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Influenza surveillance systems in Africa: A systematic review protocol

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Keywords:	Influenza infrastructure systems, surveillance systems, burden of influenza, sub Saharan Africa, influenza preparedness

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Peer Review Only

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3 Influenza surveillance systems in Africa: A systematic review protocol
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Abstract

Introduction: Influenza infrastructure systems are a crucial aspect in maintaining operations of surveillance, mitigating and responding to the disease. The role of surveillance is to isolate and identify as rapidly as possible any new influenza strains and collate this information for the preparedness for and response to an impending influenza activity in the humans. However, sources of surveillance information, particularly in Africa, are meagre. This systematic review will critically evaluate the existing surveillance systems in sub Saharan Africa that are available to detect and quantify the burden of influenza.

Method and analysis: We will build multiple electronic database search strategies using Medline, Cinahl, PubMed Central, Embase, Cochrane, African Journal Online (AJOL), Web of science and Google scholar to identify as many titles as possible. The medical subject heading (MeSH) and keywords will include a wide range of synonyms, both in index terms and free-text words. We will also perform hand searches of the reference sections of all relevant studies. All the identified titles and abstracts will be examined for inclusion. If relevant, a full text article would be obtained and read carefully. We will include full text studies published from 2002 in order to coincide with the establishment of the Integrated Disease Surveillance Response system in Africa by the WHO. Our primary outcome will be surveillance systems or types that quantifies transmission patterns and burden of influenza (e.g. hospitalization, mortality and incidence). A narrative synthesis of all studies will be performed and assessed for quality and risk of bias.

Ethics and communication: This study does not require ethics approval because it uses publicly available data. Our findings will be published in a peer review journal and disseminated to policymakers.

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3 **Protocol registration number:** This protocol has been submitted to PROSPERO pending
4 registration.
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11 **Strengths and limitations of this study**

- 14 • This systematic review aims to evaluate influenza surveillance systems in sub Saharan
15 Africa capable for the early detection of the burden of influenza; and it will not be
16 restricted to any language.
17
- 20 • A comprehensive search of published and unpublished reports that describe surveillance
21 of influenza-related illnesses or syndromes will be double screened and retrieved for
22 inclusion.
23
- 27 • Our findings will enhance the utility to respond rapidly to the early warning signs of an
28 influenza outbreak and subsequently strengthen the overall surveillance systems.
29
- 32 • The systematic review will adhere to the guidelines on preferred reporting items for
33 systematic review and meta-analysis protocols (PRISMA-P).
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- 37 • Potential limitations include the possibility of underreporting the review findings if we
38 are unable to find all the published and unpublished materials on surveillance systems.
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Introduction

Surveillance of seasonal or pandemic influenza is an important public health task. However, quantifying influenzas is generally more difficult because influenza viruses tend to undergo continuous antigenic variations, either because of mutation (antigenic drift) or genetic recombination (antigenic shift).^{1 2} The WHO recommends the continuous monitoring of influenza cases during each influenza season to identify the virus strains circulating in the population. The role of surveillance is to isolate and identify as rapidly as possible any new influenza strains and collate this information for the preparedness for and response to an impending influenza activity in the humans. Surveillance further provides information for production of vaccines for treatment, prevention and control of influenza.³ However, sources of such information, particularly in Africa, are meagre.⁴

There are undoubtedly general difficulties in surveillance systems in Africa, not only in the robustness of the data needed to send early signals for health service response, but also in the financial resources and leadership required for efficient and timely decision-making.⁵ Influenza surveillance is persistently characterised by low completeness and timeliness reporting due to inadequate laboratories, communication structures and poor public health human resource.⁵ A related difficulty despite the use of standard case definitions of influenza like illness (ILI) and Severe Acute Respiratory Infections (SARI) are sampling issues which are often biased towards collecting more specimen from patients suspected on clinical grounds to have influenza.⁶ In some cases, calculation of death associated to ILI and SARI is difficult to ascertain especially where such deaths are not attributable to influenza illness as primary cause.

Epidemiological observations including inferential statistics that explain epidemiological events, are important and crucial for any public health decision that inform prevention and control

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3 strategies. Indirect indices such as excess mortality, attack rates and clinical symptoms are
4
5 signature measures of the impact of influenza. A measure in the sudden increase in illness or
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7 death from complications of influenza remains a challenge, these mathematical models are no
8
9 means a direct one. Epidemiologists in seasonal climates determine excess deaths attributable to
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11 influenza, including influenza burden on hospitalization (during winter months), by use of
12
13 serfling-like cyclical regression models and arima models.⁷ However, these models are not
14
15 applicable in tropical climates where seasonality is all year round whereas these methods require
16
17 cyclic seasonal patterns of viral activity interrupted by influenza-free periods. Due to several
18
19 limitations, quantifying influenza surveillance deploy other methods such as use of the pyramid
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21 of severity, the spread of disease and risk factor determination, which often do not require
22
23 emphasis on viral culture and laboratory isolation.

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28 Influenza infrastructure systems are a crucial aspect in maintaining operations of surveillance,
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30 mitigating and responding to the disease. This systematic review critically evaluates the existing
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32 surveillance systems and types to detect influenza. The findings will inform public health
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34 policymakers on the role of strengthening surveillance systems.
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40 **Objective**

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42 To evaluate influenza surveillance systems that are designed to detect transmission patterns and
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44 burden of influenza.
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49 **Methods**

50 **Design**

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3 We designed this study protocol using the guidelines on preferred reporting items for systematic
4 review and meta-analysis protocols (PRISMA-P).⁸ We considered all the 17 items in the
5
6 PRISMA-P in the facilitation of this protocol development. The protocol is yet to be registered
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8 on PROSPERO. Any amendments to the protocol will subsequently be updated in the
9
10 PROSPERO systematic review registry.
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17 **Search**

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19 We will build multiple electronic database search strategies using Medline, Cinahl, PubMed
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21 Central, Embase, Cochrane and Google scholar to identify as many titles as possible.
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24 The medical subject heading (MeSH) terms Influenza Like Illnesses (ILI) and Severe Acute
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26 Respiratory Infections (SARI), surveillance, virologic, outpatient illness, mortality, morbidity,
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28 hospitalization, laboratory confirmed, influenza, sentinel, seasonal, pandemic, infrastructures and
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30 Africa will be used to combine searches systematically. The search terms will include a wide
31
32 range of synonyms, both in index terms and free-text words. The exact terms for the search in
33
34 PubMed are presented in Table 1. A computerised search will be followed by manual checks of
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36 reference sections of all relevant studies. All the identified titles and abstracts will be examined
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38 for inclusion. If relevant, a full text article would be obtained and read carefully. The titles
39
40 searched by hand from the reference lists will be retained into the database search for a full text.
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47 [Insert Table 1 about here]
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49 **Type of participants**

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51 Influenza surveillance systems target either animals or human beings. This review will draw on
52
53 all human participants. Although young children, elderly and persons with underlying medical
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3 conditions are at higher risk of severe influenza, the disease can affect any individual. For
4 example, the 2009 pandemic H1N1 virus remained antigenically unchanged in May 2012, still
5 affecting young adults (as in the 2010/11 season) as seasonal influenza.⁹ Surveillance systems
6 are designed such that to detect the disease in all individuals for prevention and control.
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14 **Type of intervention**

15 The types of surveillance interventions will be as follows:

16 Virologic Surveillance e.g. public health and clinical laboratories

17 Outpatient Illness Surveillance e.g. patient visits to health care providers for influenza-like
18 illness

19 Mortality Surveillance e.g. influenza-associated deaths

20 Hospitalization Surveillance e.g. laboratory confirmed influenza-associated hospitalizations

21 Summary of the geographic spread of influenza e.g. no activity, sporadic, local, regional, or
22 widespread.
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26 **Eligibility criteria**

27 We will include studies if they meet the following criteria:

28 Studies that have investigated influenza surveillance system reporting at least one measurement
29 property (i.e. incidence, prevalence, mortality, excess mortality, clinical symptoms, transmission
30 patterns)

31 Articles published and unpublished reports in any language (e.g. English, French, Arabic,
32 Afrikaans, etc)

33 All human surveillance systems in sub Saharan Africa established in 2002
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3 No restriction on age

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5 Articles available in full text.

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8 All studies reporting on animal surveillance system will be excluded.
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10 11 12 **Data extraction and management** 13

14 The WHO defines surveillance systems as those that collect and analyze morbidity, mortality,
15 and other relevant data and facilitate the timely dissemination of results to appropriate decision
16 makers. We will therefore examine reports that describe or evaluate systems for collecting,
17 analyzing, or presenting surveillance data for influenza-related illnesses or syndromes. Two
18 reviewers (EZS and DN) will screen and retrieve reports or study titles and abstracts
19 independently for eligibility. Any disagreements or discrepancies that arise in the inclusion and
20 exclusion criteria will be resolved by the third reviewer (CSW). Where studies need clarification,
21 we will contact the author(s) for information. We will include full text studies published from
22 2002 in order to coincide with the establishment of the Integrated Disease Surveillance Response
23 system by the WHO. Where identified studies are not in English, full text articles will be
24 translated into English.
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42 **Assessment of the risk of bias in the included studies** 43

44 The Grading of Recommendations Assessment, Development and Evaluation (GRADE) tool will
45 be used to assess risk of bias in the included studies. The tool encompasses six domains of which
46 each domain includes one or more specific entries in the risk table describing the study and
47 assigning judgement relating to the risk of bias for that entry.¹⁰ Two independent reviewers
48 (EZS and DN) will assess the risk of bias and based on their judgement and score the risk as
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3 either high risk, low risk or unclear risk based on the quality evidence for each study. We will
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5 develop a risk of bias table to summarize our assessments. Any disagreements or discrepancies
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7 concerning the risk of bias will be resolved by discussion and if any disagreement cannot be
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9 resolved an involvement of a third reviewer (CSW) will be recommended.
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14 **Types of the outcomes measures**

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16 We acknowledge that there is little consensus as to which sources of surveillance data or which
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18 collection, analysis, and reporting technologies are probably the most timely, sensitive, and
19
20 specific for detecting and managing diseases. For this review, we will include primary and
21
22 secondary outcome measures for assessing surveillance systems. Primary outcome will include
23
24 surveillance system that capture hospitalization, attack rates, susceptibility, mortality, incidence,
25
26 prevalence, transmission patterns and laboratory isolation and testing. Secondary outcomes will
27
28 include school absenteeism, pyramid of severity, the spread of disease and risk factor
29
30 determination as other methods of quantifying influenza surveillance.
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38 **Ethics and communication**

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40 Our study is based on publicly available published studies which does not require ethical
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42 approval and consent from participants. The results from this systematic review will be
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44 communicated in peer review journal and presented at international conferences.
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49 **Patient and public involvement**

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51 Patient and public were not involved.
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Discussion

This protocol for systematic review will evaluate seasonal or pandemic influenza surveillance systems using available literature. We will explore the existing types of surveillance tools used to gather data and evaluate the techniques in surveillance reporting and monitoring of seasonal or pandemic influenza. We hope our findings will enhance the utility to respond rapidly to the early warning signs of new influenza viruses and subsequently strengthen the overall surveillance systems by informing public health policy. Seasonal surveillance systems are important because it offers as predicative indicator to aid estimates of additional capacities that may be needed to detect increases in the pandemic activity by collecting up to date virological, epidemiological and clinical information on human seasonal influenza.¹¹ Potential limitations include the possibility that most existing surveillance systems may not have been studied or published thus we may likely underreport the review findings.

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Table 1: Search Strategy

<p>((((((((("africa"[MeSH Terms] OR "africa"[All Fields]) OR ("africa south of the sahara"[MeSH Terms] OR ("africa"[All Fields] AND "south"[All Fields] AND "sahara"[All Fields]) OR "africa south of the sahara"[All Fields] OR ("sub"[All Fields] AND "saharan"[All Fields] AND "africa"[All Fields]) OR "sub saharan africa"[All Fields])) OR ("africa, western"[MeSH Terms] OR ("africa"[All Fields] AND "western"[All Fields]) OR "western africa"[All Fields] OR ("west"[All Fields] AND "africa"[All Fields]) OR "west africa"[All Fields])) OR ("africa, northern"[MeSH Terms] OR ("africa"[All Fields] AND "northern"[All Fields]) OR "northern africa"[All Fields] OR ("north"[All Fields] AND "africa"[All Fields]) OR "north africa"[All Fields])) OR ("africa, southern"[MeSH Terms] OR ("africa"[All Fields] AND "southern"[All Fields]) OR "southern africa"[All Fields] OR ("southern"[All Fields] AND "africa"[All Fields])) OR ("africa, central"[MeSH Terms] OR ("africa"[All Fields] AND "central"[All Fields]) OR "central africa"[All Fields] OR ("central"[All Fields] AND "africa"[All Fields])) OR ("africa, eastern"[MeSH Terms] OR ("africa"[All Fields] AND "eastern"[All Fields]) OR "eastern africa"[All Fields] OR ("east"[All Fields] AND "africa"[All Fields]) OR "east africa"[All Fields])) AND (((((((((((((((("epidemiology"[Subheading] OR "epidemiology"[All Fields] OR "surveillance"[All Fields] OR "epidemiology"[MeSH Terms] OR "surveillance"[All Fields]) OR ("epidemiology"[Subheading] OR "epidemiology"[All Fields] OR "surveillance"[All Fields] OR "epidemiology"[MeSH Terms] OR "surveillance"[All Fields]) AND systems[All</p>
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Fields))) OR (("epidemiology"[Subheading] OR "epidemiology"[All Fields] OR
 "surveillance"[All Fields] OR "epidemiology"[MeSH Terms] OR "surveillance"[All Fields])
 AND types[All Fields])) OR sentinel[All Fields]) OR ("virology"[MeSH Terms] OR
 "virology"[All Fields] OR "virologic"[All Fields])) OR infrastructure[All Fields]) OR
 ("mortality"[Subheading] OR "mortality"[All Fields] OR "mortality"[MeSH Terms])) OR
 ("epidemiology"[Subheading] OR "epidemiology"[All Fields] OR "morbidity"[All Fields]
 OR "morbidity"[MeSH Terms])) OR (pyramid[All Fields] AND severity[All Fields])) OR
 (("risk factors"[MeSH Terms] OR ("risk"[All Fields] AND "factors"[All Fields]) OR "risk
 factors"[All Fields] OR ("risk"[All Fields] AND "factor"[All Fields]) OR "risk factor"[All
 Fields]) AND ("analysis"[Subheading] OR "analysis"[All Fields] OR "determination"[All
 Fields])))) OR (spread[All Fields] AND ("disease"[MeSH Terms] OR "disease"[All Fields]))))
 OR (("virology"[MeSH Terms] OR "virology"[All Fields] OR "viral"[All Fields]) AND
 ("ethnology"[Subheading] OR "ethnology"[All Fields] OR "culture"[All Fields] OR
 "culture"[MeSH Terms])) OR (("laboratories"[MeSH Terms] OR "laboratories"[All Fields]
 OR "laboratory"[All Fields]) AND ("isolation and purification"[Subheading] OR
 ("isolation"[All Fields] AND "purification"[All Fields]) OR "isolation and purification"[All
 Fields] OR "isolation"[All Fields])) OR ("death"[MeSH Terms] OR "death"[All Fields])
 AND attributable[All Fields])) OR (("laboratories"[MeSH Terms] OR "laboratories"[All
 Fields] OR "laboratory"[All Fields]) AND confirmed[All Fields])) OR ("hospitalisation"[All
 Fields] OR "hospitalization"[MeSH Terms] OR "hospitalization"[All Fields])) OR
 admission[All Fields]) OR ("outpatients"[MeSH Terms] OR "outpatients"[All Fields]))
 AND (((((((seasonal[All Fields] OR ("pandemics"[MeSH Terms] OR "pandemics"[All
 Fields] OR "pandemic"[All Fields])) OR ("influenza, human"[MeSH Terms] OR
 ("influenza"[All Fields] AND "human"[All Fields]) OR "human influenza"[All Fields] OR
 "influenza"[All Fields])) OR ("influenza, human"[MeSH Terms] OR ("influenza"[All
 Fields] AND "human"[All Fields]) OR "human influenza"[All Fields] OR "influenza"[All
 Fields]) AND like[All Fields] AND illness[All Fields])) OR (severe[All Fields] AND
 acute[All Fields] AND ("respiratory tract infections"[MeSH Terms] OR ("respiratory"[All
 Fields] AND "tract"[All Fields] AND "infections"[All Fields]) OR "respiratory tract
 infections"[All Fields] OR ("respiratory"[All Fields] AND "infections"[All Fields]) OR
 "respiratory infections"[All Fields])))) OR SARI[All Fields]) OR ILI[All Fields])) AND
 (((serfling[All Fields] AND like[All Fields] AND cyclical[All Fields] AND ("regression
 (psychology)"[MeSH Terms] OR ("regression"[All Fields] AND "(psychology)"[All Fields])
 OR "regression (psychology)"[All Fields] OR "regression"[All Fields]) AND ("Model
 Driven Eng Lang Syst"[Journal] OR "models"[All Fields])) OR ("moclobemide"[MeSH
 Terms] OR "moclobemide"[All Fields] OR "arima"[All Fields]) AND ("Model Driven Eng
 Lang Syst"[Journal] OR "models"[All Fields])))) OR ("transmission"[Subheading] OR
 "transmission"[All Fields])) OR (cyclinic[All Fields] AND seasonal[All Fields] AND
 patterns[All Fields]))

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Evaluation of influenza surveillance systems in sub Saharan Africa: A systematic review protocol

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Manuscript ID	bmjopen-2018-023335.R1
Article Type:	Protocol
Date Submitted by the Author:	07-Aug-2018
Complete List of Authors:	Sambala, Evanson; South African Medical Research Council, Cochrane Ndwandwe, Duduzile; South African Medical Research Council, Cochrane South Africa Mwayi, Love; Malawi Public Health Forum Wiysonge, Charles; Stellenbosch University, Centre for Evidence-Based Health Care
Primary Subject Heading:	Epidemiology
Secondary Subject Heading:	Respiratory medicine, Public health, Infectious diseases, Health policy
Keywords:	Influenza infrastructure systems, surveillance systems, burden of influenza, sub Saharan Africa, influenza preparedness

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3 Evaluation of influenza surveillance systems in sub Saharan Africa: A systematic review
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Abstract

Introduction: Influenza infrastructure systems are a crucial aspect in maintaining operations of surveillance, mitigating and responding to the disease. The role of surveillance is to isolate and identify as rapidly as possible any new influenza strains and collate this information for the preparedness for, and response to, an impending influenza activity in the humans. However, sources of surveillance information, particularly in Africa, are meagre. This systematic review will critically evaluate the existing influenza surveillance systems in sub Saharan Africa.

Method and analysis: We will build multiple electronic database search strategies for use in PubMed, Scopus, African Journal Online (AJOL), Web of Science and Google scholar to identify as many studies as possible. The medical subject heading (MeSH) and keywords will include a wide range of synonyms, both in index terms and free-text words. Database search will be followed by hand searching of reference lists of all relevant studies. We will include eligible full text studies published from 2002 in order to coincide with the establishment of the Integrated Disease Surveillance and Response system in Africa by the WHO. We will examine the influenza surveillance performance systems using the US Centers for Disease Control and Prevention (CDC) guidelines on evaluating public health surveillance systems. Our outcome measures will include surveillance system attributes such as timeliness, sensitivity, specificity, acceptability, representativeness, simplicity and usefulness. We will conduct a narrative synthesis of all studies.

Ethics and communication: This study does not require ethics approval because it uses publicly available data. Our findings will be published in a peer review journal and disseminated to policymakers.

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3 **PROSPERO registration number:** Registration in PROSPERO is underway
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9 **Strengths and limitations of this study**
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- 11 • A comprehensive search of published and unpublished literature in any language will be
12 included hence minimizing the risk for publication bias.
13
- 14 • The search strategy excludes stochastically or computer simulated modelling techniques
15 thus placing limitation on surveillance methods that potentially may have greater
16 sensitivity and specificity.
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- 18 • Data extraction tool used in this study to evaluate African surveillance systems was
19 specifically developed to assess advanced systems outside Africa hence; the review
20 findings of this study may be biased.
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Introduction

The overarching goal of influenza surveillance systems is to isolate and identify as rapidly as possible any new influenza strains and collate this information for control and mitigation of the impacts of influenza in the humans. However, quantifying influenza cases in real time is generally more difficult because influenza viruses tend to undergo continuous antigenic variations, by either mutation (antigenic drift) or genetic recombination (antigenic shift).^{1,2} The World Health Organization (WHO) recommends the continuous monitoring of influenza viruses during each influenza season to identify the virus strains circulating in the population and track the burden of influenza related illnesses. Surveillance further provides information on the candidate viruses for vaccine production and monitoring of the antiviral sensitivity.³

Surveillance of influenza is an important public health task. However, sources of surveillance information, particularly in Africa, are meagre.⁴ There are undoubtedly general difficulties in surveillance systems in Africa, not only in the robustness of the data needed to send early signals for health service response, but also in the financial resources and leadership required for efficient and timely decision-making.⁵ Influenza surveillance is persistently characterised by low completeness and timeliness reporting due to inadequate laboratories, communication structures and poor public health human resources.⁵ A related difficulty despite the use of standard case definitions of influenza like illness (ILI) and Severe Acute Respiratory Infections (SARI) are sampling issues, which are often biased towards collecting more specimen from patients suspected on clinical grounds to have influenza.⁶ In some cases, calculation of death associated

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3 to ILI and SARI is difficult to ascertain especially where such deaths are not attributable to
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5 influenza illness as primary cause.
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8 Epidemiological observations including inferential statistics that explain epidemiological events
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10 are important and crucial for any public health decision that inform prevention and control
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12 strategies. Indirect indices such as excess mortality, attack rates and clinical symptoms are
13
14 signature measures of the impact of influenza. A measure in the sudden increase in illness or
15
16 death from complications of influenza remains a challenge, these mathematical models are no
17
18 means a direct one. Epidemiologists in seasonal climates determine excess deaths attributable to
19
20 influenza, including influenza burden on hospitalization (during winter months), by use of
21
22 serfling-like cyclical regression models and arima models.⁷ However, these models are not
23
24 applicable in tropical climates where seasonality is all year round whereas these methods require
25
26 cyclic seasonal patterns of viral activity interrupted by influenza-free periods. Due to these
27
28 limitations, quantifying influenza surveillance data deploy other methods such as use of the
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30 influenza pyramid of severity, the spread of disease and risk factor determination, which often
31
32 do not require emphasis on viral culture and laboratory isolation.
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38 Influenza infrastructure systems are a crucial aspect in maintaining operations of surveillance,
39
40 mitigating and responding to the disease. The WHO defines surveillance systems as a
41
42 “continuous, systematic collection, analysis and interpretation of health-related data needed for
43
44 the planning, implementation, and evaluation of public health practice”⁸ However, there is little
45
46 agreement as to which sources of surveillance data is most appropriate to serve as an early and
47
48 sensitive warning system for influenza outbreaks and management.
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3 This systematic review critically evaluates the existing surveillance systems used to collect and
4 analyze surveillance data to detect when and where influenza activity is occurring. Our findings
5 will inform public health policymakers on the role of strengthening surveillance systems.
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11 12 **Objective**

13
14 To evaluate and describe influenza surveillance systems designed to detect the occurrence,
15 circulation and impacts of influenza related illnesses.
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21 22 **Methods**

23 24 **Patient and public involvement**

25 Patients were not involved in the design of this study.
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30 31 **Eligibility criteria**

32 33 **Types of studies to be included**

34
35 Observational studies on influenza surveillance systems or methods that describe or evaluate the
36 collection, analysis and reporting of influenza surveillance. We will include the following
37 categories of surveillance systems:
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- 41
42 • Virologic Surveillance e.g. public health and clinical laboratories that test specimens to
43 understand when and where influenza viruses are circulating.
- 44
45 • Outpatient Illness Surveillance e.g. patient visits to health care providers for influenza-
46 like illness/contact tracing
- 47
48 • Mortality Surveillance e.g. influenza-associated deaths
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- Hospitalization Surveillance e.g. laboratory confirmed influenza-associated hospitalizations
- Geographic spread of influenza e.g. no activity, sporadic, local, regional, or widespread.

All studies that report mathematical models or use hypothetical surveillance data will be excluded.

Type of participants

This review will draw on all human participants. Although young children, elderly and persons with underlying medical conditions are at higher risk of severe influenza, the disease can affect any individual. For example, the 2009 pandemic H1N1 virus remained antigenically unchanged in May 2012, still affecting young adults (as in the 2010/11 season) as seasonal influenza.⁹ Surveillance systems are designed such that to detect the disease in all individuals for prevention and control. All studies reporting on animal surveillance system will be excluded.

Type of exposure

Identifying and quantifying influenza cases is generally more difficult compared to other infectious diseases, which have clear-cut clinical signs. Influenza illnesses, especially mild ones, may go unreported and sometimes may warrant no medical attention although influenza virus infections can lead to fatal complications and death associated with pre-existing medical conditions such as cardiovascular diseases.¹⁰ In cases of death associated with pre-existing medical conditions, influenza would not be typically identified as the primary cause of death. We will adopt the WHO case definitions for ILI and SARI. ILI is defined as “an acute respiratory illness with measured temperature of $\geq 38^{\circ}$ C and cough, with onset within 10 days”¹¹ SARI is

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3 “an acute respiratory illness with a history of fever or measured fever of $\geq 38^{\circ}\text{C}$ and cough,
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5 with onset within the past 10 days, requiring hospitalization.¹¹
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10 **Types of the outcomes measures**

11
12 The primary outcomes include the following influenza surveillance system attributes:

- 13 1. Simplicity i.e. ease of operation
 - 14 2. Flexibility i.e. adapting to changing information such as case definitions
 - 15 3. Data quality i.e. completeness and validity
 - 16 4. Acceptability i.e. willingness of staff to use the system
 - 17 5. Sensitivity i.e. timely detection of influenza
 - 18 6. Predictive value positive i.e. proportion of true cases
 - 19 7. Representativeness i.e. distribution in the population by place and person
 - 20 8. Timeliness i.e. speed between steps in a public health surveillance system,
 - 21 9. Stability i.e., the ability to collect, manage, and provide data properly without failure
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37 The secondary outcomes measures will include the following descriptions of the surveillance
38 system tasks:
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- 40 1. Public health importance
 - 41 2. System under evaluation
 - 42 3. Resources to operate the surveillance system
 - 43 4. Usefulness of the surveillance system
 - 44 5. Design
 - 45 6. Conclusion and recommendations of the system
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3 7. Utilization of the findings and how these are shared as lessons learned with stakeholders
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8 **Search strategy**
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10 We will build multiple electronic database search strategies for use in PubMed, Scopus, African
11 Journal Online (AJOL), Web of Science, and Google scholar to identify as many titles as
12 possible in any language. The medical subject heading (MeSH) terms Influenza Like Illnesses
13 (ILI) and Severe Acute Respiratory Infections (SARI), surveillance, virologic, outpatient illness,
14 mortality, morbidity, hospitalization, laboratory confirmed, influenza, sentinel, seasonal,
15 pandemic, infrastructures and Africa will be used to combine searches systematically. The search
16 terms will include a wide range of synonyms, both in index terms and free-text words. The exact
17 terms for the search in PubMed is presented in Table 1. Hand searching of reference lists of all
18 relevant studies and reports will be completed to identify additional studies that might be eligible
19 for the review. All the identified titles and abstracts will be examined for inclusion. If relevant, a
20 full text article will be obtained and read carefully. The titles searched by hand from the
21 reference lists will be retained into the database search for a full text. We will search for studies
22 published from 01 January 2002 in order to coincide with the establishment of the Integrated
23 Disease Surveillance and Response system by the WHO.
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45 **Searching other resources**
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48 We will identify country eligible reports or preliminary analysis from respective National
49 Influenza Centres and fluNet where surveillance data is shared. We will search the websites of
50 relevant government's agencies, the WHO's Global Influenza Surveillance and Response System
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3 (GISRS), Global Influenza Surveillance Network (GISN) and Global Influenza Programme
4 (GIP). We will also search conference reports and abstracts from the African Network for
5 Influenza Surveillance and Epidemiology (ANISE) and the Africa Flu Alliance Meeting.
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11 12 13 **Selection of studies**

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15 Two authors (EZS and DN) will screen titles and abstracts for eligibility independently of each
16 other based on the inclusion criteria. Refworks manager will import the identified titles and
17 abstracts into the reference database. The full text of potentially eligible studies will be screened
18 for duplications by two independent authors (EZS and DN). All the duplicate articles and reports
19 will be removed. Where disagreement arise on the study eligibility due to lack of information on
20 the study manuscript or report, we will contact the authors of the article for additional
21 information or clarification. All discrepancies and disagreement will be resolved by consensus
22 and if necessary by arbitration of the third author (CSW). We will translate words, phrases and
23 web pages into English from other languages using google translation software.
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38 39 **Data extraction and management**

40 We will examine studies and reports that describe surveillance systems for collecting, analyzing,
41 or presenting surveillance data for influenza-related illnesses or syndromes. Two independent
42 authors (EZS and DN) will abstract information from eligible studies using a standard data
43 extraction form shown in Table 2. In addition, we will abstract details from studies and reports
44 such as the year of study, settings, study design, methods, participants, source of funding,
45 participants and risk of bias. Two authors will compare the extracted data and discrepancies or
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any disagreements that arise will be resolved by the third author (CSW). Where there is missing data in the studies and reports, we will contact the study author(s) for additional information.

Assessment of the risk of bias in the included studies

Two independent authors (EZS and DN) will assess the risk of bias. We will develop a risk of bias table to summarize our assessments. In context of surveillance systems, biases arise in case definitions (i.e. SARI/ILI) and the type of diagnostic equipment (RT-PCR versus Immunofluorescence assays) used to test influenza as such these variations can lead to selection or misclassification bias in the surveillance techniques. Any disagreements or discrepancies concerning the risk of bias will be resolved by discussion and if any disagreement cannot be resolved an involvement of a third reviewer (CSW) will be recommended.

Data synthesis

We will score each surveillance task including its element by assigning values from 5 (excellent) to 1 (absent). Table 3 shows the point scoring criteria for evaluating the studies and reports. We will describe the surveillance performance system using the US Centers for Disease Control and Prevention (CDC) guidelines on evaluating public health surveillance systems.^{12,13} First developed in 1988 and updated in 2001, the guidelines ensure that the influenza surveillance system operates efficiently and effectively in meeting its intended purpose and objectives. In order to gauge the strength of these surveillance systems we will sum up the scores for each surveillance system using averages and percentages. In addition, we will also generate the predefined themes captured in the data collection form.

Reporting of this review

We designed and wrote this study protocol following the guidelines on Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P).¹⁴ We considered all the 17 items in the PRISMA-P in order to facilitate the transparent and complete reporting of systematic reviews and meta-analysis. We will report our results of this review according to guidance contained in the PRISMA Statement.¹⁵ Any amendments to the protocol will subsequently be updated in the PROSPERO systematic review registry.

Timeline for the systematic review

We plan to conduct the searches and select eligible studies between August and October, 2018. We hope to complete the data analysis, write up and submit the first draft of the manuscript by December 2018.

Ethics and communication

Our study is based on publicly available published studies which does not require ethical approval and consent from participants. The results from this systematic review will be communicated in peer review journal and presented at international conferences.

Data sharing statement

Additional information beyond that contained within this manuscript can be obtained from the corresponding author.

Discussion

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3 This protocol for systematic review will evaluate influenza surveillance systems using available
4 literature. We will explore the existing types of surveillance tools used to gather data and
5
6 evaluate study techniques in surveillance reporting and monitoring of influenza. We hope to
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8 identify gaps in our findings and recommend direction for the future evaluation of the systems.
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10 In addition, our findings will enhance the utility to respond rapidly to the early warning signs of
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12 new influenza viruses and subsequently strengthen the overall surveillance systems by informing
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14 public health policy. Influenza surveillance systems particularly those designed for seasonal
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16 influenza outbreaks is important. They can serve as a predictive indicator for new events such as
17
18 an influenza pandemic and systematically aid pandemic planners to plan for additional capacities
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20 and resources needed to deal with a more severe outbreak.¹⁶
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26 There are potential limitations to this study. Firstly, we anticipate that reported surveillance
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28 systems at the country level will lack geographic representativeness because sentinel data
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30 aggregated at the national influenza centers often are unevenly distributed. Subsequently, this
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32 may introduce bias in our review findings. Secondly, our search strategy excludes stochastically
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34 and computer simulated modelling techniques yet these methods have high sensitivity and
35
36 specificity. This substantially limits our understanding of the types of surveillance systems that
37
38 may exist. Thirdly, we use a data extraction tool specifically developed for the surveillance
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40 systems in United States to describe and assess the strength of surveillance systems in Africa.
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43 With such a limitation, our findings may not be a true reflection of the established surveillance
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45 systems in Africa.
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51 **Authors' contributions**

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3 EZS, DN, ML and CSW contributed to the conceptualization of the review. EZS wrote the
4 manuscript draft. EZS, ML developed the search strategy. All authors revised and edited the
5 manuscript draft and search strategy. All authors approved the manuscript.
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12
13
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15 not-for-profit sectors.
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20 **Competing interests statement:**

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24 None
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28 **Patient consent:**

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31 Not required.
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Table 1: Search Strategy

```

((((((((("africa"[MeSH Terms] OR "africa"[All Fields]) OR ("africa south of the
sahara"[MeSH Terms] OR ("africa"[All Fields] AND "south"[All Fields] AND "sahara"[All
Fields]) OR "africa south of the sahara"[All Fields] OR ("sub"[All Fields] AND
"saharan"[All Fields] AND "africa"[All Fields]) OR "sub saharan africa"[All Fields])) OR
("africa, western"[MeSH Terms] OR ("africa"[All Fields] AND "western"[All Fields]) OR
"western africa"[All Fields] OR ("west"[All Fields] AND "africa"[All Fields]) OR "west
africa"[All Fields])) OR ("africa, northern"[MeSH Terms] OR ("africa"[All Fields] AND
"northern"[All Fields]) OR "northern africa"[All Fields] OR ("north"[All Fields] AND
"africa"[All Fields]) OR "north africa"[All Fields])) OR ("africa, southern"[MeSH Terms]
OR ("africa"[All Fields] AND "southern"[All Fields]) OR "southern africa"[All Fields] OR
("southern"[All Fields] AND "africa"[All Fields])) OR ("africa, central"[MeSH Terms] OR
("africa"[All Fields] AND "central"[All Fields]) OR "central africa"[All Fields] OR
("central"[All Fields] AND "africa"[All Fields])) OR ("africa, eastern"[MeSH Terms] OR
("africa"[All Fields] AND "eastern"[All Fields]) OR "eastern africa"[All Fields] OR
("east"[All Fields] AND "africa"[All Fields]) OR "east africa"[All Fields])) AND
((((((((((((((((("epidemiology"[Subheading] OR "epidemiology"[All Fields] OR
"surveillance"[All Fields] OR "epidemiology"[MeSH Terms] OR "surveillance"[All Fields])
OR (("epidemiology"[Subheading] OR "epidemiology"[All Fields] OR "surveillance"[All
Fields] OR "epidemiology"[MeSH Terms] OR "surveillance"[All Fields]) AND systems[All
Fields])) OR (("epidemiology"[Subheading] OR "epidemiology"[All Fields] OR
"surveillance"[All Fields] OR "epidemiology"[MeSH Terms] OR "surveillance"[All Fields])
AND types[All Fields])) OR sentinel[All Fields]) OR ("virology"[MeSH Terms] OR
"virology"[All Fields] OR "virologic"[All Fields])) OR infrastructure[All Fields]) OR
("mortality"[Subheading] OR "mortality"[All Fields] OR "mortality"[MeSH Terms])) OR
("epidemiology"[Subheading] OR "epidemiology"[All Fields] OR "morbidity"[All Fields]
OR "morbidity"[MeSH Terms])) OR (pyramid[All Fields] AND severity[All Fields])) OR
(("risk factors"[MeSH Terms] OR ("risk"[All Fields] AND "factors"[All Fields]) OR "risk
factors"[All Fields] OR ("risk"[All Fields] AND "factor"[All Fields]) OR "risk factor"[All
Fields]) AND ("analysis"[Subheading] OR "analysis"[All Fields] OR "determination"[All
Fields])) OR (spread[All Fields] AND ("disease"[MeSH Terms] OR "disease"[All Fields]))))

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OR (("virology"[MeSH Terms] OR "virology"[All Fields] OR "viral"[All Fields]) AND ("ethnology"[Subheading] OR "ethnology"[All Fields] OR "culture"[All Fields] OR "culture"[MeSH Terms])) OR (("laboratories"[MeSH Terms] OR "laboratories"[All Fields] OR "laboratory"[All Fields]) AND ("isolation and purification"[Subheading] OR ("isolation"[All Fields] AND "purification"[All Fields]) OR "isolation and purification"[All Fields] OR "isolation"[All Fields])) OR (("death"[MeSH Terms] OR "death"[All Fields]) AND attributable[All Fields]) OR (("laboratories"[MeSH Terms] OR "laboratories"[All Fields] OR "laboratory"[All Fields]) AND confirmed[All Fields]) OR ("hospitalisation"[All Fields] OR "hospitalization"[MeSH Terms] OR "hospitalization"[All Fields]) OR admission[All Fields] OR ("outpatients"[MeSH Terms] OR "outpatients"[All Fields])) AND (((seasonal[All Fields] OR ("pandemics"[MeSH Terms] OR "pandemics"[All Fields] OR "pandemic"[All Fields])) OR ("influenza, human"[MeSH Terms] OR ("influenza"[All Fields] AND "human"[All Fields]) OR "human influenza"[All Fields] OR "influenza"[All Fields])) OR ("influenza, human"[MeSH Terms] OR ("influenza"[All Fields] AND "human"[All Fields]) OR "human influenza"[All Fields] OR "influenza"[All Fields]) AND like[All Fields] AND illness[All Fields]) OR (severe[All Fields] AND acute[All Fields] AND ("respiratory tract infections"[MeSH Terms] OR ("respiratory"[All Fields] AND "tract"[All Fields] AND "infections"[All Fields]) OR "respiratory tract infections"[All Fields] OR ("respiratory"[All Fields] AND "infections"[All Fields]) OR "respiratory infections"[All Fields])) OR SARI[All Fields] OR ILI[All Fields]) AND (((serfling[All Fields] AND like[All Fields] AND cyclical[All Fields] AND ("regression (psychology)"[MeSH Terms] OR ("regression"[All Fields] AND ("psychology)"[All Fields]) OR "regression (psychology)"[All Fields] OR "regression"[All Fields]) AND ("Model Driven Eng Lang Syst"[Journal] OR "models"[All Fields])) OR ("moclobemide"[MeSH Terms] OR "moclobemide"[All Fields] OR "arima"[All Fields]) AND ("Model Driven Eng Lang Syst"[Journal] OR "models"[All Fields])) OR ("transmission"[Subheading] OR "transmission"[All Fields]) OR (cyclinic[All Fields] AND seasonal[All Fields] AND patterns[All Fields]))

Table 2: Evaluation checklist

Category	Criteria	1	2	3	4	5	NA
Stakeholders	Describe persons or organizations who will utilize the data gathered by the surveillance system.						
Description of the system	Describe the importance of the public health problem under surveillance.						
	Explain the reason/purpose						

	behind collecting data, and how the data is intended to be used.								
	Describe resources required to operate the system.								
Evaluation design	Describe the specific purpose of the evaluation .								
	Propose uses of the evaluation results.								
	Include the specific questions that the evaluation answered.								
Credible evidence	Describe usefulness of the information generated by analyzing data.								
	Assess surveillance system attributes in terms of:								
	Simplicity								
	Flexibility								
	Data quality								
	Acceptability								
	Sensitivity								
	Predictive value positive								
	Representativeness								
	Timeliness								
	Stability								
Conclusions and Recommendations	Present conclusions based on evaluation results. Propose appropriate and applicable recommendations to improve the system or discontinue its operation								
Lessons learned	Describe how lessons learned will be communicated to those who need to know								

Table 3: Scoring sheet

Points	Description
5 = excellent	The element is present, consistent with the standard described in the instructions and provided in the classroom, and is of a remarkable/outstanding quality.
4 = good	The element is present and consistent with the standard described in the instructions and provided in the classroom.
3 = satisfactory	The element is present and may be used even though it may not completely follow the standard described in the instructions and provided in the classroom
2 = poor	The element is present but flawed or of poor quality.
1 = absent	The element is absent from the report.
NA = not applicable	The element is not relevant to this report.

BMJ Open

Evaluation of influenza surveillance systems in sub Saharan Africa: A systematic review protocol

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2018-023335.R2
Article Type:	Protocol
Date Submitted by the Author:	08-Nov-2018
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Primary Subject Heading:	Epidemiology
Secondary Subject Heading:	Respiratory medicine, Public health, Infectious diseases, Health policy
Keywords:	Influenza infrastructure systems, surveillance systems, burden of influenza, sub Saharan Africa, influenza preparedness

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Manuscripts

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3 Evaluation of influenza surveillance systems in sub Saharan Africa: A systematic review protocol
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Abstract

Introduction: Influenza infrastructure systems are a crucial aspect in maintaining operations of surveillance, mitigating and responding to the disease. The role of surveillance is to isolate and identify as rapidly as possible any new influenza strains and collate this information for the preparedness for, and response to, an impending influenza activity in the humans. However, sources of surveillance information, particularly in Africa, are meagre. This systematic review will critically evaluate the existing influenza surveillance systems in sub Saharan Africa.

Method and analysis: We will build multiple electronic database search strategies for use in PubMed, Scopus, African Journal Online (AJOL), Web of Science and Google scholar to identify as many studies as possible. The medical subject heading (MeSH) and keywords will include a wide range of synonyms, both in index terms and free-text words. Database search will be followed by hand searching of reference lists of all relevant studies. We will include eligible full text studies published from 2002 in order to coincide with the establishment of the Integrated Disease Surveillance and Response system in Africa by the World Health Organization. We will examine the influenza surveillance performance systems using the US Centers for Disease Control and Prevention (CDC) guidelines on evaluating public health surveillance systems. Our outcome measures will include surveillance system attributes such as timeliness, sensitivity, specificity, acceptability, representativeness, simplicity and usefulness. We will conduct a narrative synthesis of all studies.

Ethics and dissemination: This study does not require ethics approval because it uses publicly available data. Our findings will be published in a peer review journal and disseminated to policymakers.

PROSPERO registration number: CRD42018103042

Strengths and limitations of this study

- Extraction of information from eligible studies using a standard evaluation checklist will efficiently summarise findings on the sensitivity, quality and usefulness of surveillance systems.
- A comprehensive and through search of published and unpublished literature in any language will be included to minimise the risk for publication bias.
- The search strategy excludes stochastically or computer simulated modelling techniques thus placing limitation on surveillance methods that potentially may have greater sensitivity and specificity.

Introduction

The overarching goal of influenza surveillance systems is to isolate and identify as quickly as possible any new influenza strains and collate this information for control and mitigation of the impacts of influenza in the humans.¹ However, measuring influenza cases in real time is often a challenge because influenza viruses tend to undergo continuous antigenic variations, by either mutation (antigenic drift) or genetic recombination (antigenic shift).^{2,3} The World Health Organization (WHO) recommends the continuous monitoring of influenza viruses during each influenza season to identify the virus strains circulating in the population and track the burden of influenza related illnesses.⁴ Surveillance further provides information on the candidate viruses for vaccine production and monitoring of the antiviral sensitivity.⁵

Surveillance of influenza is an important public health task. However, sources of surveillance information, particularly in sub Saharan Africa are insufficient.^{1,6} There are undoubtedly general difficulties in surveillance systems in Africa, not only in the robustness of the data needed to send early signals for health service response, but also in the financial resources and leadership required for efficient and timely decision-making.⁷ Influenza surveillance is persistently characterised by low completeness and timeliness reporting due to inadequate laboratories, communication structures and poor public health human resources.⁷ A related challenge despite the use of standard case definitions of influenza like illness (ILI) and Severe Acute Respiratory Infections (SARI) are sampling issues within surveillance systems, which are often biased towards collecting more specimen from patients suspected on clinical grounds to have influenza.⁸ In some cases, calculation of death associated to ILI and SARI is difficult to ascertain especially where such deaths are not attributable to influenza illness as primary cause.

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3 Epidemiological methods using inferential statistics can explain epidemiological events, and are
4 important for any public health decision that inform influenza prevention and control strategies.
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6 Indirect indices such as excess mortality, attack rates and clinical symptoms are signature measures
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8 of the impact of influenza. A measure in the sudden increase in illness or death related to influenza
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10 remain an issue, these mathematical models are no means a direct one. Epidemiologists in seasonal
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12 climates determine excess deaths attributable to influenza, including influenza burden on
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14 hospitalization (during winter months), by use of serfling-like cyclical regression models and
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16 arima models.^{1,9} However, these models are not applicable in tropical climates where seasonality
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18 is all year round whereas these methods require cyclic seasonal patterns of viral activity interrupted
19
20 by influenza-free periods. Due to these limitations, quantifying influenza surveillance data deploy
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22 other methods such as use of the influenza pyramid of severity, the spread of disease and risk factor
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24 determination, which often do not require emphasis on viral culture and laboratory isolation.
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Influenza infrastructure systems are a crucial aspect in maintaining operations of surveillance, mitigating and responding to the disease. The WHO defines surveillance systems as a “continuous, systematic collection, analysis and interpretation of health-related data needed for the planning, implementation, and evaluation of public health practice”.¹⁰ However, there is little agreement as to which sources of surveillance data is most appropriate to serve as an early and sensitive warning system for influenza outbreaks and management.

This systematic review critically evaluates the existing surveillance systems used to collect and analyze surveillance data to detect when and where influenza activity is occurring. Our findings will inform public health policymakers on the role of strengthening surveillance systems.

Objective

To evaluate and describe influenza surveillance systems designed to detect the occurrence, circulation and impacts of influenza related illnesses.

Methods

Eligibility criteria

Types of studies to be included

Observational studies on influenza surveillance systems or methods that describe or evaluate the collection, analysis and reporting of influenza surveillance. We will include the following categories of surveillance systems:

- Virologic Surveillance e.g. public health and clinical laboratories that test specimens to understand when and where influenza viruses are circulating.
- Outpatient Illness Surveillance e.g. patient visits to health care providers for influenza-like illness/contact tracing.
- Mortality Surveillance e.g. influenza-associated deaths.
- Hospitalization Surveillance e.g. laboratory confirmed influenza-associated hospitalizations.
- Geographic spread of influenza e.g. no activity, sporadic, local, regional, or widespread.

All studies that report mathematical models or use hypothetical surveillance data will be excluded.

Type of participants

This review will draw on all human participants. Although young children, elderly and persons with underlying medical conditions are at higher risk of severe influenza, the disease can affect any individual. For example, the 2009 pandemic H1N1 virus remained antigenically unchanged in

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2
3 May 2012, still affecting young adults (as in the 2010/11 season) as seasonal influenza.^{4,11}
4
5 Surveillance systems are designed to detect the disease in all individuals for prevention and
6
7 control. All studies reporting on animal surveillance system will be excluded.
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11 12 **Type of exposure**

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14 Identifying and quantifying influenza cases is generally more challenging compared to other
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16 infectious diseases, which have clear-cut clinical signs. Influenza illnesses, especially mild ones,
17
18 may go unreported and sometimes may warrant no medical attention.¹ Influenza virus infections
19
20 can lead to fatal complications and death associated with pre-existing medical conditions such as
21
22 cardiovascular diseases.¹² In cases of death associated with pre-existing medical conditions,
23
24 influenza would not be typically identified as the primary cause of death. We will adopt the WHO
25
26 case definitions for ILI and SARI. ILI is defined as “an acute respiratory illness with measured
27
28 temperature of $\geq 38^{\circ}\text{C}$ and cough, with onset within 10 days”¹³ while SARI is defined as “an
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30 acute respiratory illness with a history of fever or measured fever of $\geq 38^{\circ}\text{C}$ and cough, with
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32 onset within the past 10 days, requiring hospitalization.”¹³
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40 **Types of the outcomes measures**

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42 The primary outcomes include the following influenza surveillance system attributes:

- 43 1. Simplicity i.e. ease of operation
 - 44 2. Flexibility i.e. adapting to changing information such as case definitions
 - 45 3. Data quality i.e. completeness and validity
 - 46 4. Acceptability i.e. willingness of staff to use the system
 - 47 5. Sensitivity i.e. timely detection of influenza
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6. Predictive value positive i.e. proportion of true cases
7. Representativeness i.e. distribution in the population by place and person
8. Timeliness i.e. speed between steps in a public health surveillance system,
9. Stability i.e., the ability to collect, manage, and provide data properly without failure

The secondary outcomes measures will include the following descriptions of the surveillance system tasks:

1. Public health importance
2. System under evaluation
3. Resources to operate the surveillance system
4. Usefulness of the surveillance system
5. Design
6. Conclusion and recommendations of the system
7. Utilization of the findings and how these are shared as lessons learned with stakeholders

Search strategy

We will build multiple electronic database search strategies for use in PubMed, Scopus, African Journal Online (AJOL), Web of Science, and Google scholar to identify as many titles as possible in any language. The medical subject heading (MeSH) terms Influenza Like Illnesses (ILI) and Severe Acute Respiratory Infections (SARI), surveillance, virologic, outpatient illness, mortality, morbidity, hospitalization, laboratory confirmed, influenza, sentinel, seasonal, pandemic, infrastructures and Africa will be used to combine searches systematically. The search terms will include a wide range of synonyms, both in index terms and free-text words. The exact terms for

1
2
3 the search in PubMed is presented in Table 1. Hand searching of reference lists of all relevant
4 studies and reports will be completed to identify additional studies that might be eligible for the
5 review. All the identified titles and abstracts will be screened for inclusion. If relevant, a full text
6 article will be obtained and read carefully. The titles searched by hand from the reference lists will
7 be retained into the database search for a full text. We will search for studies published from 01
8 January 2002 to coincide with the establishment of the Integrated Disease Surveillance and
9 Response system by the WHO.
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22 **Searching other resources**

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24 We will identify country eligible reports or preliminary analysis from respective National
25 Influenza Centres and FluNet where surveillance data is shared. We will search the websites of
26 relevant government's agencies, the WHO's Global Influenza Surveillance and Response System
27 (GISRS), Global Influenza Surveillance Network (GISN) and Global Influenza Programme (GIP).
28 We will also search conference reports and abstracts from the African Network for Influenza
29 Surveillance and Epidemiology (ANISE) and the Africa Flu Alliance Meeting.
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43 **Selection of studies**

44 Two authors (EZS and DN) will screen titles and abstracts for eligibility independently of each
45 other based on the inclusion criteria. We will import the identified titles and abstracts into the
46 reference database using Endnote X7. The full text of potentially eligible studies will be screened
47 for duplications by two independent authors (EZS and DN). All the duplicate articles and reports
48 will be removed. Where disagreement arise on the study eligibility due to lack of information on
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3 the study manuscript or report, we will contact the authors of the article for additional
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5 information or clarification. All discrepancies and disagreement will be resolved by consensus
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7 and if necessary by arbitration of the third author (CSW). We will translate words, phrases and
8
9 web pages into English from other languages using google translation software.
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14 **Data extraction and management**

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16 We will examine studies and reports that describe surveillance systems for collecting, analyzing,
17
18 or presenting surveillance data for influenza-related illnesses or syndromes. Two independent
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20 authors (EZS and DN) will extract information from eligible studies using a standard data
21
22 extraction form shown in Table 2. In addition, we will extract details from studies and reports such
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24 as the year of study, settings, study design, methods, participants, source of funding, participants
25
26 and risk of bias. Two authors will compare the extracted data and resolve discrepancies or any
27
28 disagreements by discussion to reach consensus. If the two authors are unable to resolve
29
30 disagreements a third author (CSW) will be consulted. Where there is missing data in the studies
31
32 and reports, we will contact the study author(s) for additional information.
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40 **Assessment of the risk of bias in the included studies**

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42 Two independent authors (EZS and DN) will assess the risk of bias in observation studies using
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44 the ROBINS-I tool.¹⁴ We will evaluate the following domains for risk of bias: confounding,
45
46 selection of participants, classification of interventions, deviations from intended interventions,
47
48 missing data, measurement of outcomes and selection of the reported results. We will develop a
49
50 risk of bias table to summarize our assessments. In context of surveillance systems, biases arise in
51
52 case definitions (i.e. SARI/ILI) and the type of diagnostic equipment (RT-PCR versus
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3 Immunofluorescence assays) used to test influenza as such these variations can lead to selection
4 or misclassification bias in the surveillance techniques. Any disagreements or discrepancies
5 concerning the risk of bias will be resolved by discussion and if any disagreement cannot be
6 resolved an involvement of a third reviewer (CSW) will be recommended.
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14 **Data synthesis**

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16 We will score each surveillance task including its element by assigning values from 5 (excellent)
17 to 1 (absent). Table 3 shows the point scoring criteria for evaluating the studies and reports. We
18 will describe the surveillance performance system using the US Centers for Disease Control and
19 Prevention (CDC) guidelines on evaluating public health surveillance systems.^{15,16} First developed
20 in 1988 and updated in 2001, the guidelines ensure that the influenza surveillance system operates
21 efficiently and effectively in meeting its intended purpose and objectives. In order to gauge the
22 strength of these surveillance systems we will sum up the scores for each surveillance system using
23 averages and percentages. In addition, we will also generate and organise data using the predefined
24 themes captured in the data collection form.
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40 **Reporting of this review**

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42 We designed and wrote this study protocol following the guidelines on Preferred Reporting Items
43 for Systematic Review and Meta-Analysis Protocols (PRISMA-P).¹⁷ We considered all the 17
44 items in the PRISMA-P to facilitate the transparent and complete reporting of systematic reviews
45 and meta-analysis. We will report our results of this review according to guidance contained in
46 the PRISMA Statement.¹⁷ Any amendments to the protocol will subsequently be updated in the
47 PROSPERO systematic review registry.
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Timeline for the systematic review

We plan to conduct the searches and select eligible studies between November - December 2018.

We hope to complete the data analysis, write up and submit the first draft of the manuscript by December 2018.

Ethics and dissemination

Our study is based on publicly available published studies which does not require ethical approval and consent from participants. The results from this systematic review will be communicated in peer review journal and presented at international conferences.

Data sharing statement

Additional information beyond that contained within this manuscript can be obtained from the corresponding author.

Patient and public involvement

Patients were not involved in the design of this study. The study does not require the recruitment of patients and/or for the public to be involved as this systematic review only assesses available influenza surveillance systems

Discussion

This protocol for systematic review will evaluate influenza surveillance systems using available literature. We will explore the existing types of surveillance tools used to gather data and evaluate

1
2
3 study techniques in surveillance reporting and monitoring of influenza. We hope to identify gaps
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5 in our findings and recommend direction for the future evaluation of the systems. In addition, our
6
7 findings will enhance the utility to respond rapidly to the early warning signs of new influenza
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9 viruses and subsequently strengthen the overall surveillance systems by informing public health
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11 policy. Influenza surveillance systems particularly those designed for seasonal influenza outbreaks
12
13 is important. They can serve as a predictive indicator for new events such as an influenza pandemic
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15 and systematically aid pandemic planners to plan for additional capacities and resources needed to
16
17 deal with a more severe outbreak.¹⁸

18
19 There are potential limitations to this study. Firstly, we anticipate that reported surveillance
20
21 systems at the country level will lack geographic representativeness because sentinel data
22
23 aggregated at the national influenza centers often are unevenly distributed. Subsequently, this may
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25 introduce bias in our review findings. Secondly, our search strategy excludes stochastically and
26
27 computer simulated modelling techniques yet these methods have high sensitivity and specificity.
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29 This substantially limits our understanding of the types of surveillance systems that may exist.
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31 Thirdly, we use a data extraction tool specifically developed for the surveillance systems in United
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33 States to describe and assess the strength of surveillance systems in Africa. With such a limitation,
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35 our findings may not be a true reflection of the established surveillance systems in Africa.
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44 **Authors' contributions**

45
46 EZS, DN, ML and CSW contributed to the conceptualization of the review. EZS wrote the
47
48 manuscript draft. EZS, ML developed the search strategy. All authors revised and edited the
49
50 manuscript draft and search strategy. All authors approved the manuscript.
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Competing interests statement:

None

Patient consent:

Not required.

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9 [mentInterimGuidance_Jun2013.pdf](http://www.who.int/influenza/preparedness/pandemic/GIP_PandemicInfluenzaRiskManagementInterimGuidance_Jun2013.pdf)
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16 Table 1: Search Strategy
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19 (((((((("africa"[MeSH Terms] OR "africa"[All Fields]) OR ("africa south of the
20 sahara"[MeSH Terms] OR ("africa"[All Fields] AND "south"[All Fields] AND
21 "sahara"[All Fields]) OR "africa south of the sahara"[All Fields] OR ("sub"[All Fields]
22 AND "saharan"[All Fields] AND "africa"[All Fields]) OR "sub saharan africa"[All
23 Fields])) OR ("africa, western"[MeSH Terms] OR ("africa"[All Fields] AND
24 "western"[All Fields]) OR "western africa"[All Fields] OR ("west"[All Fields] AND
25 "africa"[All Fields]) OR "west africa"[All Fields])) OR ("africa, northern"[MeSH Terms]
26 OR ("africa"[All Fields] AND "northern"[All Fields]) OR "northern africa"[All Fields]
27 OR ("north"[All Fields] AND "africa"[All Fields]) OR "north africa"[All Fields])) OR
28 ("africa, southern"[MeSH Terms] OR ("africa"[All Fields] AND "southern"[All Fields])
29 OR "southern africa"[All Fields] OR ("southern"[All Fields] AND "africa"[All Fields]))
30 OR ("africa, central"[MeSH Terms] OR ("africa"[All Fields] AND "central"[All Fields])
31 OR "central africa"[All Fields] OR ("central"[All Fields] AND "africa"[All Fields])) OR
32 ("africa, eastern"[MeSH Terms] OR ("africa"[All Fields] AND "eastern"[All Fields]) OR
33 "eastern africa"[All Fields] OR ("east"[All Fields] AND "africa"[All Fields]) OR "east
34 africa"[All Fields])) AND (((((((((((((((("epidemiology"[Subheading] OR
35 "epidemiology"[All Fields] OR "surveillance"[All Fields] OR "epidemiology"[MeSH
36 Terms] OR "surveillance"[All Fields]) OR (("epidemiology"[Subheading] OR
37 "epidemiology"[All Fields] OR "surveillance"[All Fields] OR "epidemiology"[MeSH
38 Terms] OR "surveillance"[All Fields]) AND systems[All Fields])) OR
39 ("epidemiology"[Subheading] OR "epidemiology"[All Fields] OR "surveillance"[All
40 Fields] OR "epidemiology"[MeSH Terms] OR "surveillance"[All Fields]) AND types[All
41 Fields])) OR sentinel[All Fields]) OR ("virology"[MeSH Terms] OR "virology"[All
42 Fields] OR "virologic"[All Fields])) OR infrastructure[All Fields]) OR
43 ("mortality"[Subheading] OR "mortality"[All Fields] OR "mortality"[MeSH Terms])) OR
44 ("epidemiology"[Subheading] OR "epidemiology"[All Fields] OR "morbidity"[All Fields]
45 OR "morbidity"[MeSH Terms])) OR (pyramid[All Fields] AND severity[All Fields])) OR
46 ("risk factors"[MeSH Terms] OR ("risk"[All Fields] AND "factors"[All Fields]) OR "risk
47 factors"[All Fields] OR ("risk"[All Fields] AND "factor"[All Fields]) OR "risk factor"[All
48 Fields]) AND ("analysis"[Subheading] OR "analysis"[All Fields] OR "determination"[All
49 Fields])) OR (spread[All Fields] AND ("disease"[MeSH Terms] OR "disease"[All
50 Fields])) OR ("virology"[MeSH Terms] OR "virology"[All Fields] OR "viral"[All
51 Fields])) OR ("virology"[MeSH Terms] OR "virology"[All Fields] OR "viral"[All
52 Fields])) OR ("virology"[MeSH Terms] OR "virology"[All Fields] OR "viral"[All
53 Fields])) OR ("virology"[MeSH Terms] OR "virology"[All Fields] OR "viral"[All
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59 Fields])) OR ("virology"[MeSH Terms] OR "virology"[All Fields] OR "viral"[All
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Fields]) AND ("ethnology"[Subheading] OR "ethnology"[All Fields] OR "culture"[All Fields] OR "culture"[MeSH Terms])) OR (("laboratories"[MeSH Terms] OR "laboratories"[All Fields] OR "laboratory"[All Fields]) AND ("isolation and purification"[Subheading] OR ("isolation"[All Fields] AND "purification"[All Fields]) OR "isolation and purification"[All Fields] OR "isolation"[All Fields])) OR (("death"[MeSH Terms] OR "death"[All Fields]) AND attributable[All Fields]) OR (("laboratories"[MeSH Terms] OR "laboratories"[All Fields] OR "laboratory"[All Fields]) AND confirmed[All Fields]) OR ("hospitalisation"[All Fields] OR "hospitalization"[MeSH Terms] OR "hospitalization"[All Fields]) OR admission[All Fields] OR ("outpatients"[MeSH Terms] OR "outpatients"[All Fields])) AND (((((seasonal[All Fields] OR ("pandemics"[MeSH Terms] OR "pandemics"[All Fields] OR "pandemic"[All Fields])) OR ("influenza, human"[MeSH Terms] OR ("influenza"[All Fields] AND "human"[All Fields]) OR "human influenza"[All Fields] OR "influenza"[All Fields])) OR ("influenza, human"[MeSH Terms] OR ("influenza"[All Fields] AND "human"[All Fields]) OR "human influenza"[All Fields] OR "influenza"[All Fields]) AND like[All Fields] AND illness[All Fields])) OR (severe[All Fields] AND acute[All Fields] AND ("respiratory tract infections"[MeSH Terms] OR ("respiratory"[All Fields] AND "tract"[All Fields] AND "infections"[All Fields]) OR "respiratory tract infections"[All Fields] OR ("respiratory"[All Fields] AND "infections"[All Fields]) OR "respiratory infections"[All Fields])) OR SARI[All Fields] OR ILI[All Fields])) AND (((serfling[All Fields] AND like[All Fields] AND cyclical[All Fields] AND ("regression (psychology)"[MeSH Terms] OR ("regression"[All Fields] AND "(psychology)"[All Fields]) OR "regression (psychology)"[All Fields] OR "regression"[All Fields]) AND ("Model Driven Eng Lang Syst"[Journal] OR "models"[All Fields])) OR (("moclobemide"[MeSH Terms] OR "moclobemide"[All Fields] OR "arima"[All Fields]) AND ("Model Driven Eng Lang Syst"[Journal] OR "models"[All Fields])) OR ("transmission"[Subheading] OR "transmission"[All Fields]) OR (cyclinic[All Fields] AND seasonal[All Fields] AND patterns[All Fields]))

Table 2: Evaluation checklist

Category	Criteria	1	2	3	4	5	NA
Stakeholders	Describe persons or organizations who will utilize the data gathered by the surveillance system.						
Description of the system	Describe the importance of the public health problem under surveillance						

	Explain the reason/purpose behind collecting data, and how the data is intended to be used.						
	Describe resources required to operate the system.						
Evaluation design	Describe the specific purpose of the evaluation . Propose uses of the evaluation results. Include the specific questions that the evaluation answered.						
Credible evidence	Describe usefulness of the information generated by analyzing data.						
	Assess surveillance system attributes in terms of:						
	Simplicity						
	Flexibility						
	Data quality						
	Acceptability						
	Sensitivity						
	Predictive value positive						
	Representativeness						
	Timeliness						
	Stability						
Conclusions and Recommendations	Present conclusions based on evaluation results. Propose appropriate and applicable recommendations to improve the system or discontinue its operation						
Lessons learned	Describe how lessons learned will be communicated to those who need to know						

Table 3: Scoring sheet

Points	Description
5 = excellent	The element is present, consistent with the standard described in the instructions and provided in the classroom, and is of a remarkable/outstanding quality.
4 = good	The element is present and consistent with the standard described in the instructions and provided in the classroom.
3 = satisfactory	The element is present and may be used even though it may not completely follow the standard described in the instructions and provided in the classroom
2 = poor	The element is present but flawed or of poor quality.
1 = absent	The element is absent from the report.
NA = not applicable	The element is not relevant to this report.

PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

Section and topic	Item No	Checklist item	Information reported	Page number
ADMINISTRATIVE INFORMATION				
Title:				
Identification	1a	Identify the report as a protocol of a systematic review	Yes	1
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	NA	
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	Yes	2
Authors:				
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	Yes	1
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	Yes	13
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	Yes	9
Support:				
Sources	5a	Indicate sources of financial or other support for the review	NA	
Sponsor	5b	Provide name for the review funder and/or sponsor	NA	
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	NA	
INTRODUCTION				
Rationale	6	Describe the rationale for the review in the context of what is already known	Yes	4-5
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	Yes	6
METHODS				
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	Yes	6
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	Yes	8-9
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that	Yes	Table 1: 16-17

		it could be repeated		
Study records:				
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	Yes	10
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	Yes	9-10
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	Yes	10
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	Yes	7
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	Yes	7-10
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	Yes	10-11
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	Yes	11
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2 , Kendall's τ)	Yes	11
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	Na	
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	NA	
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	NA	
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	NA	