



Durability of Antibody Responses After Seasonal Influenza Vaccination in Adults Over Seventy: A Review of the Evidence

Anahit Campbell^{1*}, Amara Peralta², Kavita Martirosyan³

¹Department of Life Sciences, Tamiraparani Center for Life Sciences, Ghana

²Department of Life Sciences, Rhone Research Institute of Life Sciences, Uganda

³Department of Life Sciences, Nile Delta Graduate Institute of Life Sciences, Saudi Arabia

Article Info

Volume 1, Issue 1, 2026

doi: [10.62715/ijiid.2026.v1.i1.pp1-7](https://doi.org/10.62715/ijiid.2026.v1.i1.pp1-7)

Received: 22 May 2026

Accepted: 14 July 2026

Published: 30 August 2026

Abstract

Older adults carry most of the severe burden of seasonal influenza, and annual vaccination is offered to them on the assumption that the protection it gives will last through the months of virus circulation. Whether that assumption holds for people in their seventies and beyond has been argued over for decades. This narrative review brings together three bodies of published work that bear on the question: serological studies that follow haemagglutination inhibition titres after vaccination, observational studies that estimate how vaccine effectiveness changes with time since vaccination, and immunological studies of the plasma cells that sustain serum antibody. The serological literature shows that older adults start from a lower peak, and that titres fall over the following months at a rate not clearly faster than in younger adults. The effectiveness literature, mostly from test-negative studies, points to a loss of protection within a single season, most consistently against A(H3N2), although part of that signal may reflect bias and antigenic drift. Work on bone marrow plasma cells offers a mechanism for short-lived responses at any age. The review considers what these findings mean for the timing of vaccination and for enhanced vaccines, and identifies where data specific to the oldest age groups are still missing.

Keywords: *Influenza vaccine, Older adults, Antibody persistence, Haemagglutination inhibition, Immunosenescence, Waning immunity*

© 2026 Anahit Campbell et al. This is an open access article under the CC BY license (<https://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made.

1. Introduction

Influenza vaccination programmes in most countries give priority to older adults, and with reason: hospital admission and death from influenza are concentrated in the later decades of life. The inactivated vaccines used in these programmes are reformulated each year and given in the autumn, weeks or months before the virus begins to circulate. Protection therefore has to last. In temperate regions the season may run from late autumn into spring, and a person vaccinated at the first opportunity may need the response to hold for half a year or more.

The idea that it does not hold in the elderly is old and has been repeated often. It rests on a reasonable

* Corresponding author: Anahit Campbell, Department of Life Sciences, Tamiraparani Center for Life Sciences, Ghana. E-mail: anahit.campbell@tamiraparani.edu

© 2026 Anahit Campbell et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

chain of inference. Ageing changes the B cell and T cell compartments in ways that blunt responses to new antigens (Goronzy and Weyand, 2013), and older adults reach lower antibody titres after influenza vaccination than younger adults do (Goodwin *et al.*, 2006). A lower peak that then declines will cross any protective threshold sooner. What is less clear is whether the decline itself is faster in old age, whether it matters clinically, and how much of the evidence concerns people over seventy as distinct from the wider group aged sixty-five and over that most studies report.

This review examines that evidence. It asks what is known about the persistence of vaccine-induced antibody in adults over seventy, how far serological decline is matched by loss of protection against illness, and what the answers imply for practice.

2. Scope and Approach

The article is a narrative review of the published literature. It draws on serological follow-up studies, on earlier systematic reviews and meta-analyses, on observational studies of vaccine effectiveness by time since vaccination, and on immunological studies of the cells that produce antibody. No formal search protocol was applied and no new analysis is reported. Because few studies restrict enrolment to people over seventy, the review relies in many places on findings for adults aged sixty or sixty-five and over, and says so where the distinction affects the conclusion.

3. Measuring Antibody and Defining Protection

Almost all of the persistence literature uses the haemagglutination inhibition (HI) assay, which measures the highest serum dilution that prevents the viral haemagglutinin from agglutinating red cells. The assay owes its standing to challenge studies in healthy adult volunteers, in which a titre of about 1:40 was associated with a halving of the risk of infection (Hobson *et al.*, 1972). That figure became the working definition of seroprotection, and it has been carried into the immunogenicity criteria used in vaccine licensing ever since, with the qualification that the studies behind it were done in young volunteers.

Two cautions follow. First, the relationship between titre and protection is a continuous curve and not a step: modelling of pooled data shows protection rising steadily with titre, with no point at which it becomes complete (Coudeville *et al.*, 2010). The proportion of a group above 1:40 is a convenient summary and a crude one. Second, the correlate was established in young adults. In a vaccine trial that examined it directly, HI titre predicted protection after inactivated vaccine but left a good deal of risk unexplained (Ohmit *et al.*, 2011), and in older adults measures of T cell function have tracked protection more closely than serum antibody has (McElhaney *et al.*, 2006). Persistence of an HI titre is therefore evidence about one arm of immunity, and the arm that is easiest to measure.

4. The Peak Response in Older Adults

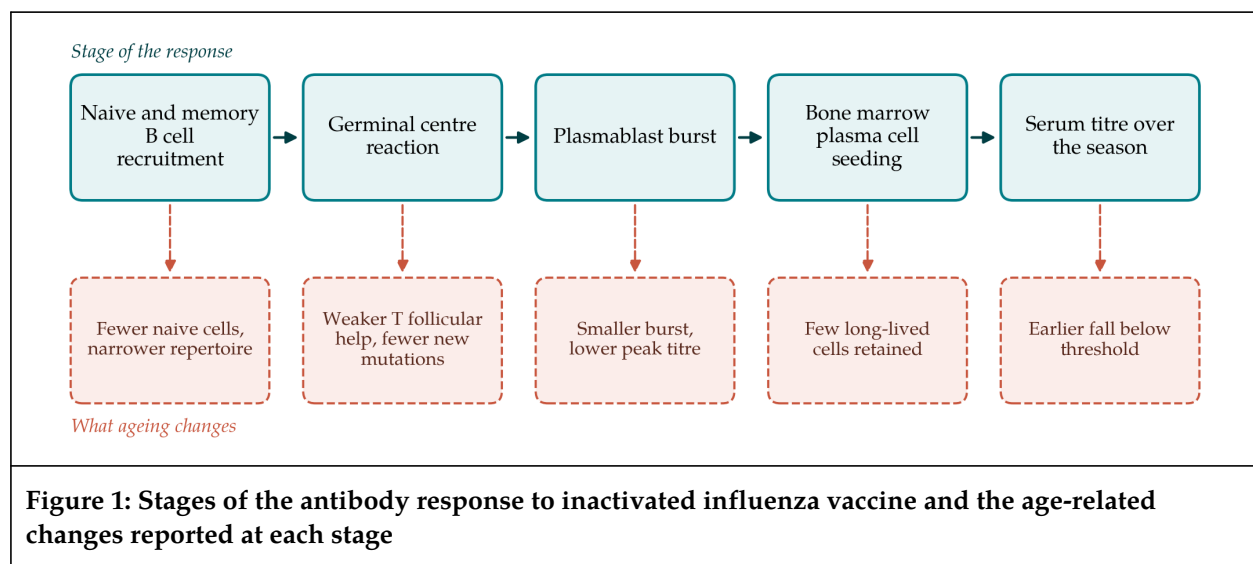
Durability cannot be judged apart from the height of the peak. A quantitative review of several decades of immunogenicity studies found that adults aged sixty-five and over were considerably less likely than younger adults to seroconvert or to reach seroprotective titres, for all three vaccine components, and that responses were lower still in those aged seventy-five and over (Goodwin *et al.*, 2006). The same review pointed out that many older adults enter the season with measurable antibody from earlier vaccinations and infections, which depresses fold-rise statistics without necessarily meaning a poor final titre.

Cellular studies explain the lower peak. Older vaccinees generate fewer vaccine-specific plasmablasts in the week after immunisation, and the smaller burst accounts for the lower serum titre; the antibodies that individual cells produce are not of obviously lower avidity (Sasaki *et al.*, 2011). The B cells that older adults recruit after vaccination carry fewer newly acquired mutations and are directed at conserved epitopes remembered from earlier exposures, which leaves them poorly adapted to drifted strains (Henry *et al.*, 2019). The lifelong layering of responses to successive influenza strains, reviewed by Krammer (2019), means that an older adult's response is to a large extent a recall of the past. Figure 1 sets the stages of the response beside the changes that ageing brings to each.

5. Serological Evidence on Persistence

The claim that vaccine-induced antibody declines rapidly in the elderly was tested against the literature by [Skowronski *et al.* \(2008\)](#). They found that the statement had been passed from one guidance document to the next with little primary support, and that in the studies which followed older vaccinees serologically, seroprotection rates, where they had been reached after vaccination, were generally maintained for at least four months and often for six or longer, particularly for the A(H3N2) and A(H1N1) components. Their conclusion was that the published record did not show a decline steep enough to justify delaying vaccination.

A later systematic review and meta-analysis asked a slightly different question: whether responses in the elderly last the whole year. Pooling studies with follow-up to about twelve months, [Young *et al.* \(2017\)](#) found that titres and seroprotection rates fell progressively after the first month, with the size of the fall varying by subtype and lineage. The two reviews are less opposed than they appear. One shows that antibody mostly lasts a season; the other shows that it does not last until the next. Individual follow-up studies of older vaccinees fit that reading, reporting a clear decline by six months and identifying low pre-vaccination titre and advanced age among the predictors of an inadequate or short-lived response ([Song *et al.*, 2010](#)).



Whether the rate of decline is greater in the old than in the young is harder to establish, because few studies follow both age groups with the same assay over the same interval. In healthy adults enrolled in a placebo-controlled trial, antibody to haemagglutinin and to neuraminidase fell only modestly over a season ([Petrie *et al.*, 2016](#)). The serological studies in older adults do not show a markedly steeper slope. The weight of the evidence is that older adults lose seroprotection earlier chiefly because they begin closer to the threshold. Table 1 summarises the main kinds of evidence and what each can and cannot show.

6. Evidence From Vaccine Effectiveness Studies

A second line of evidence does not measure antibody at all. Since about 2010, observational studies using the test-negative design have compared vaccine effectiveness among people vaccinated shortly before they fell ill with effectiveness among those vaccinated long before. In Europe, analyses of the 2011 to 2012 season, in which A(H3N2) circulated late, found that effectiveness was lower in those vaccinated more than about three months earlier, with the pattern most evident in older adults and other target groups ([Castilla *et al.*, 2013](#); [Kissling *et al.*, 2013](#)). A study in the United States reported a similar decline against A(H3N2) within one season in young children and in older adults ([Belongia *et al.*, 2015](#)).

Larger analyses followed. Data pooled over four seasons from the United States Influenza Vaccine Effectiveness Network showed effectiveness falling by several percentage points for each month since vaccination, for A(H3N2), for A(H1N1)pdm09 and for influenza B ([Ferdinands *et al.*, 2017](#)). A cohort

analysis within a large health system found that the odds of testing positive for influenza rose steadily with each additional four weeks since vaccination (Ray *et al.*, 2019). A meta-analysis of test-negative studies concluded that effectiveness declined between the first three months and the second three months after vaccination, significantly so for A(H3N2) and for influenza B (Young *et al.*, 2018).

Table 1: Kinds of evidence on the durability of influenza vaccine responses in older adults

Evidence	What it measures	Main finding	Main limitation
Serological follow-up	HI titre and seroprotection over months	Titres mostly held for a season, not a year (Skowronski <i>et al.</i> , 2008)	Correlate derived in young adults
Pooled serology	Seroprotection at fixed intervals	Progressive fall to twelve months (Young <i>et al.</i> , 2017)	Heterogeneous assays and age bands
Test-negative studies	Effectiveness by time since vaccination	Within-season decline (Ferdinands <i>et al.</i> , 2017)	Bias and drift can mimic waning
Cohort studies	Risk by weeks since vaccination	Risk rises with time (Ray <i>et al.</i> , 2019)	Timing of vaccination is not random
Cellular studies	Plasmablasts and marrow plasma cells	New plasma cells largely lost by one year (Davis <i>et al.</i> , 2020)	Small groups, few very old donors
T cell studies	Cytokine and granzyme B responses	Better correlate than HI in old age (McElhaney <i>et al.</i> , 2006)	No agreed protective threshold

These findings should be read with care. Lipsitch (2019) has set out why studies of this kind can show waning that is not there. If a vaccine protects some recipients well and others hardly at all, the unprotected among the vaccinated become infected early, as do the unvaccinated, and the two groups come to resemble each other as the season goes on. People who are vaccinated early also differ from those vaccinated late, and late-season viruses may have drifted from the vaccine strain. None of this disproves waning, and the consistency of the signal across designs and countries is hard to dismiss, but the estimates of its speed are uncertain. Few of the studies report adults over seventy as a separate stratum.

7. Why the Response May Be Short-Lived at Any Age

Serum antibody to some antigens lasts a lifetime. Longitudinal measurement in adults has shown antibody to measles, mumps and rubella declining so slowly that the estimated half-lives run to many decades, while antibody to tetanus and diphtheria toxoids declines much faster (Amanna *et al.*, 2007). The difference is thought to lie in how many long-lived plasma cells a given exposure deposits in the bone marrow. Direct sampling of marrow before and after influenza vaccination has shown that vaccine-specific plasma cells increase in the weeks after immunisation and then fall back towards their starting level within a year, with newly generated cells lost preferentially (Davis *et al.*, 2020).

This suggests that a transient response is a property of the current inactivated vaccines in adults generally, and not only a defect of old age. What ageing adds is a smaller initial burst and, plausibly, a marrow environment less able to retain new cells, although the second point has been studied mainly in animals and remains uncertain in humans.

8. Implications for Practice

Two practical responses have been pursued. The first is to raise the peak. A vaccine containing four times the standard quantity of haemagglutinin proved more efficacious than the standard-dose vaccine in a large randomised trial in adults aged sixty-five and over (DiazGranados *et al.*, 2014), and a meta-analysis of observational studies found the MF59-adjuvanted vaccine effective against influenza-related hospital admission in the elderly (Domnich *et al.*, 2017). A higher starting titre should, other things being equal, stay above a protective level for longer, but whether these vaccines slow the decline itself has not been settled.

The second response concerns timing. Guidance in the United States now expresses a preference for high-dose, recombinant or adjuvanted vaccines in people aged sixty-five and over, and advises against vaccinating older adults in the height of summer because protection may wane before the season ends (Grohskopf et al., 2022). The same guidance is clear that vaccination should not be put off so long that it is missed. That balance reflects the state of the evidence: the cost of a missed dose is certain, and the benefit of fine-tuning the date is not.

9. Gaps and Directions for Research

Several gaps stand out. Adults over seventy, and especially those over eighty or living in care homes, are underrepresented in serological follow-up, and where they are included the results are seldom reported separately. Frailty, which may matter more than chronological age, is rarely measured. Persistence has been studied almost entirely through HI titres, with little longitudinal information on neuraminidase antibody, on antibody to the haemagglutinin stalk or on T cell memory. Head-to-head comparison of the decline after standard and enhanced vaccines over a full season is sparse. Finally, the effect of repeated annual vaccination on the durability of each year's response, as opposed to its peak, is not well described. Studies that sample the same older adults at intervals across a season, with several immune measures and with clinical outcomes, would address most of these questions.

10. Conclusion

The published evidence does not support the old claim that influenza vaccine antibody disappears within weeks in the elderly, and it does not support complacency either. Older adults reach lower titres, those titres decline over the months that follow, and protection against illness appears to fall within a season, most clearly against A(H3N2). The vaccine-induced plasma cell response is short-lived in adults of any age. For people over seventy the data are thinner than their share of the disease burden warrants. Vaccinating with an enhanced product, at a date neither far ahead of the season nor so late as to risk missing it, is the course best supported by what is known.

Conflict of interest

To be declared by the author(s) before publication.

Funding

To be declared by the author(s) before publication.

References

- Amanna, I.J., Carlson, N.E. and Slifka, M.K. (2007). [Duration of humoral immunity to common viral and vaccine antigens. *New England Journal of Medicine*, 357\(19\): 1903-1915.](#)
<https://doi.org/10.1056/NEJMoa066092>
- Belongia, E.A., Sundaram, M.E., McClure, D.L., Meece, J.K., Ferdinands, J. and VanWormer, J.J. (2015). [Waning vaccine protection against influenza A \(H3N2\) illness in children and older adults during a single season. *Vaccine*, 33\(1\): 246-251.](#) <https://doi.org/10.1016/j.vaccine.2014.06.052>
- Castilla, J., Martínez-Baz, I., Martínez-Artola, V., et al. (2013). [Decline in influenza vaccine effectiveness with time after vaccination, Navarre, Spain, season 2011/12. *Eurosurveillance*, 18\(5\): 20388.](#)
- Coudeville, L., Bailleux, F., Riche, B., Megas, F., Andre, P. and Ecochard, R. (2010). [Relationship between haemagglutination-inhibiting antibody titres and clinical protection against influenza: development and application of a Bayesian random-effects model. *BMC Medical Research Methodology*, 10: 18.](#)
<https://doi.org/10.1186/1471-2288-10-18>
- Davis, C.W., Jackson, K.J.L., McCausland, M.M., et al. (2020). [Influenza vaccine-induced human bone marrow plasma cells decline within a year after vaccination. *Science*, 370\(6513\): 237-241.](#)
<https://doi.org/10.1126/science.aaz8432>

- DiazGranados, C.A., Dunning, A.J., Kimmel, M., et al. (2014). Efficacy of high-dose versus standard-dose influenza vaccine in older adults. *New England Journal of Medicine*, 371(7): 635-645. <https://doi.org/10.1056/NEJMoa1315727>
- Domnich, A., Arata, L., Amicizia, D., Puig-Barberà, J., Gasparini, R. and Panatto, D. (2017). Effectiveness of MF59-adjuvanted seasonal influenza vaccine in the elderly: a systematic review and meta-analysis. *Vaccine*, 35(4): 513-520.
- Ferdinands, J.M., Fry, A.M., Reynolds, S., et al. (2017). Intraseason waning of influenza vaccine protection: evidence from the US Influenza Vaccine Effectiveness Network, 2011-12 through 2014-15. *Clinical Infectious Diseases*, 64(5): 544-550. <https://doi.org/10.1093/cid/ciw816>
- Goodwin, K., Viboud, C. and Simonsen, L. (2006). Antibody response to influenza vaccination in the elderly: a quantitative review. *Vaccine*, 24(8): 1159-1169. <https://doi.org/10.1016/j.vaccine.2005.08.105>
- Goronzy, J.J. and Weyand, C.M. (2013). Understanding immunosenescence to improve responses to vaccines. *Nature Immunology*, 14(5): 428-436. <https://doi.org/10.1038/ni.2588>
- Grohskopf, L.A., Blanton, L.H., Ferdinands, J.M., et al. (2022). Prevention and control of seasonal influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices, United States, 2022-23 influenza season. *MMWR Recommendations and Reports*, 71(1): 1-28. <https://doi.org/10.15585/mmwr.rr7101a1>
- Henry, C., Zheng, N.-Y., Huang, M., et al. (2019). Influenza virus vaccination elicits poorly adapted B cell responses in elderly individuals. *Cell Host & Microbe*, 25(3): 357-366. <https://doi.org/10.1016/j.chom.2019.01.002>
- Hobson, D., Curry, R.L., Beare, A.S. and Ward-Gardner, A. (1972). The role of serum haemagglutination-inhibiting antibody in protection against challenge infection with influenza A2 and B viruses. *Journal of Hygiene*, 70(4): 767-777. <https://doi.org/10.1017/S0022172400022610>
- Kissling, E., Valenciano, M., Larrauri, A., et al. (2013). Low and decreasing vaccine effectiveness against influenza A(H3) in 2011/12 among vaccination target groups in Europe: results from the I-MOVE multicentre case-control study. *Eurosurveillance*, 18(5): 20390.
- Krammer, F. (2019). The human antibody response to influenza A virus infection and vaccination. *Nature Reviews Immunology*, 19(6): 383-397. <https://doi.org/10.1038/s41577-019-0143-6>
- Lipsitch, M. (2019). Challenges of vaccine effectiveness and waning studies. *Clinical Infectious Diseases*, 68(10): 1631-1633. <https://doi.org/10.1093/cid/ciy773>
- McElhaney, J.E., Xie, D., Hager, W.D., et al. (2006). T cell responses are better correlates of vaccine protection in the elderly. *Journal of Immunology*, 176(10): 6333-6339. <https://doi.org/10.4049/jimmunol.176.10.6333>
- Ohmit, S.E., Petrie, J.G., Cross, R.T., Johnson, E. and Monto, A.S. (2011). Influenza hemagglutination-inhibition antibody titer as a correlate of vaccine-induced protection. *Journal of Infectious Diseases*, 204(12): 1879-1885. <https://doi.org/10.1093/infdis/jir661>
- Petrie, J.G., Ohmit, S.E., Truscon, R., et al. (2016). Modest waning of influenza vaccine efficacy and antibody titers during the 2007-2008 influenza season. *Journal of Infectious Diseases*, 214(8): 1142-1149. <https://doi.org/10.1093/infdis/jiw105>
- Ray, G.T., Lewis, N., Klein, N.P., et al. (2019). Intraseason waning of influenza vaccine effectiveness. *Clinical Infectious Diseases*, 68(10): 1623-1630. <https://doi.org/10.1093/cid/ciy770>
- Sasaki, S., Sullivan, M., Narvaez, C.F., et al. (2011). Limited efficacy of inactivated influenza vaccine in elderly individuals is associated with decreased production of vaccine-specific antibodies. *Journal of Clinical Investigation*, 121(8): 3109-3119. <https://doi.org/10.1172/JCI57834>
- Skowronski, D.M., Tweed, S.A. and De Serres, G. (2008). Rapid decline of influenza vaccine-induced antibody in the elderly: is it real, or is it relevant? *Journal of Infectious Diseases*, 197(4): 490-502. <https://doi.org/10.1086/524146>

- Song, J.Y., Cheong, H.J., Hwang, I.S., et al. (2010). Long-term immunogenicity of influenza vaccine among the elderly: risk factors for poor immune response and persistence. *Vaccine*, 28(23): 3929-3935.
- Young, B., Sadarangani, S., Jiang, L., Wilder-Smith, A. and Chen, M.I.-C. (2018). Duration of influenza vaccine effectiveness: a systematic review, meta-analysis, and meta-regression of test-negative design case-control studies. *Journal of Infectious Diseases*, 217(5): 731-741.
<https://doi.org/10.1093/infdis/jix632>
- Young, B., Zhao, X., Cook, A.R., Parry, C.M., Wilder-Smith, A. and I-Cheng, M.C. (2017). Do antibody responses to the influenza vaccine persist year-round in the elderly? A systematic review and meta-analysis. *Vaccine*, 35(2): 212-221.