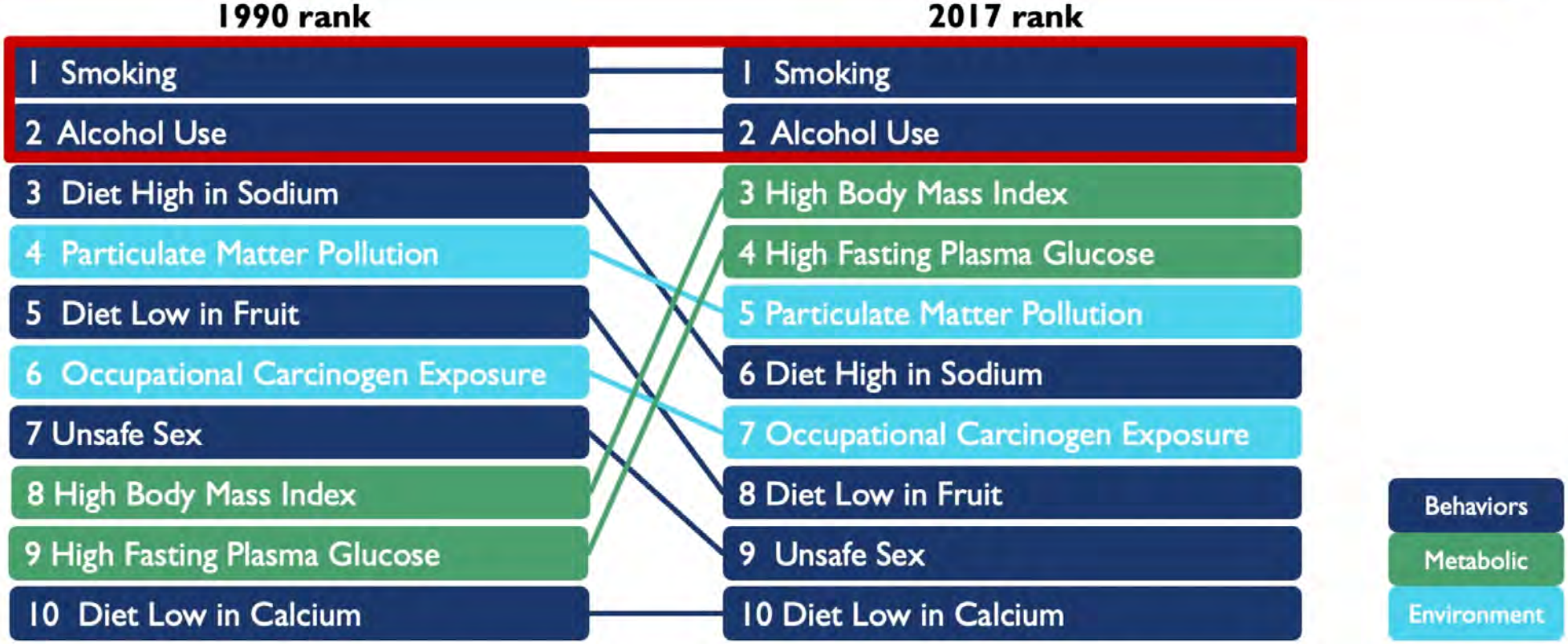


https://insidethecask.com/2017/12/05/an-end-to-prohibition-84-years-ago/

- Tobacco Con ted to smoking.
  - Policies vary
  - Global Conv 2005 (currently there are 18

FCTC
FRAMEWORK CONVENTION
TOBACCO CONTROL

RISK FACTORS FOR CANCER IN GLOBALLY
ALL AGES, BOTH SEXES, DEATHS PER 100,000



Source: Institute for Health Metrics and Evaluation (IHME). GBD Compare Data Visualization. Seattle, WA: IHME, University of Washington, 2016. Available from http://vizhub.healthdata.org/gbd-compare. (Accessed October 28th, 2019)

USE ANTI-CARCINOGENS

Poison ⟷ anti-poison

- Ex: Vitamin C or E AND Red or processed meat
- Ex: Retinoïds & lung cancer = CARET and ATBC studies
- Ex: Vaccination = HPV

REDUCTION IN EXPOSURE TO CARCINOGENS

"HARM REDUCTION"

A new concept?

No, it is a term arose in the context of drug addiction

http://afew.org/headlines/harm-reduction/
http://www.smchd.org/2018/12/what-is-harm-reduction/
http://www.smchd.org/2018/12/what-is-harm-reduction/

THE TIMES (SEPTEMBER 2ND, 2019)

IAN BIRRELL

SEPTEMBER 2 2019, 12:01AM, THE TIMES

Misguided morality is denying help to drug addicts

- 1980's Mrs. Thatcher introduced and pioneered a focus on harm reduction during the AIDS epidemic, with needle exchange and safe havens → which resulted in the lowest rates of HIV in drug users in the world
- Over the past 12 years the UK Think Tank "Centre for Social Justice" led change in drug policy → "ABSTINENCE BASED POLICY"
- Outcome: Drug-related fatalities have double since 2011

  1 in 3 drug-related deaths in Europe are in the UK

People make poor lifestyle choices despite suffering negative health effects

If you want to reduce the exposure to carcinogens …

You MUST

Identify the nature, production, and exposure source of carcinogens

EXAMPLE:

CIGARETTES
OR
SMOKING

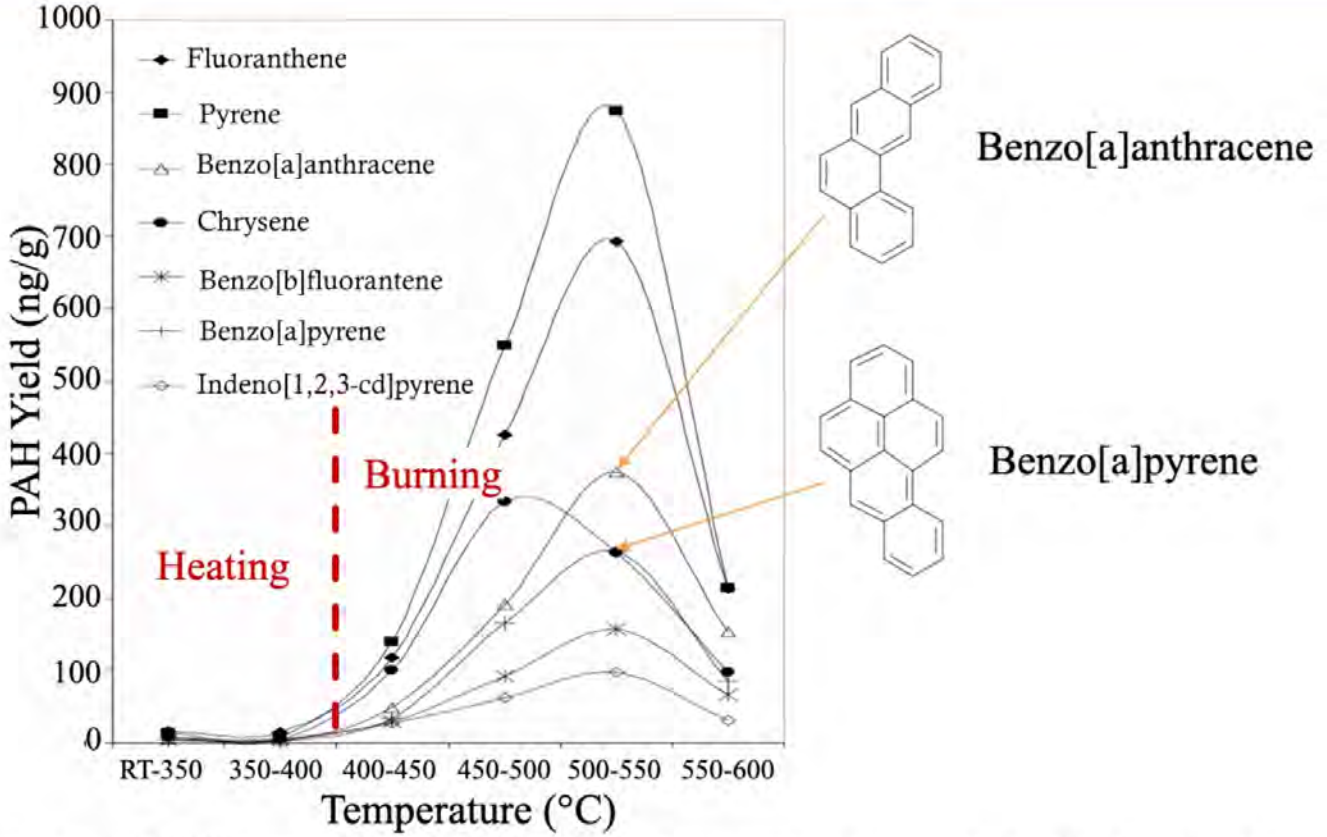
HOW DOES CIGARETTE SMOKE CAUSE CANCER?

CARCINOGENS IN CIGARETTE SMOKE

- Burning tobacco generates smoke.
- Tobacco smoke contains more than 6,000 chemicals & ultrafine particles. [1]
- 93 of them are listed by the U.S. FDA as Harmful and Potentially Harmful Constituents (HPHCs)[2].
- The majority (almost 80) are carcinogens or potential carcinogens.[2]

1 Rodgman A, Perfetti TA. The chemical components of tobacco and tobacco smoke 2nd ed: CRC Press, Taylor & Francis Inc (United States): 2013.
2 Harmful and Potentially Harmful Constituents in Tobacco Products and Tobacco Smoke: Established List; https://www.fda.gov/tobacco-products/rules-regulations-and-guidance/harmful-and-potentially-harmful-constituents-tobacco-products-and-tobacco-smoke-established-list (April 2012)

CHEMICALS EMITTED WHEN TOBACCO BURNS



Source: McGrath, T.E., Wooten, J.B., Chan W.G. and Hajaligol, M.R., 2007. Formation of polycyclic Aromatic Hydrocarbons from Tobacco: the "Link" between Low Temperature Residual Solid and PAH Formation, Food and Chemical Toxicology, 45,6,1039-1050

Remember!!!

CANCER DEVELOPMENT - A MATTER OF DOSE RESPONSE

The greater amount of carcinogens you are exposed to

the higher the risk of cancer

QUITTING TOBACCO SMOKING

IS BY FAR THE BEST OPTION !

QUITTING IS HARD – EVEN FOR PEOPLE WITH CANCER

Smokers Diagnosed with Cancer Continue to Smoke

https://www.fredhutch.org/en/news/center-news/2017/11/smoking-with-cancer.html

HARM REDUCTION

Accepting that some level of our bad behaviors are inevitable therefore

Target to minimize the harms people suffer as a consequence (not the behavior)

Driving Fast → Seatbelts, airbags, disc brakes
Unhealthy Diet → statins, stents, anti-aggregates
Sun Tanning → sunscreen
Sweet Tooth → sugar replacements
Sex → condoms, vaccination

??WHAT ABOUT FOR SMOKING??

INNOVATION IN TOBACCO SMOKING

E-Cigarettes

Heated Tobacco

FDA: Description of Heated Tobacco Products:
https://youtu.be/g2lQaIrBZpA

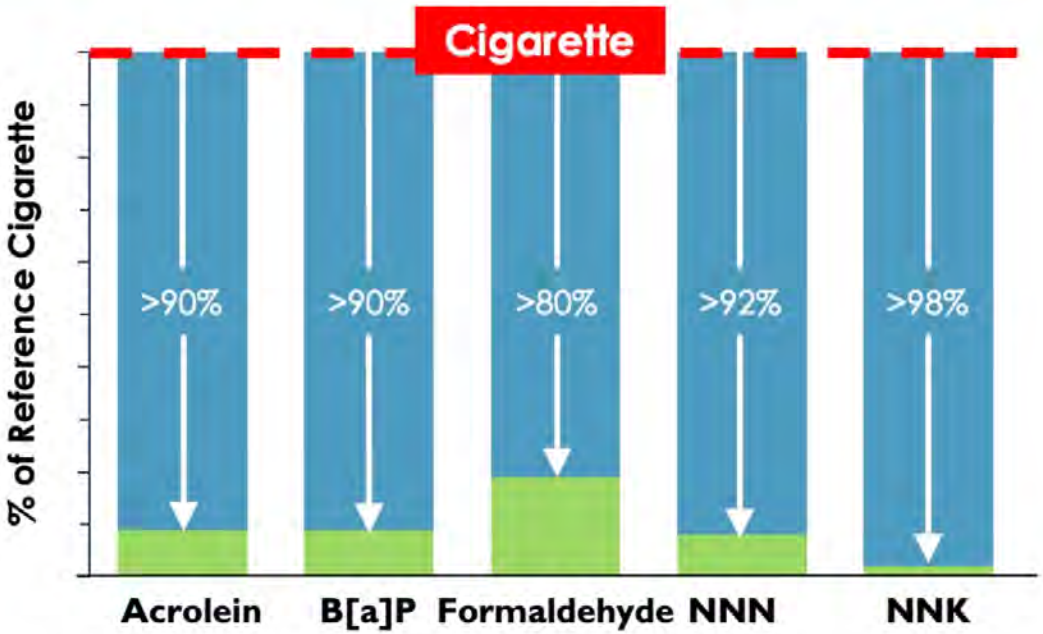
https://www.fda.gov/tobacco-products/ctp-newsroom/how-are-non-combusted-cigarettes-sometimes-called-heat-not-burn-products-different-e-cigarettes-and
https://www.health.state.mn.us/communities/tobacco/ecigarettes/index.html

JULY 2020 – U.S. FDA AUTHORIZED MODIFIED RISK TOBACCO PRODUCT WITH REDUCED EXPOSURE CLAIM (MRTPA)

FDA Conclusions

Determined that the exposure modification order for IQOS would be appropriate to **promote the public health** and is expected to **benefit the health of the population** as a whole

1. No combustion in IQOS
2. IQOS emits reduced levels of toxicants than cigarettes
3. Smokers who switch completely to IQOS reduce their exposure to toxicants
4. IQOS has a lower toxic potential than cigarettes
5. Although "Risk Reduction" has not yet been demonstrated … a substantial and measurable reduction in morbidity and mortality is reasonably likely in subsequent studies



FDA's Southeast Tobacco Laboratory (STL) tested IQOS in October 2017

https://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/TobaccoProductsScientificAdvisoryCommittee/UCM593109.pdf
https://www.fda.gov/media/139796/download

CANCER POTENCY OF CARCINOGENS OF NICOTINE AND TOBACCO CONTAINING PRODUCTS

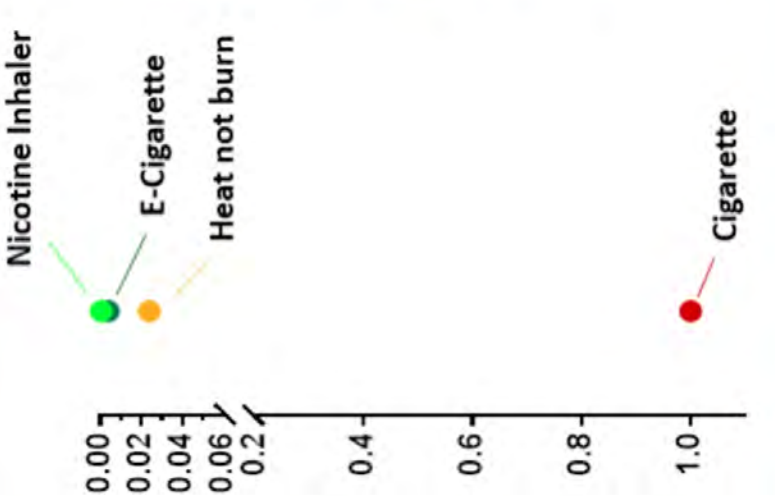
Research paper

Comparing the cancer potencies of emissions from vapourised nicotine products including e-cigarettes with those of tobacco smoke

William E Stephens

ABSTRACT

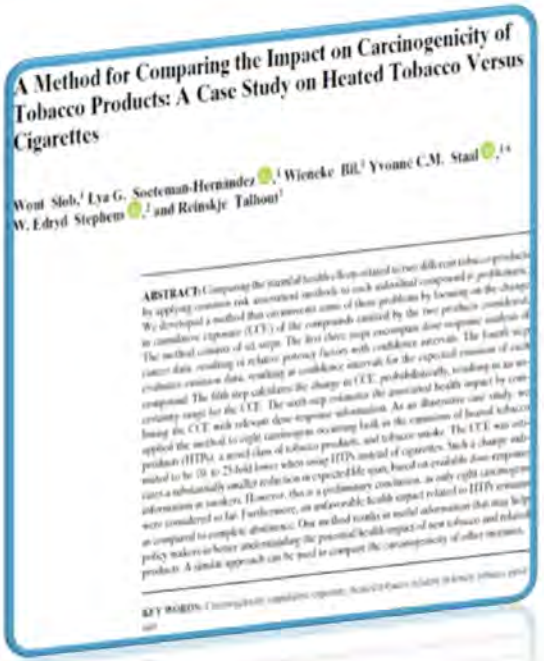
(Adapted from Stephens 2017)



It not really "a risk continuum" BUT "a risk cliff"

* Based on :Stephens WE; Comparing the cancer potencies of emissions from vapourised nicotine products including e-cigarettes with those of tobacco smoke; Tobacco Control Published Online First: 04 August 2017. doi: 10.1136/tobaccocontrol-2017-053808

RIVM (NETHERLANDS) INDEPENDENT ASSESSMENT OF HEALTH IMPACTS OF TOBACCO PRODUCTS (IQOS)


A Method for Comparing the Impact on Carcinogenicity of Tobacco Products: A Case Study on Heated Tobacco Versus Cigarettes

Wout Slob,[1] Lya G. Soeteman-Hernández,[1] Wieneke Bil,[1] Yvonne C.M. Staal,[1,*] W. Edryd Stephens,[2] and Reinskje Talhout[1]

ABSTRACT: Comparing the harmful health effects related to two different tobacco products by applying common risk assessment methods to each individual compound is problematic. We developed a method that circumvents some of these problems by focusing on the change in cumulative exposure (CCE) of the compounds emitted by the two products considered. The method consists of six steps. The first three steps encompass dose–response analysis of cancer data, resulting in relative potency factors with confidence intervals. The fourth step evaluates emission data, resulting in confidence intervals for the expected emission of each compound. The fifth step calculates the change in CCE probabilistically, resulting in an uncertainty range for the CCE. The sixth step estimates the associated health impact by combining the CCE with relevant dose–response information. As an illustrative case study, we applied the method to eight carcinogens occurring both in the emissions of heated tobacco products (HTPs), a novel class of tobacco products, and tobacco smoke. The CCE was estimated to be 10- to 25-fold lower when using HTPs instead of cigarettes. Such a change may cause a substantially smaller reduction in expectable death, based on available dose–response information in smokers. However, this is a preliminary conclusion, as only eight carcinogens were considered so far. Furthermore, an unfavorable health impact related to HTPs cannot be excluded as compared to complete abstinence. Our method results in useful information that may help policy makers in better understanding the potential health impact of new tobacco and related products. A similar approach can be used to compare the carcinogenicity of other mixtures.

KEY WORDS:

- Regulators need to assess the validity of health claims for new tobacco products.
- RIVM developed a methodology to compare the risk between tobacco products.
- To illustrate how the model functions, RIVM used PMI data to compare IQOS with cigarettes

Key Findings

- IQOS had 10 to 25-fold lower exposure to carcinogens than cigarettes.
- Exposure reductions could translate into a substantial increase in life expectancy compared to continuing to smoke.
- Although cessation still had the most substantial increase in life expectancy.

Why Is This Important?

- This model is a tool to evaluate health impacts of individuals and could be used to determine to appropriate policy and practice.

https://onlinelibrary.wiley.com/doi/full/10.1111/risa.13482

CONCLUSION – IN A PERFECT WORLD

- **The Dream**
  - To eliminate all smoking and therefore all smoking-related disease

  If not possible …

- **Detect genomic succeptibility**
  - To implement targeted prevention

CONCLUSION – IN THE REAL WORLD

- **Education & Prevention**
- **Innovations – to reduce harmful consequences of behaviors**
  - Smoking & Tobacco: stop burning tobacco → e-cigarettes or heated tobacco products or snus
  - Diet & Obesity
  - Physical activity
  - Sun exposure
  - Vaccination
  - Use of anti-carcinogens