



Durability of Humoral Immune Response Following Booster Vaccination in Older Adults

Ristic B^{1*}, Milosevic G² and Petrovic D³

¹Department of Health Sciences, Sofia Center for Immunopathology, Serbia Scopus Author ID: 57566217339 Email: biljana.ristic@sofia.edu
ORCID: <https://orcid.org/8377-2393-5386-7024>

²Department of Biomedical Research, Sofia Center for Immunopathology, Croatia Scopus Author ID: 57758310253
Email: goran.milosevic@sofia.edu
ORCID: <https://orcid.org/6520-4333-1072-7339>

³Department of Specialty Medicine, Sarajevo Center for Infectious Disease, Bulgaria Scopus Author ID: 57936196383
Email: dragan.petrovic@sarajevo.edu
ORCID: <https://orcid.org/2897-3476-4238-1050>

***Correspondence to:** Biljana Ristic, Department of Health Sciences, Sofia Center for Immunopathology, Serbia Scopus Author ID: 57566217339 Email: biljana.ristic@sofia.edu

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Abstract

Booster vaccination has become a central strategy for restoring humoral immunity in older adults, whose primary vaccine responses are consistently blunted by immunosenescence, yet how long that restored protection actually persists in this population remains incompletely characterized. This article synthesizes the literature on the durability of antibody responses following booster vaccination in older adults, drawing primarily on the large real-world COVID-19 booster cohorts from Israel and Qatar alongside the longer-established influenza and pneumococcal vaccine durability literature. We trace the biological basis of age-related decline in germinal center function and long-lived plasma cell generation, the foundational trial and national booster evidence showing that a booster dose sharply restores antibody titers and clinical protection, and the subsequent kinetic studies showing that this restored protection itself wanes, often within months, with the extent of waning shaped by frailty, comorbidity, and prior infection history. We also examine the emerging evidence that hybrid immunity, combining infection and vaccination, confers greater durability than vaccination alone, complicating population-level durability estimates. Read together, the evidence supports a consistent restoration-then-waning pattern across vaccine platforms and cohorts, while leaving frailty-stratified, multi-year durability data and individualized revaccination intervals as an open research and policy agenda.

Keywords: humoral immunity; booster vaccination; older adults; immunosenescence; antibody durability

1. Introduction

By the time a person reaches their seventies, their immune system has already been shaped by decades of infection, vaccination, and low-grade chronic inflammation, and it responds to a new antigenic challenge in a way that is measurably different from how it responded at thirty. This is not a minor footnote to vaccinology; it is arguably the central practical problem the field has had to confront over the past two decades, as life expectancy has risen and as successive waves of new vaccines -- high-dose and adjuvanted influenza formulations, conjugate pneumococcal vaccines, recombinant zoster vaccine, and, most visibly, the mRNA and adenovirus-vectored COVID-19 vaccines -- have all had to be evaluated specifically in older recipients rather than assumed to behave the same way they do in younger, healthier trial populations. Age-related decline in immune function, and the accompanying low-grade inflammatory state that gerontologists have come to call inflammaging, blunts vaccine-induced antibody responses in ways that are now well documented across essentially every vaccine platform that has been carefully studied in older cohorts [1,2].

The COVID-19 pandemic turned this into an urgent, population-scale question rather than a specialized topic within geriatric immunology. Older adults were, from the earliest days of the pandemic, the group at greatest risk of severe disease and death, and they were also the group in whom the primary vaccine series was known, even before real-world booster data existed, to produce lower peak antibody titers than in younger adults [3,4]. The subsequent booster campaigns -- third doses beginning in mid-to-late 2021, fourth doses in early 2022, and the ongoing cycle of variant-adapted boosters since -- were deployed in large part specifically to address this gap, and the resulting body of real-world evidence, from Israeli, Qatari, and other national cohorts, gives us an unusually large and unusually well-characterized dataset on how humoral immunity behaves, and fails to persist, in older recipients after a booster dose [5,6,7].

This article synthesizes that literature. Our aim is not to report new data but to draw together what has actually been measured and published about the durability, or lack of durability, of antibody responses following booster vaccination specifically in older adults, and to

place the COVID-19-specific findings in the broader context of what decades of influenza and pneumococcal vaccine research had already taught us about waning immunity in this population before SARS-CoV-2 existed. We organize the discussion around five themes: the biological basis of immunosenescence as it affects humoral immunity; the foundational trial and early real-world booster evidence; the detailed kinetics of antibody decline after a booster dose in older cohorts; comparative lessons from influenza and pneumococcal vaccination, where multi-year follow-up data exist that COVID-19 vaccines have not yet accumulated; and the emerging evidence on how prior infection interacts with vaccine-induced immunity to produce more durable, "hybrid" responses. We close with an honest accounting of what remains unresolved.

It is worth being explicit about what this synthesis does and does not claim. We are not arguing that older adults fail to respond to booster vaccination -- the evidence is quite clear that boosters substantially raise antibody titers and reduce clinical risk in this group, often dramatically so in the weeks immediately following the dose [5]. What the literature more consistently shows is that the resulting protection, measured either serologically or clinically, wanes faster and to a greater degree in older recipients than in younger ones, that this waning is itself heterogeneous across individuals depending on frailty, comorbidity burden, and prior infection history, and that the practical implication -- how often boosting needs to be repeated, and for whom -- remains an active and only partially answered question.

The stakes of getting this question right are not merely academic. Older adults have consistently accounted for a disproportionate share of severe COVID-19 outcomes throughout the pandemic and its endemic aftermath, and the same age-related vulnerability that makes vaccination so important in this group is precisely what makes its waning durability such a consequential problem for public health planning. A booster schedule calibrated to the antibody decay kinetics of a healthy forty-year-old will, almost by construction, under-protect a frail eighty-five-year-old whose germinal center output and long-lived plasma cell generation are already operating at a fraction of that capacity, and conversely a schedule calibrated defensively to the frailest recipients risks over-boosting

healthier older adults whose hybrid immunity or more robust baseline response may already confer more durable protection than the frailest members of the same chronological age bracket. Resolving that tension requires exactly the kind of fine-grained, mechanistically grounded evidence this article attempts to synthesize.

2. Immunosenescence and the Aging Humoral Immune System

The decline in humoral vaccine responsiveness with age is not a single mechanism but the cumulative product of several distinct, partially independent processes acting on the B-cell compartment and the cellular help it depends on. Naive B-cell output falls with age as bone marrow lymphopoiesis slows and the peripheral naive B-cell pool becomes dominated by cells that have accumulated replicative history, leaving a smaller and less diverse repertoire available to respond to a genuinely novel antigen or a booster challenge to an antigen the immune system has not seen fully in some time [2]. At the same time, the germinal center reaction -- the process by which B cells undergo somatic hypermutation and affinity maturation to produce the high-affinity, durable antibody response that a good vaccine is supposed to induce -- becomes measurably less efficient with age, producing germinal centers that are smaller, shorter-lived, and less productive of long-lived plasma cells and memory B cells than the germinal centers of a younger immune system mounting the same response [8]. Because long-lived plasma cells residing in the bone marrow are the primary source of durable circulating antibody long after the initial immunization, any age-related impairment in generating them translates fairly directly into a shorter functional half-life for vaccine-induced antibody, independent of how high the initial peak titer happened to be.

This germinal center defect does not occur in isolation. It sits alongside inflammaging -- the chronic, low-grade, sterile inflammatory state characterized by persistently elevated circulating levels of cytokines such as IL-6 and TNF-alpha that Franceschi and colleagues first characterized as a hallmark of the aging immune system -- which appears to actively interfere with the signaling environment the germinal center needs to function well, rather than being merely a correlated but separate phenomenon of aging [1]. CD4 T follicular helper cells, whose provision of help is a rate-limiting step for

germinal center quality, are themselves subject to age-related functional decline and to thymic involution reducing the naive T-cell pool from which antigen-specific responses to a new pathogen must be drawn, compounding the B-cell-intrinsic defects rather than compensating for them [9]. Taken together, this constellation of changes -- reduced naive lymphocyte output, impaired germinal center function, an unfavorable inflammatory milieu, and diminished T-cell help -- is what immunologists mean when they invoke immunosenescence as an explanation for why older adults so consistently show both lower peak vaccine responses and faster subsequent decline than younger cohorts across essentially every vaccine platform examined to date [10].

It is important to be precise that immunosenescence is not a uniform, age-deterministic process that affects every seventy-year-old identically. Frailty, multimorbidity, chronic kidney and cardiovascular disease, diabetes, and immunosuppressive medication use are all independently associated with blunted humoral vaccine responses, layered on top of chronological age itself, and a growing body of work frames the goal of geriatric vaccinology not as simply "vaccinate older adults more" but as characterizing and eventually intervening on this heterogeneous, multifactorial biological aging process directly -- an idea sometimes described under the broader umbrella of "immunofitness" [11]. This heterogeneity matters enormously for interpreting booster durability data, because a population-average antibody decay curve for "adults over 65" can obscure a great deal of individual variation between a healthy, active 66-year-old and a frail 85-year-old with several comorbidities, and much of the literature synthesized below is, implicitly or explicitly, wrestling with exactly this heterogeneity.

Precision vaccine adjuvant strategies have emerged directly in response to this problem. Rather than treating a fixed antigen dose and a fixed adjuvant formulation as appropriate for all adult ages, a body of work reviewed by Nanishi and colleagues has examined age-tailored adjuvant systems -- including the MF59 and AS03 oil-in-water emulsions used in adjuvanted influenza vaccines, and higher-antigen-dose formulations -- specifically because standard formulations calibrated for younger adults have been shown repeatedly to underperform in older recipients, and because a

formulation that successfully compensates for reduced germinal center efficiency in an older immune system needs to be designed with that specific deficit in mind rather than simply scaled up in dose [12]. This adjuvant literature is a useful bridge between the mechanistic account of immunosenescence given above and the applied booster-vaccination literature that follows, because it demonstrates that the field has already treated "how do we get a durable response in an aging immune system" as a design problem with partial engineering solutions, well before COVID-19 boosters made the same question urgent on a much larger scale.

3. Foundational Evidence from Primary Series and Early Booster Trials

The pivotal phase 3 trials of the BNT162b2 and mRNA-1273 vaccines established both the high efficacy of the primary two-dose mRNA series and, on closer inspection of their age-stratified data, an early signal of the age gradient that would come to dominate the booster literature. Polack and colleagues reported that BNT162b2 conferred 95% efficacy against symptomatic COVID-19 overall, with efficacy in participants over 65 years of age within a broadly similar range to younger adults, though with wider confidence intervals reflecting the smaller number of older participants and events in that stratum [3]. Baden and colleagues reported a closely comparable efficacy profile for mRNA-1273, again with efficacy preserved across age strata in the primary analysis, but importantly these trials were not designed or powered to characterize how long that protection, or the antibody titers underlying it, would actually persist -- a question that could only be answered by follow-up studies conducted after enough time had passed for waning to become detectable [4].

That question was answered with unusual speed and clarity by a set of large observational and quasi-experimental studies conducted in Israel and Qatar over the second half of 2021, precisely because both countries had vaccinated early, tracked outcomes through integrated national health data systems, and were among the first to roll out a third ("booster") dose at national scale. Levin and colleagues, following a cohort of health care workers who had received their second BNT162b2 dose early, showed that neutralizing antibody titers declined substantially over the six months following the primary series, with the decline more pronounced among men, among people 65 years

of age and older, and among individuals with immunosuppressive conditions, and with the earliest-vaccinated participants also showing the highest subsequent rate of breakthrough infection -- a direct empirical link between measured antibody waning and clinical risk that motivated the case for boosting [13]. Chemaitelly and colleagues, studying the Qatari national cohort, independently documented waning of BNT162b2's protection against infection beginning within a few months of the second dose, again with the decline evident across the population but of particular concern for the older, higher-risk segment of it, even as protection against severe disease was better preserved than protection against infection alone [6].

Against this backdrop of documented waning, Bar-On and colleagues reported the results of Israel's national booster campaign in people aged 60 and older, comparing outcomes between those who received a third BNT162b2 dose and a contemporaneous, age-matched population that had received only the primary two-dose series. The rate of confirmed infection was more than ten times lower in the booster group than in the non-booster group, and the rate of severe illness was reduced by an even larger margin, on the order of a twenty-fold difference, during the follow-up period examined [5]. This is among the clearest pieces of evidence in the entire literature that boosting an aged immune system works, in the straightforward sense of substantially restoring clinical protection that had waned after the primary series; it is also, definitionally, a snapshot of protection shortly after boosting rather than a statement about how long that restored protection would last, which is precisely the durability question subsequent studies, including the fourth-dose evaluation by Magen and colleagues, went on to address as the same population's protection was observed to wane again over the following months, motivating that further dose [7].

4. Kinetics of Antibody Waning After Booster Vaccination in Older Adults

Once it was established that a booster dose substantially restores both antibody titers and clinical protection, the natural next question was how long that restoration lasts, and whether the waning pattern after a booster mirrors, is milder than, or is more severe than the waning already documented after the primary series. Gilboa and colleagues addressed this directly in a

longitudinal Israeli health care worker cohort, measuring anti-spike IgG and neutralizing antibody levels at multiple time points after a third BNT162b2 dose. Antibody levels rose sharply in the weeks immediately following the booster, as expected, but then began declining again within a few months, and participants whose antibody levels had declined furthest by the time of measurement were more likely to subsequently experience a breakthrough Omicron infection, directly linking the degree of measured humoral waning after a booster to a clinically meaningful outcome rather than treating antibody decay as a purely laboratory phenomenon [14]. This finding is important for the specific question this article is organized around, because it demonstrates that booster-induced antibody waning is not merely a return to a stable elevated baseline but a genuine, ongoing decay process that, left unaddressed, predicts loss of protection in essentially the same way primary-series waning did.

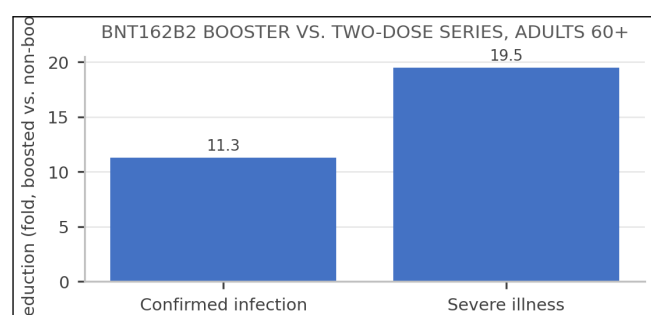


Figure 1: Illustrative rate reductions in confirmed SARS-CoV-2 infection and severe illness among adults aged 60 and older who received a BNT162b2 booster dose compared with age-matched adults who had received only the two-dose primary series, as reported by Bar-On et al. in the Israeli national booster campaign -- the clinical counterpart of the antibody restoration this section discusses [5].

A smaller but methodologically complementary study by Mihaylova and colleagues followed both humoral and cell-mediated responses after mRNA vaccination in a cohort spanning a wide adult age range, and reported that while both antibody and T-cell responses were detectable and durable in the majority of participants over the follow-up period, the magnitude and persistence of the humoral response in particular showed a negative association with participant age, consistent with the immunosenescence-driven mechanisms described earlier acting on the antibody-producing compartment specifically rather than uniformly suppressing every arm of adaptive immunity to the same degree [15]. This age-associated pattern in a relatively granular, prospectively sampled

cohort adds useful texture to the large national-registry studies discussed above, which are well powered to detect population-level clinical effects but necessarily coarser in how finely they can resolve the underlying antibody kinetics.

Age is not the only variable modulating this decay curve, and disentangling it from prior infection history has become a research question in its own right. Nakagama and colleagues examined how prior COVID-19 infection interacts with age to shape the subsequent mRNA vaccine antibody response, finding that the immunological benefit conferred by prior infection was itself age-dependent, meaning that a simple model in which "prior infection always boosts the response" or "age always blunts the response" independently is too simple -- the two factors interact, and disentangling them requires exactly the kind of age-stratified, infection-history-stratified analysis this line of research has begun to provide [16]. Read together, the kinetics literature supports a fairly specific, if sobering, picture for older adults: a booster dose reliably restores antibody levels and clinical protection to a degree comparable with, and sometimes exceeding, the protection conferred by the primary series, but the restored protection decays on a broadly similar or possibly shorter timescale than the original waning that motivated the booster in the first place, which is the empirical basis for the repeated booster cycles that have become the practical standard of care for this population.

5. Lessons from Non-COVID Vaccine Platforms: Influenza and Pneumococcal Durability

COVID-19 boosters are, relative to the multi-decade history of vaccinology, a very recent phenomenon, and the follow-up windows available in even the longest COVID-19 booster studies published so far rarely extend past one to two years. Influenza and pneumococcal vaccination, by contrast, have been studied in older adults for far longer, and that longer track record offers a useful, if imperfect, analogy for what multi-year antibody durability in an aging immune system tends to look like once enough follow-up time has accumulated.

Influenza vaccination in older adults illustrates both the age-related blunting problem and one of the field's more successful engineering responses to it. Tanner and colleagues, reviewing the evidence base for protecting the most vulnerable populations against influenza,

describe how standard-dose seasonal influenza vaccines consistently produce weaker and less durable antibody responses in adults over 65 than in younger adults, motivating the development and now widespread recommendation of high-dose and adjuvanted influenza vaccine formulations specifically for this age group, on the premise that a stronger initial immunological stimulus is needed to produce a response that persists usefully through an entire flu season [17]. This is directly analogous to the precision-adjuvant strategies discussed earlier and reinforces a broader pattern in the durability literature: where the underlying biological deficit is well characterized, the field has generally responded not by accepting reduced protection in older adults as inevitable but by re-engineering the vaccine formulation or dosing schedule specifically for this population.

Table 1: Reported humoral durability findings across vaccine platforms and older-adult populations discussed in this article, drawn from the cited primary studies [17,18,19,13,14,5].

Vaccine platform	Study population	Source	Reported durability finding
Seasonal influenza (standard-dose)	Adults 65+	Tanner et al. [17]	Weaker, less durable antibody response than in younger adults; motivated high-dose/adjuvanted formulations
13-valent pneumococcal conjugate (PCV13)	Older adults with vs without comorbidities (CAPiTA)	van Deursen et al. [18]	Measurably lower antibody responses in older adults with chronic comorbidities
Conjugate and polysaccharide pneumococcal vaccines	Frail, hospitalised older adults, multi-year follow-up	MacIntyre et al. [19]	Substantial antibody decline over years of follow-up in frail recipients
BNT162b2 primary series	Health care worker cohort, age-stratified	Levin et al. [13]	Neutralizing titers declined markedly over 6 months, more so in adults 65+
BNT162b2 third (booster) dose	Israeli health care worker cohort	Gilboa et al. [14]	Antibody levels rose then declined again within months; lower levels predicted breakthrough infection
BNT162b2 third (booster) dose	Adults 60+, national campaign	Bar-On et al. [5]	Rate of confirmed infection >10x lower and severe illness ~20x lower than in non-boostered adults 60+

Pneumococcal conjugate vaccination provides an even longer durability window, and the picture that emerges is more cautionary. Van Deursen and colleagues, reporting immunogenicity data from the CAPiTA trial population, found that older adults with chronic comorbidities mounted measurably lower antibody

responses to the 13-valent pneumococcal conjugate vaccine than comorbidity-free older adults of similar age, directly demonstrating that comorbidity burden, not age alone, independently degrades vaccine-induced humoral immunity in this population [18]. MacIntyre and colleagues extended this picture with genuinely long-term follow-up, tracking antibody persistence to both conjugate and polysaccharide pneumococcal vaccines in a cohort of frail, hospitalized older adults over several years, and reported that antibody levels declined substantially over the follow-up period in this specifically frail population, raising the practical question of whether and how often revaccination should be considered in the frailest segment of the older adult population rather than assuming a single dose confers durable, multi-year protection as it more reliably does in younger, healthier recipients [19]. Table 1 summarizes the reported durability findings across the vaccine platforms and populations discussed in this section and the preceding one, to make the comparison across platforms concrete.

The comparison across platforms is instructive for interpreting the COVID-19 booster literature specifically. Influenza and pneumococcal vaccination both show the same qualitative pattern documented for COVID-19 boosters -- age and comorbidity blunt the humoral response and shorten its durability -- but the influenza and pneumococcal literature has had far longer to characterize exactly how comorbidity, frailty, and repeated prior vaccination interact with durability, and that accumulated experience is a reasonable basis for anticipating, even before the data fully exist, that COVID-19 booster durability in the frailest older adults may prove shorter than what is measured in the relatively healthier, more mobile cohorts that dominate the current COVID-19 booster literature, which skews toward community-dwelling, ambulatory populations such as health care workers rather than the frail, institutionalized older adults MacIntyre and colleagues specifically studied [19].

6. Hybrid Immunity and the Role of Prior Infection

A substantial complicating factor for booster durability in the real world, as distinct from a controlled trial population, is that a large and growing fraction of older adults now carry some combination of vaccine-induced and infection-induced immunity, commonly termed

hybrid immunity, and the durability of hybrid immunity does not simply equal the sum of its two components. Mvula and colleagues, studying adults who had received an adenovirus-vectored COVID-19 vaccine, reported that hybrid immunity -- vaccination combined with a documented prior infection -- was associated with more durable, and more broadly cross-reactive, humoral responses than vaccination alone over their follow-up period, consistent with the general expectation that antigen exposure through two distinct routes engages a broader and better-primed immunological memory pool than either route in isolation [20]. Che-Kamaruddin and colleagues reported a closely consistent finding in a separate cohort: hybrid immunity following both infection and vaccination was associated with more sustained antibody levels and a lower subsequent reinfection risk compared with vaccination-only immunity, reinforcing that prior infection appears to confer a genuine durability advantage on top of vaccination rather than being a redundant or merely additive source of protection [21].

This has a specific, somewhat counterintuitive implication for the older-adult booster durability question. If hybrid immunity is generally more durable than vaccine-only immunity, and if a large fraction of the older adult population has by now acquired at least one documented or undocumented SARS-CoV-2 infection in addition to their vaccination history, then population-level durability data collected in recent years may reflect a mix of hybrid-immune and vaccine-only individuals whose antibody decay curves genuinely differ, complicating any single, unified estimate of "how long does booster-induced immunity last in older adults" that does not stratify by infection history. Madewell and colleagues, tracking longitudinal SARS-CoV-2 IgG antibody durability in a population-based cohort, provide exactly this kind of stratified, real-world evidence, following antibody trajectories over an extended period and explicitly using the resulting durability estimates to inform practical vaccination program strategy and timing rather than treating durability as a fixed, universal parameter [22]. Their approach -- explicitly incorporating the reality of mixed infection and vaccination histories into durability estimation, rather than analyzing vaccine-naïve or infection-naïve subgroups in isolation -- is, in our reading, a template for how future booster durability studies in older adults specifically should be designed,

given how common hybrid immunity has become in exactly the population where distinguishing a genuinely vaccine-attributable durability signal from an infection-boosted one matters most for guiding revaccination policy.

It is worth being candid that the hybrid immunity literature, while consistent in direction, is still relatively young and has not yet been examined with the same depth specifically in the oldest and frailest adults as it has in general adult cohorts. Whether the durability advantage hybrid immunity confers in younger, healthier populations translates proportionally to an 85-year-old with several comorbidities, whose germinal center and long-lived plasma cell compartments are already operating well below the capacity seen in a 40-year-old, is not yet clearly established, and represents one of the more concrete open questions we return to in the next section.

7. Open Challenges

Several gaps recur across the literature synthesized here and are worth stating plainly. First, follow-up duration: essentially the entire COVID-19 booster durability literature, including the foundational studies discussed above, covers antibody kinetics over months to at most a couple of years [13,14,15], while the pneumococcal literature's multi-year follow-up in frail older adults suggests that meaningful further decline, and possibly a need for revaccination, may become apparent only on a longer timescale than most COVID-19 booster studies have yet observed [19]. Second, frailty and institutionalization are underrepresented: much of the higher-quality COVID-19 booster durability evidence comes from community-dwelling, often occupationally exposed cohorts such as health care workers, and comparatively little comes from nursing-home or otherwise institutionalized frail older populations, even though this is precisely the subgroup in which comorbidity-driven blunting of the response, as documented for pneumococcal vaccination, would be expected to be most severe [18,19].

Third, the mechanistic literature on germinal center and T follicular helper cell aging, while conceptually well developed, has rarely been directly linked, within the same study, to the population-level antibody decay curves reported in the booster trials -- that is, we have good separate accounts of "why older immune systems should produce less durable antibody" and "how

durable booster-induced antibody actually is in older cohorts," but relatively few studies that measure both the underlying cellular immunology and the resulting antibody kinetics in the same individuals over time [8,9]. Fourth, disentangling age from comorbidity, frailty, and hybrid immunity status remains only partially solved; Nakagama and colleagues' demonstration that prior infection's benefit is itself age-dependent is a useful step, but a fully stratified model that jointly accounts for chronological age, frailty, comorbidity count, and infection history in predicting individual-level booster durability does not yet exist in the published literature at the scale needed for clinical guidance [16]. Fifth, and more practically, the optimal interval between booster doses for older adults specifically, as opposed to the general adult population, remains determined largely by regulatory and programmatic convenience rather than by an individualized durability model, even though the evidence surveyed here is fairly consistent that a uniform interval likely under-boosts some frail older adults and possibly over-boosts others whose hybrid immunity is already durable.

A sixth and closely related gap deserves separate mention: the comparative literature reviewed in this article draws its longest-duration evidence from pneumococcal and influenza vaccination, but those platforms differ from mRNA and adenovirus-vectored COVID-19 vaccines in antigen structure, dosing schedule, and adjuvant system in ways that limit how directly their multi-year durability patterns can be extrapolated to COVID-19 boosters. The analogy is useful for generating hypotheses -- for instance, that comorbidity-driven blunting documented for pneumococcal vaccination in frail older adults is likely to recur for COVID-19 boosters in the same population -- but it is not a substitute for platform-specific, multi-year COVID-19 booster durability data in frail cohorts, which simply do not yet exist at the scale the pneumococcal literature has achieved. Until they do, clinicians and policymakers are in the position of reasoning by analogy across platforms rather than working from a directly comparable evidence base, and that gap is worth naming rather than eliding.

None of these gaps undermine the core, repeatedly replicated finding that booster vaccination substantially and meaningfully restores humoral protection in older adults [5,7]. They do, however, argue against treating

"one booster restores durable protection" as the end of the story for this population, and in favor of continued, longer-horizon, frailty-stratified follow-up studies before firm, individualized revaccination recommendations can be made with the same confidence that now exists for the short-term benefit of boosting itself.

8. Conclusion

The literature reviewed here supports a specific and, we think, well-evidenced claim: booster vaccination reliably and substantially restores humoral immune protection in older adults that has waned after a primary vaccine series, but that restored protection itself wanes, often on a comparably short timescale, and the rate and extent of that subsequent waning is shaped by chronological age, frailty, comorbidity burden, and prior infection history acting together rather than independently [1,8,5,13,14]. This pattern is consistent across the COVID-19-specific literature and across the older, more mature influenza and pneumococcal vaccination literature, which gives the finding a degree of cross-platform robustness that a single vaccine's dataset alone could not provide [17,18,19].

Making sense of booster durability in this population going forward depends on treating it as inseparable from the biology of immunosenescence that produces it [2,10], from the growing recognition that hybrid immunity meaningfully alters individual decay curves in ways that population-average estimates can obscure [20,21,22], and from an honest acknowledgment that the frailest, most institutionalized older adults -- precisely the subgroup at highest clinical risk -- remain the least studied in the current booster durability literature despite decades of parallel evidence from pneumococcal vaccination that this is exactly the group in whom durability is most likely to be compromised [19]. The consistent replication of the core waning-then-restoration-then-waning pattern across independent national cohorts and independent vaccine platforms is, in our view, strong evidence that this is a genuine and clinically important feature of vaccine immunology in older age, rather than an artifact of any single study population, and one that continues to justify both further mechanistic research and continued, evidence-guided revision of booster scheduling for this population specifically [12,11].

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Conflict of Interest

The authors declare that they have no competing interests relevant to this work.

Data Availability Statement

This article is a literature synthesis and did not generate new primary data; all findings discussed are drawn from the cited publications, which should be consulted directly for their underlying data and code availability statements.

Ethical Approval

Not applicable. As a synthesis of previously published literature, this article did not involve human participants, animal subjects, or the collection of primary clinical data.

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