

# **Infectious disease surveillance**

**Learn how infectious diseases are monitored**

Jakob Schumacher

# Table of contents

<b>About the book</b>	<b>6</b>
Learning objectives . . . . .	6
Who writes this book . . . . .	6
Helpful ressources . . . . .	7
<b>Preface</b>	<b>8</b>
<b>Presentations</b>	<b>10</b>
Einführung . . . . .	10
Introduction to surveillance systems . . . . .	10
Stages of surveillance systems . . . . .	11
Types of surveillance systems . . . . .	11
Attributes of surveillance systems . . . . .	12
Evaluation of surveillance systems . . . . .	12
<b>I Introduction</b>	<b>14</b>
<b>1 Definition of surveillance</b>	<b>15</b>
Learn more . . . . .	16
<b>2 Other forms of surveillance</b>	<b>17</b>
2.1 Neighbourhood surveillance . . . . .	17
2.2 Rhizomatic surveillance . . . . .	18
2.3 Top-down-surveillance . . . . .	18
2.5 Learn more . . . . .	18
<b>3 International regulations</b>	<b>19</b>
3.1 International health regulations . . . . .	19
3.1.1 Important contents of the IHR . . . . .	20
3.1.2 History of PHEICS . . . . .	20
3.2 EU Regulation 2022/2371 . . . . .	20
3.3 Essential public health operations . . . . .	21

<b>II</b>	<b>Stages</b>	<b>22</b>
<b>4</b>	<b>Objectives of surveillance (Stage 1)</b>	<b>23</b>
4.1	Primary objectives . . . . .	25
4.1.1	Get information to initiate case based action . . . . .	25
4.1.2	Get information to initiate population based action . . . . .	25
4.1.3	Get information to initiate individual action . . . . .	25
4.1.4	Get information to initiate action by medical professionals . . . . .	26
4.2	Secondary objectives . . . . .	26
4.2.1	Scientific advances . . . . .	26
4.2.2	Evaluation . . . . .	26
4.2.3	Resource allocation . . . . .	27
4.2.4	Fullfill obligation . . . . .	27
4.3	Other concepts for objectives . . . . .	27
4.3.1	World bank . . . . .	27
4.3.2	EU/EEA surveillance . . . . .	28
4.4	Objectives in practice . . . . .	28
	Read more . . . . .	28
<b>5</b>	<b>Infection Event (Stage 2)</b>	<b>29</b>
5.1	Naming and Categorization . . . . .	29
5.2	Typical events in infectious disease surveillance . . . . .	30
<b>6</b>	<b>Collection (Stage 3)</b>	<b>31</b>
6.1	Typical collection methods . . . . .	31
6.2	Active vs. passive . . . . .	32
6.3	Enhanced and intensived . . . . .	32
6.4	Integreated and one-health . . . . .	32
<b>7</b>	<b>Classification (Stage 4)</b>	<b>33</b>
7.1	Typical classification definitions . . . . .	34
7.1.1	Example of the different usages of definitions . . . . .	35
7.2	Components of definitions . . . . .	35
7.2.1	Example for a clinical part of a case defintion . . . . .	36
7.2.2	Example for a laboratory part of a case defintion . . . . .	36
7.2.3	Example for an epidemiological part of a case defintion . . . . .	37
7.3	Specificity and sensitvity . . . . .	37
7.4	Creating you own definitions . . . . .	37
<b>8</b>	<b>Data Processing (Stage 5)</b>	<b>38</b>
8.1	Typical ways of data processing . . . . .	38
8.2	Comparing characteristics of manual vs electronic data processing . . . . .	39

8.3	Problems of data processing . . . . .	39
8.3.1	Dependence on the user interface of software . . . . .	39
8.3.2	Dependence on classification systems in manual systems . . . . .	39
8.3.3	Dependence on classification systems in automatic systems . . . . .	39
8.3.4	Single point of truth . . . . .	39
8.3.5	Errors in data handling by the software . . . . .	39
8.4	Open Data and Public Engagement . . . . .	40
<b>9</b>	<b>Analysis and Assessment (Stage 6)</b>	<b>41</b>
9.1	Analysis . . . . .	42
9.1.1	Surveillance indicators . . . . .	42
9.1.2	Graphical Display . . . . .	42
9.1.3	Time, Place, Person . . . . .	42
9.1.4	Process . . . . .	43
9.2	Assessment . . . . .	43
9.2.1	Formulating of public health recommendations . . . . .	44
9.2.2	Recommendations (post-evidence) . . . . .	44
9.2.3	Recommendations (evidence version) . . . . .	44
<b>10</b>	<b>Communication (Stage 7)</b>	<b>45</b>
10.1	Graphical . . . . .	45
<b>11</b>	<b>Public Health Measures (Stage 8)</b>	<b>46</b>
<b>III</b>	<b>Types</b>	<b>47</b>
<b>12</b>	<b>Case based surveillance</b>	<b>48</b>
12.1	Terminology . . . . .	48
12.2	Process of a case-based surveillance system . . . . .	48
12.3	Strengths and weaknesses . . . . .	49
12.4	Example of a case based surveillance system . . . . .	49
<b>13</b>	<b>Syndromic Surveillance</b>	<b>52</b>
<b>14</b>	<b>Event based surveillance</b>	<b>53</b>
14.1	Stages of event based surveillance . . . . .	53
14.2	Terminology . . . . .	53
14.2.1	Event based vs. indicator based surveillance . . . . .	53
14.2.2	Epidemic intelligence . . . . .	54
14.3	Strengths and weaknesses . . . . .	54
14.4	Sources of event based surveillance . . . . .	55
14.6	Resources . . . . .	55

<b>15 Wastewater</b>	<b>56</b>
<b>16 Mortality surveillance</b>	<b>57</b>
<b>17 Mass-Gathering Surveillance</b>	<b>58</b>
17.1 Additional reading . . . . .	58
<b>18 Active vs passive</b>	<b>59</b>
18.1 Active surveillance system . . . . .	59
18.2 Passive surveillance system . . . . .	59
<b>19 Sentinal vs comprehensive</b>	<b>60</b>
<b>About</b>	<b>61</b>
License . . . . .	61
Disclaimer . . . . .	61
Privacy Policy . . . . .	62
Acknowledgements . . . . .	62
The contents of the book . . . . .	62
Usage of images . . . . .	62
Coding and publishing of the book . . . . .	62
Usage of artificial intelligence . . . . .	62

# About the book

## Warning

This book is work in progress and currently not in an acceptable state. Please return to this book to check for updates.

[jakobschumacher.github.com/infectious-disease-surveillance](https://jakobschumacher.github.com/infectious-disease-surveillance)

This book is about infectious disease surveillance. It explains what surveillance is, how it is related with other similar concepts, what the stages of a surveillance system are and how to assess the quality of surveillance systems. The book is written for infectious disease experts in Europe, but can be used by anybody interested in the topic.

## Learning objectives

- Surveillance is information for action
- Learn how to define a surveillance system
- Get to know types of surveillance systems
- Learn the stages of a surveillance system
- Find resources about the evaluation

## Who writes this book

The contents of the book come mainly from the “EPIET-World” - the European fellowship programme for applied epidemiology. Most content of the book is written by Jakob Schumacher, but it is based upon the work of many colleagues who taught the subject beforehand. The book does not represent the opinion of the institutions that the author is affiliated. It does also not represent the opinion of the ECDC. Training section.

Read more about the background in the [About section](#)

You would like to help this book - great! Here is how to do that:

1. You can go to Github issues of this repository and say what can be improved
2. You can clone, then write something yourself and then make a pull request.

## Helpful ressources

- [ECDC Handbook: Data quality monitoring and surveillance system evaluation](#)

# Preface

On the 28th of October in 2020 German chancellor Angela Merkel and the head of the federal states stuck their heads together. They had to make tough decisions about measurements to mitigate the COVID-19 pandemic. We dont know exactly what they were talking about but we can be certain that they were making the decisions with graph in picture 1 in mind.

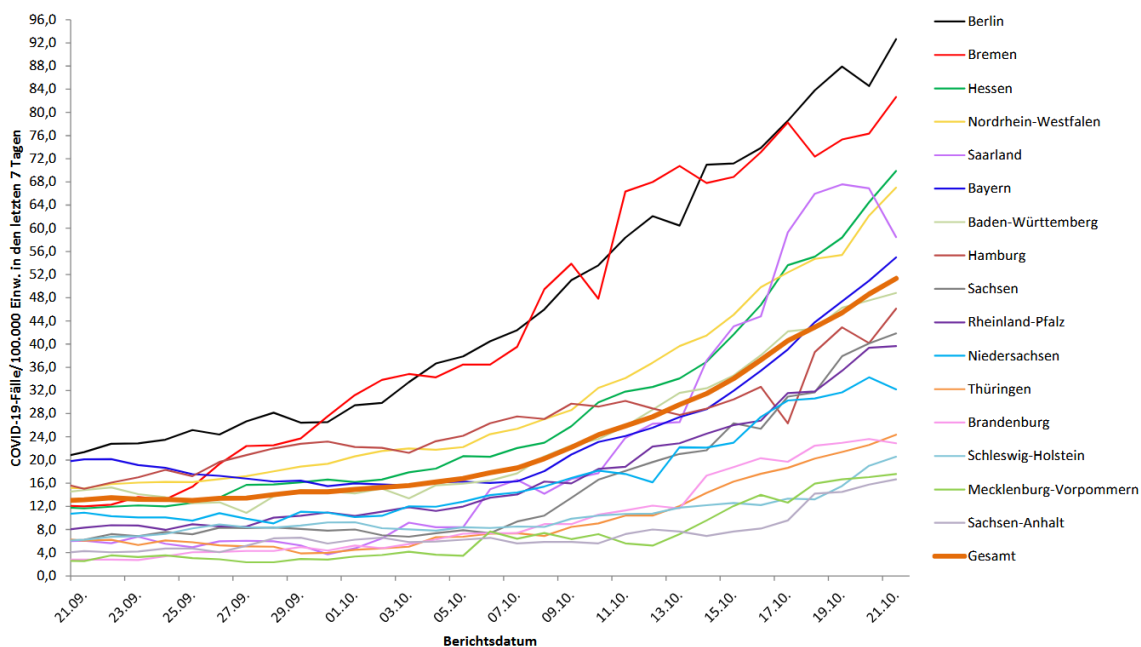


Figure 1: Picture taken from “Täglicher Lagebericht des RKI zur Coronavirus-Krankheit-2019 (COVID-19) 21.10.2020”

Infectious diseases are a threat to humanity: some have the ability to easily spread from one person to others persons and infecting all of mankind, some can be transmitted before the infectious persons knows that he is sick, some have no cure and a high fatality rate, some are able to spread long distances via air, water or food.

To combat infectious diseases mankind has developed numerous techniques throughout the ages. On very important tool that is a prerequisite to most count measures is infectious



disease surveillance. Knowing what happens when and how is one of the cornerstones of every response. And infectious disease surveillance does exactly that.

# Presentations

General presentations about infectious disease surveillance

## Einführung

Target	Description
<a href="#">Presentation</a>	The link to the presentation
Content	This presentation gives an introduction to surveillance system. How it is defined, how it falls in the domain of general surveillance, what its objectives are
Time	90 Minutes
Language	German
Intended audience	Ärztinnen und Ärzte in Weiterbildung zum Facharzt für öffentliches Gesundheitswesen.
Learning objectives	(1) Surveillance ist wichtiger denn je (2) “Daten für Taten” (3) Schritte der Surveillance (4) Surveillance muss durchdefiniert werden

## Introduction to surveillance systems

Target	Description
<a href="#">Presentation</a>	The link to the presentation
Content	This presentation gives an introduction to surveillance system. How it is defined, how it falls in the domain of general surveillance, what its objectives are

Target	Description
Time	15 Minutes
Language	English
Intended audience	Young professionals, Fellows of the European programme for intervention epidemiology
Learning objectives	(1) Know the important parts of the definition (2) Understand the domain surveillance (3) Know the objectives

## Stages of surveillance systems

Target	Description
<a href="#">Presentation</a>	The link to the presentation
Content	This presentation gives an overview of the stages of an surveillance system.
Time	10 Minutes
Language	English
Intended audience	Young professionals, Fellows of the European programme for intervention epidemiology
Learning objectives	(1) Understand that the definition of surveillance includes most stages (2) The stages are: Events, Collection, Classification, Data management, Analysis, Communication, Action

## Types of surveillance systems

Target	Description
<a href="#">Presentation</a>	The link to the presentation
Content	This presentation gives an overview of the types of surveillance system e.g. case based, syndromic, event based, wastewater, active vs passive
Time	20 Minutes
Language	English

Target	Description
Intended audience	Young professionals, Fellows of the European programme for intervention epidemiology
Learning objectives	(1) Understand that different overlapping types of surveillance system exist (2) Know what case based surveillance is (3) Know what syndromic surveillance is (4) Know what event based surveillance is

## Attributes of surveillance systems

Target	Description
<a href="#">Presentation</a>	The link to the presentation
Content	This presentation covers the attributes of a surveillance system. It covers underestimation, validity, timeliness and other attributes
Time	20 Minutes
Language	English
Intended audience	Young professionals, Fellows of the European programme for intervention epidemiology
Learning objectives	(1) Be able to describe characteristics of a surveillance system (2) Understand underestimation (3) Understand validity (4) Understand timeliness (5) Know that there are many attributes often with unclear definitions

## Evaluation of surveillance systems

Target	Description
<a href="#">Presentation</a>	The link to the presentation
Content	This presentation gives an overview of how to evaluate a surveillance system.
Time	10 Minutes
Language	English

Target	Description
Intended audience	Young professionals, Fellows of the European programme for intervention epidemiology
Learning objectives	(1) Learn the steps of an evaluation (2) need to adapt the evaluation to the trigger and the attributes (3) Surveillance is a team effort

# **Part I**

## **Introduction**

# 1 Definition of surveillance

What exactly is infectious disease surveillance?

The motto of public health surveillance is information for action. This is also the shortest definition of surveillance - although it does not capture all elements. The definition of the WHO is more comprehensive:

Public health surveillance is an *ongoing, systematic collection, analysis and interpretation* of health-related data essential to the planning, *implementation*, and evaluation of public health practice. <sup>1</sup>

This definition is very informative and gives us all important elements of a surveillance system.

Element	Explanation
ongoing	surveillance is planned for a longer time (usually). This is in contrast to a scientific study or a survey
systematic	surveillance is a planned undertaking that works with clear definitions
collection	Events are collected and stored in data systems
analysis	Indicators are calculated and the data is parsed according to time, place and person
interpretation	Assessment of the indicators and sense making
implementation of public health practice	The information guides public health responses

Infectious disease surveillance is a subset of public health surveillance that is concerned with the surveillance of infectious diseases.

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<sup>1</sup>World Health Organisation 2005 - <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3820481/table/tab5/>

## Learn more

- A history of the definitions can be found in the Article [The Past, Present, and Future of Public Health Surveillance](#) by Bernard Choi.
- The first definition in the modern form comes from Alexander Langumir - a very influential epidemiologist, who also did set up the FETP programme of the CDC. You can read about his life in his [Wikipedia-Article](#).



## 2 Other forms of surveillance

How does infectious disease surveillance fit into the landscape?

Nearly all complex biological and technical systems have mechanisms to monitor and control the system's condition. Many social systems also regularly analyze their current state. There are various terms for these status assessments: A scientific study is one form of status assessment, as is the police surveillance of a group or the evaluation of a project in the corporate sector. Surveillance is also a form of status assessment.

### 2.1 Neighbourhood surveillance

Neighbourhood surveillance is the oldest form of surveillance. In its broadest sense it is people watching other people. Small Communities such as villages usually have a strong neighbourhood surveillance. Neighbors see and know everything what other neighbors are doing. This can be framed positively as in the saying: "it takes a village to raise a child" or negatively when people blaspheme other people.

With the widespread availability of cameras and the possibility to communicate directly this form of surveillance has gained a large momentum. The largely unsuccessful Google glass project could have been an even larger driver of participatory surveillance. Now Surveillance becomes a tool that does not lie in the hands of a strong actor such as a state or less strong actors such as companies but in the hands of the individuals. This gives infectious disease specialists the opportunity to gather information from those individuals as it is done in epidemic intelligence.

This form of surveillance is sometimes also called participatory surveillance - if you want to emphasize the empowerment of the people. One rather negative example of a participatory surveillance is vividly depicted in the book and film *The Circle*. Sometimes this form of surveillance is called bottom-up-surveillance to emphasize the opposition to top-down-surveillance.

## 2.2 Rhizomatic surveillance

Rhizomatic surveillance is a term coined by Haggerty and Ericson<sup>1</sup>. The term comes from rhizom - the large underground network from Fungi. This form of surveillance shows similar characteristics of the rhizom: it is being not directly visible (being “underground”), it is horizontal in contrast to the top-down surveillance (like the rhizom that does not follow the typical direction of plants growing upwards to the sun)) and the surveillance is a group of different actors instead of one single responsible body. The surveillance done by the big tech companies is a form of rhizomatic surveillance. Collecting millions of datapoints that are left behind by users in the internet can give valuable insight that can be turned into profit. The Cambridge Analytica scandal is an example of such a surveillance system. State actors are of course also capable of doing rhizomatic surveillance as could be seen in the documents leaked to PRISM.

## 2.3 Top-down-surveillance

The top-down-surveillance is the surveillance which we usually think of first when we hear the word surveillance. There is an agent usually a dominant one like the state who watches what its constituents do. This can take the form of a Panopticon, where one person can watch many different people and after which some prisons have been modeled. This form of surveillance often aims to achieve a specific behavior among those being monitored. Epidemiological surveillance belongs to this level of surveillance.

## 2.4

## 2.5 Learn more

You can read more about different types of surveillance in the article [Timan, Tjerk and Galič, Maša and Koops, Bert-Jaap: Surveillance Theory and Its Implications for Law \(December 1, 2017\)](#)

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<sup>1</sup>Haggerty KD, Ericson RV. The surveillant assemblage. *Br J Sociol.* 2000 Dec;51(4):605-22. doi: 10.1080/00071310020015280. <https://pubmed.ncbi.nlm.nih.gov/11140886/>

# 3 International regulations

How is surveillance regulated internationally?

## 3.1 International health regulations

Surveillance is firmly anchored in national and international legal systems. The [International Health Regulations](#) (IHR) is a legally binding regulation for 196 countries. The IHR includes articles that require surveillance from the countries. The aim is to prevent cross-border threats from infectious diseases.

During the COVID-19 pandemic, the value of such international collaboration became evident. New amendments of the IHR were adopted on the first of June 2024. It will come into place in 2025/2026.

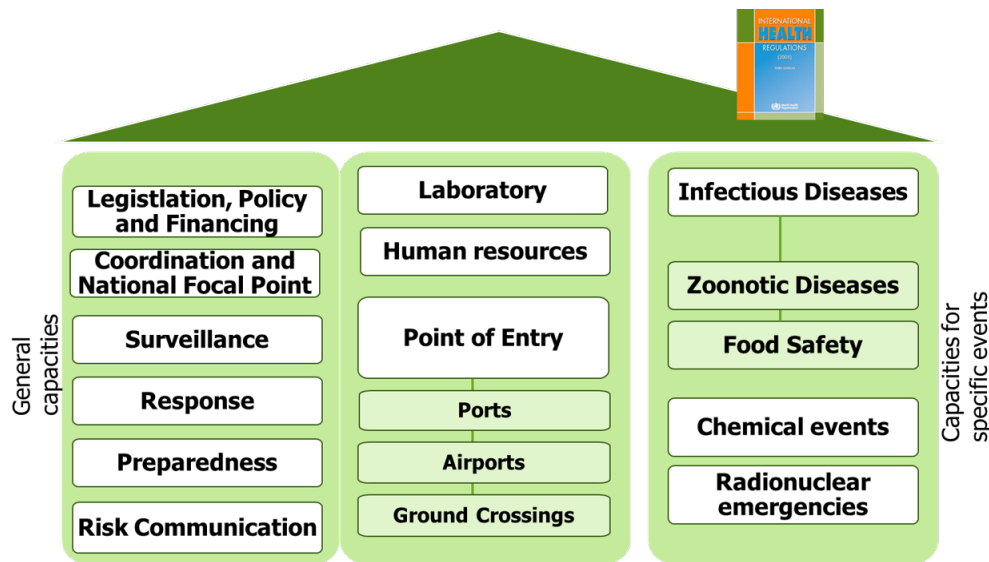


Figure 3.1: Contents of the IHR. Graph by ÖGD-Kontaktstelle RKI

### 3.1.1 Important contents of the IHR

- The IHR defines a Public Health Emergency of International Concern (PHEIC). It is defined as an extraordinary event which is determined to constitute a public health risk to other states and potentially requires a coordinated international response
- A PHEIC is declared by the Director General of WHO
- Notification according to Article 6 Annex 2: State Parties to notify WHO within 24 hours about events within their territory which can constitute a PHEIC
- Article 8: State Parties can seek consultation from WHO
- Article 10: WHO can request State Parties to verify an event and offer to collaborate on this event. States are obliged to give information within 24h
- [Annex 2](#): Decision tool for deciding if an event should be notified. It consists of a flowchart with 4 questions. There are [helpful resources to learn how to use the annex 2](#)
- The IHR Monitoring and Evaluation Framework provides an overview of approaches to review implementation of country core public health capacities under the IHR (2005)
- The [Monitoring and evaluation framework](#) describes mandatory and voluntary approaches
  - IHR State Party Self-Assessment annual report (mandatory)
  - simulation exercises (voluntary)
  - after action reviews (voluntary)
  - joint external evaluation (voluntary)

### 3.1.2 History of PHEICS

- 2009: H1N1 Pandemic
- 2014: Resurgence of Polio
- 2014: Ebola Westafrica
- 2016: Zika
- 2019: KIVU Ebola
- 2020: SARS-CoV-2
- 2022: Clade II Mpox
- 2024: Clade I Mpox

## 3.2 EU Regulation 2022/2371

- The EU has its own regulation on infectious diseases
- Regulation on serious cross-border threats to health
- Content:
  - Establishing a health security committee

- reference laboratory networks
- surveillance
- network for substances of human origin
- Mandatory events to notify in the Early warning and response system (EWRS)
  - unusual or unexpected, may cause significant morbidity or mortality in humans, may grow rapidly in scale,
  - may exceed national response capacity;
  - may affect more than one Member State; and
  - may require a coordinated response at Union level
  - Anything they notified to WHO via Annex 2

### 3.3 Essential public health operations

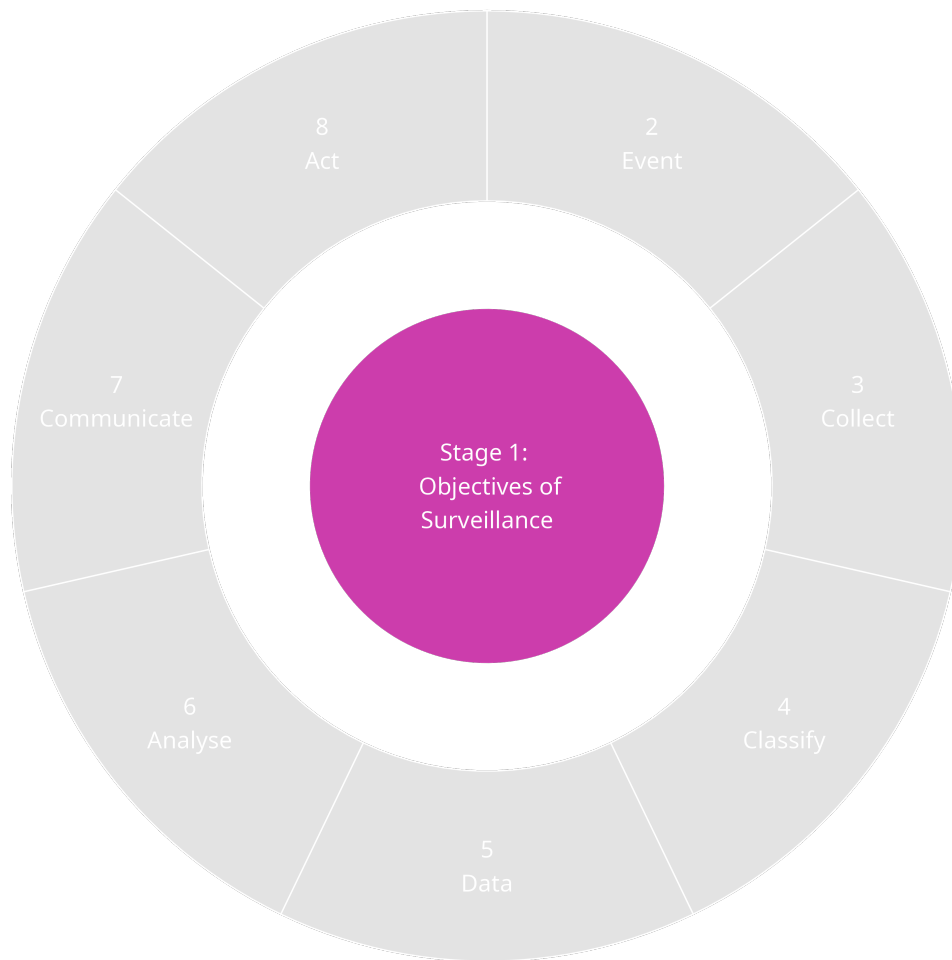
Surveillance is also a component of the [Essential Public Health Operations](#). The essential public health regulations are a tool of WHO Europe and defines central tasks for public health institutes. The goal of this [surveillance component](#) is to provide information and insights for health needs assessments, health impact assessments, and the planning of health services.

## **Part II**

# **Stages**

## **4 Objectives of surveillance (Stage 1)**

If you are clear about your objectives everything will be easier.



The objectives of a surveillance system are the reasons why a surveillance systems is set into place. The overall objective of infectious disease surveillance is described nicely in the German infection protection act:

*prevent communicable diseases in humans, detect infections at an early stage, and stop their further spread*<sup>1</sup>

The overarching objectiv can be decomposed into more concrete objectives that are based on

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<sup>1</sup>Translated from the German infection protection act [https://www.gesetze-im-internet.de/ifsg/\\_\\_1.html](https://www.gesetze-im-internet.de/ifsg/__1.html)



the interventions that can be taken. These can be subdivided into primary objectives that have a direct effect on the spread of an infectious disease or secondary objectives that exert and indirect influence.

## 4.1 Primary objectives

Objective	Description
Get information to initiate case based action	All the interventions that are taken when there is a person with an infection
Get information to initiate population based action	All the interventions that are taken that affect a large part of the population
Get information to initiate individual action	interventions taken by the individual
Get information to initiate action by medical professionals	The interventions that are taken by the medical system. A special form of the individual action

### 4.1.1 Get information to initiate case based action

Many public health interventions focus around the direct prevention of the spread from one person to another. This action is usually taken by a local public health agency. For this a surveillance systems needs to directly identify the single cases. So the objective of the surveillance system is to get all necessary information.

### 4.1.2 Get information to initiate population based action

Some public health interventions focus on the population or a group. These interventions are sometimes described as non-pharmaceutical-interventions - although this sometimes also compromises case based interventions. This kind of intervention is often done via a regulation by a federal state or a national body. But it can also be taken by a local public health agency. This action requires usually only trends and not necessarily case based information. So a surveillance system can have the objective to get the necessary information for this action

### 4.1.3 Get information to initiate individual action

The information from surveillance systems can lead to people changing their behaviour. This compromises many different interventions, that are taken by the people themselves (if it is initiated by an agency it would be a population based intervention). These interventions can

be ineffective or even counterproductive. So the surveillance can have the objective to elicit the information that is needed from the individuals to do effective and useful action.

#### **4.1.4 Get information to initiate action by medical professionals**

Some findings of surveillance systems lead to a change in practice of medical professionals. A medical professional society could change the guidelines according to findings. This intervention is initiated by the medical people and not necessarily by the public health agencies. The objective of the surveillance could be based on eliciting the information needed.

## **4.2 Secondary objectives**

Objective	Description
Scientific advances	Advance the knowledge on infectious diseases
Evaluation	Documents the impact of an intervention, or track progress towards specified goals
Resource allocation	Set priorities by the government or an institution and develop long term strategy
Fullfill obligation	Most nations have committed themselves to the International Health regulations. Thus they have to set up surveillance system

### **4.2.1 Scientific advances**

Surveillance systems collect data that can also be used for public health research. Scientists can use the data to analyse specific public health problems. The system can give information about the nature of a pathogen and epidemiological characteristics of a public health problem. One example would be the change of variants that follow the introduction of a new vaccine.

### **4.2.2 Evaluation**

Public health interventions should be beneficial for the population. The intervention can measure output, outcome and impact. Measuring the impact can be considered the most important part because it shows the benefits. This impact measurement can be done in with a surveillance system.

### 4.2.3 Resource allocation

Governments need to decide about their priorities and the distribution of resources. These decisions can be taken upon the information from surveillance systems.

### 4.2.4 Fullfill obligation

The International health regulations require: *Each State Party shall develop, strengthen and maintain [...] the capacity to detect, assess, notify and report events* Thus it can be an objective of a surveillance system to fullfill these obligations.

## 4.3 Other concepts for objectives

There are other summaries for the objectives of a surveillance system that have a similar concepts. Although they tend to be not specific but have a broader perspective.

### 4.3.1 World bank

The world bank notes the objectives of an public health surveillance system as follows<sup>2</sup>:

- recognize cases or clusters of cases to trigger interventions to prevent transmission or reduce morbidity and mortality (includes the special case in which surveillance at the national level is required to recognize multi-state clusters);
- identify new health problems and emerging diseases;
- assess public health impact of health events or determine and measure trends;
- measure causal factors in disease (e.g., risk factors) to initiate actions to prevent the onset of disease;
- demonstrate the need for intervention programs and resources, and allocate resources during health planning;
- monitor effectiveness and evaluate the impact of prevention and control measures, intervention strategies, and health policy changes;
- identify high-risk population groups or geographic areas to target interventions and guide analytic studies;
- provide data for research, and develop hypotheses that lead to analytic studies about risk factors for disease causation, propagation or progression;
- measure progress toward Millennium Development Goals, or other project or program goals, including PRSP (Poverty Reduction Strategy Paper) targets. \_\_

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<sup>2</sup><https://documents1.worldbank.org/curated/en/239131468160515361/pdf/536490BRI0ENGL10Box345621B01PUBLIC1.pdf>

### 4.3.2 EU/EEA surveillance

The EU/EEA surveillance <sup>3</sup> focuses on the need for the supranational body

- Detect and monitor any multinational infectious disease outbreaks with respect to source, time, population, and place in order to provide a rationale for public health action;
- Monitor trends in infectious diseases over time and across Member States to assess the present situation, respond to rises above warning thresholds and facilitate appropriate evidence-based action;
- Contribute to the evaluation and monitoring of prevention and control programmes targeted at infectious diseases in order to provide the evidence for recommendations to strengthen and improve these programmes at the national and European level;
- Identify population groups at risk and in need of targeted prevention measures;
- Contribute to the awareness of and the assessment of the burden of infectious diseases on the population using such data as disease prevalence, complications, hospitalisation, and mortality; and
- Generate hypotheses on (new) sources, modes of transmission and groups most at risk and identify needs for research and pilot projects

## 4.4 Objectives in practice

Although objectives play a decisive role in theory they are not as relevant in practice. Large surveillance systems tend to develop a life on its own and the focus on the objectives gets lost over time. New changes are introduced based on new needs but old parts stay in place although they might have lost their importance. Furthermore we are entangled into a complicated net of the large surveillance systems and a single person is rarely in the position to change a complete system. So to really set the focus on the objectives is a difficult undertaking.

When a surveillance system is changed there are often not purely rational and objective-based values at work. People tend to follow different decision making processes than a rational approach. Besides a rational approach one can differ between a “standard-approach” and an “environmental-approach” and a “garbage-can-approach”.

## Read more

- If you want to know more about the different approaches take the great [coursera course on organisational analysis by McFarland](#)

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<sup>3</sup><https://www.ecdc.europa.eu/sites/default/files/documents/long-term-surveillance-framework-2021-2027.pdf>

## 5 Infection Event (Stage 2)

Choosing the right event is crucial and depends on the objectives



Surveillance systems monitor a wide range of infection-related events. Understanding the event is essential for understanding a surveillance system. The choice of events to monitor in a surveillance system is a critical decision that shapes the system's in many ways. The choice depends on the Objective of the surveillance system.

- If a case-based intervention is intended the event that is monitored should be able to provide contact information of a case
- If only group-based intervention is intended only a trend is needed which can be acquired by simpler systems
- When the objective of a surveillance system is to monitor hospital capacity for resource allocation decisions, the events tracked should focus on specific indicators of hospital capacity and utilization like bed occupancy or staff coverage.

### 5.1 Naming and Categorization

Surveillance systems are often named after the events they monitor. For example:

- Emergency department surveillance (Emergency department visits)
- Syndromic surveillance (based on monitoring syndromes)
- Lab-based surveillance system (Reports by labs)
- Media surveillance (Screening of media articles)

## 5.2 Typical events in infectious disease surveillance

- The occurrence of an infectious disease
- The occurrence of an infection (infected person who is not necessarily diseased)
- An available ICU bed
- Self reports by people that they fell sick
- The colonization of a person by a pathogen
- A physician's ICD-10 classification of a patient
- The discovery of a newspaper article about a disease outbreak
- The subjective assessment of a public health department employee that something poses a threat to the population.
- A social media signal detected by a software

## 6 Collection (Stage 3)

With the collection method you will introduce the most important bias



The collection of an infectious disease Event form the foundation of any effective surveillance. The specific methods of collection can vary widely depending on the type of surveillance system. The collection is usually done by an public health agency or a commisioned insitution. The method of data collection often influences the naming of surveillance systems.

A collection processes can be based on any communication form like: Phone calls, serial interface, Reports on paper, Fax or E-Mail, direct investigation. In recent years many efforts have been put into establishing a fully seamless electronic system via electronic interfaces.

### 6.1 Typical collection methods

- Physicians report diagnosed cases to health authorities.
- Laboratories report cases that are analysed for clinical purposes to public health agencies
- Laboratories report cases that are analyses specifically for public health puropes like sequencing data to public health agencies
- Laboratories report other lab results like PCR-tests in wastewater
- A pulic health agency follows-up on an initial reports.
- Health insurance claims and ICD-10 Codes are collected via a software interface
- A public health agency gets access to a database of death records
- Public health workers go around households in a crisis situation and

- Hospital representatives fill out an online form about the number of free intensive care beds
- A specific group uses a software that screens the internet for potential public health threats
- Blood products are analysed for infectious disease

## 6.2 Active vs. passive

The collection process can be described as active or passive. Where active means that the public health agency actively collect reports, whereas passive means, that public health agency receive reports and don't directly interfere in the reporting. Many collection methods contain both, e.g. reports are sent in by a lab (passive) but in relevant cases the agency reaches out to get more information about a specific case (active)

Characteristic	Active	Passive
Ease	Complicated	Easy
Speed	slow	fast
Scalability	low	high
Operational costs	high	low
External validity	high	low

## 6.3 Enhanced and intensified

If there are several events that are looked at, that are collected via different methods the term: “enhanced” or “intensified” are used, especially in a mass-gathering surveillance.

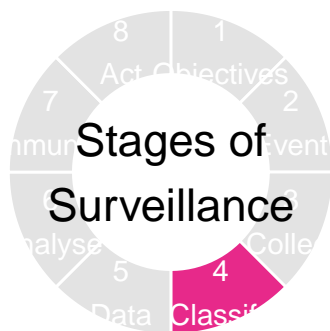
## 6.4 Integrated and one-health

If collection methods by veterinary or food-safety agencies are included the term “integrated” or “one-health” is applied.



## 7 Classification (Stage 4)

Clear definitions are crucial and avoids creating rubbish



### ⚠ Warning

The content of this chapter is the personal opinion of the author. This is especially true for the discouragement of the usage of the word case definition\_\_\_\_

Classification means categorizing the recorded events into two or more groups. Sometimes the word “collation” is used for this stage, for example in the WHO definition of surveillance. Classification means a person or software applies a set of uniform criteria to define a disease, health event or condition for infectious disease surveillance. The classification is based on the specific objective.

Usually the word “applying a case definition” is used to describe this process. But it is better to use more specific words and use the word “case definition” for the general concept. Classification is often a hidden part of the surveillance system or built into the system in a way that it is not recognized as such. For example, the application of reporting definition is built into the reporting software.

Definitions enable public health officials to classify and count cases consistently for example across reporting jurisdictions. This avoids comparing “apples to oranges”. Classification is important because recorded events can be erroneous and should not be counted. Or there may not be enough information to decide whether a real event has occurred. Without classification, the events form an unclear collection with questionable significance. Even in seemingly trivial classifications, important definitions must be agreed upon: In a mortality surveillance deaths

are counted. But does the death of a tourist with a foreign passport count as a death in the surveillance system?

## 7.1 Typical classification definitions

Table 7.1: Typical definitions used in surveillance systems

Definition	Description
<b>Reference definition</b>	A reference definition is used for official reporting (e.g. national yearly reporting)
<b>Case-finding definition</b>	A case-finding definition is applied for an the search of cases in an outbreak
<b>Notification definition</b>	A notification definition is applied by physisicans or labs whether they should notify a diseases person
<b>Reporting definition</b>	A reporting definition is applied by local public health agencies before reporting a case to a state or national level
<b>Intervention definition</b>	A intervention definition is applied when to act upon an information
<b>ECDC case definition</b>	The ECDC case definitions are used for the reports of ECDC
<b>Outbreak-study definition</b>	An outbreak study definition is used for a cohort or case-study
<b>Suspected case definition</b>	This definition is used in an outbreak response
<b>Probable case definition</b>	This definition is used in an outbreak response
<b>Confimed case definition</b>	This definition is used in an outbreak response
<b>Contact definition</b>	This definition is used in an outbreak response
<b>Clinical definition</b>	A clinical definition is applied when someone in the medical systems uses his or her knowledge whether this constitutes a disease
<b>ICD-10 definition</b>	A medical classification system that is especiall used for the reimbursment of physicians
<b>Infected person</b>	Somebody who inoculated a pathogen, that subsequently replicates within the body
<b>Diseased person</b>	Somebody with an infection with any kind of symptoms that are caused by the infection process.

Example for the application of definitions along the surveillance stages of a case-based surveillance system.

### 7.1.1 Example of the different usages of definitions

A person inoculates hepatitis B virus and the pathogen subsequently replicates in the body of the person (Fullfilling the infection definition). He then develops symptoms (therby fullfilling the diseased person definition) and he seeks the help of a doctor who gives him treatment (aplying a clinical definition) and enters the data into his software for reimbursment (applying the ICD-10 defintion). The physician notifies the local public health agency because the law requires to notify all diseased patients with acute hepatitis B (the notification definition). The local public health agency then decides to act (implicitly applying an intervention definition). They ensue an outbreak investigation and look for cases and contacts (applying case finding definitions or contact definitions). The local public health agency enters the data into their notification software that applies an algorithm and identifies that this event should be reported to the state and national agencies (reporting definition). The national agency reports the case in their official report (applying the referen definition). The software scripts in the national agency find that the event should be reported to ECDC (applying the ECDC case definition)

## 7.2 Components of definitions

Typical definitions in the field of infectious diseases include some or all of the following components

Table 7.2: Components of definitions

Component	Explanation
Time	The timeframe in which a disease is looked at (in surveillance systems this is often missing)
Place	Where a disease is looked at. E.g. a region
Person	Who is looked at. It can be everybody in a certain region or it can be only a specific group in an outbreak session
Clinical	Include common and relevant signs and symptoms of the disease under surveillance Form either individually or in combination a clear or indicative picture of the disease
laboratory	Includes a list with methods used to confirm the pathogen Usually: One of the laboratory methods on the list is sufficient for confirmation of a disease
Epidemiological criteria	Are met when an epidemiological link is established Depending on: Incubation period of the disease Transmission Routes (person-to-person, contaminated food, ...) Endemicity of the disease in the country

### 7.2.1 Example for a clinical part of a case definition

3.34. Q FEVER

**Clinical Criteria**

Any person with at least one of the following three:

- Fever
- Pneumonia
- Hepatitis

Figure 7.1: Case definition for Q-Fever by the european center for disease control

### 7.2.2 Example for a laboratory part of a case definition

**Laboratory Criteria**

At least one of the following three:

- Isolation of influenza A/H5N1 from a clinical specimen;
- Detection of influenza A/H5 nucleic acid in a clinical specimen;
- Influenza A/H5 specific antibody response (four-fold or greater rise or single high titre).

Figure 7.2: Case definition for avian flu by the european center for disease control

### 7.2.3 Example for an epidemiological part of a case definition

<b>Epidemiological Criteria</b>
<u>History of travel to, or residence in</u> an area with documented on-going transmission of Zika virus, within the two-week period prior to the onset of symptoms
OR
<u>Sexual contact with a person</u> recently exposed to or confirmed with Zika virus infection

Figure 7.3: Case definition for zika by the european center for disease control

## 7.3 Specificity and sensitivity

- A definition can be sensitive or specific. Sensitive means that more events are captured but likely this will increase the number of wrongly identified events. Specific means that less events are captured but the number of wrongly identified events is lower.

## 7.4 Creating your own definitions

- Identify the objectives of the surveillance system
- Involve a multi-sectoral team (e.g. physicians, reference laboratories, epidemiologists,...)
- Balance between sensitivity and specificity when collecting / reporting
- Define important and frequently used terms (e.g. fever)
- Use a standardised format and structure for all case definitions
- Plan the implementation of the case definitions (e.g. communicate, train, evaluate)

## 8 Data Processing (Stage 5)

The data processing is where you spend your time in infectious disease surveillance



Data processing is seldom mentioned in classical surveillance literature, but it is a stage that significantly improves surveillance systems. Many people at all levels are involved in data processing within surveillance systems. In the past, data was transmitted monthly by mail in surveillance systems, whereas today, data flow mostly occurs through interfaces between software programs and databases. The way data is transmitted affects data quality and, consequently, the evaluation of the data. Data processing also includes the application of scripts that prepare the data for subsequent evaluation. An example is automated outbreak detection. Here, data is analyzed using an algorithm or machine learning to determine whether there is a high probability of an outbreak. The resulting dataset can be made available as open data, a publication format that has increased significantly in recent times.

### 8.1 Typical ways of data processing

- Questionnaires on paper
- Software interface between laboratory information system and public health notification software
- Accessing a database via an API
- Querying persons with a survey app
- Keeping information in a large excel sheet

## 8.2 Comparing characteristics of manual vs electronic data processing

Characteristic	Manual	Electronic
Ease	Easy	Complicated
Internal validity	Low	High
Speed	slow	fast
Scalability	low	high
Setup costs	low	high
Operational costs	high	low
Acceptability	low	high
Understandability	high	low

## 8.3 Problems of data processing

### 8.3.1 Dependence on the user interface of software

The interface of the software that is used influences the data. If the variables that need to be entered are placed on different spots and described differently than one can expect different results

### 8.3.2 Dependence on classification systems in manual systems

### 8.3.3 Dependence on classification systems in automatic systems

- SnowMed
- FIHR

### 8.3.4 Single point of truth

### 8.3.5 Errors in data handling by the software

- Excel changes specific values to dates automatically
- Excel sheets have only a certain number of rows

## 8.4 Open Data and Public Engagement

Recent trends in data publication have expanded assessment beyond designated experts:

Advantages:

Enables independent verification Increases transparency Potentially leads to novel insights

Challenges:

Risk of misinterpretation by non-experts Necessitates clear communication of data limitations and context

Control group must be - representative of exposures in the source population - be identifiable as cases - have same exclusion and restctition criteria as cases



## 9 Analysis and Assessment (Stage 6)

Be true to yourself



The analysis and assessment stage involves the calculation of relevant indicators, examining data through the lenses of time, place, and person, assessing the results by drawing of conclusions and eventually formulating recommendations. Essentially, this stage transforms raw data into actionable information, aligning with the “data–information–knowledge–wisdom” hierarchy<sup>1</sup>.

The complexity of analysis varies significantly across scenarios:

- Straightforward cases: Some situations demand immediate action based on clear indicators. For instance, a reported case of Ebola in a returning traveler unequivocally signals the need for prompt intervention.
- Complex scenarios: Other situations require nuanced interpretation and extensive expertise. For example, determining whether a relative increase in a SARS-CoV-2 variant warrants action involves intricate analysis and often necessitates collaborative evaluation among experts.

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<sup>1</sup>Rowley, J. (2007). The wisdom hierarchy: representations of the DIKW hierarchy. *Journal of Information Science*, 33(2), 163-180. <https://doi.org/10.1177/0165551506070706>

## 9.1 Analysis

### 9.1.1 Surveillance indicators

The analysis process begins with data from the processing stage, typically structured in spreadsheets or databases. From this foundation, surveillance indicators are computed based on the specific objectives of the surveillance system. Here are key indicators often used in health surveillance:

Table 9.1: Typical indicators used in surveillance systems

Indicator	Description
Count	Total number of cases meeting the relevant definition
Incidence proportion	Probability that a particular event has occurred in a specified period.
Incidence rate	Frequency of new occurrences of a medical disorders in the studied population at risk of the medical disorder arising in a given period of time.
Prevalence proportion	Proportion of a defined population affected by a particular medical disorder at a given point in time, or over a specified period of time
Hospitalisation rate	Incidence rate for cases of a disease that are hospitalised

### 9.1.2 Graphical Display

In addition to computing indicators, data visualization plays a crucial role in making complex information easily interpretable. Graphs transform raw data into visual representations that are readily understood by humans. Common examples in infectious disease surveillance include:

- Epidemic curves (Epicurves): Showing the progression of cases over time
- Dot maps: Illustrating the geographic distribution of cases

### 9.1.3 Time, Place, Person

Infectious disease data is typically analyzed across three key dimensions:

- Time:
  - Data is arranged chronologically to reveal temporal patterns.
  - Example: Epicurves showing the number of cases per day or week.
- Place:

- Data is categorized by geographic distribution.
- In outbreak settings: Dot maps or incidence maps are created.
- In routine surveillance: Indicators are computed separately for each subregion.
- Person:
  - Demographic factors: Age, sex
  - Social factors: Occupation
  - Epidemiological characteristics: Risk factors, vaccination status

#### 9.1.4 Process

While manual analysis can be preferred in outbreak settings for rapid information gathering, the computation of indicators and production of graphs is typically automated using software. Common tools include:

- Spreadsheet applications (e.g., Excel)
- Statistical software packages (e.g., R, Stata)

## 9.2 Assessment

After the data has been analyzed across time, place, and person dimensions, experts evaluate the resulting indicators and graphs. This assessment process is inherently subjective and context-dependent, involving several key aspects:

- Interpretation of Patterns:
  - Analyzing graph shapes and indicator values
  - Identifying and investigating outliers (data points that deviate from typical patterns)
- Contextual Analysis:
  - Incorporating relevant literature and evidence
  - Considering information from other surveillance systems and sources
  - Understanding system limitations (e.g., changes in testing strategies affecting case numbers)
- Holistic Evaluation:
  - Experts synthesize quantitative data with qualitative insights

### 9.2.1 Formulating of public health recommendations

Sometimes the information found in a surveillance system can lead to public health recommendations

### 9.2.2 Recommendations (post-evidence)

#### Warning

Warning: This is the personal opinion of the author and not the standard theory

- Base recommendations on evidence, where evidence is available and do not give recommendations that contradict evidence
- Demphasize areas where evidence is available and emphasise areas where evidence is not available
- Convey uncertainty
- Formulate recommendations with diverse experts
- Try to create more options in the future
- Time your recommendations
- Use gut-feeling, where gut-feeling is likely to be good
- Fit recommendations to the world-view of people
- Minimize harm

### 9.2.3 Recommendations (evidence version)

- Evidence-based (Evidence that the actions recommended will control the outbreak or improve health outcomes)
- Specific (Prioritised clear list of actions that all targeted understand: Describe ‘what’, ‘who’, ‘when’, ‘how’)
- Feasible (Logistics, willingness, systems, access, sustainable)
- Acceptable
- Cost-effective
- Ethical

# 10 Communication (Stage 7)

Communication in a complex world is difficult



Communication is the dissemination of the obtained information in words, writing, and images. Communication consists of traditional elements such as press releases and press conferences or the preparation of reports. Communication now also includes social media and fact-checking. The presentation of data and information in dashboards also counts as communication.

## 10.1 Graphical

the graphical representation of information is often done in terms of time, place, and person

The communication of epidemiological information was a major focus towards the end of the pandemic and is an area with strong development potential. Almost worldwide, a significant portion of the population rejected the measures to combat the COVID-19 pandemic, thereby influencing the course of the pandemic.

# 11 Public Health Measures (Stage 8)

This is what its all about.



Measures are the goal towards which surveillance is directed. Public health measures are all deliberate efforts by commissioned actors aimed at preventing the further spread and generally minimizing the harm caused by infectious diseases. Measures are often legally defined. Measures can be divided into case-based measures and population-based measures. Case-based measures include, for example, informing an affected person about transmission routes or measures such as quarantine. Population-based measures are those that affect many people, for example, the population of a federal state.

Typical interventions taken are:

- guidance: The local public gives the case or his contact persons guidance on what to do and how to behave
- mandate: The local public health official could order a case or a contact person to do something. This could be quarantine for example
- information: the local public health agency informs everybody who needs to know about this public health event

Typical population based interventions are: - Boiling water before drinking - Requiring to wear masks - Closing schools - Giving advice

Typical interventions are: - change in calculated antibiotic therapy (so before information about resistance of the specific pathogen is available) according to a higher resistancy in an area - change in immunization strategies

Typical interventions are: - Wearing masks - Washing handy frequently - Not using public transport - Avoiding specific groups

## **Part III**

# **Types**

## 12 Case based surveillance



A case-based surveillance system focuses on identifying persons that have been diagnosed with an infectious diseases. A person diagnosed with a disease is called a case if the appropriate definition is fulfilled [See the classification stage](#). Case-based surveillance is the most important type of infectious disease surveillance.

### 12.1 Terminology

A case-based surveillance system is also called an indicator-based surveillance<sup>1</sup>. It is called indicator to convey that the focus lies on the compilation of indicators. The term case-based surveillance is - in the eyes of the author of this book - more accurate as it puts the focus on the event under surveillance which distinguishes it from other types of surveillance systems. Other surveillance systems also compile indicators e.g. the viral load in wastewater surveillance. The CDC usually describes the concept as a case surveillance but less frequently also as a notification-based surveillance system<sup>2</sup>. This type is sometimes referred to as physician-based surveillance or lab-based surveillance when physicians or labs are the main provider of information.

### 12.2 Process of a case-based surveillance system

As case-based surveillance is normally mandated by law, the objectives are often laid down during the legislative process. A typical process is that a physician is required to fill out a form when she or he finds a person that has a disease. The form is then sent to a local public health agency where the event is collected and classified. The local public health agency takes appropriate measures and enters the data into a software. This data is transferred to regional or national levels where experts analyse the data for the reporting and supranational measures.

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<sup>1</sup>The surveillance of communicable diseases in the European Union – a long-term strategy (2008-2013)  
<https://www.eurosurveillance.org/images/dynamic/EE/V13N26/art18912.pdf>

<sup>2</sup><https://www.cdc.gov/nndss/about/index.html>



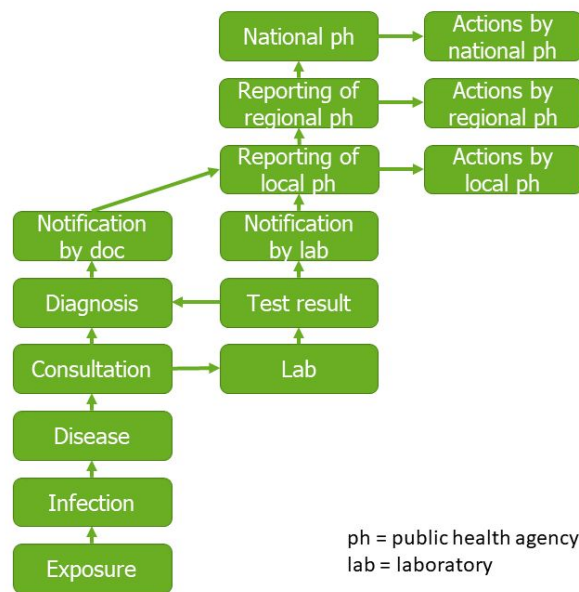


Figure 12.1: Scope of a case based surveillance system. Adapted from ECDC Handbook Data quality monitoring and surveillance system evaluation

## 12.3 Strengths and weaknesses

Strengths:

- measures one central event in infectious diseases directly - allows case-based measures - allows collecting detailed information e.g. on exposure or demographics - usually allows the measurement of the severity of a disease (e.g. hospitalisation)

Weaknesses:

- usually goes along with a strong selection bias, especially in disease with a many asymptomatic cases - expensive - depends on a reliable health system

## 12.4 Example of a case based surveillance system

The German infectious disease reporting system is governed by the Infection Protection Act (IfSG). It is the backbone of epidemiological surveillance in Germany. It has developed historically and has its roots in the Imperial Epidemic Act of 1900. This act has for example the following regulation: *“Any case of illness and any death from leprosy, cholera (Asian), typhus, yellow fever, plague (Oriental bubonic plague), smallpox [...] must be reported immediately to*

*the competent police authority.*” The current reporting system was established in 2000 with the creation of the Infection Protection Act. The reporting system is legally regulated in Sections 6 to 11 of the Act, which have been amended multiple times, usually in response to acute events such as the HUS epidemic in 2011.

The events (Stage 1) monitored are typically the occurrence of infectious diseases. However, the reporting system encompasses various reporting obligations and multiple reporting channels. It can therefore be viewed as a collection of related but essentially different surveillance systems. A significant component of the reporting system is the obligation for physicians, pathologists, and other professionals to report. The event captured in this context is the suspicion of a disease, the diagnosis of the disease, or the death from a diseases. The infectious diseases are laid out in the text of the law and consists out of severe diseases that can be medically diagnosed, such as measles, polio, or HUS. Another relevant component is the obligation for laboratories to report. The monitored event is a laboratory finding indicative of an acute infection. This laboratory reporting obligation applies to a wide range of infectious diseases. In addition to the physician and laboratory reporting obligations, there are other components, such as non-nominal reporting obligations for the laboratory detection of certain pathogens like HIV, which follow a separate reporting pathway.

The capture of physician and laboratory reports (Stage 2) is usually carried out through the reporting process and investigations by the health authorities. For many years, the method of reporting was not standardized and was typically done via fax. In the last decade, the German Electronic Reporting and Information System (DEMIS) has been developed, primarily digitizing the reporting process from the reporter to the health authority. This method of reporting is now legally required for many reporting channels under the Infection Protection Act. The way health authorities conduct investigations is not prescribed, although there are, of course, restrictions due to privacy rights. A common investigation involves a phone call from the health authority and an infection control interview with the affected individuals. The reporting system is thus a hybrid system of passive and active surveillance. It is passive because the monitored events do not exist solely because of the reporting system. For instance, in most cases, a laboratory test is performed for clinical reasons, not for epidemiological reasons. It is active because health authorities actively investigate and contact the affected individuals. Investigation is a central part of the job profile for public health inspectors.

The classification (Stage 3) within the reporting system is performed by the health authority, assisted by the respective reporting software. After entering the collected data, the software indicates whether the event matches the defined criteria. These definitions are twofold: first, there is a definition for events that must be reported to the state authority and the RKI (“reporting definition”), and second, there is a definition for cases officially counted in the RKI statistics (“reference definition”). Establishing these definitions is crucial for ensuring comparability and identifying increases or decreases in the number of cases. At the start of the COVID-19 pandemic, the Chinese government changed the case definition of COVID-19, leading to an artificial spike in the statistics. Case definitions can be sensitive, aiming to

capture as many cases as possible, or specific, aiming to include only a small number of false-positive cases. Case definitions exist not only for a surveillance system but are also often established separately for outbreaks. Additionally, case definitions are not necessarily the standard for implementing measures. For example, in a suspected case of hemorrhagic fever, action does not need to wait until a case definition is met.

Data management (Stage 4) takes place after classification. The reporting system has significantly benefited from more professional data management. Before the introduction of electronic reporting software, data was transmitted laboriously and prone to errors via mail or fax. With increasing digitization and the reduction of media disruptions, data management has become increasingly precise and faster. The most well-known reporting software, SurvNet, from the Robert Koch Institute (RKI), sets the standards for transmission from the health authority to the state authority and from there to the RKI. Data management is carried out in databases operated by the RKI. This process includes quality assurance and data preparation for the subsequent evaluation stage. The preparation also involves automated signal detection, identifying and appropriately displaying potential outbreaks.

The analysis of the reporting system's data occurs at all three levels: local, state, and national. This is similar to the interventions taken. Usually the local agency takes case based measurements, whereas the state and the nation take population-based measurements

# 13 Syndromic Surveillance

Syndromic surveillance refers to surveillance systems where the relevant event is not a diagnosed disease but rather cases from a group of illnesses. So threats can be detected if there is no specific diagnosis yet. Syndromic surveillance can use many different events that indicate a syndrom.

Typical events:

- Physician office visits
- ICD-10 Codes of Hospitals
- Self assessment of people
- Information seeking
- Prescriptions
- Absenteeism

Advantages:

- can detect unknown or lesser-known diseases
- syndromic systems can be very fast
- can often be acquired automatically because it often works well with classification systems like ICD-10 codes

Disadvantages

- Syndromic surveillance is usually a sentinel system and not comprehensive
- Difficult to interpret during high activities of several similar diseases
- Calculating incidence and prevalence is usually biased because the denominator is not clear

Examples: For example, in syndromic surveillance, instead of tracking cases of SARS-CoV-2 infection, cases of acute respiratory illness are recorded. This approach makes the surveillance system more sensitive, capturing a broader spectrum of diseases. When a signal suggests a relevant event, such as an outbreak, further investigation can be conducted to identify the exact pathogen.

# 14 Event based surveillance

How do we find public health threats that we did not anticipate?

**Warning: This is not ready**

Event based surveillance is a defined system that rapidly detects events that might be a threat to public health. These events could be news reports, rumors, social media or informations by other surveillance systems. The collected events are then analysed, assessed and the relevant information is disseminated. The goal of an event based surveillance system is to provide an early warning system and detect previously unknown or generally threats, that are not detected by indicator based surveillance systems.

## 14.1 Stages of event based surveillance

## 14.2 Terminology

### 14.2.1 Event based vs. indicator based surveillance

The term indicator based surveillance is opposite to event based surveillance. Indicator based means that there are predefined indicators that are monitored, for example a syndromic or case-based surveillance system. When you look closely the line becomes somewhat blurred because event based surveillance can also incorporate indicator based surveillance.

Table 14.1: Characteristics of indicator and event based surveillance

Characteristic	Indicator based surveillance	Event based surveillance
Process	Routine, Systematic, Pre-defined pathways and indicators	Formalized, Ad hoc and in real time, Flexible
Data	Organized data with predefined variables, Trusted and reliable, often health-care sector based	Not organized or predefined (variable), Reliability to be assessed

Characteristic	Indicator based surveillance	Event based surveillance
Sources	Formal sources (usually one sector)	All sources (Media/Internet, Communication, Indicator based surveillance)

### 14.2.2 Epidemic intelligence

Event based surveillance and epidemic intelligence are often used as synonyms. But some argue that epidemic intelligence is broader than event based surveillance to emphasize the fact that it also uses indicator based surveillance and encompasses the verification, assessment and investigation steps<sup>1</sup>. But as the usage of indicator based surveillance and steps of verification, assessment and investigation also falls within the definition of event based surveillance or surveillance in general, there is no need to use the term epidemic intelligence.

## 14.3 Strengths and weaknesses

Strengths:

- Can detect unknown or not-thought of public health threats - Is usually fast - Has a formalised way of assessing risks

Weakness: - Large subjective component - Does not give reliable statistical measurements (e.g. trends)

**Definition:** Event-based surveillance is the organized and rapid capture of information about events that are a potential risk to public health<sup>2</sup>

<sup>1</sup><https://www.eurosurveillance.org/content/10.2807/esm.11.12.00665-en>

## 14.4 Sources of event based surveillance

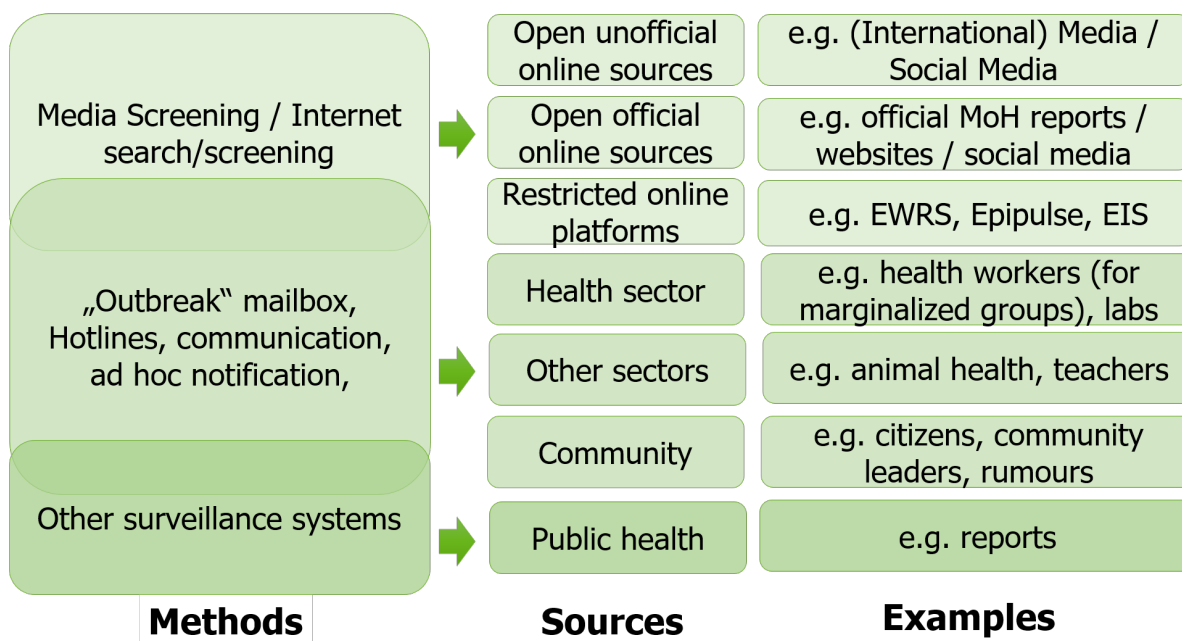


Figure 14.1: Graph adapted from the ECDC Fellowship programme

## 14.5

An example of such surveillance is an expert commission that regularly meets to collect potentially relevant events.

## 14.6 Resources

- Norzin T, Ghiasbeglou H, Patricio M, Romanova S, Zaghlool A, Tanguay F, Zhao L. Event-based surveillance: Providing early warning for communicable disease threats. *Can Commun Dis Rep*. 2023 Feb 1;49(1):29-34. PMID: 38090144

<sup>2</sup>[https://iris.who.int/bitstream/handle/10665/207737/9789290613213\\_eng.pdf?sequence=1](https://iris.who.int/bitstream/handle/10665/207737/9789290613213_eng.pdf?sequence=1)

## 15 Wastewater

Wastewater surveillance is a system that measures indicators of diseases in wastewater. Pathogens can be excreted via stool, urine or washed into the drain during shower. These pathogens can be detected at a wastewater treatment plant.



## 16 Mortality surveillance

Mortality surveillance assesses the number of deaths. One example would be the collection of death certificates by physicians. They are legally required to fill out a form after a person dies. These forms are collected by specific agencies and the number of deaths or the reasons for death can be analysed by public health experts.

# 17 Mass-Gathering Surveillance

Mass-gathering surveillance refers to surveillance systems that are set up for the duration of a special event. A mass-gathering is a planned or spontaneous event where the number of people attending could strain the planning and response resources of the community or country hosting the event<sup>1</sup>

Mass-gatherings can be a threat to public health because any large group of people poses the risk of the spread of an infectious disease. Such events are also accompanied by many small food vendors, that have limited facilities. As many mass-gatherings usually go along with lots of international attention and the attention of media, there is usually a political pressure.

Typically, different components from other surveillance systems are employed. For instance, a separate surveillance system might be implemented during a European Football Championship.

## 17.1 Additional reading

- Mass gathering events and communicable diseases - Considerations for public health authorities <https://www.ecdc.europa.eu/sites/default/files/documents/Mass-gathering-events-and-communicable-diseases-June-2024.pdf>

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<sup>1</sup>WHO Definition of mass-gathering. <https://www.who.int/news-room/questions-and-answers/item/what-is-who-s-role-in-mass-gatherings>

## **18 Active vs passive**

Case based surveillance systems can be divided whether they are active or passive. Many surveillance systems have elements of both.

### **18.1 Active surveillance system**

An active surveillance system involves a group of individuals who actively collect information for the surveillance system.

An example of an active surveillance system would if the staff of an agency goes door-to-door to gather information.

### **18.2 Passive surveillance system**

A passive surveillance system uses data collected for other purpose. Passive surveillance can be seen as secondary data analysis.

An example for a passive surveillance system could be a system that extracts data from a hospital database.

## 19 Sentinal vs comprehensive

Sentinel surveillance is a system that does not monitor all individuals about whom conclusions are to be drawn but rather only a defined portion. The term “Sentinel,” means “watchman,”. A sentinel system saves resources and generally allows for more detailed information to be collected. The level of detail is often crucial for assessing epidemiological questions, such as evaluating the severity of a disease. For example, a few medical practices might be selected to collect detailed information on respiratory illnesses, including vaccination status, disease severity, and information on individuals without respiratory illnesses as a comparison group. These practices’ data can then be extrapolated to represent all medical practices. The alternative—examining all practices directly—is much more labor-intensive and risks lowering data quality because some information may be provided reluctantly.

# About

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### The contents of the book

- Most content comes from the “EPIET-World”. One important basis is the introductory course of the ECDC Fellowship Programme and specifically the presentations that have been held there by numerous european surveillance experts. \* One important source are the publications by ECDC namely the Handbook on evaluating infectious disease surveillance
- The publications from CDC have been used especially
  - <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3820481/>

### Usage of images

- Only images that had a creative commons were used (except the pictures from Bing Image Creator). The authors of the work are written underneath each picture.
- The primary source of images is Mediawiki the image storing space of Wikipedia the greates project of the internet.

### Coding and publishing of the book

This book builds upon the wonderful software of [quarto](#), that itself uses many open source software projects. One important basis is R and Git. This book is published on github.

### Usage of artificial intelligence

- ChatGPT has been used to polish the text and help with the wording. It has neither been used to generate content or to structure the book or a text. ChatGPT has also been used to code - especially the stages graph.
- Bing Image Creator has been used to create images