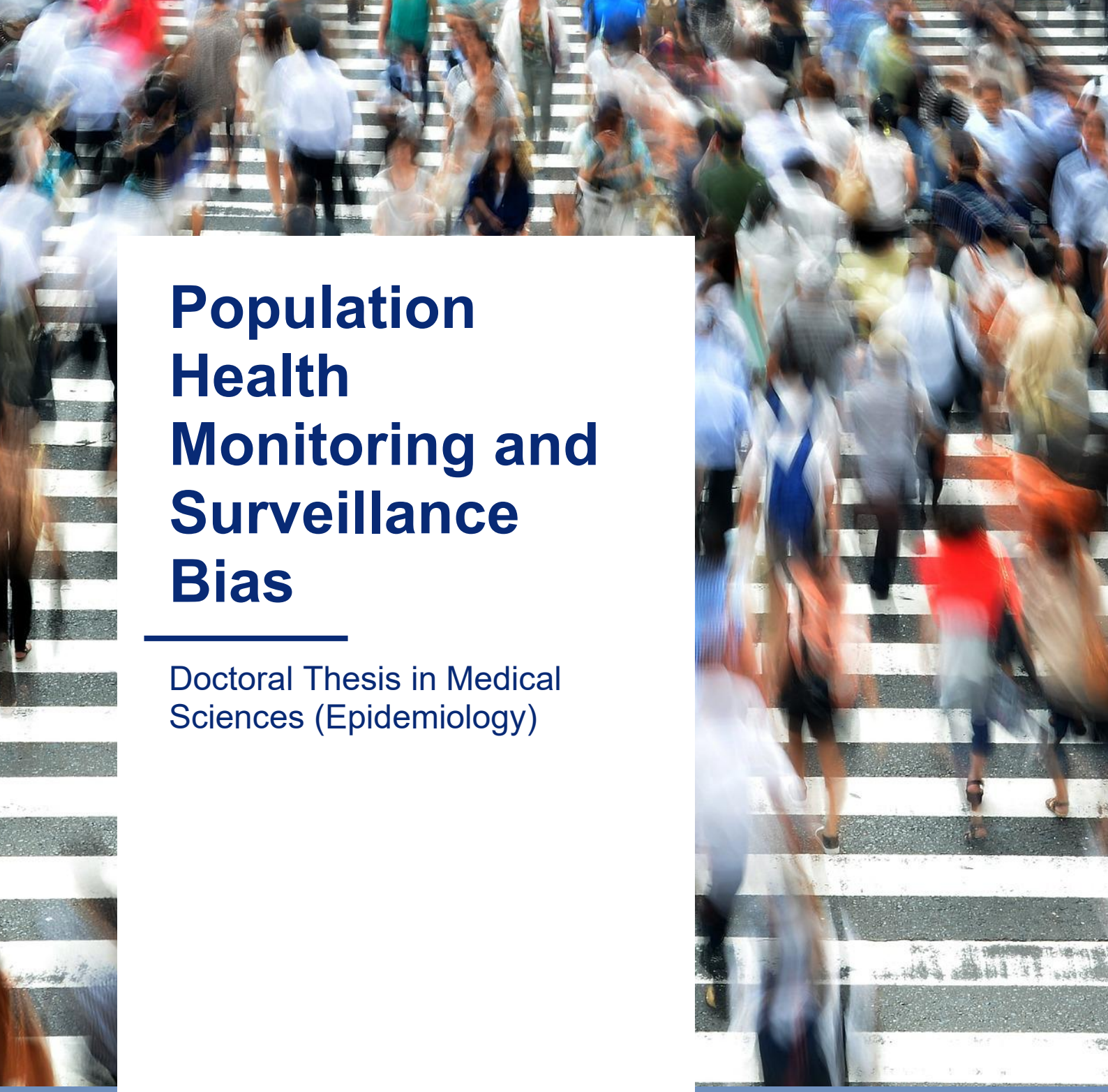

Population Health Monitoring and Surveillance Bias

Doctoral Thesis in Medical Sciences (Epidemiology)

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UNI FR

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Population Health Monitoring and Surveillance Bias

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Table of Contents

PhD committee members 2
Summaries 3
Chapter 1 | Introduction 11
What is public health surveillance? 11
Historical foundations 11
Conceptual framework 13
Tools and methods for measuring population health 14
From data to health indicators 15
Potential biases of health indicators 15
Surveillance bias 16
Summary 18
Chapter 2 | Objectives 21
Chapter 3 | Methodology 23
Corona Immunitas 23
Narrative reviews 24
National Institute for Cancer Epidemiology and Registration (NICER) 24
Chapter 4 | Surveillance bias: when appearances are misleading 29
Chapter 5.1 | Seroprevalence trends of anti-SARS-CoV-2 antibodies and associated risk factors: a population-based study 35
Chapter 5.2 | Surveillance bias in the assessment of the size of COVID-19 epidemic waves: a case study 51
Chapter 5.3 | Designing surveillance at a population level 59
Chapter 6.1 | Screening and surveillance bias in cancer 63
Chapter 6.2 | Epidemiological signatures and surveillance bias in cancer 69
Chapter 6.3 | Assessing the magnitude of surveillance bias in prostate cancer, melanoma and lung cancer 75
Chapter 7 | Discussion 93
Summary of main findings 93
Limitations and strengths 94
Chapter 8 | Conclusion 97
List of publications and courses 99
Bibliography 105

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Summaries

Abstract

Surveillance bias occurs when variations in the frequency of a health condition result from differences in the modality or intensity of detection, rather than actual changes in its underlying risk. These differences often arise from variations in detection, screening, and diagnostic strategies over time or across populations, care settings, and types of patients. As a result, surveillance indicators, such as disease incidence or quality-of-care metrics, are biased, leading to misinterpretations and potentially wrong public health decisions. This bias can also lead to incorrect estimates of the association between an exposure and a health condition due to differences in detection modalities of outcomes across exposure subgroups. Despite the widespread recognition of surveillance bias, a precise and accepted definition, as well as estimates of its magnitude in different settings, are still lacking.

Therefore, the overarching goal of my PhD thesis was to clearly define and describe surveillance bias and provide quantitative estimates of its magnitude. To achieve this, we pursued three specific aims: (1) to define surveillance bias, identify contexts and situations in which it occurs, describe its causes and consequences, and how to prevent it (Chapter 4); (2) to describe and estimate the magnitude of surveillance bias in COVID-19 (Chapter 5); and (3) to describe and estimate the magnitude of surveillance bias in cancer (Chapter 6).

Chapter 4: Overview and definition of surveillance bias

In *Chapter 4*, we explained the concept of surveillance bias and identified several situations where it occurs, including the assessment of the severity of COVID-19 epidemic waves, the evaluation of quality-of-care indicators, and the interpretation of cancer trends, chlamydia incidence or hypertension prevalence. Through these examples, we showed how surveillance bias influences trends in different ways and arises from multiple factors, including changes in testing intensity—as observed in COVID-19 surveillance and quality-of-care metrics—, changes in screening practices, as in cancer; shifts in diagnostic thresholds, as in hypertension; or variations in reporting completeness, notably in chlamydia surveillance. In this chapter, we also outlined strategies to reduce the effect of surveillance bias, like analyzing trends accounting for screening and diagnostic processes, favoring indicators less exposed to surveillance bias, or standardizing disease definitions.

Chapter 5: Surveillance bias in COVID-19

In *Chapter 5.1*, we described the spread of SARS-CoV-2 in Switzerland between 2020 and 2021. We estimated seroprevalence trends through the nationwide study Corona Immunitas and provided estimates for eleven Swiss cantons across three different periods (May–Oct 2020, Nov 2020–mid-May 2021, and mid-May–Sep

2021) of the pandemic and for various age groups. These estimates were used for the study described in the next chapter.

In *Chapter 5.2*, we used seroprevalence estimates and three other COVID-19 indicators (cases, hospitalizations, deaths) retrieved from the Federal Office of Public Health to estimate surveillance bias in the assessment of the severity of COVID-19 epidemic waves in the canton of Fribourg, Switzerland. We found that no single indicator was free from surveillance bias. The number of cases was highly biased, underestimating the magnitude of epidemic waves, especially during the first phases of the pandemic. Hospitalizations and deaths provided more consistent estimates of wave severity over time, but they were also affected by surveillance bias. Seroprevalence, initially the least biased indicator, became more biased in later stages due to widespread vaccination, as changes in seroprevalence reflected both the epidemic spread and vaccine-induced immunity.

In *Chapter 5.3*, we built on insights from the previous studies to describe how different types of COVID-19 surveillance—at both the population and healthcare provider levels—are impacted by surveillance bias and how this influences data interpretation and health policy decisions. We showed the advantages and disadvantages of these surveillance tools and argued that population-based indicators are less affected by surveillance bias compared to diagnosis-based indicators.

Chapter 6: Surveillance bias in cancer

In *Chapters 6.1* and *6.2*, we presented two narrative reviews on how surveillance bias occurs in scrutiny-dependent cancers, how it relates to screening and overdiagnosis, and how it can be identified using epidemiological signatures of cancer. We described the cases of thyroid, prostate, melanoma, breast, and kidney cancers, as well as the impact of surveillance bias on identifying certain risk factors such as obesity, sex, and socioeconomic status. Using incidence and mortality trends for prostate, melanoma, and lung cancers in Switzerland, we also demonstrated how cancer epidemiological signatures can help detecting surveillance bias and correctly interpreting cancer trends.

In *Chapter 6.3*, we provided numeric estimates of surveillance bias in prostate cancer, melanoma, and lung cancer in Switzerland using incidence and mortality trends from 1989 to 2021. We found that the bias for prostate cancer changed substantially since 1989, being moderate between 1989 and 2004, low between 2004 and 2011, and high between 2011 and 2021. The bias was high for melanoma across the entire study period 1989–2021. For lung cancer, surveillance bias was moderate over the entire period, and consistently lower compared to the other two cancers. In stage-specific analyses, surveillance bias tended to be greater for cancers diagnosed at earlier stages than for those diagnosed at later stages.

In conclusion, we assessed surveillance bias across different diseases and contexts, explored its causes, and described possible strategies to prevent it. We showed that the bias was substantial for certain indicators, such as the number of COVID-19 cases or cancer incidence for specific types of cancer, providing

estimates of its magnitude. Accurately measuring surveillance bias proved challenging, mainly due to the multiplicity of external factors influencing health indicators, which were difficult to consider all at once. Nonetheless, our work contributes to paving the way for more comprehensive and accurate methods to quantify surveillance bias, while also fostering awareness and advocating for methodological improvements.

Résumé

Le biais de surveillance se produit lorsque des variations dans la fréquence d'un événement résultent de différences dans la modalité ou l'intensité de sa détection, plutôt que de véritables changements dans son risque sous-jacent. Ces différences surviennent souvent en raison de variations dans les stratégies de détection, de dépistage et de diagnostic au fil du temps ou entre différentes populations, contextes de soins et types de patients. Par conséquent, les indicateurs de surveillance, tels que l'incidence des maladies ou les mesures de qualité des soins, peuvent être biaisés, entraînant des interprétations erronées et des décisions de santé publique incorrectes. Ce biais peut également fausser les estimations de l'association entre une exposition et un événement en raison de différences dans les modalités de détection des événements entre les sous-groupes exposés. Bien que le biais de surveillance soit largement reconnu, une définition précise et acceptée de ce biais, ainsi que des estimations de son ampleur dans différents contextes, restent encore à établir.

Ainsi, l'objectif principal de ma thèse de doctorat était de définir le biais de surveillance et de fournir des estimations de son impact. Pour cela, nous avons poursuivi trois objectifs spécifiques : (1) définir le biais de surveillance, identifier les contextes et les situations dans lesquels il survient, en décrire les causes et les conséquences, ainsi que les moyens de le prévenir ; (2) estimer l'ampleur du biais de surveillance dans le cadre du COVID-19 ; et (3) estimer l'ampleur du biais de surveillance dans le cadre du cancer. Ces objectifs sont présentés dans trois chapitres principaux :

Chapitre 4 : Vue d'ensemble et définition du biais de surveillance

Dans le *chapitre 4*, nous expliquons le concept de biais de surveillance et identifions plusieurs situations dans lesquelles il se produit, notamment dans l'évaluation de la gravité des vagues épidémiques de COVID-19, l'évaluation des indicateurs de qualité des soins et l'interprétation des tendances de l'incidence du cancer, de la prévalence de l'hypertension et des taux d'infection de chlamydia. À travers ces exemples, nous montrons comment le biais de surveillance peut influencer les tendances de manière différente, et résulter de multiples facteurs, tels que les variations de l'intensité du dépistage - comme observé dans la surveillance du COVID-19 et les indicateurs de qualité des soins -, les changements dans les pratiques de dépistage, comme pour le cancer ; les modifications des seuils diagnostiques, comme pour l'hypertension ; ou encore les variations dans l'exhaustivité des déclarations, notamment pour la chlamydia. Dans ce chapitre, nous présentons également des stratégies visant à atténuer l'effet du biais de surveillance, telles que l'analyse des tendances en tenant compte des processus de dépistage et de diagnostic, l'utilisation d'indicateurs moins exposés à ce biais, ou la standardisation des définitions des maladies.

Chapitre 5 : Biais de surveillance dans le COVID-19

Dans le *chapitre 5.1*, nous décrivons la diffusion réelle du SARS-CoV-2 en Suisse entre 2020 et 2021. Nous avons estimé les tendances de la séroprévalence grâce

à une étude nationale appelée Corona Immunitas, et avons fourni des estimations pour onze cantons suisses à trois périodes distinctes de la pandémie et pour différents groupes d'âge. Ces estimations ont été utilisées pour l'étude présentée dans le chapitre suivant.

Dans le *chapitre 5.2*, nous utilisons les estimations de la séroprévalence ainsi que trois autres indicateurs du COVID-19 (cas, hospitalisations, décès), issus de l'Office fédéral de la santé publique, afin d'évaluer le biais de surveillance dans le canton de Fribourg. Nous avons constaté qu'aucun indicateur n'était exempt de biais de surveillance. Le nombre de cas était fortement biaisé, en particulier durant les premières phases de la pandémie. Les hospitalisations et les décès offraient des estimations plus cohérentes de la sévérité des vagues épidémiques au fil du temps, mais étaient également influencés par ce biais. La séroprévalence, initialement l'indicateur le moins biaisé, est devenue plus sujette au biais dans les phases ultérieures, en raison de la vaccination.

Dans le *chapitre 5.3*, nous approfondissons les résultats des études précédentes pour décrire comment différents types de surveillance du COVID-19—tant au niveau de la population qu'au niveau individuel—sont affectés par le biais de surveillance et comment cela influence l'interprétation des données et les décisions en matière de santé publique. Nous montrons les avantages et inconvénients de ces outils de surveillance et démontrons que les indicateurs basés sur la population sont moins affectés par le biais de surveillance que ceux basés sur les diagnostics individuels.

Chapitre 6 : Biais de surveillance dans le cancer

Dans les *chapitres 6.1 et 6.2*, nous présentons deux revues narratives sur la manière dont le biais de surveillance affecte les « scrutiny-dependent cancers », comment il est lié au problème du surdiagnostic et comment il peut être identifié à l'aide de signatures épidémiologiques du cancer. Nous abordons les cas des cancers de la thyroïde, de la prostate, du mélanome, du sein et du rein, ainsi que l'impact du biais de surveillance sur l'identification de certains facteurs de risque tels que l'obésité, le sexe et le statut socio-économique. En utilisant les tendances d'incidence et de mortalité en Suisse pour le cancer de la prostate, le mélanome et le cancer du poumon, nous démontrons également comment les signatures épidémiologiques du cancer peuvent être utilisées pour détecter le biais de surveillance et interpréter correctement les tendances du cancer.

Dans le *chapitre 6.3*, nous avons fourni des estimations numériques du biais de surveillance pour le cancer de la prostate, le mélanome et le cancer du poumon en Suisse, en utilisant les tendances d'incidence et de mortalité de 1989 à 2021. Nous avons observé que le biais pour le cancer de la prostate a changé de manière significative depuis 1989 : il était modéré entre 1989 et 2004, faible entre 2004 et 2011, et élevé entre 2011 et 2021. Le biais était élevé pour le mélanome sur l'ensemble de la période étudiée (1989–2021). Pour le cancer du poumon, le biais de surveillance était modéré durant toute la période, et systématiquement plus faible que pour les deux autres cancers. Dans les analyses par stade, le biais de surveillance tendait à être plus important pour les cancers diagnostiqués à un stade précoce que pour ceux diagnostiqués à un stade plus avancé.

En conclusion, nous avons évalué le biais de surveillance dans différents contextes et pour plusieurs maladies, exploré ses causes et décrit des stratégies possibles pour le prévenir. Nous avons montré que ce biais pouvait être important pour certains indicateurs, tels que le nombre de cas de COVID-19 ou l'incidence de certains types de cancer, en fournissant des estimations de son ampleur. Mesurer précisément le biais de surveillance s'est révélé difficile, principalement en raison de la multiplicité des facteurs externes influençant les indicateurs de santé, lesquels sont difficiles à prendre en compte simultanément. Notre travail contribue à ouvrir la voie à des méthodes plus complètes et plus précises pour quantifier le biais de surveillance, tout en sensibilisant à ce biais et en promouvant des améliorations méthodologiques.

Chapter 1 | Introduction

“What gets measured, gets done.”

This well-known old cliché, with no clearly identifiable source, highlights the importance of measuring and monitoring to gather information needed for action. In public health, surveillance and monitoring of population health and well-being have a crucial role, and are among the WHO's 12 essential public health functions (World Health Organization, 2024). However, they can be hindered by several biases, which need to be examined and addressed to make appropriate public health decisions.

This thesis focuses on a specific type of bias: surveillance bias. This bias occurs when variations in the frequency of an outcome result from differences in the modality or intensity of detection, rather than actual changes in its underlying risk. To fully understand the concept of surveillance bias, it is important to first clarify what public health surveillance is, how it works, and what its main objectives are. This also includes exploring the tools used in surveillance, understanding their limitations and discussing potential biases. These topics will be covered in this introduction to provide the necessary background for the rest of the thesis.

What is public health surveillance?

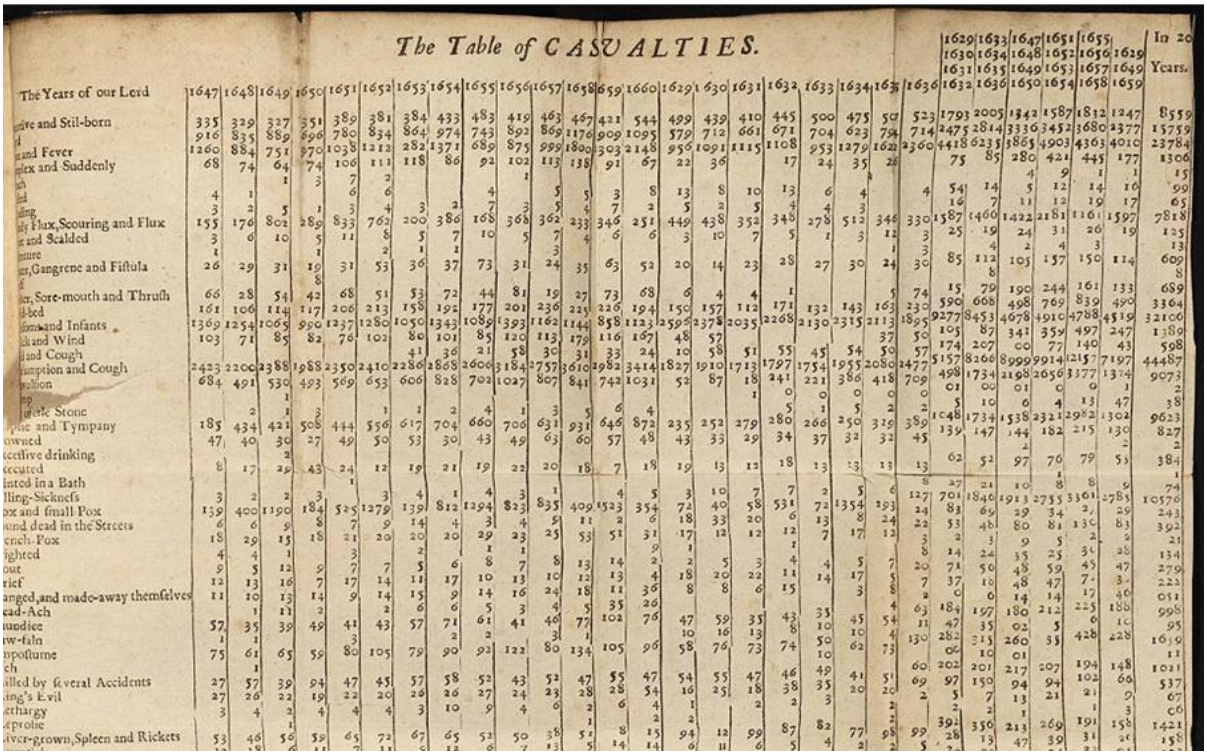
Public health surveillance is the ongoing, systematic collection, analysis, and interpretation of health data essential to the planning, implementation, and evaluation of public health practice and closely integrated with the timely dissemination of this information to guide decisions and actions in public health (Porta et al., 2014; Thacker & Berkelman, 1988).

Terms such as "population health monitoring" or "public health monitoring" are often used alongside "public health surveillance" to describe the same processes. However, there is no clear consensus on the precise use of these terms or the context in which they should be applied. In this thesis, the terms "population health monitoring," (Verschuuren & van Oers, 2020) "public health monitoring," (European Public Health Association, 2025) and "public health surveillance" will be used interchangeably.

Historical foundations

One of the earliest examples of public health surveillance dates back to 1662, when John Graunt, an English draper, analyzed death records kept by London parishes

since 1532 (Declich & Carter, 1994; Morabia, 2013). Graunt analyzed 50 years of weekly data and condensed them into clear and tables, transforming disorganized data into usable information (Figure 1). By analyzing mortality trends, Graunt revealed patterns in annual deaths from diseases like tuberculosis and linked sporadic plague outbreaks to environmental factors.



The Table of CASUALTIES.

The Years of our Lord	1647	1648	1649	1650	1651	1652	1653	1654	1655	1656	1657	1658	1659	1660	1629	1630	1631	1632	1633	1634	1635	1636	1629 1630 1631 1632	1633 1634 1635 1636	1647 1648 1649 1650	1651 1652 1653 1654	1655 1656 1657 1658	1629 1650 1649 1659	In 20 Years.
...ive and Still-born	335	329	327	351	389	381	384	433	483	419	463	467	421	544	499	439	410	445	500	475	50	523	1793	2005	1342	1587	1812	1247	8559
...d	916	835	889	896	780	834	864	974	743	892	869	1176	909	1095	579	712	661	671	704	623	758	714	2475	2814	3336	3452	3680	2377	15759
...and Fever	1260	884	751	970	1038	1212	282	1371	689	875	999	1800	303	2148	956	1091	1115	1108	953	1279	162	2360	4418	6235	3865	4903	4363	4010	23784
...plex and Suddenly	68	74	64	74	106	111	118	86	92	102	113	138	91	67	22	36		17	24	35	28		75	85	280	421	445	177	1306
...ch			1	3	7	2				1															4	9	1	1	15
...ad	4	1			6	6			4		5	5	3	8	13	8	10	13	6	4		4	54	14	5	12	14	16	99
...ling	3	2	5	1	3	4	3	2	7	3	5	4	7	2	5	2	5	4	4	3			16	7	11	12	19	17	65
...dy Flux, Scouring and Flux	155	176	802	289	833	762	200	386	168	368	362	233	346	251	449	438	352	348	278	512	346	330	1587	1460	1422	2181	1161	1597	7818
...e and Scalded	3	6	10	5	11	8	5	7	10	5	7	4	6	6	3	10	7	5	1	3	12	3	25	19	24	31	26	19	125
...ture	1			1		2	1	1			3										1	3		4	2	4	3		13
...rt, Gangrene and Fiftula	26	29	31	19	31	53	36	37	73	31	24	35	63	52	20	14	23	28	27	30	24	30	85	112	105	137	150	114	609
...f				8																				8					8
...er, Sore-mouth and Thrush	66	28	54	42	68	51	53	72	44	81	19	27	73	68	6	4	4	1				74	15	79	190	244	161	133	689
...d-bed	161	106	114	117	206	213	158	192	177	201	236	225	226	194	150	157	112	171	132	143	163	230	590	668	498	769	839	490	3364
...men and Infants	1369	1254	1065	990	1237	1280	1050	1343	1089	1393	1162	1144	858	1123	2596	2378	2035	2268	2130	2315	2113	1895	9277	8453	4078	4910	4788	4519	32100
...k and Wind	103	71	85	82	76	102	80	101	85	120	113	179	116	167	48	57					37	50	105	87	341	359	497	247	1380
...and Cough							41	36	21	58	30	31	33	24	10	58	51	55	45	54	50	57	174	207	00	77	140	43	598
...umption and Cough	2423	2200	2388	1988	2350	2410	2280	2868	2606	3184	2757	3610	2982	3414	1827	1910	1713	1797	1754	1955	2080	2477	5157	8206	8999	9914	12157	7197	44487
...pullion	684	491	530	493	569	653	606	828	702	1027	807	841	742	1031	52	87	18	241	221	386	418	709	498	1734	2198	2656	3377	1324	9073
...p			1														1	0	0	0	0	0	01	00	01	0	0	1	2
...eric Stone		2	1	3		1	1	2	4	1	3	5	6	4				5	1	5	2	2	5	10	6	4	13	47	38
...pine and Tympany	185	434	421	508	444	556	617	704	660	706	631	931	646	872	235	252	279	280	266	250	319	389	1048	1734	1538	2321	2982	1302	9623
...owned	47	40	30	27	49	50	53	30	43	49	63	60	57	48	43	33	29	34	37	32	32	45	139	147	144	182	215	130	827
...ecttive drinking				2																					2			2	2
...ecuted	8	17	25	43	24	12	19	21	19	22	20	18	7	18	19	13	12	18	13	13	13	13	62	52	97	76	79	53	384
...ifted in a Bath					1																					1			1
...illing-Sickneſs	3	2	2	3		3	4	1	4	3	1		4	5	3	10	7	7	2	5	6	8	27	21	10	8	8	5	74
...ox and small Pox	139	400	1190	184	525	1279	139	812	1294	823	835	409	1523	354	72	40	58	531	72	1354	193	127	701	1846	1913	2755	3361	2585	10576
...und dead in the Streets	6	6	9	8	7	9	14	4	3	4	5	11	2	6	18	33	20	6	13	8	24	24	53	48	80	81	130	83	392
...nch-Pox	18	29	15	18	21	20	20	20	29	23	25	53	51	31	17	12	12	12	7	17	12	22	2	3	9	5	2	2	21
...ghted	4	4	1	3		2		1	1					9	1			1				3	14	24	35	25	30	28	154
...out	9	5	12	9	7	7	5	6	8	7	8	13	14	2	2	5	3	4	4	5	7	8	71	50	48	59	43	47	279
...rief	12	13	16	7	17	14	11	17	10	13	10	12	13	4	18	20	22	11	14	17	5	20	71	56	48	47	7	3	222
...anged, and made away themſelves	11	10	13	14	9	14	15	9	14	16	24	18	11	36	8	8	6	15		3	8	7	37	18	48	47	17	46	011
...ead-Ach		1	11	2		2	6	6	5	3	4	5	35	26								2	0	0	14	14	17	46	998
...uddice	57	35	39	49	41	43	57	71	61	41	46	77	102	76	47	59	35	43	35	45	54	63	184	197	180	212	225	188	95
...w-faln	1	1			3			2			3	1			10	16	13	8	10	10	4	11	47	35	02	5	6	10	95
...poſtume	75	61	65	58	80	105	79	90	92	122	80	134	105	96	58	76	73	74	50	62	73	130	282	315	260	33	428	228	1639
...ch																			10				00	10	01				11
...illed by ſeveral Accidents	27	57	39	94	47	45	57	58	52	43	52	47	55	47	54	55	47	46	49	41	51	60	202	201	217	207	194	148	1021
...ing's Evil	27	26	22	19	22	20	26	27	24	23	28	28	54	16	25	18	38	35	20	20		69	97	150	94	94	102	66	537
...ethargy	3	4	2	4	4	4	3	10	9	4	6	2	6	4	1		2	2	3			2	5	7	13	21	1	9	67
...epſie			1									1		2	2							2	2	2	1		1	3	06
...iver-grown, Spleen and Rickets	53	46	56	58	65	72	67	65	52	50	38	51	8	15	94	12	99	87	82	77	98	99	392	356	213	269	191	158	1421
																							28	13	47	39	31	20	158

Figure 1 *The table of casualties from Graunt's manuscript.*

Another significant figure in the history of public health surveillance is Johann Peter Frank. In 1766, Frank proposed a broad approach to public health surveillance through his system of "police medicine" in Germany. This system included areas like school health, injuries, maternal and child health, and public water and sewage systems (Declich & Carter, 1994; Thacker & Berkelman, 1988).

Later, William Farr, an English statistician regarded as the father of modern surveillance, developed the first national vital statistics system and ensured its use as a public health tool (Declich & Carter, 1994; Lilienfeld, 2007). By categorizing causes of death and calculating death rates relative to population size, he allowed meaningful comparisons across different regions and time periods, laying the groundwork for modern surveillance methods.

While these examples reflect the scope of public health surveillance, i.e. monitoring to inform decision-making, the term "surveillance" in public health was, until 1950, primarily used to refer strictly to infectious diseases. Specifically, it referred to tracking contacts of infectious diseases, like smallpox, to detect symptoms early and ensure prompt isolation (Thacker & Berkelman, 1988). In 1963, the concept

of surveillance was broadened to include population-wide monitoring of communicable diseases by Alexander Langmuir, an American epidemiologist (Langmuir, 1963). It was only in 1968 that the World Health Assembly further expanded the concept of surveillance to encompass a broader range of public health issues beyond communicable diseases (Thacker & Berkelman, 1988).

Conceptual framework

The ultimate goal of public health surveillance is to use health data to inform and prompt public health action. Achieving this goal requires raw data to be collected, analyzed, and transformed into actionable information and knowledge. A conceptual framework used to illustrate this progression is the Data, Information, Knowledge, and Wisdom (DIKW) pyramid, first described by Ackoff in 1989 (Ackoff, 1989). At the base of this "information pyramid," are data. In the second tier, data are processed into usable information, such as health indicators. The next tier of the pyramid is knowledge, which emerges when indicators are contextualized within a broader and policy-relevant framework. This involves integrating indicator data with evidence from fields such as health services research, health promotion, clinical medicine, and sociology, allowing for a deeper understanding of them (Chiolero & Buckeridge, 2020). At the top of the pyramid lies wisdom, which reflects the capacity to make well-informed policy decisions based on the accumulated knowledge. Surveillance bias occurs when information is translated into knowledge: if variations in health indicators are not interpreted in light of changes in detection, screening, or diagnostic strategies, the resulting knowledge may be biased, leading to flawed policy decisions.

Recently, revisions to the DIKW pyramid have been proposed, suggesting de-emphasizing the concept of wisdom and introducing "evidence" as a new step between information and knowledge. This updated framework, referred to as DIEK, highlights how evidence serves as the basis for building actionable knowledge in public health (Figure 2) (Chiolero & Buckeridge, 2020; Dammann, 2018).

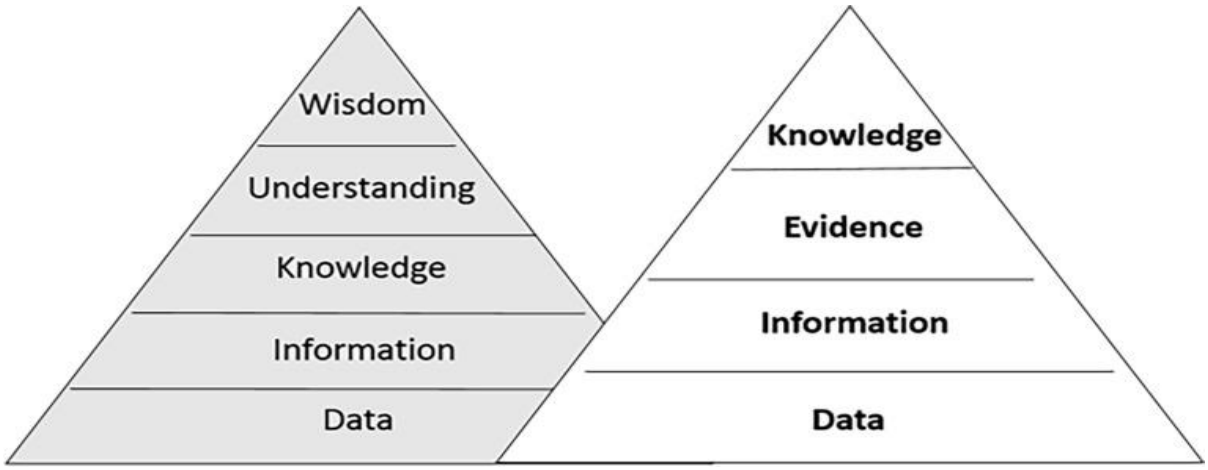


Figure 2 *DIKW and DIEK pyramid. This figure was reproduced from (Dammann, 2018)*

Tools and methods for measuring population health

Modern public health surveillance covers the monitoring of all aspects of health. This includes include diseases, accidents, mental health, subjective health, health behaviors and determinants, as well as the organization, use, and financing of healthcare systems (Groseclose & Buckeridge, 2017). Therefore, a wide range of data is needed, and various sources and methods are employed to collect it (Figure 4). This section summarizes the main types of data sources and tools used for surveillance activities.

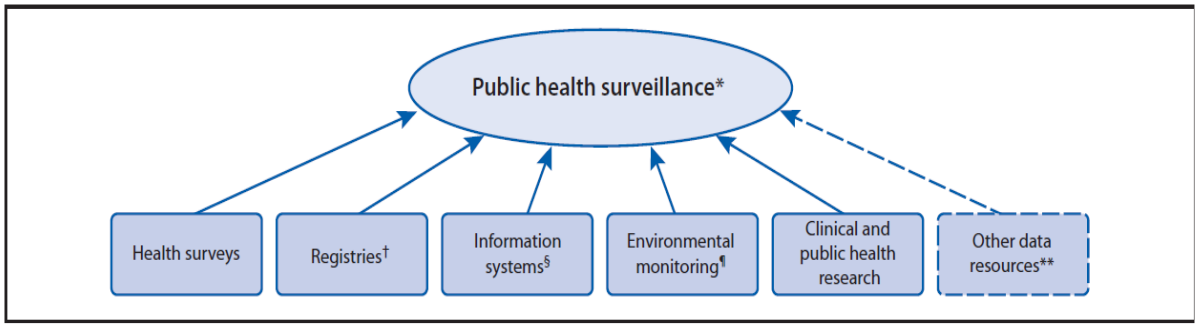
A key data source used for surveillance in public health is the civil registration and vital statistics systems, which record major life events such as births and deaths (Mahapatra et al., 2007). These systems are characterized by their universality, continuity, and compulsory nature as usually mandated by law, making them very valuable for surveillance activities (World Health Organization).

Data can also be collected through registries, which gather information on individuals with specific diagnoses, conditions, or outcomes with the aim of including all cases within a defined population or area (Brooke & World Health Organization, 1974). Registries provide epidemiological insights into the frequency and distribution of specific outcomes and serve as a foundation for research. Examples include cancer registries as well as those tracking conditions such as COVID-19 or multiple sclerosis.

Periodic population surveys are another important data source (Fisher et al., 2020). These surveys, repeated over time, collect data from a group of participants who represent a larger population. They are often used to assess sociodemographic characteristics, health behaviors, health status or healthcare use within a population (Fisher et al., 2020). Examples include surveys on health determinants and behaviors to evaluate risk factors, such as smoking or alcohol consumption.

Further, clinical and health services infrastructures also serve as a critical source of data for surveillance, such as data from hospitals, nursing homes, ambulatory care, and health insurance systems (e.g., billing information). These data repositories provide public health authorities with diverse information, including medical diagnoses, medication prescriptions or laboratory test results.

Other sources of data can also be used, including environmental monitoring and criminal justice information. Data generated by digital technologies, such as social media or sensor data, have also become potential resources for surveillance activities. However, these data sources are typically less structured compared to traditional surveillance tools like surveys or registries, which makes their interpretation more challenging (Chiolero et al., 2023; Groseclose & Buckeridge, 2017).



* Systematic and continuous collection, analysis, and interpretation of data, closely integrated with the timely and coherent dissemination of the results and assessment to those who have the right to know so that action can be taken (Porta MA, Dictionary of Epidemiology, 5th Ed., Oxford University Press, 2008).
† Vital registration, cancer registries, and exposure registries
§ Medical and laboratory records, pharmacy records.
¶ Weather, climate change, and pollution.
** Criminal justice information, Lexis-Nexis, and census.

Figure 4 *Conceptual framework for public health surveillance, which includes input from health surveys, registries, information systems, environmental monitoring, clinical and public health research, and other sources. This figure was reproduced from (Thacker et al., 2012)*

From data to health indicators

Regardless of the source, data are usually transformed into easily understandable indicators, which are succinct measures designed to summarize complex information into a few key points to facilitate the decision-making process (Verschuuren & Van Oers, 2019). Examples include the infant mortality rate, cancer incidence and mortality or incidence and mortality of COVID-19. Indicators should possess several key characteristics: they must accurately capture the phenomenon they are intended to measure; they should be based on accessible and reliable data, grounded in robust evidence; they must address relevant health issues; and they should provide actionable insights (Verschuuren & Van Oers, 2019). However, indicators are not without limitations and can be prone to bias, including surveillance bias. It is therefore essential to carefully consider these aspects to fully understand the information they convey.

Potential biases of health indicators

The meaningful interpretation of health indicators is fundamental to inform actionable decisions, and this requires a clear understanding of their limitations and potential biases.

One limitation is that indicators from population surveys can be affected by issues related to sampling design, particularly if the sample does not accurately represent the target population (Verschuuren & Van Oers, 2019). For example, if certain demographic groups—such as younger individuals or those from lower socioeconomic backgrounds—are underrepresented in the sample, the results may not generalize to the target population. This also limits the external validity of the

results, meaning their ability to be applied to similar populations or settings (Westreich et al., 2019).

In addition, survey data can be affected by non-response bias (also known as non-participation bias), which arises when individuals who choose not to participate differ systematically from those who do, as well as by measurement biases (e.g., recall bias or social desirability bias)(Verschuuren & Van Oers, 2019). For instance, the social desirability bias occurs when respondents provide answers they perceive as more socially acceptable rather than truthful, especially for sensitive topics (Krumpal, 2013). Recall bias arises if respondents misremember and inaccurately report past behaviors or events (Porta et al., 2014; Verschuuren & Van Oers, 2019). Finally, possible biases can also arise from the way a questionnaire is designed or administered, including issues related to question wording, order, or mode of administration (Choi & Pak, 2005; Cullati et al., 2020).

Regarding indicators built from registries data, their main strength relies on the fact that registries collect all cases of a specific outcome in a defined population, reducing the risk of selection bias. However, their reliability can be compromised by incompleteness, inaccuracy or delayed registration (Bray & Parkin, 2009; Donnelly et al., 2017). This is especially true in contexts where registration is not mandatory or lacks adequate resources (Valsecchi & Steliarova-Foucher, 2008).

Indicators based on medico-administrative data also offer valuable insights into healthcare usage, but their use is limited to individuals who seek medical care. This introduces a selection bias, where undiagnosed or untreated conditions are underrepresented.

Finally, indicators can also be prone to surveillance bias, the primary focus of this thesis. This bias will be explored in more detail in the following paragraph.

Surveillance bias

Surveillance bias occurs when variations in the frequency of a health outcome are caused by differences in the modality or intensity of detection, rather than actual changes in its underlying risk (Chiolero & Buckeridge, 2020; Haut & Pronovost, 2011). These differences often arise from varying detection, screening, and diagnostic strategies over time or across populations, care settings, and types of patients. Put simply, "The more you look, the more you find" (Haut & Pronovost, 2011), and the opposite is also true: the less you look, the less you find. As a result, surveillance indicators, such as disease incidence or quality-of-care metrics, are biased, leading to misinterpretations and potentially wrong public health decisions.

In the context of infectious diseases such as COVID-19, surveillance bias has been particularly problematic, as disparities in testing, reporting, and healthcare access have resulted in inflated or skewed estimates of disease incidence (Tancredi et al., 2021). Data on the number of infections was influenced by testing capacity or reporting practices, which created inconsistencies in understanding the true

burden of the disease across regions and over time. Similarly, in the surveillance of certain types of cancer, changes in screening or diagnostic practices can lead to variations in cancer incidence that are not due to changes in the true occurrence of cancer, but rather in the variation of the intensity of its detection (Welch et al., 2019), making it difficult to assess the true burden of the disease.

Beyond COVID-19 and cancer, surveillance bias affects a wide range of other health indicators. For example, quality-of-care indicators—such as hospital-acquired infections or postoperative complications—can be biased by differences in the intensity of their detection, due for instance to increased clinical awareness, rather than actual variations in care quality (Haut & Pronovost, 2011). This means that if hospitals are compared without accounting for surveillance bias, a hospital with a higher reported rate of infections or complications might erroneously appear to have worse quality of care, when in fact the higher numbers simply reflect better detection and reporting practices. Surveillance of hypertension provides another relevant example. The prevalence of hypertension depends not only on real changes in population blood pressure levels but also on evolving diagnostic thresholds and increased screening practices. For instance, if the diagnostic threshold for hypertension is lowered by just a few mmHg, the number of people classified as hypertensive will rise dramatically (Welch et al., 2012). If this shift is not considered when interpreting incidence or prevalence trends, the increase may be mistakenly attributed to a worsening public health situation rather than to a change in classification criteria. This applies to many other conditions, such as diabetes or hypercholesterolemia, whose diagnosis depends on specific thresholds of blood glucose and lipid levels (Chiolero & Paccaud, 2012).

Another issue related to surveillance bias is its potential to distort the identification of risk factors. This occurs when different detection modalities are applied across exposure subgroups. For example, postmenopausal women who use estrogen therapy have an increased risk of abnormal bleeding, which may lead to more frequent medical consultations and screenings. As a result, more cancers may be detected in this group, but this increase is influenced by the increased screening intensity, that leads to a higher detection rate. This biases the association between estrogen exposure and cancer risk (Horwitz & Feinstein, 1978). Other similar examples will be discussed in the following chapters of this thesis, including risk factors for cancer such as obesity, sex, and socioeconomic status.

Studying surveillance bias is important because misinterpreting health indicators can lead to wrong public health actions. Nonetheless, it is particularly challenging because detection, screening, and diagnostic strategies are not static. They evolve continuously due to advancements in medical technology, changes in clinical guidelines, and shifts in healthcare policies. These changes need to be considered when conducting surveillance activities, to ensure the accurate interpretation of disease trends and to support effective public health policies.

Summary

Surveillance is the process of translating raw data into actionable knowledge, making it a cornerstone of evidence-informed decision-making. It relies on multiple data sources, each with its own limitations. The accuracy of surveillance depends on understanding these limitations, including surveillance bias. This bias arises when variations in detection methods or intensities distort the true representation of disease patterns, potentially leading to flawed public health decisions.

This thesis addresses the challenge of interpreting public health surveillance data in the presence of surveillance bias, with a particular focus on COVID-19 and cancer. It explores the mechanisms driving this bias, examines its consequences on disease trends and risk factor identification, and estimates its effects in various contexts, providing estimates of its magnitude in COVID-19 and cancer.

By tackling these issues, this work aims to enhance our understanding of surveillance systems and provide actionable insights to improve the accuracy of public health monitoring.

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Chapter 2 | Objectives

The overarching objective of my PhD thesis was to clearly define and describe surveillance bias and provide quantitative estimates of its magnitude. This objective was addressed though three specific aims: (1) to define surveillance bias, identify contexts and situations in which it occurs, describe its causes and consequences and how to prevent it (Chapter 4); (2) to describe and estimate the magnitude of surveillance bias in COVID-19 (Chapter 5); and (3) to describe and estimate the magnitude of surveillance bias in cancer (Chapter 6).

These aims are investigated via several papers and research questions:

Aim 1 | Overview and definition of surveillance bias (Chapter 4)

Research questions:

What is surveillance bias?

Which conditions or outcomes are influenced by surveillance bias?

What are the mechanisms driving surveillance bias?

How does surveillance bias impact the interpretation of surveillance data?

How can we prevent surveillance bias?

Aim 2 | Surveillance bias in COVID-19 (Chapters 5.1, 5.2 and 5.3)

Research questions:

How did the COVID-19 pandemic evolve in Switzerland?

What was the magnitude of surveillance bias across different COVID-19 surveillance indicators in assessing the severity of epidemic waves?

How are different types of surveillance tools—at the population and healthcare provider levels—affected by surveillance bias in COVID-19?

Aim 3 | Surveillance bias in cancer (Chapters 6.1, 6.2 and 6.3)

Research questions:

Which cancers are prone to surveillance bias?

How does surveillance bias impact the interpretation of cancer surveillance data?

How can epidemiological signatures be used to detect surveillance bias in cancer incidence and mortality trends?

What is the magnitude of surveillance bias in prostate, melanoma, and lung cancer trends in Switzerland?

Chapter 3 | Methodology

This chapter provides a general overview of the methods and data sources relevant to the research presented in this thesis. Specific methods are detailed within each study. For Chapters 5.1 and 5.2, data were retrieved from the Corona Immunitas initiative, along with COVID-19 surveillance data obtained from the Federal Office of Public Health (FOPH). Narrative reviews were used to gather and synthesize information on surveillance bias for Chapter 4 as well as Chapters 6.1 and 6.2. Data for Chapter 6.3 was retrieved from the National Institute for Cancer Epidemiology and Registration (NICER).

Corona Immunitas

Corona Immunitas is a nationwide research program coordinated by the Swiss School of Public Health (SSPH+) to study the spread of SARS-CoV-2 in Switzerland during the COVID-19 pandemic (West et al., 2020). Launched in spring 2020, the program ended in 2023 and consisted of six rounds of population-based seroprevalence studies (Corona Immunitas Working Group & Kaufmann, 2023; Corona Immunitas Working Group et al., 2023).

The program involved 13 regional study centers across 13 cantons (Geneva, Vaud, Valais, Ticino, Basel-Stadt, Basel-Landschaft, Fribourg, Neuchâtel, Zurich, Bern, Luzern, St. Gallen, and Grisons). Participants were randomly selected adults, with additional sub-studies focusing on specific groups such as healthcare workers, children, and vulnerable populations. The study design ensured representativeness through random sampling within each participating canton and stratification by demographic factors like age and gender. The governance of Corona Immunitas was decentralized, with individual sites responsible for implementation but adhering to a centralized protocol developed by the Corona Immunitas Executive Committee (Corona Immunitas Working Group et al., 2023).

The program's primary objectives were to estimate the prevalence of COVID-19 infection through seroprevalence surveys, evaluate the duration and extent of immunity, and identify demographic and behavioral factors associated with infection risk. Data collection followed standardized methodologies across regions, including uniform antibody tests and questionnaires that allowed for reliable regional comparisons and national-level insights (Amati et al., 2022; Anker et al., 2020; Anker et al., 2022; Dupraz et al., 2021; Frei et al., 2023; Richard et al., 2022; Tancredi et al., 2023).

Narrative reviews

Narrative reviews are a non-systematic approach to synthesizing literature. Unlike systematic reviews, which are highly structured and focus on answering narrowly defined research questions, narrative reviews aim to provide a broader understanding of a topic and its interpretation (Grant & Booth, 2009; Greenhalgh et al., 2018; Sukhera, 2022).

This type of review is often criticized for relying on subjective interpretation and for the risk of "cherry-picking" evidence to support a particular perspective (Greenhalgh et al., 2018). It is also criticized for lacking transparency compared to other types of reviews, such as systematic reviews, as they often omit details on how the literature is searched and how the relevance of studies is assessed (Collins & Fauser, 2005). Nonetheless, despite these limitations, narrative reviews serve a purpose that is distinct from that of other types of reviews and can play an important role in evidence synthesis.

As Greenhalgh et al. argue, narrative review and systematic reviews should be viewed as complementary tools. Systematic reviews synthesize evidence through a highly technical process of identification, appraisal, and synthesis of evidence. While the synthesis they produce is precise, it may not always provide sufficient insight, particularly in complex situations such as decision-making contexts, where multiple factors must be considered. Conversely, narrative reviews, although lacking methodological precision, gather and contextualize research findings with a broader perspective guided by the authors' expertise, helping to better understand complex situations.

Rather than focusing on data synthesis, narrative reviews offer interpretation, clarification, and insights, relying on the authors' critical judgment. This subjective yet flexible approach to summarizing knowledge is helpful for fostering advancements in a field, proposing new theories, and exploring alternative perspectives (Sukhera, 2022).

National Institute for Cancer Epidemiology and Registration (NICER)

The National Institute for Cancer Epidemiology and Registration (NICER) is an independent foundation established in 2007 to promote and coordinate cancer registries, support population-based cancer registration, ensure data quality, and facilitate epidemiological cancer research in Switzerland (National Institute for Cancer Epidemiology and Registration).

In Switzerland, cancer registries have been progressively implemented since 1970. By 2006, they achieved full coverage of the French-speaking regions and Ticino. Since 2020, following the introduction of the Cancer Registration Act, which standardized cancer data collection nationwide, they now cover all Swiss cantons. The Cancer Registration Act mandates the compulsory reporting of cancer

diagnoses by physicians, hospitals, and laboratories and ensures a systematic and standardized registration process (Office fédéral de la statistique).

Currently, 97% of the Swiss population is covered by cancer registration, a percentage that has steadily increased over time. Data registration includes all cases of primary malignant tumors, except for non-melanoma skin cancers. In years when cancer registration is not exhaustive across the entire country, NICER extrapolates data to provide reliable national estimates, allowing researchers to track cancer incidence trends over time (Office fédéral de la statistique).

NICER also monitors cancer mortality data, sourced from the Cause of Death Statistics (COD) of the Federal Statistical Office (FSO), which comprehensively records the causes of death of Swiss residents through medical death certificates (Office fédéral de la statistique).

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Chapter 4 | Surveillance bias: when appearances are misleading

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Biais de surveillance : quand les apparences sont trompeuses

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La surveillance en santé publique consiste à recueillir et à analyser en continu des données relatives à la santé, puis à les transformer en informations utiles pour la décision. On parle de biais de surveillance lorsque les différences de fréquence d'une maladie sont dues à des variations dans les modalités de détection plutôt qu'à des changements du risque réel de cette maladie dans la population. Ce biais est fréquent car l'activité de surveillance repose de plus en plus souvent sur des données qui ne sont pas collectées primairement pour la surveillance, notamment celles provenant des prestataires de soins de santé. De nombreuses maladies (comme le Covid-19, le cancer de la prostate ou l'hypertension) sont sujettes à un biais de surveillance. Ce biais nuit également à la surveillance de la qualité des soins.

Surveillance bias: when appearances are misleading

Public health surveillance is the ongoing collection and analysis of health-related data, followed by the timely dissemination of information useful for decisions. Surveillance bias occurs when differences in the frequency of a condition are due to variations in the modalities of detection rather than to changes in the actual risk of the condition. As a result, the true burden of diseases cannot be properly assessed. This is of growing concern because surveillance activity is more and more often based on data not designed primarily for surveillance, notably data from healthcare providers. Many diseases (such as COVID-19, prostate cancer, or hypertension) are prone to surveillance bias. It also hinders quality of care monitoring.

INTRODUCTION

La surveillance en santé publique est la collecte, l'analyse et la diffusion en continu de données relatives à la santé en vue de la prise de décision. Elle constitue l'une des dix opérations essentielles de santé publique selon l'Organisation mondiale de la santé.[1] Des systèmes de surveillance informent et orientent les décisions en santé publique et permettent de fixer des priorités, de planifier des politiques et d'évaluer la nécessité et les effets des interventions. Malgré le nombre croissant de données disponibles pour les activités de surveillance, notamment celles provenant des prestataires de soins, il n'est pas toujours facile de transformer ces données en informations utiles pour la décision.

Un problème majeur est le biais de surveillance qui survient lorsque les différences de fréquence d'un problème de santé sont dues à des variations dans la modalité de détection plutôt qu'à un changement dans le risque réel de ce problème[2,3] (figure 1). Lorsque cela se produit, il est difficile d'évaluer le réel fardeau de ce problème de santé, par exemple, au cours du temps, l'évolution apparente étant interprétée à tort comme l'évolution réelle du problème dans la population. Cela peut également entraver la surveillance de la qualité des soins.

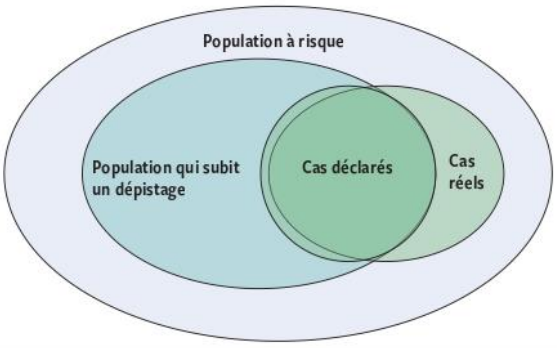
EFFET LAMPADAIRE ET SURDIAGNOSTIC

Le biais de surveillance est lié à l'effet lampadaire (streetlight effect) et au surdiagnostic (overdiagnosis). L'effet lampadaire se produit lorsque les activités de surveillance sont axées sur ce qui est facile à mesurer plutôt que sur ce qui est important. Ainsi, pour de nombreuses pathologies, il peut être relativement facile de compter le nombre de cas diagnostiqués ou hospitalisés et de récupérer ces informations auprès des prestataires de soins. Néanmoins, ce nombre dépend de la stratégie de dépistage, de diagnostic et de traitement, et ne reflète pas toujours le fardeau réel de ces maladies.

Le surdiagnostic est « le diagnostic d'une anomalie qui n'est pas associée à un risque substantiel pour la santé et dont les patients n'ont aucun avantage à être informés »,[4] et peut entraîner un surtraitement. Le biais de surveillance et le surdiagnostic ont des origines communes, par exemple, en lien avec les change-

FIG 1 **Exemple de biais de surveillance pour une maladie sujette à un dépistage**

Le biais de surveillance se produit notamment dans les maladies pour lesquelles un dépistage est effectué (par exemple, le cancer de la prostate). Pour comprendre ce qui influence le nombre de cas détectés dans une population, il faut considérer: a) la population à risque, c'est-à-dire les personnes qui peuvent développer la maladie; b) la population qui subit un dépistage et c) les cas déclarés qui peuvent être identifiés par le dépistage ou par d'autres moyens. Pour un problème de santé dont le diagnostic dépend de la modalité de détection, les cas déclarés ne sont pas un reflet fidèle du nombre de cas réels de la maladie dans la population et le biais de surveillance provient de la différence entre le nombre de cas déclarés et celui de cas réels.[15]



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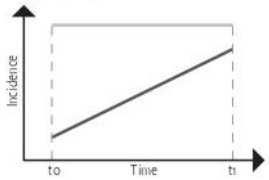
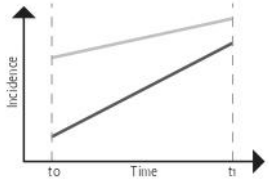
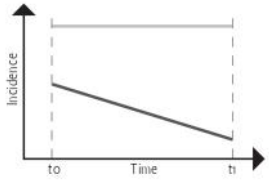
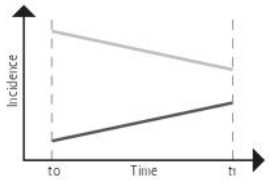
ments dans les définitions des maladies ou dans les stratégies de dépistage.[5] Ainsi, l'abaissement du seuil de glycémie pour définir le diabète peut conduire, d'une part, à un surdiagnostic et, d'autre part, à un biais de surveillance lorsque les cas diagnostiqués sont utilisés pour évaluer l'évolution du fardeau du diabète dans la population.

EXEMPLES DE BIAIS DE SURVEILLANCE

Pour mieux comprendre ce qu'est le biais de surveillance et son impact sur l'activité de surveillance, nous avons sélectionné des exemples de problèmes de santé exposés à ce biais. En lien avec ces exemples, nous avons distingué quatre scénarios hypothétiques de l'évolution réelle des problèmes de santé et de l'évolution sur la base des cas déclarés (**tableau 1**).

TABLEAU 1 **Impact du biais de surveillance sur l'analyse de tendances**

Exemples de problèmes de santé pour lesquels le biais de surveillance entrave les analyses de l'évolution du fardeau de la maladie dans la population.

Tendances	Exemples et explications
Évolution du fardeau de la maladie dans la population Cas déclarés 	• Mélanome • Thrombose veineuse profonde • Infection du site chirurgical Alors que le fardeau réel des maladies reste stable, l'évolution des cas déclarés augmente en raison d'une plus grande intensité de détection
Évolution du fardeau de la maladie dans la population Cas déclarés 	• Covid-19 Le fardeau réel de la maladie et le nombre de cas signalés augmentent tous deux, mais à des rythmes différents, en raison de différences dans la modalité et l'intensité de la détection au fil du temps
Évolution du fardeau de la maladie dans la population Cas déclarés 	• Cancer de la prostate Alors que le fardeau de ce cancer reste stable, la tendance des cas déclarés diminue en raison de la baisse des activités de dépistage en lien avec la modification des recommandations en la matière. Lorsque l'activité de dépistage augmente, l'incidence des cas déclarés augmente
Évolution du fardeau de la maladie dans la population Cas déclarés 	• Chlamydia Alors que l'évolution des cas déclarés est à la hausse en raison de l'augmentation des dépistages et des déclarations, l'incidence réelle des infections pourrait être à la baisse

Évaluer l'intensité des vagues épidémiques du Covid-19

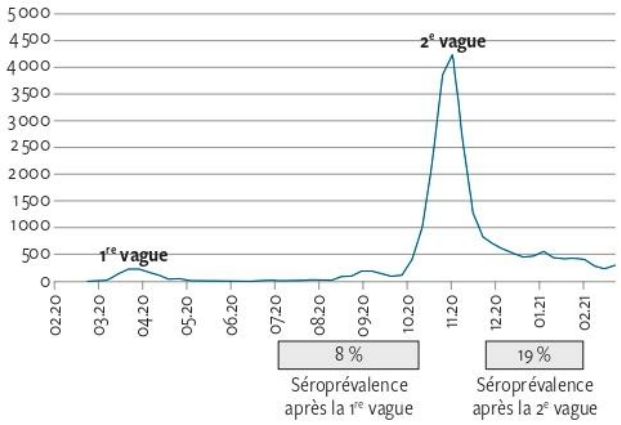
La plupart des cas de Covid-19 sont pauci- ou asymptomatiques et non diagnostiqués, et la surveillance basée sur ces cas est exposée à un BS. Les taux d'incidence des cas à différents moments de la pandémie ne sont pas systématiquement corrélés aux taux d'hospitalisation et de mortalité. Cela est dû notamment à des différences dans les stratégies et capacités de dépistage car, en bref, plus on effectue des tests, plus on diagnostique de cas.[6] La **figure 2** montre un exemple de biais de surveillance du Covid-19 dans une région en Suisse. Alors qu'une grande différence dans le nombre de cas a été constatée entre la première et la deuxième vague de la pandémie, la différence de séroprévalence, un bien meilleur marqueur de la propagation de l'épidémie, a été nettement plus modeste.

La thrombose veineuse profonde comme marqueur de la qualité des soins

Il existe un biais de surveillance potentiel sur les taux de thrombose veineuse profonde (TVP) après un traumatisme.[7] De nombreux centres médicaux ont des stratégies de prévention des TVP et utilisent son incidence comme un indicateur de la qualité des soins; plus le taux est bas, plus la qualité des soins serait élevée. Cependant, le taux de TVP diagnostiquée notamment par échographie duplex augmente directement avec le nombre d'échographies de dépistage postchirurgicales. L'incidence de la TVP peut donc être révélatrice de l'intensité des activités de dépistage postchirurgical plutôt que des activités de prévention et de la qualité des soins fournis.

FIG 2 **Biais de surveillance du Covid-19 dans le canton de Fribourg**

Cette figure montre l'incidence des nouveaux cas diagnostiqués de Covid-19 (en bleu) et les estimations de séroprévalence (cases grises) après les 1re et 2e vagues de la pandémie en 2020. Le nombre cumulé de cas diagnostiqués était de 2355 après la 1re vague et de 23 321 après la 2e, soit une différence de 20 966. Si on se base sur le nombre de cas diagnostiqués, le nombre estimé d'infections était donc 8 à 9 fois plus élevé lors de la 2e vague que lors de la 1re. La séroprévalence après la 1re vague de la pandémie était de 8% et a atteint 19% après la 2e vague, soit une différence de 11%. Si on se base sur la séroprévalence, le nombre estimé d'infections était moins de 1,5 fois plus élevé lors de la 2e vague que lors de la 1re. Dès lors, si on se base uniquement sur les cas déclarés, on surestime la gravité de la pandémie au cours de la 2e vague.



(Source: Corona Immunitas Fribourg, Laboratoire de santé des populations (#PopHealthLab)).

Surveillance des infections du site opératoire

Les systèmes de surveillance des infections du site opératoire constituent un outil de suivi essentiel pour informer les stratégies de prévention et de contrôle des infections et améliorer la qualité des soins. En Suisse, un programme de surveillance à l'échelle nationale a été mis en œuvre en 2011 et les premiers résultats ont montré des taux d'infection élevés par rapport aux autres pays.[8] Alors que cela pourrait être interprété comme un signe de mauvaise qualité des soins en Suisse, cela peut aussi être dû à des différences dans la stratégie de surveillance, notamment pour minimiser le risque de sous-déclaration. Des travaux ultérieurs ont ainsi montré que la qualité de la surveillance était corrélée aux taux d'infection du site opératoire.[9]

Incidence du cancer de la prostate et du mélanome

Le cancer de la prostate est sensible à l'intensité des activités de dépistage, ce qui peut créer un biais de surveillance.[10] En Suisse, après une augmentation initiale jusqu'au début des années 2000, l'incidence du cancer de la prostate a diminué. Néanmoins, ces changements d'incidence ne sont pas associés à des changements concomitants de mortalité. Ainsi, il y a un découplage entre les taux d'incidence et de mortalité, que l'on peut mettre en rapport avec des changements dans les recommandations de dépistage et du surdiagnostic.[11] Le mélanome est également exposé au risque de surdiagnostic et de biais de surveillance,[12] et dans de nombreux pays, y compris en Suisse, l'incidence a augmenté alors que la mortalité est restée stable ou a diminué. Tant pour le cancer de la prostate que pour le mélanome, l'incidence ne reflète pas directement le fardeau réel de la maladie alors que la mortalité est un indicateur moins biaisé.

Évaluation de la prévalence de l'hypertension

Les changements dans la définition d'une maladie ou dans les seuils d'un facteur de risque peuvent créer un biais de surveillance. Par exemple, les seuils de pression artérielle pour définir l'hypertension ont été progressivement abaissés au cours du temps, ce qui a augmenté le nombre de cas diagnostiqués. Ainsi, alors que les niveaux moyens de pression artérielle systolique et diastolique ont diminué dans les pays à revenu élevé au cours des dernières décennies,[13] le nombre de personnes diagnostiquées hypertendues a augmenté. Cela est dû à la croissance et au vieillissement de la population mais aussi au fait qu'au fil du temps l'hypertension a été diagnostiquée et traitée à des niveaux de pression artérielle de plus en plus bas. Les seuils de diagnostic ont également été abaissés pour l'hypercholestérolémie, le diabète et de nombreuses autres affections. Ces changements peuvent être les moteurs de pseudo-épidémie et cacher les améliorations réelles de la santé de la population.

Y a-t-il une épidémie de chlamydia?

Dans l'Union européenne, les taux d'incidence de chlamydia ont augmenté entre 2000 et 2009 et sont restés relativement stables entre 2009 et 2018.[14] Cependant, le nombre de cas de chlamydia déclarés est dépendant de l'exhaustivité des déclarations, de l'intensité des activités de dépistage et du type de test utilisé. Ainsi, sur la base de données nord-américaines, en ajustant les estimations d'incidence en fonction des changements dans la couverture du dépistage, des tests de diagnostic et du degré d'exhaustivité des déclarations, il a été démontré que l'incidence était en fait en baisse.[15] Par conséquent, l'augmentation du nombre de cas signalés[14] pourrait ne pas refléter une augmentation réelle du nombre d'infections à chlamydia.

COMMENT FAIRE FACE

Il existe plusieurs méthodes pour tenir compte du biais de surveillance (**tableau 2**). Globalement, il faut préférer les indicateurs qui sont moins sujets à ce biais et s'assurer que ceux-ci sont construits sur des données standardisées avant de faire des comparaisons. Nous encourageons l'emploi de plusieurs indicateurs. Ainsi, il faut éviter d'évaluer les tendances

TABLEAU 2 **Méthodes pour prévenir ou tenir compte du biais de surveillance**

Exemples	Causes ou conséquences	Solutions
Covid-19 (cas diagnostiqués)	Interprétation erronée de la situation épidémiologique	• Utiliser des indicateurs multiples, par exemple, les cas, les hospitalisations, les hospitalisations en soins intensifs et les décès • Utiliser des indicateurs moins biaisés pour évaluer la courbe épidémique réelle (séroprévalence, nombre d'infections estimé par enquête avec échantillonnage aléatoire)
Qualité des soins (incidence des infections du site opératoire, incidence des thromboses veineuses profondes)	Mesures biaisées de la qualité des soins, conduisant à une évaluation comparative non fiable des hôpitaux et des cliniques	• S'assurer que tous les hôpitaux utilisent les mêmes protocoles de surveillance (standardisation) • Utiliser des méthodes permettant d'ajuster pour les sous- ou surdéclarations[9]
Cancers (cancer de la prostate, mélanome)	Surdiagnostic; changement dans les modalités de détection au cours du temps	• Se concentrer sur les indicateurs moins sujets aux biais de surveillance, tels que le taux de mortalité ou l'incidence des cancers avancés (stades 3 et 4)[12] • Tenir compte des différences dans les stratégies de dépistage selon les régions et les périodes
Modification des définitions des maladies (hypertension, diabète, hypercholestérolémie)	Surdiagnostic; les problèmes de santé considérés changent au fil du temps	• Évaluer l'évolution en tenant compte des changements dans les définitions ainsi que dans les stratégies de traitement et de diagnostic • Évaluer l'évolution en se concentrant sur les mesures qui ne sont pas influencées par les changements dans les définitions des maladies (par exemple, les mesures objectives de la pression artérielle plutôt que les diagnostics d'hypertension autodéclarés)

du nombre de cas de Covid-19 ou celles de l'incidence du cancer de manière isolée, sans tenir compte, par exemple, de la mortalité.

CONCLUSION

Les professionnels de la santé, les spécialistes des données, les décideurs politiques et les citoyens doivent être conscients du biais de surveillance car il faut en tenir compte pour interpréter correctement les données de surveillance de la santé des populations et du monitoring de la qualité des soins.

Conflit d'intérêts: Les auteurs n'ont déclaré aucun conflit d'intérêts en relation avec cet article.

IMPLICATIONS PRATIQUES

- De nombreux problèmes de santé sont sujets à des biais de surveillance car ils sont sensibles à l'intensité et aux modalités de détection
- Lorsque cela se produit, il est difficile d'évaluer le réel fardeau de ce problème de santé, par exemple, au cours du temps, l'évolution apparente étant interprétée à tort comme l'évolution réelle du problème dans la population
- La prise en compte des biais de surveillance est essentielle pour une activité adéquate de surveillance de la santé des populations et de monitoring de la qualité des soins

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* **à lire**
** **à lire absolument**

Chapter 5.1 | Seroprevalence trends of anti-SARS-CoV-2 antibodies and associated risk factors: a population-based study

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RESEARCH

Seroprevalence trends of anti-SARS-CoV-2 antibodies and associated risk factors: a population-based study

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Abstract

Purpose We aimed to assess the seroprevalence trends of SARS-CoV-2 antibodies in several Swiss cantons between May 2020 and September 2021 and investigate risk factors for seropositivity and their changes over time.

Methods We conducted repeated population-based serological studies in different Swiss regions using a common methodology. We defined three study periods: May–October 2020 (period 1, prior to vaccination), November 2020–mid-May 2021 (period 2, first months of the vaccination campaign), and mid-May–September 2021 (period 3, a large share of the population vaccinated). We measured anti-spike IgG. Participants provided information on sociodemographic and socioeconomic characteristics, health status, and adherence to preventive measures. We estimated seroprevalence with a Bayesian logistic regression model and the association between risk factors and seropositivity with Poisson models.

Results We included 13,291 participants aged 20 and older from 11 Swiss cantons. Seroprevalence was 3.7% (95% CI 2.1–4.9) in period 1, 16.2% (95% CI 14.4–17.5) in period 2, and 72.0% (95% CI 70.3–73.8) in period 3, with regional variations. In period 1, younger age (20–64) was the only factor associated with higher seropositivity. In period 3, being aged ≥ 65 years, with a high income, retired, overweight or obese or with other comorbidities, was associated with higher seropositivity. These associations disappeared after adjusting for vaccination status. Seropositivity was lower in participants with lower adherence to preventive measures, due to a lower vaccination uptake.

Conclusions Seroprevalence sharply increased over time, also thanks to vaccination, with some regional variations. After the vaccination campaign, no differences between subgroups were observed.

Keywords COVID-19 pandemic · SARS-CoV-2 · Seroprevalence · Epidemiology · Public health · Surveillance

Introduction

An accurate description of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spread dynamics is key to informing and driving policymakers' decisions. Yet, surveillance based on PCR or antigen-reported cases resulted in biased estimates of the virus spread [1] due to a large share of a- or pauci-symptomatic infections [2, 3], changes in care-seeking behaviours, and different screening and diagnostic strategies across regions and over time. For instance, when SARS-CoV-2 first emerged, many European countries had limited testing capacities [4], and some, including Switzerland, restricted testing to patients admitted to hospitals. This led to a surveillance bias [5], with an underestimation of the number of SARS-CoV-2 cases. By contrast, serological studies account for all infections,

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providing a more representative, albeit less timely, picture of the extent and dynamics of the COVID-19 pandemic.

So far, many SARS-CoV-2 seroprevalence studies have been conducted, both in the general population and in specific subgroups, to monitor the pandemic and inform on population levels of immunity [6–8]. A recent literature review [9] showed substantial worldwide geographical variability in seroprevalence estimates, caused by differences in the extent of infections and vaccination coverage. It also showed evidence of considerable infection under-ascertainment, highlighting the importance of seroprevalence estimates to describe the true number of SARS-CoV-2 infections. However, variabilities in research designs, tests used, or studies quality and reporting, make it challenging to compare estimates between countries or between regions within the same country. In addition to their role in assessing immunity levels and monitoring the virus's spread, seroepidemiological studies are also a strong tool to understand the drivers of the spread and to identify groups at higher risk of infection. During the pandemic, many factors have been linked to increased seropositivity, including socioeconomic, sociodemographic, or health characteristics. A higher exposure to SARS-CoV-2 is possible in socioeconomically disadvantaged individuals [10] (e.g., with a lower income or lower educational level), and differences in exposure have been found in different age groups [11, 12] or according to job type, health behaviours (e.g., smokers versus non-smokers) or health characteristics (e.g., with respect to different BMI levels or number of comorbidities) [11, 13, 14]. Additionally, the evidence suggests that different levels of stringency of mitigation policies [9] and adherence to preventive measures were also associated with seropositivity [15]. However, countries experienced a wide range of different epidemiological situations; governments recommendations and individual behaviours changed, and vaccines have been rolled out. It is therefore likely that factors associated with seropositivity have also changed over time.

In Switzerland, the Swiss School of Public Health (SSPH +) launched in the early phases of the pandemic the Corona Immunitas research program [16], implementing repeated population-based seroprevalence studies, with the aim of estimating the proportion of the population who developed anti-SARS-CoV-2 antibodies over time. Conducting repeated studies using a common methodology, at regular intervals, and with shared coordination, offers unique strengths to provide a clear picture of the population immunological status over time and across regions, and allows investigating trends in seroprevalence of SARS-CoV-2 antibodies, making comparisons between regions, and investigating differences in the virus's exposure between different populations' groups. In light of the above, using data from Corona Immunitas, we aimed to (1) assess the seroprevalence trends of SARS-CoV-2 antibodies in Switzerland between May 2020 and September 2021, both at a quasi-national and cantonal level (descriptive aim), and (2) investigate risk factors for seropositivity and their changes over time (etiologic aim).

Methods

Study design

This study is part of Corona Immunitas [16]. Repeated population-based serological studies were conducted in different regions of Switzerland. Testing periods could change for each participating site. Invited participants were randomly selected from the national residential registry by the Swiss Federal Statistical Office for each new assessment wave; 65,500 participants were invited, the average participation rate was around 21%, with regional differences (from 16 to 39%). For this study, we defined three study periods: period 1 from May 2020 to October 2020 (before the launch of the vaccination campaign in Switzerland), period 2 from November 2020 to mid-May 2021 (in the first months of the vaccination campaign), and period 3 from mid-May 2021 to September 2021 (a significant share of the population vaccinated). Each period corresponds to a time window following each of the first three pandemic waves in Switzerland (Fig. 1). This choice was made because estimating seroprevalence after each epidemic wave was deemed more informative for descriptive purposes, and it is in line with the World Health Organization (WHO) recommendations for cross-sectional seroprevalence studies [17]. At each period, participants provided a venous blood sample and filled out a questionnaire on demographic and socioeconomic characteristics, adherence to COVID-19 preventive measures, health status and, once available, vaccination status. The questionnaire could be completed either in person or online (data were collected using REDCap, Research Electronic Data Capture) [18].

Study population

We included 13,291 participants (in period 1 n = 3402, in period 2 n = 5611, and in period 3 n = 4278) aged 20 and older from 11 Swiss cantons (Additional file1: Fig. S1). Around 5.9 million people live in these cantons, that is roughly 68% of the entire Swiss population. Those aged below 65-years of age and those above were sampled in a ratio of 1:1, with few exceptions in some cantons where only one age group has been recruited. For the second objective of this study, we excluded participants who completed the questionnaire more than 30 days before or after having provided the blood sample for the serology test. The reason for this exclusion was to avoid a possible mismatch between

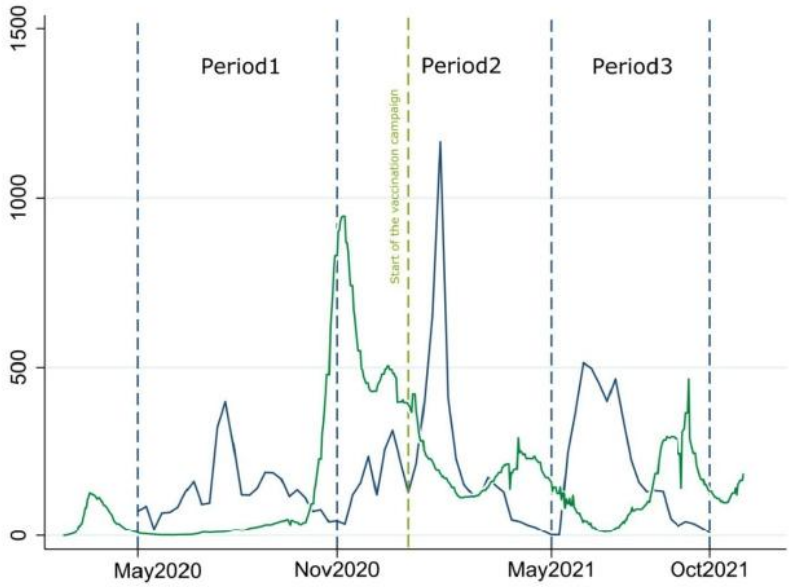


Fig. 1 Blood samplings per week and daily confirmed COVID-19 cases reported in Switzerland, May 2020–September 2021

Note: In green, daily new COVID-19 cases per million people in Switzerland; 7-day rolling average. In blue, number of Corona Immunitas blood samplings per week

serology results and information reported in the questionnaires (preventive behaviours, health status and socioeconomic status). For the same reason, we also excluded participants who provided information on vaccination status more than 11 days before or after providing the blood sample for the serology test. Figure S2 (Additional file1: Fig. S2) shows a flow diagram of the participants included in the study for each study objective.

Testing procedure

We analysed venous blood samples using the SenASTrIS assay, developed by the Vaud Central University Hospital (CHUV), the Swiss Federal Institute of Technology in Lausanne (EPFL) and the Swiss Vaccine Center [19]. The assay measures the amount of human immunoglobulins G (IgG) that binds the trimeric SARS-CoV-2 spike protein, induced either by infection or vaccination. The test was validated on a sample of the general population and specificity and sensitivity were 99.7% and 96.6% for the detection of IgG antibodies. Borderline test results (i.e., a signal just below the predefined cut-off) were categorized as seronegative (n = 140, 1%). A detailed description of the test is available elsewhere [19].

Potential risk factors

For the second objective of this study, we investigated the following potential risk factors, selected based on findings of previous studies, background expert knowledge and a priori reasons for having an increased risk of being seropositive [10, 11, 13, 14, 20–22]: sex, age (20–64 years old vs 65 years and older), educational level (primary, secondary, tertiary), body mass index (BMI; < 18.5; 18.5- 24.9; 25–29.9, ≥ 30 kg/m^2), household monthly income (≤ 3000 CHF, > 3000–6000 CHF, > 6000–9000 CHF, > 9000 CHF; 1 Euro equalled 1.046 to 1.112 CHF between 1st January 2020 and 25th November 2021), employment status (retired, outside the labour force, self-employed, employed), number of children in the household (none, one child, two or more children), comorbidity score (0, 1, ≥ 2), smoking habit (current smokers vs non-smokers; former smokers were included in the non-smokers category), physical distancing during the previous seven days (frequently, occasionally/rarely), staying at home during the previous seven days (frequently, occasionally/rarely), wearing a mask during the previous seven days (frequently, occasionally/rarely), hygiene measures during the previous seven days (frequently, occasionally/rarely). BMI was categorized according to the World Health Organization standard categories [23]. Educational level was categorized according to the International Standard Classification of Education (ISCED). Physical distancing, staying at home and hygiene measures' variables were defined as having implemented the measures recommended by public health authorities (e.g.: keeping a distance of 1.5 m, staying at home whenever possible, avoiding unnecessary activities outside the home, no handshaking or hugging, washing hands regularly, sneezing into the elbow, using tissues, etc.). The comorbidity score goes from 0 to ≥ 2 and was calculated using the following possible answers (one point for each disease) to the question "Do you suffer from one or more of the following diseases?": cancer, immunological diseases, cardiovascular diseases, diabetes, hypertension, respiratory diseases and allergies.

Statistical analysis

To estimate seroprevalence (objective 1), we used a Bayesian logistic regression model, adjusted for the antibody test sensitivity and specificity performances [24]. Seroprevalence estimates were weighted by the age and sex distribution of the population of each canton. We investigated the association between potential risk factors and seropositivity (objective 2) using Poisson regression models and expressed as prevalence ratios (PR) and 95% confidence intervals. Robust variance estimators were used to relax the assumption that the outcome distribution followed a Poisson distribution. Sex, age, educational level, BMI, income, employment status, number of children in the household, comorbidity score and smoking habit were included in the models (hereafter, model 1). Results were stratified by study period. Models for period 3 were adjusted for vaccination status (hereafter, model 2; in Switzerland the vaccination campaign started at the end of December 2020, during the second period of this study). To investigate seropositivity risk factors and their changes over time (objective 2), we used multiple imputation by chained equations to impute any missing data (30 imputations). Statistical analyses were conducted using Stata 17 software (Stata Corp, TX, 2021) and R Statistical Software (version 4.1.2; R Foundation for Statistical Computing, Vienna, Austria).

We also performed several sensitivity analyses: (1) including participants who had completed the questionnaire on demographic and socioeconomic characteristics, adherence to COVID-19 preventive measures, and health status, more than 60 days before and after their blood sample; (2) including a third age category (from 20 to 34 years old; based on the hypothesis that people in this category could have had more social interactions and therefore an increased risk of being infected) and (3) using a score computed from the preventive behaviours variables (hereafter, preventive behaviours score). The score goes from 0 to 4; one point for every "occasionally/rarely" answer to the questions on preventive behaviours. The higher the score, the less frequent the adherence to preventive behaviours.

Results

Characteristics of the sample

We included 13,291 respondents (53% females), with a mean age of 55.9 years (SD = 16.9). Characteristics of the participants are summarized in Table 1. Participants' characteristics across study periods and by cantons are detailed in Tables S1 and S2 (Additional file 1: Tables S1 and S2). Some 61% of participants were aged between 20 and 64 years and 39% were 65 years and older. 46% of

Table 1 Characteristics of participants (n = 13,291), Corona Immunitas study, Switzerland, May 2020—September 2021

Sociodemographic characteristics	
Sex	
Female	53%
Male	47%
Age group	
≥ 65	39%
20–64	61%
Children in the household	
No children	77%
One child	9%
More than one child	14%
Socioeconomic characteristics	
Educational level[a]	
Tertiary	46%
Secondary	48%
Primary	6%
Household income	
> CHF 9000	34%
CHF > 6000–9000	28%
CHF > 3000–6000	28%
CHF ≤ 3000	10%
Employment status	
Retired	38%
Outside the labour force[b]	10%
Self employed	10%
Employed	42%
Health status	
Body Mass Index	
< 18.5	3%
18.5–24.9	52%
25–29.9	33%
≥ 30	12%
Comorbiditiy score[c]	
0	53%
1	32%
≥ 2	15%
Smoking	
Non-smoker	84%
Smoker	16%
Preventive behaviours	
Physical distancing during previous 7 days	
Frequently	91%
Occasionally/rarely	9%
Staying at home during previous 7 days	
Frequently	69%
Occasionally/rarely	31%
Wearing mask during previous 7 days	
Frequently	83%
Occasionally/rarely	17%

Table 1 (continued)

Hygiene measures during previous 7 days	
Frequently	94%
Occasionally/rarely	6%

[a]International Standard Classification of Education (ISCED)

[b]Outside the labour force includes participants in training/studying and unemployed participants

[c]Comorbidity score goes from 0 to ≥ 2 and was calculated using the following possible answers: cancer; immunological diseases; cardiovascular diseases or diabetes or hypertension; respiratory diseases; allergies

participants were highly educated, 42% were employed and 23% lived with children. 47% had one or more comorbidities. In our sample people aged over 65 years were overrepresented by design, and smokers, employed participants, households with one or more than one child, low-income households and people with only primary education were slightly underrepresented [25].

Seroprevalence estimates and trends

During period 1, seroprevalence was 3.7% (95% CI 2.1–4.9). It increased to 16.2% (95% CI 14.4–17.5) during period 2 and to 72.0% (95% CI 70.3–73.8) during period 3. Seroprevalence varied by age group, with higher estimates in younger participants (20–64 years) during period 1 and in older participants (65 years and older) during period 3 (Additional file 1: Table S3). There were some regional variations between cantons (Table 2 and Fig. 2). During period 1, seroprevalence in cantons from the French and Italian speaking regions of Switzerland ranged from 3.0 to 7.7%, and in cantons from the German speaking regions from 2.1 to 5.0%. We found substantial differences between cantons during periods 2 and 3.

Factors associated with seropositivity

Table 3 shows the results of the multivariable models by study period. Information on missing data are reported in Tables S4 and S5 (Additional file1: Tables S4 and S5). Before the start of the vaccination campaign (period 1), participants aged between 20 and 64 years had a higher prevalence of seropositivity (PR = 2.32, 95% CI 1.03–5.22) compared to older participants. After the start of the vaccination campaign (period 3), participants aged 20–64 years old (PR = 0.85, 95% CI 0.78–0.93), with a low household income (PR = 0.75, 95% CI 0.68–0.82) or with an employment status different from retired had a lower prevalence of seropositivity compared to reference categories. Participants with a BMI of 25 or more (PR = 1.12, 95% CI 1.04–1.19) or with one or more comorbidities (PR = 1.12, 95% CI 1.06–1.18) had a higher prevalence

Table 2 Seroprevalence estimates[a] (IgG anti Sars-CoV-2 Spike) by study period and canton, Corona Immunitas study, Switzerland, May 2020–September 2021

Time window	Period 1, n = 3402 01/05/2020–31/10/2020	Period 2, n = 5611 01/11/2020–15/05/2021	Period 3, n = 4278 16/05/2021–31/09/2021
	% (95%CI)	% (95%CI)	% (95%CI)
National level	3.7 (2.1–4.9)	16.2 (14.4–17.5)	72.0 (70.3–73.8)
Basel-Landschaft	2.9 (1.3–5.4)	16.5 (13.4–19.9)	82.8 (78.0–87.3)
Basel-Stadt	5.0 (2.6–7.8)	19.7 (16.2–23.2)	77.2 (72.7–81.6)
Bern	NA	10.9 (7.4–14.7)	78.1 (74.1–82.0)
Fribourg	5.9 (3.2–9.1)	22.5 (18.7–26.6)	73.5 (68.4–78.4)
Grisons[b]	NA	15.7 (11.5–20.3)	43.2 (37.2–49.3)
Lucerne	NA	15.5 (11.7–19.7)	58.9 (54.4–63.6)
Neuchâtel	3.0 (1.4–5.4)	19.2 (15.4–23.1)	79.2 (74.8–83.2)
Saint Gallen[b]	NA	11.7 (7.8–16.5)	62.2 (56.6–68.0)
Ticino[c]	7.7 (5.3–10.3)	6.8 (4.1–9.7)	NA
Vaud	6.5 (3.8–9.8)	23.7 (20.3–27.1)	NA
Zurich	2.1 (1.0–3.6)	9.7 (6.7–13.0)	78.5 (74.3–82.5)

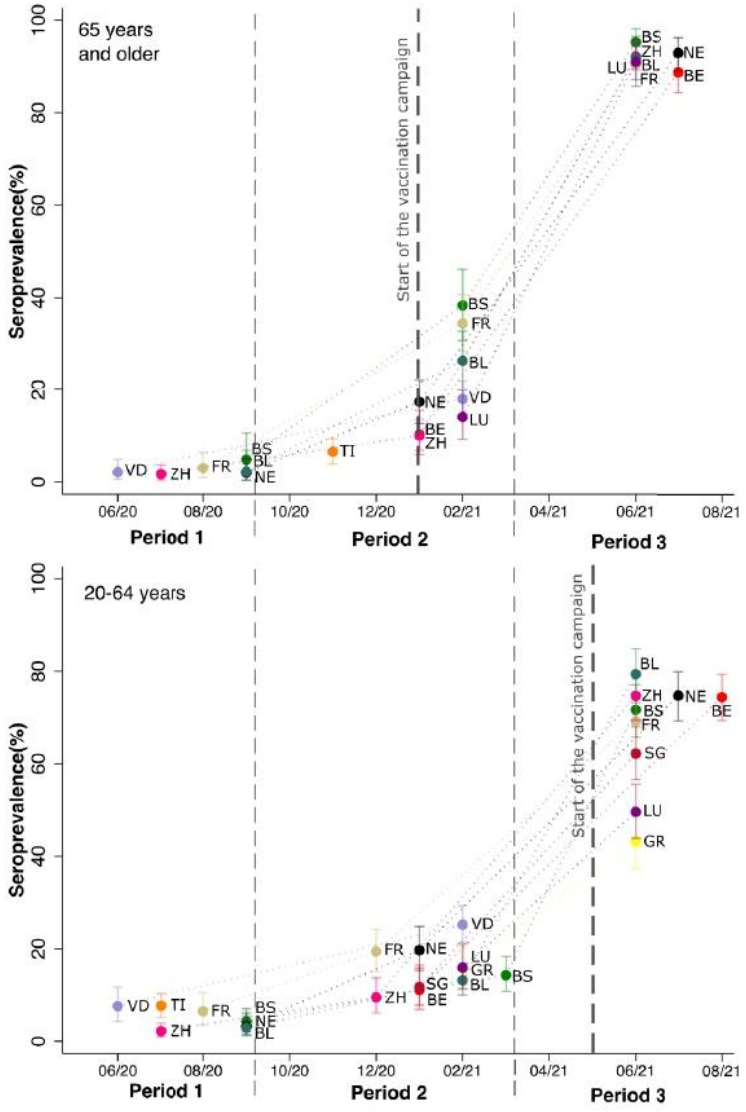
Samplings in Bern, Grisons, Lucerne and Saint Gallen started after period 1. Data for Ticino and Vaud period 3 were not available for the analyses presented in this study

IgG immunoglobulin G, *NA* not available

[a]Seroprevalence was estimated using Bayesian regression adjusted for the antibody test sensitivity and specificity performances and weighted by age and sex of the general population of each canton

[b]In cantons Grisons and Saint Gallen, only participants aged from 20 to 64 years were tested

[c]In canton Ticino, during period 1, only participants aged from 20 to 64 were tested. During period 2 only data from people aged 65 years or more were available for these analyses



Note: estimates are reported with 95% CIs
Abbreviations: BL= Basel-Landschaft; BS= Basel-Stadt; BE= Bern; FR= Fribourg; GR= Grisons; LU= Lucerne; NE= Neuchâtel; SG= Saint Gallen; TI= Ticino; VD= Vaud; ZU= Zürich

Fig. 2 Trends of seroprevalence estimates (IgG anti SARS-CoV-2 Spike) per canton and by age group, Corona Immunitas study, Switzerland, May 2020–September 2021

of seropositivity. However, all these differences disappeared upon adjustment for vaccination status in period 3 (percentages of vaccinated participants in period 3 are reported in additional file 1: Table S6).

None of the self-reported preventive behaviours (Table 4) were associated with seropositivity before the start of the vaccination campaign (period 1). In period 3, participants who reported to occasionally or rarely practice physical distancing (PR = 0.81, 95% CI 0.75–0.89), stay at home (PR = 0.94, 95% CI 0.90–0.98), wear a mask (PR = 0.76, 95% CI 0.70–0.84) and perform hygiene measures (PR = 0.79, 95% CI 0.72–0.87) had a lower prevalence of seropositivity compared to participants who frequently adhered to preventive behaviours. All these differences disappeared after adjusting for vaccination status.

Sensitivity analyses gave similar results as the main analyses and results are shown in supplementary material (Additional file1: Tables S7–S10).

Discussion

Main findings

Seroprevalence in Switzerland rose sharply between May 2020 and September 2021, with some regional variations,

Table 3 Association of sociodemographic, socioeconomic characteristics and health status with SARS-CoV-2 seropositivity across study periods, Corona Immunitas study, Switzerland, May 2020–September 2021

Factor	Period 1, n = 3108 (01/05/2020–31/10/2020)	Period 2, n = 4969 (01/11/2020–15/05/2021)	Period 3, n = 2836 (16/05/2021–31/09/2021)	
	Model 1[a], PR (95%)	Model 1[a], PR (95%)	Model 1[a], PR (95%)	Model 2[b], PR (95%)
Sex				
Female	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
Male	1.15 (0.82–1.62)	1.05 (0.92–1.20)	0.93 (0.89–0.98)	0.97 (0.94–1.00)
Age groups				
≥ 65	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
20–64	2.32 (1.03–5.22)	1.22 (0.96 -1.54)	0.85 (0.78–0.93)	0.94 (0.89–0.99)
Children in the household				
No children	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
One child	0.71 (0.40–1.24)	1.20 (0.96–1.49)	0.90 (0.82–1.00)	0.97 (0.90–1.04)
More than one child	1.01 (0.64–1.60)	1.11 (0.90–1.35)	0.92 (0.85–0.99)	1.06 (0.99–1.12)
Educational level				
Tertiary	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
Secondary	1.62 (1.12–2.35)	0.83 (0.72–0.96)	0.95 (0.91–0.99)	1.01 (0.98–1.04)
Primary	1.49 (0.59–3.79)	1.15 (0.89–1.50)	0.92 (0.82–1.03)	1.01 (0.93–1.10)
Household income				
> CHF 9000	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
CHF > 6000–9000	0.72 (0.44–1.19)	1.07 (0.90–1.27)	0.88 (0.83–0.93)	0.99 (0.95–1.03)
CHF > 3000–6000	0.76 (0.46–1.27)	1.25 (1.04–1.51)	0.83 (0.78–0.88)	0.97 (0.94–1.01)
CHF ≤ 3000	0.79 (0.38–1.65)	0.94 (0.71–1.26)	0.75 (0.68–0.82)	0.94 (0.89–1.01)
Employment status				
Retired	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
Outside the labour force[b]	1.09 (0.46–2.60)	0.69 (0.54–0.89)	0.84 (0.72–0.97)	1.00 (0.90–1.10)
Self employed	1.10 (0.50–2.41)	0.68 (0.49–0.95)	0.78 (0.69–0.88)	0.97 (0.90–1.06)
Employed	0.56 (0.25–1.26)	0.81 (0.63–1.04)	0.84 (0.77–0.93)	1.00 (0.95–1.06)
Body Mass Index				
18.5–24.9	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
< 18.5	0.49 (0.12–1.96)	1.07 (0.70–1.63)	0.99(0.86–1.14)	1.04 (0.93–1.16)
25–29.9	0.72 (0.49–1.07)	1.12 (0.97–1.30)	1.08(1.03–1.13)	1.04 (1.00–1.07)
≥ 30	0.67 (0.38–1.17)	1.18 (0.97–1.44)	1.12(1.04–1.19)	1.04 (1.00–1.09)
Comorbiditiy score[d]				
0	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
1	1.23 (0.82–1.79)	0.95 (0.82–1.10)	1.08(1.03–1.13)	1.01 (0.98–1.04)
≥ 2	1.26 (0.74–2.16)	1.24 (1.04–1.48)	1.12(1.06–1.18)	1.00 (0.97–1.03)
Smoking				
Non-smoker	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
Smoker	0.80 (0.49–1.29)	0.81 (0.66–0.99)	0.93 (0.86–1.00)	0.97 (0.92–1.01)

[a]Model adjusted for: sex, age, educational level, body mass index, income, employment status, children in the household, comorbidity score and smoking habit

[b]Model additionally adjusted for vaccination status

[c]Outside the labour force includes participants in training/studying and not employed participants

[d]Comorbidity score goes from 0 to ≥ 2 and was calculated using the following possible answers: cancer; immunological diseases; cardiovascular diseases or diabetes or hypertension; respiratory diseases; allergies

from 3.7% (95% CI 2.1–4.9) in May–October 2020, to 16.2% (95% CI 14.4–17.5) between November 2020 and mid-May 2021, and finally 72.0% (95% CI 70.3–73.8) between mid-May and September 2021. Before the start of the vaccination campaign, seropositivity differed by age but not by other factors. After the start of the vaccination campaign,

Table 4 Association of recommended preventive behaviours with SARS-CoV-2 seropositivity across study periods, Corona Immunitas study, Switzerland, May 2020–September 2021

Factor	Period 1, n = 2151 (01/05/2020–31/10/2020)	Period 2, n = 4969 (01/11/2020–15/05/2021)	Period 3, n = 2836 (16/05/2021–31/09/2021)	
	Model 1[a], PR (95%)	Model 1[a], PR (95%)	Model 1[a], PR (95%)	Model 2[b], PR (95%)
Physical distancing during previous 7 days				
Frequently	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
Occasionally/rarely	1.25 (0.61–2.59)	1.52 (1.18–1.96)	0.81 (0.75–0.89)	0.97 (0.92–1.02)
Staying at home during previous 7 days				
Frequently	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
Occasionally/rarely	1.43 (0.86–2.37)	1.13 (0.96–1.33)	0.94 (0.90–0.98)	1.02 (0.99–1.05)
Wearing mask during previous 7 days				
Frequently	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
Occasionally/rarely	0.68 (0.41–1.13)	1.06 (0.78–1.43)	0.76 (0.70–0.84)	0.96 (0.91–1.02)
Hygiene measures during previous 7 days				
Frequently	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
Occasionally/rarely	0.97 (0.31–3.02)	0.88 (0.62–1.25)	0.79 (0.72–0 .87)	1.01 (0.94–1.08)

Data from Ticino and data from Vaud period 1 were not included because not harmonizable with data from other sites

[a]Model adjusted for sex, age, educational level, body mass index, income, employment status, children in the household, comorbidity score and smoking habit

[b]Model additionally adjusted for vaccination status

seropositivity was higher among participants over 65 years, with a high income, retired, overweight or obese, or with other comorbidities, due to a higher vaccination uptake. Seropositivity was lower in participants with lower adherence to preventive measures, due to a reduced propensity for vaccination uptake.

Comparison with other studies

This study's findings describe the evolution of the SARS-CoV-2 spread and of population immunological status in the first phases of the COVID-19 pandemic in several cantons of Switzerland, accounting for under-ascertainment and differences in testing strategies across Swiss cantons. European seroprevalence estimates varied widely during the pandemic, depending on study populations, study periods and methods used. However, our seroprevalence estimates were roughly similar to estimates found by other seroprevalence surveys in the same periods in other Swiss cantons [24, 26] and to pooled estimates from other European high-income countries [9]. We found some variations in seroprevalence estimates between cantons during period 1, with estimates ranging from 3.0 to 6.5% in the French speaking cantons, being 7.7% in Ticino, and ranging from 2.1 to 5.0% in German speaking cantons. These results are particularly interesting in light of the fact that, especially at the beginning of the pandemic, comparisons between studies were hindered by differences in study designs. We also found substantial differences during period 2 and 3. However, these results are difficult to interpret, since seroprevalence estimates were strongly influenced by vaccination rates during these periods, and differences in testing periods could have resulted in different estimates.

During the first period of this study, i.e., before the start of the vaccination campaign, we found a higher prevalence of seropositivity in participants aged between 20 and 64 years compared to those aged 65 years and older. Other studies showed higher seroprevalence in younger adults [10–13] compared to older population's groups, and this could be due to the fact that younger populations were considered at lower risk of severe illness and therefore could have had more social interactions. No other factor was associated with seropositivity during the first period of this study, despite several studies showing differences in seropositivity according to socioeconomic characteristics (e.g., higher seroprevalence in people with lower income or lower educational level) [10], health behaviours (e.g., higher seroprevalence in smokers vs non- smokers) [11, 13] or other sociodemographic characteristics (e.g., higher seroprevalence in households with more than one child) [13]. The higher prevalence of seropositivity found during the third period of this study among participants aged over 65 years, overweight or obese, retired and with other comorbidities, was due to a higher vaccination rate in these subgroups. These results were expected, since the vaccination campaign in Switzerland prioritised people with a higher risk of severe illness and death (i.e., older people and people with comorbidities or a high BMI) [27]. Having a high household income was also associated with

higher seropositivity due to a higher vaccination uptake. This finding is consistent with other studies conducted in Switzerland [28] and elsewhere [29, 30].

Regarding preventive behaviours, despite several personal and social preventive measures associated with a reduction in the incidence of COVID-19 [21, 31], we did not find associations between adherence to preventive behaviours and seropositivity before the start of the vaccination campaign (period 1). This result could be due to selection bias, as people who adhered less to preventive measures were also less likely to participate in this study. Another hypothetical explanation is that people who did not frequently adhere to the recommended measures benefited from the collective adherence to those same measures, or from the low seroprevalence in period 1. During the last study period, we found a lower prevalence of seropositivity in people with lower adherence to recommended preventive behaviours, especially in participants who less frequently wore masks. This was explained by a lower vaccination uptake in these groups. Other studies investigated the associations between willingness to receive the COVID-19 vaccine and adherence to preventive behaviours [32], showing that people who are more prone to follow prevention recommendations are also more likely to get vaccinated. Overall, the associations between risk factors and seroprevalence during period 2 were difficult to interpret because period 2 included blood sample collected both before and after the vaccination campaign and because, during the first months of the vaccination campaign, self-reported information on vaccination status was less reliable, due to organizational difficulties in promptly modifying the questionnaires to include questions on vaccination status.

Strengths and limitations

This study has some limitations. Overall, the participation rate was moderate (21%). Moreover, despite random representative samples of the population being invited, selection bias is possible, with a higher participation rate of highly educated participants compared to the Swiss general population. Further, seroprevalence could be underestimated due to waning immunity [33], people failing to produce antibodies [34] and due to the fact that we only measured the amount of anti-SARS-CoV-2 IgGs, without assessing other types of antibodies. We were therefore not able to distinguish between infection-related and vaccination-related antibodies. Information bias is also possible, since the information collected through the questionnaire was self-reported. The key strengths of our study include the use of a large population-based sample covering a significant proportion of the country and with repeated samplings over time, the use of a previously validated test with high sensitivity and specificity, and post-stratification weights to account for differences in sex and age.

Conclusions

Seroprevalence in Switzerland has increased sharply over time, also thanks to the increasing vaccination coverage, with some regional differences. After the vaccination campaign, no differences between subgroups were observed.

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Data availability Deidentified individual participant data underlying the findings of this study will be available for researchers submitting a methodologically sound proposal to achieve the aims of the proposal after the publication of this article. Access to data requires contacting Corona Immunitas.

Declarations

Conflict of interest The authors declare no competing interests.

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Chapter 5.2| Surveillance bias in the assessment of the size of COVID-19 epidemic waves: a case study

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Original Research

Surveillance bias in the assessment of the size of COVID-19 epidemic waves: a case study

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ABSTRACT

Objectives: To estimate the size of COVID-19 waves using four indicators across three pandemic periods and assess potential surveillance bias.
Study design: Case study using data from one region of Switzerland.
Methods: We compared cases, hospitalizations, deaths, and seroprevalence during three periods including the first three pandemic waves (period 1: Feb–Oct 2020; period 2: Oct 2020-Feb 2021; period 3: Feb–Aug 2021). Data were retrieved from the Federal Office of Public Health or estimated from population-based studies. To assess potential surveillance bias, indicators were compared to a reference indicator, i.e. seroprevalence during periods 1 and 2 and hospitalizations during the period 3. Timeliness of indicators (the duration from data generation to the availability of the information to decision-makers) was also evaluated.
Results: Using seroprevalence (our reference indicator for period 1 and 2), the 2nd wave size was slightly larger (by a ratio of 1.4) than the 1st wave. Compared to seroprevalence, cases largely overestimated the 2nd wave size (2nd vs 1st wave ratio: 6.5), while hospitalizations (ratio: 2.2) and deaths (ratio: 2.9) were more suitable to compare the size of these waves. Using hospitalizations as a reference, the 3rd wave size was slightly smaller (by a ratio of 0.7) than the 2nd wave. Cases or deaths slightly underestimated the 3rd wave size (3rd vs 2nd wave ratio for cases: 0.5; for deaths: 0.4). The seroprevalence was not useful to compare the size of these waves due to high vaccination rates. Across all waves, timeliness for cases and hospitalizations was better than for deaths or seroprevalence.
Conclusions: The usefulness of indicators for assessing the size of pandemic waves depends on the type of indicator and the period of the pandemic.

Introduction

During the COVID-19 pandemic, surveillance systems and indicators were crucial to monitor the size and severity of the pandemic, evaluate control measures, assess population-level immunity and vaccination, and adapt preventive strategies accordingly.[1,2] However, interpreting and translating information from indicators into practical actions was challenging. One major problem was that indicators could be prone to surveillance bias, a bias that occurs when differences in an indicator result from differences in the frequency or modality of detection of an health event over time or across healthcare settings and regions, rather than an actual difference in the frequency of this event.[1] This problem was particularly relevant when indicators built on data from healthcare providers were used to assess the size of the COVID-19 epidemic waves, leading to misinterpretations of trends, and potentially wrong public health actions.

A prime example of an indicator prone to surveillance bias is the number of COVID-19 reported cases. This indicator was frequently used to monitor the virus spread but is influenced by differences over time or across regions in screening and diagnostic strategies, test availability, or care-seeking behaviors.[3] Hence, especially in the early stages of the pandemic, the number of reported cases largely underestimated the actual spread of the virus.[4] In Switzerland, a

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seroprevalence study showed that for every confirmed case reported in April/May 2020, there were roughly 12 infections in the community.[5] A study conducted in France found that 9 out of 10 cases were missed by the COVID-19 surveillance system in May/June 2020.[6] These high shares of missed cases were mainly due to a large proportion of non-tested, asymptomatic, or mildly symptomatic individuals, and greatly biased the assessment of the actual size of pandemic waves at the beginning of the pandemic. Later, the vaccine rollout also influenced case reporting rates because vaccinated individuals experienced milder COVID-19 symptoms[7,8] and vaccine availability altered the risk perception, changing health-seeking behaviors and reducing the willingness to get tested.[9] Other indicators, such as deaths or hospital admissions, were probably prone to surveillance bias as well. For instance, the accuracy of the number of COVID-19 deaths depended on definition or testing practices at or close to death.[10] Hospitalization rates could be biased by the threshold for hospitalization changing over time, based on changing risk perception, medical attitudes about who should be hospitalized, and beliefs about the availability of effective in-hospital treatments, and hospital bed capacity.[11]

No matter the epidemic indicator, the degree to which each indicator was biased could change across different stages of the pandemic, depending on testing capacity, diagnostic strategies, hospital capacity, vaccine availability, and other factors. It is therefore challenging to determine the reliability of each indicator to assess the size of epidemic waves during different pandemic periods, since the information provided by each indicator changed over time. Therefore, to ease the critical evaluation of surveillance data, using data from one region in Switzerland, we aimed to estimate the size of epidemic waves using various indicators across different periods of the pandemic. This allowed us to compare their variation between waves and to assess to what extent each indicator is prone to surveillance bias.

Methods

This is an observational, retrospective study conducted using data from one region in Switzerland, the canton of Fribourg. We estimated the size of COVID-19 epidemic waves, comparing four indicators: 1) seroprevalence, expressed as the proportion of the population who developed SARS-CoV-2 antibodies due to infections or vaccination, 2) number of COVID-19 reported cases, 3) number of COVID-19 hospitalizations, and 4) number of COVID-19 deaths. These indicators were compared across three different periods, i.e. period 1: from 24 February 2020 to 14 October 2020; period 2: from 15 October 2020 to 5 February 2021; and period 3: from 6 February to 16 August 2021. The three periods included the first three pandemic waves in the canton of Fribourg (Fig. 1). These periods were chosen based on the dates of the end of each seroprevalence study, i.e. following each of the first three pandemic waves in Switzerland, in line with the World Health Organization (WHO) recommendations for cross-sectional seroprevalence studies.[12] To better interpret our results, it is key to specify that the vaccination campaign in Switzerland started in January 2021 for people aged above 65 years and in May 2021 for younger adults. During period 1, vaccination was not available in Switzerland. Period 2 included a very short time window in which vaccination was available, but the proportion of vaccinated people was overall negligible (roughly 4%). Period 3 covered a time window in which vaccination was broadly available in Switzerland.[13]

Seroprevalence estimates

Seroprevalence was estimated by carrying out three population-based studies at the end of each study period on random samples of the adult population in the canton of Fribourg. These studies were conducted within the framework of Corona Immunitas, a nationally coordinated Swiss research project that consisted of repeated population-based seroprevalence studies conducted in several Swiss cantons with shared coordination and methodology.[14] Random samples of the general population were drawn from the population register of the Federal Statistical Office. The first serosurvey was conducted between July 8th and October 14th, 2020, at the end of the first pandemic wave. The second serosurvey was conducted after the second pandemic wave, between November 30th, 2020, and February 5th, 2021, and the third serosurvey was conducted between May 20th and August 13th, 2021, after the third pandemic wave (Fig. 1).

Participants provided venous blood samples that were analyzed using the SenASTrIS assay to measure the amount of human immunoglobulin G (IgG) that binds the trimeric SARS-CoV-2 spike protein, induced either by infection or vaccination. The test was validated on a sample of the general population, specificity and sensitivity were 99.7% and 96.6% for the detection of IgG antibodies, respectively.[15] Seroprevalence was estimated using a Bayesian logistic regression model, adjusted for the test sensitivity and specificity performances. Estimates were weighted by age and sex distribution of the general population of the canton of Fribourg. Seroprevalence estimates were reported as percentages. The Ethics Committees of the canton of Vaud, Switzerland, approved the seroprevalence studies used in this study (BASEC 2020-01247).

COVID-19 cases, hospitalizations, and deaths

Data on the number of COVID-19 reported cases, hospitalizations, and deaths were retrieved from the Swiss Federal Office of Public Health (FOPH).[16] The number of COVID-19 reported cases included data on individuals in the canton of Fribourg diagnosed with a laboratory-confirmed SARS-CoV-2 infection (polymerase chain reaction or antigen tests). This data was provided by laboratories, physicians, and hospitals to the FOPH. The number of COVID-19 hospitalizations included data on individuals admitted to hospitals in Switzerland who had been diagnosed with a laboratory-confirmed SARS-CoV-2 infection, regardless of the reason for hospitalization. The number of COVID-19 deaths included data on individuals in Switzerland who had died with a laboratory-confirmed SARS-CoV-2 infection. The information was based on data submitted by physicians using the form for reporting clinical findings related to a death to the FOPH. All these indicators were unadjusted. The number of COVID-19 cases, hospitalizations, and deaths were reported as counts.

Analyses

We compared the size of the 1st epidemic wave (period 1) with the 2nd wave (period 2), and the size of the 2nd wave (period 2) with the 3rd wave (period 3), respectively. Our analysis consisted of two steps. First, we calculated three simple metrics for each indicator (absolute difference, percentage difference, and ratio) to describe how the indicators changed between waves. The formulas for the metrics were as follows: (p_1 and p_2 represent the values of each indicator at period 1 and period 2, respectively):

Metric 1, absolute difference:

$$p_2 - p_1$$

Metric 2, percentage difference:

$$\frac{p_2 - p_1}{p_1} \times 100$$

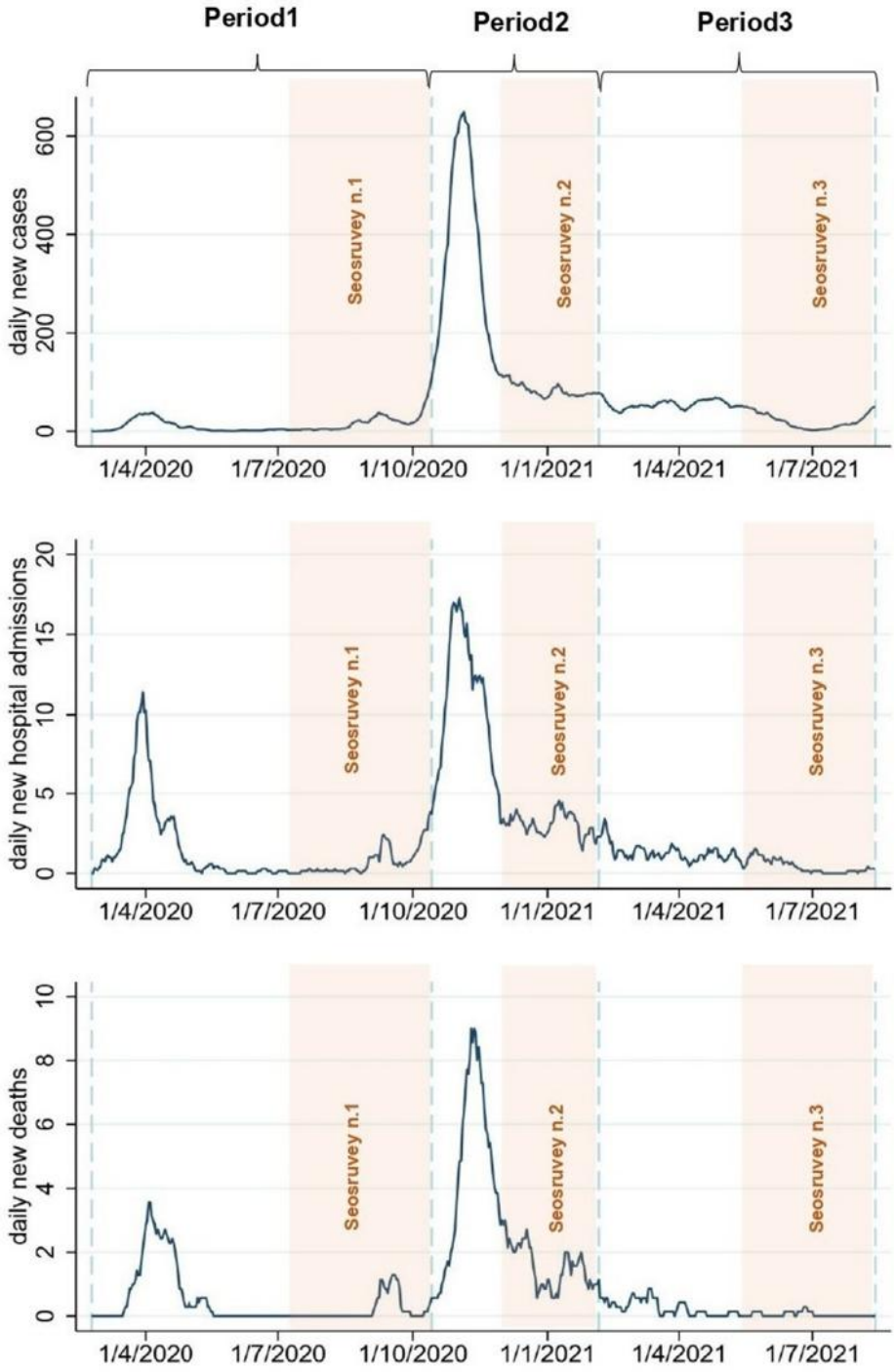

Fig. 1. 7-days rolling average of daily cases, hospital admissions and deaths in the Canton of Fribourg across the 3 periods. In orange, the time windows during which blood samples for the seroprevalence studies were taken.

Metric 3, ratio:

$$\frac{p_2}{p_1}$$

The same formulas were used to compute these metrics between period 2 and period 3, using the respective indicators' values from those periods.

The second step of our analyses consisted of selecting a reference indicator to benchmark surveillance bias in other indicators. We chose as reference indicators—the indicators that we judged to be the least bias in each comparison. This choice was made based on the authors' expertise, with the aim of clearly highlighting the phenomenon of surveillance bias through the comparison of different indicators. Specifically, we selected seroprevalence as the reference indicator when comparing indicators between period 1 and period 2, and the number of hospitalizations when comparing indicators between period 2 and period 3. Seroprevalence was chosen because during the initial two periods of the pandemic, testing strategies and

availability frequently changed, and population-based seroprevalence was the only indicator not influenced by testing differences. During period 3, seroprevalence was not directly informative due to the vaccination, and the number of cases was potentially exposed to the same type of bias seen during periods 1 and 2. Hospitalizations were therefore considered a better marker of the size of the epidemic.

To better interpret our results and the usefulness of surveillance indicators, we also descriptively assessed the timeliness of each indicator. We defined timeliness as the duration in days between the generation of the information, such as a positive test for cases, hospitalizations, and deaths, and the availability of this information to decision-makers for making informed decisions. Specifically, the timeliness of the number of cases, hospitalizations, and deaths was defined as the time between the conduction of the test and the availability of results for the public health officials of the canton of Fribourg. This information was retrieved from the 'Service du médecin cantonal' which is the medical health authority of the canton of Fribourg. For seroprevalence studies, timeliness was assessed by calculating the difference in days between the average date of the recruitment process and the average date of result availability, as results were progressively available for different batches of samples as participants were enrolled (e.g. for serosurvey 1, results were available in two batches in September and November 2020; for serosurvey 2, in three batches in January, February, and April 2021; and for serosurvey 3, in four batches in July, the end of July, September, and November 2021).

Results

The characteristics of participants of the three serosurveys are reported in Table 1. Seroprevalence was 8% (confidence interval (CI) = 4%–12%) at the end of period 1, 19% (CI = 15%–23%) at the end of period 2, and 74% (CI = 69%–79%) at the end of period 3, meaning that 8%, 11%, and 55% of the population became seropositive in the periods 1, 2, and 3, respectively. The number of cases, hospitalizations, and deaths were, respectively, 3′488, 330, and 108 for period 1, 22′771, 721, and 318 for period 2, and 10′675, 487, and 135 for period 3 (Tables 2 and 3). The absolute difference, the percentage difference, and the ratio computed for each indicator comparing period 1 vs period 2 and period 2 vs period 3 are also shown in Tables 2 and 3.

Comparison of the size of epidemic waves in period 1 and period 2

Based on seroprevalence (our reference indicator when comparing indicators between period 1 and period 2), 8% of the population got infected in period 1, and 11% got infected during period 2, representing a 38% increase between the two periods. In other words, the size of the epidemic wave of COVID-19 during period 2 was slightly larger (by a ratio of 1.4) than the size of the wave in period 1 (Table 2).

Compared to seroprevalence, other indicators provided a different description of the epidemiological situation: based on the number of reported cases, hospitalizations, and deaths, the size of the epidemic wave during period 2 compared to period 1 was overestimated (a ratio of 6.5, 2.2, and 2.9, respectively). From period 1 to period 2, reported cases, hospitalizations, and deaths increased by 553%, 118%, and 154%, respectively. Compared to the 38% increase of the chosen reference indicator (seroprevalence), the number of cases was a very biased indicator (553% increase between waves vs 38% increase), followed by the number of deaths (154% increase vs 38%) and the number of hospitalizations (118% vs 38%).

Comparison of the size of epidemic waves in period 2 and period 3

Based on the number of hospitalizations (our reference indicator when comparing indicators between period 2 and period 3), the size of the epidemic wave of COVID-19 during period 3 was slightly smaller (by a ratio of 0.7) than the wave in period 2, representing a 32% decrease in hospitalizations (Table 3).

Other indicators provided a different description of the epidemiological situation: based on seroprevalence, the size of the epidemic waves during period 3 was much higher (by a ratio of 5) than period 2. Cases or deaths slightly underestimated the size of the 3rd wave (3rd vs 2nd wave ratio for cases: 0.5; for deaths: 0.4). Seroprevalence increased by 400%, and cases and deaths decreased by 53% and 58%, respectively. Compared to our reference (hospitalizations), seroprevalence resulted to be a very biased indicator in

Table 1
Characteristics of the participants of the three serosurveys conducted in the canton of Fribourg, Switzerland.

Characteristics	Serosurvey 1	Serosurvey 2	Serosurvey 3
	July–October 2020	November 2020–February 2021	May 2021–August 2021
Number of participants (%)	418 (100%)	449 (100%)	504 (100%)
Female/male, *n* (%)	226 (54%)/192 (46%)	245(55%)/104 (45%)	277 (55%)/227 (45%)
Age, mean (SD)	58 (17)	54 (16)	58 (16)
Age groups, *n* (%)			
20–64	227 (54%)	302 (67%)	261 (52%)
≥ 65	191 (46%)	147 (33%)	243 (48%)
Educational level, *n* (%)			
Primary	38 (9%)	29 (6%)	39 (8%)
Secondary	207 (50%)	222 (49%)	254 (50%)
Tertiary	169 (40%)	198 (44%)	211 (42%)
Employment status, *n* (%)			
Retired	190 (45%)	160 (36%)	251 (50%)
Student	12 (3%)	16 (4%)	12 (2%)
Self employed	32 (8%)	30 (7%)	34 (7%)
Employed	176 (42%)	240 (53%)	209 (41%)
Not employed	17 (4%)	17 (4%)	21 (4%)
Comorbidities, *n* (%)			
Cancer	15 (4%)	10 (2%)	12 (2%)
Diabetes	26 (6%)	22 (5%)	20 (4%)
Immunological diseases	20 (5%)	10 (2%)	19 (4%))
Hypertension	94 (22%)	74 (16%)	115 (23%)
Cardiovascular diseases	39 (9%)	45 (10%)	47 (9%)
Respiratory diseases	22 (5%)	32 (7%)	31 (6%)

Table 2
Surveillance indicators in period 1 and 2, and metrics computed to compare period 1 and 2, canton of Fribourg, Switzerland.

Indicators	Period 1 (24 Feb 2020–14 Oct 2020)	Period 2 (15 Oct 2020–5 Feb 2021)	Metrics comparing period 1 and period 2			Surveillance bias magnitude
			Absolute difference	Percentage difference	Ratio	
Proportion of individuals who became seropositive	8%	11%	3%	38%	1.4	Ref
Reported cases	3488	22,771	19,283	553%	6.5	++
Hospitalizations	330	721	391	118%	2.2	+
Deaths	108	318	210	194%	2.9	+

Table 3
Surveillance indicators in period 2 and 3, and metrics computed to compare period 2 and 3, Canton of Fribourg, Switzerland.

Indicators	Period 2 (15 Oct 2020–5 Feb 2021)	Period 3 (6 Feb 2021–13 Aug 2021)	Metrics comparing period 2 and period 3			Surveillance bias magnitude
			Absolute difference	Percentage difference	Ratio	
Proportion of individuals who became seropositive	11%	55%	44%	400%	5.0	++
Reported cases	22,771	10,675	−12,096	−53%	0.5	−
Hospitalizations	721	487	−234	−32%	0.7	Ref
Deaths	318	135	−183	−58%	0.4	−

this pandemic phase due to the large share of vaccinated individuals (400% increase between waves vs 32% decrease), while deaths and cases were much less biased (58% decrease vs 32% and 53% decrease vs 32%).

Timeliness of surveillance indicators

Across all periods, the number of cases and hospitalizations were the timeliest indicators, followed by deaths and seroprevalence. Decision-makers in the canton of Fribourg were able to obtain information on days and hospitalizations within 1–2 days for cases and hospitalizations, regardless of the period under consideration. Information on deaths was less timely: although sometimes unofficial information was available for decision-makers in a few days, it took up to several weeks to receive official certificates filled out by physicians. For seroprevalence, the average time between recruitment and availability of results was 53 days (37, 64, and 57 days for serosurveys 1, 2, and 3, respectively).

Discussion

This case study shows that different surveillance indicators used during the COVID-19 pandemic provided information on the impact of pandemic waves that vastly varied depending on the indicator used and the period of the pandemic taken into consideration.

Many studies have investigated biases in COVID-19 surveillance.[17–21] Here, we focused on four commonly used indicators of epidemic size at once, to gain insights on challenges in surveillance and decision-making during the pandemic. We found that the number of confirmed cases of COVID-19, routinely used as a primary indicator of the size of epidemic waves due to the daily availability and ease of collection of this data, was greatly biased at the beginning of the pandemic. This was likely due to the unavailability of tests during period 1 and was observed in many other countries and regions.[17,22] Comparing our estimates with other studies is challenging, as most studies estimated under ascertainment by comparing the number of cases with seroprevalence within the same period, which differs from our approach that consisted of comparing waves. However, if we compare seroprevalence estimates to the number of cases found in period 1, the level of under-ascertainment we found was similar to estimates found during a comparable period in other regions of Switzerland (for every case found during period 1, there were roughly 8 infections in the population of the canton of Fribourg and 12 in the population of the Canton of Geneva).[5] As test availability improved and testing strategies became more consistent, the bias in this indicator diminished in periods 2 and 3.

Seroprevalence was considered the least biased indicator to assess the size of epidemic waves in periods 1 and 2. Nevertheless, it became the most biased indicator in period 3, due to the large share of vaccinated individuals in the population. Although we selected seroprevalence as a reference indicator in periods 1 and 2, it is important to underline that it has some limitations. For instance, it's not always feasible to select a representative sample of the general population, and seroprevalence can be underestimated because of waning immunity,[23] people failing to produce antibodies[24] or low participation rates.[25] Hospitalization and deaths, although biased to a certain degree, appeared to be indicators that could estimate the size of COVID-19 epidemic waves more consistently over time. Although these indicators were also prone to surveillance bias, they were more reliable than case counts or seroprevalence when assessing the size of waves over time during the periods examined in this case study.

The timeliness of surveillance indicators plays a major role in the decision-making process and was also estimated in this study. Across all waves, cases, and hospitalizations were timelier than deaths or seroprevalence. It must be noted that timeliness is difficult to assess due to under-reporting, and that timeliness can be defined differently than the way we defined it in this case study. For instance, if we defined timeliness as the time lag between the spread of the virus in a setting and the availability of information to be able to control the spread, deaths would be much less timely, as the time lag between infection and information on death is influenced by the fact that individuals need time to become ill, die, and then have their deaths reported.[26–29] Seroprevalence was the least timely indicator and to be more useful in the decision-making process, seroprevalence studies should be conducted more promptly. In general, surveillance tools that collect data at a population level, such as seroprevalence studies are less timely than indicators based on data from healthcare providers, such as cases,

hospitalizations, and deaths, because it takes time to design and execute the studies and retrieve data at a population level. However, since in some pandemic phases population-based methods are less prone to surveillance bias, these methods should be made more timely. This could be achieved, for instance, by establishing rapidly scalable surveillance teams with ad hoc infrastructures and preplanned protocols.[10]

This case study has several limitations. First, other surveillance strategies, such as population-based random surveys of infections[30] or wastewater surveillance[31] were not assessed. These population-based surveillance tools could be used in phases where testing strategies were not consistent or standardized, and are not influenced by vaccination. Unfortunately, we could not include these indicators in our analyses because wastewater surveillance in Switzerland only started in January 2022, and, to our knowledge, no study to randomly test a sample of the population was conducted in the canton of Fribourg. Data from these methods would have probably offered less biased information compared to data reported by healthcare providers (e.g. cases, hospitalizations, and deaths) since they are population-based. Second, by focusing on one single Swiss region, we only assessed surveillance bias over time, and we could not assess the impact of this bias on surveillance indicators due to regional differences in data collection. Third, we have not taken into account factors like the impact of changing SARS-CoV-2 variants. The spread of more or less aggressive variants over time may have influenced the number of cases, hospitalizations, and deaths. During periods 1 and 2, the distribution of variants was roughly similar in Switzerland.[32] During period 3, the most common variants were Alpha and Delta,[32] which could have negatively impacted the number of hospitalizations and deaths (although these indicators decreased compared to period 2, likely due to the COVID-19 vaccination). Moreover, the implementation of new treatments, such as corticosteroids, could have also had an influence on the number of deaths.[33] Fourth, in this case-study, we only evaluated surveillance indicators as markers of epidemic size, despite their usefulness for other purposes. For instance, seroprevalence studies are used to assess the level of protection against infection and severe outcomes, identifying COVID-19 cases plays a key role in contact tracing and interrupting the transmission chain, and hospitalizations and deaths are needed to evaluate the pressure of the pandemic on the healthcare system. Fifth, we did not evaluate the costs of producing each indicator, which is an important factor in designing a surveillance system.[34] Finally, our definition of waves may be imprecise, as providing an exact definition of epidemic waves proves challenging.[35,36]

The main strength of this case study is that, despite its simple methodology, it highlights that each indicator should have a different weight in the decision-making process depending on the pandemic phase. Possible questions to consider when making decisions include: How many tests were available during the examined period? What was the share of vaccinated individuals in the population? What were the admission criteria in the hospitals in my region? Have the definitions of COVID-19 cases or deaths changed over time? Are there new treatments available that are currently used that can reduce the hospitalization rate? This information is needed to correctly interpret indicators in each pandemic phase and to make sound public health decisions.

Conclusions and implication

The usefulness of indicators for assessing the size of pandemic waves depends on the type of indicator and the period of the pandemic under consideration. No indicator proved to be without bias at any stage, and each of them could be influenced by several external factors, such as vaccination, testing capacity and compliance, or access and effectiveness of treatment. The weight of the surveillance bias of each indicator should be taken into consideration in different pandemic phases before making any critical decisions. Population-based surveillance strategies, such as seroprevalence, were less biased in the early phase of the pandemic but lacked timeliness. Diagnosed-based tools, such as the number of cases and hospitalizations were more timely but also more biased in some pandemic periods. Integrating population-based tools, preferably with improved timeliness, and diagnosis-based surveillance strategies could ensure both timeliness and a lower risk of bias during different pandemic phases.

Author statements

Ethical approval

The Ethics Committees of the canton of Vaud (BASEC 2020-01247) approved the seroprevalence studies used in this study.

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Competing interests

None declared.

Author contributions

AC and ST conceived the study. ST, AC, and SC drafted the manuscript. All authors made substantial contributions and approved the final version of the manuscript before submission.

Informed consent

The subjects of the seroprevalence studies provided written informed consent prior to their participation in the study.

Data availability

Data on the number of cases, hospitalizations and deaths are publicly available and retrievable from the website of the Swiss Federal Office of Public Health. Deidentified individual participant data from seroprevalence studies will be available for researchers submitting a methodologically sound proposal to achieve the aims of the proposal after the publication of this article. Access to data requires contacting Corona Immunitas.

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Chapter 5.3 | Designing surveillance at a population level

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Designing Surveillance at a Population Level

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See also Ward et al., p. 1201.

As a core activity of public health, surveillance is paramount for managing crises such as the COVID-19 pandemic. Efficient surveillance systems are needed for disease monitoring, timely intervention, and informed decision-making, so that public health officials can track the spread of the virus, identify hotspots, assess population-level immunity and vaccinations, inform the population, and evaluate the impact of control measures. Ideally, these systems would capture high-quality data in a timely manner for proactive and evidence-based responses. However, during the COVID-19 pandemic, especially in its early phases, surveillance systems were insufficient in many jurisdictions; they were not timely and had poor data accuracy. As a result, information needs were only partially fulfilled.[1] How can we build more robust and efficient surveillance systems for future outbreak preparedness and response?

One problem with surveillance during the pandemic was that it relied essentially on data from health care providers and not on data designed primarily for surveillance. This is not surprising, because health care providers are the first to track emerging diseases and are key players in rapid identification, especially at the start of an epidemic. Furthermore, with basic information systems, it can be relatively easy to count the number of diagnosed or hospitalized cases.

However, these numbers are difficult to interpret because they are exposed to a large "surveillance bias": they are influenced by differences in screening, diagnosis, and treatment strategies and cannot be used directly to assess the true disease burden in populations, over time, and across areas.[2] For instance, trends in the number of cases based on diagnosis might be biased by variations in health care–seeking behaviors, testing availability, and changes in reporting rates. As a case in point, there were roughly eight times more cases in the second than the first wave of the pandemic in Switzerland, but this huge difference was explained by much more frequent testing during the second wave, rather than a massive spread of the virus in the population.[3] And currently, most cases are missed because people are no longer getting tested.

To overcome the low accuracy of diagnosis-based surveillance, it is better to have data collected primarily for surveillance purposes at a population level. The REal-time Assessment of Community Transmission-2 (REACT-2) study, conducted in England and presented in detail in this issue of *AJPH* (p. 1201), along with studies like ENE-COVID in Spain and Corona Immunitas in Switzerland, exemplify the benefits of this approach.[3,4] Using randomly selected population-based samples, these studies aim to capture the true disease dynamics and the extent of virus spread and give information on the evolution of population-level immunity. These studies are much less exposed to a surveillance bias. Hence, using population-based seroprevalence estimates as a proxy for virus spread in the population (before people were vaccinated),[3] the severity of the second wave was estimated to be slightly higher (roughly 1.5 times) than the first wave in Switzerland; this is in sharp contrast with severity estimates using the number of diagnosed cases.

However, like any other surveillance method, these population-based surveillance strategies come with limitations, such as difficulties acquiring representative samples of the general population or lack of timeliness (Box 1).[5–8] Therefore, they should be integrated with other surveillance strategies to create multilayer surveillance systems that ensure timeliness, comprehensiveness, and accuracy.[9] The basic layer of this system can be provided by health care provider diagnoses, for example, using sentinel surveillance to track new cases as early as possible. But the main layer should consist of population-level tools, such as surveys based on random sampling using antigenic or PCR (polymerase chain reaction) tests, wastewater surveillance, and population-based seroprevalence studies.

The diversity of these approaches ensures comprehensiveness, and the use of population-based methods improves accuracy, which reduces surveillance bias. To improve decision-making, population-based methods

BOX 1— Advantages and Disadvantages of Diagnosis- and Population-Based Surveillance

	Advantages	Disadvantages
Diagnosis-based surveillance		
Diagnosed cases	• Timely • Relatively easy to collect • Useful for identifying local spreads and clusters in specific populations (e.g., pregnant women, nursing homes residents)	• Strongly influenced by differences in screening and diagnostic strategies, test availability, care-seeking behaviors, and reporting rate • Burdened by standardization and interoperability issues
Hospitalizations	• Less prone to surveillance bias than cases • Relatively easy to collect • Useful for assessing the severity of the epidemic and pressure on health care systems • Useful for identifying local spreads and clusters	• Influenced by changes in admission criteria, hospital bed capacity, and availability of effective in-hospital treatments • Less timely than diagnosed cases • Burdened with standardization and interoperability issues
COVID-19 deaths	• Less prone to surveillance bias than cases or hospitalizations • Useful for assessing the severity of the epidemic	• Influenced by differences in COVID-19 death definition, testing availability, and test practices at death[5] • Not timely owing to the lag between diagnosis and death • Not timely because data can be provisional or incomplete for months or years
Population-based surveillance		
Population-based seroprevalence studies	• Less prone to surveillance bias than diagnosis-based surveillance • Useful for providing information on population-level immunity	• Not timely[6] • Burdened by possible low representativeness • Not designed to reach underprivileged and other at-risk populations • Prone to underestimation because of waning immunity[7]
Population-based surveys of infections	• Less prone to surveillance bias than diagnosis-based surveillance • Not dependent on care-seeking behaviors or reporting test results	• Not timely • Burdened by possible low representativeness • Not designed to reach underprivileged and other at-risk-populations[8]
Wastewater surveillance	• Less prone to surveillance bias than diagnosis-based surveillance • Not dependent on care-seeking behaviors or reporting test results[8,9]	• No individual-level information • Burdened by lack of information on the specific location of the epidemic or subpopulation[8]
Excess mortality	• Useful for estimating the global impact of COVID-19[5]	• Not timely • Burdened by differences in registration and reporting practices of deaths between countries

must be made more timely. This could be achieved by, for example, establishing quickly scalable surveillance teams with ad hoc infrastructures and preplanned protocols, creating pipelines that could work for more than one pathogen, or exploring new testing methods (as in the case of the REACT-2 study, in which, using at-home self-administered tests, information on seroprevalence was produced within days).

We believe that giving more weight to population-based surveillance systems is needed. As countries continue to navigate the challenges of the COVID-19 pandemic and prepare for future outbreaks, designing integrated and comprehensive surveillance strategies with a focus on populations is essential for accurate monitoring and better management of future epidemics. AJPH

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CONFLICTS OF INTEREST

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Chapter 6.1 | Screening and surveillance bias in cancer

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Opinion

Screening and Surveillance Bias in Cancer

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Abstract: Surveillance bias arises when differences in the frequency of a condition are due to changes in the modality of detection rather than to a difference in the actual risk of the condition. This bias hampers the surveillance of scrutiny-dependent cancers, leading to misinterpretations of cancer trends, risk factor identification, and, consequently, to the wrong public health actions.

Keywords: surveillance bias; cancer; cancer risk factors; cancer surveillance

1. Surveillance Bias of Cancer

What is the true burden of cancer? According to data from the International Agency for Research on Cancer (IARC), 10 million people worldwide died of cancer and 19 million new cases arose in 2020 [1]. It is standard to use mortality, incidence, and survival to assess the burden of cancer and the progress made in cancer control. However, for some types of cancers, specifically the so-called "scrutiny-dependent cancers" (Table 1) [2], using incidence or survival rates to assess the burden of cancer can be problematic because these metrics are influenced by the modality of detection of these cancers. Therefore, in settings of intense screening activities, the incidence and survival rates can be relatively high compared to settings without this level of screening activities, whatever the benefits of screening. If these rates are taken for granted, this results in "surveillance bias", a type of bias that occurs when differences across time, settings, or populations in the detection activities of scrutiny-dependent cancers lead to differences in the incidence, which are wrongly attributed to changes in the actual risk of these cancers [3].

To understand what surveillance bias is, it helps to consider how it relates to the problem of overdiagnosis. In oncology, as in other fields of medicine, the ever-evolving testing and imaging techniques allow us to find anomalies previously not detected. On the one hand, this opens the way to great opportunities for new early detection and screening strategies for cancer. On the other hand, because these anomalies are not all associated with a substantial health hazard, there is no benefit to being aware of them; moreover, if these harmless anomalies are diagnosed as diseases, this is a situation of overdiagnosis [4]. More broadly, this is linked to the well-known "length-time bias" associated with all types of early detection and screening activities. Much less known is the major impact of this phenomenon on the surveillance of some types of cancer because it biases incidence trends due to the confusion between the diagnosis of harmless anomalies and the diagnosis of clinically relevant disease [5].

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Table 1. Surveillance bias in scrutiny-dependent cancers.

Type of Cancer	Comment
Thyroid cancer	Thyroid cancer is particularly sensitive to the intensity of screening and clinical detection activities due to a large reservoir of indolent cancer subtypes, such as small papillary thyroid cancers [6,7].
Prostate cancer	The incidence of prostate cancer changed in many countries following changes in the proportion of people having PSA-based screening [8,9].
Melanoma	Routine screening is not recommended, but melanoma incidence is influenced by the frequency of skin checks [10].
Breast cancer	Breast cancer screening leads to some cases of overdiagnosis, influencing the analysis of incidence trends [11].
Kidney cancer	The incidence of kidney cancer is influenced by incidental detection due to increased utilization of imaging techniques [12].

2. Screening as a Cause of Cancer

Screening has a major influence on the incidence of some types of cancer. There are several examples of how surveillance bias due to screening activities hinders the analysis of cancer trends. For instance, in the United States, the incidence of prostate cancer sharply increased at the beginning of the 1990s following the introduction of prostate-specific, antigen-based screening; however, following the 2012 USPSTF recommendation against routine screening, the incidence has decreased (predominantly for early stage and low-grade cancers) [8,9]. However, these changes in incidence were not associated with concomitant changes in mortality. If surveillance was based only on the analysis of incidence, one could suspect that these trends are due to increased exposure to carcinogenic agents or unhealthy behaviors, yet they result from changes in early detection and screening activities over time.

Melanoma is also at risk of surveillance bias [6]. As for prostate cancer, mortality is less likely to bias the assessing of the true burden of this cancer. While melanoma incidence rates have risen in many countries, mortality has either remained stable or decreased in the past few years, likely due to new treatments for metastatic disease. This decoupling between incidence and mortality rates can be the sign of overdiagnosis. Recent estimates showed that roughly 60% of melanoma cases could be overdiagnosed in the United States, and similar proportions of overdiagnosis were reported in Australia [13,14]. Although routine screening is not recommended in most countries, melanoma incidence is influenced by the intensity of skin checks [10,15]. Due to differences in skin checks, the huge differences in incidence across countries do not reflect true differences in the risk of clinically meaningful melanoma—that is, cases that require treatment and that we aim to prevent.

3. Bias in Risk Factor Identification

Surveillance bias can also lead to a misinterpretation of potential risk factors for the occurrence of cancer since screening uptake, screening availability, access to health services, and care-seeking behaviors differ between population subgroups. A higher frequency of medical examinations in specific population groups can indeed lead to a higher probability of detecting scrutiny-dependent cancers, and this higher probability can be misinterpreted as higher disease risk [2]. For example, a higher risk of cancer in obese people could be due, on the one hand, to a genuine effect of obesity on cancer risk, or, on the other hand, the higher risk could be due to the fact that obesity is associated with more frequent medical inquiries and hence a greater probability of finding cancers [16]. Another example is the higher incidence of thyroid cancer in women compared to men. While one explanation is that higher estrogen levels in women may increase the risk of developing thyroid cancer, this difference in incidence may only be apparent [17] and could be the result of differences in care-seeking behavior or physicians' clinical practice. Actually, women may be more

likely to have their thyroids checked, and physicians may be more likely to investigate thyroid cancer in women.

A final example is the increased rates of breast cancer in women with a high socioeconomic status, which could be due to a higher screening uptake rather than a genuinely higher risk of breast cancer in women with a high socioeconomic status [2].

4. Prevention of Surveillance Bias

There are several strategies to cope with surveillance bias (Table 2). When looking at cancer trends, it is important to account for differences in screening and diagnostic strategies over time and to focus on indicators that are less susceptible to surveillance bias. Accounting for this bias is particularly important for the communication of information about cancer to the population because people are highly fearful of cancer and easily misinterpret changes in incidence. Moreover, we should also be aware that assessing the risk factors, such as socioeconomic determinants linked to health care use, for scrutiny-dependent cancers based on incidence data can be misleading.

Table 2. Four strategies to prevent surveillance bias in cancer burden assessment.

1)	Analyze trends accounting for screening and diagnostic processes.
2)	Focus on indicators that are less susceptible to surveillance bias, such as mortality trends or incidence trends of advanced cancer (stages 3 and 4).
3)	Prefer data specifically designed for surveillance purposes (e.g., data from cancer registries).
4)	Standardize the definition of the condition across surveillance systems and across time.

In conclusion, surveillance bias can influence cancer trends and the identification of cancer risk factors, hindering surveillance activities and potentially leading to the wrong public health actions. Being aware of this bias allows for a better assessment of the true evolution of the burden of cancer.

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Chapter 6.2 | Epidemiological signatures and surveillance bias in cancer

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Signatures épidémiologiques et biais de surveillance du cancer

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Le biais de surveillance se produit lorsque les variations d'incidence d'un cancer sont le résultat d'un changement dans les pratiques de dépistage ou de diagnostic plutôt que d'une augmentation de la fréquence réelle de ce cancer. Ce biais est lié au concept du surdiagnostic et peut être appréhendé en examinant les signatures épidémiologiques des cancers. Nous expliquons le concept de signature épidémiologique à l'aide des exemples du mélanome et des cancers du poumon et de la prostate. La prise en compte des biais de surveillance est particulièrement importante pour évaluer le fardeau réel du cancer et communiquer avec précision l'information sur le cancer à la population et aux décideurs.

Epidemiological signatures and surveillance bias in cancer

Surveillance bias occurs when variations in cancer incidence are the result of changes in screening or diagnostic practices rather than increases in the true occurrence of cancer. This bias is linked to the issue of overdiagnosis and can be apprehended by looking at epidemiological signatures of cancer. We explain the concept of epidemiological signatures using the examples of melanoma and of lung and prostate cancer. Accounting for surveillance bias is particularly important for assessing the true burden of cancer and for accurately communicating cancer information to the population and decision-makers.

INTRODUCTION

Évaluer le fardeau du cancer nécessite un système de surveillance sanitaire comprenant la collecte, l'analyse et l'interprétation de données épidémiologiques sur les cancers afin de produire des informations utiles pour guider les stratégies de prévention et la planification sanitaire. Mesurer correctement ce fardeau nécessite une bonne compréhension des indicateurs utilisés et des biais auxquels ils sont exposés.

L'incidence, la survie et la mortalité sont trois indicateurs utilisés fréquemment pour mesurer ce fardeau (**tableau 1**). L'incidence est le nombre (ou le taux, si rapporté à la taille de la population) de nouveaux cas diagnostiqués au sein d'une population au cours d'une période définie. Ainsi, en Suisse, en 2020, plus de 45 000 nouveaux cancers ont été diagnostiqués.[1] Le nombre de cas augmente régulièrement en raison de la croissance démographique et du vieillissement. Le taux d'incidence standardisé pour l'âge, c'est à dire le nombre de cas rapporté à la population et normalisé selon l'âge, est demeurée relativement stable.[1] La survie est le pourcentage de patients atteints de cancer toujours vivants après une période définie suivant le diagnostic, le plus souvent de 5 ans. En Suisse, le taux de survie à 5 ans standardisé pour l'âge est passé de 54 à 62 % entre 2000-2004 et 2016-2020.[2] Un autre indicateur est la mortalité par cancer, c'est-à-dire nombre (ou le taux, si rapporté à la taille de la population) de décès dus au cancer d'une population au cours d'une période définie. En 2020, 17 000 personnes sont mortes d'un cancer en Suisse.[1] Le nombre de décès a augmenté en raison de la croissance démographique et du vieillissement, mais le taux de mortalité standardisé, c'est dire le nombre de cas rapporté à la population et normalisé selon l'âge, a diminué de 40% en Suisse entre 1981-1985 et 2016-2020.[2]

Bien que les informations fournies par ces indicateurs semblent simples à interpréter, l'incidence et la survie peuvent être influencées par les pratiques de dépistage et de diagnostic. Cet article vise à expliquer comment les pratiques de dépistage et de diagnostic peuvent biaiser la surveillance du cancer et comment appréhender ce biais en utilisant le concept relativement nouveau de signature épidémiologique du cancer.

DÉPISTAGE ET SURDIAGNOSTIC DU CANCER

L'incidence et la survie peuvent fournir des informations biaisées sur le fardeau réel de certains types de cancers que l'on appelle «scrutiny-dependent cancers» car ils sont influencés par les activités de dépistage et peuvent être surdiagnostiqués. Le dépistage est effectué chez des personnes apparemment en bonne santé afin de détecter le cancer à un stade précoce, de permettre un traitement précoce et avec pour but une réduction des complications et de la mortalité par cancer. Toutefois, celui-ci peut également détecter des cancers qui n'auraient jamais été cliniquement apparents et n'auraient pas nécessité de soins médicaux s'ils n'avaient pas été détectés (**figure 1**); ces cas sont surdiagnostiqués (**encadré 1**).[3] Au niveau individuel, le surdiagnostic entraîne des traitements inutiles. Au niveau de la population, il gonfle artificiellement à la fois la survie et l'incidence et entraîne un biais de surveillance.[4]

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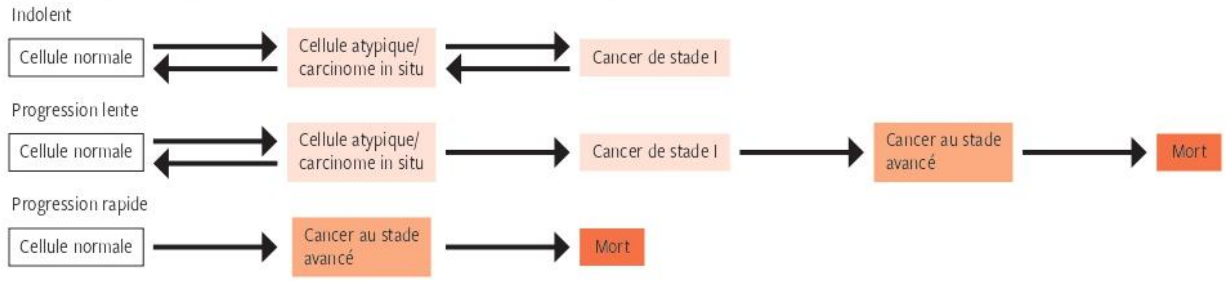
TABLEAU 1 Indicateurs utilisés pour la surveillance du cancer

Indicateur	Définition	Points forts et limites
Incidence	Le taux de nouveaux cas de cancer diagnostiqués au sein d'une population spécifique à risque au cours d'une période définie, généralement exprimé en nombre de cas pour 100000 personnes par an et ajusté en fonction de l'âge (par standardisation)	L'incidence de certains cancers est influencée par l'intensité et les modalités de détection. Par exemple, un nombre plus élevé de cancers détectés par les activités de dépistage peut donner l'impression d'une augmentation du risque du cancer même si cela est dû à des cancers surdiagnostiqués. Si on se base uniquement sur l'incidence, cela conduit à un biais de surveillance
Survie	Pourcentage de personnes survivant au cancer pendant une période définie après le diagnostic, souvent exprimé en pourcentage après un certain intervalle de temps (par exemple, taux de survie à 5 ans)	La survie peut être influencée par l'intensité et les modalités de détection du cancer, par exemple, la détection précoce par dépistage peut entraîner des temps de survie apparente plus longs que les cas diagnostiqués après l'apparition des symptômes (length time bias: biais de devancement)[14]
Mortalité	Le taux de mortalité par cancer au sein d'une population spécifique au cours d'une période définie, généralement exprimé en nombre de décès pour 100000 personnes par an et ajusté en fonction de l'âge (par standardisation)	Comme le taux de mortalité n'est pas influencé directement par l'intensité et les modalités de détection, il offre des informations plus simples à interpréter sur le fardeau du cancer. Ainsi, une baisse de la mortalité est le signe d'une diminution du risque de cancer, d'une amélioration du traitement du cancer ou de l'effet des activités de dépistage

FIG 1 Différents types de progression du cancer

Les cancers n'ont pas tous le même type de progression. La progression indolente indique que le cancer passe de l'atypie ou de la maladie in situ au cancer à un stade précoce sans évoluer vers une maladie cliniquement sévère ou causer la mort. Une progression lente signifie que le cancer progresse lentement de l'atypie ou de la maladie à un stade précoce (en orange clair), puis évolue lentement à un stade avancé (en orange foncé) jusqu'à la mort (en rouge). Une progression rapide signifie que le cancer progresse rapidement des stades précoces aux stades avancés et à la mort. Le surdiagnostic est susceptible de se produire lorsque le cancer a une évolution indolente ou lente.[15] Les dépistages peuvent être utiles pour les cancers à progression lente ; ils sont le plus souvent inutiles en cas de progression rapide et créent un surdiagnostic pour les cancers indolents.



Encadré 1. Qu'est-ce que le surdiagnostic ?

Le surdiagnostic fait référence au diagnostic, chez des personnes asymptomatiques, d'une véritable anomalie mais ne présentant pas de risque pour la santé au cours de leur vie restante.3 Le dépistage de certains cancers est une cause de surdiagnostic. D'autres causes sont la sensibilité accrue des tests diagnostiques permettant de trouver des anomalies auparavant non détectées, les résultats fortuits d'examens de laboratoire ou radiologiques (par exemple, des masses rénales ou surrénales accidentelles trouvées sur les CT abdominaux), ou l'élargissement des critères diagnostiques pour identifier les conditions nécessitant une intervention. Le surdiagnostic conduit à un surtraitement, sans aucun bénéfice potentiel pour le patient. Il n'est pas une erreur de diagnostic ni un résultat faussement positif (test positif en l'absence d'anomalie réelle).

BIAIS DE SURVEILLANCE

Le biais de surveillance se produit lorsque des différences dans la modalité de détection des « scrutiny-dependent cancers » entraînent des différences dans l'incidence pouvant être attribuées à tort à des changements dans le risque réel de ces cancers. Par exemple, l'introduction d'un nouveau test de dépistage ou de diagnostic peut gonfler artificiellement l'incidence. Si la surveillance est basée uniquement sur l'analyse de l'incidence sans tenir compte de l'introduction du nouveau test, l'augmentation de l'incidence pourrait être attribuée à tort à une exposition accrue à des agents cancérigènes ou à des comportements malsains. Par exemple, les dépistages mis en place au Japon à la suite de l'accident nucléaire de Fukushima ont permis la détection de nombreux cancers de la thyroïde, notamment chez les enfants, suggérant que cet incident a eu un impact majeur sur le nombre de cancer. Cependant, la plupart des cas n'étaient pas directement attribuables à l'exposition aux rayonnements, comme en témoigne le court laps de temps entre l'accident et la détection ainsi que l'absence de corrélation entre l'incidence régionale et les niveaux de rayonnement régionaux.[5] Il est probable qu'une part importante de ces cas n'auraient jamais été diagnostiqués s'ils n'avaient pas été dépistés.

SIGNATURE ÉPIDÉMIOLOGIQUE DES CANCERS

La signature épidémiologique des cancers est utile pour comprendre leurs tendances dans la population et mettre en exergue les situations de biais de surveillance.[6] Nous illustrons ici les signatures épidémiologiques du mélanome et des cancers du poumon et de la prostate en Suisse en utilisant des

FIG 2 **Signature épidémiologique du mélanome en Suisse**

A. Évolution des taux d'incidence et de mortalité standardisés pour l'âge, 1981-2020. **B.** Évolution relative des taux incidence et de mortalité par rapport à la période 1981-1985.

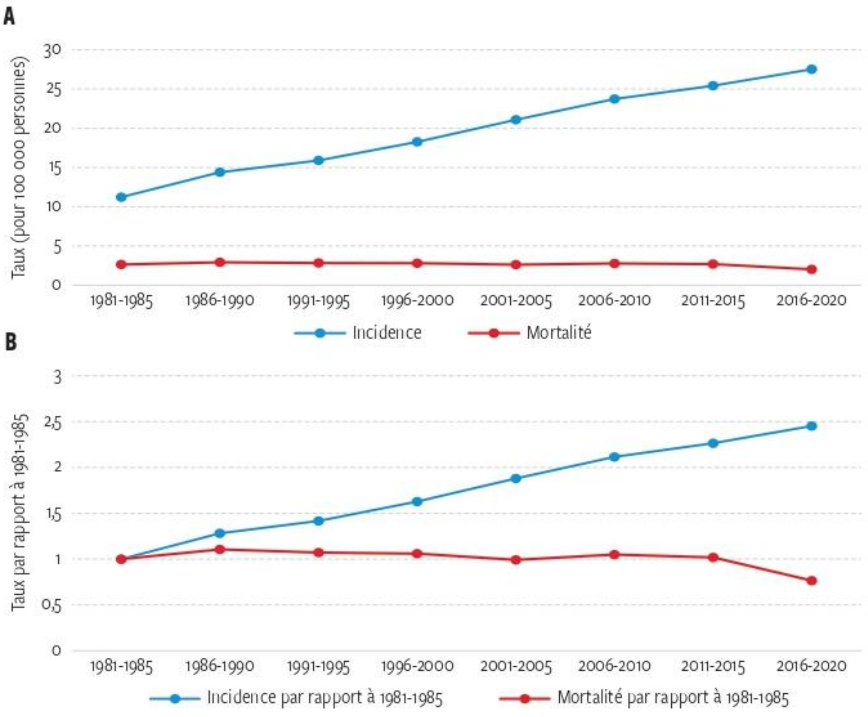
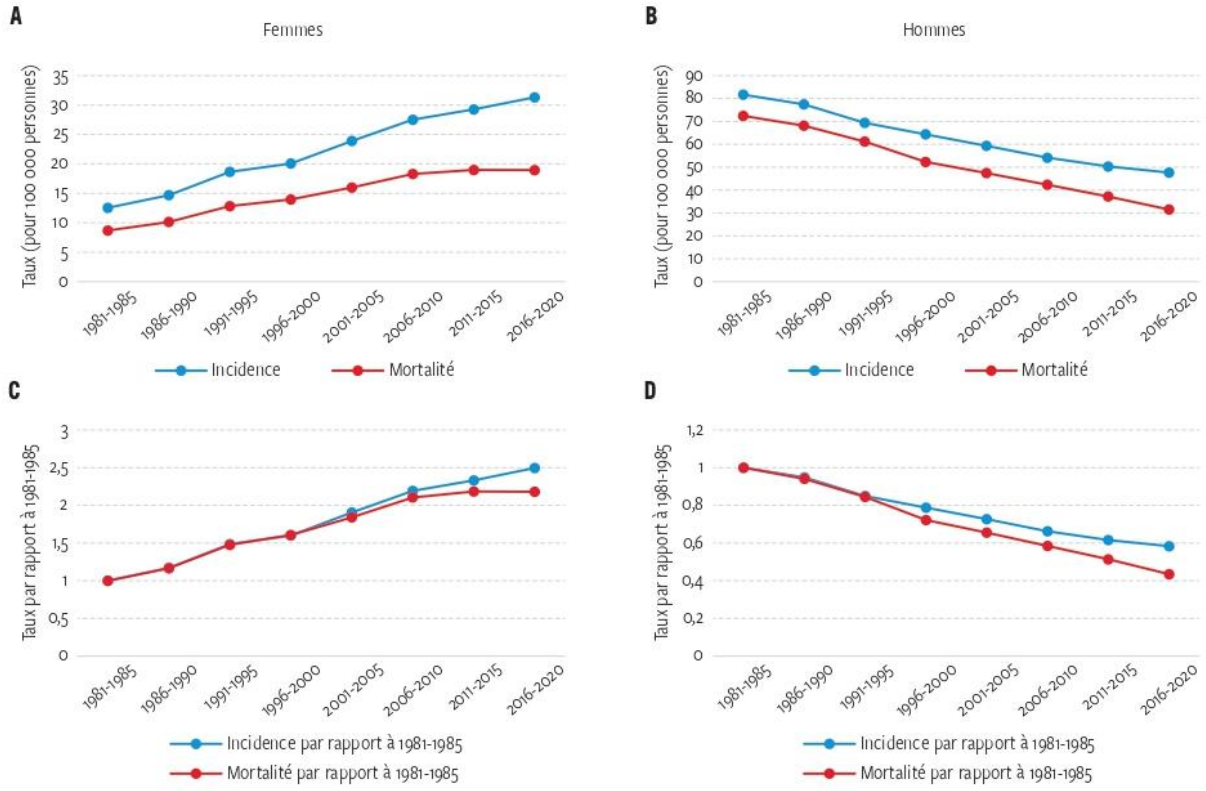


FIG 3 **Signature épidémiologique des cancers du poumon en Suisse**

A. et **B.** Évolution des taux d'incidence et de mortalité standardisés pour l'âge, chez les femmes et les hommes, 1981-2020. **C.** et **D.** Évolution relative des taux d'incidence et de mortalité par rapport à la période 1981-1985, chez les femmes et les hommes.



données extraites de l'Institut national pour l'épidémiologie et l'enregistrement du cancer (NICER). Elles sont constituées de l'incidence et de la mortalité normalisées selon l'âge ainsi que de l'évolution de ces taux au fil du temps par rapport à une période de référence (1981-1985).

Mélanome

Le mélanome a une signature épidémiologique fortement influencée par les pratiques de dépistage et de diagnostic. Son incidence a augmenté au fil du temps, tandis que la mortalité est demeurée relativement stable ou a légèrement diminué au cours des dernières années grâce aux nouveaux traitements (**figure 2**). Il est probable que l'incidence ait augmenté parce qu'un nombre croissant de cas de mélanome indolents sont diagnostiqués et c'est pourquoi cette augmentation n'entraîne pas une hausse de la mortalité.[7] On pourrait supposer que la mortalité n'a pas augmenté au fil du temps car les cancers diagnostiqués précocement sont traités plus tôt, et aussi par l'amélioration des traitements. Toutefois, cela impliquerait que ces traitements auraient permis de contrebalancer parfaitement l'augmentation de l'incidence, ce qui est peu réaliste. Il est plus probable que l'incidence du mélanome ait été influencée par la fréquence élevée des examens cutanés, bien que le dépistage systématique ne soit pas recommandé.[8,9] Si l'on ne tient pas compte de la fréquence des examens et du surdiagnostic, la surveillance est biaisée à la hausse.

Cancer du poumon

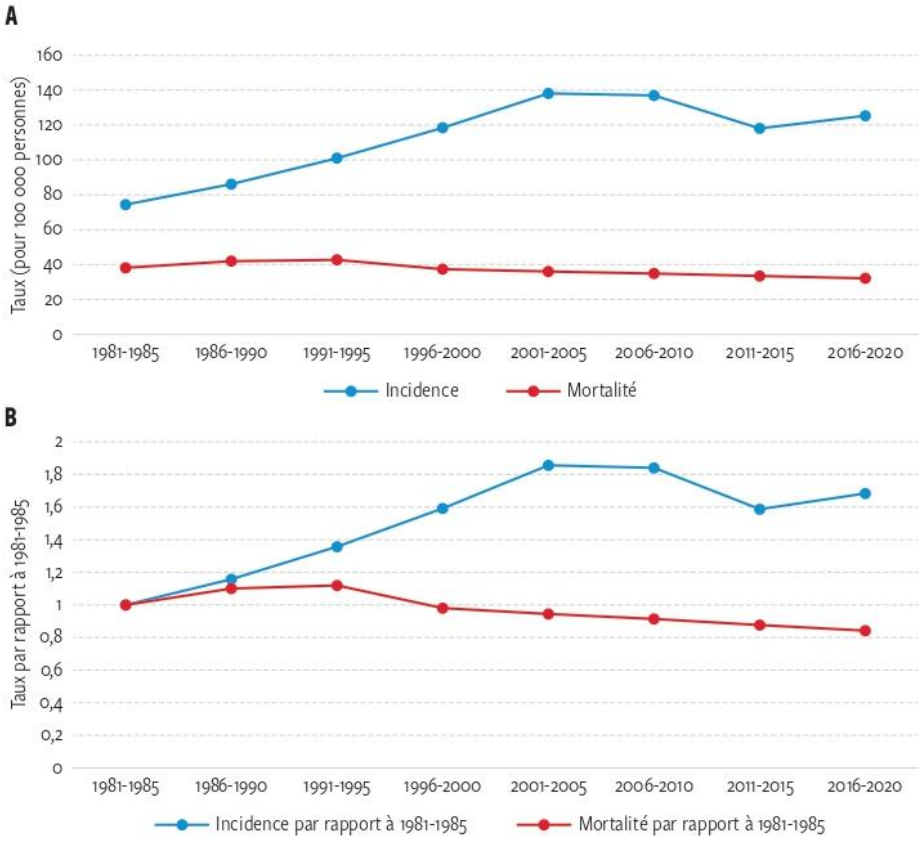
Le cancer du poumon a une signature épidémiologique n'étant que peu, voire pas, influencée par les pratiques de dépistage et de diagnostic. L'évolution de son incidence et de sa mortalité suit l'évolution de la prévalence du tabagisme dans la population, avec un décalage de 20 à 30 ans. Ainsi, entre 1985 et 2020, l'incidence et la mortalité ont diminué chez les hommes; chez les femmes, elles ont augmenté (**figure 3**). La différence selon le sexe est due à des tendances historiques différentes en matière de tabagisme entre les hommes et les femmes, et non pas à des différences dans les modalités de détection.[10] Les changements dans l'incidence reflètent les modifications réelles dans la survenue du cancer du poumon dues à des changements dans les habitudes tabagiques, avec la mortalité suivant l'incidence. Avec l'avènement du dépistage du cancer du poumon, cette signature pourrait toutefois changer.

Cancer de la prostate

La signature du cancer de la prostate est complexe, en partie influencée par les pratiques de dépistage et de diagnostic, l'incidence évoluant rapidement au fil du temps et la mortalité diminuant constamment (**figure 4**). En Suisse, l'incidence du cancer de la prostate a d'abord fortement augmenté, puis diminué, et ces dernières années, elle augmente à nouveau.

FIG 4 **Signature épidémiologique du cancer de la prostate en Suisse**

A. Évolution des taux d'incidence et de mortalité standardisés par âge, chez les hommes, 1981-2020. **B.** Évolution relative des taux d'incidence et de mortalité par rapport à 1981-1985.



Ces variations sont liées aux changements dans les pratiques de dépistage. L'incidence a augmenté après l'introduction du test PSA dans les années 1990.[11] Plus tard, lorsque certaines études contrôlées randomisées n'avaient pas encore montré de réduction de la mortalité par cancer de la prostate,[12] le dépistage a été moins encouragé et l'incidence a alors diminué.[13] La mortalité par cancer de la prostate a légèrement baissé au fil du temps, reflétant les améliorations dues aux nouveaux traitements et au dépistage.

COMMENT FAIRE FACE AU BIAIS DE SURVEILLANCE DU CANCER?

Les signatures épidémiologiques sont puissantes pour décrire et comprendre les tendances du cancer dans la population, en tenant compte des pratiques de dépistage et de diagnostic. Elles permettent également d'appréhender le biais de surveillance du cancer. Si l'on ne tient pas compte de l'effet des pratiques de dépistage et de diagnostic sur l'incidence, le fardeau réel de certains types de cancer est mal compris et cela peut conduire à prendre de mauvaises mesures de santé publique ou de planification. Pour éviter d'être induit en erreur par le biais de surveillance, une stratégie consiste à se concentrer sur la mortalité et l'incidence des cancers à stade avancé, ayant tendance à être moins biaisés par le dépistage et le surdiagnostic. Il faut aussi tenir compte des pratiques, historiquement et localement, de dépistage et de diagnostic.

CONCLUSION

L'utilisation des signatures épidémiologiques aide à mieux comprendre les données de surveillance du cancer, le biais de surveillance, le surdiagnostic et l'impact de la prévention et du traitement du cancer à l'échelle de la population. La prise en compte des biais de surveillance est particulièrement importante pour évaluer le fardeau réel du cancer et communiquer avec précision l'information sur le cancer à la population et aux décideurs.

Conflit d'intérêts: Les auteurs n'ont déclaré aucun conflit d'intérêts en relation avec cet article.

IMPLICATIONS PRATIQUES

- Les activités de dépistage et diagnostic peuvent fausser les données sur le cancer en raison du surdiagnostic, entraînant un biais de surveillance.
- L'utilisation de signatures épidémiologiques permet d'identifier les biais et de distinguer les changements réels dans le risque de cancer et les résultats associés, évitant ainsi une mauvaise interprétation du fardeau du cancer.
- Les taux de mortalité et de cancer à un stade avancé sont souvent plus faciles à interpréter pour évaluer le fardeau réel du cancer.

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* **à lire**
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Chapter 6.3 | Assessing the magnitude of surveillance bias in prostate cancer, melanoma and lung cancer

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Assessing the magnitude of surveillance bias in prostate cancer, melanoma and lung cancer

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ABSTRACT

Background. Changes in cancer incidence can result from changes in screening and diagnostic practices rather than changes in the true occurrence of cancer, leading to surveillance bias. Quantitative approaches to estimate this bias are lacking.

Objectives. To develop an approach to estimate surveillance bias in prostate cancer, melanoma, and lung cancer.

Methods. We used population-based data from Swiss cancer registries on incidence and mortality from 1989 to 2021. Age-standardized incidence was analyzed using Joinpoint regression to identify periods with distinct trends. The same periods were used to segment mortality. The magnitude of surveillance bias was assessed for each period by computing the natural logarithm of the ratio (Ln-ratio) between the mean annual changes in age-standardized incidence and mortality rates, since mortality is less affected by screening and diagnostic practices than incidence. Higher Ln-ratios indicated greater bias. Analyses were also conducted by cancer stage.

Results. Surveillance bias for prostate cancer was moderate in 1989-2004 (Ln-ratio = 1.6), low in 2004-2011 (Ln-ratio = 0.6), and high in 2011-2014 and 2014-2021 (Ln-ratio = 2.4 and 1.9). For melanoma, the bias was high across the entire study period (Ln-ratio = 2.8). For lung cancer, it was moderate over the entire study period (Ln-ratio = 1.1), and lower than other cancers. In stage-specific analyses, surveillance bias was greater for early-stage than advanced-stage cancers.

Conclusions. We estimated surveillance bias using a simple approach that can be used in daily monitoring activities. Further studies are needed to refine these estimates.

BACKGROUND

Cancer incidence trends, namely age-standardized rates, are widely used to describe and monitor changes in the risk of cancer in populations over time. Age-standardization adjust for differences in age distribution and enables comparisons of risk across populations and periods (1). However, for scrutiny-dependent cancers like prostate cancer or melanoma (2), even after adjusting for age, incidence trends do not reflect changes in cancer risk because they are influenced by changes in screening and detection practices (2). Such changes can indeed substantially increase or decrease incidence, without any actual change in the risk of developing cancer. Failing to consider the effect of changes in cancer screening and diagnostic practices leads to surveillance bias (3).

Surveillance bias is defined as a bias that occurs when changes across time, settings, or populations in the detection of cancers lead to changes in incidence, which can be wrongly attributed to changes in the actual risk of these cancers (4). It is suspected if there is a marked divergence between incidence and mortality trends, or between trends in early and advanced cancer stages, since mortality and incidence of advanced-stage cancers are less affected by changes in detection practices (4, 5). These descriptive patterns are used to visually suggest the presence of surveillance bias, but there are currently no established methods to quantitatively estimate the magnitude of the bias. Quantitative rather than visual assessment would reduce subjectivity, allow comparisons, improve transparency and reproducibility, and support clearer communication and interpretation of incidence trends by epidemiologists, decision-makers, and the public.

We therefore attempted to develop a method to estimate the magnitude of surveillance bias of prostate cancer, melanoma, and lung cancer. We selected prostate cancer and melanoma because they are scrutiny-dependent cancers for which screening and diagnostic practices have changed considerably over time (2, 5-9). Lung cancer was chosen as a comparator because it is not considered scrutiny-dependent (5).

METHODS

We conducted a population-based study using aggregated data from cancer registries in Switzerland on the incidence and mortality of prostate cancer, melanoma, and lung cancer.

In Switzerland, all new cancer cases, including information on stage at diagnosis, are systematically collected by population-based regional cancer registries and then aggregated by the National Institute for Cancer Epidemiology and Registration (NICER) (10). Cancer registration coverage has steadily increased over time, reaching approximately 97% of the Swiss population in 2021. For years in which coverage was not nationwide, NICER extrapolated data to provide national estimates (10). Primary tumors are defined according to the rules of the International Association of Cancer Registries (IACR) and the European Network of Cancer Registries (ENCR). For our analyses, we included all cases of prostate cancer (International Classification of Diseases for Oncology, 3rd edition [ICD-O-

3]: C61), melanoma (C43) and cancers of the lung, bronchus, and trachea (C33-34) recorded in the Swiss cancer registries between 1989 and 2021 (11). Cancer mortality data included deaths attributed to prostate cancer, melanoma or cancers of the lung, bronchus, and trachea, according to the Federal Statistical Office coding of causes of death. Before 1995, an earlier revision of the ICD was used, and cancer was listed as the cause of death whenever the word "tumor" appeared, either as the primary or associated cause, except when conditions such as accidents, poisoning, trauma, or influenza were also reported on the certificate. Cancer mortality rates before 1995 may therefore be overestimated and should be interpreted with caution (12).

We described trends in age-standardized incidence and mortality rates over time, as well as incidence trends by stage. Age-standardized rates were calculated using the direct method, using the 1976 European standard population (12).

To estimate surveillance bias, we followed three steps. First, we used Joinpoint regression (Joinpoint Regression Statistical Software version 5.2.0; Surveillance Research Program, National Cancer Institute, Bethesda, MD) to analyze variations in incidence trends and to identify inflection points that segment the time series into periods with distinct trends. Second, for each period, we calculated the absolute difference and the ratio between the mean annual change in age-standardized incidence and the corresponding mean annual change in age-standardized mortality. Surveillance bias was considered to be present when incidence trends diverged from mortality trends, i.e., the further the ratio was from 1, the greater the bias. Third, we applied a natural logarithm transformation to the absolute value of the ratio (hereafter referred to as "Ln-ratio") to account for the wide range of ratio values and express all values as positive numbers. The "Ln-ratio" represented our quantitative estimation of surveillance bias. For the interpretation, we defined three cut-offs to categorize it into low, moderate and high bias. An "Ln-ratio" less than or equal to 0.7 corresponded to low bias, indicating a change in incidence at most 2 times as fast or as slow as mortality. An "Ln-ratio" between 0.7 and 1.6 corresponded to moderate bias, indicating a change in incidence between 2 and 5 times as fast or as slow as mortality. An "Ln-ratio" above 1.6 corresponded to high bias, indicating a change in incidence more than 5 times as fast or as slow as mortality (Table 1).

The same analyses were conducted by cancer stage at diagnosis, categorized according to the Union for International Cancer Control (UICC; Stage I, II, III and IV) (13). Analyses by stage were performed only from 2010 onward, as data on stage at diagnosis was available starting that year. For this analysis, we computed the Ln-ratio between the mean annual change in age-standardized stage I, II and III incidence and the corresponding mean annual change in age-standardized stage IV incidence, under the assumption that incidence of Stage IV cancers is less influenced by screening than incidence of stage I, II and III cancers.

RESULTS

Main analyses

For prostate cancer, three inflection points in the age-standardized incidence trend were identified, segmenting it into four periods: 1989–2004, 2004–2011, 2011–2014, and 2014–2021 (Figure 1 and Supplementary Table S1). Age-standardized incidence and comparison with age-standardized mortality (difference, ratio, and Ln-ratio) for each period are presented in Table 2. Age-standardized incidence of prostate cancer increased from 1989 to 2004, declined between 2004 and 2011, and dropped more sharply from 2011 to 2014. From 2014 to 2021, the incidence rose again. Mortality consistently decreased over the entire period. Surveillance bias was moderate between 1989 and 2004 (Ln-ratio: 1.6), low between 2004 and 2011 (Ln-ratio: 0.6) and high from 2011 onwards (Ln-ratio: 2.4 between 2011–2014 and Ln-ratio: 1.9 between 2014-2021).

For melanoma, one inflection point was identified, segmenting the age-standardized incidence trend into two periods: 1989–2003 and 2003–2021 (Figure 2 and Supplementary Table S1). Age-standardized incidence and comparison with age-standardized mortality (difference, ratio, and Ln-ratio) are presented in Table 2. Age-standardized incidence of melanoma increased from 1989 to 2003. Between 2003 and 2021, the growth in incidence slowed but continued. Mortality remained relatively stable over both periods. Surveillance bias was high from 1989 to 2003 (Ln-ratio: 2.8) and remained high between 2003 and 2021 (Ln-ratio: 2.8).

For lung cancer, no inflection points in the age-standardized incidence trend were identified, indicating a continuous trend from 1989 to 2021 (Figure 3 and summarized in Supplementary Table S1). Age-standardized incidence and comparison with age-standardized mortality (difference, ratio, and Ln-ratio) are presented in Table 2. Age-standardized incidence showed a slight decline between 1989 and 2021, and mortality also decreased. Surveillance bias was moderate (Ln-ratio: 1.1) throughout the entire period.

Stage specific analyses

The results of the Joinpoint regression stratified by stage are shown in supplemental Figures S1-S12. Overall, surveillance bias tended to be greater for cancers diagnosed at lower stages (Stage I and II) than at higher stages (Stage III), across the three cancer types.

For prostate cancer (Table 3), Stage I incidence declined from 2010 to 2015 and then increased from 2015 to 2021. Stage II incidence showed a decrease between 2010 and 2014, followed by an increase from 2014 to 2017 and a smaller increase between 2017 and 2021. For Stage III, incidence decreased from 2010 to 2014 before slightly increasing from 2014 to 2021. Stage IV incidence slightly increased from 2010 to 2014 and increased from 2014 to 2021. Surveillance bias for Stage I was high between 2010 and 2015 and moderate from 2015 to 2021. Stage II had high surveillance bias between 2010 and 2014 and between 2014 and 2017 and low between 2017 and 2021. For Stage III, surveillance bias was moderate between 2010 and 2014 and low from 2014 to 2021.

For melanoma (Table 4), Stage I incidence increased between 2010 and 2021. Stage II incidence remained relatively stable between 2010 and 2021. For Stage III, incidence showed a modest increase between 2010 and 2021, and, for stage IV, incidence remained stable from 2010 to 2019 and increased modestly from 2019 to 2021. Surveillance bias was high for all stages over the 2010-2021 period.

For lung cancer (Table 5) Stage I incidence increased between 2010 and 2021. For Stage II, incidence increased slightly between 2010 and 2013, then declined between 2013 and 2019, with a further decrease from 2019 to 2021. For Stage III and Stage IV, incidence remained stable between 2010 and 2021. Surveillance bias for Stage I was high over the 2010–2021 period. For Stage II, surveillance bias was low between 2010 and 2013 and between 2013 and 2019, and moderate from 2019 to 2021. For Stage III, surveillance bias was low between 2010 and 2021.

DISCUSSION

To our knowledge, this is the first attempt to quantitatively assess surveillance bias of various cancers. Using nationwide population-based data, we found that surveillance bias of prostate cancer changed substantially since 1989, being moderate between 1989 and 2004, low between 2004 and 2011, and high between 2011 and 2021 in Switzerland. The bias was high for melanoma across the entire study period 1989–2021. For lung cancer, surveillance bias was moderate, and consistently lower compared to the other two cancers. In stage-specific analyses, we showed that surveillance bias tended to be greater for cancers diagnosed at earlier stages than for those diagnosed at advanced stages.

The observed patterns of surveillance bias are consistent with changes in incidence due to changes in screening and diagnostic practices in Switzerland. For prostate cancer, the initial increase in the incidence in the 1990s coincided with the introduction of PSA testing. After 2003, a decline occurred, coinciding with the retrenchment of PSA testing, and incidence trends aligned with mortality trends, resulting in a low degree of surveillance bias. A more pronounced decrease was observed after 2011, following updated guidelines that discouraged PSA use, notably guidelines from the Swiss Medical Board (14). More recently, incidence has started to rise again. For melanoma, despite no changes in screening recommendations, early diagnosis has probably increased over time in Switzerland, influencing incidence and resulting in consistently high surveillance bias (15, 16). For lung cancer, surveillance bias was lower than for the other two cancers because incidence trends largely reflect smoking patterns rather than changes in detection practices (4). These smoking-related patterns are clear when stratifying by sex, with both incidence and mortality declining among men and increasing among women (4).

Several factors beyond screening influence both incidence and mortality trends and have effects on our estimates of the degree of surveillance bias. In prostate cancer, for instance, diagnostic and therapeutic practices have evolved significantly, with increasing use of magnetic resonance imaging, active surveillance for low-risk cases, and, more recently, imaging modalities such as prostate-specific membrane antigen positron emission tomography and genetic

testing (6, 17, 18). Similarly, the diagnostic landscape for melanoma is changing, with advances in non-invasive imaging and molecular techniques such as fluorescence in situ hybridization, comparative genomic hybridization, sequencing, mass spectrometry, and immunohistochemistry being increasingly used to refine diagnosis and classification (19, 20). These developments can influence detection rates independently of any true change in the risk of developing the disease, and their implementation should therefore be taken into account to correctly interpret trends and surveillance bias estimates. Moreover, new technologies such as artificial intelligence tools are likely to further change strategies for the detection and management of cancer in the near future, highlighting the need for new estimates in the future (21, 22). For instance, lung cancer detection may evolve in the coming years: although no national lung cancer screening program currently exists in Switzerland, from 2024 a pilot project is underway in the Canton of Vaud, and its expansion may impact future incidence rates (23-25).

This study has several limitations. First, we calculated surveillance bias by comparing incidence and mortality changes over the same periods, even though changes in incidence may affect mortality after a time lag of several years. Not accounting for this delay may lead to a misinterpretation of the relationship between the two trends, potentially biasing estimates of surveillance bias. Second, our approach relies on the assumption that incidence and mortality should move in parallel, meaning that an increase or decrease in true cancer occurrence should result in a proportional change in mortality, unless biased by changes in detection intensity. The same assumption holds for surveillance bias estimates based on the divergence between early- and advanced-stages. However, a major limitation of our method is that this assumption does not hold in all cases, as mortality trends are influenced by factors such as improvements in treatment. For instance, if incidence remains stable while mortality declines due to better therapies, the two trends will diverge, but this does not indicate surveillance bias. This may explain the moderate estimated bias observed for lung cancer, where mortality declines reflect improvements in treatment. However, when incidence is changing rapidly and substantially, the divergence from mortality, whatever its trends, suggests surveillance bias. The same is true when early-stage incidence changes rapidly and substantially without substantial changes in advanced-stage incidence (4) . Third, the method used in this study is based on a relative measure, the Ln-ratio, that is sensitive to small annual changes. When variations in mortality (or advanced-stage incidence for stage-specific analyses) are very small, the ratio becomes very high. For example, in melanoma, the Ln-ratio was elevated despite relatively small absolute differences between incidence and mortality trends (e.g., differences of 0.4 and 0.7 per 100’000). In contrast, for prostate cancer, the absolute differences were sometimes much larger, even when the estimated bias was lower.

One strength of this study is that it is based on population-level data spanning a long observation period, during which substantial changes in screening and diagnostic practices occurred. It also includes multiple cancer types, allowing for comparisons across different contexts. Another important strength is that it provides a simple quantitative approach that can be used in daily monitoring activities and that goes beyond the graphical and descriptive analyses typically used to illustrate the presence of surveillance bias. It is worth noting that some

approaches have already been developed to adjust incidence trends for changes in screening and detection practices, or to distinguish temporal patterns that may reflect the impact of screening/diagnostic practices from those potentially related to underlying risk factors on cancer incidence (26, 27). For example, some models use secular trends that reflect incidence in the absence of screening (28), others use changes in the distribution of cancer stages over time, assuming that without changes in detection practices the stage distribution remains approximately constant (29), and age–period–cohort analyses can be used to assess the effects of changes in screening and diagnostic practices on incidence (27). However, these methods do not provide direct estimates of the magnitude of surveillance bias. Although not precise and hindered by several limitations, our method could be a starting point for estimating potential surveillance bias and offers a practical framework that can be adapted and expanded using more sophisticated data and modeling strategies.

CONCLUSION

This study provided quantitative estimates of surveillance bias for three different cancers. Although the method used to assess the magnitude of the bias has several limitations, it represents an initial and exploratory step toward more precise methods for quantifying surveillance bias. Finding a way to quantitatively assess surveillance bias and integrating this information into the interpretation of incidence trends is important for correctly understanding cancer incidence and for guiding public health decisions.

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TABLES AND FIGURES

Table 1: Thresholds to define low, moderate and high bias and examples for interpreting surveillance bias estimates. Low bias (light red) indicates that incidence changes at most 2 times as fast or as slow as mortality (or stage IV incidence in stage specific analyses); moderate bias (medium red), between 2 and 5 times; high bias (red), more than 5 times.

Ln-ratio ≤ 0.7	**Low bias**
0.7 < Ln-ratio ≤ 1.6	**Moderate bias**
Ln-ratio > 1.6	**High bias**

Ratio between mean annual change in age-standardized incidence and mortality	Ln-Ratio	Interpretation
-7	1,9	Incidence decreasing 7× faster than mortality
-5	1.6	Incidence decreasing 5× faster than mortality
-3	1.1	Incidence decreasing 3× faster than mortality
-2	0.7	Incidence decreasing 2× faster than mortality
-1	0	Incidence and mortality changing at same rate
1	0	Incidence and mortality changing at same rate
2	0.7	Incidence increasing 2× faster than mortality
3	1.1	Incidence increasing 3× faster than mortality
5	1.6	Incidence increasing 5× faster than mortality
7	1,9	Incidence increasing 7× faster than mortality

Table 2. Age-standardized incidence of prostate cancer, melanoma and lung cancer and comparison with age-standardized mortality (difference, ratio, and Ln-ratio) by period, 1989–2021

Ln ratio ≤ 0.7	**Low bias**
0.7 < Ln ratio ≤ 1.6	**Moderate bias**
Ln ratio > 1.6	**High bias**

Period*	Absolute change in age-standardized incidence (per 100'000)	Absolute change in age-standardized mortality (per 100'000)	Mean annual change in age-standardized incidence (per 100'000)	Mean annual change in age-standardized mortality (per 100'000)	Difference between the mean annual change in age-standardized incidence and mortality	Ratio	Ln ratio
Prostate cancer							
1989-2004	54.4	-11.5	3.6	-0.8	4.4	-4.7	1.6
2004-2011	-7.2	-4.1	-1.0	-0.6	-0.5	1.8	0.6
2011-2014	-26.9	-2.5	-9.0	-0.8	-8.1	10.8	2.4
2014-2021	33.1	-4.9	4.7	-0.7	5.4	-6.9	1.9
Melanoma							
1989-2003	9.4	-0.5	0.7	-0.04	0.7	-16.8	2.8
2003-2021	6.2	-0.4	0.3	-0.02	0.4	-17.0	2.8
Lung cancer							
1989-2021	-3.9	-11.2	-0.1	-0.4	-3.9	0.3	1.1

* Periods were defined analyzing incidence trends using Joinpoint regression; the same periods were used for mortality

Table 3. Age-standardized prostate cancer incidence by stage and comparison with stage IV incidence (difference, ratio, and Ln-ratio) by period, 2010–2021

Ln ratio ≤ 0.7	**Low bias**
0.7 < Ln ratio ≤ 1.6	**Moderate bias**
Ln ratio > 1.6	**High bias**

Period*	Absolute change in age-standardized incidence (per 100'000)	Absolute change in age-standardized stage IV incidence (per 100'000)	Mean annual change in age-standardized incidence (per 100'000)	Mean annual change in age-standardized stage IV incidence (per 100'000)	Difference between the mean annual change in age-standardized incidence and stage IV incidence	Ratio	Ln ratio
Stage I							
2010-2015	-11.8	2.2	-2.4	0.4	-2.8	-5.4	1.7
2015-2021	14.1	6.2	2.4	1.0	1.3	2.3	0.8
Stage II							
2010-2014	-8.5	1.0	-2.1	0.3	-2.4	-8.5	2.1
2014-2017	13.6	1.6	4.5	0.5	4.0	8.5	2.1
2017-2021	5.7	5.8	1.4	1.5	-0.03	1.0	0.02
Stage III							
2010-2014	-4.6	1.0	-1.2	0.3	-1.4	4.6	1.5
2014-2021	6.5	7.4	0.9	1.1	-0.1	0.9	0.1
Stage IV							
2010-2014	1.0	1.0	0.3	0.3	NA	NA	Ref
2014-2021	7.4	7.4	1.1	1.1	NA	NA	Ref

* Periods were defined analyzing incidence trends for each stage using Joinpoint regression; the same periods were used for Stage IV incidence

Table 4. Age-standardized melanoma incidence by stage and comparison with stage IV incidence (difference, ratio, and Ln-ratio) by period, 2010–2021

Ln ratio ≤ 0.7	**Low bias**
0.7 < Ln ratio ≤ 1.6	**Moderate bias**
Ln ratio > 1.6	**High bias**

Period*	Absolute change in age-standardized incidence (per 100'000)	Absolute change in age-standardized stage IV incidence (per 100'000)	Mean annual change in age-standardized incidence (per 100'000)	Mean annual change in age-standardized stage IV incidence (per 100'000)	Difference between the mean annual change in age-standardized incidence and stage IV incidence	Ratio	Ln ratio
Stage I							
2010-2021	12,4	0,3	1,1	0,003	1,1	448,0	6,1
Stage II							
2010-2021	0,7	0,3	0,1	0,003	0,1	24,0	3,2
Stage III							
2010-2021	0,9	0,3	0,1	0,003	0,1	32,0	3,5
Stage IV							
2010-2019	0,03	0,03	0,003	0,003	NA	NA	Ref
2019-2021	0,3	0,3	0,1	0,1	NA	NA	Ref

* Periods were defined analyzing incidence trends for each stage using Joinpoint regression; the same periods were used for Stage IV incidence

Table 5. Age-standardized lung cancer incidence by stage and comparison with stage IV incidence (difference, ratio, and Ln-ratio) by period, 2010–2021

Ln ratio ≤ 0.7	**Low bias**
0.7 < Ln ratio ≤ 1.6	**Moderate bias**
Ln ratio > 1.6	**High bias**

Period*	Absolute change in age-standardized incidence (per 100'000)	Absolute change in age-standardized stage IV incidence (per 100'000)	Mean annual change in age-standardized incidence (per 100'000)	Mean annual change in age-standardized stage IV incidence (per 100'000)	Difference between the mean annual change in age-standardized incidence and stage IV incidence	Ratio	Ln ratio
Stage I							
2010-2021	3,9	-0,2	0,4	-0,02	0,4	-23,3	3,1
Stage II							
2010-2013	0,7	0,8	0,2	0,3	-0,04	0,9	0,2
2013-2019	-0,4	-0,3	-0,1	-0,04	-0,02	1,4	0,4
2019-2021	-0,5	-1,5	-0,3	-0,8	0,5	0,3	1,1
Stage III							
2010-2021	-0,2	-0,2	-0,02	-0,02	-0,01	1,3	0,3
Stage IV							
2010-2021	-0,2	-0,2	-0,02	-0,02	NA	NA	Ref

* Periods were defined analyzing incidence trends for each stage using Joinpoint regression; the same periods were used for Stage IV incidence

Figure 1: Prostate cancer age-standardized incidence and mortality rates, all ages, 1989-2021, Switzerland

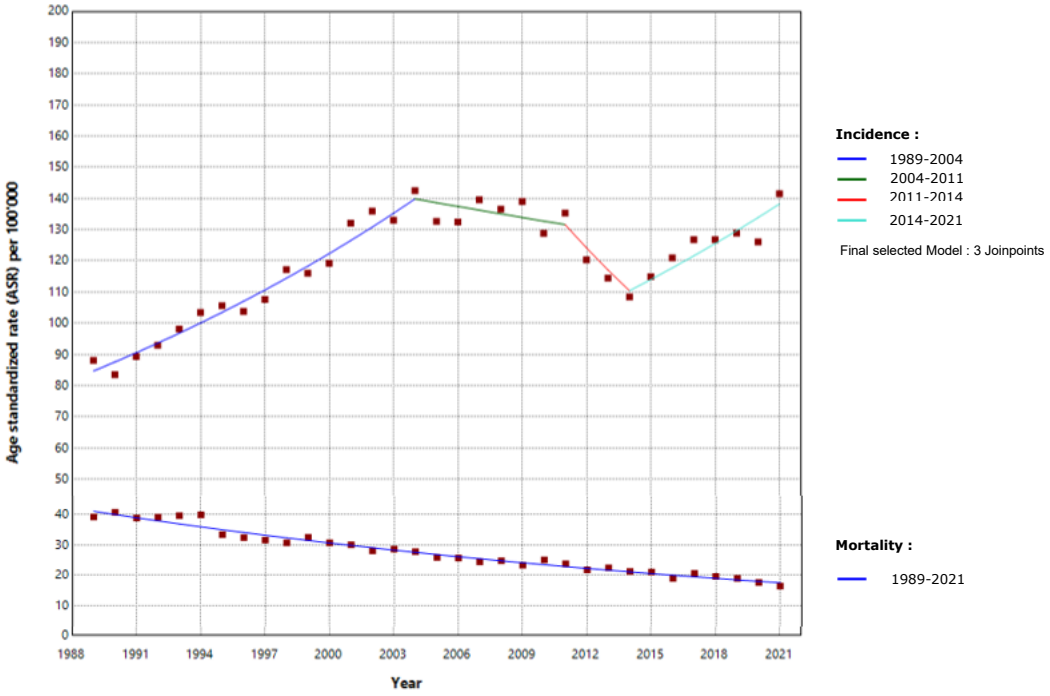


Figure 2: Melanoma age-standardized incidence and mortality rates, both sexes, all ages,1989-2021, Switzerland

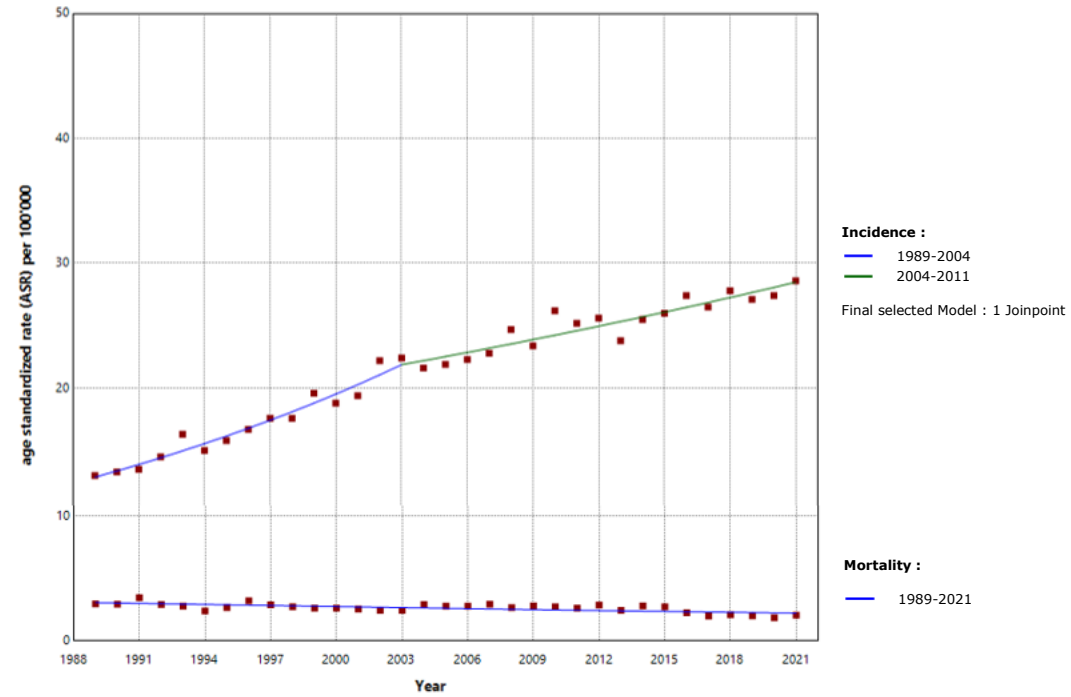
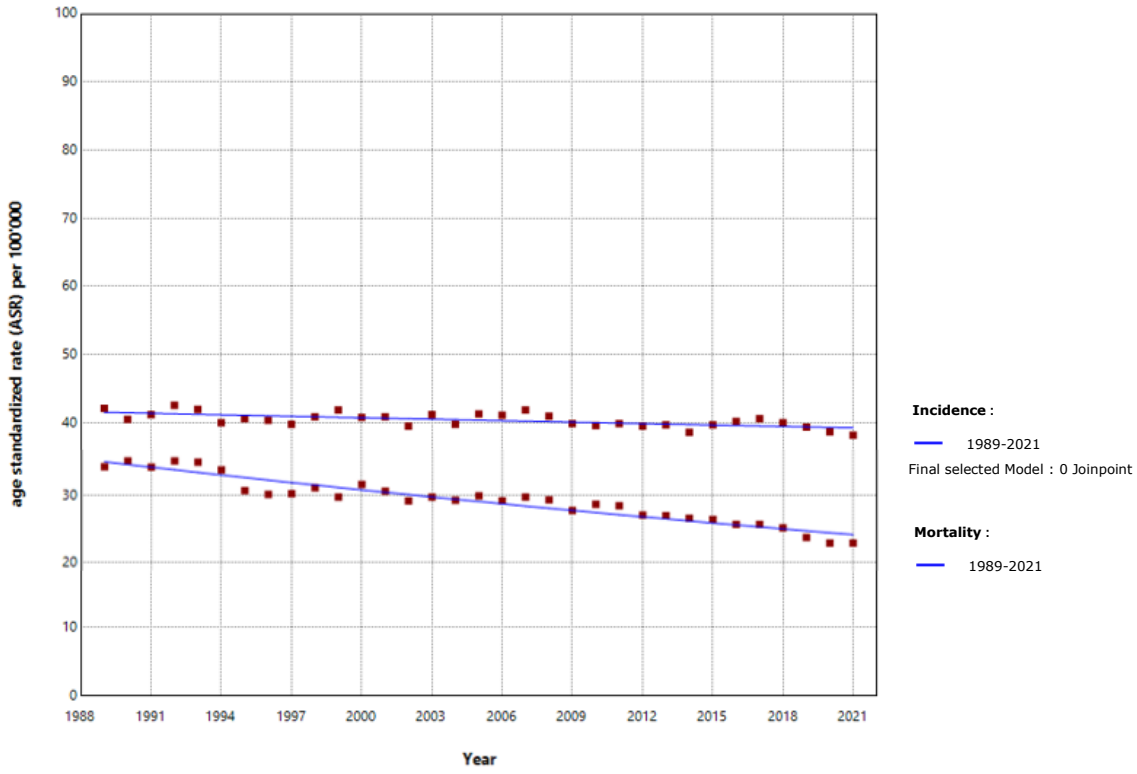


Figure 3: Lung cancer age-standardized incidence and mortality rates, both sexes, all ages,1989-2021, Switzerland



Chapter 7 | Discussion

Summary of main findings

In this thesis, we assessed surveillance bias across different diseases and contexts, explored its causes and consequences, and described possible strategies to prevent it. We showed that the bias was substantial for certain indicators, such as the number of COVID-19 cases or cancer incidence for specific types of cancer, and provided some estimates of its magnitude.

In Chapter 4, we defined surveillance bias and highlighted that it occurs in multiple contexts and arises from different causes. For COVID-19, surveillance bias resulted from differences in testing intensity. Quality-of-care indicators were biased by differences in screening intensity and resources for measurement and reporting. Incidence trends for prostate cancer and melanoma were also influenced by differences in screening intensity. For hypertension, the bias arose from changes in diagnostic thresholds. For chlamydia, the bias resulted from variations in testing and reporting. We also outlined strategies to mitigate the effect of the bias, including analyzing trends accounting for screening and diagnostic processes, favoring metrics less exposed to surveillance bias, standardizing disease definitions, and ensuring the stability of surveillance systems.

In Chapter 5.1, we measured seroprevalence and examined seroprevalence trends of SARS-CoV-2 antibodies in Switzerland between May 2020 and September 2021. We analyzed three periods of the pandemic: before vaccination, during the initial phase of the vaccination campaign, and after widespread vaccination. Seroprevalence estimates were 3.7% in period 1, 16.2% in period 2, and 72.0% in period 3, with some cantonal variations.

In Chapter 5.2, we assessed surveillance bias in the Canton of Fribourg across three pandemic waves. For the first two waves, the case count was highly biased, while hospitalizations and deaths were less influenced by surveillance bias. During these waves, seroprevalence was considered the least biased indicator and was used as reference. In the third wave, we used hospitalizations as reference, since seroprevalence was very influenced by vaccination, and we found that cases and deaths underestimated the size of the third wave.

In Chapter 5.3, we described the strengths and limitations of different COVID-19 surveillance strategies. Healthcare providers-based surveillance provided timely data but were prone to surveillance bias. Population-based surveillance was less prone to surveillance bias, but faced challenges in representativeness, feasibility, and timeliness. We emphasized that no single indicator is sufficient and called for

integrated surveillance systems combining multiple approaches to improve accuracy and reliability in disease monitoring.

In Chapter 6.1, we reviewed how surveillance bias affects cancer surveillance, using examples of scrutiny-dependent cancers. We also examined how surveillance bias can distort the identification of cancer risk factor if detection and screening strategies differ between population subgroups— for example, by biasing the associations between sex and thyroid cancer, or between obesity and cancer risk. In this review, we also outlined strategies to reduce surveillance bias in the assessment of cancer burden, including accounting for screening and diagnostic processes when interpreting incidence trends, or prioritizing less biased surveillance indicators, such as mortality and the incidence of advanced-stage cancers.

In Chapter 6.2, we illustrated how epidemiological signatures help identify surveillance bias in cancer data, using melanoma, lung cancer, and prostate cancer incidence and mortality trends from 1981 to 2020 as examples. In Switzerland, melanoma incidence markedly increased, while mortality remained stable, suggesting surveillance bias likely due to increased screening uptake over time. Prostate cancer incidence was biased by differences in screening intensity over time, while mortality showed a steady decline. This also suggests a surveillance bias due to variations in screening practices. Lung cancer was less prone to surveillance bias: incidence followed mortality trends, with incidence and mortality both declining in men and increasing in women.

In Chapter 6.3, we quantified surveillance bias in prostate cancer, melanoma, and lung cancer in Switzerland by analyzing incidence and mortality trends from 1989 to 2021. For melanoma, surveillance bias remained high throughout the entire study period. In the case of prostate cancer, the level of bias varied over time, ranging from low to high. For lung cancer, the bias was moderate and consistently lower than that observed for the other two cancer types.

Limitations and strengths

This thesis has both limitations and strengths. One key limitation is the use of narrative reviews, meaning that the examples used to illustrate surveillance bias were drawn from our own knowledge and expertise, rather than from a systematic search for all possible situations in which the bias might occur. However, in this case, being exhaustive was not necessary, given the rapid and ongoing evolution of diagnostic technologies that influence surveillance bias. The transition from traditional to digital tools has already had an impact on the diagnosis of diseases (Farber et al., 2024) and new technologies, such as artificial intelligence or wearable devices, are likely to play an increasingly important role in disease diagnosis (Hernström et al., 2025; Scholte et al., 2024; Zhou et al., 2021). Rather than being exhaustive, what mattered most in the context of this thesis was to clarify the concept of surveillance bias, its drivers, and its implications.

When we attempted to quantify surveillance bias in COVID-19 and cancer, we also faced many limitations. Although we provided some simple estimates of the magnitude of the bias, they remain far from precise and rely on simple approaches. Our work in this regard was exploratory, and several important challenges remained unaddressed. One key example of an important limitation in our attempt to measure surveillance bias in cancer was the assumption that a parallel trend between incidence and mortality would indicate a low level of surveillance bias. This assumption was made based on the work of Welch et al. (Welch et al., 2019); however, in some cases, incidence and mortality trends may diverge for reasons unrelated to surveillance bias. Another factor that hindered our work was the difficulty of accounting for all the factors that may influence surveillance indicators, such as measurement errors or changes in coding practices and reporting, which undermine the precision of bias estimation.

It is also important to note that it was difficult to clearly define the concept of surveillance bias because it intersects with several related epidemiological notions. It overlaps with detection bias, which describes the distortion of associations resulting from variations in diagnostic intensity. Surveillance bias may also be interpreted as a form of selection bias (for example, when individuals who are more closely monitored are more likely to be diagnosed and included in registries) and it is closely related to ascertainment bias. Nonetheless, the term surveillance bias aims to be more comprehensive. For instance, some causes of surveillance bias, such as changes in population screening campaigns or advances in diagnostic technologies, may not fit neatly into definitions of selection bias yet still distort surveillance indicators. More importantly, surveillance bias is directly tied to the purpose of surveillance itself. Its main consequence is not merely a biased estimate of risk or association, but the potential to mislead public health decisions by distorting our understanding of disease trends and patterns.

Despite all these limitations, this thesis contributes to a better understanding of surveillance bias and its role in public health surveillance. The broad range of examples discussed helps clarify the mechanisms through which surveillance bias arises and highlights the importance of accounting for it in epidemiological analyses. Using multiple examples is particularly useful because, in some cases, the impact of surveillance bias is more evident than in others. Moreover, we believe that refining our approach to assess the magnitude of the bias will lead to more accurate methodologies for measuring surveillance bias across different contexts. Recognizing this bias is essential not only for interpreting results and making sound public health decisions but also for ensuring effective communication with the general population. Changes in the incidence of certain types of cancer, for example, could be misinterpreted as alarming if not correctly explained in the context of surveillance bias, potentially leading to unnecessary stress and concern. For this reason, we have sought to keep the concept accessible and understandable, with the aim of raising awareness not only among surveillance experts but also within the broader public.

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Chapter 8 | Conclusion

This thesis explored the concept of surveillance bias, its causes, its consequences, and how to prevent it. It provided numerical estimates of the impact of surveillance bias, particularly in the context of COVID-19 and cancer surveillance.

We aimed to clearly define surveillance bias, and our definition, refined over the course of this work, will be published in the next edition of the Dictionary of Epidemiology (7th ed.). We described the bias through multiple real-world examples and identified several mechanisms through which it can influence epidemiological indicators, including changes in testing intensity, screening practices, diagnostic thresholds, and reporting practices. These findings highlight the pervasiveness of this bias and the need for ongoing vigilance in public health surveillance.

Quantifying the extent of surveillance bias proved challenging. No gold standard exists to measure it, and surveillance indicators are influenced by many factors, making it difficult to isolate the effect of bias. Additionally, different approaches are required for different diseases, and evolving public health policies and medical technologies make its precise estimation particularly complicated.

Beyond describing the problem, this thesis has also discussed potential strategies to mitigate surveillance bias in various contexts, including accounting for changes in screening and diagnostic processes when interpreting trends, prioritizing the use of less biased indicators, and integrating multiple surveillance approaches to improve accuracy and reliability.

Future research should focus on refining methods to quantify surveillance bias and developing standardized approaches to account for it in epidemiological analyses. In the context of cancer surveillance, for example, further work is needed to determine how best to incorporate information on screening practices into routine incidence reporting. Similarly, for infectious diseases, developing real-time correction methods for surveillance indicators could help improve the responsiveness of public health interventions.

This thesis underscores the importance of considering surveillance bias in many aspects of public health surveillance. As diagnostic technologies and screening practices continue to evolve, the challenges posed by surveillance bias will also change. By fostering awareness of surveillance bias and advocating for methodological improvements, we work toward more reliable and meaningful surveillance systems that support effective public health actions.

Declaration of Generative AI and AI-assisted technologies in the writing process

During the preparation of this work the authors used ChatGPT to check the English grammar and readability. After using this tool/service, the authors reviewed and edited the content as necessary and take full responsibility for the content of the publication.

List of publications and courses

Publications in peer-reviewed and non–peer-reviewed scientific journals related to this thesis or conducted as part of the PhD training

1. Gastens, V., **Tancredi, S.**, Kiszio, B., Del Giovane, C., Tsuyuki, R. T., Paradis, G., Chiolero, A., & Santschi, V. (2025). Pharmacists delivering hypertension care services: a systematic review and meta-analysis of randomized controlled trials. Frontiers in cardiovascular medicine, 12, 1477729. https://doi.org/10.3389/fcvm.2025.1477729
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List of courses

Date	Name	Location	ECTS
Jun 2021	Life Course Epidemiology and Public Health	Fribourg	1 ECTS
Sept 2021	Systematic Reviews and Meta-Analysis: a Practical Approach	Bern	1 ECTS
Sept 2022	Nondetects and other types of missing data in observational epidemiologic studies	Basel	1 ECTS
Sept 2022	Introduction to the Statistical Software R	Basel	1 ECTS
Oct 2022	Applied Logistic Regression	Bern	2 ECTS
Nov 2022	Introduction to the Statistical Software Stata and Electronic Data Capture Software REDCap	Basel	1 ECTS
Dec 2022	Public Health Surveillance and Population Health Monitoring	Lausanne	2 ECTS
Feb 2023	Basics of scientific writing in English: A structured method for organizing and writing better, faster papers	Online (Bern)	2 ECTS
Apr 2023	Understanding social inequalities and social problems in health!	Basel	1 ECTS
May 2023	Migration Health	Basel	1 ECTS
Aug 2023	NCD control in a global health perspective: public health and health systems strengthening approaches	Lugano	1ECTS
Oct 2024	Causal inference for population health sciences	Basel	2 ECTS
Nov 2024	Foundations of Public Health	Zurich	2 ECTS
Total ECTS			**18 ECTS**

Curriculum vitae

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01/2022 – present
PhD student in Medical Sciences
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Medical specialty training (Postgraduate) (110/110 cum laude)
Hygiene, Preventive Medicine and Public Health; University of Modena and Reggio Emilia

15/02/2017
State Exam for Abilitation to Medical Practice (270/270)
University of L'Aquila

22/10/2016
Degree in Medicine and Surgery (110/110 cum laude)
University of L'Aquila

2009
High School Diploma (95/100)
Liceo Scientifico "A.Bafile" – L'Aquila

Courses

03/2021 – 11/2021
Healthcare Management Specialization Course
Catholic University of the Sacred Heart, Rome
Management of human and technological resources, continuous quality improvement, hospital performance evaluation

06/2018 – 01/2019
Clinical Governance Core Curriculum
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Strategy and tools for clinical governance actions, audits and clinical guidelines/pathways

WORK EXPERIENCE

10/2023 – present
Epidemiologist (Médecin Epidémiologue) 60%
Observatoire Valaisan de la santé, Sion, Switzerland
Activities: Population health monitoring and quality of care

01/2021 – 12/2021
Visiting Researcher c/o Population Health Laboratory
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Supervisors: Prof. Arnaud Chiolero, MD PhD; Dr. Stéphane Cullati, PhD

30/03/2020 – 31/12/2020
Public Health Physician
Public Health Department, local health unit of Modena (AUSL Modena)

Activities: Vaccination counselling, COVID-19 contact tracing

01/11/2019 – 30/03/2020 **Resident Doctor c/o Public Health Department "AUSL Modena "**
University of Modena and Reggio Emilia
Activities: Vaccination counselling
Supervisor: Dr. Giovanni Casaletti, MD

08/01/2019 – 01/11/2019 **Resident Doctor c/o Teaching Hospital "Azienda Ospedaliero - Universitaria di Modena "**
University of Modena and Reggio Emilia
Activities: Infection prevention and control, risk management and operation theatres' efficiency
Supervisor: Dr. Elda Longhitano, MD

10/2018 – 2020 **Academic Representative c/o "Consulta degli Specializzandi" (2018 – 2020)**
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29/12/2017 – 08/01/2019 **Resident Doctor c/o Department of Biomedical, Metabolic and Neural Sciences**
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Activities: Nutritional, environmental epidemiology and healthy lifestyle promotion
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11/04/2016 – 22/10/2016 **University Tutor**

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PERSONAL SKILLS

Mother tongue: Italian

Other languages

	UNDERSTANDING		SPEAKING	WRITING
	Listening	Reading		
English	Excellent	Excellent	Excellent	Excellent
French	Good	Good	Good	Good

Digital skills

SELF-ASSESSMENT			
Information processing	Communication	Safety	Problem solving
Proficient	Proficient	Proficient	Independent

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