Review

The impact of administering vitamin D supplements on handgrip strength and performance in the timed-up-and-go test in frail elderly individuals: A meta-analysis involving randomized controlled trials

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ABSTRACT
BACKGROUND: Ongoing debates continue regarding the specific effects of vitamin D intake on the timed-up-and-go test and handgrip strength.
OBJECTIVES: To assess the impact of vitamin D supplementation on handgrip strength and performance in the timed-up-and-go test.
METHODS: Between May and June of 2023, a systematic review and meta-analysis were undertaken to assess the effects of vitamin D intake on handgrip strength and performance in the timed-up-and-go test. A comprehensive search was performed on Google Scholar, Web of Science, and PubMed to search for relevant articles published until June 2023. The analysis exclusively incorporated randomized controlled trials (RCTs) available in English publications, with a specific emphasis on evaluating the impact of vitamin D supplementation on both handgrip strength and performance in the timed-up-and-go test. Inverse variant meta-analysis was employed to evaluate the impact of vitamin D intake on the timed-up-and-go test and handgrip strength.
RESULTS: A total of 21 appropriate studies were incorporated into the systematic review. Our findings revealed a favorable impact of vitamin D administration on enhancing performance in the timed-up-and-go test. Conversely, we could not ascertain any advantageous effects of vitamin D intake on handgrip strength. Despite the notable enhancement observed in the timed-up-and-go test, our analysis did not yield statistically significant evidence supporting the impact of vitamin D intake on handgrip strength based on the included studies.
CONCLUSION: Our study findings reveal that vitamin D is an essential component in improving the timed-up-and-go test.

KEYWORDS: vitamin D; frailty; timed-up-and-go test; handgrip strength.

INTRODUCTION

Functional decline, disability, and frailty represent common geriatric conditions classified within the broader spectrum of geriatric syndromes. These conditions have various effects on the well-being of individuals. Approximately 20-30% of individuals aged 70 years and older report experiencing disability in mobility, instrumental activities, and/or basic activities of daily living (ADLs).[1] At a certain threshold of decline, this may progress to disability. However, the rate of decline varies significantly among individuals and is governed by intrinsic factors such as the aging process, comorbid diseases, and impairments, as well as environmental factors including social, nutritional, behavioral, and economic aspects. Targeted interventions have the potential to mitigate age-related declines in functional capacity and performance, thus extending the disability-free lifespan.[2,3] Frailty is another prevalent issue associated with aging and is linked to various negative health consequences, including mortality, falls, and hospitalization. It is characterized by weight loss, reduced activity, diminished handgrip strength, slowed mobility, and indicators of decreased endurance, balance, and walking performance.[3] Several factors contribute to frailty, including patient age, neuromuscular disorders, cognitive impairments, and nutrition. Among these factors, nutrition plays a crucial role and can be utilized as an intervention to address frailty.[4]

Nutrition is widely acknowledged as a pivotal aspect of healthy aging, encompassing the intake of essential vitamins and minerals crucial for maintaining overall well-being. Among these nutrients, vitamin D emerges as particularly significant. Its levels decline progressively with age, and this decline has been correlated with various adverse health outcomes in the elderly, including sarcopenia, increased susceptibility to falls, hip fractures, and higher mortality rates. Notably, studies carried out in the last decade has provided insights into the potential of vitamin D supplementation to lessen sarcopenia and reduce the likelihood of falls among the elderly.[5,6] Nevertheless, ongoing debates persist regarding the precise impact of vitamin D intake on key aspects such as performance in the timed-up-and-go test and handgrip strength. Hence, recognizing the importance of resolving these debates, our study sought to rigorously evaluate the efficacy of vitamin D intake specifically concerning performance in the timed-up-and-go test and handgrip strength. Through this investigation, we aimed to contribute substantively to the ongoing discourse surrounding the function of vitamin D in promoting optimal physical function and mobility in aging individuals.

METHODS

Study design

From May to June 2023, we performed a meta-analysis, according to the procedures specified by the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines.[7] To fulfill the objectives of our study, we meticulously executed and organized searches across multiple databases including Google Scholar, PubMed, and Web of Science. Subsequently, we meticulously collected the necessary data to evaluate the effectiveness of vitamin D intake concerning both functional mobility and cognitive function.

Eligibility criteria

Prior to commencing the systematic search, we established clear eligibility criteria. The analysis incorporated articles that met the following criteria: (1) implementation of randomized controlled trial methodologies, (2) exploration of the impacts of vitamin D intake on both functional mobility and cognitive function, (3) inclusion of elderly populations, and (4) provision of data pertaining to post-intervention mean and standard deviation. Conversely, reviews, commentaries, letters to the editor, grey literature, and duplicate publications were excluded from consideration.

Quality assessment

All prospective articles earmarked for inclusion in the study underwent a comprehensive quality assessment employing a modified Jadad Score. Quality was categorized as high, moderate, or low based on scores falling within the ranges of 3-5, 2-3, or 0-2, respectively.[8] Articles deemed to be of low quality were subsequently excluded from the analysis. The assessment of the modified Jadad Score was carried out independently by two separate teams, denoted as EJP and CYR, utilizing a pilot form. Any disparities arising during the assessment process were diligently addressed through open dialogue and consensus-building discussions, ensuring the integrity and consistency of the quality evaluation process.

Search strategy

In May 2023, an organized search of Google Scholar, PubMed, and Web of Science was conducted as part of our study methodology. The search utilized keywords generated from Medical Subject Headings (MeSH), encompassing terms such as "vitamin D", "supplementation" or "administration", "functional", "mobility", "cognitive" or "strength", and "elderly" or "geriatric" or "older adults". To maintain consistency, the search was confined to articles published in English. In instances where duplication was encountered, preference was given to studies with larger sample sizes to ensure comprehensive coverage of relevant literature. Additionally, we systematically scrutinized the citations within relevant articles to locate and retrieve any additional papers that could contribute to our investigation.

Data extraction

The selected articles underwent meticulous data collection, encompassing key information such as the first author's name, study design, study duration, sample size, population characteristics focusing on frail elderly individuals, and pertinent data regarding the average and deviation of combined timed up-and-go test and handgrip strength test post-vitamin D intake. To ensure accuracy and reliability, the article search and data extraction processes were conducted independently by two distinct teams, denoted as CYR and WF. Prior to commencing the systematic search, the agreement between the two investigators was quantitatively assessed using the kappa statistic. An established agreement was deemed to have occurred if the kappa statistic surpassed the designated p-value threshold, indicative of a satisfactory level of inter-rater reliability.

Table 1. Baseline characteristics of studies included in our analysis

Author	Country	Sample Size	Study Period	Population	Intervention	Duration of Intervention	Measurement Instrument	Quality (Jadad)
Bauer et al 2015	Multicenter	380	June 2010 - May 2013	Malnourished Elderly (>65 years)	800 IU Vitamin D, 20 gram whey protein, 3 gram total leucine, 9 gram carbohydrates, 3 gram fat, combine with mixture vitamins, minerals, and fibers	3 months	Hydraulic hand dynamometer	High
Bo et al 2019	China	60	April 2016 - July 2016	Malnourished Elderly (>65 years)	702 IU Vitamin D	6 months	Electronic Hand Dynamometer	High

Canggusu et al 2015	Brazil	160	September 2013 - February 2014	Postmenopausal women with history of fall in past 12 months	1000 IU Vitamin D3	9 months	Hydraulic hand dynamometer	Moderate
de Luis et al 2015	Spain	70	January 2012 - December 2013	Malnourished Elderly (>65 years)	HMB, Vitamin D3 12 IU	3 months	HGS by dynamometry	Moderate
El Hajj et al 2019	Lebanon	128	July 2015 - September 2015	Malnourished Elderly (>65 years)	10.000 IU Cholecalciferol (Vitamin D)	6 months	Martin Vigorimeter	Moderate
Glendenning et al 2012	Australia	686	February - July 2009	Postmenopausal women	150.000 IU Vitamin D	9 months	Hydraulic hand dynamometer	High
Imaoka et al 2016	Japan	91	September 2013 - June 2014	Frail elderly	900 IU Vitamin D	3 months	Hand dynamometer	Poor
Kim et al 2016	Japan	139	Comprehensive Geriatric Health Examination 2012	Sarcopenic Obesity Community-Dwelling Elderly	20 ug vitamin D	3 months	handheld Smedley-type dynamometer	High
Lin et al 2021	Taiwan	56	March 2017 - December 2017	Sarcopenia Elderly	120 IU vitamin D	3 months	Dynamometer	High
Rondanelli et al 2016	Italy	130	January 2013 - June 2014	Sarcopenia Elderly	7.8 IU Vitamin D3	3 months	JAMAR Hand Dynamometer	High
Takeuchi et al 2018	Japan	68	September 2011 - December 2013	Sarcopenia Elderly undergoing hospital-based rehabilitation	12.5 ug vitamin D	2 months	Smedley's hand dynamometer	Moderate
Verreijen et al 2014	Netherland	80	March 2011 - June 2012	Obesity Elderly	20 ug vitamin D3	3 months	JAMAR Hand Dynamometer	High
Bauer et al 2015	Multicenter	380	June 2010 - May 2013	Malnourished Elderly (>65 years)	800 IU Vitamin D, 20 gram whey protein, 3 gram total leucine, 9 gram carbohydrates, 3 gram fat, combine with mixture vitamins, minerals, and fibers	3 months	Hydraulic hand dynamometer	High
Bunout et al 2006	Chile	96		Community-dwelling elderly with low vitamin D levels	800 mg/day calcium plus vitamin D3 (cholecalciferol) 400 IU/day	9 months	Handgrip dynamometer; General physical fitness, measuring the timed up and go expressed	High

							in seconds and fraction	
Janssen et al 2010	Netherlands	70		Community-dwelling elderly with low serum 25OHD 20-50 nmol/L	Vitamin D (Cholecalciferol) 400 IU + Calcium 500 mg/day	6 months	Hydraulic hand dynamometer	High
Pfeifer et al 2009	Germany	242	May 2001 - March 2003	Community-dwelling elderly with low serum vitamin D < 78 mmol/l	500 mg of calcium plus 400 IU vitamin D	12 months	Hydraulic hand dynamometer	High
Sakalli et al 2012	Turkey	149	November - April	Community-dwelling elderly with low vitamin D levels	300.000 IU Vitamin D	1 months	Hydraulic hand dynamometer	High
Verreijen et al 2014	Amsterdam, Netherland	80	March 2011 - June 2012	Obesity Elderly	20 ug vitamin D3	3 months	JAMAR Hand Dynamometer	High
Zhu et al 2010	Australia	302	April 2003 - October 2004	Community-dwelling ambulant elderly with serum 25-hydroxyvitamin D < 24 ng/mL	Vitamin D2 1000 IU/day; calcium citate (1 gram calcium/day)	12 months	Mobility functioning was measured using Timed Up and Go Test	High

Note, The study design of all studies is randomized controlled trial.

Covariates

In our study, the predictor covariate under investigation was the supplementation of vitamin D. This covariate served as the independent variable, allowing us to assess its potential impact on the outcome of interest. The outcome covariate, on the other hand, pertained to functional strength and mobility in frail elderly individuals. This encompassed a range of physical capabilities and mobility-related measures, covering the timed up-and-go test and muscle strength.

Statistical analysis

Before computing the mean and standard deviation of the timed up-and-go test and handgrip strength, a thorough examination of possible bias in publication and variation among the studies was conducted. We evaluated the risk of publication bias using Egger's test, interpreting a significance level of $p < 0.05$ as an indication of bias. Additionally, heterogeneity among studies was evaluated using the Q test, where a p-value threshold of <0.10 indicated significant heterogeneity. Accordingly, a random effects model was applied for data analysis in cases of observed heterogeneity, and in instances where there was no heterogeneity, we utilized a fixed-effects model. An Inverse variance meta-analysis was carried out using the continuous covariate method to compute the mean, standard deviation, and sample size of post-intervention data from each study. These analyses were executed utilizing the Comprehensive Meta-Analysis (CMA, New Jersey, USA) version 2.1. The effect estimates pertaining to mobility and cognition, assessed through the TUG test and handgrip strength, were depicted in a forest plot, illustrating the combined mean difference (MD) and its corresponding 95% confidence interval (CI) for each outcome measure.

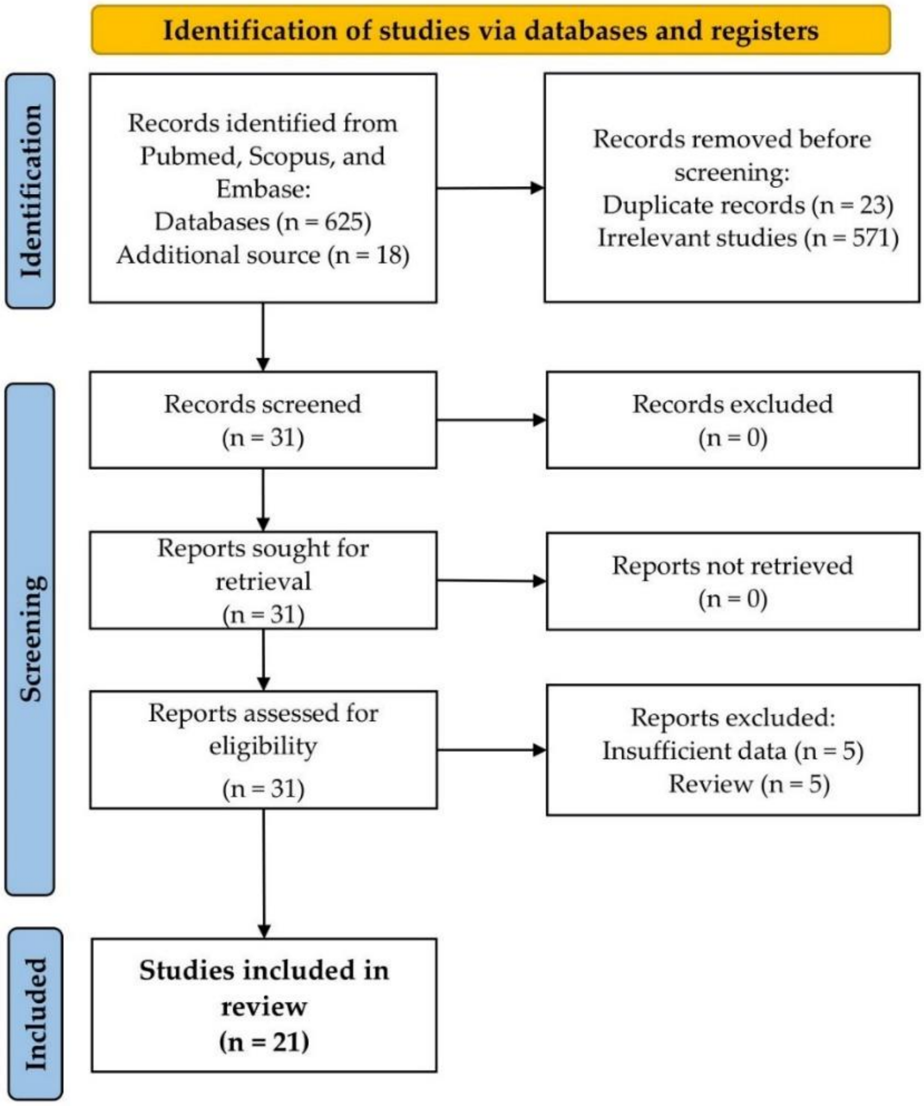

Figure 1. A flowchart of article selection in this review.

RESULTS

Patient selection

A total of 625 potential papers were retrieved from the specified databases, with an additional 18 identified from the reference lists of related articles. Among these, 23 papers were excluded due to duplication, while 571 were deemed not pertinent to the study's objectives. Consequently, 31 articles underwent full-text review. Following review, ten articles were excluded due to insufficient data, leaving 21 articles eligible for final analysis.[9-25] These articles were utilized to calculate the timed up-and-go test and handgrip strength, serving as measures of functional mobility and cognitive evaluation in frail elderly individuals. The process of article selection is visually represented in Figure 1, while the characteristics of the included articles are detailed in Table 1.

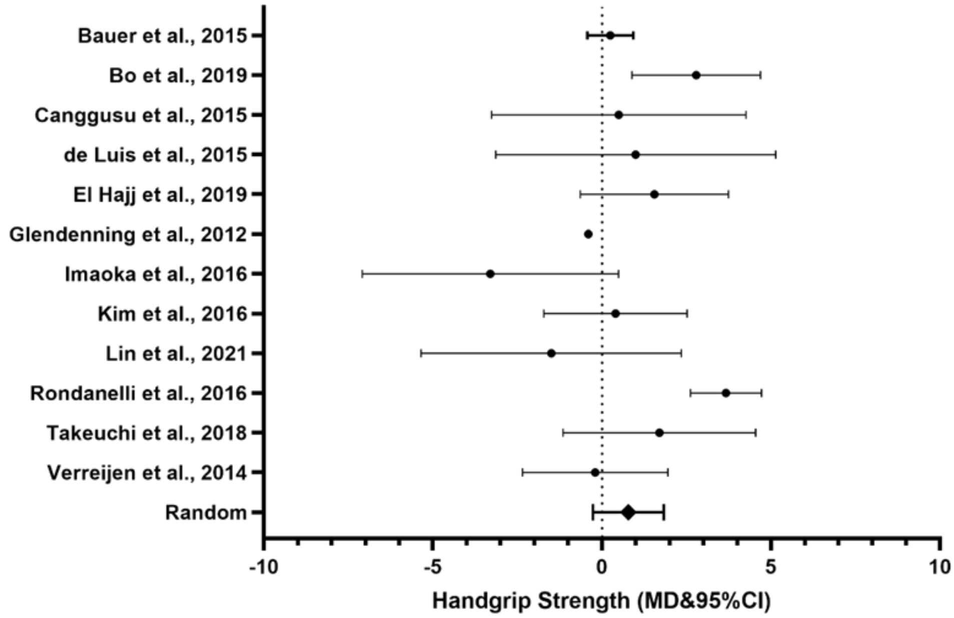

Figure 2. The effect of vitamin d supplementation on handgrip strength (MD: 0.78; 95% CI: -0.26, 1.83; p Egger: 0.464, p heterogenecity <0.0001; p: 0.0870).

The impact of vitamin D intake on handgrip strength

In our analysis aimed at determining the impact of vitamin D intake on handgrip strength, a total of 12 articles were included. Applying the random effects model for data analysis, we did not identify any significant association between vitamin D supplementation and handgrip strength (MD: 0.78; 95% CI: -0.26, 1.83; p Egger: 0.464, p heterogeneity <0.0001; p: 0.0870). The detailed effect estimates are depicted graphically in Figure 2A, illustrating the findings regarding the influence of vitamin D on handgrip strength.

The influence of vitamin D supplementation on performance in the timed-up-and-go test

In our analysis aiming to determine the impact of vitamin D intake on the timed-up-and-go test, a total of 9 articles were included. Analysis of the data using the random effects model revealed an association between vitamin D supplementation and enhanced performance in the timed-up-and-go test (MD: -0.768; 95% CI: -1.43, -0.11; p Egger: 0.286, p heterogeneity <0.0001; p < 0.0001). These effect estimates are visually presented in Figure 3, illustrating the influence of vitamin D intake on timed-up-and-go test outcomes.

DISCUSSION

Our results suggested that administering vitamin D was linked to a decrease in the timed-up-and-go test, a metric closely associated with functional mobility. However, we were unable to clarify the impact of vitamin D intake on handgrip strength. These results were consistent with previous meta-analyses, which similarly observed no noticeable enhancement in muscle strength but did find a small yet noteworthy enhancement in mobility.[26,27] Notably, our meta-analysis possessed several strengths, including a larger sample size compared to previous analyses. Furthermore, our analysis exclusively included RCTs, indicating a higher quality of evidence in our study. This rigorous methodology enhanced the reliability and validity of our findings, highlighting the potential advantages of supplementing with vitamin D to enhance functional mobility among older adults.

The underlying theory behind our findings remains a subject of debate. However, several factors may potentially elucidate the mechanisms underlying the outcomes of our study. Theoretically, vitamin D is found within the nucleus of human muscle cell lines, adult skeletal muscle, and myoblasts. It plays a role in inducing cell proliferation, influencing signaling pathways related to calcium and phosphate homeostasis, initiating muscle regeneration, and facilitating an increase in the size of muscle fibers and myogenic initiation.[28-30] A study has demonstrated that reduced levels of circulating vitamin D are linked with a rapid decline in muscle strength, decline in mobility, and heightened likelihood of falling. Therefore, this may impact an individual's muscle strength and influence timed-up-and-go test.[31] Such explanations could potentially bridge the gap regarding the implementation of vitamin D intake and timed-up-and-go test as reported by our study.

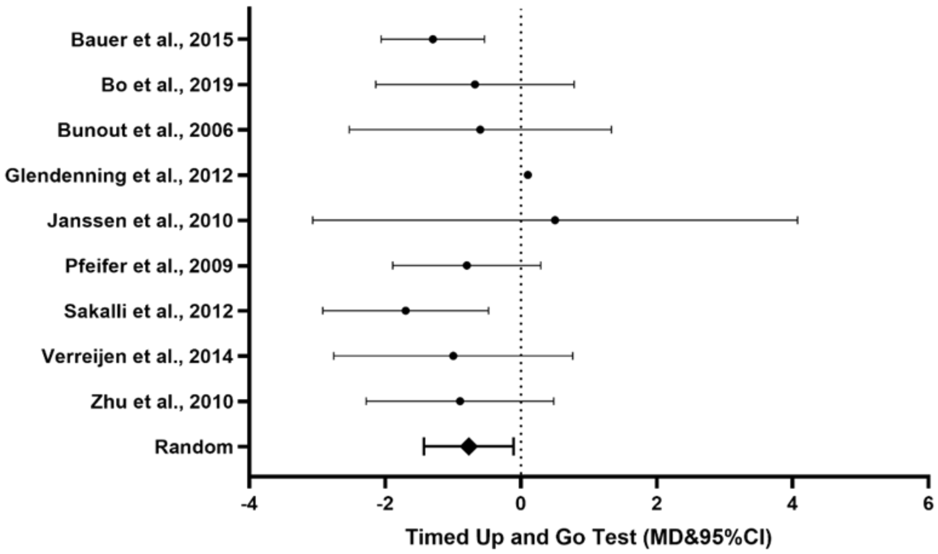

Figure 3. The effect of vitamin d supplementation on the timed up-and-go test (MD: -0.768; 95% CI: -1.43, -0.11; p Egger: 0.286, p heterogenecity <0.0001; p < 0.0001).

Our study findings confirmed that vitamin D intake had beneficial effects in improving the timed-up-and-go test. This study provided enhanced comprehension of the potential influence of vitamin D on mobility function, serving as a basis for recommending vitamin D intake to enhance individual mobility. Furthermore, the study provided the necessary scientific evidence to support clinical practices in addressing decreased mobility linked to a deficiency in vitamin D, especially in populations vulnerable to physical function decline, such as the elderly. Additionally, the study expanded our understanding of the mechanisms underlying the relationship between vitamin D levels and mobility function, paving the way for further research in this field. Moreover, the study provided a stronger knowledge base for developing intervention strategies aimed at improving mobility and independence, particularly in the context of fall prevention and mobility-related accidents. Furthermore, the study may have raised awareness of the importance of adequate vitamin D intake in maintaining physical health, including mobility, and enhancing overall quality of life.

Several limitations in this study required acknowledgment. First, we did not evaluate several potential factors that could have impacted the time-up-and-go test, such as patient age subgroups, balance function, neuromuscular disorders, and cognitive impairments. Second, differences in follow-up times and time-up-and-go test methods used in each article may have led to potential false positive results that warranted consideration. Third, variations in the dosage of vitamin D administered across articles raised concerns about the consistency of our study results. Fourth, differences in population sources in each article may have also introduced potential biases. Therefore, while this study provided valuable insights, it was crucial to take into account these limitations when interpreting the overall findings.

CONCLUSION

Our findings indicate that vitamin D intake has a beneficial effect on improving functional mobility, as demonstrated by the timed-up-and-go test. Interventions of this nature could potentially serve as preventive measures if administered earlier in adulthood. Looking ahead, larger-scale trials may be necessary to elucidate standard doses, optimal timing, and potential combinations of interventions aimed at enhancing the quality of life among the elderly population. These future endeavors will be crucial in further understanding the role of vitamin D intake in promoting mobility and overall well-being in aging individuals.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

CONFLICTS OF INTEREST

We have no conflict of interest

FUNDING SOURCES

We have no source of funding

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AUTHOR CONTRIBUTION

Conceptualization: EJP; Data Curation: EJP, CYR, WF; Formal Analysis: EJP, CYR, WF; Investigation: EJP, CYR, WF; Project Administration: EJP; Resources: EJP; Methodology: EJP, CYR, WF; Software: EJP, CYR, WF; Visualization: EJP, CYR, WF; Supervision: SS; Validation: SS; Writing – Original Draft Preparation: EJP, CYR, WF; Writing – Review & Editing: SS. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

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