Review Article

COVID-19 Vaccination in Cancer Patients: A Systematic Review of Safety, Efficacy, and Post-COVID Implications

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Abstract

Background and Aim: Since SARS-CoV-2 emerged in 2019, individuals with cancer have been particularly vulnerable due to immunosuppression. Although the acute pandemic phase has ended, the virus remains endemic, making it important to assess the safety and immunogenicity of COVID-19 vaccines in this high-risk population. Understanding vaccine responses in cancer patients can help guide post-COVID-era strategies, including booster policies, treatment scheduling, and mitigation of long-term COVID-19 complications in oncology care.

Materials and Methods: A systematic search of PubMed/Medline, Web of Science, and Scopus was conducted using the terms *"SARS-CoV-2," "COVID-19," "malignancy," "cancer," "tumor,"* and *"vaccine."* Eligible studies reported safety or effectiveness outcomes of COVID-19 vaccination in patients with solid or hematologic malignancies.

Results: Vaccination elicited measurable immune responses in most patients, with seroconversion rates generally higher in solid tumors compared with hematological malignancies. Booster doses substantially improved antibody responses across all cancer populations. Vaccines were generally well tolerated, with common adverse effects including local reactions, fatigue, and myalgia, while serious vaccine-related complications were rare. Breakthrough infections and severe COVID-19 were uncommon

Conclusion: COVID-19 vaccination is safe and induces immune responses in the majority of patients with cancer. Booster doses enhance immunity across all patient groups. Vaccination remains a key strategy to protect cancer patients, support treatment continuity, and reduce COVID-19–related complications. Further research is needed to assess long-term immunity, responses to different vaccine platforms, and efficacy across cancer treatments.

Keywords: Cancer, COVID-19 vaccination, SARS- CoV-2, Safety, Efficacy, Adverse effect

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Introduction

Since its emergence in late 2019, SARS-CoV-2 has caused a global pandemic, with continued circulation and recurrent outbreaks worldwide[1,2]. Patients with cancer are particularly vulnerable to COVID-19, experiencing higher rates of severe disease, hospitalization, and mortality compared with the general population[3-7]. Immunologic impairment arising from the malignancy itself, as well as from systemic therapies such as chemotherapy, targeted treatments, and immunomodulatory agents, can compromise vaccine-induced immune responses[8-10]. Although COVID-19 vaccination has substantially reduced morbidity and mortality in the general population, cancer patients were largely underrepresented in early clinical trials[11-16]. Subsequent studies have reported variable immunogenicity and safety outcomes, with some patients achieving robust seroconversion and clinical protection, while others—particularly those with hematologic malignancies or undergoing intensive immunosuppressive therapy—exhibit attenuated responses[15-19].

The heterogeneity of existing evidence underscores the need for a systematic review to evaluate the safety, efficacy, and immunogenicity of COVID-19 vaccines in patients with cancer. In the post-COVID era, such information is particularly important for guiding ongoing vaccination strategies, optimizing protection in high-risk populations, supporting continuity of cancer care, and informing preparedness for future SARS-CoV-2 variants or other emerging infectious threats.

Methods

This systematic review was performed based on the "Preferred Reporting Items for Systematic Reviews and Meta-Analyses" (PRISMA) statement[20].

Search Strategy: We performed a systematic literature search of PubMed/Medline, Web of Science, and Scopus, using the terms "SARS-CoV-2," "COVID-19," "coronavirus," "cancer," "malignancy," "tumor," and "vaccine." Original articles published up to March 2025 were included.

Eligibility Criteria and Study Selection: We systematically reviewed all observational studies reporting COVID-19 vaccination outcomes in adult patients with cancer. Studies published in English were included, while review articles, editorials, correspondence, letters, pediatric populations, and non-English publications were excluded. Both hematologic and solid organ malignancies were considered to evaluate differences in antibody responses, adverse events, and post-vaccination COVID-19 incidence. Additional variables, including vaccine type, ongoing anti-neoplastic therapy, comorbidities, and follow-up duration, were extracted to assess potential associations with immunogenicity and safety outcomes.

After removal of duplicates, all remaining articles were screened for relevance through a stepwise evaluation of titles, abstracts, and full texts. Each stage was independently reviewed by a second reviewer, and discrepancies were resolved through discussion with a third reviewer when necessary.

Data Extraction: For each included study, we extracted key characteristics, including first author, publication year, study design, country, median age, and study population (limited to cancer patients). Patient-level data included cancer type, ongoing antineoplastic treatments, comorbidities, prior COVID-19 infection, vaccine type administered, post-vaccination adverse events, and post-vaccination COVID-19 infections. The follow-up duration was also recorded. All data were independently extracted and cross-checked by a second reviewer, with discrepancies resolved through discussion with a third reviewer.

Risk of bias assessment: The risk of bias in the included observational studies was evaluated using the ROBINS-I (Risk of Bias in Non-randomized Studies of Interventions) tool. Assessment was performed across seven domains: bias due to confounding, bias in participant selection, bias in intervention classification, bias due to deviations from intended interventions, bias due to missing data, bias in outcome measurement, and bias in selection of the reported result. Each domain was independently assessed by two reviewers, with discrepancies resolved through discussion or consultation with a

third reviewer. The results of the risk of bias assessment were used to inform the interpretation of the reliability and validity of the findings in this review.

Results

Studies characteristics: The article selection process is summarized in Figure 1, and the key characteristics of the included studies are detailed in Table 1. A total of 29 studies met the inclusion criteria. The included studies were conducted across a broad international scope, spanning the USA, the UK, France, the Netherlands, Belgium, Austria, Denmark, and Switzerland. All study designs ranged from single-centre and multicentre cohort studies. The included studies comprised a total of 7737 participants, with a mean age of 67 years. Study populations included patients with hematologic malignancies such as lymphoid and myeloid cancers, multiple myeloma, and other blood cancers, as well as early- and advanced-stage solid tumors. Some studies also included specialized subgroups such as hematopoietic stem-cell transplant or CAR-T recipients. COVID-19 vaccines evaluated included BNT162b2 (Pfizer-BioNTech), mRNA-1273 (Moderna), AZD1222 (AstraZeneca), Ad26.COV2.S (Johnson & Johnson), and inactivated vaccines such as CoronaVac. Vaccination status ranged from first-dose and incomplete schedules to complete two-dose regimens and booster doses. Mixed vaccine strategies were reported in some cohorts. Serological assessments varied across studies, using multiple commercial platforms, with some also measuring neutralizing antibodies or cellular responses. The studies were conducted across hospital oncology departments, multicentre networks, and registry programs. Patient treatments varied, including chemotherapy, immunotherapy, chemo-

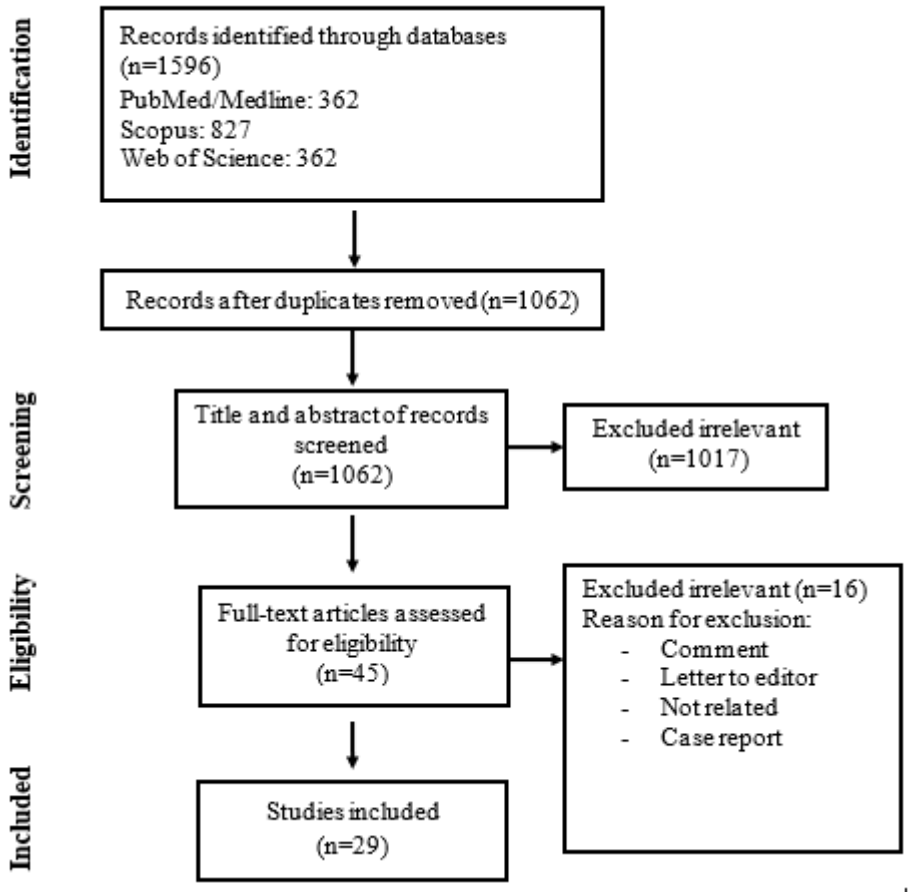

Figure 1. Flowchart of study selection for inclusion in the systematic review.

immunotherapy, targeted therapy, hormonal therapy, and cellular therapies.

Table 1. Characteristics of Included Studies.

Author (Ref)	Design	No. of patients	Mean Age	Vaccine type	Scheme
Hematological malignancies					
Agha et al. [49]	Single-centre, prospective	67	71	mRNA (BNT162b2 / mRNA-1273)	Complete
Benjamini et al. [50]	Multicentre, prospective	373	70	mRNA (BNT162b2)	Complete
Bird et al. [51]	Single-centre, retrospective	93	67	mRNA + AZD1222	Incomplete
Cohen et al. [52]	Single-centre, prospective	54	68.8	mRNA (BNT162b2)	Complete
Ghione et al. [53]	Multicentre, prospective	86	60	mRNA + AD26.COV2.S	Complete
Greenberger et al. [54]	Prospective	1445	68	mRNA (BNT162b2 / mRNA-1273)	Complete
Lavallade et al. [55]	Single-centre, prospective	21	55	mRNA (BNT162b2)	Incomplete
Herishanu et al. [56]	Multicentre, prospective	167	71	mRNA (BNT162b2)	Complete
Lim et al. [57]	Multicentre, prospective	129	69	mRNA + ChAdOx1	Incomplete + complete
Malard et al. [58]	Single-centre, retrospective	195	68.8	mRNA (BNT162b2)	Complete
Haggenburg et al. [59]	Prospective	584	60	mRNA-1273	3rd dose
Sherman et al. [60]	Prospective	94	60	mRNA (BNT162b2 / mRNA-1273)	3rd dose
Thakkar et al. [25]	Prospective	200	67	BNT162b2, mRNA-1273, Ad26.COV2.S	2nd or 1st
Maneikis et al. [61]	Prospective	855	65	BNT162b2	1st + 2nd
Gurion et al. [62]	Prospective	162	65	BNT162b2	2nd
Gavriatopoulou et al. [63]	Prospective	271	75	BNT162b2, AZD1222	1st
Roeker et al. [64]	Prospective	44	71	BNT162b2, mRNA-1273	2nd
Parry et al. [65]	Prospective	356	69	BNT162b2, AZD1222	1st + 2nd
Tzarfati et al. [65]	Prospective	423	71	BNT162b2	2nd
Ram et al. [66]	Prospective	80	65	BNT162b2	2nd
Solid tumors					
Barrière et al. [67]	Single-centre, prospective	122	69.5	mRNA (BNT162b2)	Incomplete + complete
Goshen-Lago et al. [68]	Single-centre, prospective	86	66	mRNA (BNT162b2)	Incomplete
Karacin et al. [69]	Multicentre, prospective	47	73	Inactivated (CoronaVac)	Complete
Massarweh et al. [70]	Single-centre, prospective	102	66	mRNA (BNT162b2)	Complete
Oosting et al. [71]	Prospective	503	62	mRNA-1273	1st / 2nd dose
Mixed (Hematological + Solid)					
Addeo et al. [72]	Multicentre, prospective	244	63	mRNA (BNT162b2 / mRNA-1273)	Incomplete + complete
Benda et al. [73]	Single-centre, prospective	259	65.1	mRNA (BNT162b2)	Incomplete + complete
Ehmsen et al. [74]	Single-centre, prospective	524	70	mRNA	Complete
Monin et al. [75]	Multicentre, prospective	151	73	mRNA (BNT162b2)	Incomplete + complete

Risk of Bias: The overall risk of bias in the included observational studies was assessed using the ROBINS-I framework. Studies in patients with hematological malignancies were generally at moderate risk of bias, mainly due to single-center designs, incomplete adjustment for confounding factors such as age, cancer type, and treatment, and inconsistent reporting of cellular immune responses. Studies in solid tumor populations were at low to moderate risk of bias, as most were prospective, multicenter, and employed validated assays for antibody measurement, although small sample sizes and incomplete outcome reporting slightly increased bias in some cohorts. Studies including mixed populations were at moderate risk of bias due to heterogeneity in patient characteristics, treatment regimens, and immune response assessment, which could introduce confounding and selective reporting.

Overall, while the majority of studies were prospective and used validated methods to measure vaccine-induced humoral responses, variability in study design, population characteristics, and outcome reporting contributed to a moderate risk of bias across the included studies.

Cancer Types and Anti-neoplastic Treatments: The included studies encompassed a wide spectrum of cancer types, with a substantial proportion focusing on patients with hematological cancers, followed by cohorts of solid tumors and several mixed-population studies including both groups.

Across hematologic malignancies, the most frequently represented disease categories were chronic lymphocytic leukemia (CLL), non-Hodgkin lymphoma (NHL), multiple myeloma (MM), myeloproliferative neoplasms (MPN), Waldenström macroglobulinemia (WM), and amyloidosis. Several studies also included patients who had undergone hematopoietic stem cell transplantation (HCT) or CAR-T cell therapy, reflecting populations with profound immune dysregulation. Mixed-diagnosis cohorts frequently combined lymphoid, myeloid, and plasma cell dyscrasias, as well as transplant recipients, in a single analysis.

Studies involving solid tumors included a broad range of adult malignancies typically managed within medical oncology units, although individual tumor types were not uniformly specified. These cohorts commonly included patients receiving standard systemic therapies such as chemotherapy, immunotherapy, chemo-immunotherapy, or targeted therapy.

Anti-cancer treatment status varied widely across studies. Many cohorts included patients undergoing active anticancer treatment, while others incorporated individuals on maintenance therapy, watchful waiting, or post-treatment surveillance. In hematologic malignancies, treatments frequently involved B-cell–depleting regimens (e.g., anti-CD20 monoclonal antibodies), Bruton tyrosine kinase inhibitors, immunomodulatory agents, proteasome inhibitors, lenalidomide-based regimens, and post-transplant immunosuppression. Mixed-cohort studies similarly reflected real-world treatment heterogeneity, including patients receiving cytotoxic therapies, biologic therapies, hormonal treatments, and combination systemic regimens.

Overall, the included studies captured a clinically diverse oncology population characterized by substantial variability in cancer types, disease stages, and ongoing anti-neoplastic treatments, representing the broad spectrum of immunocompromised states encountered in routine oncology practice.

Efficacy of COVID-19 vaccines: The efficacy of COVID-19 vaccines in cancer patients was assessed primarily by measuring anti-spike (anti-S) antibodies, which indicate an immune response to the vaccine. The presence of these antibodies after vaccination, known as seroconversion, indicates the vaccine's ability to stimulate an immune response. A smaller number of studies additionally measured neutralizing antibodies and T-cell responses, providing further insight into immune protection.

In patients with hematological malignancies, the proportion of individuals achieving seroconversion after the primary vaccination series was generally lower compared with patients with solid tumors. Immune responses were particularly reduced in patients receiving immunosuppressive therapies or those who had undergone hematopoietic stem cell transplantation or CAR-T therapy. Administration of booster (third) vaccine doses substantially increased the proportion of patients with detectable antibodies, and in some cases, neutralizing antibodies against SARS-CoV-2 variants were also observed. T-cell responses were detected in a subset of patients, suggesting additional cellular immunity in those with compromised humoral responses.

Patients with solid tumors showed higher rates of seroconversion following the primary vaccination series. Most patients developed detectable antibodies after one or two doses, and booster doses further increased antibody levels. Neutralizing antibodies and T-cell responses, when measured, supported the presence of effective immune activation.

In mixed cohorts containing both hematological and solid tumor patients, seroconversion rates were generally intermediate. Booster doses consistently enhanced antibody responses across all patient groups, with higher rates observed in patients with solid tumors compared to those with hematological malignancies. T-cell responses were detected in selected cohorts, complementing the humoral

response.

Overall, the data indicate that COVID-19 vaccines induce measurable immune responses in most cancer patients, but the magnitude of the response is influenced by cancer type and ongoing anti-neoplastic therapy. Booster vaccinations improve immune responses in both hematological and solid tumor patients, highlighting the importance of additional vaccine doses in immunocompromised populations.

Safety of COVID-19 vaccines: Across the included studies, COVID-19 vaccines were generally well tolerated in patients with cancer (Table 2). Reported adverse events were predominantly mild to moderate and consistent with those observed in the general population, including pain at the injection site, fatigue, headache, and low-grade fever. Serious adverse events were rare, and no new safety signals specific to cancer patients were identified.

Overall, the available data suggest that COVID-19 vaccination is safe and well tolerated in cancer patients, supporting its use in both primary and booster immunization schedules.

Discussion

The findings of this systematic review indicate that COVID-19 vaccination elicits measurable immune responses and is generally safe in patients with cancer. While most patients achieve seroconversion following complete vaccination, the magnitude of the immune response varies by cancer type and treatment, with patients with hematological malignancies or those receiving immunosuppressive therapies demonstrating lower responses compared with patients with solid tumors. Booster doses substantially improve antibody responses across all cancer populations, reinforcing their importance in this immunocompromised group.

Table 2. Efficacy of COVID-19 Vaccines in Cancer Patients.

Patient Group	Primary Vaccine Response	Booster / 3rd Dose Response	Neutralizing Antibodies (nAb)	T-cell Response	Notes
Hematological malignancies	Seroconversion generally lower than solid tumors; reduced in patients receiving immunosuppressive therapy or post-HCT/CAR-T	Booster doses substantially increased seroconversion; some studies reported nAb against SARS-CoV-2 variants	Detected in some studies post-booster; limited data overall	Measured in a subset of patients; indicates additional cellular immunity	Immune response influenced by cancer type, therapy, and prior treatments
Solid tumors	Higher seroconversion rates compared to hematological malignancies; most patients developed antibodies after 1–2 doses	Booster doses further enhanced antibody responses	Reported in select studies; supports effective humoral immunity	Detected in some cohorts; complements humoral response	Immune responses generally robust; therapy type may influence seroconversion
Mixed populations (hematological + solid)	Seroconversion rates intermediate between hematological and solid tumor patients	Booster doses consistently enhanced antibody responses across all groups	Limited nAb data; some detected post-booster	Detected in selected cohorts; supports overall cellular immunity	Responses generally stronger in solid tumor patients; booster important for immunocompromised patients

Safety profiles were similar across hematological malignancies, solid tumors, and mixed cancer populations, regardless of the vaccine type administered or whether patients had received primary or booster doses. In most studies, adverse events did not lead to discontinuation of cancer therapy or hospitalization, indicating that vaccination was generally safe even in immunocompromised patients.

This is particularly meaningful in the post-COVID era, as cancer patients represent a vulnerable population that continues to face increased risk from SARS-CoV-2 infection due to immunosuppression from both the malignancy itself and ongoing treatments such as chemotherapy, immunotherapy, targeted therapies, and hematopoietic stem cell transplantation[21-24].

Furthermore, seroconversion in cancer patients not only indicates the presence of vaccine-induced

antibodies but also reflects the broader capacity of COVID-19 vaccines to stimulate both humoral and cellular immunity[25-27]. While antibody titers are the most commonly measured markers of immune response, they may underestimate protection in patients with compromised B-cell function, such as those receiving anti-CD20 therapies, Bruton's tyrosine kinase inhibitors, or undergoing hematopoietic stem cell transplantation. In these populations, robust T-cell–mediated immunity—including CD4+ helper and CD8+ cytotoxic T-cell responses—is critical, as it can mediate viral clearance and limit disease severity even in the absence of high antibody levels[28-31]. Evidence suggests that T-cell responses may recognize conserved epitopes across SARS-CoV-2 variants, providing cross-protective immunity and partially compensating for reduced neutralizing antibody activity[29-31]. This dual arm of immunity is particularly vital in oncology populations, where vaccine-induced cellular responses may mitigate severe COVID-19, prevent hospitalization, and reduce mortality, even among patients with profound immunosuppression.

In the context of ongoing SARS-CoV-2 circulation and the emergence of new variants with partial immune escape, these findings underscore the necessity of personalized and adaptive vaccination strategies in oncology care[32-37]. The timing of vaccination relative to cancer therapy is a major determinant of efficacy: administration during periods of hematologic recovery, between chemotherapy cycles, or before initiation of highly immunosuppressive treatments may enhance seroconversion and T-cell responses[38,39]. Conversely, vaccination during active myelosuppressive therapy, post-B-cell-depleting treatment, or during profound lymphopenia may result in attenuated humoral responses, necessitating additional strategies to achieve protection. Specific subgroups, such as patients with hematologic malignancies, those receiving chimeric antigen receptor (CAR) T-cell therapy, allogeneic stem cell transplantation, or high-dose corticosteroids, may benefit from repeated booster doses, heterologous prime-boost strategies, or variant-adapted vaccines[40-43]. These strategies should ideally be guided by regular monitoring of both antibody titers and cellular immunity markers, including interferon-γ release assays or flow cytometric analysis of virus-specific T-cell responses, allowing individualized vaccination schedules that maximize protection without compromising cancer therapy efficacy.

Beyond immediate prevention of infection, high vaccination coverage in cancer patients may mitigate post-acute sequelae of COVID-19 (long COVID), which can be particularly debilitating in immunocompromised individuals[44,45]. Long COVID symptoms—ranging from chronic fatigue, dyspnea, cognitive impairment, and myalgia to cardiovascular, renal, and pulmonary complications—can disrupt cancer therapy schedules, reduce treatment adherence, prolong hospitalization, and negatively impact quality of life and functional independence[46-48]. Vaccination may attenuate the severity and incidence of these sequelae, preserve performance status, and enable timely completion of potentially curative or life-prolonging therapies. Moreover, reducing infection risk in oncology populations has broader systemic benefits: it decreases viral transmission in healthcare settings, protects other vulnerable patients, and reduces strain on oncology care resources—a critical consideration in the post-pandemic era, where SARS-CoV-2 is expected to become endemic with periodic surges.

This review faced several limitations. Variability in the categorization of anti-neoplastic therapies and cancer types limited data extraction, as some studies used broad categories while others were more detailed. Most studies were observational, lacked randomized controlled designs, and included heterogeneous patient populations, spanning treatment-naïve, actively treated, and palliative care patients, without separate subgroup analyses. Follow-up periods were often short, and the timing of serologic assessments varied, limiting assessment of long-term immunity. Comorbidities and other health conditions were inconsistently reported, and data on less-studied vaccines, such as Sputnik V and Sinovac, were insufficient. Additionally, the effects of COVID-19 vaccination on cellular and T-cell–mediated immunity remain poorly characterized, especially in patients receiving immunomodulatory or lymphodepleting therapies. Finally, heterogeneity in outcome

definitions and reporting across studies may have introduced bias.

Future studies should include larger cohorts, longer follow-up, diverse vaccine types, and detailed stratification by cancer type, stage, and treatment regimen. Dynamic monitoring of both humoral and cellular immune responses, as well as systematic assessment of adverse events, is needed to fully evaluate vaccine safety and efficacy in cancer populations.

Conclusion

COVID-19 vaccination appears to be both immunogenic and generally safe in patients with cancer, with most fully vaccinated individuals achieving seroconversion. These findings suggest that vaccination can provide meaningful protection even in immunocompromised populations, potentially reducing the risk of severe disease and post-COVID complications. In the post-COVID era, with SARS-CoV-2 expected to persist as an endemic virus, vaccination remains a critical component of ongoing oncology care, helping to protect patients, maintain treatment schedules, and reduce healthcare burden. Optimizing vaccination strategies—including timing relative to cancer therapy, consideration of booster doses, and monitoring of immune responses—may further enhance protection. While the evidence is encouraging, further research is needed to assess long-term immunity, variant-specific responses, and efficacy across different cancer types and treatment regimens.

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None.

Conflict of interest

The authors further declare that; they have no conflict of interest.

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