Estimating the global cancer burden attributable to modifiable risk factors: methodological challenges and uncertainty

Hanna Fink
PhD Student
Cancer Surveillance Branch, International Agency for Research on Cancer (IARC/WHO)
finkh@iarc.who.int

Data
Discovery
Prevention
Knowledge

60 years | International Agency for Research on Cancer
Cancer research into action

01 GENERAL INTRODUCTION

THE CHALLENGE: FROM EVIDENCE TO A GLOBAL COMPARATIVE RISK ASSESSMENT

nature medicine

Article

https://doi.org/10.1038/s41591-026-04219-7

Global and regional cancer burden attributable to modifiable risk factors to inform prevention

Aim: To provide estimates of cancer incidence attributable to 30 modifiable risk factors in order to identify and support prioritization of key opportunities for cancer prevention.

THE PAF FORMULA IS THE EASY PART

$$PAF = \frac{\int RR(x)P(x)dx - \int RR(x)P^*(x)dx}{\int RR(x)P(x)dx}$$

$$Attributable\ Cases = PAF \times Incidence$$

60 years | International Agency for Research on Cancer
Cancer research into action

02 THE METHODOLOGICAL CHALLENGES

CHALLENGE 1: FINDING A COMPATIBLE RELATIVE RISK

1. Established causal relationship
2. Available meta-analysis/pooled evidence
3. Correct cancer endpoint
4. Correct unit/category
5. Compatible with available prevalence data

Cancer	Measure	Total no. of studies	No. of studies in meta-analysis	No. of cases	Risk estimate (95% confidence intervals [CI])	Increment	I^2 (%)	Conclusion[1]	Date of CUP cancer report[2]
Oesophagus (*adenocarcinoma*)	BMI	9	9	1,725	1.48 (1.35–1.62)	5 kg/m²	37	**Convincing: Increases risk**	2016
	Waist circumference	2	2	335	1.34 (1.17–1.52)	10 cm	10		
	Waist-hip ratio	3	3	380	1.38 (1.10–1.73)	0.1 unit	27		
Pancreas	BMI (cancer incidence)	30	23	9,504	1.10 (1.07–1.14)	5 kg/m²	19	**Convincing: Increases risk**	2012
	BMI (cancer mortality)	30	7	8,869	1.10 (1.02–1.19)	5 kg/m²	61		
	Waist circumference	5	5	949	1.11 (1.05–1.18)	10 cm	0		
	Waist-hip ratio	4	4	1,047	1.19 (1.09–1.31)	0.1 unit	11		
Liver	BMI	15	12	14,311	1.30 (1.16–1.46)	5 kg/m²	78	**Convincing: Increases risk**	2015
Colorectum	BMI	57	38	71,089	1.05 (1.03–1.07)	5 kg/m²	74	**Convincing: Increases risk**	2017
	Waist circumference	13	8	4,301	1.02 (1.01–1.03)	10 cm	0		
	Waist-hip ratio	6	4	2,564	1.02 (1.01–1.04)	0.1 unit	17		

CHALLENGE 2: CAN ONE RR TRAVEL AROUND THE WORLD?

Comparative

Epub 2014 No

Global l
mass in

Melina Arnold
Gretchen A St
Rajesh Dikshit

Affiliations +

PMID: 254674

Table 7. Population attributable fraction using regional relative risk estimates and difference (PAF Δ)* compared with the main results (Table 1a for males and 1b for females)

*PAF Δ= PAF main analysis – PAF sensitivity analysis

MALES

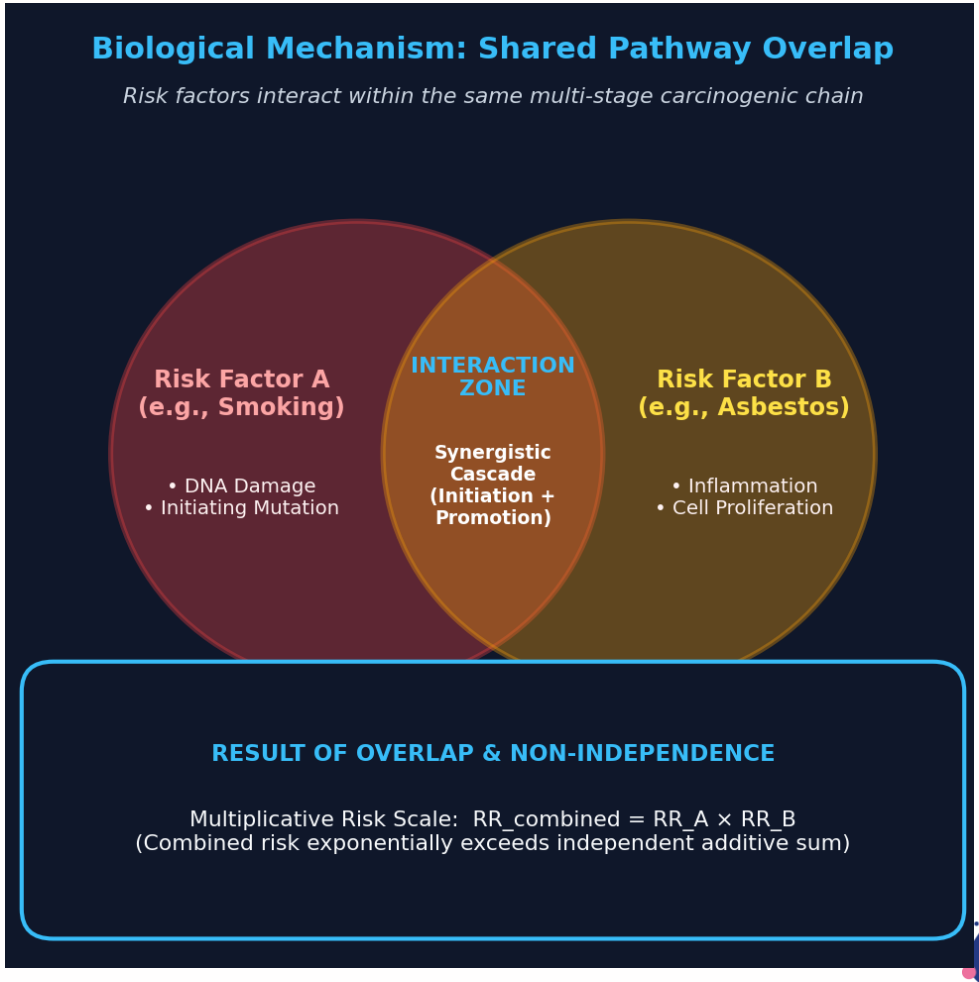
region	*Pancreas*		*Colon*		*Rectum*	
	PAF	PAF Δ	PAF	PAF Δ	PAF	PAF Δ
North America	41%	-27%	30%	-9%	6%	5%
East Asia	0%	4%	9%	-2%	2%	2%
South-East Asia	0%	3%	5%	-1%	1%	1%
South-Central Asia	0%	3%	5%	-1%	1%	1%
Eastern Europe	6%	4%	16%	0%	8%	0%
Northern Europe	8%	5%	18%	0%	9%	0%
Southern Europe	7%	4%	18%	0%	9%	0%
Western Europe	8%	5%	17%	1%	10%	0%
Oceania	8%	5%	23%	-4%	10%	0%

FEMALES

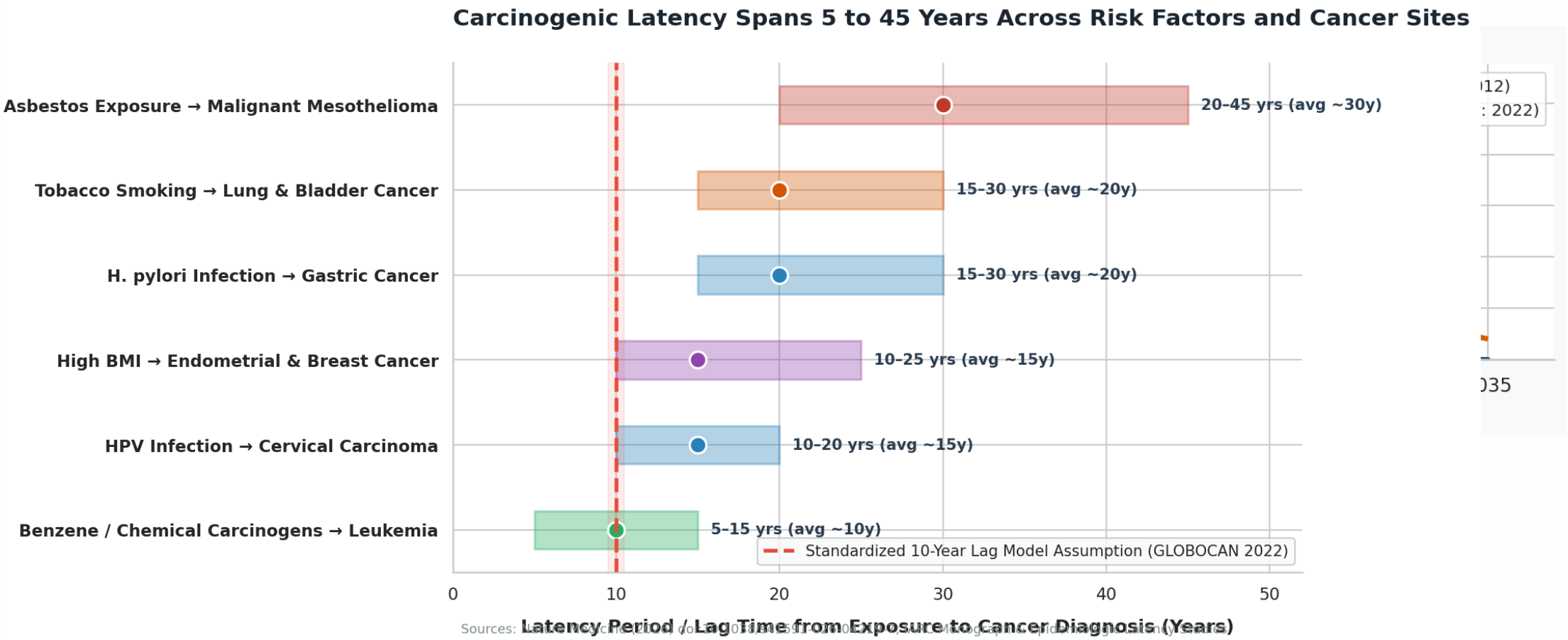
region	*Pancreas*		*Corpus uteri*		*Ovary*		*Colon*		*Rectum*		*Breast (premenopausal)*		*Breast (postmenopausal)*	
	PAF	PAF Δ	PAF	PAF Δ	PAF	PAF Δ	PAF	PAF Δ	PAF	PAF Δ	PAF	PAF Δ	PAF	PAF Δ
sub-Saharan Africa											-2%	-1%		
Middle East and Northern Africa											-4%	-2%		
North America	18%	-6%	52%	-4%	0%	7%	16%	-5%	16%	-11%	-7%	0%	17%	-3%
East Asia	14%	-10%	29%	-9%	15%	-13%	4%	0%	4%	-2%	1%	-3%	13%	-8%
South-East Asia	12%	-9%	27%	-9%	15%	-13%	4%	0%	4%	-2%	2%	-4%	12%	-7%
South-Central Asia	11%	-8%	24%	-7%	11%	-9%	3%	0%	3%	-1%	1%	-3%	10%	-6%
Eastern Europe	14%	-4%	50%	-5%	3%	3%	5%	5%	0%	5%	-4%	0%	10%	4%
Northern Europe	13%	-4%	47%	-5%	3%	3%	5%	5%	0%	5%	-5%	0%	9%	3%
Southern Europe	14%	-4%	46%	-5%	3%	3%	5%	5%	0%	5%	-3%	0%	9%	3%
Western Europe	13%	-4%	46%	-5%	3%	3%	5%	5%	0%	5%	-3%	0%	8%	3%
Oceania	14%	-4%	48%	-5%	3%	3%	5%	5%	0%	5%	-5%	0%	9%	3%

CHALLENGE 3: RISK FACTORS DON'T OCCUR IN ISOLATION

$$Total\ PAF = 1 - \prod_{i=1}^{n} (1 - PAF_i)$$



CHALLENGE 4: CANCER HAS A LONG MEMORY



Sources: [illegible]

International Agency for Research on Cancer

Cancer research into action

CHALLENGE 5: HOW UNCERTAIN IS THE FINAL NUMBER?

1. E

Comparative Study > Lancet Oncol. 2015 Jan;16(1):36-46. doi: 10.1016/S1470-2045(14)71123-4.

2. R

> Lancet. 2022 Aug 20;400(10352):563-591. doi: 10.1016/S0140-6736(22)01438-6.

The global burden of cancer attributable to risk factors, 2010–19: a systematic analysis for the Global Burden of Disease Study 2019

h body–
udy

> Lance

Glob
alco

han [4],
, Isabelle Romieu [9],

GBD 2019 Cancer Risk Factors Collaborators

Collaborators + expand

PMID: 35988567 PMCID: PMC9395583 DOI: 10.1016/S0140-6736(22)01438-6

Harriet
Isidore

Affiliations + expand

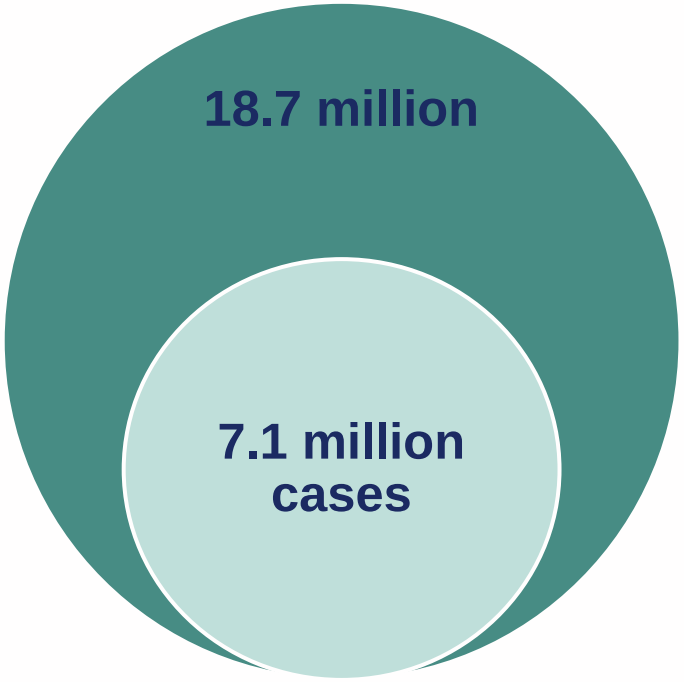
PMID: 34270924 PMCID: PMC8324483 DOI: 10.1016/S1470-2045(21)00279-5

International Agency for Research on Cancer

Cancer research into action

03 GENERAL TAKE-AWAYS

WHAT DID WE LEARN, AND WHAT SHOULD IMPROVE?



7.1 million out of 18.7 million of new cancer cases (37%) in 2022 could be prevented

1. Better RR evidence
2. Better evidence on joint exposures
3. Better exposure histories
4. Better uncertainty inputs



International Agency for Research on Cancer

Cancer research into action