

Question 1. (This question is based on 2 studies)

A.) Petousis-Harris H, Paynter J, Morgan J, Saxton P, McArdle B, Goodyear-Smith F, Black S. Effectiveness of a group B outer membrane vesicle meningococcal vaccine against gonorrhoea in New Zealand: a retrospective case-control study. The Lancet. 2017 Sep 30;390(10102):1603-10.

This was a case-control study among young adults (15 – 30 years) in New Zealand who attended a sexual health clinical, 2010-2014.

The aim was to assess vaccine effectiveness of the outer membrane vesicle meningococcal B vaccine (MeNZB) against gonorrhoea.

Cases: laboratory confirmed *Neisseria gonorrhoeae* infection

Controls: laboratory confirmed chlamydia infection

co-infected patients were excluded from the main analysis

Vaccination status was established by data linkage to National Immunisation Register via a unique patient identifier. People were considered to be vaccinated if they received three doses of vaccine.

New Zealand had a major, population-wide meningococcal B vaccination programme from 2004 to 2008, using the locally developed MeNZB vaccine. It was specifically an epidemic-control programme, with a vaccine developed specifically for the epidemic strain. The MeNZB program was effective in reducing the incidence of disease caused by the epidemic strain. (Currently, MenB is a routine funded childhood vaccine in NZ, with catch-up/late completion through age 4.)

Results

	cases	controls
n	1241	12487
fully vaccinated	511	6424
odds ratio	0.67 (0.59, 0.76)	
adjusted odds ratio	0.69 (0.61, 0.79)	
adjusted vaccine effectiveness	31% (21%, 39%)	

Adjusted for ethnicity, sex, age group, deprivation, and geographical location.

B.) Seib KL, Donovan B, Jin F, Thng C, Yeung B, Comninou N, Bopage RI, Ray A, Mahony A, Chow EP, Chen MY. Meningococcal B vaccine to prevent *Neisseria gonorrhoeae* infection. New England Journal of Medicine. 2026 Jul 8. (GoGoVax)

RCT conducted July-2021 to May-2023 at five publicly funded sexual health clinics (Sydney Sexual Health Centre, Western Sydney Sexual Health Centre, Melbourne Sexual Health Centre, Gold Coast Sexual Health Service, and RPA Sexual Health) and two private primary care clinics (Taylor Square Private Clinic and Prahran Market Clinic).

PICO Table

Participants	men who have sex with men (MSM)
Intervention	two doses of 4CMenB
Control	two saline injections
Outcome	The pre-specified primary outcome was a first <i>N. gonorrhoeae</i> infection after the receipt of vaccine or placebo in the per-protocol population.

	Screening for sexually transmitted infections, including N. gonorrhoeae nucleic acid amplification testing of samples obtained from urogenital, anorectal, and oropharyngeal sites, was performed quarterly for 2 years.
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Results

Analysis and population	4cMenB				Placebo			
	No. events	No. p-y	incidence	No. events	No. p-y	incidence	IRR (95% CI)	VE (95% CI)
per-protocol first infection	160	330.0	48.1 per 100 p-y	155	324.2	47.8 per 100 p-y	1.01 (0.80, 1.26)	-1 (-26, 20)
modified ITT first infection	184	388.5	47.4 per 100 p-y	173	400.7	43.2 per 100 p-y	1.10 (0.89, 1.36)	-10 (-36, 11)

Describe and interpret the results from the two studies.

Discuss why the studies obtained different results

Question 2

VITAL was a RCT with a 2-by-2 factorial design (Vitamin D and Omega-3) that investigated whether supplemental vitamin D3 (2000 IU per day), n-3 fatty acids (1 g per day), or both would prevent cancer and cardiovascular disease in men 50 years of age or older and women 55 years of age or older in the United States. This question focuses on Vitamin D.

After a 3-month placebo run-in phase, participants who took at least two thirds of the trial pills underwent randomization. Nearly 40,000 participants entered the run-in stage and 14,000 were excluded (largely because they did not take at least two-thirds of the pills), leaving about 26,000 patients to be randomised.

The design did not fully meet the classic placebo-controlled ideal, because by 5 years, 6.4% of the vitamin D group versus 10.8% of the placebo group reported using outside vitamin D above 800 IU/day, likely reflecting participants or their physicians independently starting supplementation.

VITAL measured serum 25-hydroxy vitamin D levels in a nested biomarker sub-cohort at baseline (n ~ 16000) and follow-up (n ~ 1700), which let investigators conduct a pre-specified subgroup/effect-modification variable tested against the primary outcomes (result: null treatment-effect modification).

Previous reports from VITAL reported no effect of Vit D supplementation no pre-specified primary endpoints of CV disease and cancer; and also no effect on various ancillary endpoints: cognitive decline, diabetes, depression, macular degeneration, knee pain, kidney function, and others.

There were positive findings in two subgroups for the cancer endpoint

- Cancer-related deaths excluding the first 2 years for follow-up: HR 0.75; 95% CI 0.59–0.96
- Cancer incidence in normal weight individuals: HR 0.76; 95% CI 0.63–0.90

The positive finding outside of the cancer subgroups was a reduction in autoimmune disease incidence: HR 0.78, 95% CI 0.61–0.99.

The tables below are for the paper published on the fracture endpoints, LeBoff MS, Chou SH, Ratliff KA, Cook NR, Khurana B, Kim E, Cawthon PM, Bauer DC, Black D, Gallagher JC, Lee IM. Supplemental vitamin D and incident fractures in midlife and older adults. New England Journal of Medicine. 2022 Jul 28;387(4):299-309.

PICO table

Participants	n ~ 26,000 no history of cancer or cardiovascular disease agreed to limit supplemental Vit D intake men: 50+ years women: 55+ years
Intervention	supplemental vitamin D3 (2000 IU per day)
Control	placebo
Outcome	Incident fractures were reported by participants on annual questionnaires and adjudicated by centralized medical-record review. The pre-specified co-primary end points were incident total, nonvertebral, and hip fractures. Median follow-up was 5.3 years.

Results

Pre-specified co-primary endpoint	Vit D (n = 12,927)	Placebo (n = 12,944)	HR (95% CI)
Total incident fractures	769	782	0.98 (0.89, 1.08)
Nonvertebral	721	744	0.97 (0.87, 1.07)
Hip	57	56	1.01 (0.70, 1.47)

Describe and interpret the results in the Results table

Discuss the findings from Vital (summarised above). Comment particularly on why there was no effect observed for fractures and on the pros and cons of Vit D testing and supplementation for primary prevention at a population level.