

Paucity of Laboratory-confirmed Failures of High-dose Influenza Vaccine in an Elderly Population, 2012-2013

Last year we reported our experience with high-dose influenza vaccine, which bolstered the view that high-dose vaccine was more effective than standard vaccine in preventing laboratory-confirmed influenza in the elderly.¹ Accompanying commentary² noted that this evidence was welcome, albeit weak. Additionally, the commentary noted the disproportionate impact of influenza on the elderly, the disappointingly low efficacy of influenza vaccine, and the interest in results of clinical trials. Subsequently, the results of a randomized, controlled trial (RCT) of 31,989 patients have been reported, showing 24.2% better efficacy of high-dose vaccine in preventing laboratory-confirmed clinical influenza.³ These results increase interest in confirmatory observational studies. Observational studies and RCTs produce similar results,⁴ and observational studies reflect less-selected populations, unlike the RCT,³ which required subjects who were available for weekly phone contact for 3 months and twice weekly contact for 2 months. Consequently, we looked at our more recent experience with high-dose vaccine. This strengthened our observations by providing data from an additional year—one which was particularly troublesome for the elderly⁵—and analyzing the data with more rigorous statistical methods.

As in 2010-2011,¹ the high-dose vaccine was used overwhelmingly for those 65 and over in the Veterans Health Administration's Nebraska-Western Iowa Health Care System, but sister facilities in our region's Veterans Integrated Service Network (VISN) 23 overwhelmingly used standard vaccine. VISN 23 laboratories documented 90 positive influenza tests among 67,993 standard vaccines and 8 positive tests among 11,320 receiving high-dose vaccine. (Sample odds ratio 1.87, Fisher exact test 2-tailed, $P=.04921$). Our institutional review board approved this study.

Although consistent with our previous results and the RCT³ (odds ratio 1.3257), this data has limitations resembling those of our earlier report: variation in laboratory methods and decisions to test, geographic variation in impact of influenza, absence of research staff to control data quality, and confounding by herd immunity. Our odds ratio exceeded that of the RCT, possibly reflecting an older population; the RCT odds ratio was 1.49 for those 75 and older.⁶ The larger amount of vac-

cine compared to 2010-2011 may reflect trends in vaccine use.

We agree with the observation that our earlier report has limitations, as does efficacy of standard vaccine. For that reason, the current report is important in providing additional support to the RCT³, showing that high-dose vaccine is an improvement in protecting the especially vulnerable elderly population.

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References

1. Bittner MJ, Gorby GL, Parks CC. Absence of laboratory-confirmed failures of high-dose influenza vaccine in an elderly population. *WMJ*. 2013;112(2):45.
2. Temte JL. Commentary: Solid evidence is lacking, but signs are hopeful. *WMJ*. 2013;112(2):45.
3. DiazGranados CA, Dunning AJ, Kimmel M, et al. Efficacy of high-dose versus standard-dose influenza vaccine in older adults. *N Engl J Med*. 2014; 371(7):635-645.
4. Concato J, Shah N, Horwitz RJ. Randomized, controlled trials, observational studies, and the hierarchy of research designs. *N Engl J Med*. 2000;342(25):1887-1892.
5. Centers for Disease Control and Prevention. Estimated influenza illnesses and hospitalizations averted by influenza vaccination—United States, 2012–13 influenza season. *MMWR Morb Mortal Wkly Rep*. 2013;62(49):997-1000.
6. Greenberg D. Fluzone high-dose vaccine efficacy trial results. Slide presentation at October 23-24, 2013 meeting of the Advisory Committee on Immunization Practices of the Centers for Disease Control and Prevention. <http://www.cdc.gov/vaccines/acip/meetings/downloads/slides-oct-2013/04-Fluzone-Greenberg.pdf>. Accessed September 12, 2014.

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