

Preparedness for and response to meningococcal outbreaks: preliminary results of a Canadian Immunization Research Network (CIRN) randomized controlled trial of two schedules of 4CMenB vaccine in adolescents and young adults

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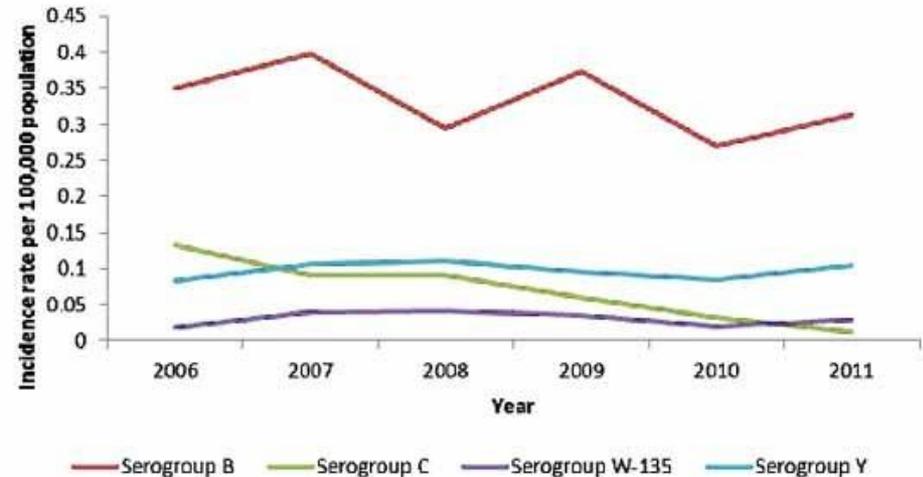


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Background

- *Neisseria meningitidis* type B most common cause of IMD in Canada
- IMD is usually sporadic
- Institutional outbreaks are rare (<5% of cases) but create public health crises; response:
 - Education
 - Antibiotic prophylaxis for close contacts
 - MenB vaccine



Serogroup specific Invasive Meningococcal Disease (IMD) incidence rates in Canada 2006-2011

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Acadia University dealing with 'institutional outbreak' of meningitis

Public Health will offer free meningococcal B vaccine to all Acadia students

CBC News Posted: Feb 13, 2015 9:33 AM AT | Last Updated: Feb 13, 2015 6:34 PM AT

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An Acadia University student hospitalized with meningococcal meningitis is suffering from the B strain — the same strain that killed another Acadia student earlier this month — according to Nova Scotia's chief public health officer.

"Two cases of the same strain of meningococcal meningitis in one location, such as a university campus, constitutes an institutional outbreak," said Dr. Robert Strang.

■ **Meningitis: Answers to frequently asked questions**



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Meningococcal B vaccines

- Two MenB vaccines are authorized in Canada:
 - 4 component (4CMenB) vaccine (Bexsero®, GlaxoSmithKline) authorized Dec 13 for those 2 months to 17 years of age, in Aug 2018 up to 25 years of age
 - Bivalent (Factor H binding protein) vaccine (Trumemba®, Pfizer) authorized October 2017 for 10 to 25 years of age
- Increased incidence in Saguenay-Lac-Saint-Jean, Quebec 2006 – 2013; 4CMenB program for age 2 months to 20 years
- Institutional outbreaks
 - Five in US college campuses 2013-2016
 - Acadia University 2015
 - Logistics of delivering vaccine program during academic year
 - 2 doses two months apart or shorter?
 - Public health goal is outbreak control v individual protection

Methods

- Randomized, controlled, observer-blinded trial in 3 CIRN sites (Halifax, Montreal, Vancouver)
- Compare safety and immunogenicity of two 4CMenB vaccination schedules:

Accelerated (0, 21 days) vs. Standard schedule (0, 60 days)

Hep A vaccine given as control

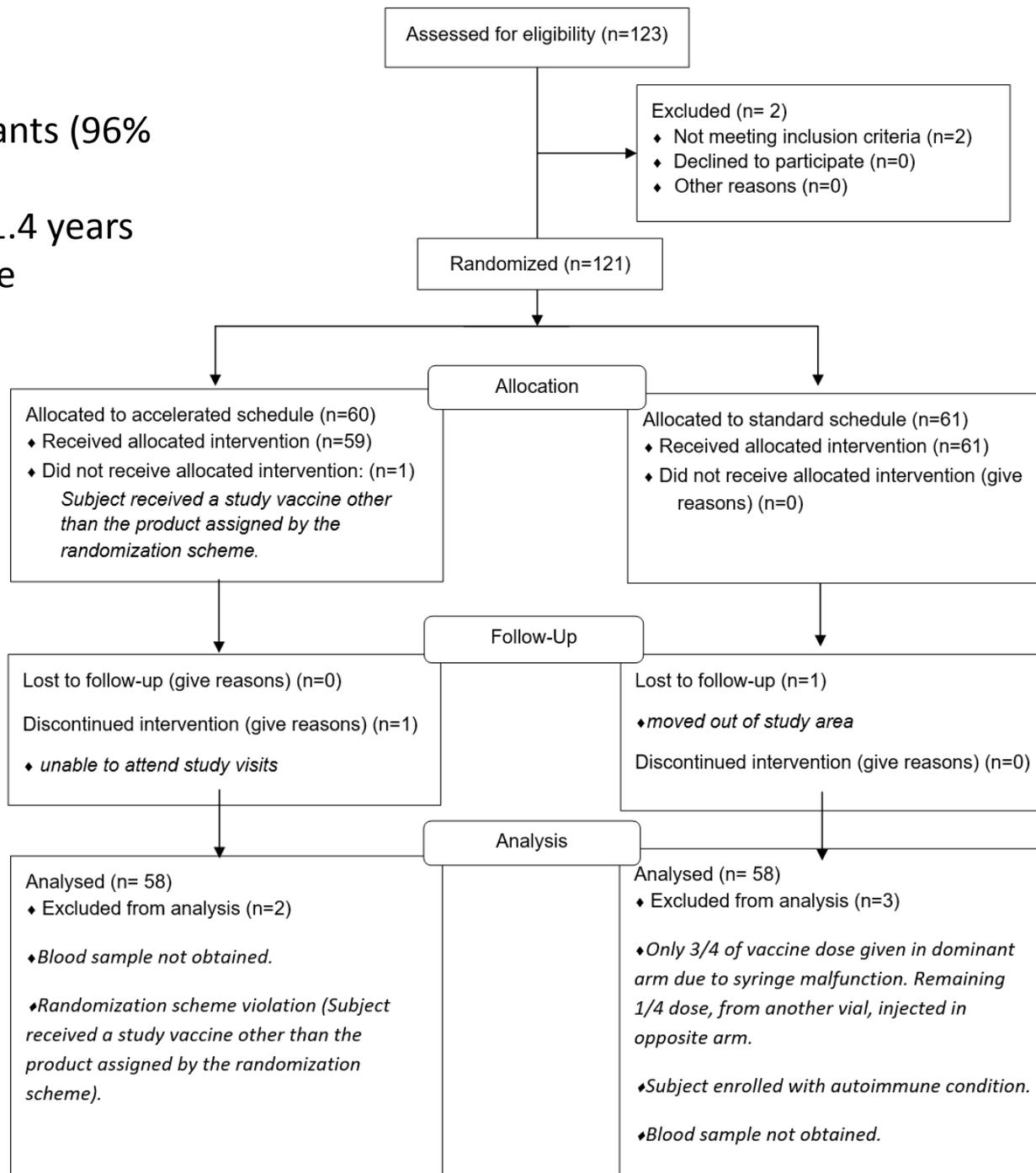
- Eligibility
 - 17-25 years of age, healthy
 - attending school
- Enrolment in first term of academic year (Sept 2015-April 2016) over 4 to 6 weeks

Results:

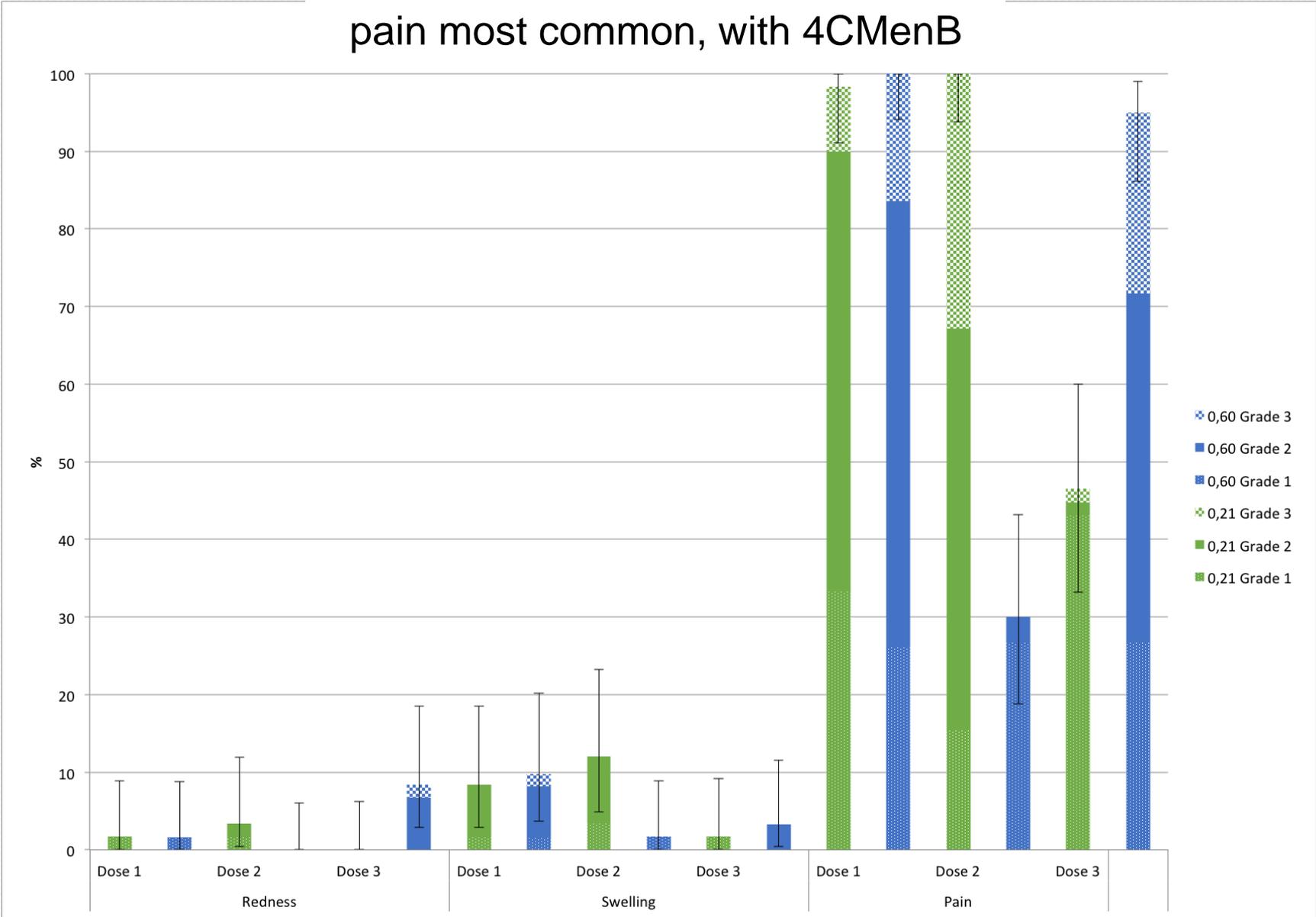
121 participants (96%
in ATP)

Mean age 21.4 years

69.4% female

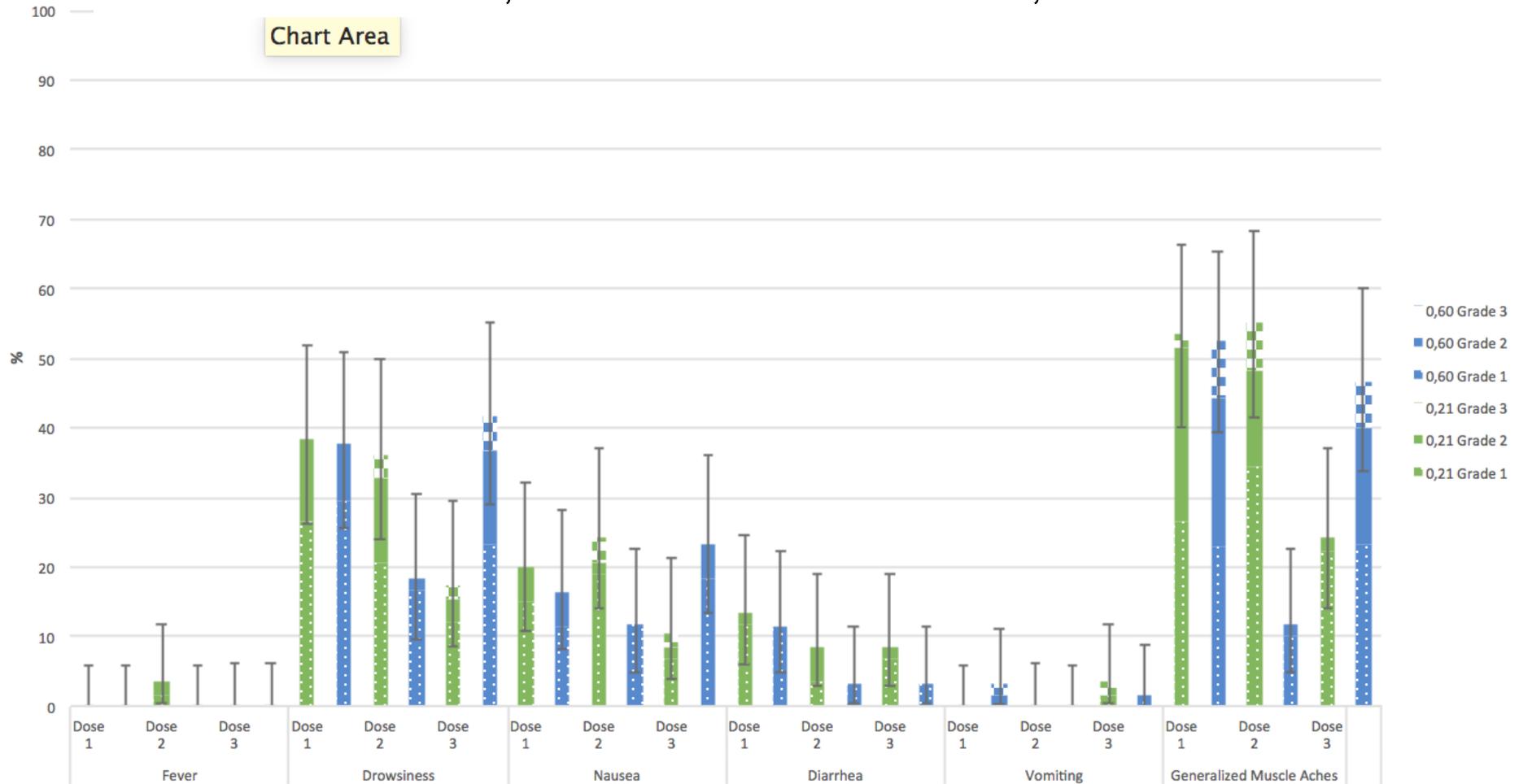


Solicited Local Events: pain most common, with 4CMenB



Solicited General Adverse Events: Muscles aches, drowsiness most common; with 4CMenB

Chart Area

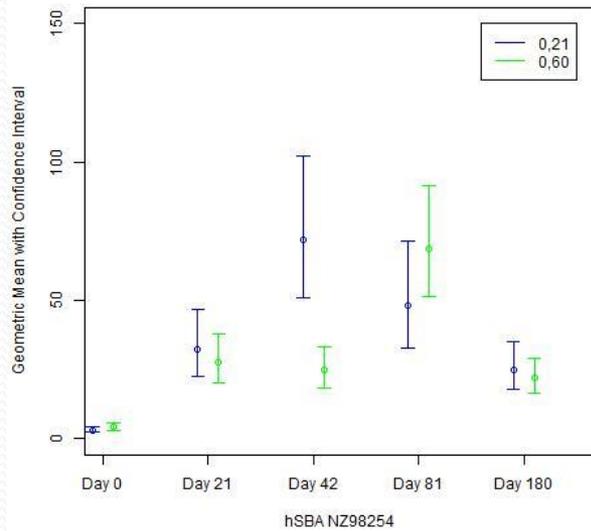


Immunogenicity outcomes

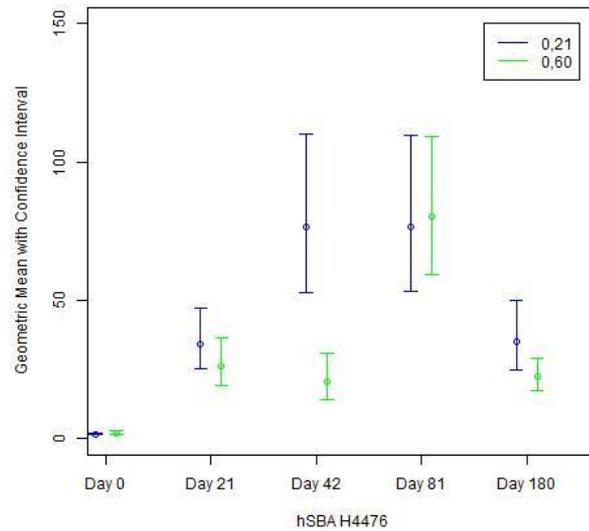
- Human Serum Bactericidal Titres (hSBA) on days 0, 21, 42, 81, 180 using MenB strains 5/99, H44/76 and NZ98/254
- Geometric Mean Titers (GMTs)
- Reverse Cumulative Distribution graphs

GMTs by strain, days 0 to 180

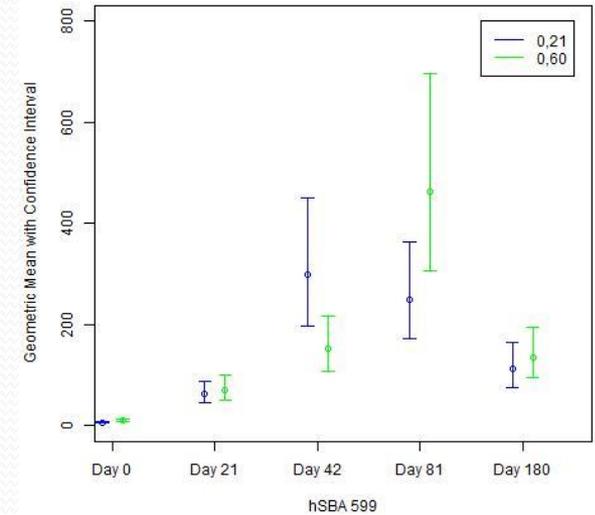
NZ98/254



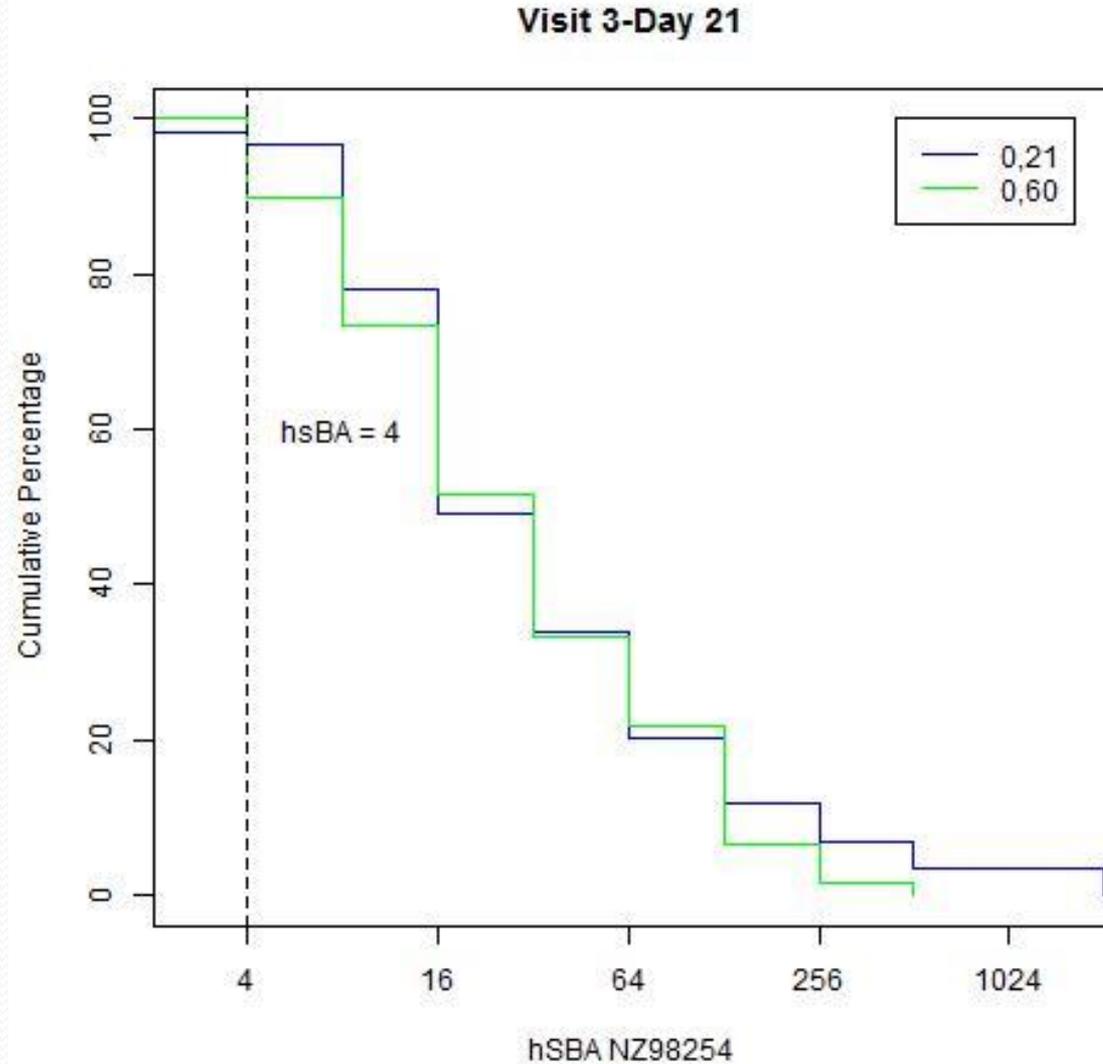
5/99



H44/76



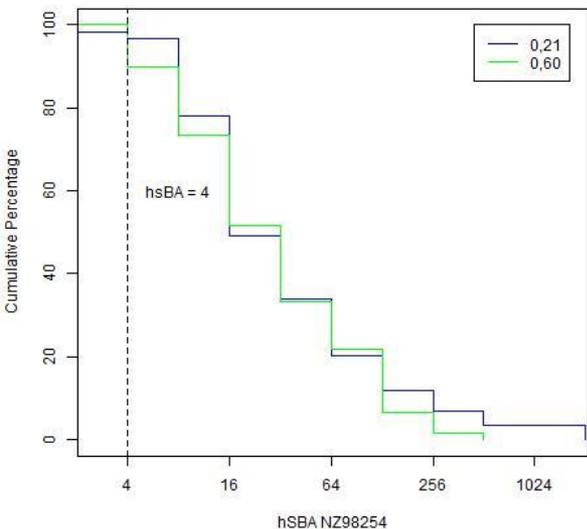
Reverse
cumulative
distribution
curve



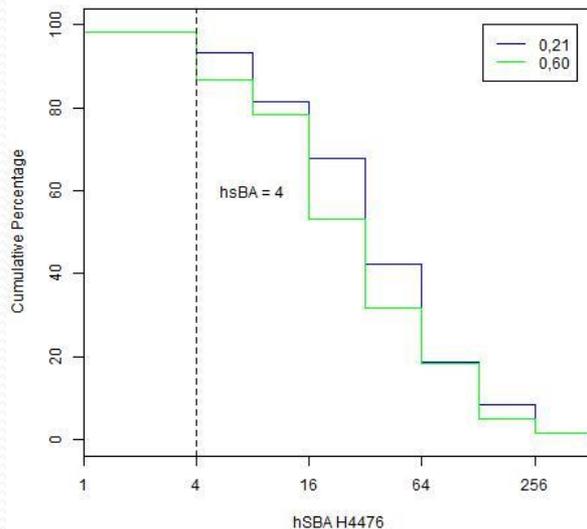
hSBA Titers: Reverse Cumulative Distribution

Day 21

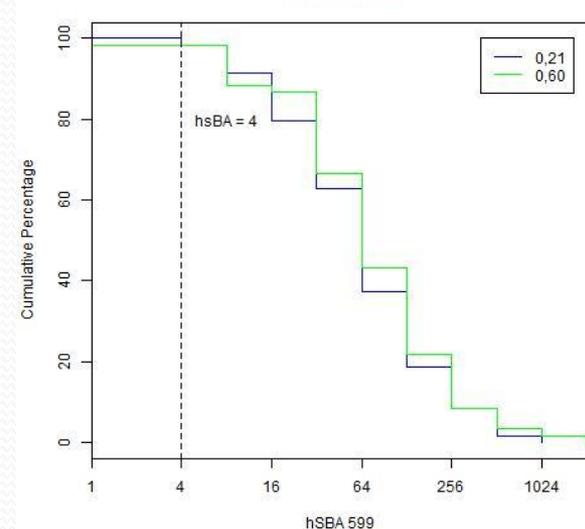
Visit 3-Day 21



Visit 3-Day 21

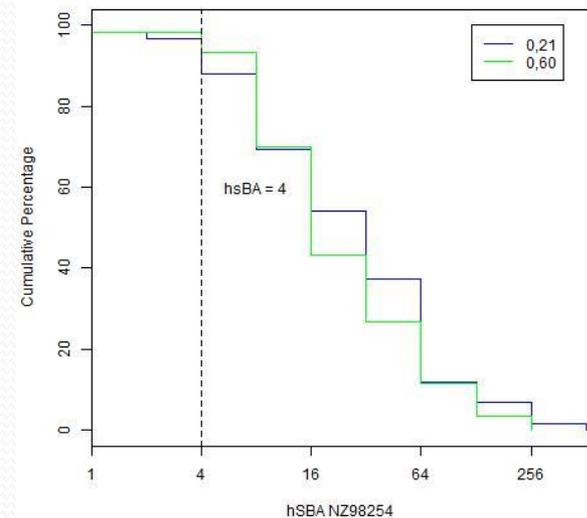


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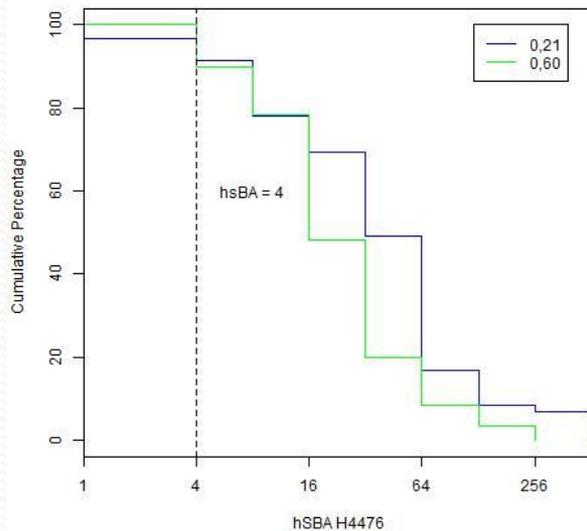


Day 180

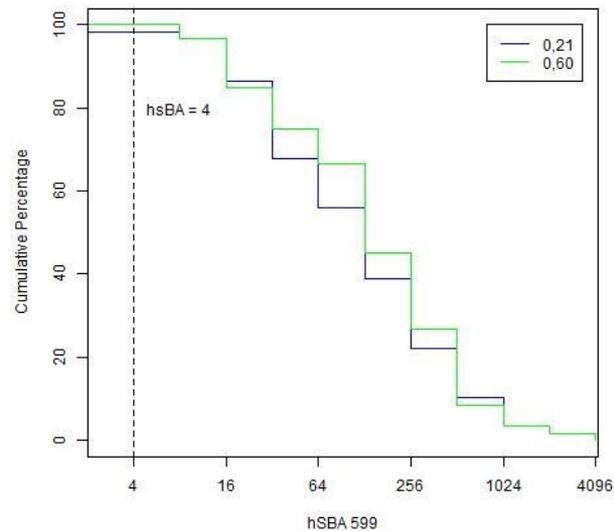
Visit 9-Day 180



Visit 9-Day 180



Visit 9-Day 180



Conclusions: RCT of 0,21 vs. 0,60 day 4CMenB schedule in 17-25 year old students

- *Capacity building* for rapid trials: conducted rapidly in 1st term of academic year at 3 sites, >99% retention at six months
- *Safety*: reactogenicity greater in 4CMenB recipients: injection site pain in >96%, muscles aches and drowsiness in ~50% (*tolerability outcomes pending*)
- *Immunogenicity*: protective titers present in all 4CMenB recipients 21 days after first dose, sustained in >90 % at Day 180 (*hSBA to outbreak strains pending*)
- An accelerated 4CMenB schedule (0, 21 days) could be used to control outbreaks in adolescents/young adults