

# VALIDATION OF A CODE-BASED DATA COLLECTION METHOD IN PRIMARY CARE

for influenza-like illness surveillance in Belgium:

**Protocol** 

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## **ABSTRACT**

**BACKGROUND** 

Internationally, researchers have explored alternative data sources beyond historical sentinel surveillance systems (based on questionnaires) to address their inherent limitations and enable real-time estimates of influenza activity. In this context, Electronic Health Records (EHR) data collection method have shown promise, although comparative studies with the traditional method are limited in the literature.

In Belgium, the COVID-19 Barometer in General Practices (cBGP) rapidly provided COVID-19 data during the pandemic. This EMR-based semi-automated tool also captured daily data on Influenza-like Illness (ILI).

Meanwhile, the long-running questionnaire-based ILI surveillance of the Sentinel General Practitioners network (SGP) is hampered in its expansion.

This study aims to determine the gains and losses of replacing the questionnaire-based method with a code-based method for ILI surveillance data collection in Belgian general practices.

#### **METHODS**

The Centers for Disease Control and Prevention (CDC) guidelines for evaluating surveillance systems will serve as a framework for a retrospective comparison of cBGP with established ILI data collection methods.

First, requirements for the ILI surveillance system in Belgium will be defined. Then, the surveillance systems will be evaluated based on nine attributes: Data Quality, ILI Incidence, Sensitivity, Representativeness, Timeliness, Stability, Simplicity, Acceptability and Flexibility.

Quantitative and qualitative measures, as well as thresholds, will be determined to ensure a comprehensive performance evaluation.

The Simple Multi-Attribute Rating Technique (SMART) method will be applied to identify the optimal approach among three defined alternatives: to retain, complement, or replace the SGP data collection method, outlining focus points. Experts will score and assign importance-related weight to attributes per alternative. The alternative receiving the highest endorsement will be recommended.

#### **RESULTS**

The results will allow the appraisal of the shift from questionnaire- to code-based ILI data collection method in Belgium and highlight key points for optimising cBGP use.

#### **CONCLUSIONS**

This assessment will improve the understanding and strengthening of ILI surveillance data collection methods in Belgian primary care.

## **ABBREVIATIONS**

ARI	Aguta Rospiratory Infactions
ATC	Acute Respiratory Infections
	Anatomical Therapeutic Chemical
AVIQ	Agence pour une Vie de Qualité
BE	Belgium
сВGР	COVID-19 Barometer in General Practices 2.0
CDC	Centers for Disease Control and Prevention
CNK	Code National / Nationale Kode
ECDC	European Centre for Disease Prevention and Control
eForm	Electronic form
EFPC	European Forum for Primary Care
EGPRN	European General Practice Research Network
EHR	Electronic Health Records
EISS	European Influenza Surveillance Scheme
EMR	Electronic Medical Records
EU	European Union
GISRS	Global Influenza Surveillance and Response System
GP	General Practitioner
GP OOH posts	General Practitioner Out-Of-Hours posts
HD	Healthdata.be
HSR	Health Service Research
ICD-10	International Classification of Diseases 10 <sup>th</sup> Revision
ICPC-2	International Classification of Primary Care 2 <sup>nd</sup> edition
GI	Goldstein Index
ILI	Influenza-Like Illness
MCDM	Multi-Criteria Decision Making
MEM	Moving Epidemic Method
NH	Nursing Homes
NIC	National Influenza Centre
NIHDI	National Institute for Health and Disability Insurance
NRC	National Reference Centers
NUTS	Nomenclature of Territorial Units for Statistics
ООН	Out-Of-Hours
RSV	Respiratory Syncytial Virus
SARI	Severe Acute Respiratory Infection
SGP	Sentinel General Practitioners Network
SMART	Simple Multi-Attribute Rating Technique
TESSY	The European Surveillance System
WHO	World Health Organisation
WONCA	World Organization of National Colleges, Academies
	and Academic Associations of General Practitioners /
	Family Physicians

## **GLOSSARY**

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#### The labelling of attributes

For the sake of clarity, the attributes – representing the characteristics of the surveillance systems – will be denoted with a capitalised first letter throughout the document (unless explicitly accompanied by the term 'attribute'), as follows: Data Quality, ILI Incidence, Sensitivity, Representativeness, Timeliness, Stability, Simplicity, Acceptability, and Flexibility.

#### The surveillance systems

Across this protocol, the terms 'surveillance systems' and 'systems' will be used interchangeably to refer to public health setups established to carry out the ongoing and systematic collection, analysis, and interpretation of health data for the purpose of describing and monitoring health events<sup>1</sup>. This approach aims to enhance readability and fluency.

#### The CDC guidelines

The expression 'CDC guidelines' will serve as a concise reference to the 'Updated Guidelines for Evaluating Public Health Surveillance Systems' issued by the Centers for Disease Control and Prevention.

## INTRODUCTION

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## 1. Background

#### 1.1. INFLUENZA GENERAL INFORMATION

Seasonal influenza, caused by globally circulating influenza viruses, spreads easily in crowded settings. In temperate regions of the Northern Hemisphere, influenza epidemics primarily occur in winter.

Most cases, characterised by symptoms such as sudden onset of fever, cough, headache, muscle and joint pain, sore throat and a runny nose, resolve within a week without any specific medical attention. The transmission occurs via respiratory droplets expelled by infected individuals through coughing or sneezing. However severe complications can arise, particularly in high-risk groups (adults>65y, children<5y, pregnant women and people with chronic medical conditions)<sup>3</sup>.

In Belgium, on average, 1 person in 1000 influenza cases encounters complications that necessitate hospitalisation and more than 90% of deaths concern people of 65 years and over<sup>4</sup>.

Due to significant disease burden<sup>5,6</sup>, socio-economic impact<sup>6</sup>, vaccine-preventability<sup>7</sup>, and pandemic potential<sup>8</sup>, effective influenza surveillance is essential for public health.

#### 1.2. NEED FOR INFLUENZA-LIKE ILLNESS SURVEILLANCE SYSTEMS

#### 1.2.1. Measuring influenza activity

Clinically distinguishing influenza from other respiratory viruses is particularly challenging outside epidemic periods or during low influenza activity. Flu-like symptoms can also be caused by viruses such as SARS-CoV-2 or Respiratory Syncytial Virus (RSV). Moreover, since the COVID-19 pandemic, the relationship between the incidence of suspected influenza and actual influenza rates has been disrupted due to the co-circulation of influenza viruses and SARS-CoV-29.

To assess influenza activity with post-pandemic data, one possible method is the Goldstein Index (GI)<sup>10</sup> calculation. As a proxy for influenza rates, the GI adjusts the incidence of suspected cases by accounting for the proportion of positive influenza tests.

With regards to the confirmed diagnosis of influenza, it is not routinely established and requires laboratory analysis of respiratory specimens using techniques such as Reverse Transcription Polymerase Chain Reaction (RT-PCR) or antigen detection assays<sup>11</sup>.

In view of the above, the WHO ILI case definition, updated in 2018, supports surveillance systems in capturing ILI cases and aims to enhance the case definition's specificity without considerably compromising its sensitivity<sup>12</sup>.

Table 1 • Revision of ILI case definition by the WHO

ILI case definition from the WHO (2011)	ILI case definition from the WHO (2018)
'A sudden onset of fever, a temperature >38°C and cough or sore throat in the absence of another diagnosis'.	'An acute respiratory illness with a measured temperature of ≥ 38 °C and cough, with onset within the past 10 days'.

The notion of ILI was therefore introduced to facilitate monitoring, acknowledging the non-specific nature of influenza symptoms and the limited testing of individuals for the virus.

#### 1.2.2. From sentinel surveillance systems to combined surveillance systems

#### 1.2.2.1. Internationally

#### a. The early days of sentinel surveillance systems

The importance of flu surveillance had been recognised and encouraged by experts before the WHO was created in 1948. The Spanish flu pandemic of 1918 and later the first isolation of an influenza virus in 1933 provided the impetus for influenza surveillance<sup>13</sup>.

The WHO Global Influenza Surveillance and Response System (GISRS) was presented in September 1952 in Geneva as the WHO influenza surveillance network to provide the global mechanism for surveillance, preparedness and response to seasonal, pandemic and zoonotic influenza.

Continuing this approach on an international scale, national networks of sentinel GPs were gradually set up around the world, notably in the Czech Republic (1951), the United Kingdom (1967), the Netherlands (1970), Belgium (1979) and many other countries<sup>14,15</sup>.

#### b. The growth of interest and research in Electronic Health Records (EHR)

In the early '90s, hardware became more affordable and access to the Internet made it possible to obtain information more quickly and easily. In addition, personal computers became more widespread, as more powerful and compact hardware became available <sup>16</sup>.

In this context, Electronic Health Records (EHR) were developed with the main advantage of saving medical staff time, initially on simple tasks such as photocopying, eliminating filing and retrieving files<sup>17</sup>. Then, physician workstation has enabled more clinical uses, with GPs accessing their notes, nurses' notes, prescriptions, lab results and also the linkage to tools such as pharmaceutical references, bibliographic search engines and electronic communication tools<sup>18</sup>.

The number of articles published on EHR increased considerably between 1991 and 2005 in 39 countries located in America, Europe, Africa, Asia and Oceania<sup>19</sup>. This significant growth demonstrates the worldwide interest in the potential of EHR.

#### c. Combined ILI surveillance systems

To address the need for real-time estimates of influenza-like illness (ILI) activity and to overcome certain limitations of sentinel surveillance systems, such as timeliness and representativeness, research in various countries has explored alternative data sources. These include data derived from direct citizen participation<sup>20</sup>, school absenteeism<sup>21</sup>, and EHR<sup>22</sup>.

A recent scoping review<sup>23</sup> was conducted, covering international articles published between 2007 and 2022, which compared at least one non-traditional influenza surveillance system with a traditional system, focusing on the correlation of activity or timeliness. Among the 57 articles included, EHR-based surveillance systems were the most frequently studied, with 15 dedicated investigations. Of the alternative approaches, EHR-based and participatory systems demonstrated the greatest consistency across studies in their potential to complement sentinel surveillance systems.

#### 1.2.2.2. In Europe

By 1990, influenza surveillance was well established in most European countries, although it operated in an uncoordinated manner. To harmonise these activities, the European Commission funded the Eurosentinel<sup>24</sup> project in 1988. This initiative led to the launch of several programmes, including one specifically focused on influenza. This initial project evolved into ENSCARE, later becoming the European Influenza Surveillance Scheme (EISS) in 1996, and finally the current European Influenza

Surveillance Network (EISN) in 2008, which is coordinated by the European Centre for Disease Prevention and Control (ECDC).

At first, sentinel surveillance systems relied predominantly on questionnaire-based data collection. Over time, code-based data collection methods have emerged, enabling data registration through diagnosis code classifications embedded in EHR.

There is limited research directly comparing EHR-based surveillance systems with sentinel GP surveillance systems in Europe, and a comprehensive evaluation of their characteristics remains scarce. Nonetheless, a literature review indicates a promising correlation between data from code-based and traditional ILI surveillance systems. In Switzerland, data based on ICPC-2 codes extraction showed a strong correlation with sentinel system data and demonstrated potential to support the sentinel reporting system<sup>25</sup>. Similarly, researchers in Portugal identified a high correlation between weekly primary care consultations coded with ICPC-2 R80<sup>26</sup> and the weekly incidence rates reported by sentinel general practitioners. In Belgium, a prior study found that ILI detection was as rapid in the sentinel system as in the computerised network<sup>27</sup>.

#### 1.2.2.3. In Belgium

#### a. The established ILI/influenza surveillance systems

In Belgium, an integrated surveillance system has been set up to monitor influenza at different stages of severity, aiming to cover all levels of the influenza surveillance pyramid<sup>28</sup>, bringing together and coordinating the efforts of each system to enable better management and response by public health authorities.

The surveillance pyramid in Figure 1 shows the levels of severity of influenza cases: asymptomatic and symptomatic cases of suspected influenza, consultations for suspected influenza and possible testing for confirmed influenza diagnosis, hospital admissions and deaths.

The systems at each level of the pyramid are briefly described, including, where applicable, details on their implementation date, coordinating body, number of participating entities, data collection methods, and added value.

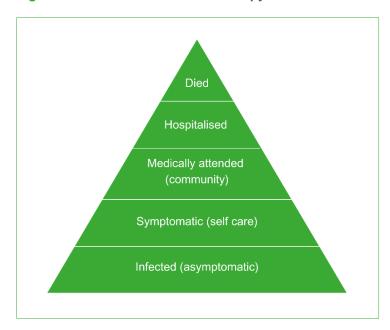


Figure 1 • The influenza surveillance pyramid

#### a.1. Asymptomatic and symptomatic cases of suspected influenza:

#### Infectieradar.be<sup>29</sup>

Part of the European consortium Influenzanet, Infectieradar.be is a participatory surveillance platform active in Belgium since 29 March 2021. It invites voluntary participants (mostly adults), to complete a brief weekly questionnaire about ILI symptoms, other infection symptoms and health complaints. During the tenth week of 2025, 2324 participants submitted their completed questionnaires<sup>30</sup>.

Given that many individuals with mild or minimal symptoms do not consult a GP or undergo testing, this platform enhances the tracking of pathogen spread in Belgium by taking into account individuals regardless of medical consultation. In addition, by accounting for asymptomatic cases, Infectieradar.be also helps refine the estimation of the catchment population.

#### a.2. Consultations for suspected influenza:

#### Sentinel General Practitioners Network (SGP)<sup>31</sup>

Established in 1979, the Sentinel General Practitioners Network (SGP) has provided Belgian surveillance of ILI through the voluntary participation of GPs<sup>32</sup>. Since 2007, this network, whose data collection method is questionnaire-based, has operated as a continuous national surveillance system monitoring ILI and acute respiratory infections.

Sciensano (formerly WIV-ISP) organises the SGP and publishes related epidemiological data, among other findings, in weekly reports (Bulletin of Acute Respiratory Infections<sup>33</sup>). These reports include incidence data and analyses of samples collected from a subset of the patient population by accredited laboratories (National Reference Centers (NRC)).

During week 12 of this year, 50 practices<sup>33</sup> provided data for the ILI incidence calculation, offering high-quality data to fulfil both national and European (ECDC) requests.

#### Improving Care And Research Electronic Data Trust Antwerp (iCAREdata)<sup>34</sup>

Since 2014, the iCAREdata project has been providing a central clinical research database infrastructure enabling the collection, linking and integration of clinical individual patient data from electronic records of emergency departments, GP out-of-hours (OOH) posts and pharmacies.

This project is coordinated by the University of Antwerp and aims to optimise primary and interdisciplinary OOH care. Among other potential benefits, the data provided by OOH services could constitute a timely source of information<sup>35</sup> and make it possible to link patient data from the different iCAREdata sources to the same individuals, while complying with privacy regulations.

This unique infrastructure currently collects data, using an EMR-based method, on several diagnoses, including infectious diseases, from GPs working in 36 OOH posts<sup>36</sup> in Flanders (see Annex 1).

#### • ILI sentinel surveillance in Belgian nursing homes (ILI-NH)<sup>37,38</sup>

The ILI-NH was initiated on 17 October 2022, following the COVID-19 pandemic, which highlighted the significant burden of ILI in this vulnerable population<sup>39,40</sup>. Participating Nursing Homes (NH) complete, on a weekly basis, a questionnaire to report ILI cases encountered.

Coordinated by Sciensano, the system monitors emerging infectious diseases in NH populations and the data on ILI is reported in the 'Bulletin of Acute Respiratory Infections'.

As of season 2024/2025 (from week 40 to week 4), on weekly average, 73 NH were part of the network.

#### a.3. Possible testing for confirmed influenza diagnosis:

#### Sentinel laboratories network<sup>41</sup>

Since 1983, Sciensano coordinates a network of microbiology laboratories, referred to as sentinel laboratories, which provide diagnostic data on various pathogens on a weekly basis. Participating laboratories complete questionnaires to report the data.

The system relies on the voluntary cooperation of laboratories and facilitates the identification of circulating pathogens.

In 2013, the participation rate was 59%<sup>42</sup> (97 participating laboratories out of 163 microbiology laboratories). Currently, although the participating sentinel laboratories are not sufficiently representative at the national or regional level to provide incidence data, they remain essential for complying with international obligations to report pathogen-specific data.

#### National Reference Centre (NRC)<sup>43</sup>

For over a decade, Belgium has established a network of NRCs for human microbiology.

The NRC Influenza (also known as the National Influenza Centre) is a WHO-recognised centre responsible for conducting first-line and second-line specialised diagnostic tests on suspected influenza samples. These samples are provided by sentinel surveillance systems, including SGP, NH-ILI, and the Severe Acute Respiratory Infection (SARI) surveillance network, as well as non-sentinel systems such as hospital laboratories. These epidemiological and microbial data are reported at national and international levels.

Since the beginning of this year, NRC influenza is part of NRC Respiratory Pathogens, which is coordinated by UZ Leuven/KU Leuven in association with Universiteit van Antwerpen, Universitair Ziekenhuis Antwerpen and Sciensano.

#### a.4. Hospital admissions:

Severe Acute Respiratory Infection (SARI) surveillance by a sentinel network of hospitals<sup>44</sup>

Since 2012, general hospitals can take part in Belgian surveillance of SARI. The network covers patients in all Belgian provinces. In 2023, the SARI network comprised 10 actively participating hospitals. The aim of this surveillance is to detect, at a relatively early stage, signs of increased severity of seasonal influenza and other acute respiratory infections, and to report them to the health authorities<sup>45</sup>.

The BELSARI-NET research group, made up of people responsible for surveillance in the participating hospitals and involved Sciensano researchers, is managing this project. The surveillance is coordinated by the Service Epidemiology of Infectious Diseases of Sciensano.

#### a.5. Deaths:

#### Be MOMO<sup>46,47</sup>

Be-MOMO carries out the surveillance of all-cause mortality at both the national and regional levels in Belgium and is also part of the European Mortality Monitoring project, EuroMOMO.

Launched in 2004, it provides near real-time surveillance of unusual mortality patterns that may arise from various circumstances, including disease outbreaks such as influenza.

The Epidemiology of Infectious Diseases Service at Sciensano conducts weekly analyses of the mortality data from the Belgian National Register.

Be-MOMO serves as a tool for the rapid detection and quantification of excess mortality, supporting the guidance and reinforcement of new or existing public health measures, such as influenza vaccinations.

#### b. The code-based surveillance system to be validated for ILI data collection

In the early stages of the COVID-19 pandemic (March 2020), an instrument<sup>48</sup> was developed to monitor the burden on GPs during the first wave, informing on the GPs' workload, the availability of personal protective equipment and COVID-19 activity.

In September 2020, this instrument was updated into a real-time syndromic surveillance tool, called the COVID-19 Barometer in General Practices 2.0 (cBGP)<sup>49</sup>. This version expanded to include all Belgian Electronic Medical Records (EMR) software packages, each with its own using electronic forms (eForms) for daily data entry and transfer.

During the pandemic, ILI and Acute Respiratory Infections (ARI) were also used as early markers for monitoring COVID-19, as initial symptoms such as cough and fever were difficult to distinguish from other respiratory infections. Consequently, the epidemiological data collected from the tool were COVID-19 (suspected or confirmed), ARI, ILI, and viral syndrome based on recorded diagnostic codes ICPC-2<sup>50</sup> and ICD-10 codes (see Annex 2).

Although it has not been formally validated for ILI surveillance and was not associated with virological sampling, it has demonstrated potential, particularly in the early detection of COVID-19 and the engagement of a large number of general practitioners. Additionally, this semi-automated tool could ease GPs' workload and provide timely data, making it a promising system for future surveillance initiatives in Belgium.

Since October 2024, the GP Infection Barometer has replaced cBGP, broadening its scope with more diagnostic codes extracted (see Annex 3) and therefore covering a wider range of health topics. It also introduces new features, including full automation, age categories and a proxy for episodes. This study will focus on the cBGP, which provided data from 2020 to 2024, but the results and recommendations will then be examined in the context of the new version of the cBGP.

## 2. Research question

'What are the gains and losses of replacing the questionnaire-based method with the code-based method for ILI surveillance data collection in Belgian general practices, to support data-based decision-making?'

## 3. Objectives

The objectives outlined below will support answering the research question and provide a robust understanding of ILI surveillance in Belgium.

#### 3.1. PRIMARY OBJECTIVES

The first objective of this study is to determine if and to what extent the cBGP is comparable to other established ILI surveillance systems in Belgium. This purpose entails conducting both quantitatively and qualitatively an evaluation comparing the systems' performance based on defined criteria (attributes).

#### INTRODUCTION

The second objective is to provide information on the suitability and reliability of cBGP tool to ensure ILI surveillance. This study intends to measure and describe the gains and losses of using the cBGP data collection method instead of the current SGP method.

Thirdly, the study aims to highlight areas for improvement and determine how potential solutions or recommendations could be implemented to enhance ILI surveillance system in Belgium, hence help with data-based decision-making.

#### 3.2. SECONDARY OBJECTIVE

Another objective of this study is to document the process, beginning with a pilot project set up during the pandemic, and evolving into a tool with the potential to support sustainable and reliable surveillance of respiratory infectious diseases, while also advancing knowledge of EMR-based surveillance systems.

## **METHODS**

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## 1. Methodological framework

#### 1.1. THE FRAMEWORK FOR THE CURRENT STUDY

The CDC guidelines (<u>see 1.2.</u>) will be used to provide evidence on the systems' strengths and weaknesses, while the Simple Multi-Attribute Rating Technique (SMART) method will guide the decision-making process (<u>see 1.3.</u>).

Regarding the surveillance systems' performance, the study will focus on 'gathering credible evidence of surveillance performance' to enable an informed decision for the validation of the cBGP system. Other tasks, outlined in the CDC guidelines, could help to evaluate additional elements, but will not be detailed in this protocol.

First, the requirements of ILI surveillance system in Belgium will be defined. Then, to evaluate the code-based data collection method in addressing these identified needs, a comparative assessment will be conducted against established surveillance systems for ILI and influenza, based on selected attributes. For each attribute, quantitative and qualitative measures will be determined, along with thresholds based on the 'Global Epidemiological Surveillance Standards for Influenza'<sup>51</sup> and the 'Operational considerations for respiratory virus surveillance in Europe'<sup>52</sup>, to ensure a thorough evaluation.

The SMART method will be adopted to guarantee an appropriate choice regarding the future ILI surveillance system. A group of experts will choose one of three alternatives, each with specific recommendations: maintaining, replacing, or supplementing the long-standing SGP system for ILI data collection. The experts will score and assign an importance-related weight to each attribute for each alternative based on the performance assessment results. The highest-endorsing alternative will be presented as the recommended option, and will then be discussed with experts and researchers to facilitate its implementation.

#### 1.1.1. ILI surveillance system needs

The needs for ILI surveillance in Belgium are directly related to the necessity for EU member states to strengthen the coordinated surveillance of communicable diseases. Member states are obliged to provide information on the evolution of the situation regarding communicable diseases, including influenza. The importance of early detection and evidence-based decision-making is at the heart of regulatory document<sup>53</sup>.

Based on this EU perspective and taking into account the long Belgian experience in ILI surveillance, the following points have been targeted as priorities:

- Continuous monitoring and description of epidemic stages (start, intensity, duration)
- Rapidly detecting changes: early warning system
- Matching the global effort (internationally and in Europe) to timely estimate epidemics or pandemics based on sustainable surveillance systems
- Supporting evidence-based decision-making

#### 1.1.2. Identification of attributes

#### 1.1.2.1. In accordance with the ILI surveillance systems needs

#### a. Continuous monitoring and description of epidemic stages

An evaluation of **Data Quality**, **Stability**, **ILI Incidence** and **Representativeness** addresses these needs. If the surveillance systems deliver complete and reliable data on ILI activity and are free from operational interruptions, the primary task required of the ILI surveillance system is assured.

#### b. Rapidly detecting changes: early warning system

Three key elements can be underscored with respect to detection and rapidity.

Firstly, the ability to detect potential influenza cases is intrinsically linked to the accurate identification of the cases encountered, making an assessment of **Sensitivity** essential in this context. Secondly, the rapidity of detection can be assessed by comparing the time at which the ILI incidence curve crosses the so-called epidemic threshold for the different systems analysed. An evaluation of **ILI Incidence** will shed light on this point. Thirdly, the rapidity of the process between the onset of symptoms in an individual and the notification of the case in the epidemiological situation report can be apprehended by evaluating the **Timeliness**.

## c. Matching the global effort (internationally and in Europe) to timely estimate epidemics or pandemics based on sustainable surveillance systems.

Firstly, this point highlights the European and international requirements regarding the nature of the data transmitted. Therefore, consideration of the relevant standards is essential.

Secondly, the sustainable aspect of a system is crucial to ensure effective and lasting surveillance of ILI, as well as to anticipate potential obstacles to the proper functioning of surveillance systems during a health crisis, for example. Assessing **Acceptability**, **Flexibility** and **Simplicity** supports the evaluation of the systems' long-term viability.

The existence of the primary care systems developed in this protocol relies on the involvement of GPs. The evaluation of Acceptability will therefore be important in this respect.

To ensure the system endures, if greater GP participation is necessary, the complexity of the system in which they are being asked to engage may hinder their involvement. Flexibility analysis is useful in assessing the system's ability to adapt to changes, whether in preparation for a pandemic, or in modifying the variables used in data collection to enhance its quality.

#### d. Supporting evidence-based decision-making

The notion of evidence-based decision-making is multi-dimensional<sup>54</sup> and not all of its aspects will be considered in this analysis. Instead, this study will focus on the assessment of **Timeliness** and **Data Quality** to determine whether authorities have access to valid data promptly.

#### 1.1.2.2. List and definition of attributes

Among the attributes presented in the CDC guidelines, the following will be examined:

- Data Quality will pertain to the completeness and validity of the data recorded.
- **Positive Predictive Value** will not be considered as such, but the **ILI Incidence** will be used instead. This attribute will reflect the ability to provide reliable incidences of ILI.
- Sensitivity will refer to the capacity to record cases.
- **Representativeness** will refer to the population covered by surveillance systems and the distribution of participants at different geographical scales.

- **Timeliness** will represent the speed at which each step in the system operation is executed.
- **Simplicity** will refer to the ease of use from the user's point of view, as well as the ease of system operation.
- **Stability** will denote the system's capacity to deliver data without failures and to operate without disruptions.
- Acceptability will indicate the willingness of GPs to participate in the surveillance system.
- Flexibility will reflect the system's ability to adapt to change.

#### 1.1.3. Relationship between attributes

The CDC guidelines depict the potential relationships that may be observed between attributes. Although these interactions are not exhaustively listed below and may be downplayed by the results, they remain important points of attention for discussing the findings as well as scoring and weighting attributes.

**Data Quality** could influence all the data provided by the surveillance systems, as it constitutes a foundational step for using the data and ensures that data is accurate and consistent.

**Sensitivity** may impact **ILI Incidence**. For instance, if the system fails to record ILI cases, it will affect the total number of recorded cases and, consequently, the calculation of incidence.

**Acceptability** may influence **Representativeness**. For example, if more GPs are willing to participate, a more representative group of participants is likely to be obtained.

**Simplicity** could influence **Flexibility**, **Acceptability**, and **Timeliness**. A simpler system will be easier to modify, and if the system is easier for users too, it may lead to improved participation. Additionally, the time taken to transition between stages of the data flow could be reduced.

**Stability** could affect **Data Quality** and **Acceptability**. A system prone to frequent failures could lead to missing data, negatively impacting **Data Quality** and **Acceptability** by discouraging participants due to operational disruptions. High-quality data could encourage greater participation, as GPs might be more motivated if they can visualise the outcomes of their contributions and apply these results to their practice.

#### 1.1.4. Prioritisation and scoring of attributes

Once the attributes have been assessed, three options will be considered for ILI surveillance data collection: the first is to rely only on the cBGP system; the second is to maintain the SGP system alongside the cBGP system; and the third is to conclude that there is insufficient evidence to depend on ILI data provided by the cBGP system.

For each alternative, a group of experts will be responsible for ranking the attributes according to their importance, assigning weight accordingly and scoring them. In this way, each option will be assigned a value based on the score and weighting of each attribute, enabling the selection of the alternative that garners the most approval.

The formula<sup>55</sup> in Figure 2, shows the scoring and weighting principles of the SMART method, considering a set of k attributes, ranging from 1 to k, and an alternative j.  $W_k$  represents the normalised weighting of attribute k, and  $u_{jk}$  denotes the score assigned to attribute k for alternative j. The product of

 $W_k$  and  $u_{jk}$  provides a value for attribute k. Summing these values across all attributes from 1 to k yields  $U_i$ , the overall value associated with alternative j.

Figure 2 • Equation for calculating the value of an alternative55

$$U_j = \sum_k w_k u_{jk}$$

Note: the reference article indicates objectives rather than attributes.

#### 1.2. THE CENTERS FOR DISEASE CONTROL AND PREVENTION (CDC) GUIDELINES

The CDC Guidelines for the Evaluation of Public Health Surveillance Systems which are intended to ensure that issues of public health importance are monitored effectively and efficiently, provide a robust and comprehensive framework for the evaluation of surveillance systems.

The guidelines report is designed as a practical document comprising several steps, called tasks, for carrying out the evaluation. Six main tasks are described: engaging the stakeholders, describing the surveillance system, focusing on the evaluation design, gathering credible evidence regarding the performance of the surveillance system, providing a conclusion and recommendations, and finally ensuring the use of evaluation findings.

In order to start the performance evaluation, firstly, the surveillance system's purpose and objectives have to be defined and accordingly appropriate attributes should be assessed.

Nine attributes are used to assess surveillance systems' performance: Simplicity, Flexibility, Data quality, Acceptability, Sensitivity, Predictive value positive, Representativeness, Timeliness, and Stability.

Each attribute is defined and accompanied by a method of assessment and discussion. The attributes' description also includes the relationship between attributes, given that certain overlaps or links may be observed.

- Simplicity refers to both the structure and the ease of use of the surveillance system.
- Flexibility refers to the system's ability to adapt to changes (i.e. information needs).
- Data quality includes the completeness and validity of the data recorded.
- Acceptability reflects the willingness of individuals and organisations to participate in the surveillance system.
- **Sensitivity** may comprise two levels in the CDC guidelines: a case notification level, but also a level referring to the ability to detect epidemics.
- **Positive predictive value** indicates the proportion of reported cases that actually present the disease under surveillance.
- **Representativeness** describes the occurrence of a health event over time and its distribution in the population by place and by person.
- Timeliness reflects the speed between steps in a public health surveillance system.
- **Stability** refers to the capacity to provide data correctly without failure, and the ability to be operational when needed.

#### 1.3. THE SIMPLE MULTI-ATTRIBUTE RATING TECHNIQUE (SMART)

The Multi-criteria decision making (MCDM) method is a tool which aims to help the understanding and handling of the several criteria that are involved in the decision-making process and allows the choice of a workable option among a finite set of alternatives. This approach has been used in several domains, including for communicable diseases<sup>56</sup> to prioritise what diseases should receive the greatest public health attention.

SMART has been adopted as a suitable MCDM approach in decision-making for, among other advantages, its ease of use and calculation<sup>57</sup>.

In a recent article, Taherdoost and Mohebi outline the steps for applying SMART as follows<sup>57</sup>(see Annex 4): identifying the decision-maker(s), defining the problems and alternatives, determining the relevant value factors for assessing alternatives, ranking the identified dimensions in order of importance, normalising their weights, calculating utilities for alternatives, and making the decision.

## 2. Study design

#### 2.1. STUDY TYPE

We will conduct a retrospective observational study based on aggregated data collected during 2021–2024 in general practices, in Belgium.

#### 2.2. STUDY PERIOD

The study period will extend from 20 June 2021 to 15 June 2024, covering three influenza seasons.

Although monitoring for ILI is continuous, and the reference period typically runs from week 40 (October) to week 20 (May) of the following calendar year, observing ILI activity from week 25 (June) provides a baseline before the usual onset of a new influenza epidemic. The seasons will thus start from week 25, each year and run through to week 24 of the following year.

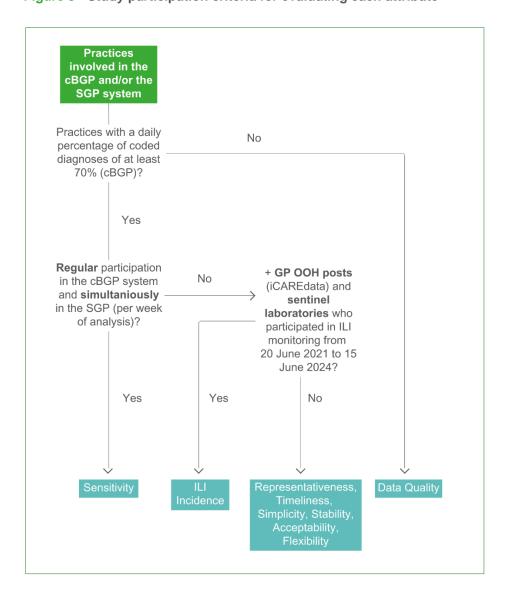
Furthermore, this study period has been set to exclude the five months during which Belgian GPs received payment for their participation in the cBGP system (26 October 2020 to 31 March 2021)<sup>58</sup>.

#### 2.3. POPULATION

#### 2.3.1. Population based on practices

#### 2.3.1.1. Summary of participation criteria

Figure 3 • Study participation criteria for evaluating each attribute



#### 2.3.1.2. Inclusion criteria (for the assessment of most attributes)

The following practices will be **included** in the study for the analysis of Representativeness, Timeliness, Simplicity, Stability, Acceptability and Flexibility.

#### a. Regarding the cBGP:

Practices must have participated in the cBGP system between the 20<sup>th</sup> of June 2021 and the 15<sup>th</sup> of June 2024.

#### b. Regarding the SGP:

Practices must have taken part in the SGP between the 20th of June 2021 and the 15th of June 2024.

#### 2.3.1.3. Exclusion criteria (for the assessment of most attributes):

#### a. Regarding the cBGP:

Practices with a low daily coding percentage will be **excluded** from the study.

A low daily coding percentage at the practice level is defined as

daily coding below 70%.

This value was determined through expert consensus during the development of the cBGP tool.

#### b. Regarding the SGP:

No specific exclusion criteria

#### 2.3.1.4. More specific criteria or exceptions

#### **Data Quality**

Regarding Data Quality assessment, the exclusion criterion for low daily coding percentage will not be applied, as low coding will be part of the evaluation.

#### ILI Incidence

GP OOH posts will be included if they have taken part in the iCAREdata project between 20 June 2021 and 15 June 2024 as well as laboratories who participated in the sentinel laboratories network during the same period.

A clarification needs to be made regarding iCAREdata and sentinel laboratories, for which data prior to the study period will be taken into account (see 4.2.5.2. and 4.2.5.3.) from the 2014/2015, 2015/2016, 2016/2017, 2017/2018 and 2018/2019 seasons. This data will be considered only for the calculation of the epidemic and intensity thresholds enabling ILI and influenza activity assessment.

For SGP system, these thresholds have already been determined and communicated by the ECDC, therefore data from previous seasons will not be necessary, while for the cBGP system, credible data for calculating thresholds is not available before the study period (see 4.2.2.).

#### Sensitivity

For the Sensitivity assessment, the analysis will compare the ability of the SGP and cBGP systems to capture ILI cases. This will include practices that participate in both surveillance systems simultaneously per week analysed. Additionally, for the cBGP system, regular participation – defined as engagement for at least three days per week – will be required. Within the SGP system, it is assumed that data is collected by GPs every weekday.

#### 2.3.2. Patient population

The population included consists of individuals of all ages who consulted a GP for influenza-like symptoms during the predefined period, and whose GP practice has participated in the surveillance systems being studied.

#### 2.4. SAMPLE SIZE

Practice participation data for the two main surveillance systems studied are presented below. Data from the iCARE project (which is based on 36 GP OOH posts) and sentinel laboratories (which provide absolute figures) will be used exclusively for the assessment of ILI Incidence.

#### 2.4.1. cBGP

All Belgian general practices with EMR software could be eligible to participate in the cBGP, on a voluntary basis.

During the period from 26/10/2020 to 31/03/2021, a financial incentive was provided to encourage regular participation, and 4,773 general practices (11,935 GPs)<sup>58</sup> took part at least once.

#### 2.4.2. SGP

During the study period, and for each year, the number of practices that regularly participated in the SGP surveillance (for at least 26 weeks per year) is as follows: 73 practices (96 GPs)<sup>59</sup> in 2021, 75 practices (103 GPs) in 2022<sup>59</sup>, 64 practices (91 GPs) in 2023<sup>60</sup> and 68 practices (108 GPs) in 2024.

### 3. Data sources

In order to determine whether there is sufficient evidence for the cBGP system to take over ILI surveillance from the SGP and become part of the integrated Belgian ILI surveillance system, these two systems will be the main data sources.

Additionally, the comparison of incidence curves and the rapidity of epidemic peak detection between the two EMR-based systems (cBGP and iCAREdata) will allow strengthening the assessment of ILI Incidence and highlighting the differences between practices and GP OOH posts. The influenza-specific data source (sentinel laboratories) will determine whether influenza data derived from the cBGP data can be used for reporting to EU authorities, thus ensuring a more accurate assessment of the epidemiological situation, complementary to ILI data.

#### 3.1. cBGP

The cBGP semi-automatically captured epidemiological data from GPs' EMR.

GPs ran an audit (via a statistical module) in their EMR software, which generated the daily number of recorded diagnostic codes. These numbers were then manually entered by GPs into an electronic form (eForm). The completed eForm (see Annexes 5 and 6 for example) was submitted to Healthdata.be by the end of the day, or no later than 10 a.m. the following day. Healthdata.be<sup>61</sup> is a platform developed by Sciensano to ensure the secure collection and storage of health data transmitted by various healthcare professionals.

GPs reported the total daily number of patient contacts for ILI, classified under the ICPC-2 code 'R80'. ICPC-2<sup>50</sup> refers to the second edition of the International Classification of Primary Care, set up by the World Organization of Family Doctors (WONCA). This classification system is designed to enable the systematic capture and organisation of clinical information in primary care.

Each contact with the GP was recorded, meaning that a patient who had multiple consultations for persistent symptoms of ILI could be found in several eForms. Episodes of care<sup>62</sup>, allowing the grouping of several contacts with a GP for the same health complaints, were not taken into account.

The number of practices or the corresponding number of GPs who participated each day can be determined (a practice ID is linked to a number of GP members of the practice) and the incidences can be calculated at both national and sub-national levels.

#### 3.2. SGP

Of the 14 health topics monitored by the SGP with varying continuity from 2019 to 2024 (see Annex 7), ILI is continuously monitored.

The network undertakes the two following activities related to ILI surveillance: ILI cases registration and virological sampling.

#### 3.2.1. ILI cases registration

The sentinel GPs report, on a weekly basis, aggregated data on all consultations for ILI diagnoses in different age categories (<1, 1–4, 5–14, 15–19, 20–64, 65–84, 85+) using a LimeSurvey standardised form (see Annex 8). The GPs fill in the form online and send it to the secured server of Sciensano. Based on these data, the ILI weekly incidence of GP consultations per 100,000 inhabitants can be calculated and is reported in the weekly Bulletin of Acute Respiratory Infections<sup>33</sup>.

#### 3.2.2. Virological sampling

Another part of SGP surveillance is virological sampling. GPs systematically take virus samples from a subset of their patients with acute respiratory infections for virological analysis to determine which viruses are currently circulating in the population.

Samples from a maximum of 5 patients (who agreed to the procedure by signing an informed consent form) are taken each week.

The first 3 patients who meet the ILI case definition and the first 2 patients who meet the ARI case definition (and are willing to participate) are selected for the nasopharyngeal swab.

Sciensano includes a WHO-certified National Influenza Centre (NIC or NRC influenza)<sup>63</sup> for virological analyses. This NIC performs diagnostic PCR tests on the collected virus samples nationally and carries out preliminary analyses. Then, the samples are sent to the WHO coordination centres for a panel of multiple respiratory viruses, as well as antigenic and genetic analyses on a subset of the samples. Based on the results of the NICs, the WHO can make recommendations on the composition of influenza vaccines each year and conduct risk assessment activities<sup>64</sup>.

#### 3.3. ICAREDATA

Physicians working in OOH posts record a range of diagnoses daily, including ILI, using thesaurus terms mapped to their corresponding ICPC-2 codes. For each consultation, information is collected on patient characteristics, reason and timing of the consultation, the diagnosis, and any prescribed medication. Free-text fields are available for recording clinical examinations and subjective patient complaints.

Prescribed medicines are registered with their corresponding CNK (Code National / Nationale Kode) codes, which are unique identifiers assigned to medication available in Belgian retail pharmacies. CNK codes are linked to the international Anatomical Therapeutic Chemical (ATC) classification system, allowing medicinal substances to be associated with their main therapeutic use. Data on dispensed medicines (including CNK code), the date of purchase, and the prescriber's NIHDI code are also captured at the pharmacy level.

To guarantee the transfer of data to iCAREdata while safeguarding the privacy of both physicians and patients, a compartmentalised approach to handling medical and personal data was implemented (see Annex 9). iCAREdata receives encrypted messages and decrypts the medical information, while personal data remain securely encoded<sup>65</sup>.

On a daily basis, ILI data extracted from GPs' EMR are made available online via the iCAREdata project dashboard<sup>36</sup>. The dashboard data can be filtered by various criteria, such as age group, patient location, and other relevant factors.

#### 3.4. SENTINEL LABORATORIES

On a voluntary basis, participating laboratories for microbiology submit weekly diagnostic data, for approximately 40 pathogens, including influenza, to Sciensano.

When required, isolates may be forwarded by sentinel laboratories to reference laboratories for specific investigations, such as certain typing and subtyping<sup>42</sup>.

The recorded data include the patient's age and sex, as well as additional details such as occupation and recent foreign travel for certain microorganisms. Information on the sample source and the diagnostic method used is also collected.

Laboratories can transfer their data as Excel files via email to the sentinel laboratories general mailbox. Alternatively, data can be transferred through the sentinel laboratories platform with access limited to participating sentinel laboratories.

For this data source, no straightforward catchment population is available; hence absolute numbers of diagnoses are reported instead of incidences.

## 4. Attributes assessment / Outcome measures and analysis

The nine attributes selected are described below. A research question linked to each attribute is formulated and corresponds to a more specific aspect of the overarching research question: 'What are the gains and losses of replacing the questionnaire-based method with the code-based method for ILI surveillance data collection in Belgian general practices, to support data-based decision-making?' Qualitative and quantitative outcome measures are also presented to answer each sub-question of research, followed by a detailed statistical analysis plan for each characteristic of the surveillance systems.

The analysis will be carried out using SAS 7.1 software.

#### 4.0. SUMMARY TABLE

Table 2 • Systems performance assessment framework (Part I)

	DATA QUALITY	ILI INCIDENCE	SENSITIVITY	REPRESENTATIVENESS	TIMELINESS
QUALITATIVE OUTCOME MEASURES	Comparison of data entry  Comparison of error  detection and handling in  data cleaning	Heat maps comparison	Comparison of case definitions  Comparison of other factors potentially impacting sensitivity	Comparison of how to calculate the population at risk	Comparison of systems' timelines for reporting ILI cases
QUANTITATIVE OUTCOME MEASURES	Comparison of practices' information errors  Comparison of epidemiological information errors	Comparison of weekly ILI incidences or ILI activity  • <u>cBGP-SGP</u> • <u>cBGP-iCAREdata</u> • <u>cBGP-sentinel</u> <u>laboratories</u>	Comparison of the number of cases registered in both systems by the same practices	Comparison of population coverage  Comparison of practices geographic distribution in Belgium municipalities	Comparison of case reporting times for both systems  Late reporting assessment
THRESHOLDS	At least 80% of the reports are validly completed	Heat charts correspondence The earliest detection of ILI epidemics Agreement of the ILI curves	Correlation between ILI cases reported by common practices	Best coverage (typically covering 1–6% of the population)  Best represented surveillance system	At least 80% of the results are reported within the targeted time frame
DATA	COVID-19 Barometer Sentinel GP Network	COVID-19 Barometer Sentinel GP Network iCAREdata Sentinel Laboratories	COVID-19 Barometer Sentinel GP Network	COVID-19 Barometer Sentinel GP Network	COVID-19 Barometer Sentinel GP Network

Table 3 • Systems performance assessment framework (Part II)

	STABILITY	SIMPLICITY	ACCEPTABILITY	FLEXIBILITY
QUALITATIVE OUTCOME MEASURES	Comparison of issue types encountered	Comparison of the data flows  Comparison of the variables collected  Comparison of GPs User Experiences	Cited reasons to participate  Cited reasons to exit the system	Comparison of the type and role of the organisations involved in the operation of the systems  Comparison of the resources required to adapt the system
QUANTITATIVE OUTCOME MEASURES	Comparison of the number of issues encountered	Comparison of the number of variables collected	Frequency of cited reasons to participate  Frequency of cited reasons to exit the system  Comparisons of participation rate  Comparison of participation duration	Comparison of the number of organisations involved in the systems' operation
THRESHOLDS	The minimum number of interruptions and system failure	The maximum ease of use  The minimum number of variables needed for decision making	Highest participation rate  Highest participation duration	The easiest to change / modify
DATA	COVID-19 Barometer Sentinel GP Network	COVID-19 Barometer Sentinel GP Network	COVID-19 Barometer Sentinel GP Network	COVID-19 Barometer Sentinel GP Network

#### 4.1. DATA QUALITY

#### 4.1.1. Research question

How comparable are the questionnaire-based and the code-based methods to ensure the quality (completeness and validity) of ILI data collection?

#### 4.1.2. Qualitative outcome measures

#### 4.1.2.1. Comparison of cBGP and SGP data entry

The validity of the data recorded may be influenced by, but not limited to, the design of the forms (user-friendly features) regarding the SGP system, the variability in the design of the software from which the cBGP data is extracted, or the coding behaviour of GPs<sup>66</sup> (cBGP).

The various technical implementations for entering consultation data will be investigated by reviewing related documentation, reports, and operational procedures. These interface elements (drop-down menus, autocomplete search boxes, multiple-choice options and free-text zones) can vary between systems (cBGP and SGP) and also between software packages within the cBGP system. These implementations determine the type of data that will be collected, i.e. structured, semi-structured or unstructured, and consequently the potential problems of standardisation of the data collected.

#### 4.1.2.2. Comparison of error detection and handling in the cBGP and SGP data cleaning

The quality checks coded in the data cleaning scripts of cBGP and SGP systems can be divided into two categories.

Firstly, we will analyse the information relating to practices, such as names, NIHDI numbers of associated GPs, addresses and dates of diagnosis.

Secondly, we will look at the quality of the epidemiological data: the number of ILI cases and the denominator.

In both categories, missing data, duplicates and values outside the expected range or inadequate values will be listed and described, together with the way in which they are handled.

A comparative table will be drawn up to highlight the differences between the data cleaning methods.

#### 4.1.3. Quantitative outcome measures

#### 4.1.3.1. Comparison of practices' information errors

Missing data, instances of duplicate recording (whether in error or for correction), and inconsistencies in values entered during the registration of participating practices will be quantified.

Missing information may include, for example, the absence of a sender NIHDI number, practice name, or postcode for the barometer data and the missing dates of diagnosis for SGP data.

Regarding duplicate entries, if sentinel GPs register multiple times for the same week, any additional registrations will be identified as duplicates, and the correct record must be identified and retained. For GPs who participated in the cBGP system, any supplementary eForm corresponding to the same day will similarly be considered duplicate.

Inadequate values encompass cases such as a NIHDI code containing fewer than eight digits or a practice with a reported number of GPs equal to zero in cBGP data, while in SGP data an incorrect GP code or inconsistent date of diagnosis will be counted.

The number and proportion of missing, duplicate, and inadequate values will be calculated. Error percentages below 20% will be deemed acceptable<sup>51</sup>.

#### 4.1.3.2. Comparison of epidemiological information errors

ILI incidence is calculated as the number of ILI cases reported in the system within a specific time frame and geographic area, divided by the population served by the SGP or for the cBGP, the number of active patients (defined for each practice as patients who had at least one contact with the practice between September 2018 and August 2020).

Missing data, duplicates and outliers can affect the incidence of ILI by reducing or increasing the value of its numerator or denominator, leading to an underestimate or overestimate of its real value.

The errors of epidemiological significance to be quantified and their potential impact on ILI incidence are outlined below.

#### a. Errors with the potential to underestimate ILI incidence

#### a.1. Reducing the numerator

#### Missing values:

In the cBGP system, missing values will be quantified following the qualitative assessment, which will provide insights into the circumstances under which such values may have occurred in the data.

In SGP, as illustrated in Figure 4, GPs can technically report that they have encountered a case of ILI but either record '0' cases or leave the number unspecified, as completing this field is not mandatory to submit the questionnaire. Both '0 cases' and empty fields will be included in the count of missing values.

Figure 4 • This scheme shows how a missing value can be generated in the SGP system.



The percentage of missing values will be calculated and compared.

#### Low coding percentage:

The coding percentage aims to estimate the extent to which diagnostic codes are applied daily in EMR and is therefore exclusively calculated for the cBGP system. Assessing this measure ensures that a sufficient number of diagnoses are coded each day per practice, thereby ensuring the reliability of the data.

This approach minimises errors in interpretation by excluding data from practices that do not code enough diagnoses compared to the total number of consultations, which may indicate insufficient coding rather than an actual low number of observed cases.

Consequently, during the cBGP data analysis, practices with a coding percentage below 70% will be excluded from the ILI incidence calculation to reduce the risk of underestimating the incidence.

The number of practices with low (<70%) coding percentages will be determined, along with the minimum, maximum, and average coding percentages.

#### a.2. Increasing the denominator

The denominator for the ILI incidence provided by the cBGP is the number of active patients, defined as those who had at least one contact with the practice the two years preceding the second version launch of the barometer. This two-year pre-pandemic period was agreed upon by consensus with general practitioners, representatives from the NIHDI, and public health experts to avoid the pandemic's impact on the estimation of practice size.

It is also possible to calculate the ratio between the number of active patients per practice and the number of GPs working in that practice, yielding the **active patients per GP ratio**.

For sentinel GPs, the population served per GP can also be estimated, allowing for a comparison between this estimate and the active patients per GP ratio.

This comparison ensures that the number of active patients assigned to each GP is consistent.

#### b. Errors with the potential to overestimate ILI incidence

#### b.1. Increasing the numerator

**Duplicates** must be sorted based on their relevance to retain the correct record and avoid counting ILI cases included in supplementary records.

The proportion of duplicates will be compared relative to the total number of records submitted in both systems.

#### b.2. Decreasing the denominator

The low number of active patients will be examined at the regional and national levels.

The number of active patients, nationally, was verified for each day of analysis, and a cut-off of 16,000 was established. If the number of active patients was below this cut-off, the results were excluded from the incidence per 100,000 inhabitants calculation.

The same approach was used at the regional level.

This criterion applies only to the cBGP system and, therefore, cannot be directly compared with the SGP system. However, it is important to determine how frequently these low values occur.

#### c. Other errors with potential to impact ILI incidence

Reference will be made to the list of checks included in the data analysis scripts to ensure the consistency of the collected values with one another. The frequency of detected errors in each system and their potential impact on the incidence calculations will be assessed.

#### 4.2. ILI INCIDENCE

#### 4.2.1. Research question

'How valid is the incidence of weekly GP contacts for ILI provided by the cBGP compared to ILI incidence provided by other Belgian surveillance systems?'

#### 4.2.2. Surveillance systems and period for comparison

The objective is to compare the incidence of ILI provided by the cBGP system with data from other surveillance systems monitoring the same syndrome.

A comparison will be conducted with two primary care surveillance systems: the SGP system and the out-of-hours care cooperative surveillance of the iCAREdata project.

The network of sentinel laboratories, which provides pathogen-specific data, will be used as a data source to evaluate the estimation of influenza virus activity by the cBGP system.

The period considered for analysis will be shortened to minimise, as much as possible, the impact of the 2020 pandemic. COVID-19 activity during this period created significant overlap with observed ILI activity, and the usual patterns of ILI activity may have been disrupted<sup>67</sup>. A time frame to be excluded from the analysis was identified (2019/2020, 2020/2021, 2021/2022 seasons) based on a thorough review of historical data and prior knowledge of typical ILI activity trends.

The analysis will therefore focus on data from week 40 in 2022 to week 25 in 2024.

#### 4.2.3. Quantitative outcome measures

## 4.2.3.1. Comparison of weekly ILI incidences between two data collection methods: cBGP and a primary care questionnaire-based system (SGP)

#### a. Data set preparation

Adjustments will be made to transition from daily to weekly cBGP incidences. In the cBGP system, daily data were collected from Monday to Friday, excluding official holidays. The daily incidences will be aggregated into weekly incidences by adding up the daily figures for each five-day week. These aggregated weekly incidences will then be compared with the SGP data.

In regard to the SGP system, data is collected for each week, assuming that each day of the week is taken into account. As GP consultations do not normally take place at weekends, data collection can be considered to occur over five days.

#### b. Measures of central tendency and dispersion

The data will be plotted on a line graph, allowing visual comparison of incidence patterns over time. In addition, statistical measures of central tendency and dispersion will be calculated and presented. The mean, the associated standard deviation, the minimum and maximum values of incidence will be determined as well as the weeks in which these values were reached.

#### c. Correlation coefficient

The weekly incidences of both surveillance systems, as continuous variables, will be examined to determine whether there is a correlation and how strong this correlation is between them.

The Spearman's correlation coefficient will be used as the correlation statistic. It ranges from -1 to +1. The closer the coefficient is to 1, the stronger the monotonic relationship is. The correlation may be positive, indicating that as the values of one variable increase, the values of the other tend to increase as well, or negative, signifying that as the values of one variable increase, the values of the other tend to decrease.

Results of the Spearman's correlation test will be considered significant at p-value under 0.05.

#### d. Degree of time series agreement

The previous correlation test quantifies the strength of the relationship between two variables obtained from different data collection methods. However, a high correlation does not necessarily imply good agreement. To evaluate agreement, the differences between the paired measurements provided by the two methods need to be examined.

The analysis will be conducted using the Bland-Altman plot<sup>68</sup>. This method, which visually represents the difference between two measurements relative to their mean, has already been used to compare data from different ILI surveillance systems<sup>69</sup>. A key advantage of this approach is its ability to assess the agreement between two measurement techniques. Bland-Altman diagrams facilitate the

visualisation of the degree of agreement and help identify the extent of disagreement, whether arising from systematic bias or random error.

The graph will include a horizontal line representing the mean difference between the two measurements, along with additional lines at ±2 standard deviations of the difference, in order to highlight any potential outliers in the data.

## 4.2.3.2. Comparison of weekly ILI incidences between two data collection methods: cBGP and another primary care EMR-based system (iCAREdata)

#### a. Data set preparation

Adjustments will be made to obtain weekly incidences for both systems.

In the iCAREdata surveillance, ILI data is provided for all seven days of the week. However, this data typically demonstrates a distribution with significantly higher daily incidences during weekends compared to weekdays. In contrast, in the cBGP data, weekends were not taken into account.

To enable the comparison, iCAREdata figures will be aggregated by week, summing up daily incidences of all seven days. While for the cBGP data, it will be assumed that the five-day incidence totals are representative of ILI activity over the entire week, including weekends.

This approach will partially address discrepancies in the distribution of daily ILI data between two surveillance systems, though the implications of this distribution will be considered in the discussion of the results.

As the iCAREdata is restricted to Flanders, the comparison will be limited to cBGP data from the same region.

#### b. Measures of central tendency and dispersion

Descriptive statistics will be calculated and compared as well as a graphical representation of the weekly incidences over time.

#### c. Correlation coefficient

A Spearman's correlation will be performed to assess the relationship between incidences from both data collection methods.

#### d. Degree of time series agreement

Bland Altman analysis will be held to assess the degree of agreement between incidences provided by iCAREdata and cBGP systems.

## 4.2.3.3. Comparison of weekly influenza activity between two data collection methods: cBGP and a pathogen-specific surveillance system (sentinel laboratories)

#### a. Data set preparation

Adaptations will be implemented to convert cBGP incidences to pathogen-adjusted cBGP incidences. The Goldstein Index (GI) will be used to estimate weekly influenza activity from the cBGP data. It is calculated as the product of the weekly ILI incidence and the proportion of positive influenza cases detected each week.

However, the cBGP system was not linked to virological surveillance for determining the number of positive influenza virus tests.

Therefore, our analysis will rely on tests conducted by the NRC for influenza virus in Belgium, using specimens from the SGP virological surveillance, with the assumption that both systems represent the same population and that the samples analysed are representative of this population.

The GI derived from the cBGP data will then be compared with the weekly influenza data provided by the sentinel laboratories.

#### b. Measures of central tendency and dispersion

The weekly number of positive tests for influenza from the sentinel laboratories and the weekly GI related to cBGP data will be plotted on a double Y-axis graph to represent their differing units (absolute numbers vs pathogen-adjusted incidence) and descriptive statistics will be provided.

#### c. Correlation coefficient

Spearman correlation will be carried out to assess the correlation between influenza activity data provided by the sentinel laboratories and cBGP systems.

#### d. Degree of time series agreement

The Bland Altman plots will be performed to assess the degree of agreement between the GI derived from the cBGP data and influenza data from the sentinel laboratories.

#### 4.2.4. Transformation from quantitative into qualitative data

#### 4.2.4.1. Need for qualitative ILI data

The European Surveillance System (TESSy) is provided by the ECDC to gather, evaluate, and disseminate surveillance data on infectious diseases in Europe. In 2025, TESSy will be integrated into the European Surveillance Portal for Infectious Diseases (EpiPulse).

In its 'Reporting Protocol for Integrated Surveillance of Respiratory Viruses' (version 1.83)<sup>70</sup> countries are encouraged to use qualitative and semi-quantitative indicators to assess the epidemiological situation of influenza. It is also recommended that both influenza virus detections and syndromic data are taken into account in the analysis.

Therefore, it is necessary to assess whether the qualitative ILI data for the cBGP system are reliable enough to be transmitted to ECDC by being compared with data from other surveillance systems. This comparison will be based on epidemic thresholds, which indicate the level of incidence above which the epidemic period is considered to have been entered, and more specific thresholds for assessing the intensity of ILI activity. Among the various methods for establishing these thresholds, the Moving Epidemic Method (MEM) will be applied due to its robustness in detecting influenza epidemics<sup>71</sup>.

#### 4.2.4.2. Principle of the Moving Epidemic Method (MEM)

The main objective of the MEM is to define ILI activity on the basis of historical data and to establish an epidemic threshold and intensity thresholds, as follows (with the assigned colours):

Table 4 • MEM intensity levels

Baseline	no activity or activity at baseline
Low	low levels of activity
Medium	usual levels of activity
High	levels of activity higher than usual
Very high	exceptionally high levels of activity

This information enables the determination of the start, duration, end, and intensity of ILI activity, which can then be compared across different surveillance systems or countries.

For the purposes of this study, the analyses will be carried out using version 2.11 of the MEM web application, which is based on version 4.3.1 of R (2023-06-16).

#### 4.2.4.3. Heat maps visualisation

Once the thresholds have been established, each weekly ILI rate will be assigned to an epidemic stage and, consequently, to a specific predetermined colour. The weekly rates of the surveillance systems under analysis will then be mapped to the corresponding colour. Finally, a heat map will be generated, with each threshold reached each week represented by a distinct colour.

#### 4.2.5. Qualitative outcome measures

The period will be similar to the quantitative analysis, namely from the 40<sup>th</sup> week of 2022 to the 25<sup>th</sup> week of 2024.

## 4.2.5.1. Comparison of epidemic detection and intensity levels between cBGP and SGP data using heat maps

The MEM thresholds suggested by the ECDC for application on ILI data of 2022–2023 and 2023–2024, and applied for reporting ILI data, are presented in Table 5. These thresholds are based on 5 seasons excluding 2019–2020, 2020–2021 and 2021–2022.

For the cBGP data, the determination of MEM thresholds will be limited to data from the 2022–2023 and 2023–2024 seasons. Consequently, the minimum of 5 seasons required to calculate the MEM thresholds will not be met, and the application of these thresholds will be done on the data from the same period, rather than on the following year's data. This limitation will be discussed with the results.

In the MEM application, the cBGP data will be uploaded as rates, representing the number of GP consultations for ILI per 100,000 inhabitants. The table to be uploaded will be structured with a row for each epidemiological week and a column for each surveillance season. In the parameters to be defined, the selected seasons will be indicated, and no transformations will be applied. The 'one wave per season observed' option will be selected, with the first week defined as week 40 and the last week as week 20. The pre-epidemic and intensity thresholds will then be determined.

A visual comparison of both related heat maps will be performed.

Table 5 • MEM thresholds to apply for seasons 2022/2023 and 2023/2024 regarding SGP data

Thresholds	2022–2023	2023–2024
baseline	0–128.07	0–183
low	128.07–507.41	183–503
medium	507.41-782.60	503–792
high	782.60–947.80	792–968
very high	947.80 –	968 –

Seasons	Pre-Epidemic	Post-Epidemic
2022/23	128.07	105.36
2023/24	183	93

## 4.2.5.2. Comparison of epidemic detection and intensity levels between cBGP data and iCAREdata using heat maps

The MEM thresholds determined previously for the cBGP data (see 4.2.5.1) will be applied.

Regarding iCAREdata, the MEM thresholds will be calculated based on 2014/2015, 2015/2016, 2016/2017, 2017/2018 and 2018/2019 seasons for application to ILI data of the season 2022–2023, and based on 2015/2016, 2016/2017, 2017/2018, 2018/2019, and 2022–2023 seasons for application to ILI data of the season 2023–2024. The MEM model will assume one peak per season (week 40 to week 20).

Two heat maps will be drawn up accordingly to compare the start, end, intensity and duration of ILI activity.

### 4.2.5.3. Comparison of epidemic detection and intensity levels between cBGP data and sentinel laboratories using heat maps

The previously calculated GI for cBGP data will be loaded into the MEM application for thresholds determination.

For the network of sentinel laboratories data, the model of one peak per season from week 40 to week 20 will be used and 5 influenza seasons will be considered without taking into account the period between 2019 and 2022.

Once created, the heat maps will provide influenza-specific information for comparison.

#### 4.3. SENSITIVITY

#### 4.3.1. Research question

'To what extent is the detection of ILI cases comparable between the cBGP and SGP systems?'

#### 4.3.2. Qualitative outcome measures

Two aspects will be explored in this qualitative assessment of Sensitivity.

The first aspect, the case definition, is a fundamental element of a system's capacity to detect cases. Furthermore, the use of standardised case definitions can enhance the utility of the data generated by such systems by enabling valid comparisons over time and across different locations<sup>72</sup>.

The second aspect pertains to measures aiming to support case detection within surveillance systems, or rather those designed to minimise underreporting of disease occurrences. For instance, the implementation of weekly reminders for participants to complete their forms on time could positively influence the number of reported cases and, consequently, the sensitivity of the system.

#### 4.3.2.1. Comparison of case definitions

Case definitions are used to establish clinical diagnoses for individual patients, with the goal of ensuring that cases of a given disease are systematically and consistently counted. This enables incidences derived from these cases to be meaningfully compared and analysed.

By reviewing reports and literature on case definitions in Belgium, as well as in European and international contexts, we will compare the different approaches. The case definition used for recording ILI cases within the SGP system will be delineated. For the cBGP system, the practical application of the ICPC-2 code R80 will be described, highlighting its advantages and limitations in comparison to the clinical case definition.

#### 4.3.2.2. Comparison of other factors potentially impacting sensitivity

Reports, newsletters and informational websites detailing procedures aimed at encouraging the completion of forms will be reviewed to show differences in follow-up measures. These measures, such

as reminders, may impact positively the number of recorded cases; hence, the sensitivity of the surveillance system.

#### 4.3.3. Specificity of the population based on practices for quantitative analysis

The evaluation will be restricted to practices who participated regularly (see 2.3.1.4) in both the SGP and cBGP systems. These common practices will be identified through the correspondence of practice addresses.

For each week of the study period, only ILI cases reported by practices actively participating in both systems simultaneously will be included.

#### 4.3.4. Quantitative outcome measures

#### Comparison of the number of cases registered in both systems by the same practices

The data reported by practices involved in both systems at the same time will be analysed to determine whether a relationship exists between the data reported in each system.

A regression analysis, taking into account the cluster effect by practice, will be conducted to assess whether a linear relationship exists between the data from the two systems and to determine whether the data provided by the SGP system (as the dependent variable) can be predicted using the data from the cBGP tool (as the predictor).

#### 4.4. REPRESENTATIVENESS

#### 4.4.1. Research question

'Are the population coverage and geographical distribution of practices comparable between the cBGP and the SGP surveillance systems?'

#### 4.4.2. Selection of indicators

As highlighted by ECDC in the document 'Operational considerations for respiratory virus surveillance in Europe', evaluating representativeness requires consideration of factors such as geographical distribution, population density (urban versus rural), age structure, and social characteristics specific to the population under study. This approach ensures that the sample analysed is representative of the broader population at either the national or subnational level.

Population coverage will be evaluated at the district level, with a minimum target coverage of 1% to be achieved. It will also be examined whether practices are present in all districts across Belgium. The geographical distribution of practices will be determined in order to assess whether rural and urban areas are represented. In addition, a comparison will be conducted with the geographical distribution of practices that are not included in the systems being studied.

The age structure of the sampled population is available only in the data collected by the SGP, and therefore cannot be compared with the cBGP data.

Finally, data obtained from the cBGP and the SGP do not allow for the direct inclusion of social characteristics, as these are not collected within both systems.

#### 4.4.3. Qualitative outcome measures

#### Comparison of how to calculate the population at risk

The population at risk for ILI is the specific group of individuals who are potentially exposed to and could develop ILI symptoms. This notion is part of the population coverage determination.

By detailing how this denominator of ILI incidence is calculated, we will describe the population from which data is collected, revealing both its strengths and inherent limitations of the system's representativeness.

#### 4.4.4. Quantitative outcome measures

#### 4.4.4.1. Comparison of population coverage

For the cBGP system, in each district, the calculation will involve multiplying the number of participating practices by the number of active patients allocated to each practice. The minimum and maximum weekly coverage during a season will be determined, alongside the average population covered.

For the SGP system, population coverage will be calculated as the product of the number of participating practices and the number of inhabitants allocated to an active GP (defined as a GP who, as of 31/12, had a minimum of 1,250 patient contacts during the same year) in each district. The population covered by the network will be determined by season and by week of participation. Additionally, the average, minimum, and maximum values of this coverage will be calculated.

#### 4.4.4.2. Comparison of practices geographic distribution in Belgium municipalities

The analysis is based on the classification of urban and rural areas outlined in Eurostat's Methodology Manual on Territorial Typologies<sup>73</sup>. The NUTS<sup>73</sup> (Nomenclature of Territorial Units for Statistics), a system referring to regions within European countries for statistical analyses and harmonisation, will be used. This urban-rural typology is specifically applied at the NUTS 3 level, which corresponds to districts in Belgium.

Three types of geographical areas are identified in this document: predominantly rural areas (where less than 50% of the population resides in urban clusters), intermediate areas (where 50% but less than 80% of the population resides in urban clusters), and predominantly urban areas (where at least 80% of the population resides in urban clusters). An urban cluster is defined as 'a cluster of contiguous grid cells of 1 km² (including diagonals) with a population density of at least 300 inhabitants per km² and a minimum total population of 5,000 inhabitants'<sup>74</sup>.

Each district will be assigned to one of these three categories, and the geographical distribution of practices will be assessed to determine whether one or the other system is more represented in urban, intermediate, and rural areas. A comparison will also be made with practices that do not participate in these two systems.

#### 4.5. TIMELINESS

#### 4.5.1. Research question

'Is the timeline for reporting ILI cases comparable between the cBGP and SGP systems?'

#### 4.5.2. Qualitative outcome measures

#### Comparison of systems' timelines for reporting ILI cases:

A timeline will be established for each system to track the reporting of ILI cases. Each stage of the timeline, from the onset of symptoms to the researchers' reporting to the authorities, will be described and compared.

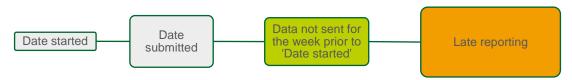
#### 4.5.3. Quantitative outcome measures

#### 4.5.3.1. Comparison of case reporting times for both systems

The maximum and minimum number of days for each of the stages described above will be compared between the SGP and cBGP data.

#### 4.5.3.2. Late reporting assessment

Figure 5 • This scheme shows how late reporting can be generated in the SGP system



In the SGP, questionnaires can be initiated by the sentinel GPs without being submitted immediately. The forms are saved and assigned a registration date. If the same questionnaire is submitted several weeks later, the delay can be calculated by subtracting the registration date from the submission date, providing the number of days in between.

This measurement allows late reporting (see Figure 5) within the SGP system to be quantified, whereas for the cBGP system, only the submission date is available.

The proportion of late reporting of ILI data will be calculated. This will provide additional information on the timeline for reporting ILI cases. Furthermore, this analysis could offer insights into the acceptability of the SGP system by sentinel GPs. For instance, due to work overload, questionnaires may be started by GPs but returned much later, when more time is available.

Therefore, this measurement is considered valuable, even if it is not available for the cBGP system.

#### 4.6. STABILITY

#### 4.6.1. Research question

'To what extent are the data collection problems encountered in the cBGP and SGP systems comparable in terms of their type, frequency, and consequences for data reporting?'

#### 4.6.2. Qualitative outcome measures

#### Comparison of issue types encountered

Within Sciensano, an IT ticketing system, ServiceNow, is used to track and assist in addressing IT service requests, incidents, and alerts. Tickets sent to Healthdata.be agency will therefore be collected to provide information on incidents for cBGP.

However, as this tool was implemented during the current study, access to the tickets will not be available before 2023.

The 'Bulletin of Acute Respiratory Infections' will also be used to find out whether, for technical reasons, researchers were unable to report data for cBGP and SGP.

Details of how the problems occurred will be outlined to identify their origin at a technical level, their consequences, and, where applicable, the solutions that were implemented at the time to resolve them. The descriptions will be presented in a table to facilitate the highlighting of the most significant aspects identified during the examination.

#### 4.6.3. Quantitative outcome measures

#### Comparison of the number of issues encountered

The number of emails, HD tickets, and Bulletins of acute respiratory infections reporting a problem with data collection will be provided for the SGP and cBGP systems.

In addition, the period during which data remained unreported due to a notified problem will be determined to measure the impact of the issue. The means, minimums, and maximums of time without reporting will be compared.

#### 4.7. SIMPLICITY

#### 4.7.1. Research question

'How simple is the operation of the cBGP system compared to the SGP system in terms of steps involved, data collected and user-friendliness for GPs?'

#### 4.7.2. Qualitative outcome measures

#### 4.7.2.1. Comparison of the data flows

Data will be collected from a literature review of reports and articles that shed light on how the two systems work. The data flow, from consultation by GPs to the reporting of data by researchers, will be examined along with the important steps associated.

A data flow diagram will be created to visually represent the findings.

The two systems will be displayed side by side to enable comparison and bring the distinctive features to attention.

#### 4.7.2.2. Comparison of the variables collected

The eForms will serve as a source of information for the cBGP data, while for the SGP data, the standardised questionnaires will be reviewed.

#### 4.7.2.3. Comparison of GPs User Experiences

The appraisal of GPs user experience will focus on ease of use.

This will be assessed by describing how GPs are required to register or enrol in both systems, how their data is submitted, and how additional information, useful to GPs when needed, is made available.

The website and procedure reports will be analysed to gather evidence on ease of use.

#### 4.7.3. Quantitative outcome measures

#### Comparison of the number of variables collected

A comparison will be made between the number of variables required to establish an ILI case in each of the studied systems.

#### 4.8. ACCEPTABILITY

#### 4.8.1. Research question

'To what extent is the willingness of GPs to participate in the SGP and cBGP surveillance systems comparable?'

#### 4.8.2. Qualitative outcome measures

#### 4.8.2.1. Cited reasons to participate

For the cBGP system, GPs could participate directly without specifically informing the cBGP coordination team. Feedback on the use of the cBGP tool could be sent via email to the general cBGP mailbox, but it was not often done.

The participation request emails, feedback, and the annually adapted survey on the profile of GPs in the SGP, called the 'profile enquête', which provides information on the characteristics of participating GPs and their practices will be examined.

However, the reasons for participation are rarely, if ever, indicated by GPs, nor do they provide feedback on their current participation. The main source of information will be the results of the 2024 'profile enquête'. For respondents participating in the ILI case registration, the responses to the question, 'Why are you participating in the sentinel GP network as a registration partner?' will be reviewed. In this survey, eight possible answers are provided: scientific interest, newsletters on the network's activities, individual annual report on practice data, access to scientific webinars and events organised by the network, financial compensation, being cited in scientific publications (author group), the possibility of representing the network on the steering committee/participating in decision-making, and 'other'.

Some of the reasons mentioned in the categories above may provide an indication of the willingness to participate in the cBGP system as well.

#### 4.8.2.2. Cited reasons to exit the system

Regarding the cBGP system, GPs could directly end their participation at any time by no longer submitting the eForms. Occasionally, some GPs have asked to be removed from the cBGP mailing list, often without giving their reasons. Thus, their email may have indicated that they wished to end their participation and no longer receive reminders or simply continue to participate without receiving daily reminders.

The reasons why GPs of the network no longer wished to participate in the system were sometimes specified in the emails they sent to the network coordination team to indicate their decision to leave the network.

#### 4.8.3. Quantitative outcome measures

#### 4.8.3.1. Frequency of cited reasons to participate

The reasons provided and their relative frequencies will be presented.

#### 4.8.3.2. Frequency of cited reasons to exit the system

The reasons will be first categorised and then their relative frequencies will be determined.

#### 4.8.3.3. Comparisons of participation rate

Participation will be assessed for each of the following seasons: 2021/2022, 2022/20223, 2023/2024.

#### a. Descriptive statistics

The data will be plotted on a line graph, enabling a visual comparison of weekly practice participation. Furthermore, the number of participating GPs, along with the mean, minimum, and maximum values, will be determined.

These values will be specified by district, region and nationally.

#### b. Participation rate calculation

The participation rate of a system will be calculated as the average number of participating GPs divided by the number of non-participating GPs, then multiplied by one hundred.

The number of non-participating GPs will be the number of active GPs minus the number of GPs participating in the system to be analysed.

The results will compare the national, regional and district participation rates.

#### 4.8.3.4. Comparison of participation duration

The number of weeks of practice participation for each season will be calculated, and the corresponding box plot for each system will be presented.

Subsequently, the results will be compared using the Mann-Whitney test to evaluate differences, with the p-value threshold set at 0.05.

#### 4.9. FLEXIBILITY

#### 4.9.1. Research question

'How comparable is the ease of adapting SGP and cBGP systems to potential changes required for ILI surveillance in the future?'

#### 4.9.2. Changes considered in this study

As highlighted in the CDC guidelines, a good way to assess flexibility is likely through a retrospective approach, examining how systems have responded to new requests or changes in the past.

Unfortunately, this will not be possible in this study due to the limited historical information we have for the cBGP system. The scope of the Flexibility assessment will therefore focus on the organisations involved in the functioning of the systems and the evolving information needs, particularly regarding the granularity of variables.

It is assumed that a system will tend to be less flexible if numerous organisations are involved in its operational processes, as this could increase the number of communications or negotiations required before a change can be implemented. However, this is not always true, as some organisations may have limited roles confined to specific actions and may not necessarily participate in all decisions.

Regarding the granularity of variables, specific needs may require the division of a category within a recommended variable. For instance, a very young population with a high infant mortality rate may be impacted by severe influenza, necessitating the observation of cases involving children under six months of age, as noted by the WHO in its 'Global Standards for Epidemiological Surveillance of Influenza'51. This suggests that the 0–1 year age existing category could be further divided to obtain data specifically for infants aged 0–6 months.

#### 4.9.3. Qualitative outcome measures

### 4.9.3.1. Comparison of the type and role of the organisations involved in the operation of the systems

Organisations or groups of researchers, GPs, policy-makers, developers, software vendors and partners directly involved in the operating process will first be listed and described. Their role and importance in the surveillance systems will be detailed.

All organisations that have an impact by participating in the decisions taken concerning the operation of the systems will be taken into account, whatever the level at which they are involved in the surveillance. They will then be divided into categories according to their roles, such as data providers, software providers, data users and data collectors.

A summary table will be used to gather the findings.

#### 4.9.3.2. Comparison of the resources required to adapt the system

Flowcharts will be drawn up from the categories described above. These diagrams will emphasise the critical stages that could potentially hinder the systems' adaptation to the desired change.

Then, we will present the hypothetical situation of adding an age category to the data collection in order to meet a specific information need.

The resources required to integrate this more detailed age variable will be listed and described.

Finally, a table will summarise the time required and the corresponding human resources to enable both systems to integrate this change into their data collection.

#### 4.9.4. Quantitative outcome measures

#### Comparison of the number of organisations involved in the systems' operation

Following the qualitative analysis, the number of organisations or groups involved in the systems will be determined by category. This will show whether a system depends more on organisations that have a critical impact on the data flow.

### 5. Limitations

#### **5.1. SELECTION BIAS**

The study acknowledges the existence of a potential selection bias arising from disparities in health-seeking behaviour and healthcare accessibility. To mitigate this bias, we will determine the differences in accessibility to care through the density of practices in urban and rural areas assessment.

This will not eliminate selection bias, but it will provide valuable insights into its nature and magnitude, reinforcing the robustness of our results.

#### **5.2. CONFOUNDING BIAS**

We should also note the presence of potential confounding factors in this study, especially with regard to the underlying health status of the population and variation in vaccination rates. This could be particularly true if the populations covered by the systems are very different. These factors may influence the results independently of the effectiveness of surveillance systems. Unfortunately, due to limited data availability, we are unable to directly account for or adjust for these confounding variables in our analysis. These factors could have an impact on the differences observed between the two surveillance systems.

#### **5.3. OTHER LIMITATIONS**

Since the study results will consider the characteristics of the cBGP, and this tool has evolved into the infection barometer, the findings may not be directly applicable. Therefore, if the cBGP is recommended for ILI surveillance, this aspect will have to be taken into account. Additionally, the cBGP was initially designed to monitor COVID-19 activity, which might be a constraint for its ILI surveillance usage.

# 6. Evaluation of the results and recommendations

The results obtained will be shared with the **expert group**, after which an online survey will be sent to them to evaluate these results by attribute and for each proposed alternative, allowing the identification of an appropriate choice.

The results of this evaluation will be discussed with the experts in order to make a final decision regarding the future of ILI surveillance. **Recommendations** will then be formulated to point out the key areas for improvement identified by the comparative study and to support the implementation of the final chosen option.

### PROJECT MANAGEMENT

### 1. Study timeline estimation

Table 6 • General study timeline



### 2. Data governance

This non-interventional retrospective study does not fall within the scope of the law on experimentation. GPs have given their consent for data transmission by either their registration to the SGP or by their voluntary participation in the cBGP system. The aim of this study, optimising the surveillance systems, is within the scope of the original systems.

No patient informed consent is required by Sciensano, as the data consists of **aggregated** weekly totals of ILI cases without any identifiable patient information (e.g. name, address). At the practice level, results will be either aggregated or assigned a practice ID to prevent identification. All necessary technical and organisational measures have been implemented to ensure secure data management, in full compliance with applicable data protection regulations.

Regarding cBGP, data was collected through GP's medical software, then retained and safeguarded by Healthdata.be. Secure data transfer methods were used via an approved **SFTP** site and required authentication by username and password.

Each participating practice from the sentinel network has provided data, which is collected through LimeSurvey and automatically stored on a **secured server** managed by Sciensano.

Only researchers from the Health Service Research (HSR) and Epidemiology of Infectious Diseases departments from Sciensano, involved in these two surveillance systems, are authorised to access the stored data. This will also apply to data from sentinel laboratories and the iCARE project.

### 3. Results

The dissemination strategy will include peer-reviewed publications, conference presentations, reports, and targeted outreach initiatives such as webinars and newsletters. This approach intends to enhance scientific knowledge, inform public health policy, and engage key contributors, including general practitioners.

Methodological advances have already been published and presented at international conferences. The 99th meeting of the European General Practice Research Network (EGPRN) in Budapest provided an opportunity to share the development of the protocol and receive peer feedback. In mid-September 2024, at the European Forum for Primary Care (EFPC) in Ljubljana, the study's perspective on sustainability was presented. These conferences facilitated valuable exchanges with researchers, contributing to methodological progress.

The protocol, detailing the methodology and analytical framework, will be published as a report to document the study's implementation. It will also be submitted for publication in a recognised scientific journal, providing a valuable reference for future research and system enhancements.

The findings will be published in a report and sent to designated experts for scoring and weighting of the attributes. Following their evaluation, a document outlining the results of the online survey and the recommendations associated with the final selected alternative will be provided. The publication of a peer-reviewed article is also planned to share the final results.

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We hereby declare that the researchers involved in this study have no relevant conflicts of interest to disclose.

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### **ANNEXES**

Annex 1 • Distribution of GP OOH posts (iCARE)



Annex 2 • Diagnostic codes extracted by cBGP<sup>58</sup>

Diagnostics	Codes
Suspected COVID-19	ICPC-2 R80
	ICD-10 J11.1
Confirmed COVID-19	ICPC-2 A77
	ICD-10 B34.2
ARI	ICPC-2 H71, ICPC-2 R74, ICPC-2 R75, ICPC-2 R76,
	ICPC-2 R77, ICPC-2 R78, ICPC-2 R81
ILI	ICPC-2 R80

ARI: acute respiratory infection; ICD: international classification of diseases ICPC: international classification of primary care; ILI: influenza-like illness.

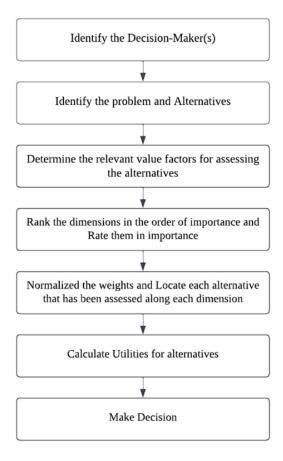
Annex 3 • Diagnostic codes extracted by the GP infection Barometer

Name indicator	ICPC2 Code(combination)	Description
Respi H71	H71	Otitis media
Respi R74	R74	acute upper respiratory tract infection
Respi R75	R75	acute/chronic sinusitis
Respi R76	R76	acute tonsillitis
Respi R77	R77	acute laryngitis/tracheitis
Respi R78	R78	acute bronchitis/bronchiolitis
Respi R80	R80	Influenza
Respi R81	R81	Pneumonia
STI X70	X70	Syphilis woman
STI X71	X71	Gonorrhoea woman
STI X73	X73	Genital trichomoniasis woman
STI X74	X74	Inflammation of the small pelvis/PID
STI X90	X90	Genital herpes woman
STI X91	X91	Condylomata acuminata woman
STI X92	X92	Chlamydia infection genitalia female
STI Y70	Y70	Syphilis man
STI Y71	Y71	Gonorrhoea man
STI Y72	Y72	Genital herpes man
STI Y76	Y76	Condylomata acuminata male
VPD A71	A71	Measles
VPD A72	A72	Chicken pox
VPD A74	A74	Varicella
VPD D71	D71	Mumps
VPD N70	N70	Poliomyelitis
VPD N71	N71	Meningitis/encephalitis
VPD N72	N72	Tetanus
VPD R71	R71	Whooping cough
VPD S70	S70	Herpes zoster
VPD Y74	Y74	Orchitis/epididymitis
other S84	S84	Impetigo
other S72	S72	Scabies/other diseases caused by mites

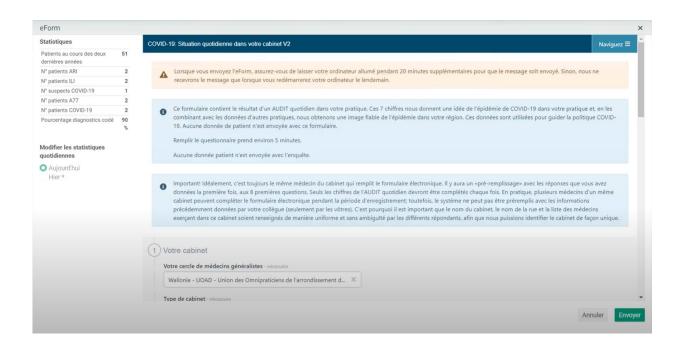
	_	
other D70	D70	Gastrointestinal infection
other D72	D72	Viral hepatitis
other D73	D73	Presumed infectious gastroenteritis
Intego U70	U70	Pyelonephritis/pyelitis
Intego U71	U71	Cystitis/urinary infection other
Intego U73	U73	Prostatitis/seminal vesiculitis
Intego U74	U74	Orchitis/epididymitis
Intego R72	R72	Laryngitis (streptococcus)
Intego S76	S76	Skin infection other (cellulitis)
Intego S13	S13	Animal/human bite
Intego D92	D92	Diverticular disease
group_Suspected_COVID- 19	IBUI 10,118,856 (ICPC-2 R80 - ICD-10 J11.1)	suspicion COVID-19
group_confirmed_COVID- 19	IBUI 10118837 (ICPC-2 A77 – ICD-10 B34.2)	confirmed COVID-19
	ICPC-2 H71 or	
	ICPC-2 R74 or	
	ICPC-2 R75 or	
group_ARI	ICPC-2 R76 or	group codes for ARI
	ICPC-2 R77 or	
	ICPC-2 R78 or	
	ICPC-2 R81	
group_WHO_ILI	R05 AND A03	WHO ILI definition: cough and fever
group_EU_ILI	(A03 OR A05 OR N01 OR L18) AND (R05 OR R02 OR	EU ILI case definition (Sudden onset of symptoms
	R21)	
		AND at least one of the following symptoms: – Fever or feverishness – Malaise – Headache – Myalgia
		AND at least one of the following: – Cough – Sore throat – Shortness of breath)
group_mumps_orchitis	D71 AND Y74	(= mumps + orchitis) in the same patient with maximum interval of 28 days
group_varicella_meningitis	A72 AND N71	(= chicken pox + meningitis/encephalitis) in the same patient with maximum interval of 28 days
group_varicella_pneumonia	A72 AND R81	(= chicken pox + pneumonia) in the same patient with maximum interval of 28 days
group_GEA	D70 or D73	group codes for gastrointestinal infections
group_Viral_syndrome1	(A03 OR A02)	fever OR chills
		1

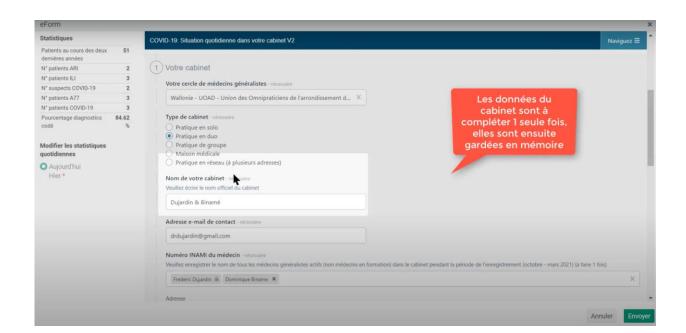
group_Viral_syndrome2	(A03 OR A02) AND (A04 OR A05)	(Fever OR chills) AND (General fatigue/weakness OR feeling sick)
-----------------------	----------------------------------	--

Annex 4 • SMART approach process<sup>57</sup>

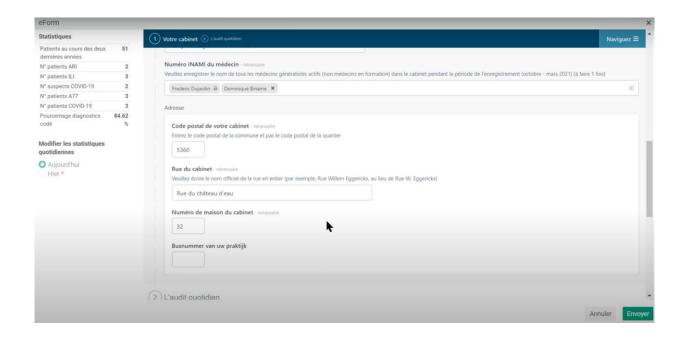


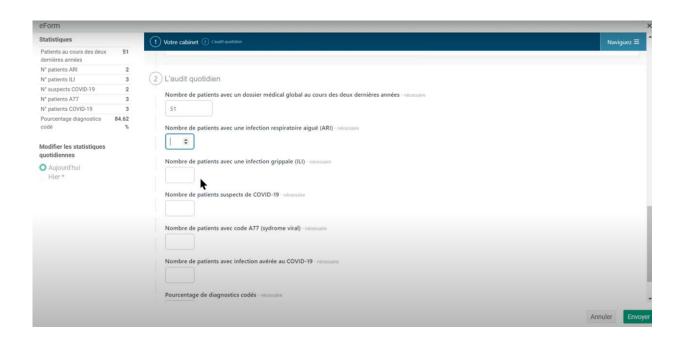
#### Annex 5 • Medispring eForm overview



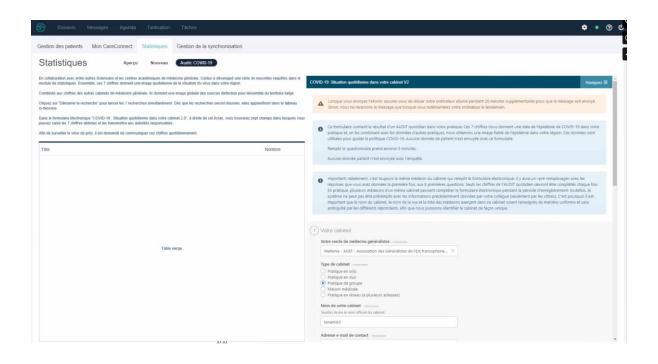


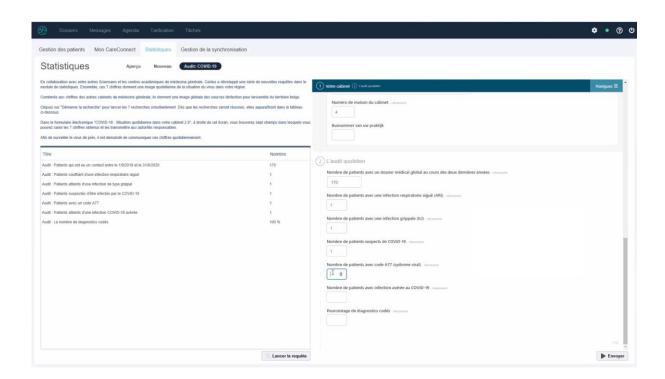
#### **ANNEXES**

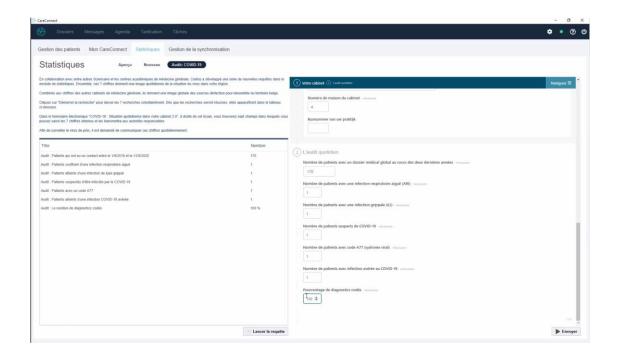


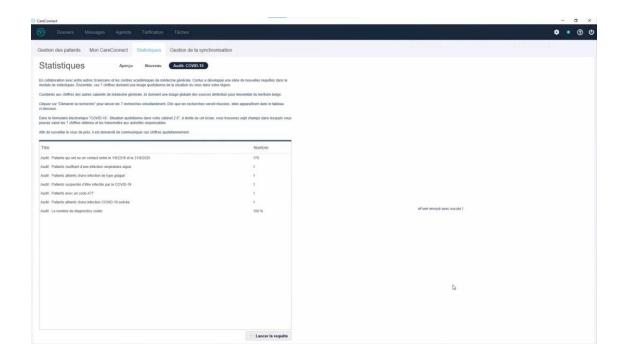


#### Annex 6 • Careconnect eForm overview









Annex 7 • Overview of health topics registered by the SGP (since 2019)

Hardeb Arrian arriatement by CCD waterway	Registration period					
Health topics, registered by SGP network	2019	2020	2021	2022	2023	2024
Acute respiratory infections	X	Χ	X	Χ	X	X
Influenza-like illness	X	Х	Х	X	X	Χ
Acute diarrhea	X	X	X	X	X	X
SARS-CoV-2 test results		Χ	X	Χ	X	
Fall incidents among people >=65 years	X	Χ	Χ			
Problematic substance use	X	Χ				
Sexual Transmitted Infections (STIs)	X	Х	Χ	Χ	X	Χ
Tick bites and/or suspicion of Lyme disease	X	Х		X	X	Χ
Varicella	X	Х	X	Χ	Х	X
Zona or post herpetic neuralgia			Χ	Χ	X	Χ
Psychopharmaceuticals in children, adolescents and young adults			Χ	Χ	Χ	Χ
Physical activity on prescription (PAP)					Χ	
Long Covid					X	X
Advanced Care Planning (ACP)				Χ	X	Χ

Annex 8 • Paper version of the ILI case reporting form (SGP)

Sciensano	Wallonie families santé handi	icap (Vlaa	nderen		mission communaut imune # Bruxelles-C	
7SSMG 50 ans		ecins Vigi ogie et Santé Pub be - R. DE SCHREYE	lique	20 73	domus medica	
Code du médecin:	Code du médecin:/202 au//202 au//202					
Code d'activité: ☐ ac	tif 🗆 oubli 🗆 cor	ngé 🛮 maladie	au	tre raison		
	INFECTIONS RE rhume banal, la rhinite, la (rh (laryngo-)trachéite, la brond		ine, la sinus	ite, l'otite moye	nne aiguë, la laryngi	te, la

Cas d'IRA à enregistrer pour cette semaine? ☐ oui ☐ non

		Nombre de cas
Groupe	< 1 an	
d'âge	1 - 4 an(s)	
l	5 - 14 ans	
	15 - 19 ans	
	20 - 64 ans	
	65 - 84 ans	
	85 ans et +	

#### SYNDROMES GRIPPAUX

Un syndrome grippal est une affection fébrile d' es respiratoires et des symptômes généraux Cas de syndromes grippaux à enregistrer pour cette semaine?  $\square$  oui  $\square$  non

		Nombre de cas	Traitements antiviraux (nombre de cas avec oui)	(nombre de cas avec oui)	Vacciné à partir d'octobre 2022 contre la grippe saisonnière (nombre de cas avec oui)	Décédé* (nombre de cas avec oui)
Groupe	<1an					
d'âge	1 – 4 an(s)					
	5 – 14 ans					
	15 - 19 ans					
	20 - 64 ans					
	65 - 84 ans					
	85 ans et +					

\*Décès parmi les patients diagnostiqués avec syndromes grippaux ces dernières semaines

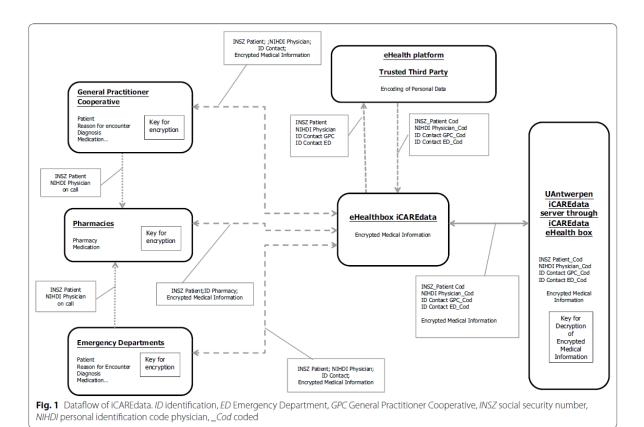
DIARRHEE AIGUE

Diarrhée aiguë = au moins 3 selles liquides ou molles par jour datant de moins de 14 jours motivant la consultation Cas de diarrhée aiguë à enregistrer pour cette semaine? ☐ oui ☐ non

		Nombre de cas	(nombre de cas avec oui)	(nombre de cas avec oui)	(nombre de cas avec oui)
Groupe	< 1 an				
d'âge	1 - 4 an(s)				
	5 - 14 ans				
	15 - 19 ans				
	20 - 64 ans				
	65 – 84 ans				
	85 ans et +				

Enregistrez de préférence par voie électronique sur le site web des Médecins Vigies (https://www.sciensano.be/fr/reseau-des-medecins-vigles) ou envoyez par e-mail à PPMV@sciensano.be (avant le mercredi).

#### Annex 9 • Dataflow of iCAREdata



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