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ARTICLE COMMENTARY

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Characteristics of COVID-19 vaccine hesitancy in university students: Methodological insights from a syndemic perspective

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ABSTRACT

This paper offers a methodological critique of the study by AlShurman et al. that examined whether COVID-19 vaccine hesitancy (VH) and COVID-19-related factors interact to influence booster dose uptake among university students in Canada from a syndemic perspective. The original cross-sectional survey was conducted among 4453 students at the University of Waterloo in 2024. VH was measured retrospectively for primary doses and concurrently for booster doses, with a change score computed to capture shifts in hesitancy over time. Logistic regression models were used to assess the main effects and interactions on additive and multiplicative scales. While the original study provides a valuable application of syndemic theory, notable limitations warrant caution in interpretation. These include substantial recall bias in the retrospective VH change score, the inability of the cross-sectional design to establish temporal dynamics and bidirectional reinforcement required by syndemic theory, low response rate (approximately 11%) raising concerns about selection bias, dichotomization of key variables, untested linearity of the change score, and potential overinterpretation of statistical interactions as mechanistic syndemic synergy. Unmeasured factors such as student stressors, social media exposure, and psychological reactance may also influence the observed associations. The findings should be interpreted conservatively. Targeted interventions such as rebuilding trust and addressing misinformation remain important. However, stronger longitudinal studies with prospective measurement of hesitancy, mediation analyses, and sensitivity testing are needed to more robustly examine syndemic interactions in vaccine uptake.

KEYWORDS

Syndemics; vaccine hesitancy; COVID-19; interactions; booster doses; cross-sectional design; recall bias

Dear Editor,

The recent publication by AlShurman and team on the interplay between COVID-19 vaccine hesitancy and various pandemic experiences in shaping booster dose uptake among Canadian university students offers an intriguing application of syndemic theory to a timely issue.[1] By framing hesitancy as a socially driven epidemic that synergizes with biological aspects of COVID-19, the work highlights potential pathways where factors like prior infection, guideline compliance, and conspiracy beliefs might amplify reluctance toward additional shots. This is particularly relevant in a student population where primary vaccinations were often mandated, potentially masking underlying doubts that surface with voluntary boosters. Yet, a closer look reveals notable methodological and interpretive challenges. Drawing from epidemiological principles and behavioral research, our discussion centers on two core concerns: substantial recall bias in retrospective measurement of hesitancy change, the inherent limitations of the cross-sectional design in supporting syndemic claims, and the risk of overinterpreting statistical interactions as mechanistic synergy.

Measurement of vaccine hesitancy in this study relies on the COVID-19 Vaccine Hesitancy Scale, adapted from tools like the Parent Attitudes about Childhood Vaccines survey, with participants rating attitudes toward primary doses retrospectively and boosters concurrently.[2] The resulting change score – booster minus primary hesitancy – aims to capture evolving reluctance. While this method is practical for a single survey, it opens the door to recall bias, a common pitfall in self-reported health data where current views distort memories of past ones.[3] In the context of a prolonged pandemic, participants' recollections in

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2024 are likely distorted by subsequent events (e.g., information about variants, personal infection experiences, or policy changes). Non-boosted participants, in particular, may unconsciously inflate their recalled hesitancy toward primary doses to maintain consistency with their current behavior, thereby exaggerating the computed change score.[4] Similarly here, non-boosted participants could retroactively heighten primary hesitancy scores to align with their current stance, especially if intertwined with conspiracy leanings.

This issue is amplified by the cross-sectional nature of the data. Syndemic theory, as articulated in foundational works, emphasizes temporal dynamics where conditions mutually reinforce over time, such as how social stressors worsen disease progression and vice versa.[5] A one-time snapshot struggles to disentangle these cycles and cannot establish the bidirectional reinforcement central to syndemic theory. Did rising hesitancy deter boosting, or did skipping boosters prompt a reevaluation of earlier attitudes? Longitudinal designs are better suited to address this limitation; for example, a 2022 cross-sectional study of German university students identified key determinants of vaccination intentions and behavior.[6] We acknowledge that the current design limits causal inference and that observed associations should not be interpreted as demonstrating syndemic synergy. Excluding the small unvaccinated subset (about 2%) for analytic reasons is pragmatic but omits a baseline for comparing entrenched versus emergent hesitancy, further limiting insights into progression.

The change score's treatment as a continuous predictor in models assumes a linear relationship with uptake, yet hesitancy often operates in thresholds – subtle increments may not sway decisions until surpassing a critical point. Behavioral models from the era suggest incorporating non-linear terms, like splines, to detect such patterns.[7] In related work on measles vaccine hesitancy, economic modeling demonstrated how reluctance produces threshold-dependent consequences for population uptake and outbreak risk.[8] The reported 23% odds reduction per unit increase should therefore be interpreted cautiously until the assumption of linearity is formally tested.

Response rates pose another layer of concern. With only 11% of over 40,000 invited students participating, selection bias looms large – those with polarized views, pro or con vaccination, might self-select, skewing hesitancy estimates.[9] Online surveys in vaccine research from 2021 to 2023 frequently overrepresented skeptics, raising serious concerns about non-response bias.[10] While the authors cite minimal missing data and random patterns via Little's test, this doesn't capture non-response mechanisms.[11] Comparing responders to university demographics or applying weights could mitigate this, but absent such steps, the sample's representativeness remains uncertain. For instance, over half being employed or from specific faculties might underplay hesitancy in more isolated groups, like full-time undergraduates in dorms where peer norms heavily sway decisions.[12]

Variable categorization also merits attention. Binning guideline adherence into high versus low loses granularity; partial adherence often mirrors outright non-compliance in fostering ambivalence, as seen in 2022 compliance studies.[13] Conspiracy beliefs as a simple yes/no overlooks subtypes – efficacy doubts versus systemic distrust – with differential ties to hesitancy.[14] A 2024 cluster analysis of childhood-vaccine-hesitant individuals identified three distinct profiles, including those with high endorsement of conspiracy theories.[15] Such dichotomization may obscure important heterogeneity and affect estimates of interactions.

On the interaction front, employing relative excess risk due to interaction and adjusted odds ratios aligns with established guidance for quantifying synergies.[16] However, interpreting these statistical interactions as direct evidence of syndemic synergy is premature. Observed interactions may stem from unmeasured confounders (e.g., trust levels, media exposure), small subgroup sizes (especially "don't know" responses), or statistical artifacts rather than true mechanistic reinforcement.[17,18] We therefore view the reported interactions as preliminary associations that warrant further investigation rather than conclusive proof of syndemic processes.

To substantiate a true syndemic interaction in this context, stronger evidence would typically be required, including longitudinal data with repeated measures of hesitancy before and after key pandemic experiences, mediation analyses demonstrating pathways such as eroded trust or reactance, and qualitative insights exploring how participants themselves describe the interplay between their experiences and vaccination decisions. Without such evidence, statistical interactions remain suggestive but insufficient to confirm syndemic synergy.

Interactions with adherence and conspiracies – sharper uptake drops amid rising hesitancy for compliers and non-believers – invite alternative readings. Compliers under mandates might harbor reactance, where forced actions breed later pushback. Student stressors such as academic pressure, social media exposure, and peer

influences – known correlates of vaccine hesitancy – are not accounted for and represent potential omitted variables.[6] Non-believers' shifts could proxy unmeasured misinformation exposure.[19] These alternative explanations, including eroded trust and psychological reactance, should be treated as hypotheses requiring empirical testing through mediation analysis, qualitative data, or longitudinal studies, rather than as established explanations.[20]

The syndemic lens itself invites scrutiny. Traditionally anchored in biological-social feedbacks, like poverty fueling HIV via weakened immunity, extending to hesitancy as a "social epidemic" requires solid evidence of bidirectional reinforcement.[21] To support syndemic claims, longitudinal data with prospective measurement, mediation analyses, and qualitative insights are typically needed. Network studies document hesitancy clustering, but contagion isn't directly tested here.[22] We therefore recommend framing findings more conservatively.

Overlooked contexts add to this. Mandates likely suppressed primary hesitancy, so changes might echo relief from coercion rather than organic synergy. German 2022 research identified determinants of vaccination behavior among university students that were influenced by mandate-related contexts and fatigue.[6] Student stressors – social media, academics, peers – key in 2021 U.S. surveys, aren't factored, potentially confounding results.[12]

These limitations shape implications. Advocating trust-building and anti-misinformation efforts is sound, but basing them on possibly biased synergies could misdirect.[23] Longitudinal replication, with prospective hesitancy tracking and network data, would bolster claims.[24] For campuses, integrating brief video interventions has shown efficacy in increasing booster intentions among young adults.[14]

In essence, while the original study makes a valuable contribution to applying syndemic theory to vaccine hesitancy, the combination of recall bias, cross-sectional limitations, selection bias, variable dichotomization, and overinterpretation of statistical interactions constrains the robustness of its conclusions. Tempered inferences and future longitudinal, mechanistic research would significantly strengthen its contribution to both theory and policy.

Author contributions

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Data availability statement

No datasets were generated during the current study.

Ethics statement

Due to the nature of this study, an ethics approval is not required.

ICMJE criteria for authorship

All authors attest they meet the ICMJE criteria for authorship.

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