

**A SYNDEMIC APPROACH TO UNDERSTANDING AND EXPLORING
COVID-19 VACCINE HESITANCY AMONG UNIVERSITY OF
WATERLOO STUDENTS, CANADA**

by

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This thesis consists of material all of which I authored or co-authored: see Statement of Contributions included in the thesis. This is a true copy of the thesis, including any required final revisions, as accepted by my examiners.

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STATEMENT OF CONTRIBUTIONS

Bara' Abdallah AlShurman was the sole author for Chapter 1 and Chapter 5 which were written under the supervision of Dr. Zahid Butt and were not written for publication.

The manuscripts presented in this thesis, including four that have been submitted to or published in scientific journals, are the work of Bara' AlShurman, in collaboration with her co-authors and committee members.

Exceptions to sole authorship include:

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As lead author of the four chapters, I was responsible for conceptualizing the study designs, developing the questionnaire, leading data collection and cleaning, conducting the statistical analysis, interpreting the results, creating tables and figures, drafting the submitted manuscripts, and addressing revisions based on co-author and reviewers' feedback.

Dr. Zahid A. Butt provided overall supervision and methodological guidance, contributed to the conceptualization of the studies, and offered detailed feedback and revisions on each manuscript.

Dr. Joslin Goh provided guidance on statistical analysis and interpretation of results and contributed to the review and editing of the manuscripts. Dr. Shannon E. Majowicz offered critical feedback on the data analysis, interpretation of findings, and the structure, clarity, and framing of the manuscripts. Dr. Kelly Grindrod provided feedback on the overall content and the structure, clarity, and framing of the manuscripts. Xisi Zhang assisted with statistical analysis in Chapter 3. All co-authors reviewed and approved the final versions of the manuscripts.

ABSTRACT

Vaccine hesitancy (VH) remains a persistent challenge to achieving widespread COVID-19 vaccination. Although initial vaccine rollout efforts witnessed high uptake of the primary series, booster dose uptake has declined, particularly among younger adults. Universities, where primary doses were mandated but boosters remained optional, offer a unique setting to study VH dynamics. These institutions encompass socially connected, information-exposed populations who navigate a developmental stage for forming health-related decisions.

Recent scholarship has conceptualized VH not only as an individual behavioral issue but as a social phenomenon that spreads across communities, often amplified by misinformation and peer influence. Given that COVID-19 has been described as a biological pandemic and VH as a social epidemic, their co-occurrence may constitute a syndemic, where each amplifies the effects of the other and suppresses vaccine uptake. As booster coverage continues to decline, applying a syndemic lens to VH among students is essential for guiding future vaccination strategies.

This dissertation addresses critical gaps in COVID-19 VH research. First, existing scales offered limited constructs that did not capture the multidimensional nature of VH or were not validated for booster-specific attitudes. Additionally, most prior studies assessed VH at a single vaccine stage, overlooking how attitudes evolve from mandatory primary series to voluntary booster decisions. Moreover, while syndemic theory has gained traction conceptually, its empirical application in the context of VH remains limited, with most studies relying on theoretical or qualitative descriptions rather than quantitative tests of interaction effects. To address these gaps, the objectives of this thesis were to (1) validate a COVID-19 Vaccine Hesitancy Scale (CVHS) to measure VH for COVID-19 primary and booster doses among students at the University of Waterloo (UW) in Canada, (2) estimate COVID-19 VH prevalence and identify key factors driving VH across primary and booster doses, and (3) examine the

syndemic interaction between VH and COVID-19-related factors (e.g., COVID-19 diagnosis, COVID-19 hospitalization, adherence to public health guidelines, and beliefs in conspiracy theories) in shaping booster uptake.

This dissertation is based on a cross-sectional survey of 4,453 students at UW, Canada, conducted in 2024. The first study adapted the CVHS to measure VH toward both primary and booster COVID-19 doses among university students. Exploratory and confirmatory factor analyses, along with reliability and validity tests, were conducted to assess the underlying factor structure and evaluate model fit. Results indicated a three-factor structure across both scales, with high internal consistency and excellent model fit. The scale demonstrated adequate convergent, discriminant, and criterion validity. VH was significantly higher for booster doses (33.4%) than primary doses (19.3%) with more students delaying (32.1%) or refusing boosters (29.3%) than delaying (11.5%) or refusing (6.2%) primary doses.

The second study examined how VH shifted from primary to booster doses and what factors contributed to this VH change using Generalized Estimating Equations. Results showed a marked increase in VH, with mean scores rising from 7.3 (SD = 7.1) for primary doses to 10.9 (SD = 8.1) for boosters. VH prevalence doubled from 17% to 33.4%. The largest VH increases were seen among women and younger students. Students with low perceived risk, negative booster perceptions, low trust in government recommendations, and lack of prior flu or meningococcal vaccination showed greater VH change. Conversely, students with no religious affiliation and those less influenced by vaccine mandates showed smaller VH shifts.

The third study tested the central syndemic hypothesis and investigated whether changes in VH interacted with COVID-19-related experiences to influence booster dose uptake. Logistic regression models were used to estimate main and interaction effects on booster uptake. Increased VH was associated with a 23% reduction in the likelihood of receiving a booster.

Younger age, no COVID-19 hospitalization, absence of flu vaccination, non-compliance with public health guidelines, and belief in conspiracy theories predicted lower booster uptake.

Interaction analyses revealed that the negative effect of VH on booster uptake was stronger among students who complied with public health guidelines and those who rejected conspiracy beliefs. Interestingly, among participants uncertain about their hospitalization status, increased VH was associated with higher booster uptake.

This dissertation contributes new evidence that VH is dynamic and context-dependent, evolving significantly between vaccine phases. Findings underscore that the effect of VH is magnified when interacted with COVID-19 experiences such as pandemic fatigue, stigma, and conspiracy beliefs, together constituting a syndemic. This indicates the presence of a “latent hesitancy” among individuals who may outwardly engage in preventive behaviors but internally remain skeptical or fatigued by ongoing vaccine messaging. As such, vaccine mandates, broad awareness campaigns, or generic messaging may be insufficient to address the complex drivers of booster hesitancy. Instead, interventions should be segmented and tailored to specific behavioral profiles, such as compliant-but-hesitant versus disengaged-and-distrustful, rather than treating students as a homogeneous group. Strategies should go beyond one-size-fits-all models and adopt dialogic and supportive approaches, such as vaccine counseling sessions, peer-led discussions, or transparent communication from trusted campus figures. Furthermore, institutions should recognize that VH may shift over time. Ongoing monitoring of VH levels and underlying factors through rapid surveys can support targeted public health interventions.

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DEDICATION

Alhamdulillah¹

IT IS THE DAY, FINALLY

Yes, it is the day I get to dedicate this hard work, to dedicate these years of distance, growth, and struggle to the people who've been with me in every unspoken way.

To **my family**, whom I have been deeply attached to, yet lived away from for the past four years. Every day apart from you was felt, but your presence never left.

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I started this journey with a quote, and I'll end it with the same:

“I am a dreamer. I have to dream and reach for the stars”

¹ *Alhamdulillah* — An Arabic expression, meaning “All praise is due to GOD,” expressing contentment and thankfulness.

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LIST OF ABBREVIATIONS

ADHD	Attention Deficit Hyperactivity Disorder
AGFI	Adjusted Goodness of Fit Index
AIDS	Acquired Immunodeficiency Syndrome
BIPOC	Black, Indigenous, and People of Color
CCHS	Canadian Community Health Survey
CDC	Centers for Disease Control and Prevention
CFA	Confirmatory Factor Analysis
CFI	Comparative Fit Index
CI	Confidence Interval
COPD	Chronic Obstructive Pulmonary Disease
COVH	COVID-19 and Vaccine Hesitancy
COVID-19	Coronavirus Disease 2019
CR	Composite Reliability
AVE	Average Variance Extracted
CVHS	COVID-19 Vaccine Hesitancy Scale
EFA	Exploratory Factor Analysis
EMS	Emergency Medical Services
GEE	Generalized Estimating Equations
GFI	Goodness of Fit Index
HCW	Healthcare Worker
HIV	Human Immunodeficiency Virus
HPV	Human Papillomavirus
ICU	Intensive Care Unit
IFI	Incremental Fit Index
KMO	Kaiser-Meyer-Olkin
MCAR	Missing Completely at Random
MMR	Measles, Mumps, and Rubella
NCDs	Non-Communicable Diseases
NFI	Normed Fit Index
NPIs	Non-Pharmaceutical Interventions
OCVHS	Oxford COVID-19 Vaccine Hesitancy Scale
OR	Odds Ratio

PACV	Parent Attitudes about Childhood Vaccines
PGFI	Parsimony Goodness of Fit Index
PHAMILIS	Physical Health problems, Abuse, Mental Illness, Loss, Instability, and Substance use
PNFI	Parsimony Normed Fit Index
PPE	Personal Protective Equipment
PTSD	Post-Traumatic Stress Disorder
QIC	Quasi-likelihood under the Independence model Criterion
RERI	Relative Excess Risk due to Interaction
RFI	Relative Fit Index
RMSEA	Root Mean Square Error of Approximation
SAGE	Strategic Advisory Group of Experts
SAVA	Substance Abuse, Violence, and AIDS
SAVID	Substance Abuse, Childhood and Adolescent Sexual Abuse, Violence, Internalized Homonegativity, and Depression
SD	Standard Deviation
SPSS	Statistical Package for the Social Sciences
SRMR	Standardized Root Mean Square Residual
SUMIC	Substance Use, Mental Illness, and Familial Conflict non-negotiation
TB	Tuberculosis
TLI	Tucker-Lewis Index
UK	United Kingdom
US	United States
USD	United States Dollar
UW	University of Waterloo
VH	Vaccine Hesitancy
VHS	Vaccine Hesitancy Scale
VIDDA	Violence, Immigration, Depression, Diabetes, Abuse
WHO	World Health Organization
aOR	Adjusted Odds Ratio

CHAPTER 1: INTRODUCTION

1.1. Background

The COVID-19 pandemic has created one of the most significant global health crises, with more than 770 million confirmed cases and nearly seven million deaths reported by early 2024 [1]. Vaccines have remained central to the pandemic response and have offered strong protection against severe illness, hospitalization, and transmission [2]. In Canada, the national vaccine rollout began in December 2020, first targeting high-risk groups before gradually expanding to the broader public by mid-2021 [3]. As eligibility widened, individuals were considered fully vaccinated upon completing the recommended primary series, either one or two doses, depending on the vaccine product [3]. However, evidence soon emerged that protection against infection declined significantly by six months after the second dose, dropping below 20% [4]. In response, health authorities introduced booster doses to reinforce immunity, particularly during the spread of the Delta and Omicron variants in 2021. This shift also led to the introduction of bivalent vaccines tailored to address emerging variant mutations [5].

While uptake of the primary series was high, with 86.8% of Canadians aged five and older deemed fully vaccinated, booster coverage has been substantially lower, with only 51.6% receiving a third dose [6], and just 40% of those aged 18–39 receiving three or more doses by September 2023 [4,7]. Similar patterns have been observed globally and for other routine immunizations like the influenza vaccine [8,9]. Booster hesitancy has also emerged across multiple groups including younger adults [8,10,11], healthcare workers [12], parents [13,14], and students [15]. Studies from Canada and abroad consistently show that vaccine hesitancy (VH) is more prevalent among younger populations [16,17]. Commonly reported reasons include doubts about booster safety or necessity, low perceived risk, and distrust in health

authorities.

VH, defined by the World Health Organization (WHO) as the “delay in acceptance or refusal of vaccines despite the availability of vaccination services,” is not simply the opposite of vaccine acceptance [18]. Rather, it exists on a continuum where individuals may accept some vaccines while delaying or refusing others. For example, someone might complete the COVID-19 primary series but decline subsequent booster doses. In this context, vaccine mandates played a key role in vaccination efforts [19,20]. By September 2021, all ten provinces in Canada had implemented proof-of-vaccination policies for students to attend in-person academic activities and campus residences [21,22]. The literature shows that COVID-19 vaccine uptake increased significantly following mandate announcements in multiple provinces in Canada [23]. The goals of these mandates were to reduce COVID-19-related absenteeism, curb community transmission, and facilitate a return to normal school life. Nonetheless, their implementation raised debates about personal autonomy and freedom, and concerns about division between vaccinated and unvaccinated students [20]. Within university settings, the distinction between compulsory COVID-19 primary series and voluntary booster doses provides further insights into VH. University students may have received primary doses to comply with the institutional mandates, whereas their decisions to get booster doses were likely influenced by personal beliefs, peer norms, and prior experiences with COVID-19 [24–26].

Beyond individual attitudes, VH seems to operate within broader social systems and spread across communities through shared narratives, mistrust, and online misinformation [27–29]. Research suggests that VH may function not merely as a personal belief or behavioral outcome, but as a socially transmitted phenomenon with epidemic-like characteristics [27–29]. In this light, VH has been conceptualized as a social epidemic [30] that could overlap with and

amplify the impact of the COVID-19 pandemic. When both coexist, particularly in populations navigating uncertainty, they can lead to worse outcomes than either would alone.

1.2. Literature Review

The theoretical and conceptual lens for this thesis is grounded in syndemic theory. The term syndemic was introduced over two decades ago to describe the synergistic interaction of co-occurring epidemics, where the combined effect is greater than the sum of their individual impacts, thereby intensifying the health burden on affected populations [31,32]. The concept was originally developed to explain health inequities linked to HIV/AIDS, substance use, and violence (the SAVA syndemic) [33]. More recently, COVID-19 has been described as a syndemic due to its intersections with chronic illness, mental health, structural inequities, and broader sociopolitical forces [34–36]. Importantly, syndemics are not limited to biological conditions, they also encompass behavioral and social factors that interact to worsen health outcomes [37]. Extending this logic, this thesis takes a unique approach by applying the syndemic framework to examine how a behavioral condition like VH interacts with a biological pandemic like COVID-19 to shape vaccine behaviors.

This section provides a detailed and focused literature review on syndemic theory, VH, and the COVID-19 pandemic, as presented in a published paper. The aim of conducting this review was to establish the theoretical foundation of this thesis and to position it within the broader scholarly context. In particular, we framed a novel syndemic framework to understand how VH and COVID-19 may co-occur and interact in ways that amplify negative health outcomes, such as reduced vaccine uptake.

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Proposing a New Conceptual Syndemic Framework for COVID-19 Vaccine Hesitancy: A Narrative Review

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Keywords: vaccine hesitancy; COVID-19; syndemics; framework; COVID-19 vaccination

Abstract

Background: Discussions regarding syndemics have dominated research in recent years.

Vaccine hesitancy has also been propelled to the forefront. In this narrative review, we aim to frame a novel syndemic framework to understand the interaction between vaccine hesitancy, COVID-19, and negative health outcomes.

Methods: A non-systematic electronic search was conducted in PubMed and Google Scholar. Search criteria were limited to articles published between November 2019 and June 2022. Articles related to the COVID-19 syndemic and vaccine hesitancy were included.

Results: Our review revealed that the adherence to COVID-19 regulations—although they were effective in preventing COVID-19 transmission, cases, and deaths—created a dynamically unstable ‘vicious cycle’ between undesirable health, economic, and social outcomes. The “accumulation” of complex stressors decreased individuals’ cognitive flexibility and hindered them from making decisions and getting vaccinated. Furthermore, it increased individuals’ risk of acquiring COVID-19, losing their employment, increasing poverty, and decreasing healthcare utilization. We illustrated how the amalgamation of sociodemographic and contextual factors associated with COVID-19 might impact people’s vaccine decisions, making them more hesitant toward COVID-19 vaccination. Failing to receive vaccinations increases the chances of COVID-19 transmission, hospitalization, and other negative health outcomes.

Conclusions: Understanding the interaction between these factors is essential to provide policymakers with inspiration to set appropriate interventions for promoting COVID-19 vaccination acceptance to decrease the overall burden of pandemics.

1. Introduction

A syndemic, or synergistic epidemic, is defined as the accumulation of two or more epidemics or disease clusters that are present concurrently or sequentially in a population, and that have biological, social, or environmental interactions that worsen the burden of the disease [1,2,3]. The theory of syndemics was first proposed in the early 1990s to investigate how social, biological, environmental, political, and economic conditions cluster and interact synergistically with other epidemics, enhancing adverse health outcomes and multiplying the burden of disease interaction [1,2,3]. After the emergence of Singer's syndemic theory (1996), the concept of syndemics and disease interaction has become broadly used and accepted in public health and biomedical fields, epidemiology research, and among healthcare providers and physicians [1,2,4]. Multimorbidity and dual diagnosis have been extensively captured in the last two decades, and the syndemic approach to understanding either disease-behavioural conditions or disease-disease interaction has been documented in the previous literature [4]. Regarding disease-disease interactions, many articles discussed the syndemic interaction between HIV and tuberculosis [5,6], diabetes and depression [7,8], and COVID-19 and non-communicable diseases [9,10]. At the same time, disease-behavioural condition interactions were conceptualized by using lexicalized acronyms and multidimensional syndemic frameworks to understand the clustering of population-level/individual-level health, and its determinants across different dimensions [4]. For instance, the term "VIDDA" was used to illustrate the complex interactions of Violence, Immigration, Depression, Diabetes, and Abuse [11,12]. Other researchers coined the "SAVA" term to characterize a triplex health condition that involves the interaction between Substance Abuse, Violence, and AIDS [13,14]. In the present, these lexicalized acronyms have become widely published, and new frameworks have appeared, such as the "SUMIC" syndemic (i.e., Substance Use, Mental Illness, and Familial Conflict non-

negotiation) [15], “SAVID” (i.e., Substance abuse during condomless sex, childhood and adolescent sexual abuse, violence, internalized homonegativity, and depression) [16], and “PHAMILIS” (i.e., Physical Health problems, Abuse, Mental Illness, Loss, Instability, and Substance use) [17,18].

On the other hand, other authors have argued that little attention has been drawn to syndemics from a medical anthropological perspective [12]. Syndemics were viewed by anthropologists as examples of how the concept of co-morbidities affects humans from multidimensional and ecological perspectives, and the ways in which culture and society are organized around or influenced by issues of health, healthcare and related issues [19]. In doing so, they stressed the importance of studying the biosocial processes that reflect how social, cultural, and economic factors influence individual-level experience, instead of only studying disease–disease interaction [12,19].

During the COVID-19 pandemic, much attention has been drawn to syndemics, and discussions regarding disease interactions have dominated research in recent years [20,21,22]. Vulnerability to acquiring COVID-19 was seen as a syndemic, as it increases in the presence of poor social, economic, and environmental factors [23,24,25,26]. These factors, such as social inequality, marginalization, poverty, and injustice, can contribute to COVID-19 clustering, which in turn increases treatment costs [22,23,24,25]. Hundreds of articles demonstrated the intertwined relationship between the COVID-19 pandemic and many adverse health and socio-economic outcomes [24,27]. The outcomes were mainly linked to non-communicable diseases (such as diabetes and cardiovascular disease) [10,28,29], infectious diseases (such as tuberculosis, malaria, and HIV) [29,30,31,32], nutrition insecurity [33,34], mental health inequities [35], climate change, gender-based violence [36], and racism [35,37,38]. A recent

rapid review published in 2021 revealed that health emergencies resulting from the COVID-19 pandemic and its associated risk factors (e.g., financial stress, service closure, social distancing, and quarantine) exacerbated gender disparities in terms of income level, work environment, and job security [36]. Consequently, these pandemic-related constraints increased women's vulnerability to violence and discrimination and reduced their access to mental health and healthcare services [36]. Another study found that the COVID-19 pandemic complicated the treatment and management of tuberculosis and diabetes due to socioeconomic inequalities and hospital inaccessibility faced by people during the lockdown [29]. Taken together, the COVID-19 pandemic–syndemic acts as the nexus between intensifying health inequalities and worsening the burden of other diseases.

On the other hand, Vaccine Hesitancy (VH) for COVID-19 vaccines has been propelled to the forefront [39,40]. VH is defined by the SAGE working group as “the delay in acceptance or refusal of vaccination despite the availability of vaccination services” [41]. Additionally, prior research substantiates the belief that VH is an attribute ascribed to people who hold an intermediate position along a continuum ranging from full support for vaccination to strong opposition to any vaccine [42,43,44]. Understanding the factors and determinants that influence VH have become increasingly important, especially during the COVID-19 pandemic, as governments around the globe have been struggling to convince groups of their populations to participate in vaccination protocols [39,40,45,46,47]. In a scoping review published in 2021, the authors investigated and identified significant predictors of COVID-19 vaccination acceptance, refusal, and hesitancy [48]. The findings showed that many demographic, social, and contextual factors were associated with triggering VH, such as age, gender, education level, race/ethnicity, vaccine safety and effectiveness, influenza vaccination history, health history/medical conditions, and lack of trust [48]. Other previous studies and systematic reviews revealed that

different population subgroups may experience greater tendency towards VH [49,50,51,52,53,54,55,56]. These groups were mainly women, less-educated populations, low-income individuals, black adults, people with comorbidities (e.g., HIV, chronic kidney disease, and substance abuse), and people living in rural or semi-urban settings [49,54,55,57,58,59,60].

Previous studies and reviews were only limited to investigating the factors that influence COVID-19 VH. None of them explored how social, demographic, and contextual factors can facilitate the interactions between COVID-19 and VH, and escalate morbidity and mortality, by using a syndemic framework. Therefore, this narrative review has two main objectives: (1) to map and synthesize the literature that captures the COVID-19 syndemic and VH during the COVID-19 pandemic; and (2) to frame and conceptualize a novel syndemic conceptual framework to understand how different factors interact, resulting in a disparate risk of increasing VH, COVID-19 transmission, and worsening negative health outcomes.

2. Literature Review Search Strategy

This narrative review targeted the existing literature on the COVID-19 syndemic and COVID-19 VH to identify and summarize what has previously been published. Since this is a narrative review without a strict protocol to be followed, a non-systematic electronic literature search was conducted primarily in health science databases, such as PubMed, using the following MeSH terms and search strategies: ((COVID-19 OR SARS-CoV-2 OR Pandemic*) AND syndemic*) OR ((Vaccine OR Vaccin* OR Immuniz*) AND syndemic*) OR (syndemic*) OR (Vaccine hesitancy AND COVID-19 syndemic*) OR (syndemic* AND interaction*) OR (Syndemic* AND coronavirus AND vaccine acceptan*) OR (SARS-CoV-2 AND vaccine hesitancy AND syndemic*). Google Scholar was also searched to find a broader number of related articles using a plain-language search such as: “Syndemics and COVID-19” or

“Syndemics and COVID-19 vaccine hesitancy” or “Syndemics in COVID-19 era”. Search criteria were limited to articles published in English between November 2019 and June 2022. As a result, 104 articles were yielded from the search.

Non-standardized inclusion and exclusion criteria were used. Relevant studies were selected only if they (1) focused on the COVID-19 syndemic and (2) were contextualized to COVID-19 VH. All relevant studies were reviewed regardless of their types or designs, and all countries of origin were eligible for inclusion. In addition, any relevant articles found outside our search strategy were included if their content related to this review. Articles were excluded if they were (1) not published during the COVID-19 pandemic, (2) irrelevant to either COVID-19 VH or the COVID-19 syndemic, and (3) non-journal articles. Finally, the included articles ($n = 40$) were peer-reviewed articles, perspectives, reviews, editorials, and commentaries. These articles were reviewed, and relevant data were extracted to report the key findings.

3. Key Findings from the Literature

3.1. COVID-19 as a Syndemic

Since November 2019, the abrupt, unpredictable, and quickly growing number of COVID-19 cases has resulted in significant and devastating adverse health, economic, and environmental outcomes all over the world [61]. The exacerbating burden of COVID-19 caused a direct impact on people’s health, patient care, hospital capacities, workplaces, country productivity, and financial stability [62]. Based on the COVID-19 level of severity and spread, it was classified as a pandemic by the WHO [63]. At that time, COVID-19 research had recently started, and scientists, public health professionals, medical researchers, and medical anthropologists did not have a deeper knowledge about the unintended consequences of the

COVID-19 pandemic. As time went by, seminal contributions were made examining the nature of COVID-19, as well as its cumulative and intertwined characteristics [37,64,65]. From there, research began to be oriented toward the term syndemic, and authors started to drive further development of the idea that COVID-19 can be seen as a syndemic. Miller Singer and his colleagues, Nicola Bulled and Rebecca Irons, were the first medical anthropologists who coined the “COVID-19 syndemic” term, and they discussed and conceived the idea of considering and characterizing COVID-19 as a “syndemic” instead of a “pandemic” [66,67,68]. Irons argued that some researchers and observers stated that COVID-19 affected anyone, regardless of their gender, social class, background, or geographical location; thus, it is a disease that knows no discrimination [68]. However, Irons contradicted this theory and supported her argument by confirming that COVID-19 is inequitably distributed and severely affects elderly people more than younger people, and influences those with underlying health conditions more than healthy people [68]. However, it is no longer right to say that COVID-19 has nothing to do with the discrimination. Hence, many authors supported the notion of reframing COVID-19 as a syndemic instead of a pandemic.

During the same period, Singer and his colleagues shed light on the fact that, even though the COVID-19 pandemic spread globally, multiple countries were impacted by COVID-19 differently based on each country’s resource availability, contexts and demographics, previous pandemics, management plans, mitigation strategies, and healthcare systems [66,67]. As such, South Africa is a focus of attention, as it has been barely affected by the COVID-19 pandemic, besides its rich history of facing past pandemics and diseases, such as HIV/AIDS and the 2009 H1N1 Influenza pandemic [67]. If we look to South Africa as a case study, we can find a multi-faceted problem with extended demographic, environmental, social, contextual, and economic facets. First, according to the WHO statistics, South Africa had the largest number of TB cases,

as more than 25% of TB deaths occurred in the African Region [69]. Second, over one-third of people living with HIV in the African Region in 2016 were infected with TB [70]. Third, the problems that faced South Africa during previous pandemics were not only related to the severity and contagiousness of infectious diseases, but also related to poverty, gender inequality, poor health of the workforce, unemployment rates, international labor migration, and violent crime, all of which exacerbated the transmission and co-morbidity of both TB and HIV/AIDS [71,72,73]. All of these diseases together have been involved in portraying the syndemic nature of COVID-19.

However, this is not the whole picture; previous studies have also brought a more comprehensive description of the background of the COVID-19 syndemic, and how COVID-19 restriction measurements could be strongly associated with significant adverse outcomes while interacting with other surrounding social factors [67,74,75,76]. In particular, most low- and middle-income countries that imposed lockdown response strategies similar to those implemented in high-income countries have been adversely impacted by these measures [77]. This is because of their insufficient medical equipment and supplies and limited financial resources. Despite the fact that implementing Non-Pharmaceutical Interventions (NPIs) was effective in preventing COVID-19 cases and deaths in some instances, it still resulted in undesirable health, economic, and social outcomes [77]. These outcomes include physical inactivity, PTSD, high glucose intake/poor diet, domestic violence, and social isolation as a consequence of isolation policies and the long duration of shutdowns [67,75,78]. Moreover, the rigidity of isolation policies, the imposition of longer-duration shutdowns, and the restriction of all non-essential internal movement all resulted in a deterioration of the socioeconomic system, healthcare sector, and business productivity [67,75,78]. Prior to COVID-19, the majority of people living in developing countries were suffering from multidimensional poverty, including

income inequalities, healthcare, education, and living standards [79]. When COVID-19 hit these populations, other than its adverse health outcomes, a sharp increase in multidimensional poverty levels was seen [79,80]. The reason behind this phenomenon can be explained by highlighting different situations in different regions globally. For example, harsh governmental restrictions on trade ports and shipments resulted in products' supply and demand disturbances, insufficient agriculture resources, and food insecurity [33,81]. According to research carried out among developing countries, populations in South Asia, the Middle East, and Sub-Saharan Africa were significantly susceptible to food demand and scarcity, resulting in reduced economic activity and income losses for businesses and workers [81]. Food insecurity due to the COVID-19 pandemic was also described as a multifaceted syndemic that might impact household food insecurity [33]. Consequently, it had an influence on maternal and child nutrition, particularly in families with young children. Previous research has shown that when children do not get enough nourishment throughout their developmental years, it can harm their mental health, which can lead to behavioral issues that hinder their academic performance when they reach school age [33].

Business and school closure were a further two important factors that not only led to increasing unemployment rate and affecting students' education level but also triggered unprecedented waves of family violence [82,83]. In Australia, domestic violence and familial abuse have escalated as a result of isolation policies. The authors reported that one cause of this was the loss of social support from extended relatives and neighbors, while others stated that this might be a result of increased alcohol consumption at home when bars and restaurants were closed [84]. Lastly, in the case of "Tighter measures drive non-compliant behaviour", a study documented those developing countries with more restrictive regulations experienced higher rates of non-compliance to those government regulations [85]. Not surprisingly, the non-

compliance rate was associated with labor-insecure individuals' income. A justification for this is that people with decent jobs, jobs paying low wages, or informal work experienced hardships from stay-at-home orders, which created an adverse reaction and encouraged them to break the rules [85].

The syndemic approach was further expanded to include BIPOC populations (Black, Indigenous, and people of color communities), the threat of systematic racism they experienced, and the highest disease burden they suffered during the COVID-19 pandemic [25,86]. Several studies have been conducted to better understand the synergistic effect of numerous illnesses among BIPOC populations during the COVID-19 syndemic, as well as the social, economic, environmental, and political situations that surround them [25,86,87]. BIPOC groups were described as the “More Exposed and Less Protected” populations [88]. Therefore, particular attention should be given to these populations, especially during pandemics and outbreaks. Interestingly, a previous study used the syndemic framework to highlight how healthcare providers' negligence of patient-related bio- and socioeconomic factors lead to cognitive biases and diagnostic errors/misdiagnosis, which in turn can lead to inadequate treatment [86]. Muhrer et al. demonstrated the idea of disease clustering among BIPOC communities during the COVID-19 pandemic, arguing that physicians and healthcare providers should examine the patient's social, economic, and environmental aspects—not just biological causes—when diagnosing diseases. Many diseases, such as malaria, diabetes, digestive disorders, respiratory diseases, and cardiovascular diseases, were shown to be more prevalent in low-income neighborhoods than in middle-to-high-income neighborhoods [25,86]. The reason for this is because impoverished populations suffer from poor air quality, malnutrition, inadequate sanitation, and poverty [25,86,87,88]. Therefore, the “accumulation” of multiple and complex stressors left them at a higher risk of acquiring COVID-19. For example, in the U.S., the

majority of black people were found to work in low-wage frontline jobs, which put them in a dilemma between staying at home, losing their employment, and becoming unable to pay for their basic needs; or risking COVID-19 exposure and continuing to work [25,87]. Another large concern is their fear of racial discrimination, which creates a mistrust of the healthcare system. As a result, they avoid seeking help from healthcare professionals or visiting hospitals or clinics until they become seriously ill [25,87]. Poor housing, the coexistence of comorbidities, homelessness, and uninsurance issues, all lead black people to be immunocompromised to SARS-CoV-2 infection risk and disease severity [25,86,87].

3.2. Vaccine Hesitancy during the COVID-19 Pandemic

VH was described as a “wicked problem” that is challenging and has no “right or wrong” solution [89]. It is complex, multifactorial, context-specific, and varies over time, communities, and locations. VH is not a new phenomenon; widespread skepticism about vaccination has existed for a long time [90]. It first appeared after the development of the first formal vaccine for smallpox in the 1790s [91]. The anti-vaccination movements have been acknowledged as a significant public health threat and a “dangerous trend” that contributed to increasing the prevalence and mortality of vaccine-preventable diseases (e.g., infectious diseases) [92]. Recent vaccination controversies have also emerged, such as those surrounding the association between the measles, mumps, and rubella (MMR) vaccine and the development of autism [93]. As a result, in November 2011, the members of the Strategic Advisory Group of Experts (SAGE) recognized the emerging concerns and reluctance to accept immunization and established many conceptual models to understand the factors that influence the decision to accept vaccines [94]. VH was defined as an intermediate position between full acceptance and full refusal despite the availability of vaccination services [42].

Since the outbreak of coronavirus disease 2019 (COVID-19), VH has been more recognized, and the anti-vaccination movement has increased at a great rate, which undermines researchers' efforts to end the pandemic [95]. Global efforts have been made to convince groups of people to participate in vaccination protocols. VH during the COVID-19 pandemic has been linked to specific contexts and attributed to a heterogeneous range of determinants, including demographic, social, political, cognitive, environmental, and health factors [96]. Previous research has attempted to understand the complexity of interactions between different factors, vaccine dynamics, and VH by using a variety of models [42]. The most classic models that have been frequently used in the literature to capture and analyze the factors that affect VH are the "Health Belief Model", "Theory of Planned Behaviors", and "5 C's model" [97,98,99,100,101]. These models have essentially targeted a multi-factorial approach in order to understand the pathway by which multiple factors are interconnected and exacerbate VH among different populations [97,98,99,100,101].

A spectrum of determinants of VH during COVID-19 have been reported in the literature, and they were highly variable [99]. The results from the literature are inconsistent and controversial regarding which group of people are the most hesitant to vaccination. This means that VH has no stable traits, as it fluctuates across different populations in different regions. In addition, VH rates vary by country and over time [96]. Interestingly, some researchers point out how people's opinions and reluctance have changed over the last two years due to the dynamic nature, instability, and uncertainty of the COVID-19 pandemic [101]. Multiple phases of VH were proposed by Kumar (2022), which are: vaccine eagerness; vaccine ignorance; vaccine resistance; vaccine confidence; vaccine complacency; and vaccine apathy, to explain the variability of people's behaviors and attitudes toward COVID-19 vaccines [101]. Each of these phases was influenced by a major context and a national measure that was happening at that

time. For instance, at the beginning of the pandemic, people were very concerned and afraid of catching COVID-19 and of its complications, so they were very eager to take the vaccine, whereas when vaccines started to be authorized by official governments, people took a step back and were concerned about the fast development of vaccines, which can negatively affect the safety and effectiveness of vaccines. Following this, the rising number of cases and the new emerging contagious variants (e.g., Gamma, Delta, and Omicron) prompted many to reconsider vaccination, especially when the mortality rate decreased in those who were vaccinated. It has been one step forward and two steps back for people to get COVID-19 vaccines; thus, they were stuck in a loop that had no end. For this reason, the term “Hysteresis loop” was suggested to express the negative perceptions experienced by people towards vaccination [102]. This resulted in changes in vaccination trajectory, potentially impeding governments’ efforts to promote vaccine uptake.

Previous research revealed that sociodemographic factors were related to VH during the COVID-19 pandemic [40,48,103,104]. For example, gender, age, income level, occupation, employment status, religion, education level, race, and ethnicity were all associated with VH and impacted people’s intention to use COVID-19 vaccines [40,48,103,104,105]. Gender difference was one of the most prominent factors that was linked to VH during the COVID-19 pandemic [106,107]. There was a consensus in a number of reviews that women were more hesitant to be vaccinated than men due to various barriers and social norms that affect women’s decisions [48,107,108]. Many explanations have been discussed in the literature, such as gender inequality, health disparities, economic insecurity, and poverty [48,107,108]. Likewise, other family members constrain women’s movement, particularly in low-income countries, preventing them from accessing healthcare facilities, including vaccination clinics. The infertility myth was another significant hurdle to vaccination [90,109]. Therefore, the fear of vaccines’ side effects,

especially among pregnant women, was frequently reported.

In general, the VH problem was recurrently linked to unprivileged communities during COVID-19 [110,111,112]. These communities include people who live in low-middle-income countries, BIPOC communities, ethnic minorities, marginalized populations, immigrants, refugees, or even underserved groups who live in high-income countries [110,111,112,113,114]. Past evidence showed that such populations are at higher risk of having poor health and are more likely to catch COVID-19 or be hospitalized due to COVID-19 [110,111,112,113]. In a study conducted by Public Health Ontario in Canada, geographic areas with a high marginalization index were linked to higher levels of ethnic concentration [115]. The authors found that the most ethno-culturally diverse neighborhoods experienced disproportionately higher rates of COVID-19, and related deaths compared to neighborhoods that were less diverse. Additionally, hospitalization and ICU admission rates were four times higher among the most diverse neighborhoods than the least diverse neighborhoods. Similarly, death rates were twice as high in neighborhoods with the most ethnic diversity than in those with less ethnic diversity [115]. Hence, the situation becomes even more problematic when there is low vaccination coverage in these areas because of VH.

Systematic racism was recognized as a key factor that lies between COVID-19 and VH [116]. The disproportionate effects of COVID-19, including the unequal distribution of the social determinants of health, lack of transportation, job loss, high mortality rates, and reduced access to healthcare, led underserved populations to distrust unfair health systems, which in turn drove vaccine distrust [113,116]. Black communities in the U.S. are a good example of this; as of July 2021, CDC data indicated that among those who received at least one dose, the number of white people was 1.4 higher than black people [117]; whereas in June 2022, after

approximately one year, the percentage of fully vaccinated white people was 5.6 times higher than the percentage of fully vaccinated black people [118]. The growing disparity in vaccination coverage between the two populations is alarming and raises concerns about VH and equity in the healthcare system. VH linked to health inequities has had a significant impact on other parts of the world [50]. Results from a recent published review revealed that Africa, Eastern Europe, and Central Asia are the most impacted by VH [50]. Moreover, a higher VH and refusal rate was observed among Arabic nations, which was related to distrust in the health system and concerns about side effects [119]. Another study by the University of Toronto, Canada, found that immigrants had around two-fold higher risk of COVID-19 VH than their Canadian-born counterparts. Immigrants also reported higher concerns than non-immigrants on vaccine safety and side effects owing to their distrust of vaccines [120].

Skepticism of vaccine effectiveness, the expedited production of vaccines, low risk perception, fear of vaccine side-effects, parental concerns, and distrust in scientific expertise were other common barriers to COVID-19 vaccine uptake [48]. In addition to this, the problem of the misinformation from the social media “infodemic” is recognized as one of the critical obstacles which stand against providing valid and scientific information to the general population [121]. The notion of politicization, the spread of fake information on social media platforms, and false conspiracy beliefs have all contributed to decreasing vaccine uptake [121]. Health literacy was seen as a core competence to understand basic health information and make decisions about vaccination [122]. This is why people with low health literacy were the most prevalent groups to such fake news, including older adults, minority populations, those with low socioeconomic status, and those with a low education level [122].

It is worth mentioning that the devastating effect of the COVID-19 pandemic itself has

increased the level of VH compared to the pre-COVID-19 era [123]. Familial economic hardship caused by COVID-19 prompted vaccination hesitancy [124]. The majority of those affected by economic difficulty were either vulnerable workers with decent occupations or unskilled individuals working in non-essential activities [125]. As a result, these people encounter a number of logistical problems, such as a lack of money for transportation and inaccessibility to vaccination services [124]. On the other hand, the fluctuation of COVID-19 vaccination policies, the implementation of different measures, mandatory vaccination policies, and the discrepancy between regulations at the national and international levels created confusion and exacerbated hesitation about vaccines in all regions [126]. Furthermore, the poor communication and confusing messages from authority figures impacted people's confidence in COVID-19 vaccines [126]. It may not only be misinformation which affects people's decisions to reject vaccines, but also the lack of tools to reformulate the decision-making process and gain a better understanding of the benefit and risks of vaccination.

3.3. Framework Development: A Novel Conceptual Framework for COVID-19 Vaccine Hesitancy "COVH"

In order to develop our new syndemic model/framework, we carried out our search, particularly for articles that addressed COVID-19 VH (e.g., factors affecting VH, building vaccine confidence, COVID-19 VH frameworks, COVID-19 vaccine coverage, and factors associated with vaccine uptake) and COVID-19 as a syndemic. Recent syndemic research contains different models and pathways that link multiple disease-exacerbating cofactors to COVID-19 and negative health outcomes. We also reviewed research that focused on applying a syndemic lens to disease outbreaks to fight future public health disasters and ongoing health inequity.

Our framework was developed by considering the most commonly discussed factors in the literature, as well as the most prominent previous frameworks. We sought to develop a framework that included three different models: the VH model, the COVID-19 pandemic model, and the adverse health outcomes model. Furthermore, we aimed to create an extensive and comprehensive model that can (1) be easily communicated, (2) be used by researchers from various disciplines and sectors to combat VH, and (3) serve as a basic foundation for public health professionals and policy makers to identify underlying health system vulnerabilities. **Figure 1** represents our proposed conceptual framework, which illustrates the interaction between vaccine-hesitancy-associated factors and COVID-19-associated factors, resulting in adverse health outcomes.

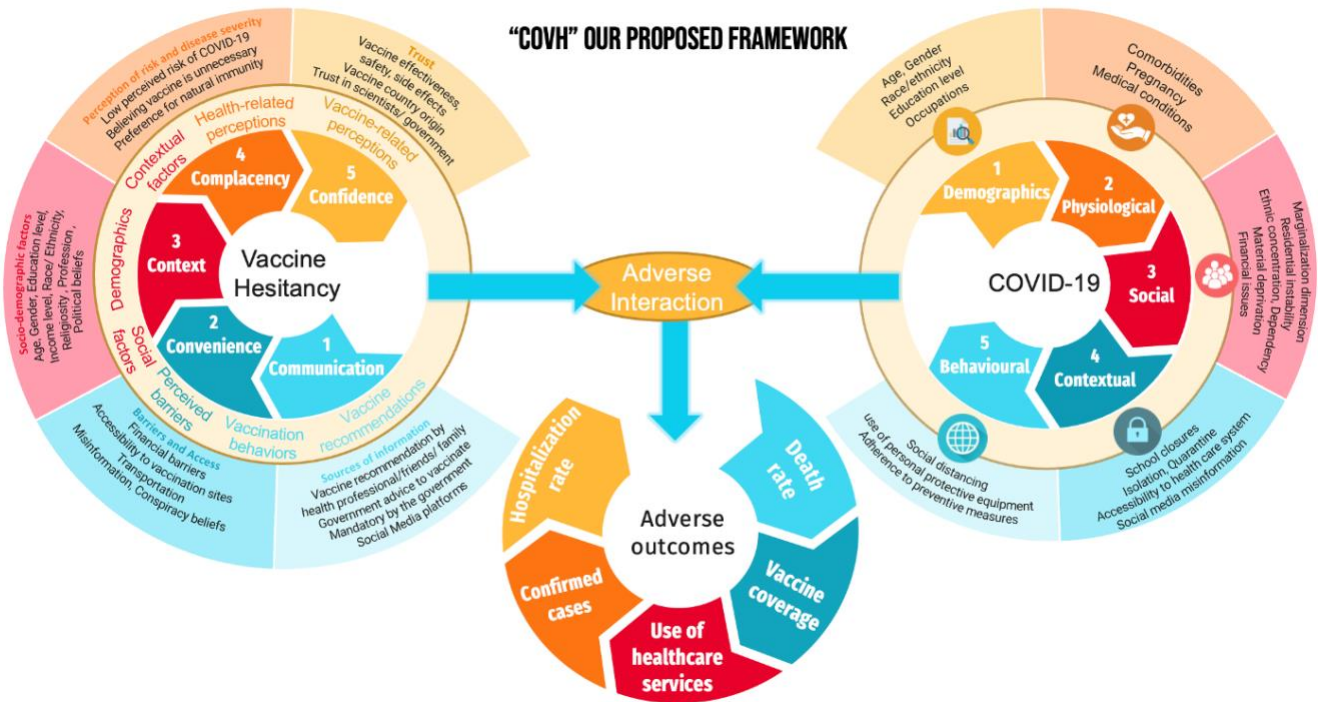


Figure 1. COVID-19 and vaccine hesitancy syndemic framework “COVH”

3.3.1. Components of the “COVH” Syndemic

The first part of the framework includes factors associated with VH. We used a modified version of the 5 Cs model to investigate the psychological drivers of VH. The idea of using this specific model is that it covers all the main drivers and barriers to getting vaccinated. The modified 5 Cs model encompasses five categories: confidence, complacency, context, convenience, and communication. Therefore, taking these in turn: first, confidence—do people trust the vaccines, the health system and the authorities more widely? This category comprises factors such as vaccine effectiveness, safety, side effects, vaccine country origin, influenza, vaccination history, and trust in scientists/government. Second, complacency—how do people perceive the potential risks of catching COVID-19? This category consists of factors such as perception of risk and disease severity, low perceived risk of COVID-19, believing the vaccine is unnecessary, and preference for natural immunity. Third, context—how socio-demographic

characteristics of people affect their decisions to get vaccines, including age, gender, education level, income level, employment status, region, race/ethnicity, religiosity, marital status, profession, and political beliefs. Fourth, convenience—is it physically and financially easy to get vaccinated, and do people have access to easily understood information about the vaccine in a language that they know? This category includes financial barriers, accessibility to vaccination sites, transportation, and vaccination policies. Lastly, communication—how do people obtain information/recommendations about vaccines and which sources do they use the most to inform their risk–benefit analysis about vaccination? This category includes vaccine recommendations by health professionals/friends/family, mandatory vaccination by the government, social media platforms, misinformation, and conspiracy beliefs. Overall, all of the previous factors are associated with VH. Therefore, the different “C’s” are important to tackle VH for different population groups, and it is important to conduct an analysis of the situation in order to ensure that appropriate interventions are implemented in response. There is no one-size-fits-all approach to this work and that can make it challenging, but it is still essential. We should remember that nobody is safe until everybody is safe.

The second part of the framework includes factors that are associated with COVID-19. These factors can be either demographic, biological, social, contextual, or behavioral. Demographics may include age, gender, race/ethnicity, education level, and occupation. Biological factors may involve comorbidities, pregnancy, and medical conditions, while social factors can be represented by marginalization, poverty, job loss, health disparities, violent crime, food insecurity, and financial issues. Contextual factors can include school closures, isolation, quarantine, access to healthcare, social media, and misinformation. Finally, behavioral factors may be related to social distancing, use of personal protective equipment, and adherence to preventive measures.

The third part of the framework represents the result of the interaction, which can be translated into five major negative health outcomes: death rate, hospitalization rate, vaccine coverage, use of healthcare services, and confirmed cases.

3.3.2. Framing the “COVH” Syndemic

Although VH is not a direct mechanism of COVID-19 transmission, it plays a catalytic role in driving the COVID-19 syndemic. Historically, low vaccine coverage pertaining to VH was associated with increased rates of infectious diseases, putting an additional burden on treatment costs [127]. Evidence dating back to 2016 indicates that a 5% decline in MMR (measles, mumps, and rubella) childhood vaccination in the U.S. was associated with a three-fold increase in measles cases, with an additional USD 20,000/case needed for measles treatment, including laboratory investigations, transportation, and vaccination [127].

During the COVID-19 pandemic, VH was attributed to many factors, such as age, gender, vaccine safety, vaccine effectiveness, misinformation, education level, lack of trust, racism, and social inequality, all of which enhanced COVID-19 transmission, morbidity, and mortality [48]. Moreover, COVID-19 has been linked to many adverse health outcomes, such as pneumonia, acute cardiac injury, acute respiratory distress syndrome, and acute liver injury [128]. Taken together, the clustering of these factors resulted in the aggravation of hospitalization rates and Intensive Care Unit (ICU) admissions; thus, subsequent demand for healthcare worker (HCW) staffing and personal protective equipment (PPE) [129,130]. Likewise, the augmentation of treatment prices (e.g., antiviral drugs) and the scarcity of face masks, ventilators, and ICU beds have created shortcomings in the delivery of patient care [129,130]. To date, global statistics show that vaccination rates in low-income countries remain low, and that only 20.9% of the population has received at least one dose of the COVID-19

vaccine [131], with some studies suggesting that VH triggered by misinformation and inequity in vaccine distribution is the driving factor behind such situations [132,133].

Mental health issues can be seen as a salient factor that provoke COVH syndemics, thereby maximizing the cost of treatment of multiple diseases convergence. On one hand, movement restriction and prolonged social isolation during the COVID-19 pandemic affected people's mental and emotional health [75]. A previous study estimated an additional 53 million cases of mental disorders due to the COVID-19 pandemic globally, which introduced an additional demand to mental health services [134]. Although implementing protective measures (e.g., lockdowns) was effective in preventing COVID-19 transmission, cases, and deaths [135], it resulted in undesirable health, economic, and social outcomes, such as PTSD, high glucose intake, unemployment, domestic violence, and social isolation [67,75]. Vaccination decisions, on the other hand, were perceived as a challenging procedure due to the abundance of infodemics and misinformation on social media [136]. This stressful pandemic and its unprecedented uncertainty weakened people's cognitive flexibility needed for behavioral adaptation to changing situations, particularly those with low health literacy. This fueled VH, which eventually resulted in not being vaccinated [136]. As a result, unvaccinated people amplified COVID-19 transmission, especially those living in high-density housing [137]. In Canada, unvaccinated adults were 31 times more likely than fully vaccinated adults to be hospitalized due to COVID-19 [138]. Another study discussed how the rates of vaccination coverage and vaccine efficacy influence the number of COVID-19 cases, direct medical costs, death rate, and productivity losses [139]. The interaction between these medical and behavioral conditions has overburdened healthcare infrastructure [129,130]. It also added cost and frustration to patients and their families who either live at a greater distance from healthcare services and cannot afford transportation costs, or those who lost their jobs and health insurance because of COVID-19

[129]. In addition, patients may suffer from other non-monetary and intangible costs, such as productivity loss and decrements in their quality of life.

The systematic discrimination experienced by marginalized populations has established skepticism about the healthcare system and governments, thus triggering VH [25]. Marginalization involves a wide spectrum of demographic indicators, such as race, ethnicity, minority/immigrant status, income level, unemployment rate, education attainment, and residential instability. Such factors make VH even more complex. Higher rates of infectious diseases and poor healthcare utilization among such groups were attributed to longstanding histories of systemic racism, stigmatization, and discrimination [89]. Because of social inequalities, these communities were heavily represented in essential industries, low-income categories, and living in multi-generational overcrowded dwellings, which were seen as “grim reapers” of COVID-19 [89,120]. Furthermore, Indigenous people have experienced centuries of Canadian colonialism and oppression. They were subjected to medical experimentation and vaccine trials in their childhood without their family’s permission [140]. Understandably, such history left scars in their memories and deeply affected their trust in government, making them hesitant to receive vaccines or healthcare.

The disparities in vaccination rates created a disproportionate impact on such populations, leaving them at higher risk of hospitalization and death due to COVID-19 [110]. For example, in Ontario, Canada, hospitalization rates were four times higher among the most ethnically diverse neighborhoods than in the least diverse neighborhoods [115]. More concerning, if unvaccinated individuals or those who are hesitant to vaccinate have existing co-morbidities (e.g., diabetes, hypertension, or cardiovascular diseases) [141], this may exacerbate their risk of hospitalization. Dong et al. found that the existence of co-morbidities in

COVID-19 cases resulted in 21.1% higher hospitalization costs compared to cases without comorbidities [142]. On the other hand, previous research has shown that due to discrimination concerns, marginalized communities tended to avoid seeking help from healthcare facilities until they became seriously ill [143,144]. The delay and avoidance of medical care by people suffering from non-communicable diseases (NCDs) and COVID-19 would create a “double burden” on the healthcare system. Additionally, it would require multiple visits to different clinics and different specialists, with increased responsibilities on HCWs, who would take the brunt of unpaid or underpaid work [8]. The occurrence of syndemics in healthcare systems structured to deliver care on a disease-by-disease basis often leads to insufficient care coordination [8]. Such care fragmentation is commonly linked to undesirable consequences and increasing costs [8,145].

Through our proposed framework, we can illustrate and conceptualize how the sociodemographic and contextual factors associated with the COVID-19 pandemic and VH can co-occur and interact with each other, resulting in magnified risk of developing adverse health outcomes. For example, according to previous research, immigrants or refugees are among the people who are most likely to encounter discrimination in the labor market, facing substantially higher levels of unemployment and lower wages [146,147]. This is because of the workplace preference to hire native people in higher-skilled jobs or the lower education level of immigrants and refugees, all of which can threaten their food security, accessibility to transport and health literacy. Low health literacy, in turn, could be a direct contributor to obtaining health information from untrustworthy social media platforms and websites.

The amalgamation of these factors can influence this group’s decisions to take vaccines, making them more hesitant toward COVID-19 vaccination. Furthermore, failing to receive

vaccinations increases their chances of becoming infected with COVID-19 and being hospitalized. On the other hand, stringent COVID-19 regulations caused the majority of immigrants and refugees to lose their employment, increasing the poverty rate, creating distrust in the healthcare system, and decreasing healthcare utilization. It should be noted that the situation is significantly worse among this sample's senior population. COVID-19 can exacerbate the symptoms of older persons who already have health problems, putting an added burden on the healthcare system. A lack of transportation can also be a significant barrier to seeking healthcare, resulting in limited healthcare utilization by this portion of the population.

Of further concern is the interactive nature of all the previous factors. As a result of this syndemic interaction, the number of confirmed COVID-19 cases, hospitalization and death rates could all increase, while vaccine coverage could decrease. From this example, we can envision how all of these factors in our suggested framework interact in a loop, with each factor being directly or indirectly connected to the others. Furthermore, the proposed pathway implied that some factors may operate as confounders, mediators, or effect modifiers. Hence, the suggested variables can distort the associations between COVID-19, VH, and adverse health outcomes. Other factors can transmit the effect between multiple variables or affect the direction and/or the strength of the relationship between the three main parts of the framework.

4. Discussion

This narrative review aims to provide a novel framework to understand and conceptualize the interaction between VH and COVID-19, resulting in negative health outcomes. The novelty of this framework comes from its method of engaging with and connecting different factors and determinants that are associated with major public health problems in recent years and linking them to undesirable health effects which can have considerable impacts on

individuals and communities. No prior research has used the syndemic perspective to understand how VH can synergistically interact with COVID-19 and exacerbate negative health outcomes.

Taken together, using a syndemic framework to explore how multiple factors interact with each other in the context of VH and COVID-19 will provide countries with a guidance tool to set up plans for future pandemic eradication. The real value of the syndemic model lies in its ability to analyze the pandemic by using cross-disciplinary perspectives including biological, psychological, political, environmental, and social interactions to visualize and predict the long-term consequences of the pandemic [20]. For instance, by understanding how determinants of VH and factors associated with COVID-19 interact and worsen adverse health outcomes, scientists, policymakers, and legislators might be encouraged to change their ways of thinking about responding to future pandemics. Therefore, employing syndemic thinking in building and preparing impactful interventions—at earlier stages—to address accessibility, equity, healthcare setting, mental health, hospitalizations, VH, official policies, financial issues, and communication platforms can result in effective solutions and long-term investment.

It is worth noting that vaccination is the most globally approved weapon to prevent infectious diseases such as COVID-19. However, a country without a robust vaccine response strategy, appropriate pandemic management, and sufficient vaccination campaigns cannot successfully eradicate viruses or vaccinate a substantial number of its inhabitants [148]. Previous articles have pointed out the significance of having a clear and ready-made deployment and vaccination plan for pandemic preparedness [148,149]. This can be accomplished by (1) conducting a pre- and post-assessment surveillance system, (2) ensuring equity and accessibility to vaccines for all target groups, especially high-risk people and vulnerable populations, (3) creating clear communication tools to inform people about the risks of pandemics and the

advantages of vaccinations, (4) maintaining adequate deployment logistics, and (5) increasing vaccination acceptability and raising vaccine awareness. For example, during the 2009 H1N1 influenza pandemic, studies showed that nations with earlier seasonal influenza prevention and control programs, such as the Americas region, were more prepared for pandemic responses than those without programs, such as low-income countries [148,149,150,151].

4.1 Implications

Taken together, using a syndemic approach to explore how VH and COVID-19 interact will help researchers and healthcare workers to consider ways to combine health services in order to focus not only on individual behavior and diseases but the context within which that behavior/disease occurs, and the emotional, structural, and social demands which drive those individuals and their VH and their risk of acquiring COVID-19. By doing so, we minimize missed opportunities for addressing such interactions more holistically. In addition, our research can inspire policymakers to move upstream and implement impactful interventions—at earlier stages—to address accessibility, equity, mental health issues, and VH in healthcare settings. The findings from this research can result in improving the delivery of healthcare, optimizing patients' health, and reducing the treatment costs in Ontario as well as Canada.

4.2 Strengths and Limitations

The strength of this study is that, to our knowledge, this is the first review proposing a framework that addresses COVID-19 and VH. In addition, it highlighted most of the peer-reviewed and non-peer-reviewed articles that discussed COVID-19 as a syndemic, as well as COVID-19 VH. However, this review still has limitations. First, a non-standardized search strategy and inclusion and exclusion criteria were used. Second, the nature of narrative reviews

is considered subjective in terms of selecting which studies to include, analyzing the findings, and drawing conclusions. Third, this review lacks a quality appraisal of the content and the methodologies of the included studies.

5. Conclusions

Understanding the interaction between the three parts of our model is essential to providing policymakers and public health researchers with guidelines to set appropriate interventions and good practices to facilitate COVID-19 vaccination acceptance and uptake, as well as COVID-19-associated measures to decrease the overall burden of disease and adverse outcomes. This framework can be a useful contribution to the huge efforts being made to increase COVID-19 vaccination coverage and bringing us towards the end of the pandemic.

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1.3. Project Rationale

This thesis addressed several key limitations in the existing VH literature by responding to gaps related to measurement tools, population focus, and theoretical frameworks. This section clearly outlines the gaps in prior research, justifies the choice of university students as a study population, and explains the theoretical contribution of adopting a syndemic approach.

1.3.1. Gaps in the Literature

Despite the growing body of research in understanding COVID-19 VH, several gaps remain in the current literature in how VH is measured, analyzed, and conceptualized, particularly in the context of booster doses and evolving pandemic conditions.

First, several existing tools have been developed over the past two decades to measure VH, yet many are limited in scope or applicability to the COVID-19 context. The most well-known among them is the WHO Strategic Advisory Group of Experts (SAGE) Vaccine Hesitancy Scale, developed in 2015 [38]. While this tool has been widely used across different countries and settings [39–42], it contains only two subscales (lack of confidence and risk of vaccination), which may not fully capture the complex and evolving nature of VH. Moreover, it is generally considered psychometrically unstable to rely on fewer than three constructs, as noted in previous research [42].

More recent instruments, such as the Oxford COVID-19 Vaccine Hesitancy Scale and the Vaccination Confidence Scale (VCS), have attempted to respond to pandemic-specific needs [43,44]. The Oxford scale, though psychometrically robust, is limited to a seven-item unidimensional structure that focuses narrowly on vaccine confidence and intention, which could potentially oversimplify and overlook behavioral patterns like vaccine delay or selective refusal. Similarly, the VCS centers on vaccine confidence but does not measure the broader attitudinal, contextual, and behavioral aspects of VH. In contrast, the COVID-19 Vaccine

Hesitancy Scale (CVHS) [45,46], adapted from the Parent Attitudes about Childhood Vaccines (PACV) scale [47], offers a broader tool that captures multiple constructs, including general vaccine attitudes, perceived safety and efficacy, and past vaccination behaviors. Although the CVHS has been validated in Chinese populations [45,46], it has not been psychometrically tested in Western settings, particularly universities, or adapted for booster-specific hesitancy, which may limit its cross-contextual utility.

Second, existing studies have generally assessed VH at a single point in time or for a single vaccine phase, with most recent work focusing on COVID-19 booster hesitancy [10,48–50]. However, little is known about how vaccine attitudes shift within a particular group in response to evolving public health policies, personal experiences, or broader social dynamics. The shift from mandatory to voluntary booster doses creates an important but understudied context. Despite evidence showing significantly lower booster uptake relative to the primary series [4,48,49], no research has examined how VH evolves across different vaccine stages within the same population.

Third, most studies measuring VH with different scales have used a cut-off point to dichotomize VH scores into “hesitant” or “not hesitant” categories [40,51–55]. While this approach is simple to interpret, it fails to capture the full range of variability in VH scores. Treating VH as a continuous construct allows for a more nuanced understanding of attitude variation and provides greater sensitivity in detecting meaningful changes over time or across subgroups.

Fourth, although several conceptual models, such as the 5C model [56], have widely guided research into VH determinants, no prior study has empirically tested how VH has changed or shifted during an era of rapidly spreading infectious disease like COVID-19. The syndemic framework offers a theoretically rich lens to explore such interactions, yet its

application has largely been limited to qualitative or narrative analyses [37]. To date, there is limited empirical research that quantitatively examines how behavioral factors like VH and COVID-19 contextual experiences interact to shape vaccine uptake.

1.3.2. Why Focus on University Students?

University students represent a uniquely important but under-explored population for VH research. Although not traditionally considered a high-risk population for severe COVID-19 outcomes, university students are of particular interest in VH research because they are highly engaged in social networks, often exposed to rapidly changing information environments, and situated at a stage of life where long-term health attitudes are being formed [57]. They are, or will soon be, making independent health decisions not only for themselves but potentially for others in their social or professional circles. University students can thus be considered a critical group for understanding vaccine behavior, given their increased exposure to misinformation, peer influence [58], and evolving sense of social responsibility.

Altogether, the combination of autonomy, social connectivity, and digital exposure makes students an ideal group for studying the dynamics of VH, particularly during the transition from mandated primary vaccination to voluntary booster decisions. Understanding how VH evolves within this population can provide valuable insights for public health strategies beyond the university context, informing targeted communication and intervention efforts during future pandemics or routine immunization campaigns.

1.3.3. Conceptual Contribution: A Syndemic Approach

This thesis extends previous VH research by employing syndemic theory as an overarching conceptual framework. Syndemic theory argues that co-occurring epidemics, whether biological, behavioral, or social, interact synergistically to amplify negative health

outcomes. Although widely discussed in public health literature, empirical applications of syndemic theory remain relatively rare, particularly within quantitative research on VH.

By adopting a syndemic perspective, this thesis explored how VH interacts with pandemic-related experiences (e.g., prior COVID-19 diagnosis, hospitalization, adherence to public health guidelines, and conspiracy beliefs) to shape vaccine behavior. Unlike previous studies, this approach conceptualizes VH as part of a broader interplay between social, behavioral, and contextual factors, providing deeper insights into how these forces interact to influence vaccine uptake.

1.4. Research Objectives

Given the identified gaps and rationale, the overarching purpose of this thesis was to examine COVID-19 VH among university students using syndemic theory. The specific objectives of this thesis were to:

- 1) Validate the CVHS to measure VH towards COVID-19 primary series and booster doses among UW students.
- 2) Estimate the prevalence of VH for both the COVID-19 primary series and booster doses among UW students.
- 3) Identify factors associated with COVID-19 VH, accounting for changes in VH between the primary series and booster doses.
- 4) Assess the syndemic interaction between COVID-19 VH and COVID-19-related factors (e.g., prior infection, hospitalization, public health guidelines compliance, and conspiracy beliefs) and its effect on the uptake of COVID-19 booster doses.

1.5. Methodological Approach

To achieve these objectives, this thesis employed a cross-sectional study design using an online survey administered to students at the University of Waterloo (UW) during the Winter 2024 academic term. A cross-sectional approach was selected because it allowed for the efficient collection of data from a large and diverse sample of university students at a single point in time. The timing of the study, which was after the lifting of vaccine mandates, was particularly well suited for capturing natural variation in VH as decisions became voluntary. The online survey format was chosen for its accessibility, efficiency, and alignment with students' digital communication habits. This mode also offered participants flexibility and anonymity, which likely increased the likelihood of honest disclosure, especially on sensitive topics such as vaccine beliefs, vaccine mandates, and conspiracy-related views.

A core component of the methodology was the adaptation and validation of the CVHS for use among university students to measure VH toward both the primary COVID-19 vaccine series and booster doses, an approach not previously reported in the literature. In the first study of this thesis, we conducted psychometric testing of the CVHS using both Exploratory Factor Analysis (EFA) and Confirmatory Factor Analysis (CFA) to evaluate the scale's validity and internal consistency. Validating the scale was essential to ensure that VH scores could be meaningfully compared across vaccine stages and subgroups.

Additionally, this thesis adopted a VH score-based approach, by keeping the scores in their continuous form instead of classifying them into binary categories such as "hesitant" or "not hesitant". This enabled a more nuanced analysis of individual and subgroup-level differences. In the second study of this thesis, we employed generalized estimating equations (GEE) to model changes in VH scores between primary and booster doses within individuals. GEE was selected because it accounts for correlated observations in repeated measures data and

provides accurate average estimates.

In the last study of this thesis, the methodological focus shifted toward testing the central theoretical framework of the thesis, the syndemic theory. We examined the effect of the interaction between VH and COVID-19-related experiences on booster vaccine uptake by using multivariable logistic regression models with both additive and multiplicative interaction terms. This approach allowed us to assess whether the combined effect of VH and contextual stressors exceeded the sum of their individual effects. Identifying such synergistic interactions aligns with the core tenets of syndemic theory and contributes to a more comprehensive understanding of the complex drivers of vaccine behavior.

1.6. Dissertation Structure

This dissertation is organized into five chapters following a manuscript-based format. Chapter 1 “Introduction” provides the background and theoretical foundation of the thesis, introduces a narrative review of the syndemic framework (presented as a published paper – “Manuscript 1”), identifies key research gaps, explains the rationale for the project, outlines the methodological approach, and states the specific research objectives.

The core objectives of the thesis were addressed in three empirical studies, each presented as a standalone manuscript that was submitted to or published in peer-reviewed journals:

- Chapter 2 presents “Manuscript 2”, which reports the psychometric validation of the CVHS for assessing VH toward both primary and booster COVID-19 doses among UW students.
- Chapter 3 presents “Manuscript 3”, which examines the prevalence of VH across both vaccine stages, explores the changes in VH between the primary and booster phases, and identifies sociodemographic and attitudinal factors associated with these changes.
- Chapter 4 presents “Manuscript 4”, which tests the syndemic framework by analyzing

whether interactions between VH and COVID-19-related experiences (e.g., prior infection, hospitalization, adherence to guidelines, conspiracy beliefs) are associated with lower booster uptake.

Finally, Chapter 5 “Discussion and Conclusion” synthesizes the main findings from the three studies, discusses their implications for public health, highlights the thesis’s strengths and limitations, and reflects on future research directions.

CHAPTER 2 PREAMBLE

The first primary research study of this dissertation (Chapter 2) was designed to address the need for a psychometrically sound tool to measure COVID-19 VH among university students. Given that VH has emerged as a central barrier to sustained vaccine uptake, a reliable and valid assessment tool is essential for both surveillance and intervention planning. Although several VH scales exist, no previous tool has been validated to measure VH toward both primary and booster doses in young adult populations who are navigating unique social, institutional, and policy contexts. Using a consistent, validated tool to assess both primary and booster dose hesitancy simultaneously allows for more accurate comparisons and helps avoid potential measurement biases. By doing so, this study lays the foundation for future research on VH trends, predictors, and interventions in this population. As vaccine campaigns evolve and public attitudes shift, the tools we use to measure VH also need to evolve. Otherwise, they might become outdated or fail to capture new forms of hesitancy.

CHAPTER 2

Manuscript 2: Psychometric validation of the COVID-19 vaccine hesitancy scale for primary and booster doses among university students: A cross-sectional study

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Psychometric validation of the COVID-19 vaccine hesitancy scale for primary and booster doses among university students: A cross-sectional study

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Highlights

- COVID-19 booster uptake was below primary doses, with higher vaccine hesitancy (VH) toward COVID-19 booster doses than primary doses in younger adults.
- Tracking VH evolution across vaccine stages is essential for targeted interventions.
- This study validated the COVID-19 Vaccine Hesitancy Scale (CVHS) to measure VH for primary and booster doses.
- The adapted CVHS reliably and accurately captured vaccine phase-specific shifts in VH among students.

Abstract

Background: Vaccine hesitancy (VH) continues to impede COVID-19 vaccine coverage. Booster dose uptake lags behind primary dose uptake, especially among younger adults. Unlike most studies that focus on initial stages of VH, the aim of this study was to validate the COVID-19 Vaccine Hesitancy Scale (CVHS) for both primary and booster doses among University of Waterloo (UW) students.

Methods: An online survey was conducted among UW students in Ontario, Canada, between March and May 2024. The CVHS items were adapted for primary and booster doses. Exploratory (EFA) and confirmatory factor analyses (CFA) assessed the factor structure and model fit. Reliability was evaluated using Cronbach's alpha and composite reliability (CR). Convergent and discriminant validity were assessed through Average Variance Extracted (AVE). Significant differences between primary and booster dose hesitancy were determined via 95 % Confidence Interval.

Results: A total of 4453 students participated. Respondents were predominantly female (57.2 %), aged 18–22 years (84.0 %), and undergraduates (94.8 %). EFA and CFA confirmed a three-factor structure for both primary and booster dose scales. Both scales had high reliability (Cronbach's alpha >0.60, CR >0.7). CFA results indicated a good model fit (Comparative Fit Index = 0.94; Root Mean Square Error of Approximation = 0.07), and demonstrated adequate convergent, discriminant, and criterion validity. Known-group validity was supported by significant differences in VH scores across gender and academic level, with men and undergraduate students reporting higher hesitancy than women and graduate students ($p < 0.001$). VH was higher for booster doses (33.4 %) than primary doses (19.3 %) with more students delaying (32.1 %) or refusing boosters (29.3 %) than delaying (11.5 %) or refusing (6.2 %) primary doses.

Conclusion: Our adapted scales performed well psychometrically to measure VH across different COVID-19 vaccine phases. These scales can help in identifying key barriers of VH to understand

shifting trajectories over time, thereby informing targeted interventions to promote vaccination uptake among younger adults.

1. Introduction

Canada launched its COVID-19 vaccination campaign in December 2020, initially prioritizing high-risk groups and later expanding eligibility to all Canadians by mid-2021 [1]. As COVID-19 vaccine effectiveness waned within six months of the primary series [2], public health authorities began recommending booster doses in response to emerging variants such as Delta and Omicron [3]. Although 86.8 % of Canadians aged five and older completed the primary series, booster dose coverage has lagged considerably, and only 51.6 % received a third dose [4]. Vaccine coverage for booster doses was higher among older age groups than younger age groups [2]. This disparity echoes broader trends in vaccine hesitancy (VH) in Canada and abroad, which is more prevalent in younger populations, even after adjusting for sociodemographic factors such as ethnicity, gender, and health status [5,6]. Common contributors to this hesitancy include doubts regarding vaccine efficacy, perceived low personal risk of severe illness, concerns about fertility and pregnancy, distrust in public authorities, and confusion stemming from inconsistent messaging [5,6].

Vaccine mandates increased vaccine uptake, particularly within educational institutions, but were not without controversy [7,8]. These policies were intended to reduce absenteeism, contain outbreaks, and facilitate a return to campus life, but also raised concerns about personal autonomy, freedom, and social division between vaccinated and unvaccinated students [8]. As a result, university students emerged as a key population through which to examine the dynamics of VH. Their high mobility, dense social environments, and independence from parental health decisions create unique conditions for infectious disease spread and vaccine decision-making [9]. Prior research highlights that factors such as peer influence, access to information, and individual beliefs shape VH in this group [10]. Yet, little is known about how VH could differ

between the mandatory COVID-19 primary vaccine series and optional booster doses. Students may have complied with mandates for primary vaccinations but relied more heavily on personal beliefs and perceived risks when deciding on receiving booster doses. This suggests that mandates may have masked the true levels of VH. Therefore, exploring students' decisions regarding booster uptake, delays, and refusals offers valuable insights into students' vaccine behaviors when not constrained by institutional policies.

Measuring VH accurately is essential for developing targeted interventions. Previous studies have attempted to measure COVID-19 VH toward booster doses, but methodological limitations persist. Some studies assessed VH using single-item questions, ad hoc questionnaires, or non-validated tools [11,12]. These approaches, while pragmatic, might constrain the ability to detect nuanced patterns across contexts, populations, and phases of vaccine rollout. Others adapted validated instruments such as the WHO's Vaccine Hesitancy Scale (VHS) and the Oxford COVID-19 Vaccine Hesitancy Scale (OCVHS) [[13], [14], [15], [16]]. For example, the VHS was adapted to measure COVID-19 booster hesitancy among pharmacists [13], yet its focus on just two dimensions (e.g., confidence and risk perception) may overlook other psychosocial or behavioral drivers of hesitancy. Similarly, the OCVHS, which has been validated across diverse populations [15,17], was used to assess hesitancy toward the second booster dose of the COVID-19 vaccine [14]. Nonetheless, it remains unidimensional, potentially limiting its scope in capturing beliefs about necessity, prior vaccine behavior, or trust in public institutions.

In contrast, the Parent Attitudes about Childhood Vaccines (PACV) scale offers a broader conceptual model [[18], [19], [20]]. It integrates three dimensions (e.g., general attitudes, beliefs about safety and efficacy, and prior vaccine behaviors) that map more closely

onto vaccine decisions [[18], [19], [20]]. In 2021, the PACV was adapted into the COVID-19 Vaccine Hesitancy Scale (CVHS) to assess VH specific to COVID-19 while preserving its conceptual structure [21]. The CVHS has been validated across Chinese populations, including students, healthcare professionals, and the general public [21], but these efforts have focused on the primary series during the early stages of the pandemic. To date, the scale has not been validated for booster doses, nor in Western university settings, which differ in cultural, institutional, and policy contexts. As vaccine decision-making shifts from mandated compliance to autonomous choice, there is a need to determine whether the CVHS remains a valid and reliable measure across vaccine phases and populations.

Using a consistent, validated tool to assess both primary and booster dose hesitancy allows for more accurate comparisons and avoids potential measurement biases. Therefore, the aim of this study was to validate the CVHS to measure VH toward COVID-19 primary series and booster doses among University of Waterloo (UW) students. In doing so, this study contributes a psychometrically sound instrument for tracking evolving patterns of VH in young adults as public health contexts and vaccination policies continue to shift.

2. Methods

2.1. Study design and target population

We conducted a cross-sectional study using an online, anonymous, self-reported questionnaire. The target population included all full-time and part-time undergraduate and graduate students at UW, a large public research university in Ontario, Canada. This included domestic and international students, across all faculties and programs, who were registered during the Winter 2024 academic term. As of Winter 2024, the university reported an enrollment

of 34,398 undergraduate and 6010 graduate students [22]. Students were excluded if they were not actively enrolled during the study period or if they declined to provide informed consent.

2.2. Sampling and data collection

We administered the survey through the Qualtrics platform and prevented duplicate submissions via the platform's settings. Students gave informed consent on the first page of the online survey and only those who consented were able to complete the 10–15 min questionnaire. Students who participated had the option to enter a draw to win one of fifty \$25 credits added to their on-campus purchasing card, by providing their names and email addresses. To preserve the anonymity of survey responses, the link where respondents could opt into the prize draw was separate from the survey.

The Registrar's Office distributed recruitment emails to all 34,398 undergraduate students, and the Graduate Studies and Postdoctoral Affairs Office shared the survey with 6010 graduate students through weekly newsletters and emails from graduate program coordinators (Fig. 1). The emails included a recruitment letter explaining the survey objectives, compensation, and the researchers' contact information alongside the survey link. We also promoted the survey on social media platforms such as LinkedIn, Twitter, and Instagram. The survey was open from March 18 to May 1, 2024. We sent weekly reminders to students who had not opted out of further communication. Our study received ethics clearance from the UW's Research Ethics Board.

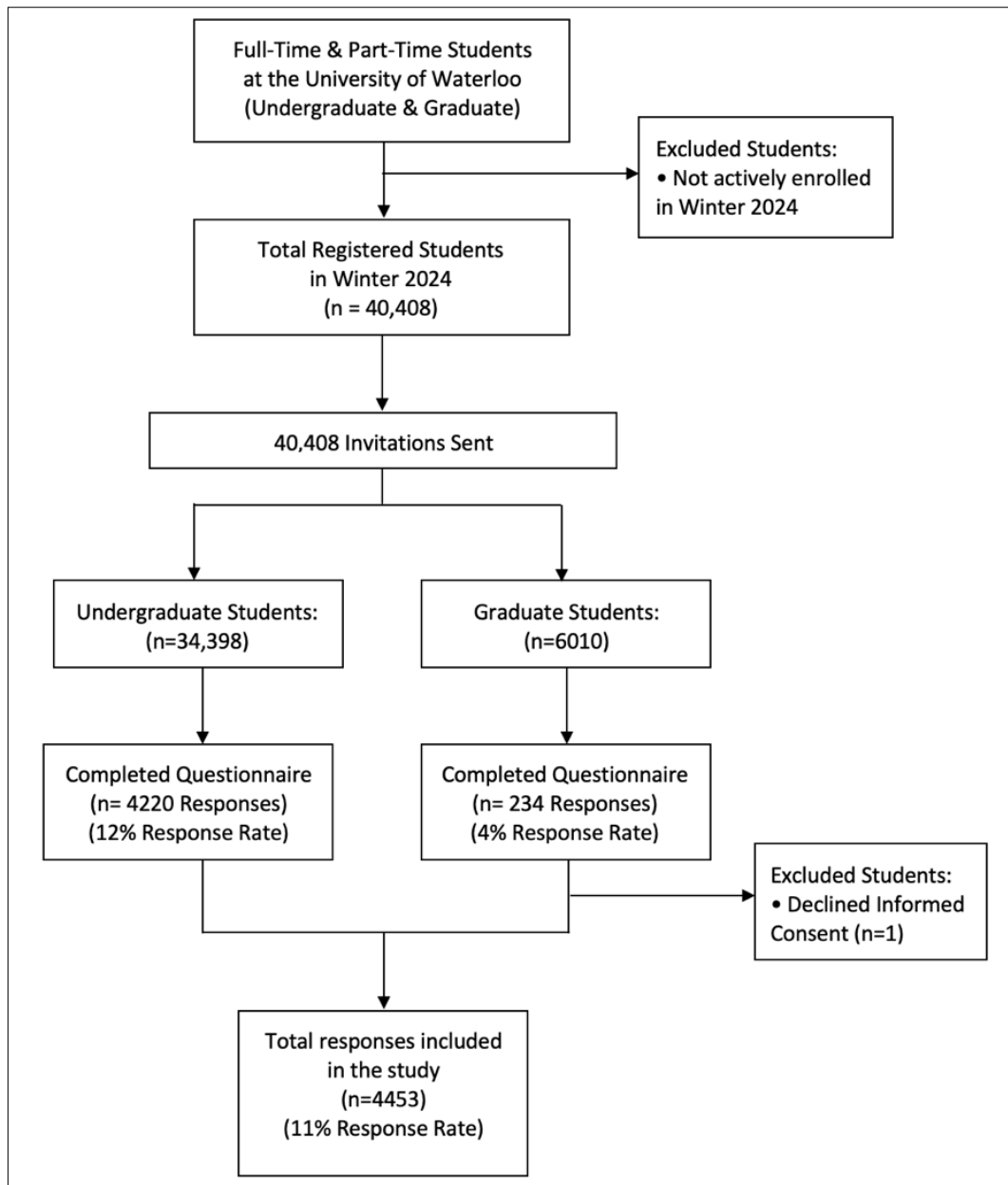


Fig. 1. Flowchart represents the selection and response rate of the study population.

2.3. Questionnaire development

We structured the questionnaire (Supplementary Material #1) into six sections and used various question formats, including multiple choice, multiple responses, yes/no/don't know, and Likert scale questions. We included a “prefer not to say” option in most of the survey questions. We adapted and derived the questions from previously published surveys and validated scales,

including the CVHS [21], the PACV [[18], [19], [20]], COVID-19 Vaccination Coverage Survey–StatCan [23], the Canadian Community Health Survey (CCHS)–StatCan [24], Vaccine Confidence Survey Question Bank [25], 5C psychological antecedents of vaccination [26], OCVHS [15], and VHS [16]. When measures were not available, items were developed by the authors.

2.4. Measurements

The primary outcome of this validation study was VH toward COVID-19 primary series and booster doses. We measured this using the 15 items of the existing CVHS [21]. We used the existing scale to capture hesitancy toward the primary COVID-19 vaccine series, and then modified the wording to focus on boosters, to capture VH toward booster doses. For the “Behavior” items, we adapted the wording to reflect past vaccination behavior, consistent with the PACV scale [[18], [19], [20]], rather than using the future tense in the CVHS [21]. The detailed wording of all items, the scale scoring system, and the permission to use the PACV scale are in Supplementary Material #2.

2.5. Content validity

We assessed content validity iteratively through multiple rounds of revisions by the research team and the Statistical Consulting and Survey Research Unit at UW.

2.6. Pretesting, piloting, and face validity

To establish face validity, we pretested the survey with 33 students across genders, ages, and academic faculties. The pretest included both in-person and online formats, where participants completed the questionnaire and provided feedback on several dimensions: clarity of the questions, ease of navigation, and any difficulties in interpretation. Ambiguities reported by

participants were addressed in subsequent revisions. We then piloted the survey with 600 undergraduate and graduate students, recruited via email from the Registrar's Office and program coordinators, to test recruitment strategies and survey procedures. The response rate was 9.5 % ($n = 57$), with no major procedural issues reported.

2.7. Sample size calculation

We calculated our target sample size of 1121 students using the primary series VH rate from the pilot (24 %), with a 95 % confidence level and a 2.5 % margin of error [27]. To ensure proportional representation, we stratified the target sample size into 955 undergraduates ($\frac{34,398}{40,408} \times 1,121$) and 167 graduates ($\frac{6,010}{40,408} \times 1,121$) [28]. Given the ~10 % response rate in the pilot, we invited the entire UW student population to participate, aiming to achieve the desired sample size. Full details of the calculations are provided in Supplementary Material #2.

2.8. Data analysis

We calculated the percentage of missing data for each question and assessed the type of missingness using Little's MCAR test [29]. Missing values were then imputed using the expectation maximization technique [30]. We analyzed demographic variables and the two scales' responses descriptively. We compared the gender, age groups, faculty of study, and study level/year characteristics of our sample with those of the overall UW student population using demographic data from the UW Institutional Analysis and Planning [28], and 95 % confidence intervals. We applied sampling weights to adjust for gender distribution. All statistical analyses were conducted using IBM SPSS version 29.0 and AMOS version 29.0, with significance level set at 0.05.

2.9. Reliability and validity assessment

i. Exploratory and confirmatory factor analyses

We used Exploratory Factor Analysis (EFA) to examine the underlying structure of the scale by grouping items based on their inter-correlations [31]. Items with high inter-correlations were loaded together under the same domain. We assessed the appropriateness of the data for EFA using Bartlett's test of sphericity and the Kaiser-Meyer-Olkin (KMO) measure for sampling adequacy [32,33]. A significant Bartlett's test ($p < 0.05$) and a KMO value of at least 0.5 were necessary to run a valid EFA (Supplementary Material #2, Table S1) [32,33]. We determined the number of factors to extract using the Kaiser criterion (Eigenvalue > 1) and further confirmed factor retention through the Scree plot [31,33]. We performed EFA using Principal Component Analysis with Varimax rotation and Kaiser Normalization [33,34]. Items were retained under a factor if they had loadings greater than 0.4, with cross-loading items assigned to the factor with the highest loading [32].

Based on the results of EFA, we performed Confirmatory Factor Analysis (CFA) to further assess the goodness-of-fit for the overall scale structure including both convergent and discriminant validity for the intra-dimensions of the domains [35]. We evaluated goodness of fit by indices, including the Chi-Square (χ^2), Root Mean Square Error of Approximation (RMSEA), Standardized Root Mean Square Residual (SRMR), Comparative Fit Index (CFI), Tucker Lewis Index (TLI), Goodness-of-Fit Index (GFI), Incremental Fit Index (IFI), Normed Fit Index (NFI), Relative Fit Index (RFI), Adjusted Goodness-of-Fit Index (AGFI), Parsimonious Normed Fit Index (PNFI), and Parsimony Goodness-of-Fit Index (PGFI), following recommended cut-off values from the literature (Supplementary Material #2, Table S2) [35,36].

ii. Reliability

We assessed the internal consistency of the two scales by calculating Cronbach's alpha for each subdomain, considering $\alpha \geq 0.60$ as moderate reliability and $\alpha \geq 0.70$ as high reliability [37]. Additionally, we calculated Composite Reliability (CR) based on standardized factor loadings from CFA, with a CR of 0.60 or higher deemed acceptable [32,38]. Recommended reliability cut-off values are presented in Supplementary Material #2, Table S3.

iii. Convergent and discriminant validity

We used standardized factor loadings from CFA to assess convergent and discriminant validity. We evaluated convergent validity by calculating the Average Variance Extracted (AVE) and CR. An AVE greater than 0.50 was considered sufficient [38,39]; however, AVE values between 0.40 and 0.50 were deemed acceptable if CR was above 0.60, as per the Fornell and Larcker rule [38]. We assessed discriminant validity using the square root of AVE, as each construct's square root AVE should exceed its Pearson correlations with other latent constructs in the model [35,38]. Validity thresholds are in Supplementary Material #2, Table S3.

iv. Criterion and construct validity

We examined criterion validity through bivariate Pearson correlation analysis between the constructs of both scales (primary vs. boosters) [21]. Adequate criterion validity was established when correlations between similar constructs were significant and higher than correlations between different constructs across the two scales.

To assess construct and known-group validity, we compared COVID-19 VH scores between the primary and booster doses across demographic groups such as age, gender, and academic level. Mean differences in VH scores were examined using a paired *t*-test. This

approach was recommended by Boateng et al., [40] as it supports the scale's ability to discriminate between known groups and thus provides evidence of construct validity.

3. Results

A total of 4453 of 40,408 students completed the questionnaire, yielding a response rate of 11 %, slightly higher than the response rate in the pilot study. Missing data were minimal, and the data were missing completely at random (p -value 1.00). Most questions had <3 % missing responses. The two questions with the most missing data were about people living in the household and were more than 93 % complete (Supplementary Material #2, Table S4).

Table 1 presents the demographic characteristics of our sample, before and after weighting, in comparison to the UW student body. Before weighting, our sample included significantly more women (57.2 %, 95 % CI: 55.7, 58.7) and younger students (84.0 %, 95 % CI: 82.9, 85.1) compared to the overall UW student population (46.8 % women and 78.1 % younger students). However, our sample was representative of the academic level and faculty of study of all UW students. After applying sampling weights, the sample demographics closely aligned with the overall population, particularly for gender representation.

Table 1. Demographic characteristics of study participants, and the University of Waterloo student population, 2024

Demographic Characteristic	Without Sampling Weight (<i>n</i> = 4453)			With Sampling Weight by Gender (<i>n</i> = 4453)			UW Students (<i>n</i> = 40,408)	
	n	%	95 % C.I. *	n	%	95 % C.I. *	n	%
Gender								
Woman	2547	57.2	(55.7, 58.7)	2083	46.8	(45.3, 48.3)	18903	46.8
Man	1689	37.9	(36.5, 39.4)	2292	51.5	(50.0, 52.9)	20807	51.5
Others ^a	126	2.8	(2.4, 3.4)	45	1.0	(0.7, 1.3)	698	1.7
Prefer not to say	91	2.0	(1.6, 2.5)	33	0.7	(0.5, 1.0)	–	–
Age								
10-22	3742	84.0	(82.9, 85.1)	3769	84.6	(83.5, 85.7)	31540	78.1
23-29	604	13.6	(12.6, 14.6)	587	13.2	(12.2, 14.2)	6478	16.0
30-39	75	1.7	(1.3, 2.1)	69	1.5	(1.2, 2.0)	1687	4.2
40-85	32	0.7	(0.5, 1.0)	28	0.6	(0.4, 0.9)	703	1.7
Academic level								
Undergraduate year 1	935	21.0	(19.8, 22.2)	945	21.2	(20.0, 22.5)	7231	17.9
Undergraduate year 2	906	20.3	(19.2, 21.6)	910	20.4	(19.3, 21.7)	8550	21.2
Undergraduate year 3	1120	25.2	(23.9, 26.5)	1104	24.8	(23.5, 26.1)	8736	21.6
Undergraduate year 4 or 4+	1258	28.3	(26.9, 29.6)	1267	28.4	(27.1, 29.8)	9034	22.4
Master's student	149	3.3	(2.8, 3.9)	147	3.3	(2.8, 3.9)	3782	9.4
PhD	64	1.4	(1.1, 1.8)	63	1.4	(1.1, 1.8)	2190	5.4
Others ^b	21	0.5	(0.3, 0.7)	18	0.4	(0.2, 0.6)	885	2.2
Faculties								
Arts	843	18.9	(17.8, 20.1)	761	17.1	(16.0, 18.2)	8225	20.4
Engineering	1077	24.2	(22.9, 25.5)	1164	26.1	(24.9, 27.5)	10852	26.9
Environment	350	7.9	(7.1, 8.7)	353	7.9	(7.2, 8.8)	2837	7.0
Health	510	11.5	(10.5, 12.4)	470	10.6	(9.7, 11.5)	3508	8.7
Mathematics	856	19.2	(18.1, 20.4)	928	20.8	(19.7, 22.1)	8622	21.3
Science	817	18.3	(17.2, 19.5)	776	17.4	(16.3, 18.6)	6364	15.7
Status								
Domestic	3879	87.1	(86.1, 88.1)	3855	86.6	(85.5, 87.6)	–	–
International	574	12.9	(11.9, 13.9)	598	13.4	(12.4, 14.5)	–	–
Indigenous identity								
Yes	63	1.4	(1.1, 1.8)	60	1.4	(1.0, 1.7)	–	–
No	4322	97.1	(96.5, 97.5)	4337	97.4	(96.9, 97.8)	–	–
Prefer not to say	68	1.5	(1.2, 1.9)	56	1.3	(1.0, 1.6)	–	–

Immigration status

Canadian citizen or Permanent resident	3867	86.8	(85.6, 87.6)	3842	86.3	(85.2, 87.3)	—	—
Temporary resident	509	11.4	(10.5, 12.4)	536	12.0	(11.1, 13.0)	—	—
Others ^c	7	0.2	(0.3, 0.7)	21	0.5	(0.3, 0.7)	—	—
Prefer not to say	70	1.6	(1.2, 2.0)	54	1.2	(0.9, 1.6)	—	—

Income level

Less than \$29 999	1125	25.3	(24.0, 26.6)	1111	24.9	(23.7, 26.2)	—	—
\$30 000 to \$59 999	413	9.3	(8.4, 10.2)	425	9.5	(8.7, 10.4)	—	—
\$60 000 to \$89 999	380	8.5	(7.7, 9.4)	378	8.5	(7.7, 9.3)	—	—
Greater than \$90 000	1092	24.5	(23.3, 25.8)	1130	25.4	(24.1, 26.7)	—	—
Don't know	759	17.0	(16.0, 18.2)	733	16.5	(15.4, 17.6)	—	—
Prefer not to say	684	15.4	(14.3, 16.5)	675	15.2	(14.1, 16.2)	—	—

Marital status

Single	4057	91.1	(90.2, 91.9)	4094	91.9	(91.1, 92.7)	—	—
Married	99	2.2	(1.8, 2.7)	95	2.1	(1.7, 2.6)	—	—
Others ^d	178	4.0	(3.4, 4.6)	166	3.7	(3.2, 4.3)	—	—
Prefer not to say	119	2.7	(2.2, 3.2)	98	2.2	(1.8, 2.7)	—	—

Employment status

Employed (full time, part time, co-op term)	2221	49.9	(48.4, 51.4)	2210	49.6	(48.2, 51.1)	—	—
Unemployed	2057	46.2	(44.7, 47.7)	2078	46.7	(45.2, 48.1)	—	—
Prefer not to say	175	3.9	(3.4, 4.5)	164	3.7	(3.1, 4.3)	—	—

(-) means that comparable data were not available for the University of Waterloo student population.

* Significant differences between study participants and the UW student body are shown in bold.

^a Others included Non-binary, Third gender, Transgender, LGBTQ+.

^b Others included Non-degree, Exchange students, Transfer students.

^c Others included Asylum, Refugees, Undocumented.

^d Others included Common law, Engaged, Separated, Divorced, Widowed, In a relationship.

Table 2 and Table 3 show students' responses to the two scale items related to COVID-19 primary series and booster doses. Overall, more students were hesitant toward booster doses (33.4 %, 95 % CI: 32.1, 34.8) than primary doses (19.3 %, 95 % CI: 18.1, 20.5). Delaying (32.1 %, 95 % CI: 30.8, 33.5) or refusing (29.3 %, 95 % CI: 28.0, 30.7) booster doses was significantly higher than delaying (11.5 %, 95 % CI: 10.6, 12.5) or refusing (6.2 %, 95 % CI: 5.5, 7.0) primary doses. Most students (79.7 %; 95 % CI: 78.5, 80.9) believed that primary doses could prevent severe COVID-19 outcomes, but significantly fewer (58.0 %; 95 % CI: 56.6, 59.5) held the same belief about booster doses. Trust in vaccine information was generally high across both primary and booster doses; however, mistrust in doctors' recommendations was nearly double for boosters (25.0 %, 95 % CI: 23.7, 26.3) compared to primary doses (15.1 %, 95 % CI: 14.1, 16.2).

Table 2. Descriptive statistics of items of the PACV–CVHS scale for COVID-19 primary doses (1st and 2nd).

Construct	Items	Response	n	%	95% CI
Behaviour T1	Have you ever delayed getting the COVID-19 primary doses (1st and 2nd) for reasons other than illness or allergy?	Yes	512	11.5	10.6, 12.5
		Don't know*	120	2.7	2.2, 3.2
		No	3821	85.8	84.8, 86.8
Behaviour T2	Have you ever decided not to get the COVID-19 primary doses (1st and 2nd) for reasons other than illness or allergy?	Yes	277	6.2	5.5, 7.0
		Don't know*	107	2.4	2.0, 2.9
		No	4069	91.4	90.5, 92.2
Safety T3	It is better for me to only get one vaccine at a time (e.g., only COVID-19 primary dose, or only Flu dose).	Agree ^a	1509	33.9	32.5, 35.3
		Not sure	1646	37.0	35.5, 38.4
		Disagree	1298	29.1	27.8, 30.5
Safety T4	How concerned are you that the COVID-19 primary doses (1st and 2nd) might not be safe?	Concerned ^b	1107	24.9	23.6, 26.2
		Not sure	325	7.3	6.5, 8.1
		Not concerned	3021	67.8	66.5, 69.2
Safety T5	How concerned are you that you might have a serious side effect from getting the COVID-19 primary doses	Concerned	1352	30.4	29.0, 31.7
		Not sure	469	10.5	9.7, 11.5

	(1st and 2nd)?	Not concerned	2632	59.1	57.6, 60.6
Safety T6	How concerned are you that COVID-19 primary doses (1st and 2nd) might not prevent the COVID-19?	Concerned	1181	26.5	25.2, 27.8
		Not sure	668	15.0	14.0, 16.1
		Not concerned	2604	58.5	57.0, 59.9
Attitude T7	How sure are you that getting the recommended COVID-19 primary doses (1st and 2nd) is a good idea for you?	0-5 ^c	705	15.8	14.8, 16.9
		6-7	838	18.8	17.7, 20.0
		8-10	2910	65.3	63.9, 66.8
Attitude T8	It is not necessary to get the COVID-19 primary doses (1st and 2nd).	Agree	640	14.4	13.3, 15.4
		Not sure	693	15.6	14.5, 16.7
		Disagree	3120	70.1	68.7, 71.4
Attitude T9	I believe that the COVID-19 primary doses (1st and 2nd) can prevent the severe outcomes of the COVID-19 disease.	Disagree	307	6.9	6.2, 7.7
		Not sure	595	13.4	12.4, 14.4
		Agree	3551	79.7	78.5, 80.9
Attitude T10	It is better for you to develop immunity by getting COVID-19 than to get the COVID-19 primary doses (1st and 2nd).	Agree	719	16.1	15.1, 17.3
		Not sure	851	19.1	18.0, 20.3
		Disagree	2883	64.7	63.3, 66.2
Attitude T11	Would you recommend your friends and family members to get the COVID-19 primary doses (1st and 2nd)?	No	532	11.9	11.0, 12.9
		Not sure	564	12.7	11.7, 13.7
		Yes	3357	75.4	74.1, 76.7
Attitude T12	Overall, how hesitant about the COVID-19 primary doses (1st and 2nd) would you consider yourself to be?	Hesitant ^d	859	19.3	18.1, 20.5
		Not sure	272	6.1	5.4, 6.8
		Not hesitant	3322	74.6	73.3, 75.9
Attitude T13	I trust the information I receive about the COVID-19 primary doses (1st and 2nd).	Disagree	526	11.8	10.9, 12.8
		Not sure	950	21.3	20.1, 22.6
		Agree	2977	66.9	65.5, 68.2
Attitude T14	I am able to openly discuss my concerns about COVID-19 primary doses (1st and 2nd) with my doctor.	Disagree	429	9.6	8.8, 10.5
		Not sure	1169	26.3	25.0, 27.6
		Agree	2855	64.1	62.7, 65.5
Attitude T15	All things considered; how much do you trust your doctor's recommendations regarding COVID-19 primary doses (1st and 2nd)? *Your family doctor if you have one. If not, indicate how much you generally trust doctors	0-5 ^c	672	15.1	14.1, 16.2
		6-7	933	21.0	19.8, 22.2
		8-10	2848	64.0	62.5, 65.4

T1, T2 – “Behaviour” subdomain.

T3, T4, T5, T6 – “Safety and Efficacy” subdomain.

T7, T8, T9, T10, T11, T12, T13, T14, T15 – “General Attitudes” subdomain.

* ‘Don’t know’ response was excluded as missing data.

^a Agree reflects combined responses of strongly agree and agree; disagree reflects combined responses of strongly disagree and disagree.

^b Concerned reflects combined responses of very and somewhat concerned; not concerned reflects combined responses of not concerned at all and not too concerned.

^c Response category on a 0–10 scale, with 0 being ‘not at all sure’ and 10 being ‘completely sure’.

^d Hesitant reflects combined responses of very and somewhat hesitant; not hesitant reflects combined responses of not hesitant at all and not too hesitant.

^e Response category on a 0–10 scale, with 0 being ‘do not trust at all’ and 10 being ‘completely trust’.

Table 3. Descriptive statistics of items of the PACV–CVHS scale for COVID-19 booster doses (3rd or more)

Construct	Items	Response	n	%	95% CI
Behaviour T1	Have you ever delayed getting the COVID-19 booster doses (3rd or more) for reasons other than illness or allergy?	Yes	1431	32.1	30.8, 33.5
		Don’t know*	240	5.4	4.7, 6.1
		No	2782	62.5	61.0, 63.9
Behaviour T2	Have you ever decided not to get the COVID-19 booster doses (3rd or more) for reasons other than illness or allergy?	Yes	1306	29.3	28.0, 30.7
		Don’t know*	223	5.0	4.4, 5.7
		No	2924	65.7	64.2, 67.1
Safety T3	It is better for me to only get one vaccine at a time (e.g., only COVID-19 booster dose, or only Flu dose).	Agree ^a	1457	32.7	31.3, 34.1
		Not sure	1705	38.3	36.9, 39.7
		Disagree	1291	29.0	27.7, 30.3
Safety T4	How concerned are you that the COVID-19 booster doses (3rd or more) might not be safe?	Concerned ^b	1043	23.4	22.2, 24.7
		Not sure	562	12.6	11.7, 13.6
		Not concerned	2848	64.0	62.5, 65.4
Safety T5	How concerned are you that you might have a serious side effect from getting the COVID-19 booster doses (3rd or more)?	Concerned	1318	29.6	28.3, 31.0
		Not sure	555	12.5	11.5, 13.5
		Not concerned	2580	57.9	56.5, 59.4
Safety T6	How concerned are you that COVID-19 booster doses (3rd or more) might not prevent the COVID-19?	Concerned	1280	28.7	27.4, 30.1
		Not sure	785	17.6	16.5, 18.8
		Not concerned	2388	53.6	52.1, 55.1
Attitude T7	How sure are you that getting the recommended COVID-19 booster doses (3rd or more) is a good idea for you?	0-5 ^c	1580	35.5	34.1, 36.9
		6-7	1040	23.4	22.1, 24.6
		8-10	1833	41.2	39.7, 42.6
Attitude T8	It is not necessary to get the COVID-19 booster doses (3rd or more) at this time.	Agree	1902	42.7	41.3, 44.2
		Not sure	1330	29.9	28.5, 31.2
		Disagree	1221	27.4	26.1, 28.8

Attitude T9	I believe that the COVID-19 booster doses (3rd or more) can prevent the severe outcomes of the COVID-19 disease.	Disagree	541	12.1	11.2, 13.1
		Not sure	1328	29.8	28.5, 31.2
		Agree	2584	58.0	56.6, 59.5
Attitude T10	It is better for you to develop immunity by getting COVID-19 than to get the COVID-19 booster doses (3rd or more).	Agree	839	18.8	17.7, 20.0
		Not sure	1102	24.7	23.5, 26.0
		Disagree	2512	56.4	54.9, 57.9
Attitude T11	Would you recommend your friends and family members to get the COVID-19 booster doses (3rd or more)?	No	1171	26.3	25.0, 27.6
		Not sure	1263	28.4	27.0, 29.7
		Yes	2019	45.3	43.9, 46.8
Attitude T12	Overall, how hesitant about the COVID-19 booster doses (3rd or more) would you consider yourself to be?	Hesitant ^d	1489	33.4	32.1, 34.8
		Not sure	519	11.7	10.7, 12.6
		Not hesitant	2445	54.9	53.4, 56.4
Attitude T13	I trust the information I receive about the COVID-19 booster doses (3rd or more).	Disagree	656	14.7	13.7, 15.8
		Not sure	1198	26.9	25.6, 28.2
		Agree	2599	58.4	56.9, 59.8
Attitude T14	I am able to openly discuss my concerns about COVID-19 booster doses (3rd or more) with my doctor.	Disagree	401	9.0	8.2, 9.9
		Not sure	1188	26.7	25.4, 28.0
		Agree	2864	64.3	62.9, 65.7
Attitude T15	All things considered; how much do you trust your doctor's recommendations regarding COVID-19 booster doses (3rd or more)? *Your family doctor if you have one. If not, indicate how much you generally trust doctors	0-5 ^e	1112	25.0	23.7, 26.3
		6-7	1013	22.7	21.5, 24.0
		8-10	2328	52.3	50.8, 53.8

T1, T2 – “Behaviour” subdomain.

T3, T4, T5, T6 – “Safety and Efficacy” subdomain.

T7, T8, T9, T10, T11, T12, T13, T14, T15 – “General Attitudes” subdomain.

* ‘Don’t know’ response was excluded as missing data.

^a Agree reflects combined responses of strongly agree and agree; disagree reflects combined responses of strongly disagree and disagree.

^b Concerned reflects combined responses of very and somewhat concerned; not concerned reflects combined responses of not concerned at all and not too concerned.

^c Response category on a 0–10 scale, with 0 being ‘not at all sure’ and 10 being ‘completely sure’.

^d Hesitant reflects combined responses of very and somewhat hesitant; not hesitant reflects combined responses of not hesitant at all and not too hesitant.

^e Response category on a 0–10 scale, with 0 being ‘do not trust at all’ and 10 being ‘completely trust’.

3.1. Exploratory factor analysis (EFA)

The KMO measure of sampling adequacy was 0.935 for the primary doses scale and 0.928 for booster doses scale; thus, the sample size was adequate for factor analysis. Bartlett's test of Sphericity was highly significant for both scales ($p < 0.001$). EFA yielded three factors for both scales (eigenvalues > 1). The three factors explained 58 % of the total variance in the primary doses scale and 61 % in the booster doses scale. For the primary doses scale, factor loadings ranged from 0.507 to 0.820. All items loaded on the expected subscales as the original scale except for T4 and T12, which cross-loaded on two factors but still had higher loadings on their respective factors (Table 4). In the booster doses scale, factor loadings ranged from 0.459 to 0.864, with all items loading on their corresponding factors, except for T4, T5, T6, and T8 (Table 5). Items T4, T5, and T6 loaded onto the “Attitude” subscale instead of the “Safety” subscale, and item T8 loaded onto the “Safety” instead of the “Attitude” factor. Hence, T4, T5, and T6 were reclassified under the “Attitude” and T8 under the “Safety”.

Table 4. Factor loadings for the COVID-19 primary doses scale

	Subscales		
	Behaviour	Safety and efficacy	General Attitudes
T1	0.820		
T2	0.758		
T3		0.621	
T4		0.665	0.417
T5		0.742	
T6		0.539	
T7			0.782
T8			0.703
T9			0.71
T10			0.592
T11			0.75
T12		0.484	0.507
T13			0.739
T14			0.53
T15			0.736

Extraction Method: Principal Component Analysis.
 Rotation Method: Varimax with Kaiser Normalization.
 Factor loadings ≥ 0.4 were retained.

Bolded item means that it is loaded on its corresponding subscale as in the original scale.

Table 5. Factor loadings for the COVID-19 booster doses scale

	Subscales		
	Behaviour	Safety and efficacy	General Attitudes
T1	0.864		
T2	0.821		
T3		0.807	
T4			0.784
T5			0.682
T6			0.632
T7			0.673
T8		0.592	
T9			0.689
T10		0.413	0.459
T11			0.622
T12			0.665
T13			0.810
T14			0.665
T15			0.768

Extraction Method: Principal Component Analysis.

Rotation Method: Varimax with Kaiser Normalization.

Factor loadings ≥ 0.4 were retained.

Bolded item means that it is loaded on its corresponding subscale as in the original scale.

3.2. Confirmatory factor analysis (CFA)

CFA results for the primary doses scale (Model 1–Primary) indicated a good model fit (CFI = 0.935; IFI = 0.935; NFI = 0.933; TLI = 0.922; GFI = 0.941; AGFI = 0.918; RMSEA = 0.071; SRMR = 0.0379) (Fig. 2 and Table 6). For the booster doses scale, two models were constructed. The first model (Model 1–Booster) was based on our EFA results as follows: “Behavior” with 2 items, “Safety and Efficacy” with 2 items (T3, T8), and “General Attitudes” with 11 items (by adding T4, T5, T6, and removing T8). The second model (Model 2–Booster) was based on the original CVHS structure. The CFA for (Model 1–Booster) demonstrated poor fit, as most of the indices did not meet the cut-off values. In contrast, (Model 2–Booster) showed improvement, yet still some indices did not achieve the recommended

criteria (e.g., AGFI = 0.881, lower than 0.9; RMSEA = 0.083, above 0.08). Modification indices for Model 2–Booster suggested that allowing error terms to covary could significantly improve the model fit. After modifications (Fig. 3), the revised CFA model (Model 3–Booster) showed a good fit across all indices (CFI = 0.942; IFI = 0.942; NFI = 0.94; TLI = 0.924; GFI = 0.942; AGFI = 0.913; RMSEA = 0.073; SRMR = 0.0401) (Table 6).

3.3. Reliability, convergent, and discriminant validity

Both scales demonstrated good internal consistency across all dimensions (Cronbach's $\alpha \geq 0.60$) and (CR ≥ 0.60) (Table 7). The “General Attitudes” dimension in both scales showed the highest reliability, whereas the “Safety and Efficacy” and the “Behavior” dimensions showed moderate to high reliability. Convergent validity was established for both scales (Table 7). All the dimensions met the AVE threshold (AVE > 0.5) except for the “Safety” (AVE = 0.413, CR = 0.706) and “Behavior” (AVE = 0.484, CR = 0.652) dimensions in the primary scale, but still met the criteria, as their AVE values were above 0.4 and their CR values exceeded 0.6. Discriminant validity was also established, as the square root of AVE for each dimension exceeded its highest correlation with other dimensions (Table 7).

3.4. Criterion and construct validity

Table 8 presents the results of the bivariate Pearson correlation analysis between the primary and booster dose scales. The three subscales and their total scores in both scales were significantly and positively correlated. Additionally, correlations between identical constructs in the two scales (e.g., “Attitude” in the primary scale and “Attitude” in the booster scale) were stronger than correlations between different constructs.

For construct and known-group validity, VH scores were significantly different across demographic groups (Supplementary Material #2, Table S5). Mean VH scores were significantly higher for booster doses compared to primary doses across all gender groups ($p < 0.001$), with men reporting higher hesitancy than women for both vaccine stages (primary and boosters). Similarly, undergraduate students showed significantly higher hesitancy scores than graduate students ($p = 0.003$). Although age-related differences were not significant ($p = 0.263$), older participants (40–85 years) showed higher VH scores overall.

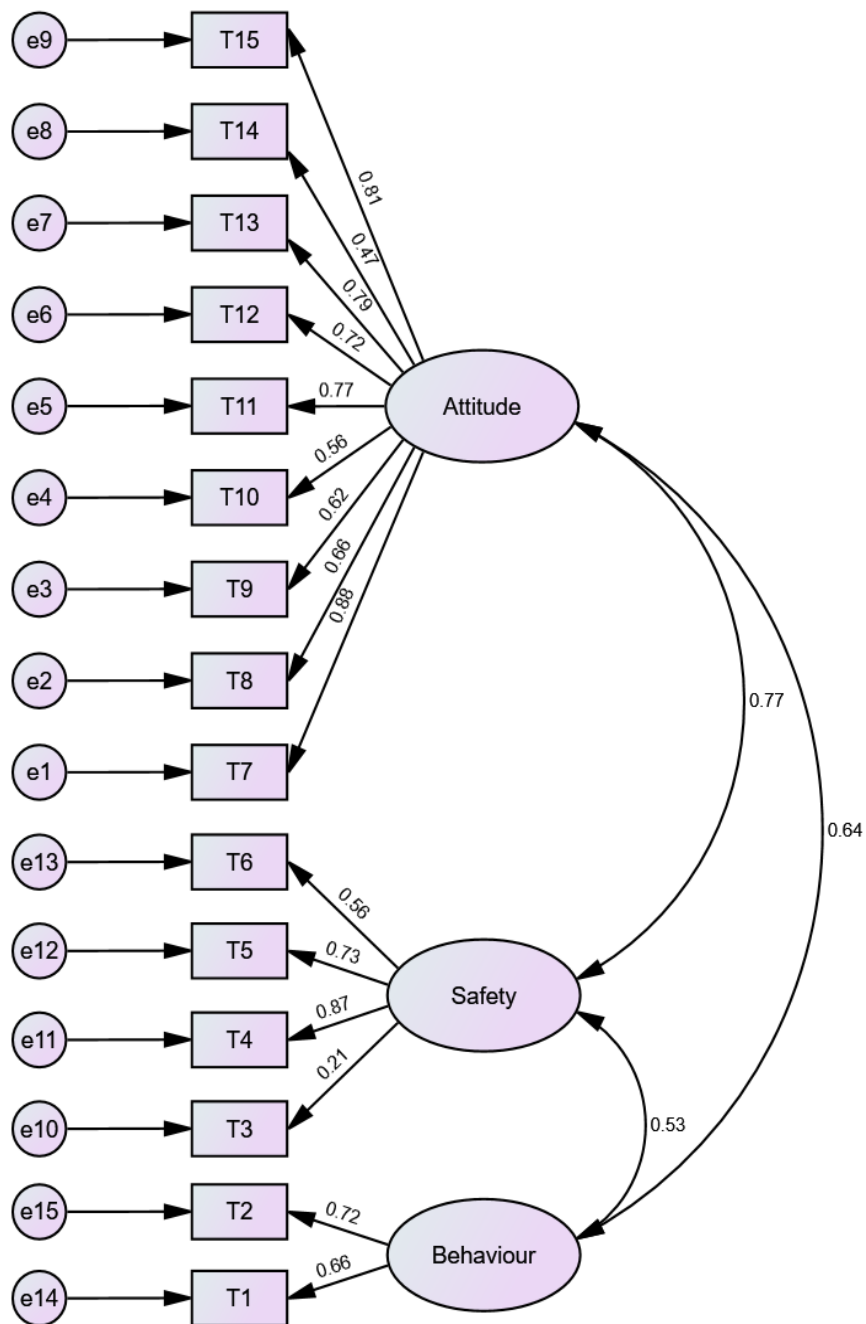


Fig. 2. Confirmatory factor analysis for model 1– primary doses scale based on the original COVID-19 Vaccine Hesitancy Scale (CVHS) structure; “Behavior” 2 items (T1, T2), “Safety and Efficacy” 4 items (T3 to T6), and “General Attitudes” 9 items (T7 to T15)

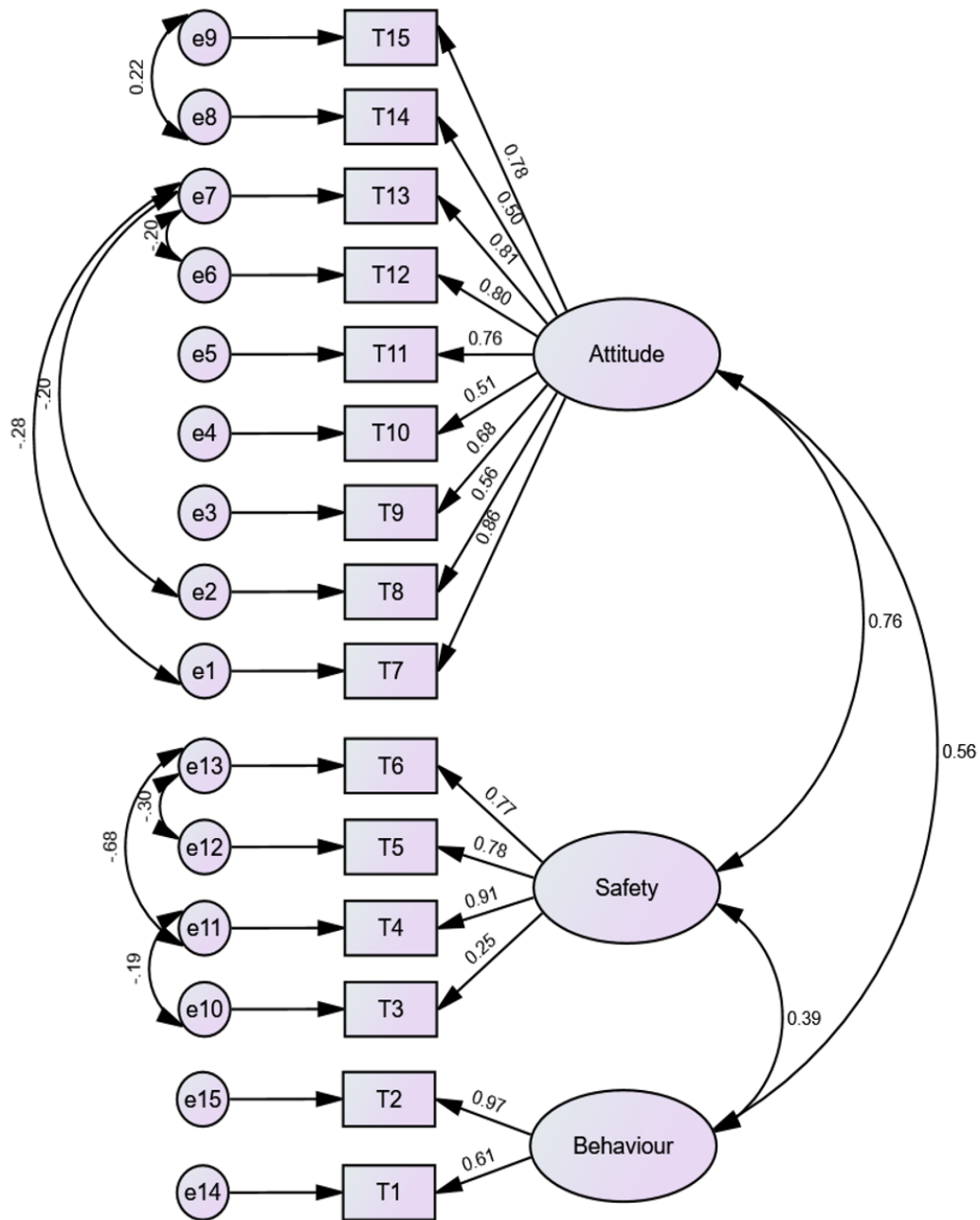


Fig. 3. Confirmatory factor analysis for model 3– booster doses scale after modifications based on the original COVID-19 Vaccine Hesitancy Scale (CVHS) structure; “Behavior” 2 items (T1, T2), “Safety and Efficacy” 4 items (T3 to T6), and “General Attitudes” 9 items (T7 to T15)

Table 6. Model fit indices of COVID-19 vaccine hesitancy scale for primary and booster doses (Total = 4 models)

Measure	χ^2	CFI	IFI	NFI	TLI	RFI	GFI	AGFI	RMSEA	SRMR	PNFI	PGFI
Cut-off Point *	p-value > 0.05	≥ 0.90	≥ .90	≥ .90	≥ .90	≥ .90	≥ .90	≥ .90	≤ .08	≤ .05	≥ .50	≥ .60
Model 1 Primary scale ^a	0.0001	0.935	0.935	0.933	0.922	0.919	0.941	0.918	0.071	0.0379	0.773	0.682
Model 1 Booster scale ^b	0.0001	0.889	0.889	0.887	0.866	0.863	0.892	0.851	0.096	0.0473	0.735	0.646
Model 2 Booster scale ^c	0.0001	0.918	0.918	0.916	0.901	0.898	0.914	0.881	0.083	0.0482	0.759	0.663
Model 3 Booster scale ^d	0.0001	0.942	0.942	0.94	0.924	0.921	0.942	0.913	0.073	0.0401	0.716	0.628

Note: Fit indices that met cutoff criteria are bolded.

^a Model 1 for primary doses based on the original scale structure which matches the results of the EFA.

^b Model 1 for booster doses based on the EFA results.

^c Model 2 for booster doses based on the original scale structure.

^d Model 3 for booster doses based on the original structure after improvement (modification model).

* References for the cut-off values of the fit indices are provided in supplementary material #2, Table S2.

Table 7. Reliability, convergent validity, and discriminant validity results of COVID-19 vaccine hesitancy scales for both primary and booster doses

COVID-19 vaccine hesitancy scale for Primary doses								
	Pearson correlation coefficient (n = 4453)							
	General Attitudes	Safety and Efficacy	Behaviour	AVE	Recommended AVE value	CR	Cronbach's alpha	Recommended Cronbach's alpha
General Attitudes	0.709			0.502	≥ 0.50	0.898	0.894	$\geq .60$
Safety and Efficacy	0.632**	0.642		0.413	$0.4 < AVE < 0.5$ if $CR > 0.6$	0.706	0.676	$\geq .60$
Behaviour	0.501**	0.355**	0.696	0.484	$0.4 < AVE < 0.5$ if $CR > 0.6$	0.652	0.636	$\geq .60$
COVID-19 vaccine hesitancy scale for Booster doses								
General Attitudes	0.708			0.501	≥ 0.50	0.897	0.892	$\geq .60$
Safety and Efficacy	0.690**	0.722		0.521	≥ 0.50	0.793	0.711	$\geq .60$
Behaviour	0.474**	0.339**	0.810	0.656	≥ 0.50	0.784	0.745	$\geq .60$

** Correlations are significant at the 0.01 level (2-tailed).

- The bolded Pearson correlation coefficient are the square roots of every AVE value to compare it with the other correlation coefficients.
- Correlations in bold mean that the square root of the AVE value for each subscale is higher than the correlation coefficients with the other subscales.
- AVE, CR, and Cronbach's alpha values that met cutoff criteria are bolded.
- References for the cut-off values of the reliability and validity tests are provided in supplementary material #2, Table S3.

Table 8. Criterion validity results: bivariate Pearson correlation between constructs in the COVID-19 primary and booster doses scales

		COVID-19 vaccine hesitancy scale for Booster doses			
	Constructs	General Attitudes	Safety and Efficacy	Behaviour	Total score
COVID-19 vaccine hesitancy scale for Primary doses	General Attitudes	0.800**	0.613**	0.347**	0.778**
	Safety and Efficacy	0.618**	0.776**	0.280**	0.697**
	Behaviour	0.398**	0.320**	0.404**	0.438**
	Total score	0.802**	0.720**	0.383**	0.819**

** Correlations are significant at the 0.01 level (2-tailed).

- Bolded diagonal values indicate that correlations between corresponding constructs in the two scales.

4. Discussion

To our knowledge, this is the first study to evaluate VH using the same multidimensional instrument across both mandated (primary) and voluntary (booster) COVID-19 vaccine stages within the same population. This two-stage approach offers a novel contribution, as VH is inherently dynamic and it shaped by evolving policies, risk perceptions, and social context. Our adapted CVHS scale demonstrated strong psychometric performance across both vaccine stages, including robust internal structure, reliability, and construct validity. Known-group validity was also supported through significant differences in VH scores across gender and academic levels, confirming the scale's ability and sensitivity to detect real-world differences in VH levels. Collectively, these findings support the utility of our tool for monitoring temporal and contextual shifts in VH, particularly in younger populations who navigate complex vaccination decisions in the absence of external mandates.

When compared with other COVID-19 VH validation studies conducted in diverse global settings (supplementary material #2, Table S6), our results are broadly aligned with prior validation efforts but also reveal important distinctions. EFA results in this study revealed three latent constructs for both scales (primary and booster), consistent with the CVHS and PACV domains [[18], [19], [20], [21]], and explained 58 % and 61 % of the total variance, respectively. These proportions are comparable to those found by Huang et al. (2022) [41], who reported 50.4 % variance explained in a Chinese sample. Although most items loaded as expected, some shifts were noted in the booster scale, particularly for items T4, T5, and T6, which loaded onto “Attitude” rather than “Safety.” This adjustment likely reflects a shift in students' evaluation of booster doses, where general attitudes take precedence over safety-specific concerns. Our CFA results further confirmed that the original structure was superior to the EFA-derived model,

aligning with Huang et al. (2022) findings, where EFA-derived models showed weaker performance [21]. Although the p -value of χ^2 was significant across all models, this metric is known to be highly sensitive to large sample sizes and may flag minor deviations even in well-fitting models [35], as is likely the case in our large sample ($n = 4453$).

For factor loadings in our scales, only one item (#3) fell below the 0.4 loading threshold, which we retained due to its conceptual importance and its role in improving CR and AVE estimates. A similar problem was noted in previous validation studies [42,43]. The low factor loading of item #3 could be attributed to the slight wording adaptation we implemented to improve its clarity, as many students in the pre-testing phase appeared to misunderstand its latent meaning. Internal consistency in our study was strong, with Cronbach's α and Composite Reliability (CR) exceeding 0.70 in most domains. The exception was the “Behavior” subscale (CR = 0.65), which is consistent with previously reported values in Arabic and Malay versions of the PACV ($\alpha = 0.57$ and 0.54 , respectively) [42,43]. However, Cronbach's α has been critiqued for potentially underestimating true reliability, especially in multidimensional scales, thus making CR a more reliable measure [44,45]. Given this, we set a CR threshold of 0.7 or higher as our benchmark, which was met in all domains except for the “Behavior” subscale in the primary doses scale (0.65), which value is still acceptable, albeit lower than that of the CVHS (0.822) [21]. This lower reliability value could be due to the limited two-item structure of the “Behavior” domain. Although a minimum of three items per domain is generally recommended for reliability [43,46], others have suggested that narrowly defined constructs can be captured adequately with two items [43,47]. Thus, the “Behavior” domain remains a valid measure in this study, supporting consistent measurement of COVID-19 VH across primary and booster doses.

The psychometric fit indices in our study (CFI = 0.935–0.942; RMSEA = 0.071–0.073) matched or exceeded the fit indices reported in the Oxford scale (CFI = 0.97; RMSEA = 0.05) [15], the Arabic 5C Scale (CFI = 0.96; RMSEA = 0.060) [48], and the CVHS (CFI = 0.90–0.93; RMSEA = 0.06 to 0.07) [21,41]. Notably, the AVE values in this study ($AVE \geq 0.50$) were relatively higher than 0.50, suggesting improved construct cohesion relative to the original CVHS, where AVE values were lower [21]. While the AVE values for the “Safety” and “Behavior” dimensions in the primary doses scale fell slightly below 0.5, they still met Fornell and Larcker's criteria due to their high CR [38]. A similar approach has been used in prior studies on vaccine scale validation [49]. This indicates that, despite some potential limitations in individual item variances, the overall constructs are sufficiently cohesive. Criterion validity further reinforced the scales' robustness in this study. Unlike previous studies that tested criterion validity using different vaccine scales [16,21], we used the same scale in two versions (one for primary doses and one for booster doses). This approach allowed us to capture phase-specific VH more effectively. Our results demonstrated significant correlations between identical constructs in the primary and booster scales. This consistency highlights the two scales' ability to accurately measure similar constructs across different vaccination stages.

Importantly, while most prior tools were developed and validated exclusively for primary vaccine series, we extended the scale to measure VH toward COVID-19 booster doses. Only a few studies have addressed booster-specific hesitancy using validated instruments [13,14]. Compared to their findings, our sample reported higher hesitancy toward COVID-19 booster doses (33 %) than primary doses (19 %), a trend consistent with previous research [[50], [51], [52]], but higher than the 26.7 % reported by Lee et al. (2023) [14]. In contrast, Al-Taie and Yilmaz (2024) reported substantially lower booster hesitancy (8.3 %) among community pharmacists in Turkey, a group that potentially has more favorable views toward

vaccination due to their medical training and occupational norms [13]. We also observed a larger proportion of students who delayed (32 %) or refused (29 %) COVID-19 booster doses than those who did the same for primary doses (12 %, 6 %, respectively), supporting the broader pattern that booster doses uptake lags behind primary vaccinations, especially among younger population [2,4,53]. Similarly, we found that (43 %) of the students viewed booster doses as unnecessary, (36 %) were unsure if getting a booster was a good idea, and more than half (55 %) were either unwilling or unsure about recommending boosters to their families or friends. Moreover, our scale detected group differences, such as higher hesitancy among men and undergraduates. These findings emphasize that VH fluctuates between different groups, waves of the pandemic, and different vaccine phases. Accordingly, the two scales validated in this study provide a reliable tool for capturing the nuanced differences in VH.

4.1. Policy implications

Our study provides a tool that policymakers and health agencies can use to track evolving patterns of vaccine acceptance over time. This is particularly critical given that booster uptake remains voluntary and more susceptible to attitudinal factors. The ability to detect subgroup differences (e.g., by gender or age) enables targeted outreach efforts and allows health authorities to design communication strategies that resonate with specific high-hesitancy groups. Moreover, by integrating validated measures into routine surveillance or large-scale health surveys, policymakers can monitor vaccine sentiment in real-time and adapt policies accordingly, whether by enhancing accessibility, addressing safety concerns, or tailoring public messaging to sustain long-term immunization coverage.

4.2. Limitations and strengths

This study has some limitations. First, self-reported data may introduce social desirability bias, as students might provide socially acceptable responses rather than their true views. To mitigate this, we assured anonymity in the informed consent. Second, as data were collected from a single institution, findings may not be fully generalizable but could apply to universities with similar characteristics. Third, recruitment differences (mass emails for undergraduates, newsletters for graduates) may have affected respondent demographics; however, we applied sampling weights to address this. Fourth, the imputation method for missing data may introduce estimates rather than relying on actual responses, though, missingness in this study was minimal and completely at random (less than 3 % per question). Fifth, varying cut-off values in EFA and CFA could yield different results, but we followed widely accepted thresholds from literature. Sixth, recall bias is possible, as students were asked about their VH and attitudes 2–3 years post-vaccine authorization. As a result, participants may have had difficulty accurately recalling their past attitudes or behaviors to the primary dose scale. This bias could have impacted the results by either underestimating or overestimating VH, depending on how participants' views may have changed over time. For example, students who currently distrust vaccines may recall being more hesitant than they actually were at the time, or vice versa. Lastly, this study validated the CVHS for both COVID-19 primary and booster doses, though its application is specific to the context of the COVID-19 pandemic. The wording and conceptual framing of certain items may be transferable to future vaccines for novel pathogens, but with appropriate modifications. Thus, adaptations would be necessary to ensure content validity if the scale were to be applied in different vaccine contexts.

Despite limitations, this study has notable strengths. First, it represents one of the largest

surveys on VH among university students, thus enhancing the reliability and generalizability of our findings. Second, our mass email sampling minimized selection bias by allowing all UW students to participate. Third, including both undergraduate and graduate students strengthened the scale's validation across academic levels. Fourth, applying sampling weights improved the demographic representation and accounted for non-response bias. Fifth, conducting this study in 2024 provided a unique perspective, as it captures VH shifts long after initial vaccine authorizations. Finally, the cross-sectional design lays a foundation for future longitudinal research on VH trends over time.

5. Conclusion

Our findings demonstrate that the COVID-19 VH scale is a reliable and valid tool for assessing hesitancy toward both primary and booster doses among university students. The scale's structure is largely consistent with its original formulation, with minor modifications needed for the booster doses scale. Given the ongoing need to monitor and address VH among younger adults, especially with booster doses, leveraging this scale to pinpoint specific drivers of VH will support the development of targeted interventions and educational campaigns to increase vaccine uptake. Academic institutions and public health departments can adapt our scales to conduct their assessments and implement tailored strategies for enhancing vaccine uptake on their campuses.

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CHAPTER 3 PREAMBLE

With a validated tool in hand from Chapter 2, the second primary research study of this thesis (Chapter 3) moved beyond measurement to explore how VH evolves and what drives it by focusing on patterns and predictors across both primary and booster doses. Although previous research has examined determinants of VH, most studies have focused on a single point in time or on the initial vaccine rollout. However, VH is not static; it changes across vaccine phases and is shaped by individual beliefs, prior experiences, and broader contextual influences such as mandates, messaging, and trust. This study compared VH levels between COVID-19 primary and booster doses and employed multivariable analysis to identify sociodemographic, psychological, and behavioral predictors. The findings offer insights into how and why VH may increase over time and highlight factors that influence hesitancy at each stage (primary vs. boosters). This study builds directly on the scale validation in Chapter 2 and sets the stage for a deeper exploration of interaction effects in Chapter 4.

CHAPTER 3

Manuscript 3: Understanding the shift in COVID-19 vaccine hesitancy and its associated factors for primary and booster doses among university students: A cross-sectional study

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Understanding the shift in COVID-19 vaccine hesitancy and its associated factors for primary and booster doses among university students: A cross-sectional study

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Highlights

- COVID-19 Vaccine Hesitancy (VH) scores increased by 51 % between primary and booster doses.
- The shift in VH was most pronounced among younger students, women, and those with low perceived risk.
- Government recommendations, prior vaccination history, and vaccine safety perceptions predicted shifts in hesitancy over time.
- Students with no religious beliefs or whose vaccination decisions were unaffected by mandates showed lower changes in VH.
- Findings support adding “Context” and “Communication” to the established 5C's model.

Abstract

Background: Vaccine hesitancy (VH) poses a major challenge to achieving high COVID-19 vaccination rates. Universities, with mandatory primary dose policies but optional boosters, offer a unique setting to study VH dynamics. This study aimed to estimate COVID-19 VH prevalence and identify key factors influencing VH across primary and booster doses among university students.

Methods: In this cross-sectional study, all actively enrolled students at the University of Waterloo, Ontario, Canada, during Winter 2024 were invited to complete an online survey. Means and standard deviations were calculated for VH scores and proportions were calculated for the binary VH.

Differences were compared using paired *t*-tests and chi-square. Generalized Estimating Equations was applied to model changes in VH scores from primary to boosters and identify key predictors of VH. Interaction terms were tested to evaluate dose-specific effects on VH.

Results: Among 4453 respondents, VH prevalence increased from 17 % for primary doses to 33.4 % for boosters, with higher VH scores for boosters (Mean $\pm$ SD: 10.9 $\pm$ 8.1) than primary doses (Mean $\pm$ SD: 7.3 $\pm$ 7.1). Women (aOR = 1.06, 95 % CI 1.01–1.11) and younger students (aOR = 1.62, 95 % CI 1.25–2.10) showed the largest VH increases, especially for boosters. Students with low perceived risk, negative perceptions of boosters' safety and effectiveness, low intention to follow government recommendations, and no prior flu or meningococcal vaccination exhibited the greatest VH increases when shifting from primary to booster doses. Conversely, students with no religious affiliation and those whose decisions were unaffected by mandates showed smaller changes in VH.

Conclusion: The rise in VH from primary to booster doses appears driven by demographic, psychological, and behavioral factors. Tailored interventions that promote clear communication, improve access, and strengthen confidence in booster recommendations rather than reliance on mandates are critical for reducing VH and sustaining vaccine uptake in this population.

1. Introduction

The definition of vaccine hesitancy (VH) has gone through a series of evolutions, reflecting its dynamic nature [1]. Since the onset of the Coronavirus Disease 2019 (COVID-19), VH has become more recognized, which continues to challenge global vaccination efforts [2]. As new COVID-19 variants continued to emerge and immunity waned over time, booster doses were introduced [3]. Global uptake of boosters has been inconsistent, with marked disparities across different regions [4]. European countries have reported relatively high booster coverage, while the Americas (US, Canada, and Peru) have experienced lower uptake rates [4]. Higher booster hesitancy rates were also recorded across diverse populations, including younger adults [[5], [6], [7], [8]], healthcare workers [9], and parents [10,11]. Common reported barriers were doubts about the necessity and safety of boosters, perceived low risk of severe disease, distrust in health authorities, and hesitancy to other vaccines [4,6].

In Canada, over 80 % of the population completed the COVID-19 primary series during the initial vaccine rollout; however, vaccination rates plateaued by mid-2021 [12]. In 2022, Canada introduced booster doses, yet, the uptake of boosters has been lower among younger populations compared to older adults [13], with only around 40 % (aged 18–39) receiving three or four doses by September 2023 [12]. Similar patterns were seen with the seasonal influenza vaccination among younger adults [5,14], where vaccine complacency—a key driver of VH where perceived risk of infection is low—has been noted [5,14].

Vaccine mandates were widely implemented in many regions, including Canada, to ensure compliance with COVID-19 primary series vaccinations, particularly in high-risk settings such as schools, workplaces, and healthcare facilities [15,16]. These policies were instrumental

in achieving high initial vaccination rates [17]. However, in settings such as universities, where mandates were often enforced for primary vaccinations, the distinction between compliance driven by mandates and genuine vaccine acceptance becomes important [[18], [19], [20]]. This distinction could highlight a key challenge: a “latent VH”– hesitancy that exists among individuals but is overridden by external pressures, such as mandates [[18], [19], [20]]. Thus, VH may not be evident during mandatory vaccination phases but can resurface when mandates are lifted, as seen in the lower uptake of optional booster doses [8,18]. This phenomenon is especially concerning among university students, who exhibit higher rates of booster hesitancy despite their significant potential to transmit the virus in high-risk occupational settings [8,[18], [19], [20], [21]].

University students have been a focal population in recent VH research. The transition to university represents a critical stage where students begin making autonomous healthcare decisions as they shift away from parental guidance [22]. For instance, a study on influenza vaccination found that 45 % of undergraduates were unvaccinated and over half reported that their parents made medical decisions for them [23]. In the context of COVID-19 booster doses, similar patterns have emerged. A 2024 survey of university students in China reported that 32.2 % were hesitant to receive additional booster doses, and 23.5 % became more hesitant after experiencing a second COVID-19 infection [8]. In the UK, 42.8 % of students expressed hesitancy toward receiving regular boosters, with lower booster acceptance influenced by low confidence, complacency, and concerns about vaccine side effects [24]. Similarly, a multi-campus study in Pennsylvania, U.S., found that although 89 % of students had completed the COVID-19 primary series, only 65 % had received a third dose and just 35 % had received the most recent boosters [18].

Beyond individual-level factors, students' perceptions of institutional policy also appear to play a role in shaping vaccine behavior. A U.S.-based study found that students who believed their university required vaccination were significantly more likely to get vaccinated, even when no formal mandate existed [20]. This suggests that perceived mandates can shape behavior as effectively, if not more so, than actual policies. Collectively, these studies suggest that although primary series coverage among this population is generally high, booster uptake is considerably lower and may reflect a complex interplay of confidence, risk perception, prior experience, and institutional messaging.

At the University of Waterloo (UW), Ontario, Canada, COVID-19 primary series (one or two doses, depending on vaccine type) were mandated for all students, faculty, and staff to access campus facilities as of September 2021 [[25], [26], [27]]. This mandate remained in place until May 1, 2022, after which the university lifted the requirement [[25], [26], [27]]. Booster doses, including third and subsequent doses, were strongly recommended, but were not mandated at any point. The university continued to encourage voluntary reporting of vaccination status through the Campus Check-in tool [27].

Universities, as microcosms of society with diverse, well-educated populations, provide a unique opportunity to explore VH dynamics. Although much effort has been invested to uncover the underlying factors of VH among students [28], no previous work has focused on the differences in VH and its drivers toward primary and booster doses. To fill this gap, the aim of our study was 1) to estimate the prevalence of VH for both the COVID-19 primary series and booster doses among UW students 2) to identify factors associated with COVID-19 VH, accounting for changes in VH between the primary series and booster doses.

2. Methods

2.1. Study design and data collection

This cross-sectional study was conducted using an online, self-reported survey administered to all actively enrolled undergraduate and graduate students during the Winter 2024 term at the UW. In Winter 2024, the UW had 34,398 undergraduate students and 6010 graduate students [29]. The survey was hosted on the Qualtrics platform, and duplicate submissions were prevented using platform settings. Informed consent was obtained on the first page of the survey, and only consenting participants were able to proceed. Students who were not enrolled during the study period or who did not consent to participate were excluded.

Recruitment emails were sent to all 34,398 undergraduate students by the UW Registrar's Office. For graduate students ($n = 6010$), the survey was shared through weekly newsletters from the Graduate Studies and Postdoctoral Affairs office, as well as direct emails from departmental program coordinators. Additional outreach was conducted on social media platforms including LinkedIn, Twitter, and Instagram. The data collection period ran from March 18 to May 1, 2024, with weekly reminders sent to students who had not opted out. To encourage participation, respondents were offered a chance to win one of fifty \$25 credits for campus purchases. Contact information for the prize draw was collected separately from survey responses to preserve anonymity. Ethics approval was obtained from the University of Waterloo Research Ethics Board (ORE #46023).

2.2. Measures and outcome

The full questionnaire is provided in the supplementary material. The questions were adapted or derived from several validated instruments and national surveys such as the COVID-

19 Vaccine Hesitancy Scale (CVHS) [30], the Parental Attitude toward Childhood Vaccination (PACV) [[31], [32], [33]], COVID-19 Vaccination Coverage Survey [34], the Canadian Community Health Survey (CCHS) [35], Vaccine Confidence Survey Question Bank [36], 5C psychological antecedents of vaccination [37], the Oxford COVID-19 Vaccine Hesitancy Scale [38], and the General Vaccine Hesitancy Scale [39]. The key variables used for this study were:

2.2.1. Outcome of interest

COVID-19 VH. We measured COVID-19 VH at two points; for the primary series and for booster doses, using the 15 items of the existing CVHS, the adapted version of the PACV tool [[30], [31], [32]]. Therefore, we modified the language of the CVHS twice; one to capture hesitancy toward the primary COVID-19 vaccine series, and one to be about boosters. Our adapted CVHS version used here was validated among university students in a prior study [40].

2.2.2. Explanatory variables

The 5C's model and two new proposed C's. The 5C's model is a widely used framework to understand VH, comprising five psychological drivers: Complacency, Confidence, Calculation, Convenience, and Collective Responsibility [37]. “Complacency” reflected perceived risk and severity of COVID-19 infection. We assessed complacency using four questions from the Oxford COVID-19 Vaccine Hesitancy Scale [38], and a previous survey [41]. “Confidence” measured trust in safety, effectiveness, and risk of COVID-19 primary and booster doses. We included two self-developed and eight adapted questions [36,41]. “Convenience” captured perceived ease of access and potential barriers to COVID-19 vaccine, such as religious beliefs, and logistical accessibility. We adapted four items from the Vaccine Confidence Survey Question Bank [36], and added two new questions. “Calculation” evaluated weighing the risks

and benefits of COVID-19 vaccines. We adapted two items from the original 5C scale [37,41]. “Collective Responsibility” measured the sense of responsibility to protect others. We asked participants one question: “I would get a COVID-19 vaccine to protect my community” (five-point scale, “strongly disagree” to “strongly agree”). Beyond the 5C's, we proposed “Context” and “Communication”. “Context” included socio-demographic characteristics, such as age, gender, income, and employment. “Communication” assessed the influence of recommendations from government, family, and healthcare professional to get COVID-19 vaccine.

Vaccine mandates. Participants were asked whether vaccine mandate policy from both the government and the university influenced their vaccination decisions.

COVID-19 related experiences. Participants were asked about whether they had been diagnosed with COVID-19 or hospitalized due to COVID-19.

Previous vaccination attitude and behavior. Participants were asked about their past vaccine uptake and attitude (e.g., influenza, human papillomavirus (HPV), meningococcal) using 13 questions adapted from the HPV vaccine hesitancy scale and other surveys [30,42].

2.3. Scale scoring system

VH scores for primary and booster doses were calculated using the scoring protocol from the CVHS and PACV scales, which are given elsewhere [[30], [31], [32]]. Responses were assigned scores: 2 points for hesitant, 1 point for not sure, and 0 points for non-hesitant answers. Raw scores were calculated by summing item scores and ranged from 0 to 30 if all items were included, 0–28 if Q1 or Q2 was excluded, or 0–26 if both were excluded, with higher scores indicating greater VH. Scores were then linearly transformed to a 0–100 scale and dichotomized into non-hesitant (<50) and hesitant (≥ 50) (supplementary material).

2.4. Pretesting and piloting

The questionnaire was refined and modified through multiple rounds of revisions by the research team and the Statistical Consulting and Survey Research Unit at UW. Pretesting was conducted among a diverse group of UW students ($n = 30$) to ensure clarity and relevance of the questions. A pilot test was then carried out with a random sample of 600 students to assess the feasibility of the recruitment strategy and survey procedures. The pilot study yielded a 9.5 % response rate, and no major issues were identified.

2.5. Sample size calculation

We estimated a target sample size of 1121 students based on ~24 % VH rate from the pilot study, using a 95 % confidence level and a 2.5 % margin of error. To ensure proportional representation, this sample was stratified into 955 undergraduates and 167 graduate students, according to the total enrolled population (34,398 undergraduates and 6010 graduates). Given the ~10 % response rate in the pilot, the entire UW student population was invited to participate to meet the sampling goal.

2.6. Statistical analysis

COVID-19 VH was assessed in two forms: discrete count score (range: 0–30, 0–28, or 0–26) and dichotomous (hesitant vs. non-hesitant). Percentage of missing data were calculated, and missing data were minimal (<3 % for most questions) and found to be completely at random ($p = 1.00$) using Little's MCAR test [43]. Descriptive statistics were generated for demographic characteristics and all study variables. Means and standard deviations were calculated for VH count scores, and proportions were calculated for the dichotomous form. Paired t -tests and Pearson's chi-square tests were conducted to compare VH mean differences and proportions

between primary and booster doses, respectively. Independent variables on a 5-point Likert scale were regrouped into three categories (e.g., agree, neutral, disagree), with “Don't know” and “Prefer not to say” retained as separate groups. To identify factors associated with the dichotomous VH outcome, two logistic regression models for primary doses and booster doses were fitted, starting with a full model of all predictors ($n = 47$), including the 5C's model, two proposed C's “Context” and “Communication”, vaccine mandates, COVID-19 related experiences, and previous vaccination attitude and behavior. Using a backward elimination approach, predictors were manually removed one by one based on their statistical significance ($p < 0.05$) and/or their potential relevance to VH (e.g., age, gender, trust in vaccine safety and effectiveness, and prior vaccination behavior have been consistently linked to VH in literature).

To estimate the association between the predictors and VH scores at two measurement points and to account for VH changes from primary to booster doses, a Generalized Estimating Equations (GEE) model was applied with a robust error estimation [44]. In the GEE model, a binomial regression was chosen to handle the distribution of the dependent variable “VH scores as discrete counts” [45]. A “Dose” variable (primary = 0, booster = 1) was created to represent dose type. Variables were manually removed one at a time based on three criteria: their plausible relationship with VH as supported by the literature, statistical significance ($p < 0.05$), and their impact on model fit as assessed by the Quasi-likelihood under the Independence Model Criterion (QIC) [46], until no further improvement in QIC was observed. Lastly, all possible interactions between “Dose” and independent variables were tested to assess whether associations differed by dose type. All significant interactions were retained in the final model. Analyses were performed using IBM SPSS 29.0 and R version 4.4.1, with significance level at <0.05 .

3. Results

Of the 40,408 students invited, 4453 completed the survey (Response rate: 11 %). Demographic characteristics of the study sample are presented in [Table 1](#). The majority of participants were women (57.2 %; $n = 2547$), undergraduate students in year 3 or 4 (53.5 %; $n = 2378$), and domestic students (87.1 %; $n = 3879$). Participants were drawn from all faculties, with the largest proportions from Engineering (24.2 %; $n = 1077$) and Mathematics (19.2 %; $n = 856$). Most students reported being single (91.1 %; $n = 4057$) and were either employed (49.9 %; $n = 2221$) or unemployed (46.2 %; $n = 2057$) at the time of the survey.

Table 1. Demographic characteristics of study participants, 2024.

Demographic Characteristic	(n = 4453)	
	n	%
Gender		
Woman	2547	57.2
Man	1689	37.9
Non-binary/Others ^a	126	2.8
Prefer not to say	91	2.0
Age		
14–22	3742	84.0
23–29	604	13.6
30–39	75	1.7
40 or more	32	0.7
Academic level		
Undergraduate year 1	935	21.0
Undergraduate year 2	906	20.3
Undergraduate year 3	1120	25.2
Undergraduate year 4 or 4+	1258	28.3
Master's student	149	3.3
PhD	64	1.4
Others ^b	21	0.5
Faculties		

Demographic Characteristic	(n = 4453)	
	n	%
Arts	843	18.9
Engineering	1077	24.2
Environment	350	7.9
Health	510	11.5
Mathematics	856	19.2
Science	817	18.3
Status		
Domestic	3879	87.1
International	574	12.9
Indigenous identity		
Yes	63	1.4
No	4322	97.1
Prefer not to say	68	1.5
Immigration status		
Canadian citizen or Permanent resident	3867	86.8
Temporary resident	509	11.4
Others ^c	7	0.2
Prefer not to say	70	1.6
Income level		
Less than \$29,999	1125	25.3
\$30,000 to \$59,999	413	9.3
\$60,000 to \$89,999	380	8.5
Greater than \$90,000	1092	24.5
Don't know	759	17.0
Prefer not to say	684	15.4
Marital status		
Single	4057	91.1
Married	99	2.2
Others ^d	178	4.0
Prefer not to say	119	2.7

Demographic Characteristic	(n = 4453)	
	n	%
Employment status		
Employed (full time, part time, co-op term)	2221	49.9
Unemployed	2057	46.2
Prefer not to say	175	3.9

a Others included Third gender, Transgender, LGBTQ+.

b Others included Non-degree, Exchange students, Transfer students.

c Others included Asylum, Refugees, Undocumented.

d Others included Common law, Engaged, Separated, Divorced, Widowed, In a relationship.

Health and vaccine-related characteristics of the study sample are provided in the supplementary material. Overall, a significant majority reported good to excellent overall health (91.3 %; $n = 4067$), yet 32.7 % ($n = 1458$) disclosed poor to fair mental health. For COVID-19-related experiences, 61.2 % ($n = 2725$) of participants had previously been diagnosed with the virus, though only 1.2 % ($n = 53$) had been hospitalized. For vaccination logistics, most participants (76.6 %; $n = 3413$) found accessing primary vaccine doses to be easy, in contrast to 59.2 % ($n = 2637$) for booster doses. Perceived risk of contracting COVID-19 was low for 64.9 % ($n = 2890$) of participants. Students reported higher trust in the safety (79.5 %; $n = 3539$) and effectiveness (79.6 %; $n = 3543$) of the primary doses compared to their trust in the safety (69.3 %; $n = 3087$) and effectiveness (56.5 %; $n = 2515$) of the booster doses. Religious beliefs had no impact on vaccination decisions for 42.6 % of students ($n = 1896$), whereas vaccine mandate policies from both the government and the university influenced 44.6 % ($n = 1988$) and 31.7 % ($n = 1412$) of students to get vaccinated, respectively. Regarding prior vaccination, 64.0 % ($n = 2851$) did not receive a flu shot in 2023–2024, while over half had received the HPV (61.4 %; $n = 2736$) and meningococcal vaccines (57.2 %; $n = 2547$).

For the overall VH scores, they were significantly higher for booster doses (Mean $\pm$ SD: 10.9 ± 8.1) than for primary doses (Mean $\pm$ SD: 7.3 ± 7.1). Binary categorization of VH scores further indicated that the proportion of hesitant participants increased significantly from 17 % ($n = 759$) for primary doses to 33.4 % ($n = 2964$) for booster doses (Table 2).

Table 2. Comparison of vaccine hesitancy scores between COVID-19 primary doses and booster doses

	Primary Doses	Booster Doses	P-value
Original Vaccine Hesitancy Score (out of 30)			<0.001*
Mean $\pm$ SD	7.3 ± 7.1	10.9 ± 8.1	
Binary Vaccine Hesitancy Scores	n (%)	n (%)	<0.001**
Non-hesitant (Score < 50)	3694 (83%)	2964 (66.6%)	
Hesitant (Score $\geq$ 50)	759 (17%)	1489 (33.4%)	

Significant values are shown in bold.

*Paired t-test was used to compare mean vaccine hesitancy scores between primary and booster doses.

**Cross-tabulation was used to compare binary vaccine hesitancy between the two doses.

The two logistic regression models (Table 3, Table 4) showed that gender generally did not predict VH. However, participants who chose not to disclose their gender were more than twice as likely to be hesitant toward COVID-19 primary doses compared to men (aOR = 2.34, 95 % CI 1.03–5.34). Age was a significant factor, with individuals aged 20–29 being more hesitant for both primary (aOR = 1.63, 95 % CI 1.18–2.25) and booster doses (aOR = 1.42, 95 % CI 1.13–1.80) than those aged 14–19. Students who made vaccination decisions independently of mandates were less hesitant overall. Specifically, they were 58 % less likely to report hesitancy for primary doses (aOR = 0.42, 95 % CI 0.30–0.59) and 46 % less likely for booster doses (aOR = 0.54, 95 % CI 0.43–0.68) compared to those influenced by mandates. Trust in the vaccine's importance, safety, and effectiveness strongly influenced VH. For example, participants who viewed primary doses as unimportant were over five times more likely to be hesitant compared to those who viewed them as important (aOR = 5.64, 95 % CI 3.45–9.22). Hesitancy for boosters was even higher, with these participants being ten times more likely to be

hesitant (aOR = 10.08, 95 % CI 6.89–14.73). Similarly, doubts about the vaccine's effectiveness or a low perceived risk of COVID-19 were associated with increased hesitancy. Prior vaccination behavior also impacted VH. Students who had hesitated or refused flu vaccines were more than twice as likely to be hesitant toward primary doses (aOR = 2.58, 95 % CI 1.71–3.87) and over three times as likely for boosters (aOR = 3.29, 95 % CI 2.37–4.56), compared to those without such a history.

Table 3. Multivariable logistic regression of predictors of COVID-19 vaccine hesitancy for primary doses among University of Waterloo students, 2024

Independent Variable	Category	Total sample, n (%)	Adjusted OR (95% CI)	P-value
Gender	Men (Ref)	1689 (37.9)	..	..
	Woman	2547 (57.2)	1.09 (0.81–1.46)	0.587
	Non-binary/Others	126 (2.8)	1.03 (0.35–3.03)	0.953
	Prefer not to say	91 (2.0)	2.34 (1.03–5.34)	0.044
Age groups	14-19 (Ref)	3742 (84.0)	..	..
	20-29	604 (13.6)	1.63 (1.18–2.25)	0.003
	30-39	75 (1.7)	0.16 (0.03–0.79)	0.025
	40 or more	32 (0.7)	0.85 (0.15–4.77)	0.849
Ever diagnosed with COVID-19	Yes (Ref)	2725 (61.2)	..	..
	No	1519 (34.1)	1.18 (0.87–1.60)	0.278
	Don't know	141 (3.2)	2.87 (1.61–5.11)	<0.001
	Prefer not to say	68 (1.5)	1.75 (0.73–4.18)	0.206
Vaccine mandate impact from the government	I decided to get vaccinated because of the mandate (Ref)	1988 (44.6)	..	..
	I decided to not get vaccinated because of the mandate	88 (2.0)	1.99 (0.60–6.56)	0.259
	No impact	2118 (47.6)	0.42 (0.30–0.59)	<0.001
	Not aware of the mandate	217 (4.9)	0.56 (0.30–1.03)	0.06
	Prefer not to say	42 (0.9)	0.78 (0.24–2.59)	0.69
Perceived importance of primary doses	Important (Ref)	3445 (77.4)	..	..
	Unimportant	401 (9.0)	5.64 (3.45–9.22)	<0.001
	Neutral	476 (10.7)	4.69 (3.36–6.55)	<0.001
	Don't know	81 (1.8)	4.36 (2.24–8.49)	<0.001
	Prefer not to say	50 (1.1)	5.82 (1.78–19.07)	0.004

Trust in primary doses safety	Safe (Ref)	3539 (79.5)	..	..
	Unsafe	268 (6.0)	4.32 (2.21–8.45)	<0.001
	Neutral	511 (11.5)	3.20 (2.26–4.55)	<0.001
	Don't know	116 (2.6)	2.71 (1.40–5.24)	0.003
	Prefer not to say	19 (0.4)	20.44 (0.70–594.04)	0.079
Trust in primary doses effectiveness	Effective (Ref)	3543 (79.6)	..	..
	Ineffective	312 (7.0)	4.05 (2.31–7.09)	<0.001
	Neutral	451 (10.1)	1.81 (1.25–2.62)	0.002
	Don't know	128 (2.9)	1.31 (0.65–2.62)	0.447
	Prefer not to say	19 (0.4)	1.06 (0.05–22.75)	0.971
Trust in primary doses riskiness	Not risky (Ref)	3013 (67.7)	..	..
	Risky	524 (11.8)	3.14 (2.04–4.82)	<0.001
	Neutral	721 (16.2)	1.95 (1.35–2.81)	<0.001
	Don't know	171 (3.8)	1.95 (0.99–3.85)	0.054
	Prefer not to say	24 (0.5)	0.69 (0.07–6.61)	0.749
Confidence in the government	Confident (Ref)	2836 (63.7)	..	..
	Not Confident	665 (14.9)	4.11 (2.85–5.93)	<0.001
	Not sure	896 (20.1)	1.54 (1.09–2.18)	0.014
	Prefer not to say	56 (1.3)	1.35 (0.45–4.08)	0.596
Convenience to get primary doses	Easy (Ref)	3413 (76.6)	..	..
	Difficult	766 (17.2)	0.81 (0.55–1.21)	0.306
	Not sure	143 (3.2)	1.28 (0.67–2.45)	0.454
	Prefer not to say	35 (0.8)	2.31 (0.69–7.74)	0.176
	I didn't get any primary doses	96 (2.2)	13.38 (2.96–60.52)	<0.001
Likelihood of getting vaccinated when recommended by healthcare professional	Likely (Ref)	3792 (85.2)	..	..
	Unlikely	299 (6.7)	1.51 (0.87–2.62)	0.144
	Not sure	316 (7.1)	1.84 (1.21–2.81)	0.005
	Prefer not to say	46 (1.0)	0.24 (0.04–1.42)	0.114
Likelihood of getting vaccinated when recommended by the government	Likely (Ref)	3110 (69.8)	..	..
	Unlikely	623 (14.0)	3.74 (2.51–5.56)	<0.001
	Not sure	681 (15.3)	1.41 (0.98–2.04)	0.068
	Prefer not to say	39 (0.9)	3.48 (0.59–20.51)	0.168
Flu vaccine uptake	Yes (Ref)	1504 (33.8)	..	..
	No	2337 (52.5)	1.38 (0.90–2.11)	0.14
	Don't know/Can't remember	548 (12.3)	0.83 (0.46–1.50)	0.542

Ever hesitant or refused the flu vaccine	Prefer not to say	64 (1.4)	1.65 (0.49–5.55)	0.416
	No (Ref)	2566 (57.6)	..	..
	Yes	556 (12.5)	2.58 (1.71–3.87)	<0.001
	Don't know/Can't remember	676 (15.2)	1.73 (1.20–2.50)	0.003
	Not applicable (my parents made the decision)	589 (13.2)	1.29 (0.83–2.00)	0.267
Concerned about side effects from the meningococcal vaccine	Prefer not to say	66 (1.5)	0.73 (0.25–2.18)	0.575
	Agree (Ref)	395 (8.9)	..	..
	Disagree	2323 (52.2)	0.40 (0.25–0.62)	<0.001
	Neutral	822 (18.5)	0.65 (0.41–1.01)	0.056
	Don't know	852 (19.1)	0.52 (0.33–0.83)	0.006
	Prefer not to say	61 (1.4)	0.73 (0.20–2.58)	0.62

Dependent variable: Binary vaccine hesitancy toward primary doses (Hesitant vs. Not hesitant).

Significant values are shown in bold.

Table 4. Multivariable logistic regression of predictors of COVID-19 vaccine hesitancy for booster doses among University of Waterloo students, 2024

Independent Variable	Category	Total sample, n (%)	Adjusted OR (95% CI)	P-value
Gender	Men (Ref)	1689 (37.9)	..	..
	Woman	2547 (57.2)	1.06 (0.84–1.34)	0.632
	Non-binary/Others	126 (2.8)	0.77 (0.33–1.81)	0.546
	Prefer not to say	91 (2.0)	1.28 (0.61–2.68)	0.514
Age groups	14-19 (Ref)	3742 (84.0)	..	..
	20-29	604 (13.6)	1.42 (1.13–1.80)	0.003
	30-39	75 (1.7)	2.00 (0.79–5.10)	0.146
	40 or more	32 (0.7)	3.70 (0.71–19.44)	0.122
Ever hospitalized due to COVID-19	Yes (Ref)	53 (1.2)	..	..
	No	4282 (96.2)	1.07 (0.45–2.56)	0.883
	Don't know	58 (1.3)	4.29 (1.32–13.93)	0.016
	Prefer not to say	60 (1.3)	5.12 (1.49–17.56)	0.009
Vaccine mandate impact from the government	I decided to get vaccinated because of the mandate (Ref)	1988 (44.6)	..	..
	I decided to not get vaccinated because of the mandate	88 (2.0)	0.87 (0.33–2.29)	0.77
	No impact	2118 (47.6)	0.54 (0.43–0.68)	<0.001
	Not aware of the mandate	217 (4.9)	0.69 (0.44–1.07)	0.096
	Prefer not to say	42 (0.9)	2.23 (0.71–6.98)	0.169

Personal likelihood of severity of COVID-19	Likely (Ref)	529 (11.9)	..	..
	Unlikely	2976 (66.8)	0.97 (0.70–1.35)	0.859
	Not sure	915 (20.5)	0.78 (0.54–1.13)	0.186
	Prefer not to say	33 (0.7)	0.10 (0.02–0.49)	0.004
Perceived importance of booster doses	Important (Ref)	1784 (40.1)	..	..
	Unimportant	888 (19.9)	10.08 (6.89–14.73)	<0.001
	Neutral	1516 (34.0)	3.16 (2.34–4.27)	<0.001
	Don't know	219 (4.9)	3.70 (2.31–5.93)	<0.001
	Prefer not to say	46 (1.0)	6.24 (1.34–28.96)	0.019
Trust in booster doses safety	Safe (Ref)	3087 (69.3)	..	..
	Unsafe	390 (8.8)	5.73 (2.71–12.12)	<0.001
	Neutral	730 (16.4)	3.50 (2.64–4.64)	<0.001
	Don't know	222 (5.0)	3.79 (2.37–6.07)	<0.001
	Prefer not to say	24 (0.5)	3.58 (0.43–29.48)	0.236
Trust in booster doses effectiveness	Effective (Ref)	2515 (56.5)	..	..
	Ineffective	528 (11.9)	3.40 (2.13–5.42)	<0.001
	Neutral	1003 (22.5)	3.03 (2.36–3.89)	<0.001
	Don't know	380 (8.5)	1.84 (1.24–2.73)	0.003
	Prefer not to say	27 (0.6)	1.76 (0.21–15.04)	0.604
Trust in booster doses riskiness	Not risky (Ref)	2671 (60.0)	..	..
	Risky	612 (13.7)	5.19 (3.33–8.09)	<0.001
	Neutral	843 (18.9)	1.63 (1.24–2.15)	<0.001
	Don't know	299 (6.7)	1.08 (0.70–1.67)	0.737
	Prefer not to say	28 (0.6)	0.66 (0.11–3.98)	0.648
Confidence in the government	Confident (Ref)	2836 (63.7)	..	..
	Not Confident	665 (14.9)	2.00 (1.40–2.86)	<0.001
	Not sure	896 (20.1)	1.45 (1.13–1.86)	0.003
	Prefer not to say	56 (1.3)	3.04 (0.97–9.51)	0.057
Convenience to get booster doses	Easy (Ref)	2637 (59.2)	..	..
	Difficult	120 (2.7)	1.86 (1.02–3.37)	0.042
	Not sure	138 (3.1)	1.28 (0.73–2.24)	0.389
	Prefer not to say	49 (1.1)	1.65 (0.66–4.12)	0.286
	I didn't get any booster doses	1509 (33.9)	2.42 (1.91–3.07)	<0.001
Likelihood of getting vaccinated when recommended by family	Likely (Ref)	3165 (71.1)	..	..
	Unlikely	520 (11.7)	1.51 (1.04–2.20)	0.033
	Not sure	721 (16.2)	1.37 (1.04–1.81)	0.027

Likelihood of getting vaccinated when recommended by the government	Prefer not to say	47 (1.1)	0.56 (0.12–2.54)	0.448
	Likely (Ref)	3110 (69.8)	..	..
	Unlikely	623 (14.0)	4.21 (2.84–6.24)	<0.001
	Not sure	681 (15.3)	1.95 (1.49–2.54)	<0.001
HPV vaccine uptake	Prefer not to say	39 (0.9)	2.86 (0.59–13.80)	0.191
	Yes (Ref)	2736 (61.4)	..	..
	No	496 (11.1)	0.44 (0.31–0.64)	<0.001
	Don't know/Can't remember	1182 (26.5)	0.71 (0.53–0.94)	0.016
Ever hesitant or refused the flu vaccine	Prefer not to say	39 (0.9)	0.39 (0.07–2.10)	0.273
	No (Ref)	2566 (57.6)	..	..
	Yes	556 (12.5)	3.29 (2.37–4.56)	<0.001
	Don't know/Can't remember	676 (15.2)	2.30 (1.71–3.08)	<0.001
Concerned about side effects from the HPV vaccine	Not applicable (my parents made the decision)	589 (13.2)	1.81 (1.33–2.46)	<0.001
	Prefer not to say	66 (1.5)	1.55 (0.50–4.80)	0.446
	Agree (Ref)	464 (10.4)	..	..
	Disagree	2368 (53.2)	0.60 (0.42–0.84)	0.004
	Neutral	850 (19.1)	1.05 (0.73–1.53)	0.779
	Don't know	713 (16.0)	0.76 (0.51–1.14)	0.183
	Prefer not to say	58 (1.3)	0.65 (0.16–2.61)	0.54

Dependent variable: Binary vaccine hesitancy toward booster doses (Hesitant vs. Not hesitant). Significant values are shown in bold.

Based on the GEE analysis (Table 5), VH scores significantly increased when moving from primary to booster doses. On average, VH scores were 51 % higher for booster doses compared to primary doses (aOR = 1.51, 95 % CI 1.18–1.93), after adjusting for age, gender, COVID-19 hospitalization, vaccine access and perceptions, trust in vaccines and government, religious beliefs, mandates, and prior vaccination behavior. Gender differences were modest but notable; on average, women's VH scores were 1.06 times greater than men's VH scores across both primary and booster doses, after adjusting for all the variables in the model (aOR = 1.06, 95 % CI 1.01–1.11). Negative perceptions of boosters as unimportant, unsafe, or ineffective

were associated with higher VH scores, on average, over both primary and booster doses. For example, students who viewed boosters as unsafe had 2.29 times higher VH scores than those who viewed them as safe (aOR = 2.29, 95 % CI 2.08–2.51). Difficulty accessing booster doses was also a key barrier, leading to 33 % higher VH scores across primary and booster doses (aOR = 1.33, 95 % CI 1.17–1.50). Vaccine recommendations by the government were another factor. Students who were unlikely to follow government vaccine recommendations had 69 % higher VH scores compared to those who were likely to follow such recommendations (aOR = 1.69, 95 % CI 1.57–1.82). As expected, religious beliefs were associated with VH. On average, those whose beliefs discouraged vaccination showed higher VH scores (aOR = 1.19, 95 % CI 1.00–1.42), and participants with no religious beliefs were significantly less hesitant (aOR = 0.89, 95 % CI 0.82–0.96). In univariate analyses ([Table 5](#)), vaccine mandates from the university were significantly associated with VH. On average, students who did not vaccinate due to the mandate had a 3.8-fold higher VH scores than those who got vaccinated because of the mandate (OR = 3.80, 95 % CI: 2.75–5.26). After adjusting for covariates, vaccine mandates continued to show an effect. Students who reported that the university mandate had no impact on their decision had lower VH scores (aOR = 0.75, 95 % CI: 0.72–0.79), and those unaware of the mandate were also less hesitant (aOR = 0.86, 95 % CI: 0.81–0.92), than those who got vaccinated because of the mandate.

Table 5. Multivariable Generalized Estimating Equation model identifying predictors of vaccine hesitancy scores across COVID-19 primary and booster doses

Independent variables	Categories	VH score ¹ Mean (SD)	Crude OR (95% CI) ²	Adjusted OR (95% CI) ³
Intercept	..	..	..	0.09 (0.07–0.11)
Dose	Primary (Ref)	14.48 (0.38)		
	Booster	18.14 (0.38)	1.78 (1.75–1.82)	1.51 (1.18–1.93)
Age groups	14-19 (Ref)	15.74 (0.35)		
	20-29	16.31 (0.34)	1.08 (1.01–1.16)	..
	30-39	16.45 (0.51)	0.87 (0.65–1.15)	..
	40 or more	16.74 (0.69)	1.38 (0.86–2.22)	..
Gender	Men (Ref)	16.11 (0.37)		
	Woman	16.38 (0.37)	0.82 (0.76–0.87)	1.06 (1.01–1.11)
	Non-binary/Others	16.02 (0.47)	0.51 (0.40–0.64)	0.95 (0.80–1.12)
	Prefer not to say	16.73 (0.47)	1.10 (0.88–1.36)	1.13 (0.99–1.30)
Ever hospitalized due to COVID-19	Yes (Ref)	15.64 (0.64)		
	No	15.44 (0.37)	0.75 (0.59–0.94)	..
	Don't know	17.32 (0.60)	1.43 (1.08–1.90)	..
	Prefer not to say	16.85 (0.56)	1.57 (1.20–2.06)	..
Convenience to get primary doses	Easy (Ref)	15.27 (0.41)		
	Difficult	15.28 (0.42)	0.88 (0.81–0.96)	1.01 (0.96–1.07)
	Not sure	15.91 (0.48)	1.51 (1.27–1.78)	1.12 (1.00–1.25)
	Prefer not to say	17.24 (0.61)	3.00 (2.15–4.21)	1.41 (1.12–1.79)
	I didn't get any primary doses	17.85 (0.55)	10.12 (8.18–12.54)	1.73 (1.42–2.09)
Convenience to get booster doses	Easy (Ref)	15.59 (0.40)		
	Difficult	16.89 (0.50)	1.69 (1.41–2.02)	1.33 (1.17–1.50)
	Not sure	16.00 (0.47)	1.80 (1.54–2.10)	1.12 (1.00–1.26)
	Prefer not to say	16.21 (0.61)	3.42 (2.64–4.43)	1.15 (0.93–1.43)
	I didn't get any booster doses	16.87 (0.40)	3.40 (3.18–3.63)	1.29 (1.22–1.35)
Religious beliefs influencing vaccination	My religious beliefs encourage vaccination (Ref)	16.24 (0.41)		
	My religious beliefs discourage vaccination	16.95 (0.55)	5.52 (3.88–7.83)	1.19 (1.00–1.42)
	No impact	16.18 (0.39)	1.22 (1.10–1.37)	0.98 (0.91–1.06)
	Prefer not to say	16.43 (0.41)	1.78 (1.53–2.08)	1.02 (0.90–1.16)
	I don't have any religious beliefs	15.76 (0.39)	0.76 (0.68–0.86)	0.89 (0.82–0.96)
Perceived risk of getting COVID-19	No-to-low risk (Ref)	16.94 (0.41)		
	Moderate-to-high	17.25 (0.42)	0.92 (0.85–0.99)	..

	risk			
	Not sure	17.22 (0.44)	1.34 (1.15–1.55)	..
	Prefer not to say	13.83 (1.06)	2.23 (1.68–2.96)	..
Perceived importance of primary doses	Important (Ref)	14.89 (0.43)		
	Unimportant	16.15 (0.45)	5.86 (5.15–6.67)	1.26 (1.15–1.39)
	Neutral	16.60 (0.44)	4.27 (3.96–4.61)	1.25 (1.17–1.33)
	Don't know	16.82 (0.52)	4.11 (3.46–4.87)	1.30 (1.14–1.48)
	Prefer not to say	17.09 (0.68)	4.25 (3.38–5.33)	1.42 (1.11–1.81)
Perceived importance of booster doses	Important (Ref)	14.37 (0.46)		
	Unimportant	17.78 (0.46)	9.25 (8.54–10.02)	2.03 (1.88–2.20)
	Neutral	16.10 (0.45)	2.70 (2.53–2.88)	1.63 (1.54–1.73)
	Don't know	16.24 (0.49)	3.70 (3.26–4.21)	1.61 (1.46–1.79)
	Prefer not to say	17.07 (0.81)	7.05 (5.53–9.00)	1.80 (1.33–2.45)
Trust in booster doses safety	Safe (Ref)	13.71 (0.47)		
	Unsafe	18.96 (0.49)	12.47 (11.33–13.72)	2.29 (2.08–2.51)
	Neutral	16.90 (0.47)	4.09 (3.85–4.34)	1.61 (1.52–1.71)
	Don't know	16.95 (0.51)	3.70 (3.30–4.15)	1.65 (1.51–1.82)
	Prefer not to say	15.03 (1.25)	4.04 (3.02–5.42)	1.22 (0.76–1.97)
Trust in booster doses effectiveness	Effective (Ref)	14.57 (0.47)		
	Ineffective	17.83 (0.50)	10.81 (9.91–11.79)	1.73 (1.58–1.88)
	Neutral	16.57 (0.47)	3.12 (2.93–3.32)	1.48 (1.40–1.56)
	Don't know	15.70 (0.50)	2.89 (2.62–3.18)	1.28 (1.18–1.39)
	Prefer not to say	16.89 (1.20)	4.63 (3.53–6.08)	1.46 (0.93–2.28)
Trust in Government	Confident (Ref)	14.99 (0.42)		
	Not Confident	17.86 (0.43)	6.69 (6.14–7.28)	1.62 (1.52–1.74)
	Not sure	16.21 (0.42)	2.23 (2.08–2.39)	1.26 (1.19–1.32)
	Prefer not to say	16.18 (0.66)	3.11 (2.48–3.90)	1.19 (0.92–1.53)
Likelihood of getting vaccinated when recommended by the government	Likely (Ref)	14.76 (0.41)		
	Unlikely	18.07 (0.42)	7.43 (6.82–8.10)	1.69 (1.57–1.82)
	Not sure	16.42 (0.41)	2.66 (2.48–2.85)	1.33 (1.25–1.40)
	Prefer not to say	16.00 (0.69)	2.55 (2.01–3.24)	1.27 (1.01–1.60)
Flu vaccine uptake in 2023-2024	Yes (Ref)	15.43 (0.43)		
	No	16.57 (0.42)	2.77 (2.54–3.01)	..
	Don't know/can't remember	16.53 (0.43)	2.18 (1.94–2.45)	..
	Prefer not to say	16.71 (0.63)	4.30 (3.53–5.24)	..
Meningococcal vaccine uptake	Yes (Ref)	16.31 (0.41)		

Vaccine mandate impact from the university	No	16.62 (0.43)	1.59 (1.41–1.79)	..
	Don't know/can't remember	16.70 (0.41)	1.28 (1.19–1.38)	..
	Prefer not to say	15.61 (0.59)	1.91 (1.47–2.48)	..
	I decided to get vaccinated because of the mandate (Ref)	16.98 (0.41)		
	I decided to not get vaccinated because of the mandate	16.78 (0.72)	3.80 (2.75–5.26)	1.04 (0.79–1.36)
	No impact	15.52 (0.40)	0.40 (0.37–0.43)	0.75 (0.72–0.79)
	Not aware of the mandate	16.17 (0.41)	0.64 (0.59–0.70)	0.86 (0.81–0.92)
	Prefer not to say	16.11 (0.68)	1.44 (1.11–1.86)	0.85 (0.66–1.10)

Interactions

		Primary doses	Booster doses
Dose × Age groups ($p < 0.001$)	14-19 (Ref)	1	1.51 (1.18–1.93)
	20-29	1.18 (1.11–1.25)	1.61 (1.24–2.09)
	30-39	1.19 (0.92–1.53)	1.67 (0.98–2.56)
	40 or more	1.58 (1.19–2.09)	1.52 (0.95–2.45)
Dose × Hospitalized due to COVID-19 ($p < 0.001$)	Yes (Ref)	1	1.51 (1.18–1.93)
	No	0.79 (0.62–1.01)	1.71 (1.12–2.59)
	Don't know	1.31 (0.96–1.79)	2.00 (1.22–3.26)
	Prefer not to say	1.22 (0.88–1.68)	1.93 (1.15–3.25)
Dose × Perceived risk of getting COVID-19 ($p < 0.001$)	No-to-low risk (Ref)	1	1.51 (1.18–1.93)
	Moderate-to-high risk	1.13 (1.07–1.20)	1.55 (1.20–2.01)
	Not sure	1.16 (1.05–1.29)	1.47 (1.11–1.96)
	Prefer not to say	0.70 (0.47–1.05)	0.80 (0.47–1.37)
Dose × Flu vaccine uptake ($p < 0.001$)	Yes (Ref)	1	1.51 (1.18–1.93)
	No	1.18 (1.10–1.28)	2.21 (1.69–2.88)
	Don't know	1.27 (1.15–1.41)	2.13 (1.60–2.83)
	Prefer not to say	1.27 (0.95–1.69)	1.94 (1.24–3.02)
Dose × Meningococcal vaccine uptake ($p < 0.004$)	Yes (Ref)	1	1.51 (1.18–1.93)
	No	1.15 (1.04–1.28)	1.53 (1.15–2.03)
	Don't know/can't remember	1.14 (1.08–1.21)	1.58 (1.22–2.05)
	Prefer not to say	0.90 (0.70–1.16)	1.19 (0.76–1.84)

Regression model: Binomial regression with logit function.

Reference groups are indicated where applicable.

Note: The main effect of each variable is presented first followed by set of interactions between five predictors and dose type (Primary vs. Booster).

Bold values indicate statistical significance at $p < 0.05$.

¹ VH = Vaccine Hesitancy scores (range from 0–30), SD = Standard Deviation.

² OR = Odds ratio; CI = Confidence Interval.

² Crude ORs represent estimates from univariate analysis with a single predictor.

³ Adjusted ORs represent estimates from the multivariable Generalized Estimating Equation model including all predictors shown and accounting for repeated measures between primary and booster doses.

We also identified five significant interactions; [Table 5](#) shows that the effect of certain variables on VH scores differed between primary and booster doses. Generally, VH scores increased significantly for booster doses than primary doses across different groups ([Fig. 1](#)). For instance, older students (40+ years) showed the highest VH scores across both primary and booster doses, but younger age groups (14–19 and 20–29 years) had the largest increase in their VH when moving from primary to boosters (aOR = 1.51, 95 % CI 1.18–1.39 and aOR = 1.61, 95 % CI 1.24–2.09, respectively). In addition, those who perceived they were at a moderate-to-high risk of getting COVID had a smaller increase in their VH when moving from primary to boosters (aOR_{interaction} = 0.91, 95 % CI 0.86–0.96), compared to those who perceived they were at no-to-low risk of getting COVID-19 (supplementary material). [Fig. 1](#) also shows that the greatest increment in VH when moving from primary to boosters occurred among students who had not previously received flu or meningococcal vaccines and those who had not been hospitalized for COVID-19, compared to those who received the flu or meningococcal vaccine and those who were hospitalized due to COVID-19. Lastly, in all the interactions, those who didn't disclose their answers showed the highest VH scores for both primary and booster doses.

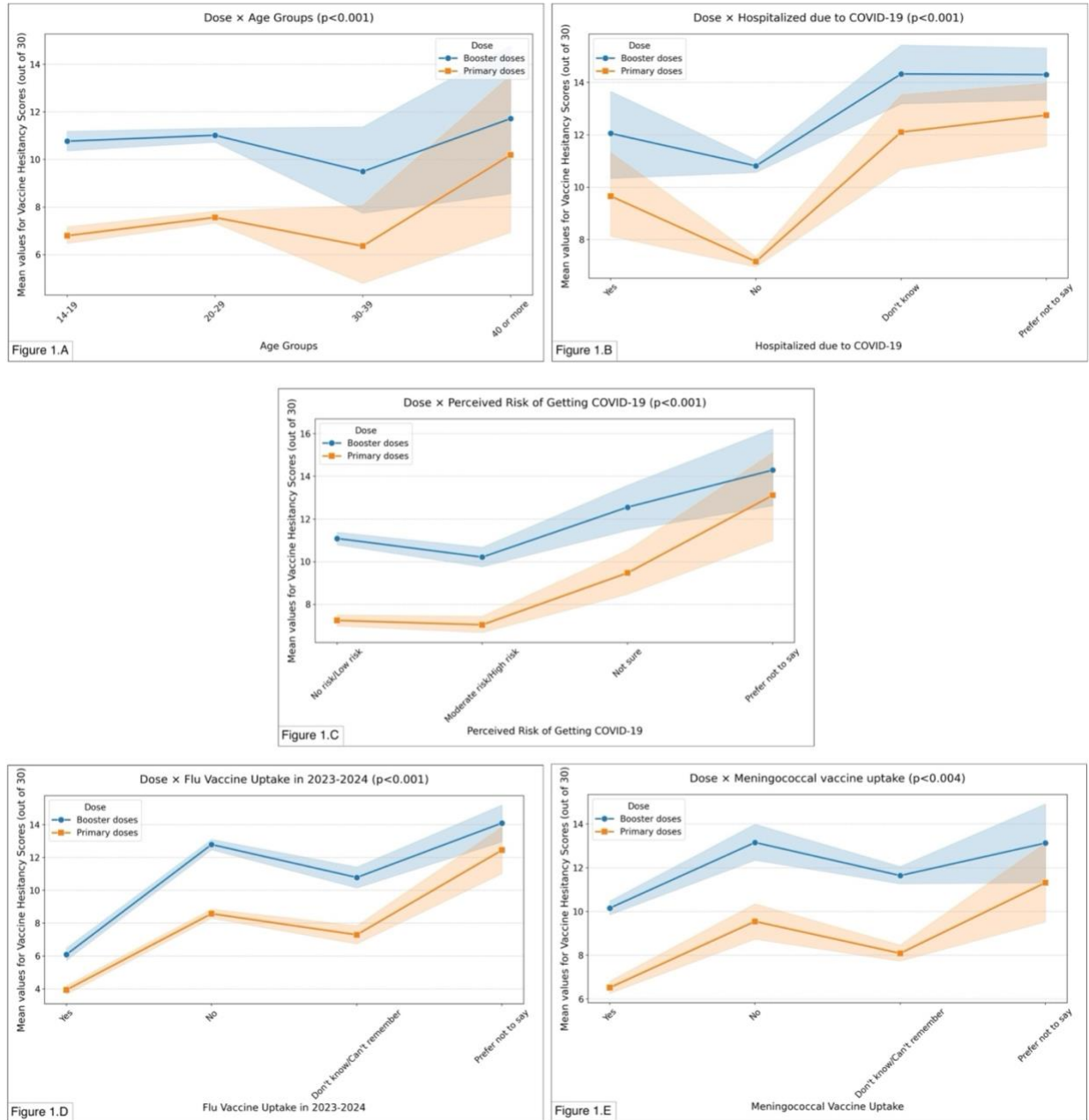


Fig. 1. The interaction effect between dose type (primary and booster) and multiple independent variables, on vaccine hesitancy scores among 4453 students at the University of Waterloo, Ontario, Canada, 2024. (A) represents the interaction between dose type and age groups. (B) represents the interaction between dose type and hospitalization due to COVID-19. (C) represents the interaction between dose type and perceived risk of getting COVID-19. (D) represents the interaction between dose type and flu vaccine uptake in 2023–2024. (E) represents the interaction between dose type and meningococcal vaccine uptake.

4. Discussion

To our knowledge, this is the first study to examine COVID-19 VH and its determinants among university students by capturing changes in VH scores between primary and booster doses. Our findings point to a substantial shift in VH as students moved from mandated primary series to optional booster doses. VH scores increased by roughly 50 %, with the proportion of hesitant students nearly doubling from 17 % to 33.4 %. The most prominent drivers of this shift were age, religious beliefs, vaccine mandates, complacency (low perceived risk), confidence in vaccine safety and effectiveness, convenience of access, government recommendations, and prior vaccination behaviors. Our GEE analysis further revealed that changes in VH scores varied significantly across subgroups, particularly by age, hospitalized due to COVID-19, vaccination history, and perceived COVID-19 risk.

The significant increase in VH prevalence between COVID-19 primary and booster doses in our study suggests a pattern of evolving vaccine-related attitudes among younger populations. Similar booster-specific hesitancy rates have been reported globally [8,24,47]. In China, nearly one-third of university students reported hesitancy toward booster doses [8], while in the United States, a national survey found that 60 % of fully vaccinated college students had not received a booster and did not intend to do so, with citing a lack of perceived necessity as the most contributing factor [47]. A multi-country survey similarly reported that about one in eight vaccinated adults were hesitant to receive a booster despite having accepted the primary series [48]. These trends reinforce that VH is not static but shifts over time, shaped by personal experience, perceived risk, and the social and institutional framing of vaccination [49]. The emergence of booster hesitancy, even among previously compliant individuals, may signal a shift from collective public health urgency to more personal, individualized decisions about

vaccination in this phase of the pandemic.

Our analysis identified gender and age as important predictors of VH across both vaccination phases. Women reported slightly higher VH scores than men for boosters, consistent with prior research indicating higher hesitancy among females that could be linked to concerns over vaccine safety, fertility, and pregnancy [6,50]. Among younger women of reproductive age, hesitancy toward additional doses may reflect heightened risk perception. Early reports of menstrual irregularities following COVID-19 vaccination, even if temporary, may have amplified these concerns [51]. For additional doses, such concerns may be compounded by the belief that repeated vaccinations could increase potential risks, despite scientific reassurance. Additionally, young women's higher engagement with social media may have increased their exposure to misinformation that links vaccination to reproductive harm [50,52]. On the other hand, older students in our study were more hesitant toward the primary series, in contrast with prior research showing greater hesitancy among younger adults [[5], [6], [7]]. However, the largest VH increase from primary to booster doses occurred among younger students, potentially reflecting lower perceived risk, previous experiences with side effects, and pandemic fatigue [5,7,8]. Prior surveys similarly found undergraduate students less likely to be vaccinated than graduate or postdoctoral peers, possibly due to younger ages, higher complacency, and lower pandemic awareness [18,47]. These findings lend empirical support to our proposed addition of “Context” (e.g. age and gender) to the 5C's model, aligning with Razai et al. [53], who emphasized incorporating socio-demographic factors into VH frameworks.

Vaccine mandates and religious beliefs also contributed to the shifts in VH between doses, supporting their inclusion within the proposed “Context” construct. Although around one-third of students reported being vaccinated due to university mandates, a larger proportion

indicated that mandates had no influence on their decisions. The latter group exhibited lower and more stable VH between doses, likely reflecting stronger internal motivation rather than reliance on external cues. Similar findings were noted by Anderson et al., who found that institutional mandates did not predict vaccine uptake, but students who believed a mandate was in place were more likely to be vaccinated [20]. Nonetheless, Bardosh et al., questioned the effectiveness and ethics of booster mandates for young adults, arguing that they lack an updated risk-benefit justification [54]. We believe that the key distinction here lies in the differential impact of mandates on vaccine uptake versus hesitancy. While mandates may prompt initial uptake, long-term vaccine attitudes could be more resilient when grounded in personal conviction rather than perceived obligation. In addition, our findings showed that having no religious beliefs was associated with lower VH scores, consistent with prior research that linked religiosity to greater hesitancy [55,56]. This may point to a broader pattern in which students with religious beliefs are more influenced by faith-based messaging or religious norms that affect VH over time. Adherence to religious beliefs can sometimes sustain VH by making individuals less receptive to new or contradictory information [57].

Consistent with the 5C's model [30,37], confidence, convenience, and complacency were key drivers of changes in VH between primary and booster doses. We found that trust in booster safety, effectiveness, and importance was associated with decreased VH over time, whereas difficulty accessing vaccines contributed to greater VH. We also observed that reduced perceived risk of contracting COVID-19 amplified VH more substantially for boosters, supporting prior research linking complacency (low perceived disease severity) to greater hesitancy and delayed uptake [6,30,41]. One possible explanation is the emerging concept of “vaccination burnout,” a phenomenon marked by emotional exhaustion from repeated vaccination efforts [58], driven by logistical burdens, pandemic fatigue, and declining

motivation. Each additional dose may be perceived as a hurdle, and without strong incentives or reminders, many students opt out. Deng et al. further documented increased VH among students even after a second COVID-19 infection [8], possibly due to assumptions of natural immunity or persistent beliefs in low personal risk tied to age or health status. Notably, we also found elevated VH among students who were uncertain about their risk or who declined to disclose it, highlighting the need for targeted communication strategies that clearly convey the role of boosters in preventing severe outcomes and maintaining long-term protection.

Another important observation was the role of government recommendations in shaping VH shifts. While most students expressed a willingness to vaccinate when recommended by government authorities, those who were unlikely to follow such recommendations showed a notable increase in VH for boosters. This echoes the work of Bronfman et al., who reported that low government trust does not directly predict preventive behaviors but instead influences young adults to follow such behaviors through social norms and perceptions of community expectations [59]. In such cases, students may turn to alternative information sources, increasing their exposure to misinformation and potentially harmful health behaviors. These findings underscore the inclusion of the proposed “Communication” construct and emphasize the role of government recommendations as a critical reference point for students navigating vaccination decisions.

Finally, prior vaccination behaviors strongly predicted VH as students who had not received flu or meningococcal vaccines were more likely to demonstrate greater increases in VH scores when shifting from primary to booster doses. Such results align with existing evidence that prior vaccination serves as a proxy for underlying vaccine attitudes and predicts future hesitancy [6,60].

Limitations of this study include the self-reported data that may introduce social

desirability bias; however, we assured anonymity in the informed consent. Second, as data were collected from a single institution, findings may not be fully generalizable but could apply to universities with similar characteristics. Third, the imputation method for missing data may introduce estimates rather than relying on actual responses, though, missingness in this study was minimal and completely at random (less than 3 % per question). Lastly, recall bias is possible, as students were asked about their VH and attitudes 2 to 3 years post-vaccine authorization, potentially affecting their responses.

This study has also notable strengths. It represents one of the largest surveys on VH among university students, thus, enhancing the reliability and generalizability of the findings. The sampling strategy, which involved mass email invitations to all students, minimized selection bias. The use of GEE provided a robust analytical framework, accounting for repeated measures and allowing for a nuanced assessment of changes in VH scores between primary and booster doses. Finally, the decision to analyze VH using its original scores rather than the dichotomized form (hesitant vs. non-hesitant) preserved the variability of VH levels and prevented potential issues associated with imbalanced categories.

5. Conclusion

This study highlights the rise in VH from COVID-19 primary series to booster doses among university students, driven by factors such as perceived risk, trust in vaccine safety and effectiveness, following government communication, religious beliefs, vaccine mandates, and prior vaccination behaviors. Our findings expand the growing literature by emphasizing the dynamic and context-dependent nature of VH across vaccination phases. The pronounced rise in booster hesitancy highlights the need for tailored strategies to address vulnerable groups, including younger adults, those with low perceived risk of COVID-19, and individuals with

limited prior vaccination experience. Targeted interventions should prioritize improving vaccine accessibility, addressing complacency and misinformation, and reinforcing the safety and benefits of boosters. Transparent, consistent communication from trusted sources such as government remains essential for building sustained vaccine trust. Public health efforts should also acknowledge the influence of religious beliefs and institutional mandates by promoting culturally sensitive engagement and building intrinsic vaccine confidence and voluntary acceptance rather than relying on mandates. This work provides a critical foundation for future longitudinal research to track VH trends and inform phase-specific public health strategies aimed at maintaining high vaccination coverage as immunization programs evolve.

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CHAPTER 4 PREAMBLE

In the previous two chapters (Chapters 2 and 3), we first validated the CVHS to measure VH toward COVID-19 primary series and booster doses, and then identified the key demographic, psychological, and contextual factors associated with changes in VH from primary to booster doses. Building on these findings, the third primary research study of this thesis (Chapter 4) was designed to examine how these shifts in VH interact with pandemic-related exposures to influence booster uptake, using a syndemic lens. This study moves beyond by exploring how VH trajectories interact with experiences such as COVID-19 infection, hospitalization, public health compliance, and conspiracy beliefs to affect the uptake of booster doses. This approach offers a more understanding of vaccine behavior during the later stages of the pandemic and highlights the importance of addressing vaccine attitudes without overlooking the pandemic experiences that shape them.

CHAPTER 4

Manuscript 4: The Syndemic Nexus: How Vaccine Hesitancy and COVID-19 Interact to Influence Vaccine Uptake among University Students

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Syndemics, Interactions, COVID-19, Vaccine Hesitancy, University Students, Primary and Booster doses, Canada

Abstract

Purpose: This study examined whether COVID-19 Vaccine Hesitancy (VH) and COVID-19-related factors interact to influence COVID-19 booster doses uptake among university students in Canada, from a syndemic perspective.

Methods: A cross-sectional survey was conducted among 4,453 students at the University of Waterloo in 2024. VH was measured toward both COVID-19 primary and booster doses. Change in VH scores were computed to capture shifts in hesitancy over time. Logistic regression models assessed the main effects of VH and COVID-19-related factors on booster uptake. Interactions were tested using additive and multiplicative scales.

Results: Increased VH was associated with a 23% decrease in booster uptake. Younger ages, not being hospitalized due to COVID-19, not receiving the flu vaccine, non-compliance with COVID-19 guidelines, and belief in conspiracy theories predicted lower booster uptake. Significant interactions were found between change in VH scores and COVID-19 diagnosis and hospitalization history, guideline adherence, and conspiracy beliefs. For students who did not receive booster doses, the change in VH was greater among those who reported following public health guidance than those who did not. Similarly, for students who did not receive booster doses, the change in VH was greater among those who reported not believing in conspiracy theories compared to those who did.

Conclusion: The findings support a syndemic model, indicating that VH and COVID-19-related experiences jointly influence booster uptake. Targeted interventions such as rebuilding trust, addressing misinformation, and reducing stigma may improve booster uptake even if not all barriers are addressed. Further research is needed to examine these interactions.

1. Introduction

Syndemics refers to the synergistic interaction of co-occurring epidemics, where their combined effect worsens health outcomes beyond individual effects [1]. Syndemics was developed to explain the clustering of HIV/AIDS, substance use, and violence (SAVA syndemic) [2], and has since been applied to the COVID-19 pandemic [3,4]. Syndemics are not limited to biological diseases but also include social and contextual factors that interact to worsen health outcomes [5].

The COVID-19 pandemic has intensified health disparities, beyond its direct health impacts [3]. Misinformation and distrust in science have further fueled the viral spread by undermining adherence to public health guidelines and acceptance of preventive measures [6]. Therefore, COVID-19 vaccines became essential tools for reducing severe illness and death, but their success has been limited by widespread vaccine hesitancy (VH), particularly toward booster doses [6,7].

VH has been widely studied as a sociocultural and behavioral phenomenon rather than a purely individual decision [8]. It predates COVID-19 and has historically affected uptake of vaccines against measles, influenza, and HPV [9,10]. Though not a biological disease, VH exhibits epidemic-like characteristics due to its rapid spread through social contagion and peer influence [11,12]. Like misinformation, VH can spread socially and cluster in specific communities in ways analogous to infectious diseases [13,14], which in turn fuels hesitancy among new individuals and compromises herd immunity [14].

The convergence of COVID-19 as a pandemic and VH as a social epidemic [16], suggests the potential for syndemic interaction. VH has shaped the pandemic by limiting vaccine uptake and prolonging transmission [6], while the pandemic has amplified VH by misinformation, conspiracy theories, and political polarization [15,16]. This reciprocal influence has given rise to new forms of

hesitancy, including booster-specific concerns and skepticism toward mRNA technology [7,17]. Therefore, the syndemic framework offers a valuable lens to understand how COVID-19-related experiences interact with VH to influence booster uptake, which requires sustained trust in evolving public health messaging [18].

Younger adults have shown higher rates of VH, particularly regarding COVID-19 booster doses [7,9]. In Canada, university students were subject to a COVID-19 primary vaccine mandate where vaccination was required to access campus facilities [19]. Therefore, primary vaccine uptake may reflect institutional compliance rather than personal conviction. In contrast, booster doses offer a better context for examining how VH influenced vaccine uptake following the removal of mandates. This combination of youth-specific vulnerabilities (e.g., high exposure to misinformation, pandemic fatigue) and a distinct policy context (mandated primary vaccination vs. voluntary boosters) makes university students a valuable population for examining the syndemic relationship between COVID-19-related experiences and VH.

Despite the increasing use of syndemic theory, empirical tests of interaction are often absent from the literature. Many syndemic studies rely on simple counts of co-occurring conditions, rather than formally testing whether conditions interact to amplify health risks [5]. To address this gap, the aim of this study was to assess whether COVID-19 VH and COVID-19-related factors such as diagnosis, hospitalization, adherence to public health guidelines, and beliefs in conspiracy theories, interact synergistically to influence the uptake of COVID-19 booster doses among university students in Waterloo, Canada.

2. Methods

2.1. Study design and data collection

The data were drawn from a cross-sectional survey conducted among undergraduate and graduate students at the University of Waterloo (UW), Ontario, Canada. Full details of the study design and data collection are presented elsewhere [20,21]. Briefly, participants were recruited through email invitations and social media platforms. Following written informed consent, participants completed an online questionnaire hosted on the Qualtrics platform. Data collection took place between March and May 2024. Incentives were provided through a random draw to win one of fifty \$25 added to the on-campus purchasing card. Overall, 40,408 students were invited to participate, and 4,453 completed the survey [20,21]. Ethical approval was obtained from the University of Waterloo's Research Ethics Board (ORE #46023).

2.2. Measures and Outcome

All measures were adapted from a questionnaire we developed in earlier studies [20,21]. The key variables used for this study were:

2.2.1. Primary exposures of interest

COVID-19 VH. COVID-19 VH scores were measured using the 15-item COVID-19 Vaccine Hesitancy Scale (CVHS) [22]. VH scores were recorded two times: once for primary doses and once for booster doses. The final scores ranged from 0–30, with higher scores indicating higher VH. The adapted CVHS version used in this study, including its scoring protocol, was validated among university students in our prior research [20,21].

COVID-19 contextual factors. Participants were asked whether they had been diagnosed with or hospitalized due to COVID-19, and if they believed in COVID-19-related conspiracy theories. Response options included: yes, no, don't know, and prefer not to say. Participants were also asked how often they followed the COVID-19 public health guidelines such as mask-wearing and physical distancing. Response options included: not at all, occasionally, most of the time, all the time, and prefer not to say. Responses were grouped into three categories: "all of the time/most of the time" and "not at all/occasionally", with "prefer not to say" retained separately.

2.2.2. Outcome measure

COVID-19 Vaccine uptake for primary and booster doses. Participants were asked whether they had received the COVID-19 primary and booster doses. For primary doses uptake, participants who reported receiving one or two doses were coded as "yes", while those who reported receiving no primary doses were coded as "no". Similarly, for booster doses uptake, participants who reported receiving one or more booster doses were coded as "yes", while those who reported receiving no booster doses were coded as "no".

2.2.3. Covariates

Previous vaccination attitude and behaviour. Participants were asked whether they usually receive the seasonal flu vaccine. Response options included: yes, no, don't know, and prefer not to say. This variable was used as a proxy for the overall attitudes and adherence to routine vaccinations.

Demographics. Socio-demographic data, including age, gender, income, and employment status, were collected.

2.3. Statistical analysis

Percentage of missing data were calculated and presented elsewhere [20]. Missing data were minimal (<3% for most questions) and found to be completely at random ($p = 1.00$) using Little's MCAR test [23]. Descriptive statistics were computed for all study variables. Means and Standard Deviations (SD) for VH scores for both primary and booster doses were previously reported [21]; with a mean and SD of 7.3 ± 7.1 for primary doses and a mean and SD of 10.9 ± 8.1 for booster doses.

Since VH scores were measured at two points, a third variable was created to assess changes in VH scores when shifting from primary to booster doses. A VH difference score was calculated as: (Change in VH scores = VH score_{Boosters} – VH score_{Primary}); where a positive score indicates an increase in hesitancy (higher hesitancy for boosters compared to primary doses), and a negative score indicates a decrease in hesitancy (lower hesitancy for boosters compared to primary doses). A score of zero reflects no change.

Participants who did not receive any primary doses (2.2% of the sample) were excluded from the main analysis due to small group size, which caused model convergence issues and unstable estimates. However, a descriptive analysis was conducted for this subgroup. Independent t-tests and chi-square tests were used to compare their demographic characteristics and VH scores with the rest of the sample (see supplementary material). Accordingly, the primary outcome of this study focused on COVID-19 booster dose uptake (yes/no).

To examine the syndemic effect between COVID-19 VH scores and COVID-19-related factors on booster doses uptake, a logistic regression model was fitted. Independent variables included change in VH scores, history of COVID-19 diagnosis, COVID-19-related hospitalization,

belief in conspiracy theories, and adherence to public health guidelines. The model was adjusted for key covariates: age, gender, income, employment status, and flu vaccine uptake. Model fit was evaluated using the Hosmer-Lemeshow goodness-of-fit test [24].

To explore potential interactions, four product terms were included in the logistic regression model, representing two-way interactions between change in VH scores and each of the following: history of COVID-19 diagnosis, hospitalization due to COVID-19, beliefs in conspiracy theories, and adherence to public health guidelines. Interactions were assessed on both additive and multiplicative scales. As noted by Knol et al. [25], the product term in logistic regression reflects interaction on the multiplicative scale. Therefore, odds ratios (ORs) and their 95% confidence intervals (CIs) were interpreted as measures of multiplicative interaction: $OR = 1$ indicates no interaction, $OR > 1$ suggests positive interaction, and $OR < 1$ indicates negative interaction [25,26]. To assess additive interaction, the Relative Excess Risk due to Interaction (RERI) was calculated using the previously established formula by Knol et al. [25]. A RERI of 0 indicates no additive interaction, $RERI > 0$ suggests a positive interaction, and $RERI < 0$ indicates a negative interaction [25,26]. All statistical analyses were conducted using IBM SPSS version 29.0, with a significance level set at 0.05.

3. Results

Of the 4,453 participants who completed the survey, 57.2% were women and 37.9% were men, with a mean age of 21 years ($SD = 3.5$). Most students (97.8%) received the COVID-19 primary doses and 66.1% received booster doses. More than half of students (52.5%) did not receive the flu vaccine. The mean of change in VH scores was 3.7 ($SD = 4.7$). Regarding COVID-19-related experiences, 61.2% had been diagnosed with COVID-19 and 1.2% had been hospitalized. Most

participants (86.6%) reported following public health guidelines all or most of the time, while 11.9% followed them only occasionally or not at all. Belief in COVID-19 conspiracy theories was reported by 20.7% of participants (Table 1).

Among participants who did not receive any COVID-19 vaccine (2.2%; $n = 96$), most were women (60.4%), employed (55.2%), had lower income (28.1%), and had a mean age of 22.3 years ($SD = 6.4$). This subgroup had significantly higher VH scores for both primary (mean $\pm$ $SD = 23.5 \pm 5.4$) and booster doses (mean $\pm$ $SD = 24.9 \pm 5.0$) compared to vaccinated participants (primary: mean $\pm$ $SD = 7.0 \pm 6.7$) and (boosters: mean $\pm$ $SD = 10.7 \pm 7.9$). They were also significantly less likely to receive a flu vaccine (6.3% vs. 34.4%; $p < 0.001$), less likely to follow COVID-19 guidelines (56.3% vs. 87.2%; $p < 0.001$), and more likely to believe in conspiracy beliefs (75.0% vs. 19.5%; $p < 0.001$) (see supplementary material).

Several key predictors of COVID-19 booster dose uptake were identified (Table 2.a). After adjusting for all variables in the model, an increase in VH scores from the time of primary doses to the booster doses was associated with a 23% reduction in booster doses uptake (aOR = 0.77, 95% CI: 0.68–0.89). COVID-19 Behaviors and beliefs were also significant factors. Participants who occasionally or never followed public health guidelines were less likely to receive booster doses (aOR = 0.48, 95% CI: 0.36–0.62). Students who endorsed conspiracy theories were 78% less likely to receive booster doses (aOR = 0.22, 95% CI: 0.18–0.28). Also, those who were uncertain (aOR = 0.41, 95% CI: 0.30–0.56) or did not disclose their conspiracy beliefs (aOR = 0.52, 95% CI: 0.28–0.97) were less likely to receive booster doses. Lastly, students who had not been hospitalized for COVID-19 were less likely to receive boosters (aOR = 0.39, 95% CI: 0.18–0.86) than those who had.

The analysis also revealed that older participants were more likely to receive booster doses, with one-year increase in age associated with an 11% increase in the likelihood of getting booster doses (aOR = 1.11, 95% CI: 1.07–1.14). Flu vaccine uptake was another predictor of booster uptake; participants who did not receive the flu vaccine were 57% less likely to get COVID-19 booster doses (aOR = 0.43, 95% CI: 0.37–0.51), compared to those who usually receive it (Table 2.a).

Regarding interactions (Table 2.b), we found evidence that the effect of increased VH on booster uptake varied by COVID-19-related experiences. Among participants who preferred not to disclose their COVID-19 diagnosis, an increase in VH from the time of primary doses to the booster doses was associated with a 28% reduction in booster uptake (aOR = 0.72, 95% CI: 0.56–0.93), compared to those who were previously diagnosed with COVID-19 (Fig. 1.A). A significant interaction was also observed with COVID-19 hospitalization history (Fig. 1.B). Among those who were uncertain about their hospitalization status, increased VH was associated with higher booster uptake on both multiplicative (aOR = 1.33, 95% CI: 1.08–1.64) and additive scales (RERI = 0.23, 95% CI: 0.13–0.34), compared to those who were hospitalized. Interactions were also significant between the change in VH and adherence to public health guidelines and conspiracy beliefs. For students who did not receive booster doses, the change in VH was greater among those who reported following public health guidance than those who did not (Fig. 1.C). Similarly, for students who did not receive booster doses, the change in VH was greater among those who reported not believing in conspiracy theories compared to those who did (Fig. 1.D).

Table 1. Sociodemographic and other characteristics of the study participants (n = 4453)

Characteristics	Mean (SD*) or Number (%)
<i>Sociodemographic and covariates</i>	
Age (in years)	21.0 (3.5)
Gender	
Man	1689 (37.9)
Woman	2547 (57.2)
Non-binary/Others	126 (2.8)
Prefer not to say	91 (2.0)
Income	
Less than \$29 999	1125 (25.3)
\$30 000 to \$59 999	413 (9.3)
\$60 000 to \$89 999	380 (8.5)
Greater than \$90 000	1092 (24.5)
Don't know	759 (17)
Prefer not to say	684 (15.4)
Employment	
Working (full time, part time, co-op term)	2221 (49.9)
Unemployed	2057 (46.2)
Prefer not to say	175 (3.9)
Seasonal flu vaccine uptake	
Yes	1504 (33.8)
No	2337 (52.5)
Don't know	548 (12.3)
Prefer not to say	64 (1.4)
<i>Independent variables</i>	
Vaccine hesitancy scores for COVID-19 primary doses	7.3 (7.1)
Vaccine hesitancy scores for COVID-19 booster doses	10.9 (8.1)
Change in vaccine hesitancy scores**	3.7 (4.7)
Diagnosed with COVID-19	
Yes	2725 (61.2)
No	1519 (34.1)
Don't know	141 (3.2)
Prefer not to say	68 (1.5)
Hospitalized due to COVID-19	
Yes	53 (1.2)
No	4282 (96.2)
Don't know	58 (1.3)
Prefer not to say	60 (1.3)

Followed the guidance (e.g., masking and physical distancing)	
All the time	1308 (29.4)
Most of the time	2546 (57.2)
Occasionally	454 (10.2)
Not at all	75 (1.7)
Prefer not to say	70 (1.6)
Beliefs in COVID-19 conspiracy theories	
Yes	922 (20.7)
No	3085 (69.3)
Don't know	356 (8.0)
Prefer not to say	90 (2.0)
<i>Outcome variable</i>	
Vaccine uptake for COVID-19 primary doses	
Yes	4357 (97.8)
No	96 (2.2)
Vaccine uptake for COVID-19 booster doses	
Yes	2944 (66.1)
No	1509 (33.9)

*SD: Standard Deviation

** Change in vaccine hesitancy (VH) scores = VH score_{Boosters} – VH score_{Primary}

Table 2.a. Multivariable logistic regression of predictors of COVID-19 booster doses uptake among University of Waterloo students, 2024

Variables	Crude OR (95% CI)	Adjusted* OR (95% CI)
Intercept	..	2.13
Change in vaccine hesitancy score	0.87 (0.86-0.88)	0.77 (0.68-0.89)
Age (in years)	1.10 (1.07-1.13)	1.11 (1.07-1.14)
Gender		
Men (Ref)	..	..
Woman	1.26 (1.11-1.43)	1.11 (0.96-1.28)
Non-binary/Others	2.06 (1.37-3.10)	1.22 (0.77-1.93)
Prefer not to say	0.89 (0.58-1.36)	0.61 (0.37-1.00)
Income		
Less than \$29 999 (Ref)	..	..
\$30 000 to \$59 999	1.23 (0.97-1.55)	1.40 (1.07-1.82)
\$60 000 to \$89 999	1.12 (0.88-1.42)	1.27 (0.97-1.67)
Greater than \$90 000	1.22 (1.03-1.45)	1.33 (1.09-1.62)
Don't know	0.93 (0.77-1.13)	1.08 (0.87-1.34)
Prefer not to say	1.12 (0.92-1.36)	1.33 (1.05-1.68)
Employment status		
Working (full/ part time, co-op term) (Ref)	..	..
Unemployed	0.85 (0.75-0.96)	0.85 (0.74-0.98)
Prefer not to say	0.91 (0.67-1.25)	1.00 (0.68-1.47)
Flu vaccine uptake		
Yes (Ref)	..	..
No	0.31 (0.27-0.36)	0.43 (0.37-0.51)
Don't know	0.36 (0.29-0.44)	0.51 (0.41-0.65)
Prefer not to say	0.59 (0.34-1.11)	0.81 (0.42-1.57)
Ever diagnosed with COVID-19		
Yes (Ref)	..	..
No	0.95 (0.84-1.09)	1.08 (0.89-1.32)
Don't know	0.62 (0.44-0.87)	0.98 (0.57-1.68)
Prefer not to say	1.05 (0.64-1.73)	4.69 (1.32-16.69)
Ever hospitalized due to COVID-19		
Yes (Ref)	..	..
No	0.69 (0.38-1.24)	0.39 (0.18-0.86)
Don't know	0.43 (0.20-0.94)	0.17 (0.06-0.50)
Prefer not to say	0.80 (0.36-1.77)	0.21 (0.05-0.83)
Followed the COVID-19 government guidance (e.g., masking)		
All/Most of the time (Ref)	..	..
Occasionally/Not at all	0.42 (0.35-0.51)	0.48 (0.36-0.62)

Prefer not to say	0.85 (0.522-1.37)	0.45 (0.18-1.12)
Beliefs in COVID-19 conspiracy theories		
No (Ref)	..	..
Yes	0.34 (0.29-0.40)	0.22 (0.18-0.28)
Not sure	0.57 (0.46-0.71)	0.41 (0.30-0.56)
Prefer not to say	0.71 (0.46-1.09)	0.52 (0.28-0.97)

*Adjusted for the following variables: change in vaccine hesitancy score, age (in years), gender, income, employment status, flu vaccine uptake, diagnosed with COVID-19, hospitalized due to COVID-19, followed the COVID-19 government guidance, and beliefs in COVID-19 conspiracy theories.

- Significant values are shown in bold.

- Reference category for the response variable is “not receiving booster doses”.

Table 2.b. Effect of change in vaccine hesitancy scores and COVID-19 related factors on the uptake of COVID-19 booster doses

Interactions	Adjusted OR* (95% CI)	RERI** (95% CI)
Change in vaccine hesitancy score × Diagnosed with COVID-19		
Yes (Ref)	..	
No	1.01 (0.97-1.04)	-0.01 (-0.08-0.06)
Don't know	0.97 (0.88-1.07)	-0.02 (-0.21-0.17)
Prefer not to say	0.72 (0.56-0.93)	-1.85 (-4.94-1.24)
Change in vaccine hesitancy score × Hospitalized due to COVID-19		
Yes (Ref)	..	
No	1.07 (0.93-1.22)	0.16 (-0.01-0.30)
Don't know	1.33 (1.08-1.64)	0.23 (0.13-0.34)
Prefer not to say	1.30 (0.97-1.76)	0.23 (0.11-0.34)
Change in vaccine hesitancy score × Followed COVID-19 government guidance		
All/Most of the time (Ref)	..	
Occasionally/Not at all	1.06 (1.02-1.11)	0.14 (0.07-0.21)
Prefer not to say	1.11 (0.91-1.36)	0.16 (-0.14-0.29)
Change in vaccine hesitancy score × Beliefs in COVID-19 conspiracy theories		
No (Ref)	..	
Yes	1.15 (1.11-1.20)	0.20 (0.12-0.28)
Don't know	1.12 (1.07-1.18)	0.17 (0.11-0.24)
Prefer not to say	1.07 (0.96-1.20)	0.14 (-0.01-0.25)

*Adjusted for the following variables: change in vaccine hesitancy score, age (in years), gender, income, employment status, flu vaccine uptake, diagnosed with COVID-19, hospitalized due to COVID-19, followed the COVID-19 government guidance, and beliefs in COVID-19 conspiracy theories.

*Adjusted odd ratios of the interactions reflect interactions on a multiplicative scale.

**Relative Excess Risk due to Interaction (RERI) reflect interactions on an additive scale.

- Significant values are shown in bold.

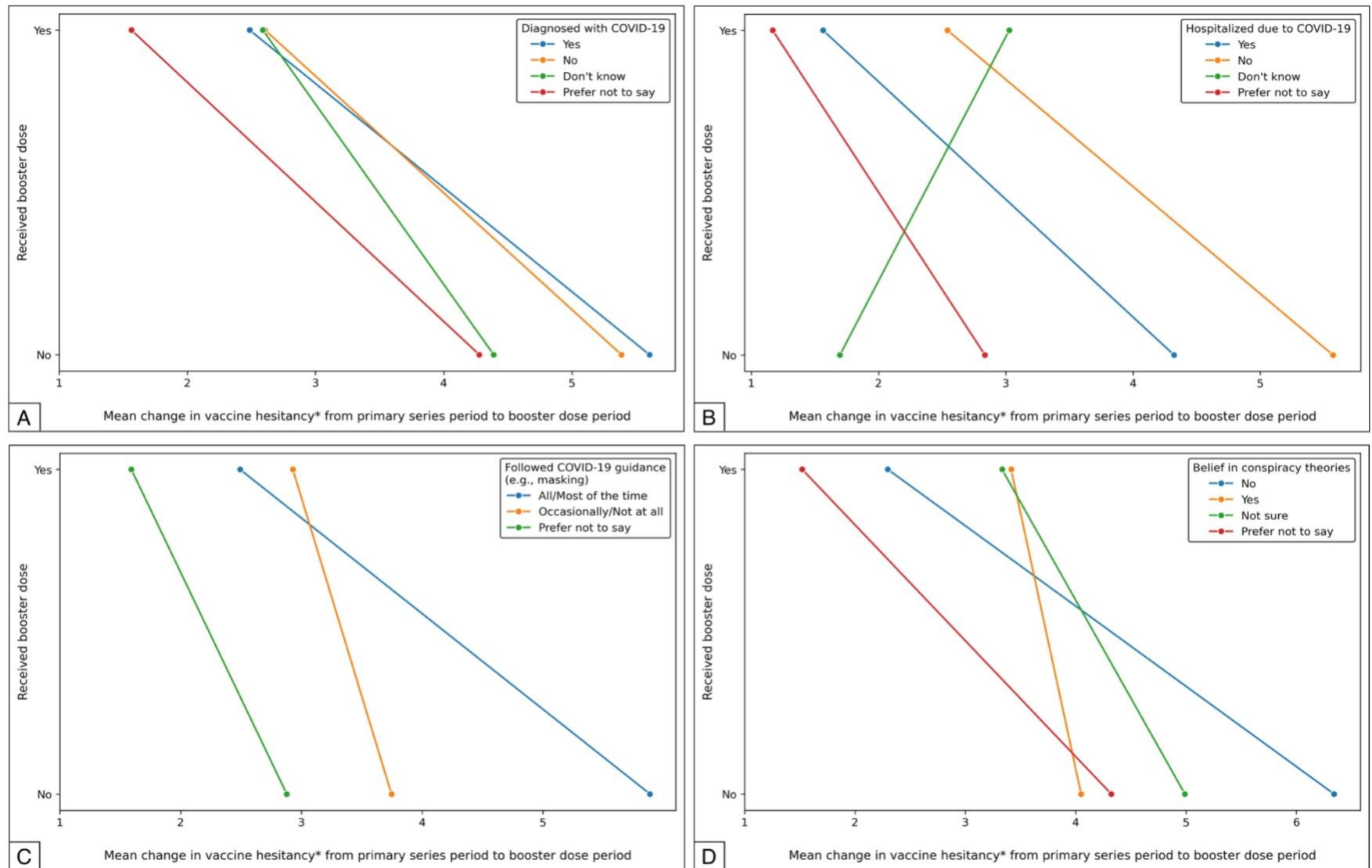


Fig. 1. Interaction between change in vaccine hesitancy score and COVID-19-related factors on booster dose uptake among 4,453 students at the University of Waterloo, Ontario, Canada, 2024. (A) represents interaction between change in vaccine hesitancy and history of COVID-19 diagnosis. (B) represents interaction between change in vaccine hesitancy and history of COVID-19 hospitalization. (C) represents interaction between change in vaccine hesitancy and adherence to COVID-19 public health guidance. (D) represents interaction between change in vaccine hesitancy and belief in COVID-19 conspiracy theories.

* Change in vaccine hesitancy score was calculated as $(VH\ score_{Change} = VH\ score_{Boosters} - VH\ score_{Primary})$, where VH scores for primary and booster doses range from 0 to 30.

4. Discussion

This study examined the syndemic interaction between changes in VH scores and COVID-19-related factors on COVID-19 booster uptake among university students in Canada. A core principle of the syndemic framework is that the joint effect of interacting conditions produces worse outcomes than each factor alone. Our findings support this model by demonstrating interactions between changes in VH scores and each of the following: COVID-19 diagnosis and hospitalization, guideline adherence, and conspiracy beliefs. Importantly, we found that VH scores fluctuated over time and these changes did not impact all groups equally. Certain individuals remained vaccine resistant regardless of their VH fluctuations, while others were more flexible and responsive to shifts in hesitancy. Such findings are novel in that they move beyond a simple analysis of hesitancy levels and instead support the syndemic model by demonstrating that VH interacts with COVID-19-related experiences, lowering booster uptake beyond what would be expected from each factor individually.

Our findings identified several key factors associated with lower booster uptake, including high VH scores, younger ages, not receiving the flu vaccine, not being hospitalized due to COVID-19, non-compliance with public health guidelines, and belief in conspiracy theories. Specifically, we found that an increase in VH from the time of primary to booster doses was associated with a 23% lower uptake of COVID-19 booster dose. This implies that while many students initially complied with primary vaccine mandates, their willingness to get additional doses declined over time. Such finding is consistent with prior research showing that booster hesitancy tends to be higher than hesitancy toward primary doses, largely due to declining perceived risk, safety concerns, and exposure to misinformation [7]. In addition, prior COVID-19 hospitalization was associated with higher booster uptake, supporting existing evidence that 64% of hospitalized patients promoted

COVID-19 vaccination upon discharge, and 69.5% intended to receive their vaccine within the recommended timeframe [27]. This suggests that perceived severity, rather than just exposure to the virus, is a strong motivator for continued vaccination.

Misinformation and conspiracy beliefs also played a significant role in vaccine decisions. We found that COVID-19 conspiracy believers were 78% less likely to receive booster doses, consistent with Silver et al. (2024), who reported that declining trust in public health institutions over time led to reduced booster uptake, whereas greater trust could increase booster uptake by at least 10% [18]. Another finding in this study was that students who did not receive the flu vaccine were significantly less likely to receive booster doses, reinforcing the idea that vaccine behaviors across different diseases are closely linked. This could be explained by that students who prioritize annual flu vaccinations might be more health-conscious or trustful of medical recommendations, leading to higher acceptance of COVID-19 boosters. Similarly, prior studies showed that prior flu vaccination predicted COVID-19 vaccine acceptance [28,29], though most research has focused on primary doses. Our findings extend this association to booster doses, underscoring the importance of long-term vaccine confidence to reinforce consistent immunization behaviors over time.

In terms of the proposed syndemic, we found three compelling interactions demonstrating that VH interacts with the COVID-19 pandemic and affects different groups in different ways. First, the interaction between change in VH and prior COVID-19 diagnosis and hospitalization highlights how COVID-19- related stigma surrounding personal health status and VH reinforce one another and thus, ultimately impacting booster uptake. Students who preferred not to disclose their COVID-19 history exhibited a decrease in booster uptake as their VH increased, suggesting that reluctance to disclose past infection is linked to heightened hesitancy, possibly driven by stigma and fear of judgment. Such findings parallel previous research showing that individuals facing stigma, such as

those with psychotic disorders, often have greater VH due to distrust in health institutions and impaired decision-making [30]. Likewise, COVID-related stigma has been directly associated with VH [31].

On the other hand, students who were uncertain about their hospitalization status showed an increase in booster uptake as their VH increased, a paradoxical trend that can be explained in two ways. One possible explanation is that some of these individuals were hospitalized but chose not to disclose it due to social stigma, particularly among younger adults who may perceive hospitalization as a sign of vulnerability or failure to manage health [31,32]. Another explanation could be that some students were hospitalized but were unsure if it was because of COVID-19 due to diagnostic uncertainty. Either way, regardless of their initial hesitancy, their hospitalization experience may have increased their health awareness, leading them to prioritize vaccination. Such that, those individuals initially concealed their hospitalization but ultimately adjusted their vaccine behaviour as risk perception evolves. Our findings further support the idea that social stigma related to disease is a key promoter of syndemic interactions [33], as it not only increases hesitancy but also decreases vaccine uptake and creates a cycle of fear and reduced public health compliance.

The second interaction was observed between change in VH and adherence to COVID-19 guidelines. Our results showed that as VH increased, the decline in booster uptake was more pronounced among those who previously followed COVID-19 guidelines compared to those who did not. This might seem counterintuitive at first, but it fits with the broader discussion of “pandemic fatigue” where prolonged exposure to strict pandemic guidelines leads to diminishing trust in continued mandates or shifting perceptions of vaccine necessity [9,34]. Previous studies have identified similar trends, where mandates played a critical role in driving primary vaccine uptake [35], but once mandates disappeared, people became less motivated to continue with boosters [7,36].

Our study suggests that even individuals who initially complied with guidelines may have experienced a loss of trust or motivation over time, making booster hesitancy a growing challenge even among pro-vaccine individuals. From a syndemic perspective, this interaction indicates that pandemic fatigue and VH collectively shape vaccine uptake in ways that would not be observed if each factor was examined separately.

The final interaction was observed between change in VH and conspiracy beliefs. An increase in VH over time had a stronger effect in reducing booster uptake among non-conspiracy believers compared to conspiracy believers. A possible explanation is that conspiracy believers already exhibit high and stable levels of VH, meaning that fluctuations in their VH scores are minimal and have little to no impact on their booster decisions. As noted previously, this group tends to distrust health authorities who advocate for vaccination [37]. Hence, they are less compliant with professional public health guidance and may exhibit deep-seated vaccine resistance rather than temporary hesitancy [38]. In contrast, non-conspiracy believers tend to be more responsive to shifts in VH, as they are generally more flexible and less bound by rigid ideological frameworks. The latter group—which could be described as the “movable middle” [39]—is not fundamentally opposed to vaccines but may express hesitancy due to factors such as fear of side effects, uncertainty about effectiveness, or exposure to conflicting information, rather than ideology.

While this study conceptualized increased VH toward booster doses as a continuation of prior vaccine attitudes, it is important to note that hesitancy toward boosters may be influenced by a different logic than that initial vaccine resistance. In particular, booster hesitancy may reflect practical concerns about utility rather than broad-based distrust or ideological opposition. COVID-19 booster doses were introduced during a period of waning public urgency, targeting a younger and lower-risk population, with messaging focused on preventing severe illness rather than infection. As

such, student hesitancy may stem less from general vaccine distrust and more from uncertainty about the personal necessity of repeat doses, especially when lifelong immunity is not conferred. This distinction is crucial in interpreting shifts in VH over time, as hesitancy toward optional boosters may involve more context-dependent cost-benefit analyses.

It is also worth noting that while VH and vaccine uptake are closely related, they are not synonymous. Uptake represents the behavioral outcome, whereas VH reflects the underlying attitudes, beliefs, and emotional responses that shape decision-making. Particularly in the context of COVID-19 boosters, vaccine confidence—defined as trust in the safety, efficacy, and importance of vaccines—plays a central role in uptake. Unlike childhood immunization programs with long-standing efficacy and broad consensus, COVID-19 boosters represented a novel intervention aimed primarily at reducing severe disease rather than preventing transmission. This added complexity to public understanding and may have reduced perceived need, especially among low-risk populations. Accordingly, booster hesitancy may reflect ambivalence rooted in shifting risk-benefit evaluations rather than categorical opposition.

Limitations of this study include its reliance on self-reported data, which may introduce social desirability bias, though anonymity was assured through informed consent. As data were collected from a single institution, the findings may not be fully generalizable but could still be applied to similar university settings. Recall bias is also possible, as students reflected on their VH 2–3 years post-vaccine rollout. Lastly, participants who did not receive any COVID-19 vaccine were excluded due to model convergence issues; however, a descriptive analysis was conducted for this subgroup.

This study has also several strengths. It represents one of the largest surveys on VH among

university students. The university-wide email recruitment minimized selection bias and increased the representativeness of the sample. Conducting this study in 2024 offers a unique perspective on VH by capturing attitudes in a post-mandate context. Finally, the use of multiplicative and additive interaction models strengthens the analytical framework and allows for a more comprehensive understanding of synergistically interacting conditions.

5. Conclusion

This study provides empirical evidence for a syndemic model of VH and COVID-19-related experiences which interact synergistically to reduce booster uptake. Our findings suggest that these factors do not act independently but rather exacerbate one another, leading to a decrease in booster uptake. The evidence for interacting conditions was strong, as VH amplified the effects of COVID-19-related stigma, pandemic fatigue, and misinformation. From a public health perspective, this suggests that addressing even one of these interconnected factors may have greater effects on vaccine uptake than if no interactions were present. Interventions aimed at rebuilding trust in public institutions, countering conspiracy beliefs, or reducing COVID-19-related stigma may each contribute to reducing VH, and thereby improving booster uptake, even if not all barriers are addressed simultaneously.

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CHAPTER 5: DISCUSSION AND CONCLUSION

5.1. Overview

University students can be considered an important population in understanding VH, given their stage of emerging independence, exposure to rapidly changing information, and evolving health decision-making. Although early COVID-19 vaccination campaigns focused on distribution and access, sustaining vaccine uptake over time, especially for booster doses, has presented new challenges. Among young adults, booster decisions were not only shaped by access or convenience but also reflected deeper personal experiences tied to changing guidance, public messaging, and broader pandemic policies.

This thesis was guided by the idea that VH is dynamic and socially influenced, especially during a time of rapid public health change. The overall goal of this dissertation was to better understand how VH shifts across different stages of the COVID-19 vaccine rollout (primary vs. booster doses) and how those shifts relate to the lived experiences of university students during the pandemic from a syndemic perspective.

5.2. Summary of Key Findings

The findings in this thesis directly engage with syndemic theory by empirically illustrating how VH trajectories do not operate in isolation but interact with other pandemic-related experiences, such as prior infection, hospitalization, conspiracy beliefs, and public health compliance, to shape vaccine behavior. This aligns with the syndemic model's emphasis on disease interaction, contextual vulnerability, and the compounding effects of co-occurring phenomena. Rather than focusing solely on individual-level determinants, this study reveals how

psychological and behavioral outcomes are amplified when social and structural stressors intersect. These findings reinforce the value of syndemic theory in understanding how public health crises—biological, informational, and institutional—converge to exacerbate risk and shape population health decisions.

This thesis had major findings from the three studies. The first study found that the adapted CVHS tool performed well and demonstrated strong psychometric properties, including internal consistency, factor structure, and known-group validity. The scale was sensitive enough to detect VH differences between groups, such as gender and academic level. Importantly, the scale revealed a noticeable increase in VH from primary to booster doses, supporting the idea that hesitancy becomes more apparent and pronounced when vaccination is no longer mandatory. This trend was further reinforced by uptake behaviors, where we found a greater number of students delayed or refused boosters compared to primary doses, and fewer students were willing to recommend boosters to others. These findings confirmed that mandates may have temporarily and apparently suppressed VH, and that a valid tool is needed to explore how VH re-emerges in voluntary settings.

The second study revealed a substantial increase in COVID-19 VH among students, with hesitancy rates doubling from 17% for primary doses to 33.4% for booster doses. This significant shift was driven by a combination of factors. In line with the 5C's model, a lack of trust in the safety and effectiveness of boosters, perceived low risk of getting COVID-19, and facing access barriers predicted higher VH scores. Pandemic fatigue and vaccine burnout further contributed to declining motivation to take additional doses, particularly after mandates were lifted and urgency declined. The findings also suggested extending the 5C's model to a 7C's model by including two additional components: "Context" and "Communication", as age,

gender, and trust in government communications emerged as key factors. Younger students and women were more hesitant toward both primary and booster doses, and students who were less likely to follow government recommendations showed higher VH, pointing to the role of institutional trust in sustaining vaccine uptake. The impact of religious beliefs and vaccine mandates was also notable. Students who reported that mandates had no effect on their decisions or who had no religious affiliation were less hesitant toward both primary and booster doses, possibly because their attitudes were more internally anchored and less shaped by external or religious pressures. In addition, the interactions observed in this study revealed that changes in VH scores varied significantly across subgroups. Younger students and those with a low perceived risk of COVID-19 demonstrated the largest increases in hesitancy over time, particularly when shifting from primary to booster doses. Prior vaccination behavior, such as not receiving flu or meningococcal vaccines, was also associated with increased VH over time, supporting the view that hesitancy reflects broader and more stable attitudes toward vaccination in general, rather than concerns about a single vaccine. Finally, the study highlighted the role of uncertainty in VH, especially among students who were unsure about their risk of infection. This group does not always fit neatly into pro- or anti-vaccine categories but instead represents a more uncertain middle group that may be hesitant or undecided. Because their views are less fixed, they can be overlooked by standard vaccine messaging, which tends to focus on individuals with more clearly defined attitudes.

The findings from the third study validate the syndemic approach by demonstrating that changes in VH over time and COVID-19-related experiences interact in complex ways that shape vaccine uptake. Notably, vaccine uptake can be considered a health behavior rather than a direct health outcome. However, it remains a critical intermediary that influences population-

level outcomes such as disease transmission, hospitalization rates, and mortality. In this thesis, vaccine uptake was used as a behavioral endpoint shaped by multiple interacting factors, including VH, prior COVID-19 experiences, and institutional trust. Understanding how VH correlates with uptake enables us to identify not just who is hesitant, but how that hesitancy translates into action or inaction. This distinction is essential for designing targeted interventions and understanding how attitudes shift into behaviors that ultimately affect public health outcomes.

The results from study 3 provide strong evidence that VH is not an isolated behavioral trait, but one that both amplifies and is amplified by COVID-19 contextual factors, forming a syndemic that ultimately undermines vaccine engagement. For example, students who became more hesitant over time and had not been hospitalized for COVID-19 were less likely to receive booster doses, highlighting how low perceived severity combined with pandemic fatigue and waning urgency can trigger hesitancy and reduce vaccine uptake. Likewise, students who consistently followed public health guidelines but later reported growing VH also showed lower vaccine uptake, suggesting that external pressures such as strict mandates, shifting recommendations, or information overload may erode trust and intensify VH over time. The findings also showed how changes in VH affected groups differently depending on their belief in conspiracy theories. Students with conspiracy beliefs demonstrated little change in VH over time and limited responsiveness to context, reflecting the fixed nature of vaccine-resistant attitudes. By contrast, students without conspiracy beliefs exhibited more variation in VH across vaccine phases and were more behaviorally sensitive to changing circumstances, which in turn affected their booster uptake. These patterns collectively point to three distinct groups: vaccine acceptors with consistently pro-vaccine views; vaccine-resistant individuals who remain

skeptical regardless of changing conditions; and a “movable middle” vaccine-hesitant students whose attitudes are more fluid and shaped by context. This differentiation underscores the need for future interventions and public health strategies that are tailored to the behavioral dynamics of each group and grounded in a deeper understanding of the social conditions shaping vaccine decision-making. As the COVID-19 pandemic evolves, and as new infectious threats emerge, public health professionals and authorities should shift from narrowly promoting COVID-19 vaccination toward the broader goal of building long-term vaccine confidence. A one-size-fits-all approach is no longer sufficient. Interventions must be segmented, responsive, and rooted in the reasons behind non-vaccination within each group. Designing vaccine policies with an understanding of each group’s characteristics and behavioral profiles may lead to more effective engagement and higher vaccine uptake.

5.3. Strengths and Limitations

This thesis offers several important strengths that are worth highlighting. First, it is, to our knowledge, the first study to apply and validate a syndemic framework by quantitatively testing whether COVID-19-related experiences and VH interact to shape booster uptake. To do this, we tested both multiplicative and additive interactions, which added analytical depth and provided direct evidence of syndemic effects. Second, the thesis focused on university students, a group that tends to be overlooked in VH research despite their significance in public health. This population offered a window into how attitudes shift once mandates fade and vaccine decisions become more voluntary and individualized. Third, the study drew from one of the largest surveys on VH conducted among university students in Ontario, which improved the reliability and generalizability of the findings. Including both undergraduate and graduate students also improved the generalizability of the results across academic levels. Fourth, the use

of a mass email invitation minimized selection bias by giving all students an equal opportunity to participate. Fifth, the study design allowed for the approximation of change in VH across vaccine phases. Although the study was cross-sectional, VH was measured separately for primary and booster doses, which allowed for a quasi-temporal comparison and offered insight into how attitudes evolved over time. These repeated measures offer a strong foundation for future longitudinal research.

From a methodological standpoint, the dissertation introduced a validated VH scale designed to assess both phases of vaccination, which enabled more consistent subgroup comparisons and reduced measurement bias. Furthermore, the use of robust statistical techniques (e.g., GEE) further helped in assessing how VH shifted across different groups and contexts. Finally, by treating VH as a continuous outcome rather than collapsing it into binary categories, “hesitant or not hesitant”, the analysis preserved meaningful variation and allowed for a more accurate and nuanced understanding of how hesitancy manifests and changes.

This thesis also has some limitations to consider. First, the study relied on self-reported data, which can introduce social desirability bias. While the survey was anonymous and this risk was minimized through the informed consent process, it is still possible that some participants adjusted their responses to align with perceived expectations. Second, as data were collected from a single institution, findings may not be fully generalizable but could still apply to universities with similar demographic and characteristics. Third, the imputation method for missing data may introduce estimates rather than relying on actual responses, though the data were missing completely at random and unlikely to have biased the results. Fourth, recall bias is possible, as students were asked about their VH and attitudes 2–3 years post-vaccine authorization. Some participants may have had difficulty recalling their past views accurately,

which could have underestimated or overestimated VH, depending on how participants' views change over time. For example, students who now distrust vaccines may remember themselves as more hesitant than they were at the time, or vice versa. Fifth, although the CVHS was validated for both primary and booster doses in the first study, the tool was developed specifically for the COVID-19 context. Its conceptual structure may be relevant to other vaccine settings, but the scale would require adaptation to ensure content validity for future applications. Lastly, in the third study, we excluded participants who had not received any COVID-19 primary doses (2.2% of the sample). This group was too small for reliable modeling, and their inclusion led to model convergence issues. Still, a descriptive sub-analysis was conducted to provide preliminary insight into their responses.

5.4. Implications for Public Health

This dissertation underscores a series of important implications for public health, particularly when it comes to COVID-19 booster campaigns and future vaccination efforts targeting younger adults. The syndemic framework validated in the last study and the synergistic interactions suggest that vaccine decision-making is not just about personal beliefs but also about the broader social and institutional contexts in which people live. Recognizing this, and in alignment with the syndemic theory [59,60], it is plausible that even partial interventions, which addressing either COVID-19-related experiences (e.g., conspiracy beliefs) or specific determinants of VH, could still increase vaccine uptake. While multicomponent interventions may yield the most substantial benefits, single-component strategies can still be effective, particularly when resources are limited. In addition, efforts to boost vaccine uptake should also address the surrounding context by acknowledging the evolving health messaging, public trust, and pandemic fatigue. Strategies that focus only on individual-level behavior may miss

important upstream factors if they do not also address the broader environment [61]. In practice, this means that outreach campaigns should not only account for vaccine safety and risk calculations but also respond to the lived experiences that shape how people come to trust or mistrust public health advice.

One of the central takeaways is that VH among university students is not a fixed trait. This underscores the limitations of standard, one-size-fits-all vaccine messaging. The findings from this thesis suggest that students are not a homogenous group, and that three broad behavioral profiles emerged: vaccine acceptors, vaccine-hesitant, and vaccine-resistant individuals. Understanding these distinctions is crucial for designing communication strategies that meet each group's specific concerns and motivations.

In the case of the resistant group, messages about collective benefit or herd immunity may have limited traction [62,63]. For this group, public health communications are more likely to succeed when they highlight personal benefits than collective benefits (e.g., caring about others), and are delivered in clear terms [62–64]. What seems more promising is to focus on personal relevance messages that speak directly to students' everyday concerns, such as missing classes, short-term side effects like allergic reactions, or protecting their health and fertility.

In contrast, the vaccine-hesitant group, students who are ambivalent rather than resistant, tend to respond better to communications that feel open, authentic, and transparent [62,63,65]. They are often more concerned about protecting those around them, rather than being motivated by their own risk of illness [62,63,65]. It has been shown that emphasizing social benefits over individual protection enhances vaccine uptake, especially when the perceived risk associated with vaccination is low [65,66]. Messages that frame vaccination as a way to safeguard specific

loved ones, such as a grandparent or a professor, can create a stronger emotional connection. Communication materials such as quotes or personal stories from peers can also help make messages feel more authentic [65]. For this group, the tone of the message often matters as much as the content.

Equally important are vaccine acceptors, who should not be overlooked. This group often demonstrates trust in public health institutions, regularly engages in preventive health behaviors, and perceives vaccines as safe and effective. Their stable attitudes make them valuable allies in promoting vaccine norms on campus. However, even among this group, confidence can waver due to side effects, shifting narratives, or exposure to misinformation. Rather than assuming continued compliance, public health strategies should actively involve these students as peer advocates and trusted messengers within their networks. In this way, vaccine acceptors can play a critical role in sustaining a culture of vaccination and countering emerging hesitancy.

Beyond these three primary groups, there is also a segment of students who are neither resistant nor hesitant, but simply disengaged or complacent. For this group, reminders and recall systems remain an effective strategy [66]. Text messages, emails, and app notifications, especially when personalized and well-timed, can nudge behavior and boost vaccine uptake [66]. We believe that these approaches could be particularly useful when VH is driven more by low perceived risk or lack of urgency rather than mistrust. Messaging that emphasizes current health threats, normalizes vaccination as a social expectation, and makes the process as convenient as possible could help minimize vaccine deferral. Campaigns that frame COVID-19 booster doses as part of routine campus health, like getting a flu shot, may encourage more consistent engagement.

It is also important to consider how students receive information. Many live in media environments saturated with emotionally charged but often misleading stories, shared on social platforms. These stories, about vaccine side effects or reproductive health, are easy to remember and hard to dislodge, even if they are not grounded in fact [65,67]. Public health campaigns can counter this by offering content that mirrors the style and emotional resonance of these stories, while still anchoring the message in science. Visuals, videos, or animations can be helpful if they are paired with links to credible sources or reinforced by peer-to-peer conversations on platforms students already trust [62,67]. Social media campaigns should also be supported by efforts to flag or remove vaccine disinformation and anti-vaccine content.

Universities also have an important role to play. They could integrate VH monitoring and vaccine coverage into ongoing campus health assessments [68]. The validated scale in this dissertation provides a reliable tool for tracking VH toward both primary and booster doses across different student subgroups. Incorporating the scale into regular student wellness surveys could offer early warning signs of declining confidence and allow for real-time adjustment of communication strategies.

Vaccine clinics on campus should also go beyond simply offering doses. Based on the finding that VH is linked to prior experiences with side effects, trust, and convenience, campus clinics can create low-barrier education and support services. For example, setting up drop-in hours where students can ask questions privately, offering information in multiple languages, or creating a “vaccine ambassador” program where trained students talk to peers [69,70]. These efforts could improve access, reduce anxiety, and foster a more supportive environment around vaccination.

For future policy planning, this work reinforces the importance of investing in trust-building infrastructure. This could include partnerships between universities and local public health units to deliver consistent messaging, engage students in co-creating vaccine communication, and establish dedicated roles (e.g., vaccine education coordinators) within campus wellness teams to lead these efforts. Ultimately, the goal is not only to increase short-term vaccine uptake but to foster long-term vaccine confidence.

Lastly, the question of whether VH toward booster vaccines is inherently problematic requires nuance. For a healthy, low-risk student population, skepticism toward repeated boosters may be a rational response rather than an indicator of misinformation or distrust. Furthermore, this study does not assume that all vaccine refusal is unfounded or irrational. Instead, it highlights patterns and predictors of hesitancy while acknowledging that ethical and scientific debates about booster necessity remain ongoing. This project also aimed to be inclusive of a spectrum of views, including those of the vaccine-resistant, by analyzing beliefs such as conspiracy endorsement and perceptions of vaccine safety. The focus on VH should not be read as implicitly endorsing universal vaccination but as a lens to understand decision-making dynamics in a complex and evolving public health landscape.

5.5. Directions for Future Research

This dissertation opens up several valuable directions for future work. First, this research focused on the interaction between VH and the COVID-19 context, but it also raises a number of important questions. One of them is whether the interaction between VH and other public health contexts behaves in a similar way to what we observed during the COVID-19 pandemic. For example, does VH amplify health risks during seasonal influenza outbreaks, responses to

other vaccine-preventable diseases, or even in the face of future pandemics? And when these forces combine, do we see negative health outcomes such as higher hospitalization rates, increased mortality, or greater demand on healthcare services? Exploring these kinds of questions would help determine whether the syndemic framework applies more broadly and whether it can be used to inform more effective strategies for pandemic preparedness.

Second, future research could include longitudinal studies to track how VH evolves over time. Ideally, such studies would begin during active vaccine mandates and continue after their removal to capture shifts from compliance to voluntary decision-making. In this thesis, we were not able to follow students across that transition because the timing of the project fell after vaccine mandates had been lifted. Therefore, a cross-sectional design was selected based on feasibility and timing constraints. Nonetheless, our findings offer a foundation for future longitudinal work by identifying key variables and behavioral profiles.

Third, future research should focus on testing real-world interventions on university campuses. These could include peer-led workshops, education programs, or vaccine ambassador campaigns. It also raises the question: when VH interacts with pandemic experiences, are single-focus interventions enough? Or do we need to address both sides of the equation to see real results? Comparing the effectiveness of single versus multi-component interventions could help validate the syndemic theory further and guide decision-making in settings where budgets and resources are limited.

Fourth, there is room to build on the CVHS validated in this thesis. Researchers could explore how well the scale works in other populations or adapt it for different vaccines or contexts. As new forms of hesitancy emerge, having a flexible and reliable tool will be essential

for ongoing public health monitoring and response.

Fifth, the syndemic interactions observed in this study are not solely attributable to the presence of vaccine mandates. Although mandates played a role in shaping initial compliance, the continued interaction between VH and pandemic-related stressors persisted even after mandates were lifted. This suggests that syndemic effects, such as the compounding influence of conspiracy beliefs, prior infection, or institutional mistrust, are not contingent on policy enforcement alone. Rather, they reflect deeper social vulnerabilities and cognitive-emotional patterns that amplify risk when co-occurring. Future research studies could explore how syndemic effects evolve in voluntary vaccination contexts and how structural interventions (not just mandates) might mitigate their impact. Furthermore, more research is needed to strengthen how syndemic theory is applied in the context of VH. In addition, future studies could explore how VH interacts with other factors such as media exposure, discrimination, marginalization, financial stress, social norms, or access to healthcare, and how these interactions shape vaccine behaviors. This would help build a broader understanding of the interconnected drivers of VH during public health crises.

Finally, to ensure that this research informs institutional and public health practices, future efforts should focus on translating the findings into actionable recommendations. One proposed step is the development of a policy brief tailored for university administrators, highlighting key insights on booster hesitancy, student perceptions, and syndemic interactions. This brief could inform updates to campus vaccine strategies, health communication campaigns, and student wellness programming. Additionally, outreach to public health partners and student health services is planned to explore opportunities for presenting these findings in policy forums and advisory meetings. Looking ahead, there is also potential to co-develop intervention

strategies with university stakeholders based on the identified behavioral profiles, supporting a more responsive and context-sensitive approach to future vaccine rollouts.

5.6. Conclusion

This dissertation showed that students' hesitancy increased as COVID-19 booster decisions became voluntary, shaped by factors such as age, trust in public messaging, religious beliefs, vaccine mandates, and prior vaccination behaviors. Just as importantly, the findings provided empirical evidence that VH interacts with pandemic-related experiences to form a syndemic, one that can suppress booster uptake even among students who outwardly comply with public health guidelines, revealing the presence of what may be called "latent hesitancy".

Given these patterns, the dissertation underscores the need to view VH as a dynamic behavior shaped by context and circumstance. Future vaccination efforts should move beyond one-size-fits-all approaches and instead adopt segmented, tailored strategies that reflect the behavioral profiles of different groups, whether resistant, hesitant, or simply complacent. Interventions should be supportive by using tools such as vaccine counseling, peer-led discussions, and transparent communication from trusted campus figures. Institutions should also recognize that VH shifts over time. Ongoing monitoring through rapid surveys can help detect emerging trends and inform timely public health responses. In doing so, this dissertation lays a foundation for more responsive interventions to sustain vaccine confidence over time.

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This section includes references from all earlier chapters, except for the “Narrative Review” from Chapter 1, and Chapters 2, 3, 4. These chapters were presented in manuscript format, their references are provided at the end of each chapter and formatted according to the respective journal’s guidelines.

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APPENDICES

This section includes supplementary materials from Chapters 2, 3, and 4, presented by Chapter.

The Questionnaire

1. [Health Status](#)
2. [Vaccination status and reason for getting/not getting vaccinated](#)
3. [Convenience/Constraints](#)
4. [Vaccine Mandate](#)
5. [Complacency](#)
6. [Confidence](#)
7. [Communication](#)
8. [Collective responsibility and calculation](#)
9. [Previous vaccination history and beliefs](#)
10. [COVID-19 contextual factors](#)
11. [Context/Demographics](#)
12. [Primary series Vaccine hesitancy scale](#)
13. [Booster doses Vaccine hesitancy scale](#)

Sections	Question	Source of question (if blank, it is self-developed)
Health Status: This section explores your health, mental health, and any health condition you may have		
Health status	1) In general, how is your overall health? • Poor • Fair • Good • Very good • Excellent • Prefer not to say	Canadian Community Health Survey (CCHS) – 2021 [71]

Mental Health Status	2) In general, how is your mental health? • Poor • Fair • Good • Very good • Excellent • Prefer not to say	Survey on COVID-19 and Mental Health - Cycle 2 [72]
Co-morbidities	3) Which of the following health conditions do you have? (Select all that apply) ☐ Brain and nervous system conditions (e.g., Epilepsy) ☐ Cardiovascular disease (e.g., stroke and hypertension) ☐ Chronic kidney disease ☐ Chronic lung disease (e.g., Asthma, COPD) ☐ Diabetes ☐ Immunocompromised or immunosuppressed (e.g., due to AIDS, an organ transplant, cancer treatment or congenital immunodeficiency) ☐ Liver disease ☐ Mental health conditions (e.g., anxiety, ADHD, depression, bipolar disorder, mania, and schizophrenia) ☐ Obesity ☐ Other (please specify) _____ ☐ I have no health conditions ☐ Prefer not to say	Modified from COVID-19 Vaccination Coverage Survey - Cycle 2 [73]
Vaccination status: This section explores your current vaccination status, including whether you have received COVID-19 vaccines or not, and the reasons and motivators behind your decision.		
Primary doses uptake	4) So far, have you received: • <u>Two</u> Primary doses (1st and 2nd) of the COVID-19 vaccine (Go to question 7) • Only <u>one</u> Primary dose (1st dose) of the COVID-19 vaccine (Go to question 5) • Not vaccinated at all (Go to question 6)	

Reason for not taking the 2nd primary dose	5) What is the main reason why you haven't received the 2nd primary dose of the COVID-19 vaccine? • Not eligible based on age or other criteria • Hesitant about receiving it • Bad experience with the first dose • Concerns about safety or side effects • Difficulty scheduling a vaccine appointment • Limited access to vaccination sites • Medical reasons or contraindications • Religious reasons • Cultural reasons • Language or communication barriers • Have a future appointment • Other (please specify) _____ • Prefer not to say	
Reason for not taking the primary doses	6) What is the main reason why you haven't received a COVID-19 vaccine? • Not eligible based on age or other criteria • Hesitant about receiving it • Bad experience with the first dose • Concerns about safety or side effects • Difficulty scheduling a vaccine appointment • Limited access to vaccination sites • Medical reasons or contraindications • Religious reasons • Cultural reasons • Language or communication barriers • Have a future appointment • Other (please specify) _____ • Prefer not to say	
Booster doses uptake	7) How many Booster doses (3rd dose or more) of the COVID-19 vaccine have you received so far? • I haven't received any booster doses (go to question 8) • One booster dose (Go to question 9) • Two booster doses (Go to question 9) • Three booster doses (Go to question 9) • Four booster doses or more (Go to question 9)	

Reason for not taking the booster doses	8) What is the main reason why you haven't received a booster dose? • Not eligible based on age or other criteria • It is not necessary to get it • Hesitant about receiving it • Got enough protection from the doses I already received • I don't see any priority in getting it • Not aware of booster eligibility or requirements • Concerns about safety or side effects • Difficulty scheduling a vaccine appointment • Limited access to vaccination sites • Medical reasons or contraindications • Religious reasons • Cultural reasons • Language or communication barriers • Have a future appointment • Other (please specify) _____ • Prefer not to say	
Reason for taking the booster doses	9) What is the main reason why you received a booster dose? • To get additional protection against COVID-19 • I am at higher risk of getting COVID-19 • To follow the recommendations from my healthcare provider • To follow the recommendations from my family and friends • To follow the recommendations from the government and health agencies • Other (please specify) _____ • Prefer not to say	

Campus-related factors	10) As a student, what "campus-related" factors and motivators that influenced your decision to get COVID-19 vaccine? (Select all that apply) ☐ To protect myself ☐ To keep my roommates/friends safe ☐ To keep my classmates/instructors/campus staff safe ☐ To follow the rules and mandates from the university ☐ To follow the rules and mandates from health authorities ☐ To avoid challenges like missed classes or needing special arrangements (e.g., attending classes online instead of in-person) ☐ To prevent outbreaks and their impact on campus life ☐ To get back to regular and normal school life ☐ Other (please specify) _____ ☐ Prefer not to say	
Convenience: This section explores the ease or challenges you faced when you got a COVID-19 vaccine		
Primary doses convenience	11) How easy do you think it was to get COVID-19 primary series (1st and 2nd) doses for yourself? • Very difficult (Go to question 12) • Somewhat difficult (Go to question 12) • Not sure (Go to question 12) • Somewhat easy (Go to question 12) • Very easy (Go to question 13) • Prefer not to say (Go to question 12)	Modified from the Vaccine Confidence Survey Question Bank [74]
Challenges to get primary doses	12) What challenges did you face when getting the primary (1st and 2nd) doses? (Select all that apply) ☐ I couldn't go on my own (I have a physical limitation). ☐ It was too far away. ☐ I didn't know where to go to get vaccinated. ☐ I have a medical reason that made me ineligible to get vaccinated. ☐ I didn't have transportation. ☐ The waiting time was too long. ☐ It was difficult to find or make an appointment. ☐ I was too busy to get vaccinated. ☐ It was difficult to arrange for childcare. ☐ I was waiting for my desired type of vaccine for primary doses. ☐ Health insurance issues ☐ I didn't find it difficult at all. ☐ Other (Please specify) _____ ☐ Prefer not to say	Modified from the Vaccine Confidence Survey Question Bank [74]

Booster doses convenience	13) How easy do you think it was to get the COVID-19 booster doses (3rd or more) for yourself? • Very difficult (Go to question 14) • Somewhat difficult (Go to question 14) • Not sure (Go to question 14) • Somewhat easy (Go to question 14) • Very easy (Go to question 15) • Prefer not to say (Go to question 14)	Modified from the Vaccine Confidence Survey Question Bank [74]
Challenges to get booster doses	14) What challenges did you face when getting the COVID-19 booster doses? (Select all that apply) ☐ I couldn't go on my own (I have a physical limitation). ☐ It was too far away. ☐ I didn't know where to go to get vaccinated. ☐ I have a medical reason that made me ineligible to get vaccinated. ☐ I didn't have transportation. ☐ The waiting time was too long. ☐ It was difficult to find or make an appointment. ☐ I was too busy to get vaccinated. ☐ It was difficult to arrange for childcare. ☐ I was waiting for my desired type of vaccine for booster doses. ☐ Health insurance issues ☐ I didn't find it difficult at all. ☐ Other (Please specify) _____ ☐ Prefer not to say	Modified from the Vaccine Confidence Survey Question Bank [74]
Religion	15) How important is religion in your life? • Very important (Go to question 16) • Somewhat important (Go to question 16) • Not very important (Go to question 16) • Not at all important (Go to question 17) • Prefer not to say (Go to question 16)	
Religious beliefs & vaccination decisions	16) To what extent do your religious beliefs impact your decision regarding vaccination? • My religious beliefs strongly encourage vaccination • My religious beliefs somewhat encourage vaccination. • My religious beliefs do not have a significant impact on my decision regarding vaccination. • My religious beliefs somewhat discourage vaccination. • My religious beliefs strongly discourage vaccination. • Prefer not to say	
Vaccine mandate: This section explores your perceptions about the vaccine mandate policy and whether or not it impacted your vaccination decisions		

Vaccine mandates from the government	17) In September 2021, proof of vaccination in Ontario was required to access certain public settings and facilities. Did this influence your decision to get vaccinated? • Yes, I decided to get vaccinated • Yes, I decided to NOT get vaccinated • No, it did not influence my decision • I am not aware of any implementation of this requirement • Not applicable, vaccine mandates were not imposed in my country (if you were outside of Canada) • Prefer not to say	
Vaccine requirements of the University of Waterloo	18) In the Fall 2021 term, the University of Waterloo required full COVID-19 vaccination for all individuals involved in any in-person activities on campus. Did this influence your decision to get vaccinated? • Yes, I decided to get vaccinated • Yes, I decided to NOT get vaccinated • No, it did not influence my decision • I am not aware of any implementation of this requirement • Not applicable, I didn't attend the University of Waterloo at that time • Prefer not to say	
Positive or negative impact of vaccine mandate	19) In general, do you think that the COVID-19 vaccine mandates have a positive or negative impact on campus life? • I think it has a negative impact • I think it has a positive impact • I think it has both (Positive and Negative) impacts • I think it has no impact • Don't know • Prefer not to say	
Advantages of vaccine mandate	20) In your opinion, what are the potential advantages of the COVID-19 vaccine mandates in universities? (Select all that apply) ☐ Reducing COVID-19-related absenteeism ☐ Minimizing community-wide COVID-19 transmission ☐ Facilitating a return to normal school life ☐ Reducing stress and concerns about in-person academic activities ☐ I don't see any positive impact ☐ Other (please specify) _____ ☐ Prefer not to say	

Disadvantages of vaccine mandate	21) In your opinion, what are the potential disadvantages of the COVID-19 vaccine mandates in universities? (Select all that apply) ☐ Creating a sense of division or exclusion among vaccinated and unvaccinated students ☐ Disrupting social interactions or events due to vaccination status differences ☐ Generating concerns about personal freedoms or autonomy ☐ Causing resistance or hesitancy among some students ☐ I don't see any negative impact ☐ Other (please specify) _____ ☐ Prefer not to say	
Complacency: This section explores your personal likelihood of contracting COVID-19 and whether you consider vaccination as a necessary preventive action		
Personal likelihood of contracting COVID-19	22) Please indicate your perceived risk of contracting COVID-19 by completing the following sentence: I consider myself at a _____ of getting COVID-19 • High risk • Moderate risk • Low risk • No risk at all • Not sure • Prefer not to say	
Personal likelihood of the severity of COVID-19	23) What do you feel is your likelihood for getting severely ill if you were to be infected with COVID-19? • Very Likely • Likely • Not sure • Unlikely • Very unlikely • Prefer not to say	
Perceived importance of COVID-19 primary doses	24) Taking the COVID-19 primary doses (1st and 2nd) is: • Really unimportant • Unimportant • Neutral • Important • Really important • Don't know • Prefer not to say	Oxford Covid-19 Vaccine Hesitancy Scale with adapted wording [43]

Perceived importance of COVID-19 booster doses	25) Taking the COVID-19 booster doses (3rd or more) is: • Really unimportant • Unimportant • Neutral • Important • Really important • Don't know • Prefer not to say	Oxford Covid-19 Vaccine Hesitancy Scale with adapted wording [43]
Confidence: This section explores your trust in the COVID-19 vaccine safety and effectiveness, your trust in the government, and your trust in the sources of information you get		
Trust in primary doses safety	26) How safe do you think the COVID-19 primary doses (1 st and 2 nd) are? • Very Unsafe • Unsafe • Neutral • Safe • Very Safe • Don't know • Prefer not to say	Modified from the Psychological characteristics and the mediating role of the 5C Model in explaining students' COVID-19 vaccination intention [75]
Trust in booster doses safety	27) How safe do you think the COVID-19 booster doses (3rd or more) are? • Very Unsafe • Unsafe • Neutral • Safe • Very Safe • Don't know • Prefer not to say	Modified from the Psychological characteristics and the mediating role of the 5C Model in explaining students' COVID-19 vaccination intention [75]
Trust in primary doses effectiveness	28) How effective do you think COVID-19 primary doses (1 st and 2 nd) are? • Very Ineffective • Ineffective • Neutral • Effective • Very Effective • Don't know • Prefer not to say	Modified from the Psychological characteristics and the mediating role of the 5C Model in explaining students' COVID-19 vaccination intention [75]

Trust in booster doses effectiveness	29) How effective do you think the COVID-19 booster doses (3rd or more) are? • Very Ineffective • Ineffective • Neutral • Effective • Very Effective • Don't know • Prefer not to say	Modified from the Psychological characteristics and the mediating role of the 5C Model in explaining students' COVID-19 vaccination intention [75]
Trust in primary doses riskiness	30) How risky do you think the COVID-19 primary doses (1st and 2nd) are? • Very Risky • Risky • Neutral • Not too • Risky • Not Risky at All • Don't know • Prefer not to say	Modified from the Psychological characteristics and the mediating role of the 5C Model in explaining students' COVID-19 vaccination intention [75]
Trust in booster doses riskiness	31) How risky do you think the COVID-19 booster doses (3rd or more) are? • Very Risky • Risky • Neutral • Not too Risky • Not Risky at All • Don't know • Prefer not to say	Modified from the Psychological characteristics and the mediating role of the 5C Model in explaining students' COVID-19 vaccination intention [75]
Trust in the government	32) How confident are you in Canada's regulatory process to approve safe and effective COVID-19 vaccines? • Not at all confident • Not too confident • Not sure • Somewhat confident • Very confident • Prefer not to say	Modified from COVID-19 Vaccination Coverage Survey - Cycle 2 [73]

Trusted sources of information	33) Please select your MOST trusted sources of information about COVID-19 vaccines: (Select all that apply) ☐ World Health Organization (WHO) ☐ Government health agencies (e.g., Health Canada) ☐ Official government social media (e.g., Health Canada) on Twitter, Facebook, and Instagram ☐ Scientific articles, journals, and published clinical trials ☐ Pharmaceutical companies producing the COVID-19 vaccines ☐ News media (TV, newspapers, online news) ☐ Social media platforms (Twitter, Facebook, and Instagram) ☐ Social media (influencers, bloggers, etc.) ☐ Healthcare providers or professionals ☐ Religious leaders ☐ Information from family and friends ☐ Other (please specify) _____ ☐ Prefer not to say	Modified from Vaccine Confidence Survey Question Bank [74]
Conspiracy theories	34) Which of the following statements have you come across regarding the COVID-19 vaccines? (Select all that apply) ☐ The COVID-19 vaccines are used to implant microchips into people ☐ The COVID-19 vaccines cause autism ☐ The COVID-19 vaccines cause sterilization or infertility ☐ Aborted fetal tissue are used in COVID-19 vaccine development ☐ There is a hidden agenda by governments to use COVID-19 vaccines for harmful purposes ☐ Taking COVID-19 booster doses will make me feel like a guinea pig ☐ Pharmaceutical companies cover up the dangers of COVID-19 vaccines ☐ I didn't come across any of these ☐ Others (please specify) _____ ☐ Prefer not to say	
Trust in conspiracy theories	35) Do you believe in any of the statements <u>you selected</u>? • Yes, All of them • Yes, Most of them • Yes, Few of them • No, not at all • Not sure • Prefer not to say	

Communication: This section explores your likelihood of getting a COVID-19 vaccine if it is recommended by others		
Family & friends' recommendation	36) What is your likelihood of receiving the COVID-19 vaccines, if they were recommended to you by family and friends? • Very unlikely • Somewhat unlikely • Not sure • Somewhat likely • Very likely • Prefer not to say	
Healthcare professionals' recommendation	37) What is your likelihood of receiving the COVID-19 vaccines, if they were recommended to you by healthcare professionals? • Very unlikely • Somewhat unlikely • Not sure • Somewhat likely • Very likely • Prefer not to say	
Government agencies' recommendation	38) What is your likelihood of receiving the COVID-19 vaccines, if they were recommended to you by government agencies? • Very unlikely • Somewhat unlikely • Not sure • Somewhat likely • Very likely • Prefer not to say	
Collective responsibility and calculation: This section explores your beliefs about vaccine and your willingness to protect others		
Willingness to protect others	39) Please indicate to what extent you agree or disagree with the following statement: I would get a COVID-19 vaccine to protect my family, friends, and others in my community. • Strongly disagree • Disagree • Not sure • Agree • Strongly agree • Prefer not to say	
Calculation	40) Please indicate to what extent you agree or disagree with the following statement: It is important for me to fully understand everything about the COVID-19 vaccines, before I get vaccinated. • Strongly disagree • Disagree	5C psychological antecedents of vaccination with adapted wording [56]

	• Neutral • Agree • Strongly agree • Prefer not to say	
Risk vs. benefits	41) Please indicate to what extent you agree or disagree with the following statement: When I think about getting the COVID-19 vaccines, I weigh the benefits and risks to make the best decision possible. • Strongly disagree • Disagree • Neutral • Agree • Strongly agree • Prefer not to say	5C psychological antecedents of vaccination with adapted wording [56]
Previous vaccination history and beliefs: This section explores your past experiences with different vaccinations (e.g., Flu, HPV, Meningitis) and your general attitudes towards them		
Flu vaccine uptake	42) Do you usually get the seasonal influenza (“flu”) vaccine? • Yes (Go to question 43) • No (Go to question 44) • Don’t know/Can’t remember • Prefer not to say	University students’ perspectives, planned uptake, and hesitancy regarding the COVID-19 vaccine: A multi-methods study
Reasons for taking the Flu vaccine	43) If yes, why? (Select all that apply) ☐ To avoid catching the flu ☐ My doctor recommends that I get it ☐ It is safe ☐ Worried about becoming seriously ill ☐ I always get the seasonal flu shot ☐ I live with people who are high risk ☐ I am high risk ☐ I am required to because of my job ☐ Other (please specify) _____ ☐ Prefer not to say	University students’ perspectives, planned uptake, and hesitancy regarding the COVID-19 vaccine: A multi-methods study [57]
Reasons for not taking the Flu vaccine	44) If no, why? (Select all that apply) ☐ Not eligible yet (based on age or other criteria) ☐ I don't see any advantage in getting it ☐ It is not a priority for me to get it ☐ Not at risk of catching the flu ☐ Concerned about safety or side effects ☐ Don't know where to get it	Modified from University students’ perspectives, planned uptake, and hesitancy regarding the

	☐ Difficulty accessing or scheduling an appointment ☐ Lack of information about the importance of flu vaccination ☐ Medical reasons or contraindications ☐ Other (please specify) _____ ☐ Prefer not to say	COVID-19 vaccine: A multi-methods study [57]
Flu vaccine uptake this year	45) Did you get the seasonal flu vaccine (2023-2024)? • Yes • No • Don't know/Can't remember • Prefer not to say	Modified from University students' perspectives, planned uptake, and hesitancy regarding the COVID-19 vaccine: A multi-methods study [57]
Flu vaccine hesitancy	46) Were you ever hesitant or refused to get the Influenza ("flu") vaccine? • Yes • No • Don't know/Can't remember • Not applicable, my parents made the decision for me • Prefer not to say	COVID-19 vaccine hesitancy among different population groups in China: a national multicenter online survey [45]
HPV vaccine uptake	47) Have you ever received the HPV (Human Papilloma Virus) vaccine? • Yes • No • Don't know/Can't remember • Not applicable • Prefer not to say	
HPV vaccine protection	48) Please indicate your level of agreement with the following statement: Getting the HPV vaccine is a good way to protect myself from developing HPV-related cancers like cervical cancer. • Strongly disagree • Disagree • Neutral • Agree • Strongly agree • Don't know • Prefer not to say	HPV- Vaccine Hesitancy Scale with adapted wording [76]

HPV vaccine side effects	49) Please indicate your level of agreement with the following statement: I am concerned about serious side effects of the HPV vaccine. • Strongly disagree • Disagree • Neutral • Agree • Strongly agree • Don't know • Prefer not to say	HPV- Vaccine Hesitancy Scale with adapted wording [76]
HPV vaccine hesitancy	50) Were you ever hesitant or refused to get the HPV vaccine? • Yes • No • Don't know/Can't remember • Not applicable, my parents made the decision for me • Prefer not to say	Modified from COVID-19 vaccine hesitancy among different population groups in China: a national multicenter online survey [45]
Meningococcal vaccine uptake	51) Have you ever received the Meningococcal (meningitis) vaccine? • Yes • No • Don't know/Can't remember • Not applicable • Prefer not to say	
Meningococcal vaccine protection	52) Please indicate your level of agreement with the following statement: Getting the meningococcal (meningitis) vaccine is a good way to protect myself from developing meningitis. • Strongly disagree • Disagree • Neutral • Agree • Strongly agree • Don't know • Prefer not to say	Modified from HPV- Vaccine Hesitancy Scale with adapted wording [76]
Meningococcal vaccine side effects	53) Please indicate your level of agreement with the following statement: I am concerned about serious side effects of the Meningococcal (meningitis) vaccine. • Strongly disagree • Disagree • Neutral • Agree	Modified from HPV- Vaccine Hesitancy Scale with adapted wording [76]

	• Strongly agree • Don't know • Prefer not to say	
Meningococcal vaccine hesitancy	54) Were you ever hesitant or refused to get the Meningococcal (meningitis) vaccine? • Yes • No • Don't know/Can't remember • Not applicable, my parents made the decision for me • Prefer not to say	Modified from COVID-19 vaccine hesitancy among different population groups in China: a national multicenter online survey [45]
COVID-19 contextual factors: This section explores your responses to the COVID-19 pandemic, including adherence to government guidance, COVID-19 symptoms, diagnoses, and hospitalizations.		
Following pandemic guidance	55) Overall, how often have you followed the guidance from the government about COVID-19, such as masking, physical distance etc.? • Not at all • Occasionally • Most of the time • All of the time • Prefer not to say	Oxford Covid-19 Vaccine Hesitancy Scale [43]
Experienced COVID-19 symptoms	56) Since the beginning of the pandemic, have you experienced any of the symptoms that led you to believe that you had COVID-19, such as fever, cough, chills, difficulty breathing or tiredness? • Yes • No • Don't know • Prefer not to say	Modified from Oxford Covid-19 Vaccine Hesitancy Scale [43]
Diagnosed/tested positive for COVID-19	57) Have you ever been diagnosed with or tested positive for COVID-19? • Yes • No • Don't know • Prefer not to say	Modified from Canadian Community Health Survey (CCHS) – 2021 [71]
Hospitalized due to COVID-19	58) Were you ever hospitalized due to COVID-19? • Yes • No • Don't know • Prefer not to say	

Context and demographics: This section explores your socio-demographic characteristics such as religious beliefs, age, gender, race, etc.		
Faculty	59) What faculty are you in? • Arts • Engineering • Environment • Health • Mathematics • Science	
Study year	60) What is your degree/year of study at the University of Waterloo? • Undergraduate year 1 • Undergraduate year 2 • Undergraduate year 3 • Undergraduate year 4 • Undergraduate year 4+ • Master's student • PhD • Other (please specify) _____	
Status	61) Are you an international or domestic student? • Domestic • International	
Gender	62) What is your gender identity? • Woman • Man • Non-binary / Third gender • Other (please specify) _____ • Prefer not to say	
Age	63) What is your age? (Please add in years) -----	
Race/ethnicity	64) Please select the racial category or categories with which you primarily identify. (Select all that apply) ☐ Black (e.g., African, Afro-Caribbean, Afro-Latine, African American, or other African descent) ☐ East Asian (e.g., Chinese, Korean, Japanese, or other East Asian descent) ☐ Latine (e.g., Latin American, Afro-Latine, or other European descent) ☐ Middle Eastern (e.g., Afghan, Egyptian, Iranian, Lebanese, Turkish, Kurdish, Arab, or other Middle Eastern descent) ☐ South Asian (e.g., East Indian, Pakistani, Bangladeshi, Sri Lankan, or other South Asian descent)	Survey Research Center at the University of Waterloo

	☐ Southeast Asian (e.g., Filipino, Vietnamese, Cambodian, Thai, Indonesian, Malaysian, or other Southeast Asian descent) ☐ White (e.g., British, German, Ukrainian, or other European descent) ☐ Other, please specify: _____ ☐ Prefer not to say	
Indigenous identity	65) Do you identify as First Nations, Métis or Inuk (Inuit)? • No • Yes, First Nations (North American Indian) • Yes, Métis • Yes, Inuk (Inuit) • Prefer not to say	Modified from COVID-19 Vaccination Coverage Survey - Cycle 2 [73]
Immigration status	66) What is your current immigration status? • Canadian citizen by birth • Canadian citizen by naturalization (e.g., an immigrant who was granted citizenship of Canada under the Citizenship Act) • Landed immigrants or permanent residents • Temporary resident (e.g., a person who has a work or study permit) • Asylum claimants (e.g., a person who has claimed refugee status) • Undocumented/Unauthorized • Other (Please specify) _____ • Prefer not to say	Modified from classification of immigrant status [77]
Income	67) What is your personal income (if you support yourself) or your family's annual household income, if they provide more than 50% of your income support (CAD)? • Less than \$14 999 • \$15 000 to \$29 999 • \$30 000 to \$44 999 • \$45 000 to \$59 999 • \$60 000 to \$74 999 • \$75 000 to \$89 999 • Greater than \$90 000 • Don't know • Prefer not to say	
Marital status	68) What is your marital status? • Single • Married • Common law (Two people who live together as a couple but who are not legally married to each other) • Separated • Divorced • Widowed • Other (Please specify) _____	

	• Prefer not to say	
Employment status	69) Are you currently employed? • Yes, working full-time, including self-employment • Yes, working part-time (e.g., Student worker, Teaching assistant...etc), including self-employment • I am in my co-op term now • Unemployed • Other (please specify) _____ • Prefer not to say	
Household information	70) During COVID-19 pandemic (2020-2022), how many people lived in your home (where you lived most of your time), including yourself? • Min = 1; Max = 20	Modified from Vaccination Coverage Survey - Cycle 2 [73]
Household health status	71) Does anyone among these people fall into one of the following categories: • Immunocompromised (Those who have a weakened immune system) • 65 years of age or more • Immunocompromised and 65 years of age or more • None of them • Don't know • Prefer not to say	

COVID-19 vaccine hesitancy scale

Questions below were adapted and adopted from the COVID-19 vaccine hesitancy scale (CVHS) developed by Huang et al., [45]. The CVHS scale is the modified validated version of the Parent Attitudes About Childhood Vaccines (PACV) original scale [78]. The scale has 15 items and is structured around three domains: "Behavior" (2 items), "Safety and Efficacy" (4 items), and "General Attitudes" (9 items).

1) Vaccine hesitancy scale questions for primary 1st and 2nd doses

	Scale item	Response		
		Hesitant responses (2 points)	Not sure or not know (1 points)	Non-hesitant responses (0 points)
T1 ¹	Have you ever delayed getting the COVID-19 primary doses (1st and 2nd) for reasons other than illness or allergy?	Yes	Don't know*	No
T2 ¹	Have you ever decided not to get the COVID-19 primary doses (1st and 2nd) for reasons other than illness or allergy?	Yes	Don't know*	No
T3 ²	It is better for me to only get one vaccine at a time (e.g., only COVID-19 primary dose , or only Flu dose).	Agree ^a	Not sure	Disagree

T4 ²	How concerned are you that the COVID-19 primary doses (1st and 2nd) might not be safe?	Concerned ^b	Not sure	Not Concerned
T5 ²	How concerned are you that you might have a serious side effect from getting the COVID-19 primary doses (1st and 2nd) ?	Concerned	Not sure	Not Concerned
T6 ²	How concerned are you that COVID-19 primary doses (1st and 2nd) might not prevent the COVID-19?	Concerned	Not sure	Not Concerned
T7 ³	How sure are you that getting the recommended COVID-19 primary doses (1st and 2nd) is a good idea for you?	0-5 ^c	6-7	8-10
T8 ³	It is not necessary to get the COVID-19 primary doses (1st and 2nd) .	Agree	Not sure	Disagree
T9 ³	I believe that the COVID-19 primary doses (1st and 2nd) can prevent the severe outcomes of the COVID-19 disease.	Disagree	Not sure	Agree
T10 ³	It is better for you to develop immunity by getting COVID-19 than to get the COVID-19 primary doses (1st and 2nd) .	Agree	Not sure	Disagree
T11 ³	Would you recommend your friends and family members to get the COVID-19 primary doses (1st and 2nd) ?	No	Not sure	Yes
T12 ³	Overall, how hesitant about the COVID-19 primary doses (1st and 2nd) would you consider yourself to be?	Hesitant ^d	Not sure	Not hesitant
T13 ³	I trust the information I receive about the COVID-19 primary doses (1st and 2nd) .	Disagree	Not sure	Agree
T14 ³	I am able to openly discuss my concerns about COVID-19 primary doses (1st and 2nd) with my doctor.	Disagree	Not sure	Agree
T15 ³	All things considered; how much do you trust your doctor's recommendations regarding COVID-19 primary doses (1st and 2nd) ? * Your family doctor if you have one. If not, indicate how much you generally trust doctors	0-5 ^e	6-7	8-10

¹ The “Behavior” subdomain – T1, T2

² The “Safety and Efficacy” subdomain – T3, T4, T5, T6

³ The “General Attitudes” subdomain – T7, T8, T9, T10, T11, T12, T13, T14, T15

* ‘Don’t know’ response was excluded as missing data.

^a Agree reflects combined responses of strongly agree and agree; disagree reflects combined responses of strongly disagree and disagree.

^b Concerned reflects combined responses of very and somewhat concerned; not concerned reflects combined responses of not concerned at all and not too concerned.

^c Response category on a 0–10 scale, with 0 being ‘not at all sure’ and 10 being ‘completely sure’.

^d Hesitant reflects combined responses of very and somewhat hesitant; not hesitant reflects combined responses of not hesitant at all and not too hesitant.

^e Response category on a 0–10 scale, with 0 being ‘do not trust at all’ and 10 being ‘completely trust’.

2) Vaccine hesitancy scale questions for COVID-19 booster doses

	Scale item	Response		
		Hesitant responses (2 points)	Not sure or not know (1 points)	Non-hesitant responses (0 points)
T1 ¹	Have you ever delayed getting the COVID-19 booster doses (3rd or more) for reasons other than illness or allergy?	Yes	Don't know [*]	No
T2 ¹	Have you ever decided not to get the COVID-19 booster doses (3rd or more) for reasons other than illness or allergy?	Yes	Don't know [*]	No
T3 ²	It is better for me to only get one vaccine at a time (e.g., only COVID-19 booster dose , or only Flu dose).	Agree ^a	Not sure	Disagree
T4 ²	How concerned are you that the COVID-19 booster doses (3rd or more) might not be safe?	Concerned ^b	Not sure	Not Concerned
T5 ²	How concerned are you that you might have a serious side effect from getting the COVID-19 booster doses (3rd or more) ?	Concerned	Not sure	Not Concerned
T6 ²	How concerned are you that COVID-19 booster doses (3rd or more) might not prevent the COVID-19?	Concerned	Not sure	Not Concerned
T7 ³	How sure are you that getting the recommended COVID-19 booster doses (3rd or more) is a good idea for you?	0-5 ^c	6-7	8-10
T8 ³	It is not necessary to get the COVID-19 booster doses (3rd or more) at this time.	Agree	Not sure	Disagree
T9 ³	I believe that the COVID-19 booster doses (3rd or more) can prevent the severe outcomes of the COVID-19 disease.	Disagree	Not sure	Agree
T10 ³	It is better for you to develop immunity by getting COVID-19 than to get the COVID-19 booster doses (3rd or more) .	Agree	Not sure	Disagree
T11 ³	Would you recommend your friends and family members to get the COVID-19 booster doses (3rd or more) ?	No	Not sure	Yes
T12 ³	Overall, how hesitant about the COVID-19 booster doses (3rd or more) would you consider yourself to be?	Hesitant ^d	Not sure	Not hesitant
T13 ³	I trust the information I receive about the COVID-19 booster doses (3rd or more) .	Disagree	Not sure	Agree
T14 ³	I am able to openly discuss my concerns about COVID-19 booster doses (3rd or more) with my doctor.	Disagree	Not sure	Agree
T15 ³	All things considered; how much do you trust your doctor's recommendations regarding COVID-19 booster doses (3rd or more) ?	0-5 ^c	6-7	8-10

	* Your family doctor if you have one. If not, indicate how much you generally trust doctors			
¹ The “Behavior” subdomain – T1, T2 ² The “Safety and Efficacy” subdomain – T3, T4, T5, T6 ³ The “General Attitudes” subdomain – T7, T8, T9, T10, T11, T12, T13, T14, T15 * ‘Don’t know’ response was excluded as missing data. ^a Agree reflects combined responses of strongly agree and agree; disagree reflects combined responses of strongly disagree and disagree. ^b Concerned reflects combined responses of very and somewhat concerned; not concerned reflects combined responses of not concerned at all and not too concerned. ^c Response category on a 0–10 scale, with 0 being ‘not at all sure’ and 10 being ‘completely sure’. ^d Hesitant reflects combined responses of very and somewhat hesitant; not hesitant reflects combined responses of not hesitant at all and not too hesitant. ^e Response category on a 0–10 scale, with 0 being ‘do not trust at all’ and 10 being ‘completely trust’.				

Chapter 2 Supplementary Material

Wording adaptation for the PACV-CVHS scale

The wording of the 15 items was carefully modified to specifically address the respective doses while keeping the wording and content as similar as possible. For instance, the item "How concerned are you that the COVID-19 vaccine might not be safe?" was reformulated as "How concerned are you that the COVID-19 primary doses (1st and 2nd) might not be safe?" and "How concerned are you that the COVID-19 booster doses (3rd or more) might not be safe?". Same was applied to the remaining items.

For the two “Behaviour” items, we used the past tense to reflect the past vaccination behaviours, like the original PACV [47,78,79], rather than using the future tense in the CVHS, which was meant to ask about the intention to get COVID-19 in 2021 when COVID-19 vaccines were newly available [45]. For example, we changed "Would you delay getting the COVID-19 vaccine for reasons other than illness or allergy?" to "Have you ever delayed getting the COVID-19 primary doses (1st and 2nd) for reasons other than illness or allergy?" and “Have you ever delayed getting the COVID-19 booster doses (3rd or more) for reasons other than illness or allergy?”. Similarly, we rephrased “Would you want to get the nationally recommended COVID-19 vaccine?” to “How sure are you that getting the recommended COVID-19 primary doses (1st and 2nd) is a good idea for you?” and “How sure are you that getting the recommended COVID-19 booster doses (3rd or more) is a good idea for you?”, aligning with the original PACV wording. Furthermore, we rephrased “If the COVID-19 vaccine becomes available, would you recommend your friends and family members to get the COVID-19 vaccine?” to “Would you recommend your friends and family members to get the COVID-19 primary doses (1st and 2nd)?” and “Would you recommend your friends and family members to get the COVID-19 booster doses (3rd or more)?”. In other items, we added clarifying details for better comprehension. Sample items: “All things considered, how much do you trust doctor?” was reworded to “All things considered, how much do you trust your doctor's recommendations regarding COVID-19 primary doses (1st and 2nd)? *Your family doctor if you have one. If not, indicate how much you generally trust doctors”.

While adapting most items was straightforward, two items were more difficult; “I believe that the COVID-19 vaccine can prevent COVID-19 (COVID-19 is a severe disease)” and “It is better for you to get fewer vaccines at the same time”. We considered the first item as a double-barreled question, hence we rephrased it to “I believe that the COVID-19 primary doses (1st and 2nd) can prevent the severe outcomes of the COVID-19 disease” and “I believe that the COVID-19 booster doses (3rd or more) can

prevent the severe outcomes of the COVID-19 disease”. Whereas for the 2nd item, there was some ambiguity in interpretation during the pre-testing stage by the students. Therefore, we changed it to” It is better for me to only get one vaccine at a time (e.g., only COVID-19 primary dose, or only Flu dose)” and “It is better for me to only get one vaccine at a time (e.g., only COVID-19 booster dose, or only Flu dose)” with adding explanation in brackets for easier understanding.

The scale scoring system

We calculated the VH score for both primary and booster doses based on the categorization methods and the scoring system of the CVHS and the PACV [45,47,78,79]. The scale items were grouped into three domains: Behavior (Q1–Q2), Safety and Efficacy (Q3–Q6), and General Attitudes (Q7–Q15). We harmonized the response formats (dichotomous, 5-point Likert, and 11-point Likert scales) into three categories: hesitant, not sure, and non-hesitant. For items using a 5-point Likert scale, responses of “strongly agree” or “agree” in (Q3, Q8, Q10) were classified as “hesitant”, while responses of “strongly disagree” or “disagree” in (Q9, Q13, Q14) were classified as “hesitant”. For (Q4, Q5, Q6) items, responses indicating “somewhat” or “very concerned” were considered “hesitant”, while responses of “not at all concerned” or “not too concerned” were categorized as “non-hesitant”. For items (Q7, Q15) using an 11-point Likert scale, we classified answers within 0–5 as “hesitant”, 6–7 as “not sure”, and 8–10 as “non-hesitant”. For items (Q1, Q2, Q11) using “yes, don’t know/not sure, no” options, we considered “yes” responses as “hesitant”, and “no” responses as “non-hesitant”, except for Q11, where the classification was reversed.

We scored students’ responses as: 2 points for hesitant answers, 1 point for not sure responses, and 0 points for non-hesitant answers. Like the original scale [47,78–80], “don’t know” responses in the Behavior domain (Q1, Q2) were excluded as missing data, as these were interpreted to reflect poor recall rather than vaccine hesitancy. We calculated the raw total score by summing the scores of all items. The total raw score ranged from 0 – 30 if all items had responses and Q1 and Q2 were not excluded as missing data. We then converted the raw score to a 0 – 100 scale using a simple linear transformation accounting for items with missing values. Higher scores indicate a higher level of VH. Lastly, we divided final scores into two categories: non-hesitant (score < 50) and hesitant (score ≥ 50).

Sample size calculation

We calculated the sample size based on the hesitancy rate from the pilot survey, with a 95% confidence level (z-score of 1.96) and a margin of error set at $\sigma = 0.025$ using the formula:

$$\frac{Z_{\alpha}^2 \times P \times (1 - P)}{\sigma^2}$$

where $Z_{\alpha}=1.96$, $P= 0.24$ (VH rate from the pilot survey), $\sigma=0.025$ to enhance survey results with greater accuracy and a lower margin of error. The calculated sample size was:

$$n = \frac{1.96^2 \times 0.24 \times (1 - 0.24)}{0.025^2} = 1121$$

We employed a proportionate stratified sampling method to ensure representation from both undergraduate and graduate students. The sample size for each stratum was calculated as:

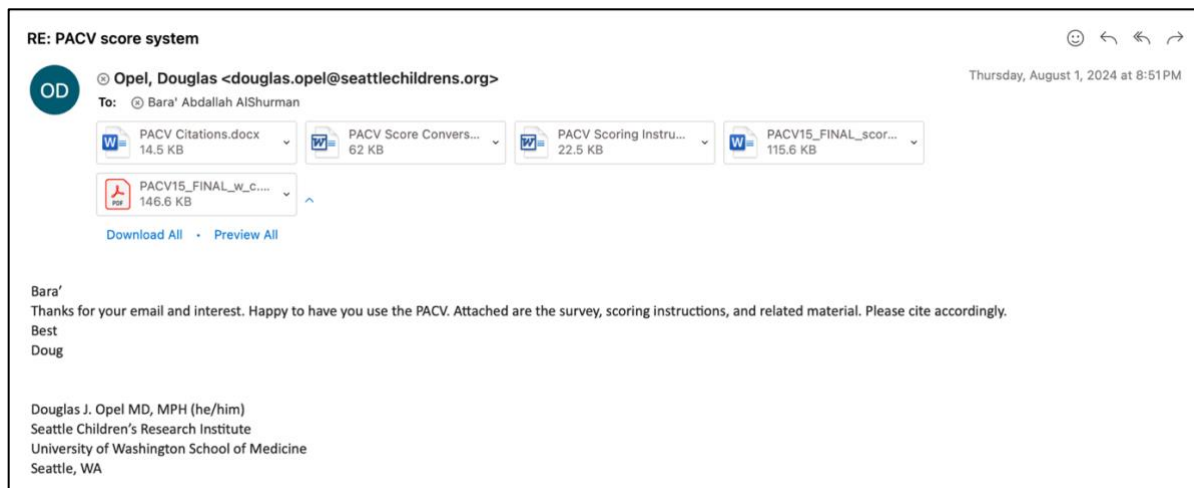
Final sample size for each stratum = (Sample size/population size) $\times$ Stratum size.

For undergraduate students: $(1121/40,408) \times 34,398 = 955$

For graduate students: $(1121/40,408) \times 6,010 = 167$

Assuming a 10% response rate based on the pilot survey, we invited the entire UW student population to participate, aiming to reach the desired sample size.

Permission to use the PACV scale



**All the below documents were provided by the author of the PACV scale

i. Citations for the Parent Attitudes about Childhood Vaccines Survey

1. Opel DJ, Mangione-Smith R, Taylor JA, Korfiatis C, Wiese C, Catz S, and Martin D. Development of a Survey to Identify Vaccine-Hesitant Parents: The Parent Attitudes about Childhood Vaccines Survey. *Human Vaccines* 2011; 7(4): 419-425.
2. Opel DJ, Taylor JA, Mangione-Smith R, Solomon C, Zhao C, Catz S, and Martin D. Validity and reliability of a survey to identify vaccine-hesitant parents. *Vaccine* 2011; 29(38): 6598–6605
3. Opel DJ, Taylor JA, Zhou C, Catz S, Myaing M, and Mangione-Smith R. The Relationship between Parent Attitudes about Childhood Vaccines Survey Score and Future Child Immunization Status: A Validation Study. *JAMA Pediatrics* 2013; 167(11): 1065-1071.
4. Cunningham R, Kerr G, Orobio J, Munoz FM, Correa A, Villafranco N, Monterrey AC, Opel DJ, Boom JA. Development of a Spanish Version of the Parent Attitudes about Childhood Vaccines Survey. *Human Vaccines and Immunotherapeutics* 2019; 15(5):1106-1110. PMID: 30735475

ii. PACV Scoring Instructions

1. Score each of the 15 PACV survey items (Q3-Q17; see attached scored version of PACV). Hesitant responses are assigned a 2, ‘don’t know or not sure’ a 1, and non-hesitant responses a 0. The two items in which the ‘don’t know’ response was excluded as missing data (Q3 and Q4) are scored as 2 for the hesitant response and 0 for the non-hesitant response.
2. Calculate the raw total PACV score by simply summing each item. The total raw score will range from 0 – 30 if all items have responses and Q3 and Q4 are not excluded as missing data. If there is at least one item without a response or Q3 or Q4 are answered as ‘don’t know’ and therefore are excluded as missing data, the total raw score needs to be adjusted. For instance, if there is one response missing or excluded, the total raw score will range from 0 – 28; if there are two responses missing or excluded, the total raw score will range from 0 – 26; etc.
3. Convert the raw score to a 0 – 100 scale using simple linear transformation accounting for items with missing values (see attached score conversion chart).

iii. PACV Score Conversion Chart

A		B		C	
If both Q3 and Q4 are Yes or No and items Q5-Q17 have no missing responses		If either Q3 or Q4 are Don't Know or Q5-Q17 has one missing response		If both Q3 and Q4 are Don't Know or Q5-Q17 has two missing responses	
Raw Score	Converted Score	Raw Score	Converted Score	Raw Score	Converted Score
0	0	0	0	0	0
1	3	1	4	1	4
2	7	2	7	2	8
3	10	3	11	3	12
4	13	4	14	4	15
5	17	5	18	5	19
6	20	6	21	6	23
7	23	7	25	7	27
8	27	8	29	8	31
9	30	9	32	9	35
10	33	10	36	10	38
11	37	11	39	11	42
12	40	12	43	12	46
13	43	13	46	13	50
14	47	14	50	14	54
15	50	15	54	15	58
16	53	16	57	16	62
17	57	17	61	17	65
18	60	18	64	18	69
19	63	19	68	19	73
20	67	20	71	20	77
21	70	21	75	21	81
22	73	22	79	22	85
23	77	23	82	23	88
24	80	24	86	24	92

25	83	25	89	25	96
26	87	26	93	26	100
27	90	27	96		
28	93	28	100		
29	97				
30	100				



Treuman Katz Center
for Pediatric Bioethics

SCORED VERSION

Parent Attitudes about Childhood Vaccines

UW Medicine
SCHOOL OF MEDICINE

READ THIS FIRST:

We are interested in your opinions about childhood shots (vaccines). Your child's doctor or nurse gives shots like MMR (measles, mumps and rubella) or Polio at check-ups to help keep your child from getting sick.

THIS SURVEY IS NOT ABOUT SEASONAL FLU OR SWINE FLU (H1N1) SHOTS.

When filling out the survey, please answer each question with the child whose appointment is today in mind. The answers to these questions will help us improve how doctors and nurses talk to parents about childhood shots.

Please check only one answer to each of the questions below.

1. Is this child your first born?

☐ Yes

☐ No

2. What is your relationship to this child?

☐ Mother

☐ Father

☐ Other _____

3. Have you ever delayed having your child get a shot (not including seasonal flu or swine flu (H1N1) shots) for reasons other than illness or allergy?

Yes

No

Don't Know

2

0

excluded

4. Have you ever decided not to have your child get a shot (not including seasonal flu or swine flu (H1N1) shots) for reasons other than illness or allergy?

Yes

No

Don't Know

2

0

excluded

5. How sure are you that following the recommended shot schedule is a good idea for your child? Please answer on a scale of 0 to 10, where 0 is *Not at all sure* and 10 is *Completely sure*.

**Not at all
Sure**

**Completely
Sure**

0	1	2	3	4	5	6	7	8	9	10
2	2	2	2	2	2	1	1	0	0	0

**Strongly
Agree**

Agree

**Not
Sure**

Disagree

**Strongly
Disagree**

6. Children get more shots than are good for them.

2

2

1

0

0

7. I believe that many of the illnesses that shots prevent are severe.

0

0

1

2

2

8. It is better for my child to develop immunity
by getting sick than to get a shot.

2 2 1 0 0

9. It is better for children to get fewer vaccines
at the same time.

2 2 1 0 0

Not at all Not too Not Somewhat Very
Concerned Concerned Sure Concerned Concerned

10. How concerned are you that your child
might have a serious side effect from a
shot?

0 0 1 2 2

11. How concerned are you that anyone of
the childhood shots might not be safe?

0 0 1 2 2

12. How concerned are you that a shot
might not prevent the disease?

0 0 1 2 2

13. If you had another infant today, would you want him/her to get all the recommended shots?

Yes

No

***Don't
Know***

0

2

1

14. Overall, how hesitant about childhood shots would you consider yourself to be?

**Not at all
Hesitant**

**Not too
Hesitant**

**Not
Sure**

**Somewhat
Hesitant**

**Very
Hesitant**

0

0

1

2

2

15. I trust the information I receive about shots.

**Strongly
Agree**

Agree

**Not
Sure**

Disagree

**Strongly
Disagree**

0

0

1

2

2

16. I am able to openly discuss my concerns about shots with my child's doctor.

0

0

1

2

2

17. All things considered, how much do you trust your child's doctor? Please answer on a scale of 0 to 10, where 0 is *Do not trust at all* and 10 is *Completely trust*.

Do Not Trust at All								Completely Trust		
0	1	2	3	4	5	6	7	8	9	10
2	2	2	2	2	2	1	1	0	0	0

The last questions are about you. Please check only one answer to each question.

18. How old are you?

- ☐ 18-29 years old
☐ 30 years or older

19. What is your current marital status?

- ☐ Single
☐ Married
☐ Living with a partner
☐ Widowed
☐ Separated
☐ Divorced

20. What is the highest level of education that you have reached?

- ☐ 8th grade or less
☐ Some high school, but not a graduate

- ☐ High school graduate or GED
- ☐ Some college or 2 year degree
- ☐ 4-year college degree
- ☐ More than 4-year college degree

21. What is your approximate household income?

- ☐ \$30,000 or less
- ☐ \$30,001-50,000
- ☐ \$50,001-75,000
- ☐ \$75,001 or more

22. How many children are in your household?

- ☐ One
- ☐ Two
- ☐ Three
- ☐ Four or more

23. What is your race/ethnicity? Please check all that apply.

- ☐ White
- ☐ Black or African American
- ☐ Hispanic/Latino
- ☐ Asian
- ☐ Native Hawaiian or other Pacific Islander
- ☐ American Indian or Alaska Native
- ☐ Other: _____

Thank you!

Supplementary Tables

Table S1. Exploratory factor analysis related measures cut-off points

Measures	Description	Recommended values	References
KMO (Kaiser-Meyer-Olkin)	Is the sample adequate for EFA?	≥ 0.5 indicates the appropriateness for the factor analysis in the data.	[81–83]
Bartlett’s test of Sphericity	To examine the hypothesis that the variables are uncorrelated in the population	A significant result (less than 0.5)	[81]
Eigen value	the total variance explained by each factor	Factors with eigenvalues > 1 are retained to identify how many constructs should we extract	[84]
Factor loadings	To assess the strength of the association between each item/variable and the identified constructs	A factor loading of ≥ 0.3 -0.4 is required for significance	[81]

Table S2. Fit indices and suggested cut-off values for overall model fit assessment

Name	Abbreviation	Cut-off Point	Description	References
Chi-Square	χ^2	p-value > 0.05	Assesses overall fit and the discrepancy between the sample and fitted covariance matrices. Sensitive to sample size. H0: The model fits perfectly.	[85]
Comparative Fit Index	CFI	≥ 0.90	A revised form of NFI. Not very sensitive to sample size. Compares the covariance matrix predicted by your model to the observed covariance matrix of the null model. A CFI value close to 1 indicates a good fit.	[86–89]
Incremental Fit Index	IFI	$\geq .90$	IFI should be .90 or higher to have an acceptable fit.	[86,90]
Normed Fit Index	NFI	$\geq .90$	An NFI statistic equal to .50 means the model improves fit by 50% compared to the null model. An acceptable fit is above .90 or above. NFI may underestimate fit for small samples and does not reflect parsimony.	[86]
Tucker Lewis Index	TLI	$\geq .90$	Also called the Non-Normed Fit Index. Above .90 equals an acceptable fit.	[86,90]
Relative Fit Index	RFI	$\geq .90$	RFI close to 1 indicates a good fit.	[86]
Goodness-of-Fit Index	GFI	$\geq .90$	Was initially created to understand the proportion of variance being captured in the estimated covariance matrix. It is very sensitive to sample size	[85,91]
Adjusted Goodness-of-Fit Index	AGFI	$\geq .90$	Was initially created to understand the proportion of variance being captured in the estimated covariance matrix. It is very sensitive to sample size	[87,91,92]
Root Mean Square Error	RMSEA	$\leq .08$	A "badness of fit" test where values close to "0" equal the best fit.	[86,87,91,93]

of				
Approximation				
Standardized Root Mean Square Residual	SRMR	$\leq .05$	The average difference between the predicted and observed covariances in the model based on standardized residuals. A SRMR of .05 and below is considered a good fit.	[86,87,93]
Parsimonious Normed Fit Index	PNFI	$\geq .50$	It is based upon the GFI by adjusting for loss of degrees of freedom.	[91,94]
Parsimony Goodness-of-Fit Index	PGFI	$\geq .60$	It is based upon the NFI by adjusting for loss of degrees of freedom.	[94,95]

Table S3. Reliability and validity cut-off points and how to establish

Measure	Name	Recommended values	References
Reliability	Cronbach's Alpha	$\alpha \geq .60$	[96]
		$\alpha \geq .70$	[97,98]
Reliability	Composite Reliability (CR)	$CR \geq .60$	[99]
		$CR \geq .70$	[100]
Convergent validity	Average Variance Extracted (AVE)	$AVE \geq .50$ for each construct	[99]
		$0.4 < AVE < 0.5$ is accepted if $CR > 0.6$	[95,99]
Discriminant Validity	Square Root of AVE	Squared root of AVE of a latent construct is higher than > the construct's highest Pearson correlation with any other latent construct	[86,99]

Table S4. Percentage of missingness in each question

Q#	% missing	Q#	% missing	Q#	% missing	Q#	% missing	Q#	% missing
Q4	0.4	Q35	0.8	Q50_2	1.7	Q67	1.2	Q87	1.5
Q5	0.3	Q36_1	0.9	Q50_3	1.7	Q68	1.3	Q88	1.8
Q7	2.2	Q36_2	1.1	Q50_4	1.8	Q69	1.5	Q89	1.6
Q10	0.5	Q36_3	1.2	Q50_5	2	Q70	1.5	Q90	1.8
Q11	0.5	Q37	0.9	Q50_6	2	Q71_1	1.4	Q91	5.7
Q12	0.5	Q38	1	Q51	1.7	Q71_2	1.6	Q92	6.1
Q13	0.6	Q39	1	Q52	1.8	Q72_1	1.6		
Q14	0.6	Q40_1	1.2	Q54_1	1.7	Q72_2	1.9		
Q95	1.6	Q40_2	1.4	Q54_2	2	Q72_3	2		
Q15	1	Q40_3	1.3	Q55_1	1.5	Q73_1	1.8		
Q18	0.6	Q40_4	1.3	Q55_2	2.1	Q73_2	1.9		
Q19	1.3	Q40_5	1.2	Q56_1	1.5	Q73_3	1.9		
Q20	0.7	Q40_6	1.3	Q56_2	1.8	Q73_4	2		
Q21	1.4	Q41	1.2	Q58	1.9	Q75	1.7		
Q23	0.6	Q42	1.2	Q59	2.1	Q76	1.8		
Q24	0.7	Q44	1.4	Q60	2	Q77	1.6		
Q25	0.7	Q45	1.4	Q61_1	1.9	Q78	1.6		
Q26	0.9	Q46_1	1.5	Q61_2	2	Q80	1.3		
Q27	1.5	Q46_2	1.7	Q61_3	2.1	Q81	1.2		
Q29	0.5	Q46_3	1.8	Q62_1	1.8	Q82	1.3		
Q30	0.7	Q47	1.7	Q62_2	1.8	Q83	1.3		
Q31	0.7	Q48	1.7	Q62_3	2	Q84	3		
Q32	0.7	Q49	1.5	Q64	1	Q85	1.5		
Q33	0.6	Q50_1	1.6	Q65	1.2	Q86	1.6		

Table S5. Comparison of vaccine hesitancy scores between COVID-19 primary doses and booster doses across demographic subgroups

Demographic Characteristic	Primary Doses*	Booster Doses*	P-value**
	Mean $\pm$ SD	Mean $\pm$ SD	
Gender			<0.001
Woman	6.9 $\pm$ 0.1	10.5 $\pm$ 0.2	
Man	8.2 $\pm$ 0.2	12.0 $\pm$ 0.2	
Non-binary/Others	5.2 $\pm$ 0.6	7.0 0.7	
Prefer not to say	9.2 $\pm$ 0.7	12.3 0.8	
Age			0.263
10-22	7.3 $\pm$ 0.1	11.1 $\pm$ 0.1	
23-29	7.7 $\pm$ 0.3	10.6 $\pm$ 0.3	
30-39	6.4 $\pm$ 0.8	9.6 $\pm$ 0.9	
40-85	10.2 $\pm$ 1.3	11.8 $\pm$ 1.4	
Academic level			
Undergraduates	7.4 $\pm$ 0.1	11.1 $\pm$ 8.1	0.003
Graduates	6.1 $\pm$ 0.5	9.5 $\pm$ 8.1	

- *Vaccine hesitancy scores are out of 30, and higher scores represent higher hesitancy.

-**Paired t-test was used to compare mean vaccine hesitancy scores.

-Significant values are shown in bold.

Table S6. Summary of COVID-19 vaccine hesitancy scale validation studies across diverse populations and vaccine stages

Study (Author, Year)	Country & Population	Scale Used	Vaccine Stage	Key Findings
Freeman et al., 2020 [43]	UK – General adult population (quota-sampled N=5,114)	Oxford COVID- 19 Vaccine Hesitancy Scale (OCVHS; 7 items)	Primary series (pre-rollout intentions)	Psychometrics: Unidimensional scale with excellent fit (CFI=0.97, RMSEA=0.05); Cronbach’s α ~0.94–0.97 (high internal consistency). Hesitancy: 28.3% expressed hesitancy (16.6% “very unsure” + 11.7% “strongly hesitant” about a COVID vaccine).
Abd ElHafeez et al., 2021 [101]	General adults in four Arab countries (multi- country, N=350)	5C Scale (Arabic version)	Primary (initial doses)	Psychometrics: 5-factor structure (15 items) confirmed with adequate fit (CFA CFI≈0.96, RMSEA≈0.06). All subscales showed Cronbach’s $\alpha \geq 0.70$. Hesitancy: Higher 5C scores (e.g. greater Confidence, etc.) predicted higher intention to vaccinate (supporting concurrent validity).
ElSayed et al., 2022 [102]	Egypt – Parents of children aged 5–18 years (Arabic-speaking)	Parent Attitudes about Childhood Vaccines (PACV; 15 items)	Primary series (child COVID-19 vaccine)	Psychometrics: EFA (3 domains matching original PACV); internal consistency (α_{total} ≈0.80; Attitudes α =0.74, Safety/Efficacy α =0.82, Behavior α =0.57). PACV score was a significant predictor of actual vaccination intent. Hesitancy: 92.4% of parents classified as hesitant (PACV score ≥ 21) to vaccinate their child against COVID-19.
Gregory et al., 2022 [103]	USA–Emergency medical service (EMS) providers (high-risk)	COVID-19 Vaccine Concerns Scale (CVCS) – focuses on fears	Primary (initial doses)	Psychometrics: Yielded a one-factor, 7-item scale with high reliability (Cronbach’s α =0.89). CFA supported one-factor model (CFI=0.95, SRMR=0.03; RMSEA=0.11).

	professionals, N=2,281)	and worries about COVID vaccines.		Hesitancy: CVCS scores correlated strongly with general vaccine hesitancy scales ($r=0.71-0.82$) and significantly predicted actual COVID-19 vaccination status.
Hamilton & Hagger, 2022 [104]	Australia/USA– General adults in Australia and US (two samples, N=522 and 499)	Vaccination Concerns in COVID-19 Scale (VaCCS) – comprehensive 35-item scale (8 subscales).	Primary (initial doses)	Psychometrics: EFA identified 8 distinct factors (35 items total) addressing diverse vaccine concerns/beliefs. CFA in both countries showed acceptable fit and confirmed configural invariance across samples. Hesitancy: Subscales demonstrated expected correlations with socio-political and health belief measures, and several subscale scores significantly predicted COVID-19 vaccination intentions (higher concern beliefs associated with lower intent).
Hrin et al., 2022 [105]	USA – Adults in the United States (online sample, N=232)	10-item COVID-19 Vaccine Hesitancy Survey (new short scale)	Primary (initial doses)	Psychometrics: Developed a unidimensional 10-item survey with strong reliability (Cronbach's $\alpha=0.89$; test–retest $r=0.87$). Hesitancy: Higher hesitancy scores correlated with greater conspiracy beliefs ($r=-0.68$) and lower trust in physicians ($r=0.58$) and were inversely associated with actual vaccination (≥ 1 dose) ($r\approx 0.68$).
Huang et al., 2022 [45]	China – Multiple groups (62.8% medical workers, 17.8% students, 10.3% general public, 9.1%	COVID-19 Vaccine Hesitancy Scale (CVHS; 15 items, adapted from PACV)	Primary series	Psychometrics: EFA (3 factors explaining 50.4% variance); CFA by subgroup (CFI 0.90–0.93, RMSEA 0.06–0.07); internal consistency ($\alpha_{\text{total}}=0.756$; subscales 0.81, 0.77, 0.71). Hesitancy: 15.6% overall prevalence; highest in students (23.9%) and general public (21.2%), lower in medical workers (13.1%) and public health professionals (10.4%).

	public health staff; n=4,227)			
Rodriguez et al., 2022 [106]	USA – People with HIV (mean age ~52; N=175)	Vaccine Hesitancy Scale (VHS; 9-item WHO/SAGE scale)	Primary series	Psychometrics: Two factors reproduced (“Lack of Confidence” and “Perceived Risks”), explaining ~57.9% of variance. Internal consistency was acceptable ($\alpha=0.72$), mirroring the original VHS structure. Hesitancy: (Not reported as a percent in abstract – study focused on scale properties among people with HIV).
Hammoud et al., 2023 [107]	Qatar – General adults (N=545)	Multidimensional COVID-19 Vaccine Hesitancy Questionnaire (developed de novo)	Primary (initial doses)	Psychometrics: Developed a 50-item instrument; EFA revealed a 7-factor structure of COVID-19 hesitancy. CFA indicated acceptable fit (e.g. CFI ≈ 0.91, RMSEA=0.05). Content validity was excellent (S-CVI/Ave=0.92). Internal consistency was satisfactory for the overall scale (Cronbach’s $\alpha=0.73$).
Lee et al., 2023 [108]	Malaysia – General adults (online sample, N=798)	Oxford COVID-19 Vaccine Hesitancy Scale (OCVHS; 7 items, adapted wording for “second booster”)	Booster (4th dose, “second booster”)	Psychometrics: Very high internal reliability (Cronbach’s $\alpha=0.959$). Higher hesitancy scores were associated with lower booster uptake. Hesitancy: Mean hesitancy scores were 17.1 (± 6.5) on 7–35 scale; ~26.7% showed some level of hesitancy toward the second booster dose. One in five Malaysians were reluctant to take the 4th dose.

Al-Taie & Yilmaz, 2024 [109]	Turkey – Community pharmacists in Istanbul (mean age 43; N=145)	Vaccine Hesitancy Scale (VHS; 9 items)	Booster dose	Psychometrics: Scale used as given; prior validation by Shapiro et al. 2018. Hesitancy: 91.7% of pharmacists intended to receive a COVID-19 booster, only ~8.3% hesitant/refusing.
Regan et al., 2025 [110]	USA – Adolescents (13– 17) and one parent each (nationwide dyads, N=764 pairs)	tVHS-COVID (Teen Vaccine Hesitancy Scale)	Primary (initial doses)	Psychometrics: EFA derived a 13-item scale with 3 factors for both adolescents and parents. CFA demonstrated excellent fit for both teen and parent scales (e.g. CFI=1.00, RMSEA ~0.03). Cronbach's $\alpha \geq 0.78$ for all versions. Hesitancy: Higher tVHS-COVID scores (greater hesitancy) were associated with lower willingness to receive future COVID-19 vaccine doses among both teens and parents, indicating good construct validity.

Chapter 3 Supplementary Material

Health and vaccine-related characteristics of the study sample

Table S1. Health and vaccine hesitancy-related characteristics of study participants (n = 4453)

		Study Participants n (%)
Overall health status	Poor/Fair	371 (8.3)
	Good/Very Good/Excellent	4067 (91.3)
	Prefer not to say	15 (0.3)
Overall mental status	Poor/Fair	1458 (32.7)
	Good/Very Good/Excellent	2967 (66.6)
	Prefer not to say	28 (0.6)
Ever diagnosed with COVID-19	Yes	2725 (61.2)
	No	1519 (34.1)
	Don't know	141 (3.2)
	Prefer not to say	68 (1.5)
Ever hospitalized due to COVID-19	Yes	53 (1.2)
	No	4282 (96.2)
	Don't know	58 (1.3)
	Prefer not to say	60 (1.3)
Convenience to get primary doses	Easy	3413 (76.6)
	Difficult	766 (17.2)
	Not sure	143 (3.2)
	Prefer not to say	35 (0.8)
	I didn't get any primary doses	96 (2.2)
Convenience to get booster doses	Easy	2637 (59.2)
	Difficult	120 (2.7)
	Not sure	138 (3.1)
	Prefer not to say	49 (1.1)
	I didn't get any booster doses	1509 (33.9)
Religious beliefs influencing vaccination decisions	My religious beliefs encourage vaccination	411 (9.2)
	My religious beliefs discourage vaccination	51 (1.1)
	No impact	1896 (42.6)
	Prefer not to say	221 (5.0)
	I have no religious beliefs	1874 (42.1)
Perceived risk of getting	No-to-low risk	2890 (64.9)

COVID-19

	Moderate-to-high risk	1316 (29.6)
	Not sure	220 (4.9)
	Prefer not to say	27 (0.6)
Personal likelihood of severity of COVID-19	Likely	529 (11.9)
	Unlikely	2976 (66.8)
	Not sure	915 (20.5)
	Prefer not to say	33 (0.7)
Perceived importance of primary doses	Important	3445 (77.4)
	Unimportant	401 (9.0)
	Neutral	476 (10.7)
	Don't know	81 (1.8)
	Prefer not to say	50 (1.1)
Perceived importance of booster doses	Important	1784 (40.1)
	Unimportant	888 (19.9)
	Neutral	1516 (34.0)
	Don't know	219 (4.9)
	Prefer not to say	46 (1.0)
Confidence in the government	Confident	2836 (63.7)
	Not Confident	665 (14.9)
	Not sure	896 (20.1)
	Prefer not to say	56 (1.3)
Trust in primary doses safety	Safe	3539 (79.5)
	Unsafe	268 (6.0)
	Neutral	511 (11.5)
	Don't know	116 (2.6)
	Prefer not to say	19 (0.4)
Trust in booster doses safety	Safe	3087 (69.3)
	Unsafe	390 (8.8)
	Neutral	730 (16.4)
	Don't know	222 (5.0)
	Prefer not to say	24 (0.5)
Trust in primary doses effectiveness	Effective	3543 (79.6)
	Ineffective	312 (7.0)
	Neutral	451 (10.1)
	Don't know	128 (2.9)
	Prefer not to say	19 (0.4)
Trust in booster doses effectiveness	Effective	2515 (56.5)

Trust in primary doses riskiness	Ineffective	528 (11.9)
	Neutral	1003 (22.5)
	Don't know	380 (8.5)
	Prefer not to say	27 (0.6)
Trust in booster doses riskiness	Not risky	3013 (67.7)
	Risky	524 (11.8)
	Neutral	721 (16.2)
	Don't know	171 (3.8)
	Prefer not to say	24 (0.5)
Likelihood of getting vaccinated when recommended by family	Not risky	2671 (60.0)
	Risky	612 (13.7)
	Neutral	843 (18.9)
	Don't know	299 (6.7)
	Prefer not to say	28 (0.6)
Likelihood of getting vaccinated when recommended by healthcare professional	Likely	3165 (71.1)
	Unlikely	520 (11.7)
	Not sure	721 (16.2)
	Prefer not to say	47 (1.1)
Likelihood of getting vaccinated when recommended by the government	Likely	3792 (85.2)
	Unlikely	299 (6.7)
	Not sure	316 (7.1)
	Prefer not to say	46 (1.0)
Understanding the importance of the vaccine	Likely	3110 (69.8)
	Unlikely	623 (14.0)
	Not sure	681 (15.3)
	Prefer not to say	39 (0.9)
Weighing vaccine benefits and risks	Agree	3621 (81.3)
	Disagree	337 (7.6)
	Not sure	446 (10.0)
	Prefer not to say	49 (1.1)
	Agree	3550 (79.7)
	Disagree	337 (7.6)
	Not sure	511 (11.5)

Taking the vaccine to protect loved ones	Prefer not to say	55 (1.2)
	Agree	3947 (88.6)
	Disagree	246 (5.5)
	Not sure	211 (4.7)
	Prefer not to say	49 (1.1)
Vaccine mandate impact from the government	I decided to get vaccinated because of the mandate	1988 (44.6)
	I decided to not get vaccinated because of the mandate	88 (2.0)
	No impact	2118 (47.6)
	Not aware of the mandate	217 (4.9)
	Prefer not to say	42 (0.9)
Vaccine mandate impact from the university	I decided to get vaccinated because of the mandate	1412 (31.7)
	I decided to not get vaccinated because of the mandate	49 (1.1)
	No impact	1864 (41.9)
	Not aware of the mandate	1088 (24.4)
	Prefer not to say	40 (0.9)
Flu vaccine uptake	Yes	1504 (33.8)
	No	2337 (52.5)
	Don't know/Can't remember	548 (12.3)
	Prefer not to say	64 (1.4)
Flu vaccine uptake in 2023–2024	Yes	1122 (25.2)
	No	2851 (64.0)
	Don't know/Can't remember	428 (9.6)
	Prefer not to say	52 (1.2)
HPV vaccine uptake	Yes	2736 (61.4)
	No	496 (11.1)
	Don't know/Can't remember	1182 (26.5)
	Prefer not to say	39 (0.9)
Meningococcal vaccine uptake	Yes	2547 (57.2)
	No	341 (7.7)
	Don't know/Can't remember	1527 (34.3)
	Prefer not to say	38 (0.9)
Ever hesitant or refused the flu vaccine	Yes	556 (12.5)
	No	2566 (57.6)
	Don't know/Can't remember	676 (15.2)
	Not applicable (my parents made the decision)	589 (13.2)

Ever hesitant or refused the HPV vaccine	Prefer not to say	66 (1.5)
	Yes	172 (3.9)
	No	2458 (55.2)
	Don't know/Can't remember	950 (21.3)
	Not applicable (my parents made the decision)	819 (18.4)
	Prefer not to say	54 (1.2)
Ever hesitant or refused the meningococcal vaccine	Yes	117 (2.6)
	No	2303 (51.7)
	Don't know/Can't remember	1164 (26.1)
	Not applicable (my parents made the decision)	816 (18.3)
	Prefer not to say	53 (1.2)
Getting the HPV vaccine provides good protection	Agree	3290 (73.9)
	Disagree	120 (2.7)
	Neutral	383 (8.6)
	Don't know	605 (13.6)
	Prefer not to say	55 (1.2)
Concerned about side effects from the HPV vaccine	Agree	464 (10.4)
	Disagree	2368 (53.2)
	Neutral	850 (19.1)
	Don't know	713 (16.0)
	Prefer not to say	58 (1.3)
Getting the meningococcal vaccine provides good protection	Agree	3175 (71.3)
	Disagree	94 (2.1)
	Neutral	421 (9.5)
	Don't know	702 (15.8)
	Prefer not to say	61 (1.4)
Concerned about side effects from the meningococcal vaccine	Agree	395 (8.9)
	Disagree	2323 (52.2)
	Neutral	822 (18.5)
	Don't know	852 (19.1)
	Prefer not to say	61 (1.4)

Significant interactions in the study

Table S2. Final Generalized Estimated Equation model, showing the interaction effect between multiple variables and the dose type (primary vs. booster) on vaccine hesitancy scores

Interactions		Adjusted OR*	95% Confidence Interval	
			Lower	Upper
Dose ** × Age groups (<i>p</i> <0.001)	10-19 (Ref)	.	.	.
	20-29	0.91	0.86	0.96
	30-39	0.93	0.73	1.18
	40 or more	0.64	0.48	0.86
Dose × Hospitalized due to COVID-19 (<i>p</i> <0.001)	Yes (Ref)	.	.	.
	No	1.43	1.13	1.80
	Don't know	1.01	0.76	1.35
	Prefer not to say	1.05	0.76	1.45
Dose × Perceived risk of getting COVID-19 (<i>p</i> <0.001)	No-to-low risk (Ref)	.	.	.
	Moderate-to-high risk	0.91	0.86	0.96
	Not sure	0.84	0.76	0.93
	Prefer not to say	0.76	0.59	1.01
Dose × Flu vaccine uptake (<i>p</i> <0.001)	Yes (Ref)	.	.	.
	No	1.24	1.16	1.33
	Don't know/can't remember	1.11	1.05	1.23
	Prefer not to say	1.01	0.80	1.28
Dose × Meningococcal vaccine uptake (<i>p</i> <0.004)	Yes (Ref)	.	.	.
	No	0.88	0.80	0.98
	Don't know/can't remember	0.92	0.87	0.97
	Prefer not to say	0.87	0.67	1.14

* Adjusted for the following factors: age, gender, COVID-19 hospitalization, convenience of getting COVID-19 vaccines, perceptions of risk and importance of COVID-19 vaccines, trust in COVID-19 vaccines and government, religious beliefs, vaccine mandates, and past vaccination behavior for influenza and meningococcal disease.

** Reference category for interaction is primary doses.

-Significant values are shown in bold.

Chapter 4 Supplementary Material

Characteristics of unvaccinated and vaccinated university students based on uptake of the COVID-19 primary vaccine series

Table S1. Sociodemographic and COVID-19-related characteristics and vaccine hesitancy scores by primary COVID-19 vaccine uptake (n = 4453)

Characteristics	Unvaccinated (n = 96)	Vaccinated (n = 4357)	P-value*
Vaccine hesitancy score for primary doses, Mean (SD)	23.5 (5.4)	7.0 (6.7)	<0.001
Vaccine hesitancy score for booster doses, Mean (SD)	24.9 (5.0)	10.7 (7.9)	<0.001
Age, Mean (SD)	22.3 (6.4)	21.01 (3.4)	<0.001
Gender, n (%)			0.911
Man	34 (35.4%)	1655 (38.0%)	
Woman	58 (60.4%)	2489 (57.1%)	
Non-binary/Others	2 (2.1%)	124 (2.8%)	
Prefer not to say	2 (2.1%)	89 (2.0%)	
Income, n (%)			0.896
Less than \$29,999	27 (28.1%)	1098 (25.2%)	
\$30,000 to \$59,999	7 (7.3%)	406 (9.3%)	
\$60,000 to \$89,999	8 (8.3%)	372 (8.5%)	
Greater than \$90,000	25 (26.0%)	1067 (24.5%)	
Don't know	13 (13.5%)	746 (17.1%)	
Prefer not to say	16 (16.7%)	668 (15.3%)	
Employment, n (%)			0.207
Employed	53 (55.2%)	2168 (49.8%)	
Unemployed	37 (38.5%)	2020 (46.4%)	
Prefer not to say	6 (6.3%)	169 (3.9%)	
Flu vaccine uptake, n (%)			<0.001
Yes	6 (6.3%)	1498 (34.4%)	
No	85 (88.5%)	2252 (51.7%)	
Don't know	5 (5.2%)	543 (12.5%)	
Prefer not to say	0 (0.0%)	64 (1.5%)	
Diagnosed with COVID-19, n (%)			0.612
Yes	59 (61.5%)	2666 (61.2%)	
No	33 (34.4%)	1486 (34.1%)	
Don't know	4 (4.2%)	137 (3.1%)	
Prefer not to say	0 (0.0%)	68 (1.6%)	
Hospitalized due to COVID-19, n (%)			0.707
Yes	1 (1.0%)	52 (1.2%)	

No	94 (97.9%)	4188 (96.1%)	
Don't know	0 (0.0%)	58 (1.3%)	
Prefer not to say	1 (1.0%)	59 (1.4%)	
Followed COVID-19 guidelines, n (%)			<0.001
All/Most of the time	54 (56.3%)	3800 (87.2%)	
Occasionally/Not at all	41 (42.7%)	488 (11.2%)	
Prefer not to say	1 (1.0%)	69 (1.6%)	
Belief in COVID-19 conspiracy theories, n (%)			<0.001
Yes	72 (75.0%)	850 (19.5%)	
No	12 (12.5%)	3073 (70.5%)	
Don't know	10 (10.4%)	346 (7.9%)	
Prefer not to say	2 (2.1%)	88 (2.0%)	

* P-values were obtained using independent t-tests for continuous variables and chi-square tests for categorical variables.

-Significant values are shown in bold.