Proposed working definition of an active case of influenza: Research Report 2

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Abstract

Background: NHS organisations lack a consistent operational definition of an “active case” of influenza. Analysis of 161 Freedom of Information responses from NHS organisations across the United Kingdom identified substantial heterogeneity in case definitions and widespread absence of reproducible criteria. Under the prespecified classification, only 2 responses were operationally adequate, while 159 of 161 (98.8%) failed to meet this standard. None incorporated all four evidential domains proposed in this framework: clinical illness, temporal relevance, influenza-specific laboratory evidence, and viral burden or activity.

Aim: To propose a working definition of active influenza suitable for NHS Trust clinical, surveillance, and analytical use, derived from the deficiencies identified in current practice.

Framework: The proposed approach distinguishes laboratory detection of influenza from evidence of current active disease. Classification is based on four complementary domains: (1) a current influenza-compatible acute clinical illness; (2) a defined temporal relationship between symptom onset, specimen collection, and ongoing illness; (3) influenza-specific detection using a validated assay; and (4) evidence of viral burden or activity, where technically available and appropriately validated. Molecular measures such as Ct/Cq/Cn or quantitative viral load should be interpreted in the context of assay platform, specimen type, sampling quality, and timing rather than through a universal Ct threshold. Serial measurements may reduce uncertainty concerning changes in viral burden but do not, in themselves, establish infectiousness.

Implications: The framework provides a reproducible distinction between suspected active influenza, laboratory-confirmed influenza infection, an active influenza case, and potentially infectious influenza. It also proposes a minimum reporting dataset that incorporates clinical features, symptom onset, specimen information, influenza-specific results, viral burden measures where available, serial trends, clinical status, and assigned case state. The framework is an analytical working definition derived from an FOI dataset rather than a consensus guideline, and influenza-specific validation of viral-burden measures, thresholds, and sampling schedules remains necessary.

Working definition for NHS Trust clinical, surveillance and analytical use

An active case of influenza is an individual with a current clinically compatible acute illness, occurring within a defined temporal relationship to symptom onset, in whom influenza virus has been specifically detected and the laboratory result provides evidence of an appreciable current viral burden. For molecular assays, viral burden should, where technically available and validated for the assay, be assessed using the

quantitative or semiquantitative output of the test (for example, Ct/Cq/Cn or viral load measurement) and interpreted in conjunction with symptom onset, clinical course, specimen type, and assay characteristics.

Rationale

In this national Freedom of Information analysis of 161 responses from NHS organisations across England, Scotland, Wales and Northern Ireland, we found substantial heterogeneity in how an “active case” of influenza was defined and, more importantly, substantial absence of an explicit operational definition. [1]

Under the original protocol classification, only 2 responses were classified as operationally adequate, 30 (19%) as partially adequate, 102 (63%) as methodologically unsound, and 27 (17%) as non-responsive or with information not held. Thus, 159 of 161 responses (98.8%) did not meet the prespecified operationally adequate category.

The secondary analysis clarified this finding, revealing variations in four evidential domains: clinical criteria, temporal relevance, influenza-specific laboratory evidence, and viral burden indications. Only two organisations included a case-level Ct threshold. Meanwhile, 26 responses combined clinical criteria, temporal information, and laboratory confirmation without specifying viral burden. Fifty-two provided mostly qualitative definitions, 71 lacked reproducible operational definitions, and 10 were unclear or non-responsive. Notably, none of the 161 responses included all four elements of the proposed evidential framework simultaneously.

These findings suggest that the principal methodological problem is not a lack of access to molecular diagnostic technology. Rather, it is the absence of a consistent conceptual and operational link between clinical illness, timing of illness, laboratory detection and evidence of ongoing viral activity. The latter is of crucial importance as an increasing viral load is suggestive of viral replication, i.e. the presence of a replication competent virus.

The four-domain framework

Domain	Minimum information	Operational interpretation	Common failure in Trust responses
1. Clinical	Current influenza-compatible acute illness/signs and symptoms.	Defines the clinical syndrome to which the laboratory result relates.	Symptoms absent; or symptoms listed without being incorporated into the case definition.
2. Temporal	Date/period of symptom onset and evidence that illness is ongoing or within a defined clinically relevant period.	Makes “active” a time-dependent construct rather than a historical positive test.	No onset date, no currentness criterion, or no rule for when a case ceases to be active.
3. Aetiological	Influenza A/B detected by a validated influenza-specific assay, with specimen and platform recorded where possible.	Establishes influenza-specific laboratory evidence.	“PCR positive” is treated as a complete case definition with little clinical or temporal context.
4. Viral burden/activity	Ct/Cq/Cn, quantitative viral load, serial molecular measurements, or	Adds information about the amount/direction of detectable	Qualitative positivity alone is often based on a single

[1] What is influenza? NHS Trust definitions in response to Freedom of Information Requests: research report 1. Trust the Evidence.September 2026 https://ora.ox.ac.uk/objects/uuid:61b0d300-60ea-4f80-b7dd-4eae4e695f09

Domain	Minimum information	Operational interpretation	Common failure in Trust responses
	validated evidence of replication competence where available.	virus and helps contextualise activity/infectious potential.	observation or on a Ct threshold used without assay-specific validation/context.

Proposed operational rule for NHS Trusts

For routine analytical use, an NHS Trust should report the following information for every suspected or laboratory-confirmed active influenza case:

- **Clinical syndrome:** Record the acute symptoms/signs that led to influenza being suspected.
- **Timing:** Record symptom onset (or best estimate), the date of specimen collection, and whether symptoms are currently present.
- **Influenza detection:** Record influenza A/B result, specimen type, assay/platform, and whether the result is qualitative or quantitative/semiquantitative.
- **Viral burden:** Where the assay provides it, record Ct/Cq/Cn or another validated viral-load measure. For serial testing, record the direction of change using the same platform where feasible.
- **Interpretation:** State explicitly whether the individual is being classified as a suspected active case, laboratory-confirmed active case, or merely laboratory-positive with insufficient information to determine activity.

Recommended case states

Case state	Suggested definition	What it does not establish
Suspected active influenza	Current compatible acute illness within the defined temporal window, with influenza suspected clinically.	Does not establish influenza aetiology.
Laboratory-confirmed influenza infection	Influenza-specific assay positive in a clinically relevant specimen.	A positive qualitative molecular result alone does not establish viral viability, infectiousness, or necessarily current biological activity.
Active influenza case	Current compatible illness + defined temporality + influenza-specific detection + viral-burden/activity evidence where technically available and validated.	Does not imply a universal Ct threshold or prove infectiousness from Ct alone. Serial Cts narrow the residual uncertainty
Potentially infectious influenza	Active case plus clinical/temporal and virological evidence indicating plausible current transmissibility; culture or other validated replication-competence evidence where definitive proof is required.	Should not be inferred from a single qualitative PCR result or a universal Ct cut-off. Serial Cts narrow the residual uncertainty

How to use Ct or viral-load information

Ct/Cq/Cn should be treated as semiquantitative or quantitative measures, with interpretation depending on the assay platform, target, specimen, sampling quality, and timing. A lower Ct generally indicates more target nucleic acid in the tested specimen; however, Ct values are not directly interchangeable across platforms and should not be used as a universal influenza threshold without assay-specific validation.

Serial measurements are preferable when the purpose is to assess changing viral burden. A falling Ct may be compatible with increasing viral burden and a rising Ct with declining burden, but these trajectories remain proxies rather than direct measures of infectiousness. Viral culture or another validated replication-competence method provides a different level of evidence when the specific question is whether replication-competent virus is present.

Important caution: the cited Ct evidence is principally from SARS-CoV-2, not influenza. It supports the methodological principle that viral burden and time interact with culture positivity, but it does not establish a universal influenza Ct cut-off. The working definition therefore requires consideration/measurement of viral burden where available, rather than mandating a Ct threshold.

Proposed minimum reporting dataset

Field	Minimum entry
Symptoms/signs	At least the clinical features supporting influenza suspicion.
Symptom onset	Calendar date or best estimate; note unknown date explicitly.
Specimen date/type	Date and respiratory specimen type.
Influenza result	A/B, detected/not detected, and assay/platform.
Ct/Cq/Cn or viral load	Value and units where available; retain assay/platform.
Serial trend	Previous value(s) and direction of change where serial testing occurs.
Clinical status	Ongoing/resolved; inpatient/ICU status where relevant.
Case state	Suspected active / laboratory-confirmed / active / potentially infectious / indeterminate.

Relationship to the NHS Trust FOI findings

The proposed framework is directly informed by the 161 Trust responses. None supplied all four domains. Two responses used a case-level Ct criterion; 26 combined clinical, temporal, and laboratory criteria without a reported viral burden measure; 52 were predominantly qualitative, laboratory-defined responses; and 71 were non-operational or insufficiently specified. The analysis therefore identified a gap between routine laboratory detection and a fully specified operational concept of an active case.

Limitations and validation requirements

- First, the framework is an analytical working definition derived from an FOI dataset, not a consensus guideline.
- Second, the use of viral burden as an evidence domain is justified conceptually and by wider respiratory-virus evidence, but the optimal influenza measure, threshold and sampling schedule require influenza-specific validation.
- Third, Ct values are assay-specific and affected by specimen collection, transport, target gene, and laboratory methods; values should therefore be interpreted within the context of the originating assay and laboratory.
- Fourth, viral burden should not be treated as synonymous with infectiousness. Where the specific question is replication competence, viral culture or another validated viability method remains the more direct evidential approach.
- Finally, immune status and vaccination status, antiviral treatment, disease severity, and host factors may influence the relationship between detectable viral burden and infectious potential; these should be considered when the definition is used in infection-control decisions.

References and evidence base

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Tom Jefferson, Carl Heneghan: What Is Influenza? NHS Trust Definitions in Response to Freedom of Information Requests. Trust the Evidence Publications: Research Report 1: 10th September 2026. https://trusttheevidence.substack.com/p/trust-the-evidence-publications-research

Practical NHS Trust implementation checklist

Element	Required reporting field	Status
Clinical syndrome	Acute compatible symptoms/signs; document whether symptoms are ongoing	☐
Temporal relationship	Symptom-onset date or best estimate; specimen date	☐
Influenza detection	Influenza A/B; specimen; assay/platform used; qualitative vs quantitative	☐

Element	Required reporting field	Status
Viral burden	Ct/Cq/Cn or validated viral load where available; serial trend if available	☐
Interpretation	Case state assigned and rationale recorded	☐

Suggested implementation statement:

The Trust records clinical features, symptom timing, influenza-specific test results, and quantitative/semiquantitative viral burden information, where available.

Qualitative molecular positivity alone is reported as influenza nucleic acid detection and, without clinical and temporal context, is not assumed to establish active or infectious influenza.