Possible impact of wide-scale vaccination against Serogroup B Neisseria meningitidis on gonorrhoea incidence rates in one region of Quebec, Canada

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Background

- *Neisseria meningitidis (Nm)* outer-membrane and outer-membrane vesicles contain a large number of proteins (n≈75) and lipopolysaccharides.
- In the human, Nm OMVs generate a bactericidal immune response against genetically-related *Nm* strains (*van der Pol et al., 2015*).
- An MenB OMV vaccine was developed and used in New Zealand to control an epidemic caused by a virulent Serogroup B Nm clone in the 1990s (*Holst et al., 2013*).
- 4CMenB (Bexsero™, Glaxo-Smith-Kline) is a licensed vaccine containing an OMV component also found in MeNZB and 3 purified surface-expressed Nm protein antigens (fHbp fused to GNA2091, NHBA fused to GNA1030, and NadA) (*Watson et al., 2016*).
- *Neisseria meningitidis* and *Neisseria gonorrhoeae* (*Ng*) belong to the same bacterial genus and share a large proportion of their primary genetic sequences (*Marri et al., 2010*).
- *Nm* PorBs present in OMV vaccines and *Ng* Por Bs have similar functions and there is a 60-70% homology in their nucleic acid sequence (*Barlow et al., 1989; Chen et al., 2013*).
- All the genes encoding the 3 other purified *Nm* proteins, except the NadA gene, are present in *Ng*, although marked differences exist in the nucleotide and aminoacid sequences in the two species (*Hadad et al., 2012*).
- Due to a persistent increase of serogroup B *Neisseria meningitidis* invasive infections in the Saguenay-Lac-Saint-Jean (SLSJ) region of the province of Quebec (Canada) since 2006, a wide-scale vaccination campaign of individuals aged 6 months to 20 years was conducted between May and December 2014 (*De Wals et al., 2017*).

- The study objective was to assess the potential impact of this mass immunization campaign on *Ng* infection rate in the SLSJ region.

Methods

- *Ng* and *Ct* cases reported to the SLSJ public health authority during pre-vaccination period (January 2006 to June 2014) and post-vaccination period (July 2014 to June 2017) were analyzed.
- The number of vaccinated individuals in the target population by age and number of doses received was extracted from the SLSJ immunization registry.
- Population denominators were estimated from census data.
- Before and after comparison of incidence rates were performed. RR estimate's 95% CI were calculated using the Byar method and two-tailed p values were computed using the Fisher exact and z-score tests when appropriate.
- The impact of this mass campaign was estimated by a Poisson regression model including the year (11 categories), age (14-20 vs 21+ years) and the intervention (0 by default and 1 in those 14-20 years in the period of July 2014 to June 2017).

Results

- Overall 4CMenB coverage was 82% in the target population, higher in newborns and school-age groups (Table 1).
- A total of 210 *Ng* and 5,688 *Ct* cases were reported among residents in the SLSJ region from January 1st 2006 to June 30th 2017.
- A decrease in *Ng* infection frequency among individuals 14-20 years was observed during the post-vaccination period whereas it increased in those 21 years and older (Figure 1). No decrease was seen in *Ct* cases following the mass campaign.
- Comparisons of *Ng* and *Ct* infection rates in the pre- and post-immunization periods are shown in Table 2.
- Results of the Poisson regression model pertaining to *Nm* infection rates are shown in Table 3. Estimate of vaccination impact was a *Ng* risk reduction of 59% (95% CI: -22% to 84%; $p = 0.1$).

Table 1. Uptake of MenB-4C in the Saguenay-Lac-Saint-Jean Region of Quebec, Canada, according to age and number of doses.

Age group	Target Number	Number of doses (%)					
		0	1	2	3	4	≥ 1
Newborns[1]	**2,168**	**7%**	**2%**	**2%**	**7%**	**82%**	**93%**
Residents[2]	**57,205**	**18%**	**6%**	**73%**	**2%**	**1%**	**82%**
2-5 months	831	6%	2%	4%	23%	65%	94%
6-11 months	1,277	8%	2%	22%	67%	-	92%
1-4 years	11,024	14%	6%	80%	-	-	86%
5-11 years	18,919	7%	3%	91%	-	-	93%
12-16 years	12,997	8%	6%	86%	-	-	92%
17-20 years	12,157	53%	14%	34%	-	-	47%
All ages	**59,373**	**18%**	**6%**	**70%**	**2%**	**4%**	**82%**

[1] *Born May 6th to December 31st, 2014.*
[2] *Born May 6th, 1993 to March 5th, 2014, and age on May 6th, 2014.*

Table 2: *Neisseria gonorrhoea* and *Chlamydia trachomatis* infections rates before and after the 4CMenB immunization campaign in the SLSJ region.

Infection	Age group (years)	Pre-vaccination (January 2010 to June 2014)		Post-vaccination (July 2014 to June 2016)		RR	p value
		No cases	IR / 100,000 p-y	No cases	IR / 100,000 p-y		
Ng	≤20	28	10.5	4	2.8	0.27	0.009
	>20	75	7.6	52	9.4	1.23	0.3
Ct	≤20	928	346.3	646	452	1.31	<0.001
	>20	1,445	147.2	1,078	194.8	1.32	<0.001

Table 3. Results of the multivariate Poisson regression analysis

Variable		Rate ratio	95% CI	P value
Year	2006	Ref		
	2007	1.57	(0.47 ; 5.21)	0.4634
	2008	3.26	(1.12 ; 9.54)	0.0306
	2009	3.96	(1.39 ; 11.33)	0.0102
	2010	3.67	(1.28 ; 10.58)	0.016
	2011	1.7	(0.52 ; 5.54)	0.3799
	2012	2.27	(0.74 ; 7.01)	0.1527
	2013	3.87	(1.35 ; 11.09)	0.0119
	2014	3.29	(1.09 ; 9.91)	0.0341
	2015	3.46	(1.16 ; 10.35)	0.0262
	2016	5.94	(2.11 ; 16.76)	0.0008
Age	Age ≤20	3.23	(2.01 ; 5.20)	<.0001
	Age>20	Ref		
Intervention	Not targeted	Ref		
	Targeted	0.41	(0.14 ; 1.22)	0.1087

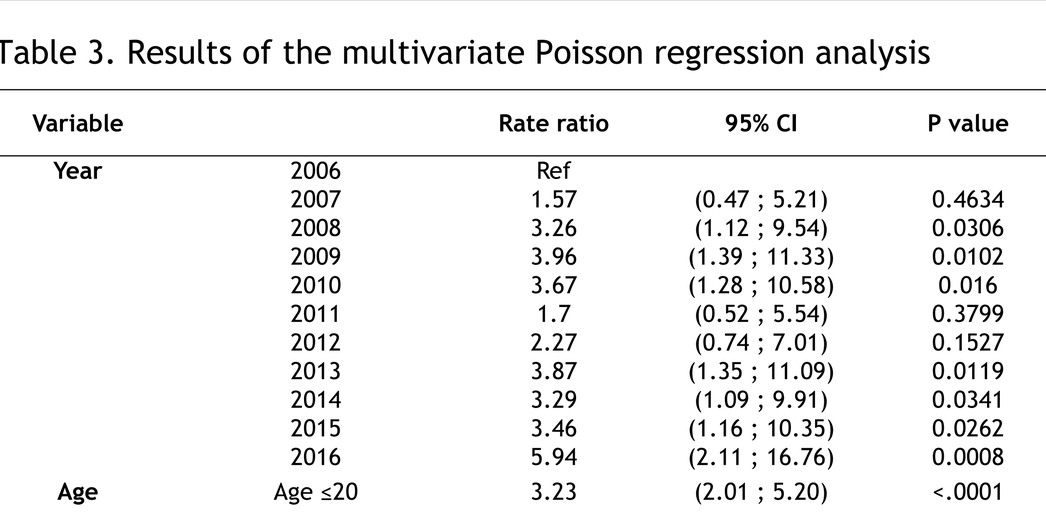

Figure 1. *Neisseria gonorrhoea* and *Chlamydia trachomatis* infections per quarter and by age group, SLSJ, January 2006 to June 2017.

Conclusions

- Results of this ecologic study suggest cross-protection of 4CMenB vaccine against *Ng* infections but an effect of unmeasured or poorly controlled confounding factors cannot be excluded.
- Results are congruent with those of a case-control study in New Zealand showing an OMV-MeNZB vaccine effectiveness of 31% (*Petousis-Harris et al., 2017*).
- A higher effectiveness of 4CMenB as compared to OMV-MeNZB is a plausible hypothesis as three additional proteins also found in Ng are included in the vaccine used in SLSJ region.
- Further studies on this topic are warranted and a more detailed analysis is planned using a retrospective cohort approach.

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