

Evaluating SARS-CoV-2 Vaccine Breakthrough Surveillance in WA

Amanda Dodd

A thesis
submitted in partial fulfillment of the
requirements for the degree of

Master of Public Health

University of Washington
2021

Committee:

Clarence Spigner

Charla A. DeBolt

Program Authorized to Offer Degree:

Department of Health Services

©Copyright 2021
Amanda Dodd

University of Washington

Abstract

Evaluating SARS-CoV-2 Vaccine Breakthrough Surveillance in WA

Amanda Dodd

Chair of the Supervisory Committee:

Clarence Spigner

Department of Health Services

Context: Severe acute respiratory coronavirus 2 (SARS-CoV-2) vaccine breakthrough surveillance is a novel surveillance program implemented in Washington. The surveillance system monitors cases of COVID-19 among those fully immunized with COVID vaccine. As of June 2021, the Washington State Department of Health has been preparing to transition SARS-CoV-2 vaccine breakthrough case identification methods from relying only on passive reporting of potential cases to inclusion of active case ascertainment facilitated by linkage of the Washington Disease Reporting Database (WDRS) and the Washington Immunization Information System (WAIIS). Process evaluation is needed to inform surveillance program protocols and optimize use of resources.

Objectives: Evaluate a proposed new surveillance method for SARS-CoV-2 vaccine breakthrough. Assess completeness of reporting under passive case reporting and compare active case ascertainment through data linkage.

Evaluation Methods: This evaluation assessed attributes defined in Centers for Disease Control and Prevention guidelines for evaluating public health surveillance systems. Outcome measures of interest are both qualitative and quantitative. Primary measures of interest were sensitivity and positive predictive value. Secondary measures of interest were system flexibility, simplicity, data quality, acceptability, representativeness, and timeliness. Assessment was informed through data collection, direct observation, and surveillance system participant feedback.

Analysis: Completeness of case identification was evaluated for both passive surveillance and active case ascertainment methodologies. The number of passively reported breakthrough cases in the first three months of surveillance was compared to the number of cases identified by linking positive COVID-19 cases to COVID-19 immunization records in the same time period. The passively detected cases that were not identified by data linkage were further examined to characterize the limitations of database linkage as an active case ascertainment methodology.

Results: Passive surveillance is reasonably sensitive, detecting a net 62.3% of the number of vaccine breakthrough cases that were identified through data linkage in the time period of interest. Active case ascertainment has much higher sensitivity, estimated at 90.8% of total cases identified by combined methods. Addition of active case ascertainment is estimated to increase overall case identification by 52%.

Conclusions: The system is flexible, acceptable to reporting organizations, and provides timely output. System simplicity is marginal but will be improved with the integration of active case ascertainment. Representativeness may be impacted by reliance on active case ascertainment only; cases whose immunization records are stored outside of WA IIS are only detected in passive surveillance. This limitation may be addressed by maintaining a passive reporting component in the surveillance system and by improving data sharing and collaboration between

public health partners. The surveillance program is effective in meeting its objectives but increases in breakthrough incidence pose a threat to system stability. Swift adoption of active case ascertainment is recommended.

Evaluating SARS-CoV-2 Vaccine Breakthrough Surveillance in Washington

1. Introduction

1.1. Background

1.2. Purpose and Objectives

1.3. SARS-CoV-2 Vaccine Breakthrough Surveillance in Washington

1.3.1. Surveillance System Objectives

1.3.2. Surveillance Methods

2. Evaluation Methods

2.1. Main Outcome Measures

2.2. Secondary Outcome Measures: Surveillance System Attributes

3. Analysis

4. Results

4.1. Surveillance Methods Analysis: Passive vs. Active Surveillance

4.1.1. Summary Data

4.1.2. Sensitivity and Percent Difference

4.1.3. Predictive Positive Value of Passive Surveillance

4.1.4. Limitations of Active Case Ascertainment

4.2. Evaluation of Surveillance System Attributes

4.2.1. Flexibility

4.2.2. Simplicity

4.2.3. Data Quality

4.2.4. Acceptability

4.2.5. Sensitivity and Positive Predictive Value

4.2.6. Representativeness

4.2.7. Timeliness

5. Discussion

5.1. Strengths

5.2. Recommendations

5.3. Implications for Public Health

Introduction

Background

Public health surveillance supports understanding of disease trends, assists with disease control and prevention, and informs public and health care policy decisions. The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic brought strain and devastation to nearly all facets of global life and has tested the limits of public health systems. Local, state, and territorial jurisdictions across the United States and the world continue to work toward community mitigation of SARS-CoV-2 transmission.

The introduction of COVID-19 vaccines brought hope to the global pandemic fight, but also new surveillance challenges for public health. A new surveillance need emerged with the introduction of vaccines: monitoring for breakthrough infections among those fully immunized against COVID-19. Monitoring for breakthrough infections among those fully immunized against COVID-19 is important because it allows for enhanced detection of signals related to vaccine effectiveness and provides timely data to inform public health policies as well as personal health behavior decisions. The Centers for Disease Control and Prevention (CDC) defines SARS-CoV-2 Vaccine Breakthrough in the following way:

“For the purposes of this surveillance, a vaccine breakthrough infection is defined as the detection of SARS-CoV-2 RNA or antigen in a respiratory specimen collected from a person $\geq$ 14 days after they have completed all recommended doses of FDA-authorized COVID-19 vaccine”

CDC SARS-CoV-2 Vaccine Breakthrough Case Definition

SARS-CoV-2 vaccine breakthrough is a novel surveillance program in Washington State, established February 1, 2021. Pre-planning began in late 2020, just prior to EUA approval and release of COVID-19 vaccines in the United States. Based upon the CDC case definition and the dates vaccines were first distributed in Washington, the first eligible day for someone to be considered a breakthrough case in Washington was January 14, 2021. The Washington State Department of Health (WA DOH) received the first report of vaccine breakthrough on February 1, 2021, regarding a patient who had a SARS-CoV-2 positive specimen collected in late January and a complete COVID vaccine series that was initiated in December of 2020.

Purpose and Objectives

As a new and novel surveillance program, early evaluation is needed to inform appropriate protocols and adjust priorities if indicated. Process evaluation is needed to determine whether the surveillance program is meeting its stated objectives and to identify ways to optimize use of resources. The purpose of this paper is to provide an evaluation of WA DOH's novel SARS-CoV-2 Vaccine Breakthrough surveillance program, share results of a methods analysis to inform future surveillance protocols and objectives, and make recommendations to improve overall surveillance program performance.

SARS-CoV-2 Vaccine Breakthrough Surveillance in Washington

Surveillance System Objectives

Washington State Department of Health's objectives for surveillance of SARS-CoV-2 vaccine breakthrough, as stated upon initiation of the program, are listed below.

Objectives of SARS-CoV-2 Vaccine Breakthrough Case Surveillance

- Assure the availability of a specimen for whole genome sequencing
 - Is breakthrough due to known variants of concern?
 - Will breakthrough follow up allow us to identify new variants?
- Assure that vaccination doses received by breakthrough cases are documented
 - Lot number
 - Administering facility
- Standardize surveillance to allow detection of signals and trends related to vaccine effectiveness

Real-time surveillance of SARS-CoV-2 vaccine breakthrough provides the opportunity to perform whole genome sequencing on eligible positive SARS-CoV-2 specimens to determine which lineages are associated with breakthrough infections and allows for earlier detection of emerging viral variants associated with breakthrough.

Scrupulous collection of vaccine data specifics, such as vaccine lot number and administering facility, allows for potential identification of vaccine mishandling events and enhances the confidence and reliability of publicly reported vaccine breakthrough metrics.

Finally, comprehensive data collection and reporting on SARS-CoV-2 vaccine breakthrough enhances the local and national ability to detect signals and early trends related to vaccine effectiveness and may inform future adjustments to formulations or to recommendations for use of COVID-19 vaccines.

Surveillance Methods

WA DOH Breakthrough Surveillance Process and Challenges

The Washington State Department of Health received reports of suspected vaccine breakthrough beginning February 1, 2021. Data elements collected include patient-level data on SARS-CoV-2 testing results and COVID-19 vaccine records. Reported cases are reviewed for classification, and for cases meeting the breakthrough case definition, clinical specimens are obtained whenever possible for whole-genome sequencing. The primary output of the surveillance system is a weekly report that summarizes vaccine breakthrough case volume, clinical and demographic information on vaccine breakthrough cases, and aggregate data on viral lineages detected in whole-genome sequencing for vaccine breakthrough cases.

Other data elements used in vaccine breakthrough reporting include patient county of residence, age, race/ethnicity, underlying health conditions or other risk factors for COVID-19, and markers of disease severity such as hospitalization and deaths. These data elements are obtained from the Washington Disease Reporting System (WDRS), which houses all notifiable conditions case data collected during disease investigation.

In this paper, passive surveillance refers to the reporting of suspected vaccine breakthrough cases by local and Tribal health jurisdictions (as well as other reporting entities, such as the Department of Veterans Affairs, the Department of Corrections, etc.) to WA DOH for inclusion in statewide vaccine breakthrough surveillance. Active surveillance refers to an aggregate case ascertainment process that matches COVID-19 cases reported via the Washington Disease Reporting System (WDRS) to administered COVID-19 vaccine doses recorded in the Washington Immunization Information System (WAIIS).

- Passive surveillance identifies potential vaccine breakthrough cases, and immunization status must be verified with appropriate documentation (e.g. WAIIS record, CDC

Vaccine Card, or another formal source of documentation that includes vaccine lot numbers and administering facility) before breakthrough status is confirmed.

- Active case ascertainment identifies true events of vaccine breakthrough only, since the identification process inherently relies on documented COVID-19 vaccine records to ascertain cases.

SARS-CoV-2 Vaccine Breakthrough surveillance was initiated as a passive surveillance program, with local jurisdictions and other public health partners reporting cases of suspected vaccine breakthrough to the Department of Health. WA DOH received passive reports beginning February 2021 and continues to receive reports from local health jurisdictions (LHJs), Tribal health, clinical laboratories, and other agencies, organizations and partners (e.g. Department of Corrections, VA Healthcare Systems, etc.). As the segment of the state population susceptible to SARS-CoV-2 Vaccine Breakthrough grew with expanded vaccine coverage, the reporting volume of breakthrough cases correspondingly increased. The reporting burden of a passive surveillance system becomes exponentially challenging with spikes in case incidence. The estimated burden of breakthrough reporting in May 2021 was approximately 5 times the number of reports received during March 2021, presenting resource-limited reporting jurisdictions with potential barriers to accurate representation and increasing the likelihood of reporting bias in statewide metrics.

The Washington State Department of Health sought to alleviate reporting burden and reduce reporting bias through development of automated active case ascertainment methods for SARS-CoV-2 Vaccine Breakthrough starting in March 2021. A challenge faced by public health in Washington is the lack of interoperability between the WA state immunization registry and the

state's notifiable conditions reporting database. Though both are maintained and operated by the State Department of Health, the Washington Immunization Information System (WAIIS) and the Washington Disease Reporting System (WDRS) are distinct, non-linked databases maintained by separate divisions within the Department of Health. Implementing a methodology for active case ascertainment in Washington requires data linkage between these two systems to match positive COVID labs with COVID vaccine records; extensive work to develop and validate this linkage was required and has been conducted.

The data linkage used to actively ascertain cases enhances the surveillance system's ability to meet its objectives by systematically identifying cases and improving overall detection of vaccine breakthrough. The data linkage also improves program efficiency. Despite the benefits offered by active case ascertainment, potential limitations and barriers to complete reporting remain. These potential limitations are described below.

The WA DOH Vaccine Breakthrough team hypothesized, based on anecdotal experience of receiving passive case reports of vaccine breakthrough, that segments of the state population may be at risk of exclusion from active case ascertainment. Federally allocated doses are required to be documented in CDC's Vaccine Administration Management System (VAMS); as sovereign governments, Tribal nations received allocations of COVID vaccine directly from the federal government rather than through state allocations. As such, many Tribal members' COVID vaccine records are recorded in VAMS and not in WA IIS.

Federal agencies such as the Department of Defense and the Department of Veterans Affairs similarly have vaccine records recorded external to WA IIS. More than 600,000 active-duty military and veterans live in Washington; family members and civilian military workers may also be administered COVID vaccines on base. Reporting of SARS-CoV-2 vaccine

breakthrough among populations not represented in the WA IIS has been made possible through the establishment of community partnerships and case-level data sharing arrangements with the WA DOH Vaccine Breakthrough team. This is predicated on the diligence, dedication, and bandwidth of clinicians and laboratorians who serve those populations and provide passive reports of vaccine breakthrough. Community partnerships established in passive surveillance have been fundamental to ensuring that the objectives of the surveillance program are met, since community partner participation in the reporting process is needed for case identification.

Another illustration of the challenges associated with vaccine data in Washington State relates to recently arrived residents and residents of counties that border other states. Many residents of Vancouver in Clark County, WA, for example, work or receive health care in neighboring Multnomah County, OR, and have COVID vaccine records stored in an out of state immunizations registry. Although data sharing does occur between states, and the use of CDC Vaccine Cards can improve the likelihood of receiving documentation of COVID vaccine for patients with vaccine records absent from WA IIS, the possibility of automation of case identification through data linkage or systematic case ascertainment is limited in this context.

WA DOH recognized the potential limitations of data linkage, as described above, and sought to quantify and fully characterize these limitations. These limitations may hinder the program's ability to meet its objective "to standardize surveillance to allow detection of signals and trends related to vaccine effectiveness." Additionally, as vaccine breakthrough case identification is a precedent to locating and retrieving specimens from vaccine breakthrough patients for whole-genome sequencing, deficits in case identification may hinder the ability of the surveillance program to meet its primary objective, "to assure the availability of a specimen for whole genome sequencing."

An evaluation of active case ascertainment methodologies and passive case surveillance methodologies was performed; the methods and results are presented in the following sections.

Evaluation Methods

Main Outcome Measures

The objectives of the surveillance program cannot be met without a strong ability to detect breakthrough cases. Therefore, the primary outcome of interest in this evaluation is the effectiveness of case ascertainment, measured in terms of sensitivity, percent difference, and positive predictive value. This evaluation assesses completeness of case identification between passive surveillance and active case ascertainment methodologies. Breakthrough cases detected in passive surveillance that were not identified in active case ascertainment were further examined to identify potential deficits in case identification using active surveillance.

Completeness and accuracy of case identification is measured in the following ways:

- Sensitivity was assessed as the proportion of cases detected by the surveillance system. Both passive and active surveillance methods were assessed for sensitivity.
- Predictive positive value was assessed as the proportion of passively reported suspected breakthrough cases that truly met breakthrough criteria.

Secondary Outcome Measures: Surveillance System Attributes

Other measures of interest include attributes outlined by the CDC as essential attributes of disease surveillance systems. In addition to sensitivity and predictive value positive, the system was evaluated according to its flexibility, simplicity, data quality, acceptability,

representativeness, and timeliness. These attributes represent a surveillance program's ability to effectively and efficiently meet program objectives. Assessments were informed primarily by direct observation and surveillance system participant feedback

Using CDC guidelines for the evaluation of public health surveillance systems, system attributes were assessed as follows:

- Flexibility was assessed by determining how easily the surveillance system responds to participant needs (i.e. ease of case reporting)
- Simplicity was assessed by investigating the surveillance system's structure and ease of operation. Indicators of simplicity include the level of integration with other systems, the methods and time requirements of managing the data, and the amount of data and time required to discern and document that the vaccine breakthrough case occurred.
- Data quality was assessed based on the completeness and validity of the breakthrough case classifications assigned REDCap, which represents all passively received and manually reviewed reports of breakthrough in the time period of interest. The validity of the breakthrough classification data in REDCap was evaluated using the WDRS-WAIIIS linkage data as the gold standard.
- Acceptability was assessed in terms of the number and type of participating entities involved in breakthrough reporting and by participant feedback
- Representativeness of passive reporting and active case ascertainment was assessed by determining if the distribution of identified cases matches the expected distribution based on total cases identified in combined active and passive surveillance methodologies.
- Timeliness was assessed by the amount of time needed to generate reports, and the reporting lag reflected in reports.

Analysis

Surveillance System Methods Analysis: Passive vs. Active Surveillance

Completeness of case identification was evaluated for both passive surveillance and active case ascertainment methodologies. The number of passively reported breakthrough cases in the first three months of surveillance was compared to the number of cases identified by linking positive COVID-19 cases to COVID-19 immunization records in the same time period. Confirmed and probable breakthrough cases that were detected in passive surveillance but not identified in active case ascertainment through data linkage were examined more closely to identify potential limitations of active case ascertainment. These reasons were categorized into themes to characterize the core barriers to complete reporting using active case ascertainment.

All passively received reports of suspected vaccine breakthrough are maintained in a reporting database housed on the secure web application REDCap. The linkage process to actively identify vaccine breakthrough events has been thoroughly vetted, and a retrospective case identification was performed. The units of analysis are confirmed and probable cases of vaccine breakthrough. The time period of interest for this analysis is the first three full months of passive surveillance, February 1, 2021 – April 30, 2021, by case report date. This dataset was also restricted to cases with specimen collection dates of April 29, 2021 or earlier to replicate the estimated reporting lag for actively ascertained cases. The number of actively ascertained breakthrough cases identified by data linkage was compared against the reported breakthrough cases identified in passive surveillance.

Results

Surveillance System Methods Analysis: Passive vs. Active Surveillance

Comparison of aggregate active case ascertainment through data systems linkage to a passive surveillance system based on individual case reporting, February 1, 2021 – April 30, 2021

To inform preparations for the adoption of active case ascertainment and to identify potential issues and limitations, an analysis comparing case identification between active and passive case ascertainment methodologies was performed. The results of this methods analysis are displayed in Figure 1 and the summary data tables below.

Summary data

Suspected vaccine breakthrough reports received under passive surveillance through April 30, 2021 (specimen collection date 4/29/2021 or earlier)

Confirmed or probable breakthrough	841
Other	102
Suspected vaccine breakthrough cases	943
Ruled out (Not a breakthrough)	129
Total suspected vaccine breakthrough cases reported	1072

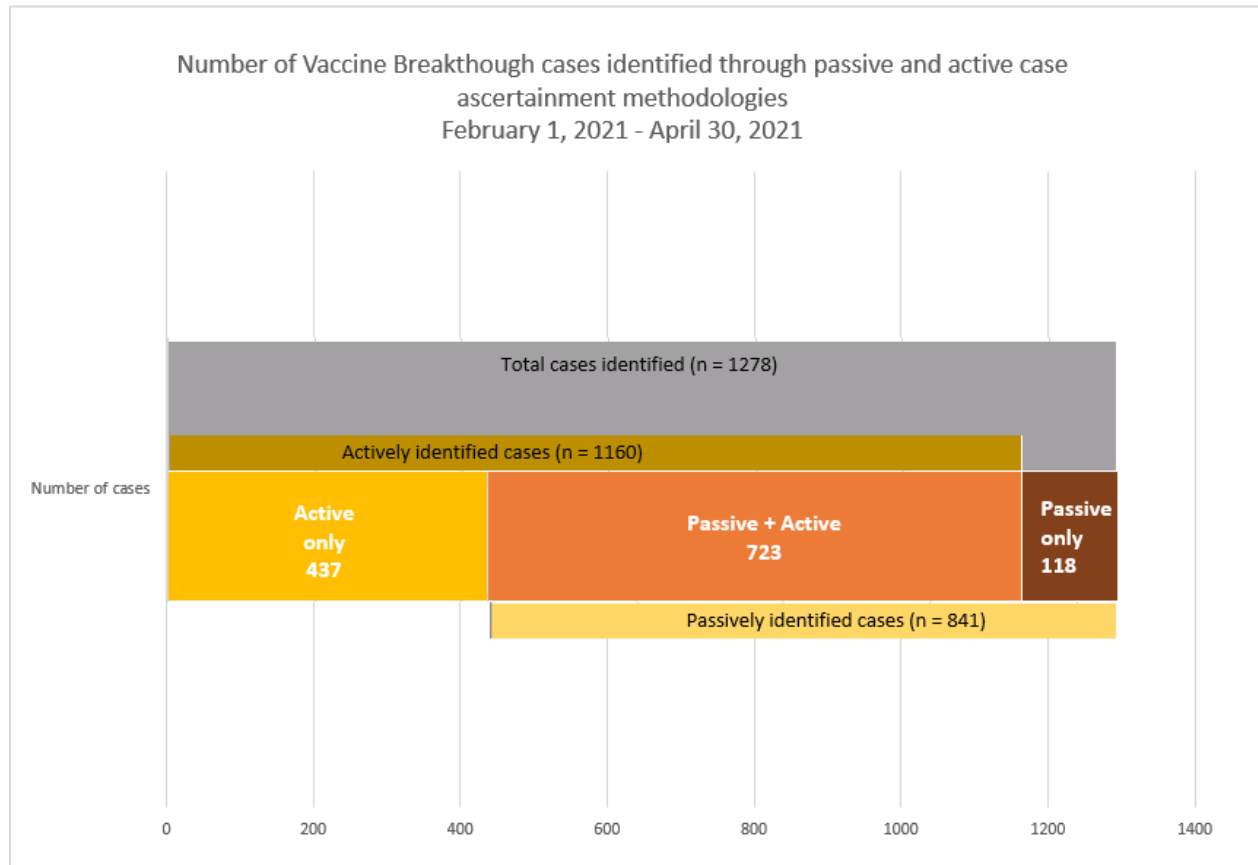
Suspected vaccine breakthrough cases identified in active case ascertainment (specimen collection date 4/29/2021 or earlier)

Confirmed or probable breakthrough	1161
Meets confirmed or probable breakthrough criteria but may represent persistent shedding	85
Total suspected vaccine breakthrough cases identified	1246

Confirmed and probable vaccine breakthrough cases identified through both methods	723
Confirmed and probable vaccine breakthrough cases identified by passive reporting only	118
Confirmed and probable vaccine breakthrough cases identified by data linkage only	437
Combined method total of active and passive case ascertainment	1278

Figure 1. Methods Analysis: Comparison of active and passive case ascertainment methodologies

Confirmed and probable SARS-CoV-2 Vaccine Breakthrough cases identified through passive and active case methodologies, Feb 1, 2021 – April 30, 2021



Sensitivity and Percent Difference. To estimate the sensitivity and percent difference of passive and active case ascertainment methodologies, the number of confirmed and probable cases identified through each methodology in the reporting period of interest was compared.

The results are shown in Table 1, Table 2 and Table 3 below.

Table 1. Methods Analysis: Evaluation of passive case reporting using active case ascertainment (through data linkage) as the gold standard

		Active case ascertainment		
		Matched	Not matched	Total
Passive case reporting	Matched	723	118	841
	Not matched	437		
	Total	1160		

Percent difference (PD) = $(841-1160)/1160 = -27.5\%$

Sensitivity = $723/1160 = 62.3\%$

Table 2. Methods Analysis: Evaluation of passive surveillance using combined methodologies (total cases identified in period of study) as the gold standard

		Combined methods		
		Matched	Not matched	Total
Passive case reporting	Matched	841	NA	NA
	Not matched	437		
	Total	1278		

Percent difference (PD) = $(841-1278)/1278 = -34.2\%$

Sensitivity = $841/1278 = 65.8\%$

Table 3. Methods Analysis: Evaluation of active case ascertainment (through data linkage) using combined methodologies (total cases identified in period of study) as the gold standard

		Combined methods		
		Matched	Not matched	Total
Active case ascertainment	Matched	1160	NA	NA
	Not matched	118		
	Total	1278		

Percent difference (PD) = $(1160-1278)/1278 = -9.2\%$

Sensitivity = $1160/1278 = 90.8\%$

Predictive Positive Value of passive surveillance. To calculate the predictive positive value of passive surveillance methods, the total number of confirmed and probable cases ascertained passively was calculated as a proportion of the total suspected vaccine breakthrough reports received in the period of interest. The estimated PPV of passive surveillance was 78.5% in the period of interest; 814 cases were identified as confirmed or probable breakthrough cases among 1072 total suspected vaccine breakthrough cases reported.

Limitations of Active Case Ascertainment: characteristics of confirmed and probable breakthrough cases not identified in active case ascertainment.

Table 4 summarizes the characteristics of the 118 confirmed and probable vaccine breakthrough cases identified by passive surveillance that were not identified in active case ascertainment methods. Of note, 11 out of 131 (8.4%) of passively reported cases classified as confirmed or

probable breakthrough that were not identified in active case ascertainment were identified as misclassification based on secondary review of vaccine data and patient identifiers, highlighting a need for strengthened data quality control. Additionally, 2 cases were missing COVID lab results in the Washington Disease Reporting System (WDRS). These 13 cases were excluded from this analysis and removed from the total number of confirmed and probable cases identified in passive surveillance only.

Table 4. Core characteristics of passively reported confirmed and probable breakthrough cases that were not identified in active case ascertainment methods.

		N	%
COVID vaccine doses not recorded in WA IIS registry ¹ (documented in alternative registry or database)		17	14.4%
• <i>Not a Washington resident</i>	7		
• <i>Tribal</i>	4		
• <i>VA</i>	3		
• <i>Naval</i>	2		
• <i>Department of Corrections</i>	1		
Missing or incomplete vaccine data in WA IIS ²		19	16.1%
Vaccine data may be absent from WA IIS repository ³		37	31.4%
Slight name or DOB discrepancies		45	38.1%
• <i>PHSKC identified via fuzzy matching</i> ⁴	9		
Total		118	

¹COVID vaccine records documented in alternative registry or database (e.g. Federal Vaccine Administration Management System (VAMS), Military Health, etc.)

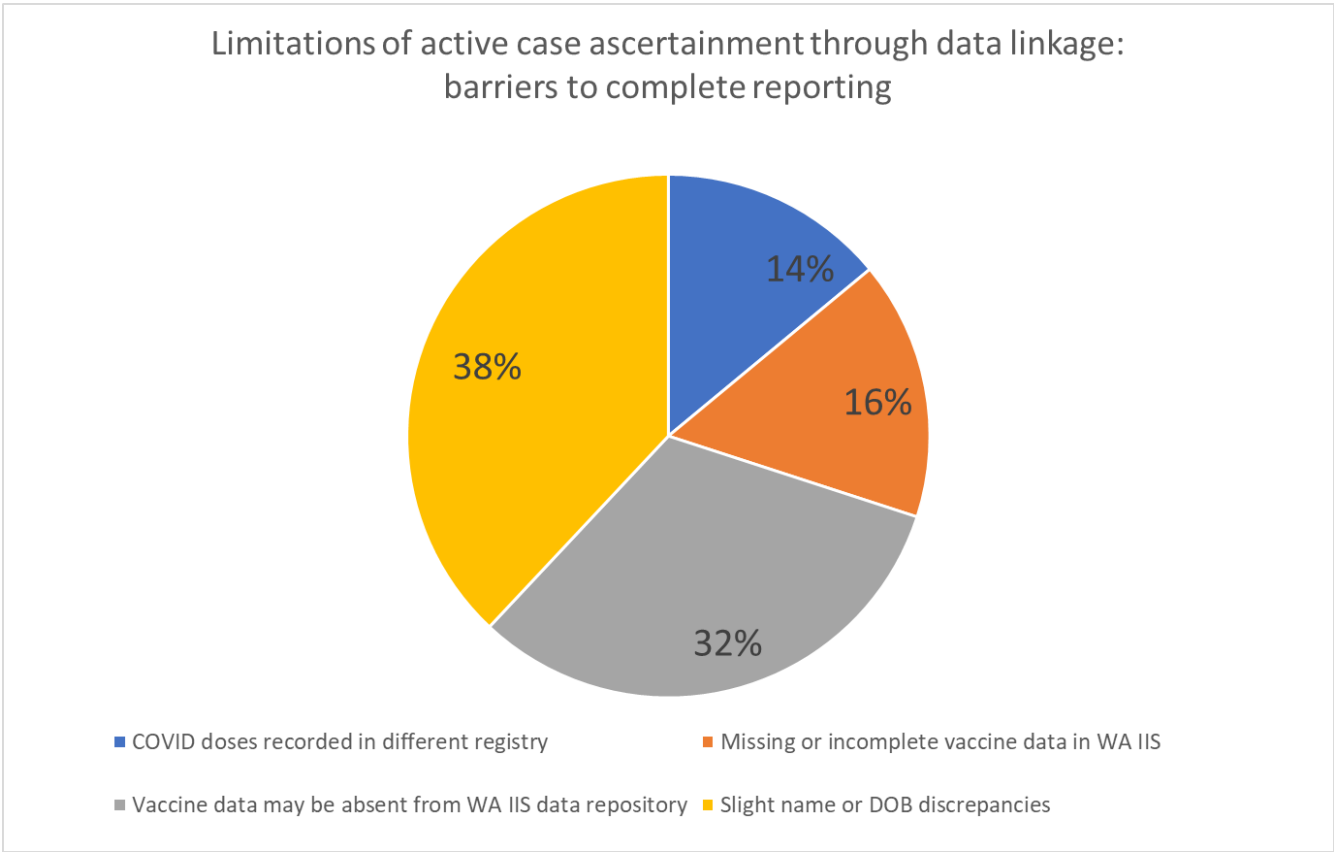
²Other valid sources of vaccine documentation include CDC Vaccine Card, medical records

³Case confirming vaccine information available in front-end of WA IIS but is absent in IIS data repository. The IIS COVID repository is the data source used in aggregate active case ascertainment

⁴Public Health – Seattle & King County employed data linkage to identify potential breakthrough cases prior to statewide implementation of WDRS – IIS data linkage. Their methods include fuzzy matching, which increases total potential matches identified but has a higher probability of “false positives”

Analysis of the limitations of active case ascertainment. Figure 2 depicts the core characteristics of passively reported confirmed and probable breakthrough cases that were not identified in active case ascertainment. Four fundamental limitations or barriers to complete reporting through active case ascertainment were identified.

Figure 2. Core characteristics of passively reported confirmed and probable breakthrough cases that were not identified in active case ascertainment methods.



Assessment of Surveillance System Attributes

Flexibility. The system is flexible, as it allows passive receipt of reports in single case format or in aggregate format and can receive reports from a broad and inclusive range of reporting entities. The system is prepared to receive both passive reports and actively ascertained reports.

Simplicity. System simplicity is marginal. Deduplication of reports received, manual data collection and case classification, and the maintenance and reconciliation of two separate databases (Vaccine Breakthrough REDCap project and the Washington Disease Reporting System) hinder program simplicity.

Data quality. The evaluation of passive vs. active case methodologies identified a need to allocate additional resources to data quality control. The overall proportion of misclassification identified in this review was 1.3% (11 of 841 total confirmed and probable cases identified in passive surveillance). Data quality may be adversely affected by increases in breakthrough incidence when manual review is needed to determine whether a case meets eligibility criteria. Automation of surveillance processes wherever possible is recommended. Automation through active case ascertainment will also improve data standardization and enhance process efficiencies related to specimen retrieval for whole genome sequencing.

Acceptability. Acceptability is high because SARS-CoV-2 breakthrough surveillance provides timely data that is highly relevant to the ongoing COVID-19 pandemic response. Reporting data related to SARS-CoV-2 is valuable, informs public health action and policy decisions, and is used by diverse audiences. 28 of Washington's 35 local health departments (80%) provided passive reports of vaccine breakthrough in the first three months of the surveillance period. This level of participation is considered very high given the lower incidence of vaccine breakthrough

in the time period analyzed. The total number of reporting entities and surveillance program participants exceeded this amount, since other public health partners contributed to vaccine breakthrough case reporting.

Sensitivity and Positive Predictive Value (PPV). Sensitivity and PPV of passive and active case ascertainment methodologies and their supporting calculations are discussed in the previous section. Sensitivity of passive case ascertainment is reasonably good, estimated at 62.3% (using data linkage/active case ascertainment as the means of comparison). PPV of passive reporting was moderately high in the time period analyzed, estimated at 78.5%. Sensitivity of active case ascertainment is excellent, estimated at 90.8% (using combined methodologies as the means of comparison).

It is estimated that the use of passive case surveillance methods only corresponds to a 27.5% deficit in the net number of cases identified compared to the use of active case ascertainment methodologies only. It is estimated that the use of active case ascertainment methodologies only would result in a 9.2% deficit in number of cases identified compared to the use of combined methodologies. Adoption of active case ascertainment is estimated to increase the volume of cases identified by 52% over the number of cases identified in passive surveillance.

Representativeness. Representativeness is good but can be improved. Local health jurisdictions in resource-limited areas may be disproportionately impacted by the burden of passive reporting, which may result in underrepresentation. Implementation of active case ascertainment will reduce this disparity. As previously discussed, representation in WA IIS data is limited for some Washington populations. This is a known limitation of active case ascertainment and can be partially addressed by maintaining a passive reporting component in the surveillance system.

Timeliness. The system timeliness is excellent. The primary system output is a report produced weekly that provides summary data on breakthrough cases reported through the end of the previous week and includes all available data on SARS-CoV-2 sequencing outcomes. Reporting has been automated and is easily generated. The timeliness of reporting supports the system objectives to monitor sequencing outcomes among vaccine breakthrough cases.

Discussion

Strengths

SARS-CoV-2 vaccine breakthrough surveillance in Washington is strong program that offers significant public health value. In a recent report from The Rockefeller Foundation, Washington state was identified as one among a small handful of states providing routine, granular data on vaccine breakthrough cases. Washington state is among the top contributors of SARS-CoV-2 sequencing data in the nation and has generated a valuable dataset for future analysis of vaccine effectiveness and the impacts of SARS-CoV-2 viral evolution over time.

Recommendations

To optimize use of resources and support continued production of high-quality output, the following recommendations are made:

- *Prioritize work on automation of surveillance processes.* SARS-CoV-2 vaccine breakthrough is a complex surveillance system that would benefit significantly from investment in identifying and developing efficiencies. Though the surveillance system is successful in meeting its stated objectives, marginal system stability poses a threat

to the system's ability to meet its objectives in the long term. The positive predictive value of passive case reporting suggests that the reporting criteria for passively reported breakthrough cases lacks specificity, resulting in lower program efficiency and increased resource needs for case investigations.

- *Strengthen community partnerships to minimize potential bias or equity concerns.* As noted in this report, distinct populations in Washington state are at risk of exclusion from breakthrough surveillance due to limited representation in WA IIS, the only vaccine data source currently used in active case ascertainment methods. Adoption of active case ascertainment methods raises the potential of bias in reporting and may result in inequitable distribution of state-funded SARS-CoV-2 vaccine breakthrough sequencing resources. SARS-CoV-2 vaccine breakthrough sequencing, the primary objective of the surveillance program, is not possible without adequate and representative case identification. With these considerations in mind, data sovereignty of Tribal Nations is also imperative to consider in program planning to address concerns of potential bias or inequities in statewide surveillance program implementation.
- *Allocate additional time and resources to Data QC.* Implementation of additional data quality checks are recommended. This analysis identified a nominal amount of misclassification in vaccine breakthrough classifications. Increases in breakthrough incidence may increase the risk of misclassification if manual processes are needed to support continued passive reporting. Continued evaluation of active case ascertainment methodologies is recommended; robust quality checks will be required for successful future integration of fuzzy-matching methodologies.

Implications for Public Health

National breakthrough surveillance changes. As of May 1, 2021, The Centers for Disease Control and Prevention transitioned from investigating all reported vaccine breakthrough cases to focus on identifying and investigating only hospitalized or fatal cases. The rationale behind this transition was to improve data quality and completeness regarding the cases of greatest clinical and public health significance.

CDC's change in breakthrough reporting policy has sparked debate among academics, clinicians, and public health practitioners. Though the burden of work is significant, the value of complete SARS-CoV-2 vaccine breakthrough surveillance data cannot be debated. There is rich opportunity presented in comprehensive ongoing surveillance of breakthrough and related SARS-CoV-2 sequencing efforts. Findings from this work may lead to enhanced detection of variants associated with vaccine escape, inform potential modifications or recommendations for COVID-19 vaccines, and ultimately help to end this devastating pandemic.

The reporting volume of SARS-CoV-2 vaccine breakthrough has grown exponentially in recent weeks beginning in mid-July, 2021. Nevertheless, Washington state continues to maintain comprehensive surveillance of SARS-CoV-2 vaccine breakthrough. This evaluation may inform adjustments to system operationalization to ensure system longevity and quality of output.

Acknowledgements

Surveillance of SARS-CoV-2 Vaccine Breakthrough in Washington State has been made possible by the hard work and dedication of public health partners across Washington state. Thank you to the LHJ, Tribal, clinical, and laboratory partners across Washington for the collaboration in these surveillance efforts.

I would like to thank Dr. Clarence Spigner of the University of Washington for his thoughtful suggestions in the development of this paper, and Charla (Chas) DeBolt for her guidance and leadership through the implementation of SARS-CoV-2 vaccine breakthrough surveillance in Washington state.

References

- Birhane, Meseret, et al. "COVID-19 Vaccine Breakthrough Infections Reported to CDC — United STATES, January 1–April 30, 2021." *MMWR. Morbidity and Mortality Weekly Report*, vol. 70, no. 21, 2021, pp. 792–793., doi:10.15585/mmwr.mm7021e3.
- Birkhead, G. S., Klompas, M., & Shah, N. R. (2015). Uses of Electronic Health Records for Public Health Surveillance to Advance Public Health. *Annual Review of Public Health*, 36(1), 345–359. <https://doi.org/10.1146/annurev-publhealth-031914-122747>
- Centers for Disease Control and Prevention. *COVID-19 Vaccine Breakthrough Case Investigation COVID-19 Vaccine Task Force Investigation Protocol*, www.cdc.gov/vaccines/covid-19/downloads/COVID-vaccine-breakthrough-case-investigations-Protocol.pdf. (Accessed June 21, 2021).
- Centers for Disease Control and Prevention. "COVID-19 Breakthrough Case Investigations and Reporting." *Centers for Disease Control and Prevention Vaccines & Immunizations*, 5 Aug. 2021, www.cdc.gov/vaccines/covid-19/health-departments/breakthrough-cases.html.
- Department of Health and Social Services. "Summary of COVID-19 Vaccine Breakthrough Cases - Alaska, February 1 through June 30, 2021." *State of Alaska Epidemiology Bulletin*, 15 July 2021.
- Fontanet, Arnaud, et al. "SARS-CoV-2 Variants and Ending the COVID-19 Pandemic." *The Lancet*, vol. 397, no. 10278, 2021, pp. 952–954., doi:10.1016/s0140-6736(21)00370-6.
- Groseclose, Samuel L., and David L. Buckeridge. "Public Health Surveillance Systems: Recent Advances in Their Use and Evaluation." *Annual Review of Public Health*, vol. 38, no. 1, 2017, pp. 57–79., doi:10.1146/annurev-publhealth-031816-044348.
- Hedegaard, H., Wake, M., & Hoffman, R. (1998). Firearm-related injury surveillance in Colorado. *American Journal of Preventive Medicine*, 15(3), 38–45. [https://doi.org/10.1016/s0749-3797\(98\)00063-4](https://doi.org/10.1016/s0749-3797(98)00063-4)
- LeMier, M., Cummings, P., Keck, D., Stehr-Green, J., Ikeda, R., & Saltzman, L. (1998). Washington State gunshot- wound surveillance system. *American Journal of Preventive Medicine*, 15(3), 92–100. [https://doi.org/10.1016/s0749-3797\(98\)00053-1](https://doi.org/10.1016/s0749-3797(98)00053-1)
- Overview of Evaluating Surveillance Systems. Atlanta, GA: Centers for Disease Control and Prevention (CDC), 2013.
- Publication of Updated Guidelines for Evaluating Public Health Surveillance Systems. (2001). *JAMA*, 286(12), 1446. <https://doi.org/10.1001/jama.286.12.1446-jwr0926-2-1>

Reicher, Mike. “Thousands of Military and Veterans' COVID-19 Vaccinations Aren't in Washington State Data, Hindering Pandemic Response.” *The Seattle Times*, 22 May 2021.

SARS-CoV-2 Sequencing and Variants in Washington State. Washington State Department of Health, 4 Aug. 2021, www.doh.wa.gov/Portals/1/Documents/1600/coronavirus/data-tables/420-316-SequencingAndVariantsReport.pdf.

SARS-CoV-2 Vaccine Breakthrough Surveillance and Case Information Resource. Washington State Department of Health, 28 July 2021, www.doh.wa.gov/Portals/1/Documents/1600/coronavirus/data-tables/420-339-VaccineBreakthroughReport.pdf.

Shmerling, Robert H. “Should We Track All Breakthrough Cases of COVID-19?” *Harvard Health*, 3 June 2021.

Singleton, J. (1999). An overview of the vaccine adverse event reporting system (VAERS) as a surveillance system. *Vaccine*, 17(22), 2908–2917. [https://doi.org/10.1016/s0264-410x\(99\)00132-2](https://doi.org/10.1016/s0264-410x(99)00132-2)

Thacker SB, Berkelman RL. 1988. Public health surveillance in the United States. *Epidemiol. Rev.* 10:164–90

Thacker SB, Berkelman RL, Stroup DF. 1989. The science of public health surveillance. *J. Public Health Policy* 10:187–203

The U.S. Can Lead the Way in Vaccine Breakthrough Reporting. Will It Squander This Opportunity? (2021, July 7). The Rockefeller Foundation. https://www.rockefellerfoundation.org/blog/the-u-s-can-lead-the-way-in-vaccine-breakthrough-reporting-will-it-squander-this-opportunity/?utm_source=Twitter&utm_medium=organic_social&utm_campaign=Health&utm_content=PPI_1

Vaccine Breakthrough Fact Sheet. Washington State Department of Health, 2 June 2021, www.doh.wa.gov/Portals/1/Documents/1600/coronavirus/420-320-BreakthroughCases.pdf.