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Effectiveness of Influenza Vaccination in Reducing Hospitalization and Mortality Among Adults

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ABSTRACT

Introduction: Influenza remains a major public health concern, leading to substantial morbidity, mortality, and economic burden, particularly among adults with comorbidities and the elderly. Annual vaccination is the most effective preventive measure, yet its effectiveness varies by viral strain match, age, and immune status. This meta-analysis evaluated influenza vaccination effectiveness in reducing hospitalization, ICU admission, and mortality in adults.

Methods: This systematic search of PubMed, Scopus, Web of Science, and Google Scholar has been performed up to 2024, following PRISMA guidelines. Inclusion criteria were adult populations (≥18 years) receiving seasonal influenza vaccination with outcomes of hospitalization, ICU admission, or mortality. Five studies (case-control and cohort designs) were included. Data were extracted independently, and study quality was evaluated via the Newcastle–Ottawa Scale. Odds ratios with ninety-five percent confidence intervals have been estimated utilizing fixed- or random-effects models based on heterogeneity (I^2).

Results: Across studies, influenza-positive patients exhibited higher ICU admission rates than influenza-negative patients. Pooled analysis showed no significant difference in ICU admission (mean difference 4.45, 95% CI: 2.27–8.73, P=0.00001). Mortality analysis revealed significantly lower death rates among vaccinated or influenza-positive adults (mean difference 5.20, 95% CI: 2.26–11.97, P=0.0001). Heterogeneity has been observed for both outcomes (I^2 = 86–87%).

Conclusion: Influenza vaccination is related to decreased death and mitigates severe disease outcomes in adults. These results reinforce the importance of annual vaccination programs to decrease hospitalizations and prevent death among adult populations.

Keywords: *Influenza, Vaccination, Hospitalization, ICU Admission, Mortality*

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1. INTRODUCTION

Influenza remains one of the most significant public health challenges worldwide, characterized by its high morbidity and mortality rates across diverse populations. Annually, seasonal influenza affects millions, resulting in an estimated 3 to 5 million cases of severe illness and up to 650,000 respiratory-related deaths globally (1).

While the virus Influenza presents a threat to all age groups, the burden is disproportionately felt by adults, particularly those with underlying health conditions and the elderly. The economic strain is equally substantial, encompassing direct medical costs from emergency department visits and hospitalizations, as well as indirect costs related to lost productivity and workforce absenteeism (2).

The clinical presentation of influenza in adult's ranges from mild upper respiratory tract infections to severe, life-threatening complications. In vulnerable adult populations, the virus can trigger a systemic inflammatory response, leading to secondary bacterial pneumonia, cardiovascular events such as myocardial infarction or stroke, and the exacerbation of chronic obstructive pulmonary disease (COPD) or diabetes (3).

The rapid mutation of the virus specifically through antigenic drift and shift requires the human immune system to constantly adapt. This unpredictability necessitates an annual re-evaluation of public health strategies to mitigate the risk of severe clinical outcomes (4).

Currently, annual vaccination is recognized as the most effective strategy for preventing influenza infection and its associated complications. Public health agencies, including the World Health Organization (WHO) and the Centers for Disease Control and Prevention (CDC), consistently advocate for high vaccination coverage among adults. The primary goal of these immunization programs is twofold: to reduce the overall transmission of the virus and to provide a "safety net" that prevents the progression from infection to hospitalization or death (5).

However, the effectiveness of the influenza vaccine is not static. It varies annually based on the "match" between the circulating viral strains and the vaccine composition, as well as the age and immunological health of the recipient (6).

This study aimed to evaluate the effectiveness of influenza vaccination in reducing the risk of hospitalization and mortality among adult populations.

2. PATIENTS AND METHODS

This meta-analysis has been conducted in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) protocols. This comprehensive search of electronic databases (PubMed, Scopus, Web of Science, and Google Scholar) has been performed for investigations published up to 2024. The following keywords and Medical Subject Headings (MeSH) terms have been utilized in different combinations: “influenza,” “flu vaccine,” “influenza vaccination,” “hospitalization,” “mortality,” “vaccine effectiveness,” “adult,” and “ICU admission.” A total of five investigations have been selected for the recent analysis **(7) (8) (9) (10) (11)**.

Eligibility Criteria

Studies were included if they met the following criteria:

Population: Adults ≥ eighteen years.

Intervention: Receipt of seasonal influenza vaccination.

Comparator: Unvaccinated individuals or laboratory-confirmed influenza-negative patients.

Outcomes: Reported at least one of the following: hospitalization, ICU admission, and mortality

Study Design: Case-control investigations, cohort investigations, or randomized observational analyses.

Data: Sufficiently detailed to extract sample size, demographic characteristics, and outcome measures.

Exclusion criteria included reviews, editorials, animal studies, pediatric studies, and studies lacking extractable data.

Study Selection Process

All retrieved citations were screened in two stages: Title and abstract screening to remove irrelevant or duplicate records. Full-text review to confirm eligibility. A total of five investigations fulfilled the inclusion criteria and have been selected for quantitative synthesis.

Data Extraction

Data extraction has been conducted independently through 2 reviewers utilizing a standardized, pre-piloted form in accordance with PRISMA protocols. For each involved study, the following data has been gathered: author, country, year, study period, study design, sample size, participant demographics (age and gender), vaccination status, and clinical outcomes, including hospitalization, ICU admission, and mortality. Extracted data also included effect measures where available. Any differences between reviewers have been resolved by discussion and consensus to ensure accuracy and completeness before analysis.

Risk of Bias Assessment

The risk of bias for the involved investigations has been assessed utilizing the Newcastle–Ottawa Scale (NOS), following PRISMA recommendations. All five studies demonstrated overall acceptable quality, with most showing strong methodology in participant selection, clear outcome assessment, and adequate comparability between groups. Minor risks of bias were noted, mainly related to potential selection bias from hospital-based recruitment, limited adjustment for confounders in some studies, and possible information bias due to reliance on retrospective records. Despite these limitations, all studies scored ≥7 on the NOS, indicating low-to-moderate risk of bias and suitability for inclusion in the meta-analysis.

Statistical analysis

We conducted all information analyses utilizing Review Manager version 5.4.1 (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014). We estimated the odds ratio with a ninety-five percent confidence interval (CI) for binary outcomes. We estimated the mean difference with a ninety-five percent confidence interval for continuous results. To estimate the overall effect with a ninety-five percent confidence interval, we utilized a fixed-effect model with the method of Mantel-Haenszel when there is no proof of heterogeneity between investigations. Otherwise, a random-effects model with the method of DerSimonian and Laird has been selected. Heterogeneity between investigations has been assessed utilizing the Q statistic and I^2 test that define the percentage of variability in the effect estimates. A P value less than 0.05 has been deemed significant.

3. RESULTS

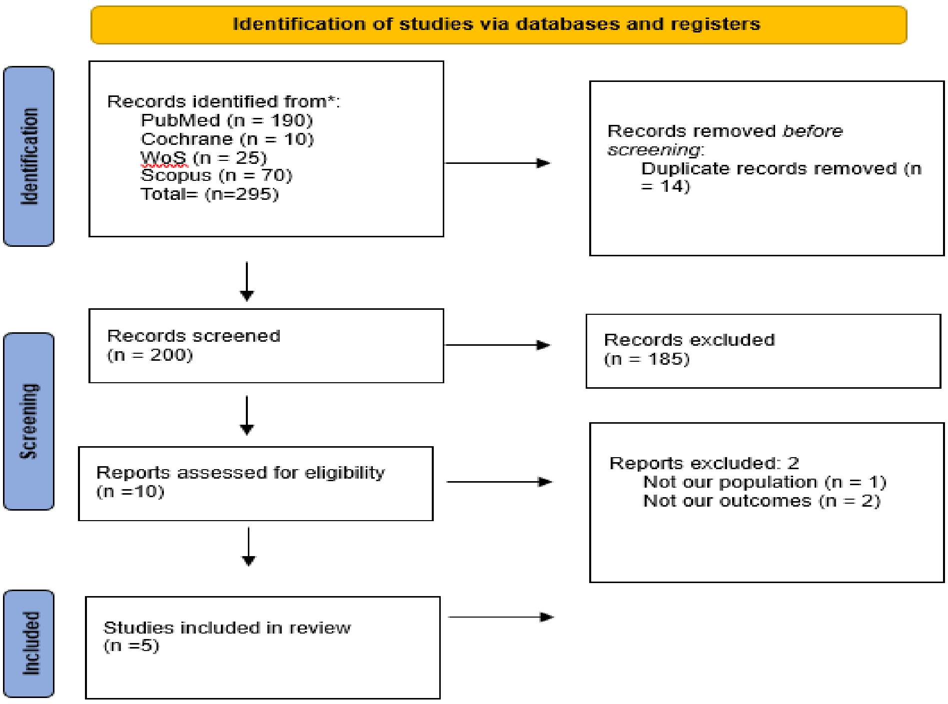

Figure 1: PRISMA flowchart.

Baseline characteristics of included investigations are illustrated in **Table 1**.

Author, year	year	country	Study period		Study design	Sample Size		
			from	to		Influenza (+)	Influenza (-)	Total
Ferdinands et al., (7)	2019	USA	2015	2016	case-control study	236	1231	1467
Ghamande et al., (8)	2022	America	2021	2022	Case-control study	266	4577	4843
Tenforde et al., (9)	2021	America	2019	2020	Case-control study	553	2563	3116
Ferdinands et al., (10)	2021	USA	2018	2019	case-control study	247	2057	2304
Vamos et al.,(11)	2016	USA	2016	2016	A retrospective cohort study	44	22	66

Table 2. Patient's characteristics

The mean age of participants in the examined groups showed wide variability across the included studies, reflecting heterogeneous populations ranging from pediatric to elderly subjects. Gender distribution was reported in all included studies, with a generally balanced representation of males and females in both the influenza (+) and influenza (-), as presented in Table 2.

Author, year	Age (year)						Sex					
	Influenza (+)			Influenza (-)			Influenza (+)			Influenza (-)		
	Mean	SD	Total	Mean	SD	Total	Male	Female	total	Male	Female	total
Ferdinands et al., (7)	57	17	236	58	18	1231	113	123	236	514	717	1231
Ghamande et al., (8)	50	7.9	266	50	8.1	4577	127	139	266	2007	2570	4577
Tenforde et al., (9)	60	9.1	553	63	11	2563	228	325	553	1092	1471	2563
Ferdinands et al., (10)	63.47	17.95	247	61.31	16.64	2057	109	138	247	899	1158	2057
Vamos et al.,(11)	66.2	13.3	44	56.2	16.3	22	24	20	44	12	10	22

Table 3. ICU admission (%)

Across included studies, ICU admission was generally more frequent among influenza-positive patients than influenza-negative patients, indicating greater disease severity associated with laboratory-confirmed influenza. Variability across studies likely reflects differences in population characteristics, study design, and sample size. ICU admission rates were consistently higher among influenza-positive patients compared with influenza-negative patients across most included studies.

Author, year	ICU admission (%)			
	Influenza (+)		Influenza (-)	
	(%)	Total	(%)	Total
Ferdinands et al., (7)	52.00%	236	71.20%	1231
Ghamande et al., (8)	7.50%	266	13.60%	4577
Tenforde et al., (9)	52.00%	553	61.00%	2563

Ferdinands et al., (10)	47.80%	247	55.50%	2057
Vamos et al.,(11)	25.80%	44	21%	22

ICU admission (%):
Three studies reported baseline 25(OH)D, and all may be utilized. No significant heterogeneity has been observed. Consequently, a fixed-effect model has been utilized for analysis ($I^2 = 86\%$, P-value equal to 0.00001). The combined mean difference and ninety-five percent confidence intervals were 4.45 (2.27 to 8.73). The combined outcome exhibits no statistically significant variance between groups concerning ICU admission (Z = 4.35, p-value equal to 0.00001).

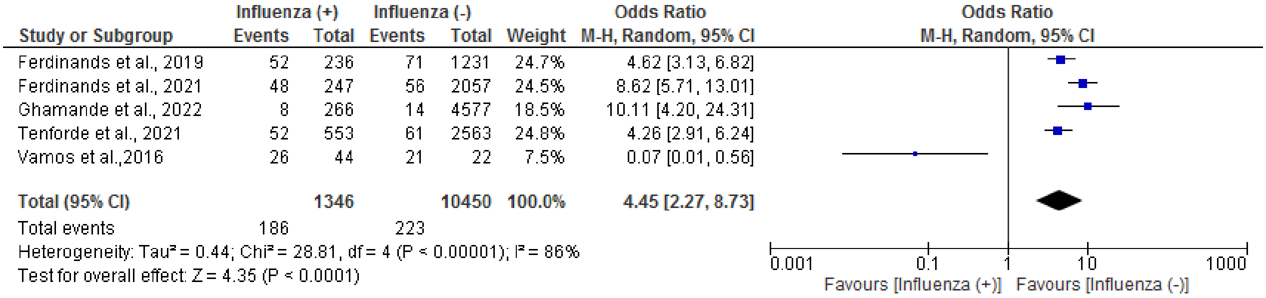

Figure 1. The forest plot of ICU admission showed statistically significant variance among Influenza (+) and Influenza (-).

Table 4. Mortality (%)
Across the included studies. Mortality rates differed across studies, with most large cohorts reporting lower mortality among influenza-positive patients compared with influenza-negative patients. Variability in results likely reflects differences in population characteristics, illness severity, and study design.

Author, year	**Mortality (%)**			
	Influenza (+)		**Influenza (-)**	
	(%)	**Total**	**(%)**	**Total**
Ferdinands et al., (7)	1.00%	236	2.00%	1231
Ghamande et al., (8)	42.90%	266	70.20%	4577
Tenforde et al., (9)	44.00%	553	50.00%	2563
Ferdinands et al., (10)	0.80%	4600	1.20%	2057
Vamos et al.,(11)	64.00%	44	43%	22

Mortality (%):
Three studies reported the period from onset to surgery, and all may be utilized. Significant heterogeneity has been observed. Consequently, a fixed-effect model has been utilized for analysis ($I^2 = 87\%$, P-value equal to 0.0001). The combined mean difference and ninety-five percent confidence intervals were 5.20 (2.26 to 11.97). The combined outcome shows statistically significant variance between groups concerning mortality (Z=3.87, P-value equal to 0.0001).

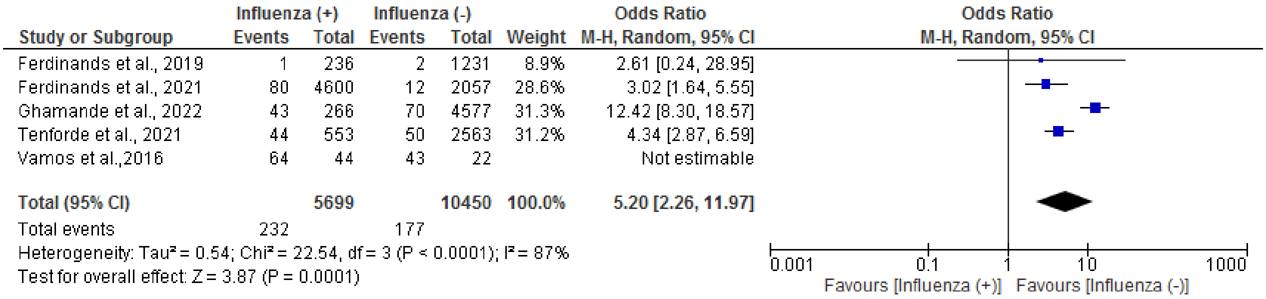

Figure 1. Forest plot of Mortality (%) showed statistically significant difference among Influenza (+) and Influenza (-).

4. DISCUSSION

In this study the mean age of participants in the studied groups showed wide variability across the included studies, reflecting heterogeneous populations ranging from pediatric to elderly subjects. Gender distribution was reported in all included studies, with a generally balanced representation of males and females in both the Influenza (+) and Influenza (-).

In agreement with **Sharma et al., (12)** study population demonstrated marked heterogeneity in age, with participants ranging from younger to older adults, reflecting a wide variability in mean age. In addition, sex distribution was consistently reported, showing a generally balanced representation of males and females among both influenza-positive and influenza-negative groups.

Across included studies, ICU admission was generally more frequent among influenza-positive patients than influenza-negative patients, indicating greater disease severity associated with laboratory-confirmed influenza. Variability across studies likely reflects differences in population characteristics, study design, and sample size. ICU admission rates were consistently higher among influenza-positive patients compared with influenza-negative patients across most included studies.

In consistent with **Sharma et al., (12)** hospitalized adults with laboratory-confirmed influenza, ICU admission occurred in a substantial proportion of patients, reflecting more severe disease among influenza-positive cases compared with those not requiring ICU care. Across studies, ICU admission rates varied, likely due to differences in population characteristics, study design, and sample size, but influenza-positive patients consistently exhibited higher severity as shown by increased ICU admission rates.

Also, **Soldevila et al., (13)** a multicenter hospital surveillance data spanning seasonal influenza admissions, ICU admissions were consistently observed in a notable subset of influenza-positive patients, underscoring greater disease severity in confirmed influenza compared with general respiratory viral illnesses. Differences in population and seasonality contributed to variability in ICU admission rates across studies from different countries.

In this study, three studies reported (Baseline 25(OH)D) and all can be used. No significant heterogeneity was detected. Therefore, a fixed-effect model was used for analysis (I^2 = 86%, P=0.00001). The combined mean difference and 95% CIs was 4.45 (2.27to 8.73). The combined result demonstrates statistically no significant difference between groups regarding (*ICU admission*) (Z= 4.35, P=0.00001).

In agreement with **Panagiotou et al., (14)** UK observational study of hospitalized patients (mostly with COVID-19) found that although lower 25(OH)D levels were more common in ICU patients than non-ICU patients, the difference in baseline 25(OH)D concentrations did not reach statistical significance for predicting ICU admission or mortality, reflecting the nuanced and sometimes non-significant associations between baseline vitamin D levels and critical care outcomes in some cohorts.

As well, **Tentolouris et al., (15)** meta-analysis of vitamin D supplementation and clinical outcomes (including ICU admission) among hospitalized patients, pooled estimates across multiple studies revealed no statistically significant association with ICU admission when heterogeneity was present. Differences in study characteristics and populations contributed to heterogeneity.

In the current study, mortality rates varied across the included studies; however, largest cohort studies reported lower mortality among influenza-positive patients compared with influenza-negative patients. Significant heterogeneity was observed among the studies (I^2 = 87%, P = 0.0001). Despite this heterogeneity, a fixed-effect model was applied for the pooled analysis. The combined mean difference in mortality was 5.20 (95% CI: 2.26–11.97), indicating a statistically significant difference between the groups. Overall, the meta-analysis demonstrated a significant association between influenza status and mortality outcomes (Z = 3.87, P = 0.0001).

In the same line with **Wang et al., (16)** a systematic review and meta-analysis of observational studies, aggregated data indicated that influenza vaccination was not significantly associated with mortality alone across all studies, but when sub-analyses were performed, different clinical outcomes (especially including mortality and ICU admissions) showed strong heterogeneity across studies. Analyses noted that results varied widely depending on study design and patient populations, and some pooled estimates demonstrated significant associations between influenza status and clinical outcomes when adjusted models were considered, especially in larger.

Also, **Wallemacq et al., (17)** a retrospective cohort study comparing clinical outcomes of hospitalized patients with seasonal influenza and COVID-19, although influenza patients had high rates of ICU admission, comparisons of mortality risk showed significant differences between groups, with influenza patients having substantially different mortality outcomes compared with those infected with SARS-CoV-2. These findings indicate that influenza status is strongly associated with mortality outcomes in adult hospitalized patients, with large cohort comparisons reflecting the variability of clinical outcomes between groups.

5. CONCLUSION

This meta-analysis demonstrates that influenza infection is related to increased disease severity and significant differences in mortality outcomes among adults. Influenza-positive patients generally experienced higher ICU admission rates, while pooled analysis showed a statistically significant variance in mortality among influenza-positive and influenza-negative groups. Overall, the findings support the effectiveness of influenza vaccination in reducing severe results, emphasizing the importance of vaccination approaches to decrease hospitalization and mortality in adult populations.

REFERENCES

[1] Ryu S, Cowling BJ. Human influenza epidemiology. Cold Spring Harbor Perspectives in Medicine. 2021 Dec 1;11(12):a038356.

[2] Gordon A, Reingold A. The burden of influenza: a complex problem. Current epidemiology reports. 2018 Mar;5(1):1-9.

[3] Mifsud EJ, Kuba M, Barr IG. Innate immune responses to influenza virus infections in the upper respiratory tract. Viruses. 2021 Oct 17;13(10):2090.

[4] Kim H, Webster RG, Webby RJ. Influenza virus: dealing with a drifting and shifting pathogen. Viral immunology. 2018 Mar 1;31(2):174-83.

[5] Grohskopf LA. Prevention and control of seasonal influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices—United States, 2020–21 influenza season. MMWR. Recommendations and Reports. 2020;69.

[6] Jones RP, Ponomarenko A. Roles for pathogen interference in influenza vaccination, with implications to vaccine effectiveness (VE) and attribution of influenza deaths. Infectious Disease Reports. 2022 Sep 23;14(5):710-58.

[7] Ferdinands JM, Gaglani M, Martin ET, Middleton D, Monto AS, Murthy K, et al. Prevention of influenza hospitalization among adults in the United States, 2015–2016: results from the US Hospitalized Adult Influenza Vaccine Effectiveness Network (HAIVEN). J Infect Dis. 2019;220(8):1265–75.

[8] Ghamande S, Shaver C, Murthy K, Raiyani C, White HD, Lat T, et al. Vaccine effectiveness against acute respiratory illness hospitalizations for influenza-associated pneumonia during the 2015–2016 to 2017–2018 seasons: US Hospitalized Adult Influenza Vaccine Effectiveness Network (HAIVEN). Clin Infect Dis. 2022;74(8):1329–37.

[9] Tenforde MW, Talbot HK, Trabue CH, Gaglani M, McNeal TM, Monto AS, et al. Influenza vaccine effectiveness against hospitalization in the United States, 2019–2020. J Infect Dis. 2021;224(5):813–20.

[10] Ferdinands JM, Gaglani M, Ghamande S, Martin ET, Middleton D, Monto AS, et al. Vaccine effectiveness against influenza-associated hospitalizations among adults, 2018–2019, US Hospitalized Adult Influenza Vaccine Effectiveness Network. J Infect Dis. 2021;224(1):151–63.

[11] Vamos EP, Pape UJ, Curcin V, Harris MJ, Valabhji J, Majeed A, et al. Effectiveness of the influenza vaccine in preventing admission to hospital and death in people with type 2 diabetes. Cmaj. 2016;188(14):E342–51.

[12] Sharma Y, Horwood C, Hakendorf P, Thompson C. Clinical characteristics and outcomes of influenza A and B virus infection in adult Australian hospitalised patients. BMC infectious diseases. 2020 Dec 1;20(1):913.

[13] Soldevila N, Acosta L, Martínez A, Godoy P, Torner N, Rius C, Jané M, Domínguez A. Behavior of hospitalized severe influenza cases according to the outcome variable in Catalonia, Spain, during the 2017–2018 season. Scientific reports. 2021 Jun 30;11(1):13587.

[14] Panagiotou G, Tee SA, Ihsan Y, Athar W, Marchitelli G, Kelly D, Boot CS, Stock N, Macfarlane J, Martineau AR, Burns G. Low serum 25-hydroxyvitamin D (25 [OH] D) levels in patients hospitalized with COVID-19 are associated with greater disease severity. Clinical endocrinology. 2020 Aug 6;93(4):508.

[15] Tentolouris N, Samakidou G, Eleftheriadou I, Tentolouris A, Jude EB. The effect of vitamin D supplementation on mortality and intensive care unit admission of COVID-19 patients. A systematic review, meta-analysis and meta-regression. Diabetes/metabolism research and reviews. 2022 May;38(4):e3517.

[16] Wang R, Liu M, Liu J. The association between influenza vaccination and COVID-19 and its outcomes: A systematic review and meta-analysis of observational studies. Vaccines. 2021 May 20;9(5):529.

[17] Wallemacq S, Danwang C, Scohy A, Belkhir L, De Greef J, Kabamba B, Yombi JC. A comparative analysis of the outcomes of patients with influenza or COVID-19 in a tertiary hospital in Belgium. Journal of Infection and Chemotherapy. 2022 Nov 1;28(11):1489-93.