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TAVOLA ROTONDA: profilassi vaccinale in popolazioni speciali

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Consensus sulla prevenzione e la gestione delle infezioni nei pazienti con SM in trattamento con farmaci biologici e non-biologici

- The available literatureon vaccination and MS is insufficient: there are few studies, with a limited range of vaccines tested (mainly influenza vaccine). In many cases different vaccines are tested simultaneously.
- The studies are usually underpowered (i.e. small samples) and few randomized controlled trials are available.
- There is no evidence to suggest that influenza vaccination in untreated multiple sclerosis (MS) patients is less effective or less safe compared with the general population. Appropriate studies to answer this question are lacking.

Vaccination in MS

- No study specifically addresses the effectiveness and safety of live vaccine immunizations in MS patients, except for one small-sized observational study on Yellow Fever vaccination, whose results are in favor of an increased risk of vaccine-induced MS reactivation

Vaccination in MS

- We may infer that IFNβ leaves unaffected the response to influenza vaccination, with the limitations due to the observational nature of studies and the small sample sizes.
- Inconclusive data are available on response to vaccines other than influenza vaccine.
- A single study showed similar humoral responses after Td, PPSV23 and MCV4 vaccination in MS patients receiving either IFNβ or dimethyfumarate
- Based on a single study, humoral responses to 23-PPV, 13-PCV, Influenza, TT appear to be significantly attenuated after ocrelizumab administration (12 weeks)

Vaccination in MS

- Conclusions, about efficacy and safety of vaccines, are difficult to be drawn during treatment with: glatiramer acetate, ocrelizumab , dimethylfumarate, teriflunomide, natalizumab, fingolimod, alemtuzumab and cladribine.
- In autoimmune diseases different from MS, rituximab hampers humoral response to inactivated vaccines, especially when administered close to vaccination. It is plausible that the same would be true in the MS population, although no studies have been performed. Inactivated vaccines should be administered at least 1 month before and 6 months after rituximab treatment.

Vaccination in MS

- All MS patients should be evaluated for immunization status with the recommended vaccines at the time of diagnosis.

- At diagnosis, vaccinations to be considered for adult MS patients should include the ones recommended by local regulations, except in cases of additional risk factors (travel, sexual habits, etc.),

Vaccinations

- Seasonal influenza every year for all patients
- Tetanus/diphtheria/pertussis acellular if never received (TD recall if needed)
- Hib if never received
- Pneumococcal conjugate vaccine (PCV13) followed by PPV23 after >2 months
- Inactivated polio vaccine if never received and planning to travel in endemic countries

Vaccinations

- Hepatitis B vaccine if HBcAb negative and HBsAb negative
- Hepatitis A vaccine if hepatitis A virus IgG negative and traveler, men who have sex with men, raw seafood eater, etc.
- MCV4 and MenB
- HPV9 for those <26 years (45 yrs?)
- Varicella vaccine for those VZV IgG negative

Vaccination

Timing and schedule of vaccinations should be tailored to:

- The timing of DMD administration (past or planned)
- The time elapsed since last acute exacerbation
- The time elapsed since last corticosteroid pulse

Vaccination

TIMING OF DMD ADMINISTRATION (past or planned)

- Inactivated vaccines (either first or recall dose) should be administered at least 2 weeks before the introduction of immunosuppressive disease modifying drugs, due to efficacy concerns.
- Similarly, even though inactivated vaccines will never pose a risk of "vaccine disease" in immunosuppressed patients, their efficacy is not guaranteed until a certain time after drug interruption: this interval is not uniformly defined. In any case, such vaccines should be re-administered when initially given during a period of intense immunosuppression.
- Nonetheless, seasonal influenza vaccine is always indicated, irrespective of concomitant MS DMDs, on the assumption that even a reduced response might be at least partially efficacious

Vaccination

TIMING OF DMD ADMINISTRATION (past or planned)

- Live attenuated vaccines should be administered at least 4–6 weeks before initiation of treatment with ~~i~~immunosuppressive DMDs.
- They should never be administered to a patient on immunosuppressive drugs, or before a certain time since their interruption, the duration of which is based on expert opinion

- <u>Specific recommendations on live vaccines</u>
  - HCDS 2014 considered 3 months to be a safe interval for live-attenuated vaccination after an immunosuppressive steroid dosage is given.
  - Fingolimod prescribing information recommends avoiding live vaccines for 2 months after discontinuation.

Vaccination

TIMING SINCE LAST ACUTE EXACERBATION

- Based on expert opinion, without any study data:
  - Wait for at least 4–6 weeks after the onset of an acute MS exacerbation before vaccination (for either first or recall dose): the situation has to be stabilized.
  - In case of an infected wound for which the TT is indicated, this can be administered even if the exacerbation is not resolved.

Vaccination

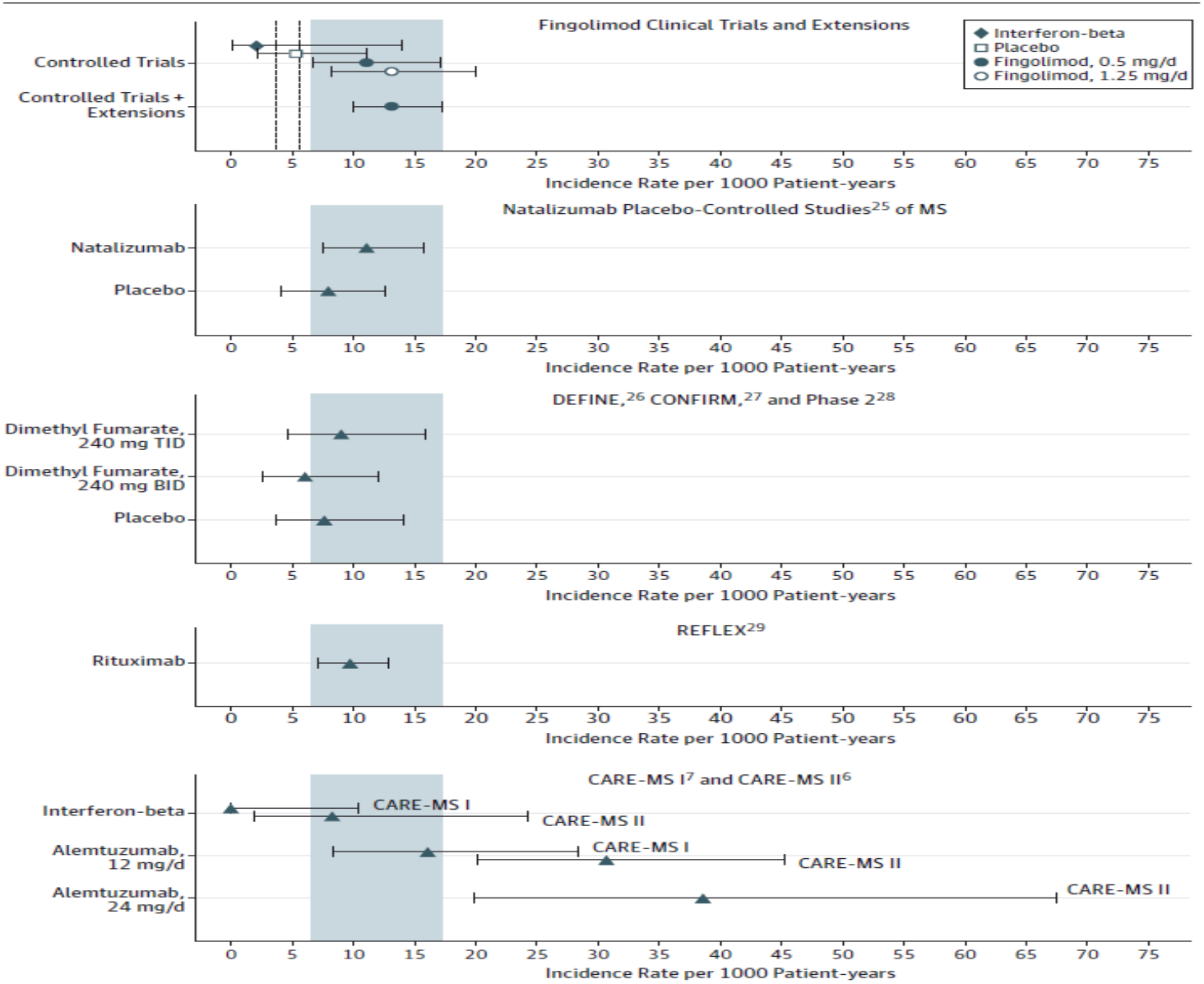
TIMING SINCE LAST STEROID PULSE

- The role of short-term pulsed steroid treatment on the immune system and its impact on response to vaccinations, in terms of safety and efficacy, warrants further research.

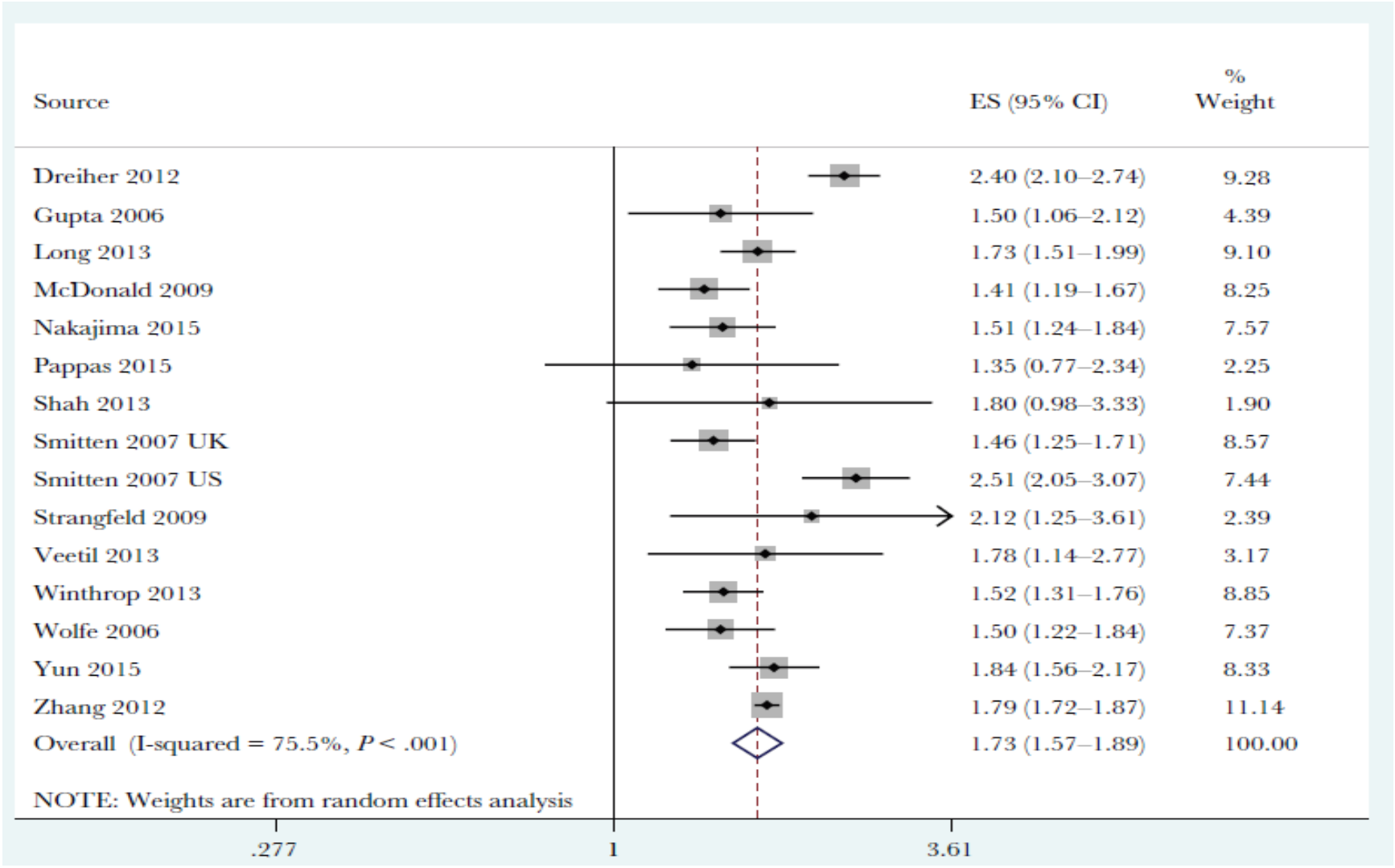
- Experts generally agree to delay vaccination with inactivated vaccines at least 4 weeks after high-dose steroid treatment. The time for live vaccines may be longer: HCDS 2014 considered 3 months after an immunosuppressive steroid dosage is given.

- There is no evidence against vaccination during MS relapses (e.g. tetanus toxoid recall when needed).

Incidence of VZV Infections in Fingolimod Trials and Comparison With Other MS DMTs



Risk of herpes zoster with corticosteroids compared with control, pooled analysis of observational studies

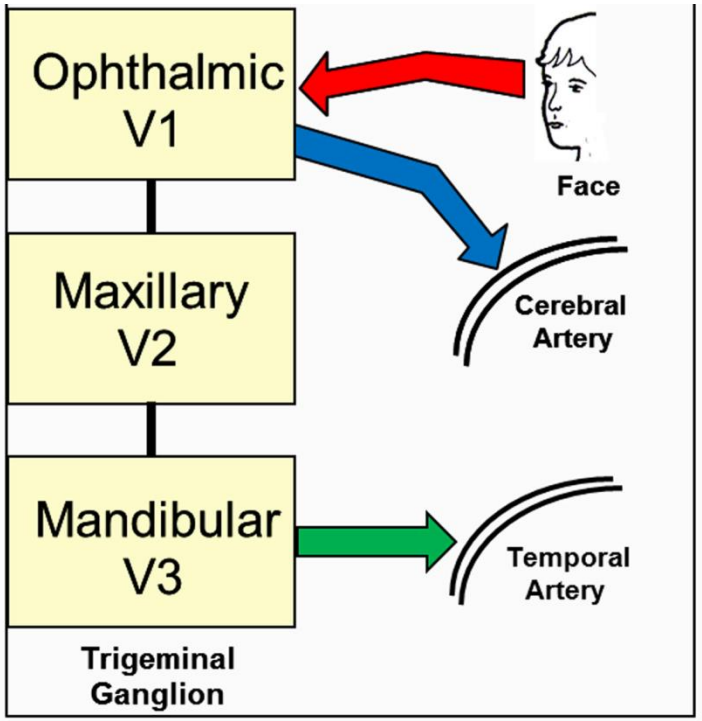


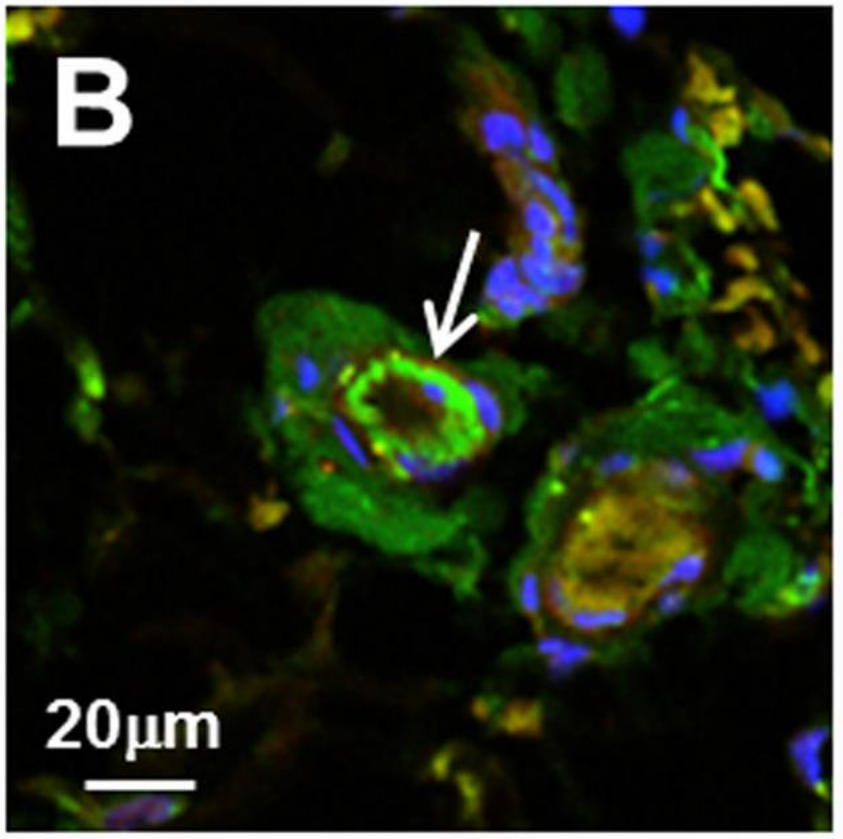
Risk of stroke after HZ and HZO compared to control periods

	All HZ		HZO	
	No. of strokes in risk period	IRR (95% CI)	No. of strokes in risk period	IRR (95% CI)
Risk period 3 months				
Stroke (any type)	352	1.29 (1.16–1.44)	31	1.59 (1.10–2.32)
Ischemic and unspecified stroke	310	1.27 (1.13–1.42)	27	1.57 (1.05–2.35)
Hemorrhagic stroke	42	1.53 (1.11–2.11)	4	1.82 (0.62–5.37)
Subdivided risk periods (secondary analysis)				
<2 weeks	59	1.30 (1.00–1.68)	2	0.63 (0.16–2.53)
week 3–4	73	1.52 (1.20–1.91)	12	3.56 (1.99–6.38)
month 2–3	219	1.24 (1.08–1.42)	17	1.37 (0.84–2.25)
month 4–6	274	1.09 (0.97–1.24)	25	1.44 (0.96–2.17)
month 7–12	444	0.96 (0.87–1.06)	29	0.63 (0.87–1.35)

Schink T, et al.. PLoS ONE 2016

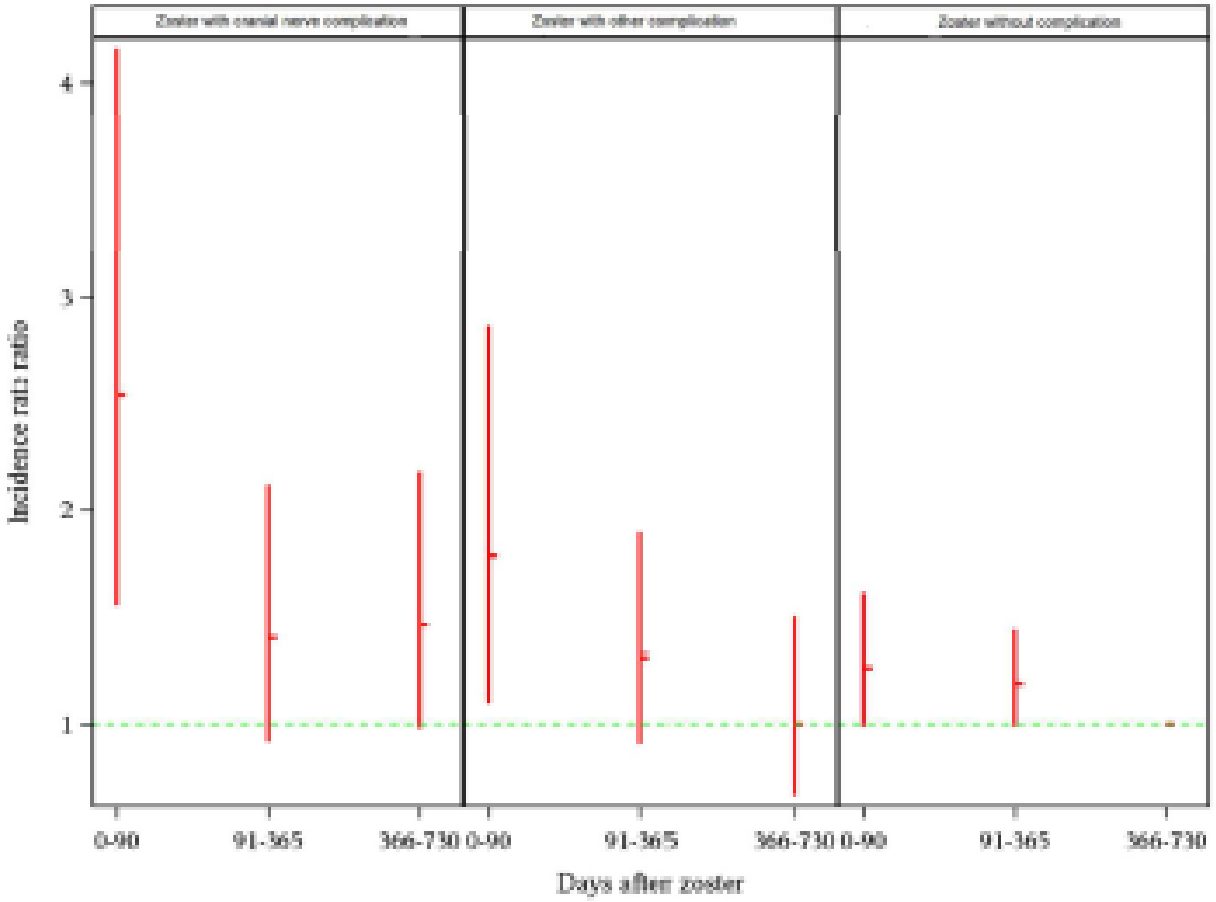
Varicella-zoster virus infection, the trigeminal ganglion and arteritis





Grose C Circulation. 2016

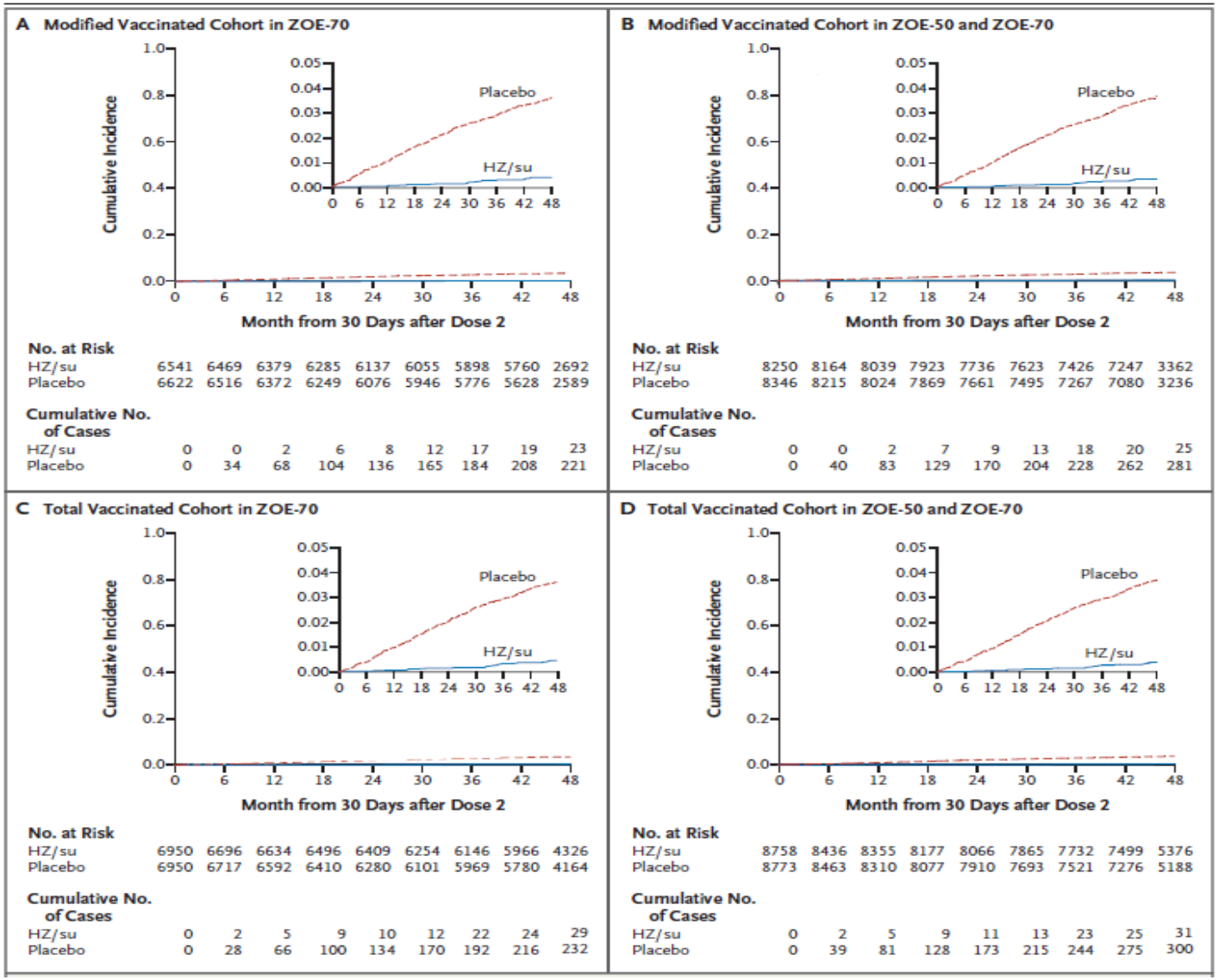
Herpes Zoster and the Risk for Stroke in Patients with Autoimmune Diseases



Incidence Rate Ratios of Hospitalized Stroke by time since Herpes Zoster and zoster phenotype

Calabrese LH et al. Arthritis & Rheumatology 2016

Efficacy of the Herpes Zoster Subunit Vaccine in Adults 70 Years of Age or Older



Risk of Development of Herpes Zoster after Vaccination

A.L. Cunningham et al.
N Engl J Med 2016

"Lady Montagu in Turkish dress" by Jean-Étienne Liotard, 1756