Carriage of *Neisseria meningitidis* and meningococcal vaccine hesitancy among students residing in residential colleges in Dunedin, New Zealand

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Abstract

Invasive meningococcal disease can cause rapid death or disability in unsuspecting healthy students residing in residential colleges. Carriage of *Neisseria meningitidis* is a precursor to the disease. While *Neisseria meningitidis* is present in an estimated 15% of the adult population, overseas studies have shown carriage is usually far higher among residential tertiary college students. This comprehensive study of meningococcal carriage and risk factors for carriage provides contemporary data relevant to students residing in residential colleges in New Zealand. Several meningococcal vaccines offer protection against invasive meningococcal disease; however, a variety of factors affect uptake of vaccinations by students residing in residential colleges. Uptake of vaccines has become an issue public interest in the context of the COVID-19 pandemic, yet there is little international literature on factors effecting vaccine uptake among students residing in residential colleges.

Following several cases of invasive meningococcal disease in University of Otago residential colleges in Dunedin in 2018, a meningococcal pharyngeal carriage and risk factor study among first year students residing in residential colleges was undertaken. This thesis reports on the 2018 carriage study and uses multivariable analysis to determine independent risk factors for carriage. Whole genome sequencing was performed on all meningococcal isolates from the carriage survey and this data are used to inform discussion on transmission pathways.

The thesis then reports on two subsequent surveys in 2019 and 2020 that examined factors that impact on the uptake of vaccinations among students residing in residential colleges. While these surveys focused on meningococcal vaccinations, the 2020 survey took place during the emerging COVID-19 pandemic and included factors that influence students' decisions to receive a COVID-19 vaccination. Both studies utilise data from the National Immunisation Register (NIR) and Student Health records to validate self-reported vaccination status.

The work presented in this thesis and subsequent publications will help to inform public heath responses to invasive meningococcal disease cases in residential college settings, inform preventative strategies such as funding for meningococcal vaccinations, and assist development of targeted health promotion strategies to raise vaccination uptake among students residing in residential colleges.

Preface

The roles of the candidate:

Full write up of this Master of Public Health thesis.

Prepared and obtained approval from the Research Advisory Committee of the Department of Preventive and Social Medicine, University of Otago, for this MPH.

Meningococcal Carriage Study 2018

- Assisted with construction and formatting of risk factor survey tool.
- Worked within the team that recruited students onsite and collected specimens.
- Prepared and obtained additional University of Otago Human Ethics Committee (Health) approval to include vaccination data from Student Health Service records in the study.
- Performed all statistical analyses of the 2018 Carriage Study data using Stata-16, with guidance from a bio-statistician.

Literature Review

- Screened the titles and abstracts of 1,110 journal articles, reviewed 27 articles.
- Screened the titles and abstracts of 1,984 journal articles, reviewed 31 articles.

Vaccine Hesitancy Study 2019 and 2020

- Prepared and submitted a Research Advisory Committee application for the Vaccine Hesitancy Study.
- Prepared and obtained additional University of Otago Human Ethics Committee (Health) approval to carry out the online survey of students residing in residential colleges in 2019 and 2020.
- Adapted the World Health Organization (WHO) Strategic Advisory Group of Experts (SAGE) on Immunisation's vaccine hesitancy survey tool for use with students residing in residential colleges in New Zealand.
- Constructed the survey tool on the RedCap platform, for use online.
- Prepared and obtained additional University of Otago Human Ethics Committee (Health) approval to include questions relating to hypothetical COVID-19 vaccine hesitancy in the online survey of students residing in residential colleges in 2020.
- Corresponded with the 14 participating residential colleges, obtained their permission to carry out the surveys, and supported them to deliver the surveys to their students.

- Cleaned survey responses in to remove duplicates and non-consenting participants.
- Collated vaccination records from the National Immunisation Record database for all participants.
- Liaised with University of Otago Student Health Service to obtain records of vaccinations they administered to study participants.
- Combined datasets, and formatted data for analysis.
- Completed basic descriptive analyses of the vaccine hesitancy data, with guidance from a bio-statistician.

Application of results:

Utilised carriage study data in a submission to Pharmac (Appendix 4) on behalf of Southern DHB advocating that Pharmac fund Meningococcal group B recombinant vaccine (4CMenB) for individuals aged 13–25 years inclusively who are entering within three months or are in their first year of living in boarding school hostels, tertiary education halls of residence (in conjunction with Medical Officer of Health Dr Susan Jack).

Coordinating the writing and submission of a paper describing carriage of *N. meningitidis* in Residential Colleges in New Zealand, for publication in the peer-reviewed literature.

Will prepare and submit a report to University of Otago Student Health Services leadership describing the vaccine hesitancy survey outcomes.

The roles of others involved in the thesis projects:

Supervisors

Dr Susan Jack collaborated with Associate Professor James Usher to design and direct the 2018 Carriage Study. She secured an Otago University Start Up Grant to fund the Carriage Study, obtained University of Otago Human Ethics Committee (Health) approval for the Carriage Study, and liaised with the Residential Colleges. She facilitated work completed by Public Health South staff and the Medical Student on an internship. She supported the candidate to secure a departmental award to fund his study, and provide funds for incentives for study participants. She provided advice and guidance to completion, aided in the preparation of the proposal for research advisory committee approval, contributed to establishing communication between the candidate and his collaborators, and advised on data collection for all projects included in this thesis. She also contributed considerably to review and editing of this thesis.

Associate Professor James Ussher collaborated with Dr Susan Jack to design the 2018 Carriage Study. He facilitated work completed by Southern Community Laboratories and The Peter Doherty Institute for Infection and Immunity, the University of Melbourne. He reviewed and provided comments on the proposal for research advisory committee approval. He also contributed to review and editing of this thesis.

Dr Ariyapala Samaranayaka designed the data analysis for all data from this study, and supported the candidate to complete the analysis. He also contributed to review and editing of this thesis.

Dr Richard Egan, as primary supervisor, provided academic guidance to the candidate, and contributed to review and editing of this thesis as well as assisting as the candidate navigated the intricacies of the academic realm.

Other contributors

Public Health South (Southern District Health Board) staff organised logistics for specimen collection, collected specimens and survey forms at study locations, and compiled student vaccination records from the NIR. They also re-identified student name and date of birth with study identification numbers when it became evident that vaccination records held on the NIR were incomplete.

University of Otago Medical Student on a summer studentship transcribed the demographic and risk factor data from the paper survey forms into Redcap, enabling analysis.

Southern Community Laboratory (Dunedin Hospital site) staff processed specimens, analysed isolates, and stored isolates pending transfer to Melbourne, Australia.

Department of Microbiology and Immunology at The Peter Doherty Institute for Infection and Immunity, the University of Melbourne, carried out Whole Genome Sequencing (WGS) on isolates. Staff (Prof Deborah Williamson and Dr George Taiaroa) also provided analysis of WGS data, and constructed figures to communicate relationships between isolates.

Student Health Service University of Otago provided records of vaccinations they administered to study participants.

Residential Colleges in Dunedin (special thanks to Jamie Gilbertson) promoted the study to their residents via email, Facebook, and other platforms, and hosted the specimen collection teams at colleges.

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I thank Doctor Susan Jack and Associate Professor James Ussher, primarily for keeping the region safe from COVID-19 during the length of my thesis, but also for entrusting their data to me. I am fortunate to have learnt from your expertise in designing and carrying out research in parallel with managing an unfolding clinical situation. I am grateful for your willingness to involve me in the project from the beginning, from specimen collection through to data analysis, and for being so willing to impart your knowledge. I thank Dr Susan Jack in particular for her encouragement to pursue study at a Master's level, and for assisting me to obtain funding from the University of Otago Department of Preventative Medicine to cover my fees. I am grateful for the time you made for me despite many more pressing concerns.

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I thank Dr Richard Egan for lighting the Public Health flame that continues to burn within me, and which motivated me to study and work within Public Health. For this thesis you took me on as an orphan and gave me a connection to the Department of Preventative and Social Medicine, and I thank you for that.

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The candidate's tuition fees were covered by a University of Otago Department of Preventive and Social Medicine Masters Scholarship.

Extracting data from the National Immunisation Register, and specimen collection, were facilitated in-kind by Public Health South, Southern District Health Board.

Southern Community Laboratories processed all the swabs from the carriage survey, and stored isolates at cost.

Additional funding for tuition fees was provided to the candidate from the Pūtea Tautoko Student Relief Fund, due to work obligations during COVID-19. This enabled an extension on the due date for this thesis.

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Table of Abbreviations

DNA	Deoxyribonucleic acid
DSP	Digital Signal Processors
e-cigarette	Electronic cigarette
ESR	The Institute of Environmental Science and Research
ICSEA	Index of Community Socio-educational Advantage
IMD	Invasive Meningococcal Disease
JBI	Joanna Briggs Institute
MALDI-TOF	Matrix-assisted laser desorption/ionization-time of flight
MDU PHL	Microbiological Diagnostic Unit Public Health Laboratory
MenACWY-D	Quadrivalent meningococcal conjugate vaccine
MenACWY-T	Quadrivalent meningococcal conjugate vaccine
MenC	Meningococcal group C conjugate vaccine
MLST	Multilocus sequence typing
MOH	Ministry of Health
N. meningitidis	Neisseria meningitidis
NHI	National Health Index
NIR	National Immunisation Register
NZSEI	New Zealand Socioeconomic Index
OR	Odds Ratio
PCR	Polymerase chain reaction
PR	Prevalence Ratio
RCT	Randomised control trial
SAGE	Strategic Advisory Group of Experts
SASG	Slide agglutination serogrouping
STROBE	Strengthening the Reporting of Observational Studies in Epidemiology
UK	United Kingdom
URTI	Upper respiratory tract infection
USA	United States of America
VR	Variable region
WGS	Whole Genome Sequencing
WHO	World Health Organization

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Chapter 1: Introduction

Neisseria meningitidis (*N. meningitidis*) often forms part of the normal human flora but can occasionally enter the blood stream and cause invasive meningococcal disease (IMD), which commonly manifests as septicaemia or meningitis.[1] IMD is preceded by carriage of *N. meningitidis*. *N. meningitidis* colonises the nasopharynx and can be spread by contact with secretions or droplets, which is thought to occur during sneezing or coughing in close proximity, or during intimate kissing.[2] Understanding factors that influence the carriage and transmission of *N. meningitidis* is important to reduce the risk of IMD to populations within our communities who are most at risk. International evidence suggests that young people in residential accommodation have a higher risk of carriage of *N. meningitidis* than children or adults.[2–5] In New Zealand adolescents have a higher incidence of IMD than adults.[6] Indeed, in 2018 there were three cases of IMD within one university residential college in Dunedin, New Zealand[7], and two further epidemiologically linked cases in the community. Following these cases, a cross sectional observational carriage study and a risk factor survey were carried out on students in their first year at University of Otago residential colleges in Dunedin. The studies aimed to establish the prevalence of carriage of *N. meningitidis*, examine the presence of risk factors associated with carriage, and examine the impact of treating an entire residential college population with antibiotics to clear carriage. Protection against IMD is available in the form of meningococcal vaccinations. In the years following the initial studies the availability and government funding of meningococcal vaccines changed. To assess the impact of these changes, and to better understand factors that impact vaccination uptake, two vaccine hesitancy surveys were undertaken, one in 2019 and one in 2020. The aforementioned studies, carried out over three years, form the basis of this thesis. Ultimately, the studies described in this thesis aim to inform public health responses to meningococcal carriage and disease.

Chapter 2: Background

2.1 Invasive meningococcal disease

IMD progresses rapidly, often in otherwise healthy young people. During 2020 IMD had a case-fatality rate of 8.6% for all age groups in New Zealand.[6] IMD most frequently manifests as meningitis or septicaemia.[8] Classic signs and symptoms of meningococcal septicaemia include sudden onset of fever, non-blanching rash and septic shock. Symptoms of meningococcal meningitis include headache, photophobia, neck stiffness, confusion, drowsiness, and coma.[1] During 2017/18 New Zealand experienced an increase in cases of IMD caused by meningococcal W serogroup, presenting with atypical symptoms and a case fatality rate of 25%.[9] IMD disproportionately effects young children under 5 years of age, who experienced 37.4% of IMD cases and 40% of IMD deaths in New Zealand in 2019[6] despite only making up 6.3% of the population in 2018.[10] In 2019 those aged 15—29 years of age accounted for 23% of IMD cases, and 20% of deaths, with the remaining deaths in those aged over 50 years.[6] Māori and Pacific peoples are over represented in IMD case statistics. The New Zealand Census 2018 showed that the population comprised 16.5% Māori, 8.1% Pacific peoples and 70.2% New Zealand Europeans[11], yet these ethnicities experienced 34%, 21% and 40% of IMD cases in New Zealand respectively in 2019.[6] Between 2013 and 2017, there were between 26 and 70 annual cases of IMD each year, and between 2 and 9 deaths, with an overall upward trend since 2014.[12] In 2018, there were 120 reported cases and in 2019 there were 139 cases. In both 2018 and 2019 there were 10 deaths.[6] The increasing incidence of IMD in New Zealand pre-COVID-19, and the relatively high case-fatality ratio, highlight the importance of understanding *N. meningitidis* and possible ways to prevent this disease.

2.2 Neisseria meningitidis

N. meningitidis is a gram negative oxidase-positive aerobic diplococcus from the bacterial family Neisseriaceae.[13] While thirteen serogroups of *N. meningitidis* have been identified, only serogroups A, B, C, W, X, and Y are commonly known to have the potential to be pathogenic and cause IMD.[14] Other serogroups that very rarely causes invasive disease include serogroup E, X and Z.[15,16] Pathogenic *N. meningitidis* are generally encapsulated in a polysaccharide layer.[17] In some very rare cases *N. meningitidis* without capsules have caused invasive disease, but only in immunocompromised individuals.[18] In immunocompetent individuals, *N. meningitidis* relies on its polysaccharide capsule for both virulence and protection from its host. The polysaccharide capsule

facilitates adhesion of *N. meningitidis* to host cells and also provides protection against the complement immune system.[17] Differences in *N. meningitidis* polysaccharide capsules, lipopolysaccharide, and the outer membrane proteins PorB and PorA, define an isolate's serogroup, immunotype, serotype, and serosubtype, respectively. This thesis will not consider the risk factors associated with immunotype, serotype, and serosubtype, but will explore potential associations between different serogroups and common risk factors for carriage.

2.3 Serogroup and disease prevalence

The six main pathogenic meningococcal serogroups, A, B, C, W, X, and Y, each have a chemically distinct capsular polysaccharide.[14] Meningococcal serogroup A rarely causes invasive disease in New Zealand, with no cases in at least the last seven years.[19] Meningococcal serogroup B has historically been the cause of over half of the annual cases of IMD in New Zealand.[6] However, during 2018–2019, just under half of all IMD was caused by meningococcal serogroup B, and just under half by serogroups C, W or Y.[19] Serogroup W has accounted for an increasing proportion of cases in New Zealand since 2018. During 2018, Northland experienced an unusually high number of IMD cases (7.4 cases per 100,000 people) compared with New Zealand overall (2.5 cases per 100,000), the majority of which were serogroup W.[19] The number of cases of IMD in New Zealand is displayed in Table 1 below. Note that low incidence in 2020 is likely due to a period of reduce community movement due to COVID-19 lockdowns, and possibly increased personal hygiene and social distancing.

Table 1: IMD Serogroup Case Distribution in New Zealand by Year, 2015–2020

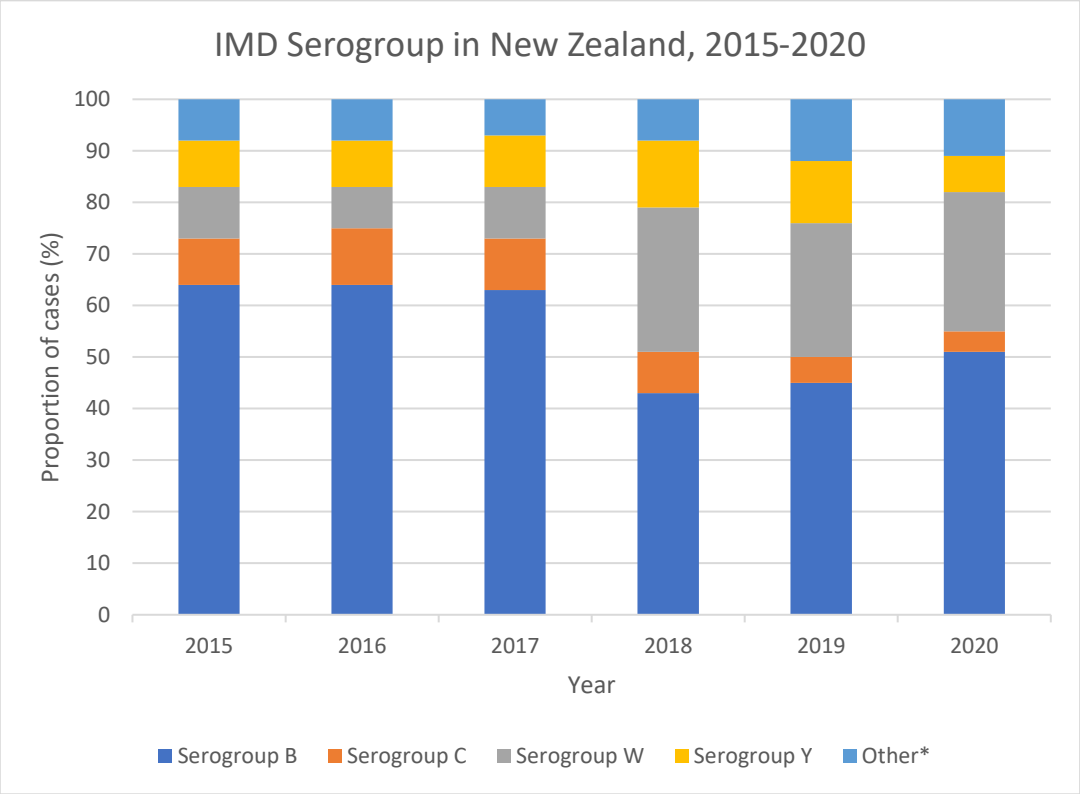
Serogroup	Year						Total
	2015	2016	2017	2018	2019	2020	
Group B	41	47	70	51	62	18	289
Group C	6	8	11	10	7	1	43
Group W	6	5	12	33	36	11	103
Group Y	6	7	11	16	16	2	58
Group E	0	0	0	0	1	0	1
Group X	0	0	0	1	0	0	1
Non-groupable[1]	0	0	1	2	6	0	9
Other lab confirmed[2]	2	3	4	4	6	1	20
Probable	3	5	3	3	5	2	21
Total	64	75	112	120	139	35	545

[1] Non-groupable – group not determined.

[2] Includes DNA laboratory-confirmed by PCR where no group or other strain characteristics were determined, or laboratory-confirmed isolates not received by ESR Invasive Pathogens Laboratory.

The proportion of invasive disease caused by each serogroup is plotted in the chart below (Figure 1) by year. This chart shows that serogroup B still accounts for highest number of IMD cases, but highlights the increasing proportion of disease associated with serogroup W.

Figure 1: IMD Serogroup in New Zealand, 2015–2020



[1] Includes serogroups X, E, Non-groupable (group not determined), other lab confirmed (DNA laboratory-confirmed by PCR where no group or other strain characteristics were determined, or laboratory-confirmed isolates not received by ESR Invasive Pathogens Laboratory), and probable cases with no serogroup data.

It is carriage of serogroups with potential to cause invasive disease that is of most interest to this carriage study.

2.4 Carriage

N. meningitidis has evolved to live in the human nasopharynx. Studies have shown carriage lasts for 15 to 23 weeks in the majority of cases[20], but can persist for 8 months or more, and that during the course of carriage the bacteria can evolve, potentially becoming better adapted to its host.[21] Carriage of serogroups B and W have been shown to persist for longer than other serogroups.[21] Carriage rates of *N. meningitidis* vary over time and differ by country, with international carriage

rates varying from 3 to 35% in the general population[14] and from 2.5%[2] to 60%[22] in adolescent populations. Adolescents entering university have the highest carriage rates, with an increase in carriage following admission[22] and following social mixing at university orientation type events.[23] The various risk factors for carriage of *N. meningitidis* will be explored in depth in the literature review, however acknowledged risk factors include adolescence, cigarette smoking, smoking of water pipes, attending pubs or night clubs, and intimate kissing.[2] All of these risk factors reflect increased risk of transmission of *N. meningitidis*.

2.5 Transmission

N. meningitidis generally colonises the nasopharynx of humans, and is therefore thought to be transmitted via direct contact with nasal or oral secretions, or via inhalation of droplets projected through the air.[14] Contact with secretions can be direct from person to person (eg; via intimate kissing), or indirect via fomites (eg; via the rim of contaminated drinking vessels). With regards to indirect contact, researchers investigating survival of *N. meningitidis* outside the human body on fomites found that despite a decline in viable organisms immediately after drying, surviving bacteria could be recovered at least two days after drying and some strains were recovered after as many as eight days, depending on environmental conditions.[24] Interestingly, a 2007 study showed the New Zealand epidemic Meningococcal B strain B:4:P1.7–2,4 survived better on glass than all other strains tested.[25] This suggests that spread via fomites, by indirect contact, is a potential mode of transmission and may account for risk factors for carriage such as smoking cigarettes or water pipes.[2] Some have hypothesised that that fomites need to be generated from secretions or droplets from the nasopharynx, not from saliva, because saliva inhibits *N. meningitidis*.[26,27] However McMillan et al were able to recover isolates of *N. meningitidis* from saliva samples during their carriage study of students residing in residential colleges, casting some doubt on the inhibitory nature of saliva.[28]

Unlike transmission by contact, transmission by droplet occurs through the air. When a person coughs[29], sneezes, sings[30] or carries out some other activity that involves forceful expulsion of air though the nasopharynx or oropharynx, bacteria or virus can be expelled in small droplets of varying size. The majority of droplets spread in this manner will be affected by gravity and will fall to the ground within a 1—2m distance.[31] However exceedingly small droplets can remain in the air, being buoyed or carried by air currents, and, if someone sneezes with force, droplets can be propelled for a long distance.[30] There has been intense interest in the degree to which humans generate organism containing droplets and aerosols during the COVID-19 global pandemic, with debate regarding the

extent to which small droplets can act as aerosols and facilitate spread of SARS-CoV2 virus[30,32], however it is unclear to what extent this recent evidence would apply to transmission of *N. meningitidis* due to a paucity of evidence related to droplet transmission of *N. meningitidis*. Regardless of the mode of transmission, living in close proximity to others, for a long period of time, increases the risk of *N. meningitidis* transmission, carriage, and therefore the risk of IMD.[33,34]

2.6 Public health response

IMD in New Zealand must be notified to the local medical officer of health, which enables a public health response.[35] To reduce the risk of meningococcal transmission, and therefore the risk of disease, public health officials follow protocols after a case of IMD has been identified and notified. These protocols are well established, and there is little variation between countries.[1,36–38] Following diagnosis of disease, cases (or their close acquaintances) are interviewed to establish their movements and identify people they have had close contact with. Close contacts are defined by the New Zealand Ministry of Health (MOH) Communicable Disease Control Manual as "Anyone who has had unprotected contact with upper respiratory tract or respiratory droplets from the case during the 7 days before onset of illness to 24 hours after onset of effective treatment".[1] This definition may include other members of the same household, healthcare workers, or any other individual that has had close exposure to the person with IMD and therefore has the potential to become unwell, or unwittingly transmit the same strain of *N. meningitidis* to other susceptible people. Anyone who is identified as a close contact of a case is offered antibiotics prophylaxis, preferably within 24 hours (regardless of immunisation status). Close contacts may also be offered immunisation. If the serogroup of the index case is either serogroup A, C, W or Y, immunisation with a quadrivalent meningococcal conjugate vaccine (MenACWY-D or MenACWY-T) is recommended and funded in New Zealand.[1] The only circumstances in which close contacts are eligible, at the discretion of the local medical officer of health, for the recombinant vaccine 4CMenB, is during a serogroup B outbreak within a multi-occupancy residential setting.[8] The New Zealand MOH Communicable Disease Control Manual defines a meningcoccal outbreak as two or more cases of disease associated in time, place or person.[1]

Clearance antibiotics are given to eradicate carriage of *N. meningitidis* [1]. Clearance antibiotics have been shown to reduce the risk of invasive disease in close household contacts by up to 89%[39]. Only those deemed close contacts are given antibiotics as unnecessary use of antibiotics is undesirable.[40–42] In a cohort at higher risk of *N. meningitidis* transmission and colonisation, such as students in their first year in a residential college, any additional evidence regarding the medium-term impact of

provision of clearance antibiotics on *N. meningitidis* carriage is useful. This is something that this thesis will examine.

2.7 Immunisation

Immunisation offers a degree of protection against IMD. There are currently four vaccines available in New Zealand that offer a degree of protection against IMD. No single immunisation offers protection against all the meningococcal serogroups. The vaccines and the serogroups each protects against are in Table 2 below:

Table 2: Meningococcal vaccinations currently available in New Zealand.

Product Name	**Description**	**Manufacturer**
Bexsero	Meningococcal group B four-component recombinant (4CMenB)[43]	GlaxoSmithKline
NeisVac-C	Meningococcal group C conjugate (MenC): contains group C polysaccharide conjugated to tetanus toxoid[44]	Pfizer
Nimenrix	Quadrivalent meningococcal conjugate (MenACWY-T): contains group A, C, W and Y polysaccharides conjugated to tetanus toxoid [45]	GlaxoSmithKline
Menactra	Quadrivalent meningococcal conjugate (MenACWY-D): contains group A, C, W and Y polysaccharides conjugated to diphtheria toxoid [46]	Sanofi-Aventis

Conjugate vaccines contain a small quantity (4—5 micrograms) of the capsular polysaccharide layer of the relevant *N. meningitidis* serogroup. This is chemically bonded to an unrelated protein (tetanus or diphtheria) to ensure a robust immune response to the polysaccharide. In contrast Bexsero is composed of three recombinant proteins (Neisserial adhesin A (NadA), Neisserial Heparin Binding Antigen (NHBA), and factor H binding protein (fHbp)) which are found on the surface of the bacteria, plus outer membrane vesicles from *N.meningitidis* group B strain NZ98/254.[43] Both types of vaccine offer varying degrees of protection against IMD.[43,44,46] However, their effect on carriage appears to differ. Recent evidence suggests recombinant vaccines targeting serogroup B have little impact on carriage of *N. meningitidis*.[2] Conversely, there is evidence that large scale vaccinations with conjugate vaccines reduces carriage.[47] This topic will be explored further in the literature review on risk factors for carriage.

What is clear is that meningococcal vaccines provide protection against IMD for between 3—5 years.[8] In New Zealand between 2004—2008 the Meningococcal group B Outer Membrane Vesicle (MeNZB) vaccine appears to have played a role in controlling the waning epidemic of serogroup B IMD.[8,48] MeNZB was developed specifically to target the *N. meningitidis* serogroup B strain B:4:P1.7b,4 (NZ 98/254), and after being delivered to New Zealand school children via a school based programme, it ceased being available in 2011. Vaccination remans an important tool for reducing the impact of IMD, particularly in groups that are at higher risk. Multiple factors determine the degree of vaccination uptake.

2.8 Vaccine hesitancy

The World Health Organization (WHO) Strategic Advisory Group of Experts (SAGE) on Immunisation defines vaccine hesitancy as "a delay in acceptance or refusal of immunisations despite availability of vaccine services".[49] As will be discussed in the literature review on vaccine hesitancy, when this study was designed, in 2018, there was limited evidence on which factors influence vaccine hesitancy among adolescents with regard to meningococcal vaccination.[50] During the study, following the emergence of firstly, COVID-19, and secondly, a vaccine for COVID-19, there was a swift increase in published literature on vaccine hesitancy. However, at the time of writing there still appears to be no literature on vaccine hesitancy among students residing in residential colleges. Vaccine hesitancy is multi-faceted and fluid, varying across time, place, and vaccinations. The WHO SAGE offer a model that allocated factors that influence vaccine hesitancy into three broad categories: confidence, complacency, and convenience.[49] Confidence refers people's perception of the safety and effectiveness of a vaccine and the services that deliver it. Complacency refers the degree of motivation people have towards receiving a vaccine, and is generally based on perceived risk, which in turn is determined by knowledge of the disease and the organism. Convenience is determined by factors external to a person, such as funding, model of delivery, and the socio-cultural and political context in which the vaccine is delivered. All three categories are affected by the broader determinants of health, but perhaps none more so than convenience. During the course of this research the availability and funding of meningococcal vaccines changed.[8] In the initial year of the study (2018), Menactra (MenACWY-D for serogroups A, C, W and Y) was available and recommended by the MOH, and Bexsero (4CMenB for serogroup B) became available part way through the year, but neither vaccine was funded or promoted by residential colleges or Student Health Services. In the second year of the study (2019), both vaccines were recommended, and were promoted to students residing in residential colleges, but neither MenACWY nor 4CMenB were

funded. In the third year of the study (2020), MenACWY was both available and funded, and 4CMenB was recommended but not funded. Understanding students residing in residential colleges' confidence, complacency and perception of convenience in relation to meningococcal vaccine uptake and vaccine hesitancy is important for informing future health policies and health promotion strategies.

2.9 Health promotion

Health promotion has been defined by WHO as "the process of enabling people to increase control over, and to improve, their health".[51] WHO stresses that health promotion moves beyond a focus on individual behaviour towards a wide range of social and environmental interventions.[51] Health promotion operates at the intersection of education, communication, community development, health science and policy development.[52] When done well, health promotion interventions facilitate healthy public policy, which in turn creates an environment that empowers people to be healthy and stay well. From a health promotion perspective, a key component of work towards reducing IMD is ensuring equitable access to meningococcal vaccine for those groups that will benefit from immunisation the most. Between 2018 and 2020 the period of data collection for this study, with respect to IMD, study participants were exposed to an increase in health education, an increase in vaccine promotion, and an increase in funding for MenACWY. As part of this thesis, the impact of each of these measures will be considered through a health promotion lens.

2.10 Invasive meningococcal disease cases in 2018 among first year university students in University of Otago residential colleges

In 2018 there were three related cases of IMD in one of the University of Otago's Dunedin residential colleges.[7] These cases were all serogroup B, and occurred over a period of four months. The usual public health protocols were followed for the first two cases, beginning with rapid contact tracing to find close contacts who were exposed.[1] Close contacts were offered clearance antibiotics, with the intention of eliminating onwards transmission of *N. meningitidis*.

However, when the third case occurred, in order to prevent further cases, a decision was made by the Public Health Unit to follow up all students and staff in the same residential college and treat them all with clearance antibiotics.[7] There are a total of 187 beds at the affected college[53], and an unknown number of support staff. Through extensive communication and close collaboration with

the residential college staff, all students and staff were offered, and accepted, a dose of antibiotic. Ultimately, this intervention was successful in preventing a further case of IMD. However, while antibiotics are effective at eliminating carriage of *N. meningitidis* immediately after administration[54], there is little evidence in the literature on the impact on rates of re-colonisation in the weeks to months after administration. Antibiotics negatively impact the microbiome of the gastrointestinal tract[55], and therefore might also negatively impact an individual's nasopharyngeal microbiome. It has been suggested that the nasopharyngeal microbiome may play a role in protecting against re-colonisation with *N. meningitidis.*[56] Given acquisition in student populations can be swift and high[57], the weeks following antibiotic administration may be a high risk period for students. In order to investigate the impact of the mass treatment, and to inform further public health action, should it be required, Public Health Unit staff conducted a carriage survey and obtained bacterial samples from the oropharynx of consenting students in the effected college, and 13 other residential colleges that did not receive antibiotics, seven weeks after antibiotic administration.

2.11 Objectives

There were four primary objectives of this thesis, and they were:

Objective A:

> To estimate the prevalence of *N. meningitidis* carriage among University of Otago students in their first year living in residential halls, including prevalence in a residential college seven weeks post *N. meningitidis* eradication therapy.

Objective B:

> To estimate the prevalence of known risk (and protective) factors of *N. meningitidis* throat carriage and any associations with the various serogroups among University of Otago first year students living in residential halls.

Objective C:

> To assess electronic cigarette (e-cigarette) use as a risk factor for *N. meningitidis* throat carriage among University of Otago first year students living in residential halls.

Objective D:

> To identify factors influencing uptake of meningococcal vaccination by University of Otago first year students living in residential halls.

2.12 Thesis structure

This thesis has two sections, followed by a discussion and conclusion. The first section, chapter two, addresses objectives A, B and C. Data sources for this section include the 2018 *N. meningitidis* carriage study and the associated 2018 risk factor survey, both carried out as part of the response to IMD cases in University of Otago residential colleges, and the NIR and Student Health immunisation records.

The second section, chapter three, describes the methods used to address objective D. Data sources for this fourth objective include the 2018 risk factor survey, additional 2019 and 2020 online vaccine hesitancy surveys, and NIR and Student Health immunisation records.

Each section, chapters two and three, include a literature review, description of methods, and results for their respective surveys. Information from both sections is combined in the discussion, chapter four, and conclusion, chapter five.

Table 3: Data Sources used to address thesis objectives.

Sections	Objective	Data Source				
		2018 Carriage Study	2018 Risk Factor Survey	NIR/Student Health Immunisation Records	2019 Vaccine Hesitancy Survey	2020 Vaccine Hesitancy Survey
Chapter Three	A: Carriage prevalence	X	X			
	B: Risk factor prevalence	X	X	X		
	C: Vaping as a risk factor	X	X			
Chapter Four	D: Vaccine Hesitancy		X	X	X	X

Chapter 3: 2018 *N. meningitidis* Carriage Study

This chapter describes the carriage study and risk factor survey carried out by Public Health South in response to cases of IMD in residential colleges in 2018. The chapter includes a literature review, methods and results of the carriage study and risk factor survey. The chapter aims to address the following objectives:

Objective A:

> To estimate the prevalence of *N. meningitidis* carriage among University of Otago students in their first year living in residential halls, including prevalence in a residential college seven weeks post antimicrobial eradication therapy.

Objective B:

> To estimate the prevalence of known risk (and protective) factors of *N. meningitidis* throat carriage and any associations with the various serogroups among University of Otago first year students living in residential halls.

Objective C:

> To assess electronic cigarette (e-cigarette) use as a risk factor for *N. meningitidis* throat carriage among University of Otago first year students living in residential halls.

3.1 *N. meningitidis* Carriage Study - Literature Review

3.1.1 Introduction

Literature investigating carriage of *N. meningitidis*, and risk factors for carriage, stretches back to at least 1918, when Captain Glover documented his observations of meningococcal carriage in military dormitories.[33] However, the methods, concepts and implementation of research into carriage and risk factors differ according to the context and resources available. To understand risk factors for carriage and methods for carriage studies of *N. meningitidis* a review of the literature was undertaken. This chapter outlines the objective of the literature review, and the strategy used. Following selection of articles, the body of literature will be assessed as a whole, before evidence underpinning each risk factor is appraised.

3.1.2 Objectives

The objectives of this review are:

To review *N. meningitidis* carriage studies, in terms of their core components and methodological strengths and weaknesses; and

To identify gaps in the literature on the topic, and to summarise the evidence surrounding known risk and protective factors for *N. meningitidis* carriage among students residing in residential colleges.

3.1.3 Methods

3.1.3.1 Search strategy

The aim of the search strategy was to identify peer reviewed journal articles describing studies on prevalence of, and risk factors for, carriage of *N. meningitidis* among university students living in residential colleges. The search strategy was restricted to articles from 1990 onwards, and articles published in English language. Studies from developing countries were excluded due the predominance of different serogroups in developing countries, and the variance in socio-economic conditions and therefore risk factors. Grey literature, including reports from governmental and nongovernmental organisations, was excluded.

3.1.3.2 Literature search

Ovid Medline, PubMed and Scopus databases were accessed via the University of Otago Library website and searched on 23 February 2020, 6 May 2020, and 29 March 2021. An initial scan of the literature was performed using the key terms “meningococcal” in conjunction with “carriage” and their truncations. Once additional key words were gained the search terms were extended to include the following terms:

Meningococcal or *Neisseria meningitidis*

AND

carriage or coloni*

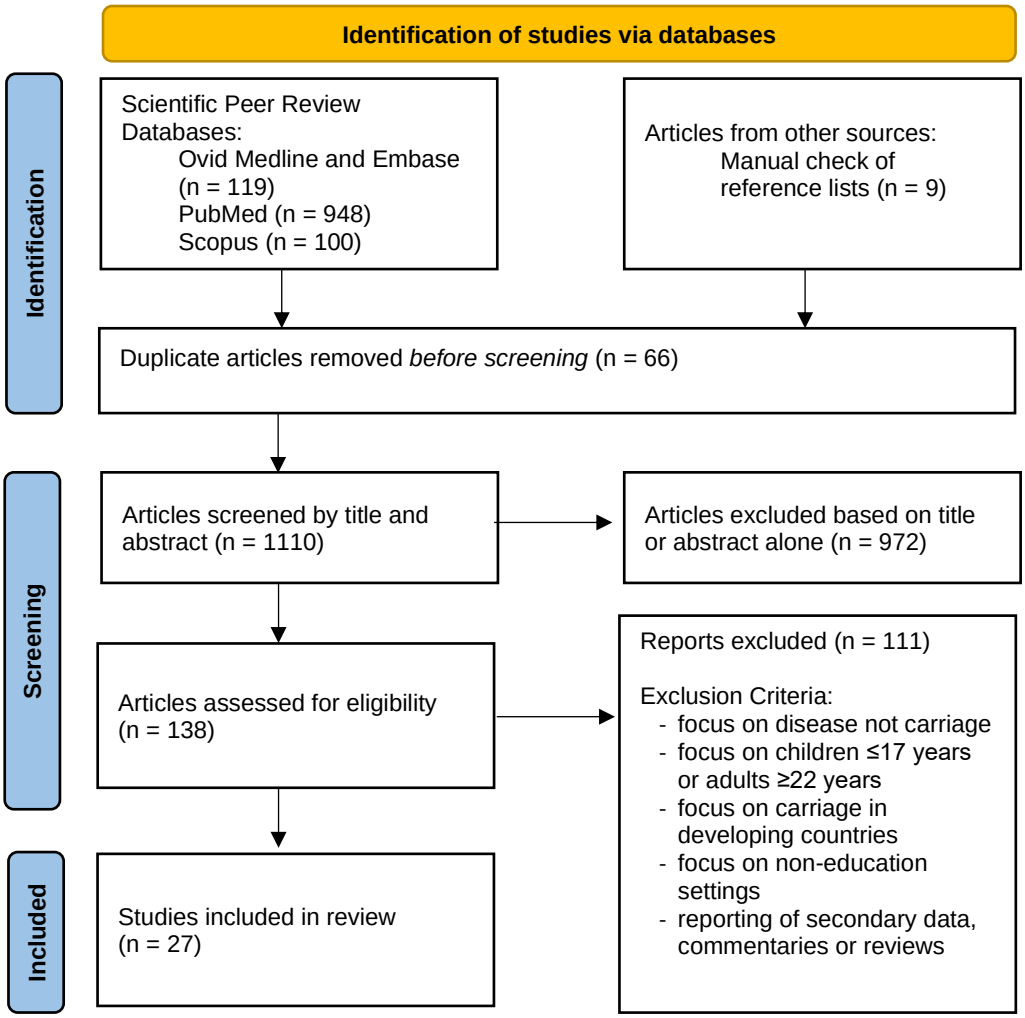
AND

Risk factor* or age or gender or ethnic* or kiss* or vap* cig* or student* or college or dorm* or university or varsity or institut* or undergraduate or communal or academy or polytech* or vaccinated or immunis* or immuniz* or occupation* or intimate or relig*

PubMed (life sciences and biomedical), Ovid Medline (life sciences and biomedical) and Scopus (life sciences, social sciences, physical sciences and health sciences) databases were chosen for their relevance to the topic and to ensure adequate coverage of the literature. The search strategy was reviewed by the subject librarian at the University of Otago Library.

Once the searches had been completed abstracts from PubMed (n=948), Ovid Medline and Embase (n=119) and Scopus (n=100) were imported into Mendeley v1.19.8 and duplicates were removed (n=66). Once duplicates had been removed titles and abstracts were screened. During screening articles with a focus on disease, organisms other than *N. meningitidis*, carriage during Hajj or within military settings, vaccine development and evaluation, and other topics unrelated to carriage among students residing in residential colleges, were excluded (n=972). Following screening of titles and abstracts 129 articles were assessed for eligibility, with exclusion criteria being: articles with focus on disease not carriage; articles with a focus on children ≤17 years or adults ≥22 years; articles with a focus on settings other than university residential dormitories/colleges; articles with a focus on carriage in developing countries; articles reporting secondary data, commentaries, or reviews. Articles that met exclusion criteria were removed (n=122), leaving only seven full text articles. Due to the paucity of carriage studies carried out exclusively within university related residential college populations (n=7), the initial exclusion criteria were altered, and carriage studies on populations of non-residential college university students (n=6) and studies that included secondary students ≥16 years of age (n=5) were included, resulting in 16 articles. Reference lists of these 16 articles were manually screened to identify additional studies, resulting in 9 additional articles being included. At the end of the literature search 27 articles remained (Figure 2).

Figure 2: PRISMA flow diagram[58] for scoping literature review of *N. meningitidis* carriage studies in University Students



3.1.3.3 Appraising literature

A literature review of *N. meningitidis* carriage in high-risk settings, published in 2018 by Peterson et al provided a reference point for the process of appraisal.[59] For this thesis the same methods were followed, including use of the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Studies Reporting Prevalence Data.[60] Studies were assessed for completeness using the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist for cross sectional studies.[61] Of the 27 articles, 11 had a JBI score indicating high quality, 12 had a score indicating medium quality, and four had a score indicating low quality. Results are displayed in Table 4. A version of this table was originally published as supplementary information by Peterson in 2018, with 15 studies and either Yes, or No, or Unclear for each of the nine questions.[59] Their table was adapted, the JBI

numerical score of each article was added, resulting in one study being excluded (set in a developing country) and 13 additional studies being included. Because studies cover a broad range of locations and risk factors, no studies were excluded from the review as a result of their low-quality score, however the limitations of individual studies have been considered when assessing their contribution to the body of knowledge, particularly in regard to assessing risk factors for carriage. Greater emphasis has been given to the findings of studies with a higher quality score, while the findings of studies with a lower quality score have been regarded with caution, as detailed in the results to follow.

Table 4: The Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Studies Reporting Prevalence Data (adapted from Peterson, et al., supplemental data[59])

Study (by date of publication)	**Score**	**Q1**	**Q2**	**Q3**	**Q4**	**Q5**	**Q6**	**Q7**	**Q8**	**Q9**
Neal[57]	6	Yes	Yes	Yes	No	Unclear	Yes	Yes	Yes	Unclear
MacLennan[62]	8	Yes	Yes	Yes	Yes	Unclear	Yes	Yes	Yes	Yes
Holmes[63]	4	Yes	Yes	No	No	Unclear	Yes	Yes	No	No
Bidmos[64]	2	Unclear	Unclear	No	No	Unclear	Yes	Yes	No	Unclear
Ala'aldeen[22]	2	Unclear	Unclear	Unclear	No	Unclear	Yes	Unclear	Yes	Unclear
Durey[65]	2	Unclear	Unclear	Unclear	No	Unclear	Yes	Yes	No	Unclear
Rodriguez[66]	3	Unclear	Unclear	No	Yes	Unclear	Yes	Yes	No	No
Read[67]	3	Yes	Yes	Unclear	Yes	Unclear	Unclear	Unclear	No	Unclear
Cleary[68]	6	No	Yes	No	Yes	Yes	Yes	Yes	Yes	No
Jeppesen[4]	4	Yes	Unclear	Yes	No	Unclear	Yes	Yes	No	No
Rodrigues[69]	6	Yes	Yes	Unclear	Yes	Unclear	Yes	Yes	Yes	Unclear
De Moras[70]	8	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes
Tryfinopoulou[71]	2	Unclear	Unclear	No	No	Unclear	Yes	Yes	No	Unclear
Rizek[72]	3	Yes	Unclear	Unclear	No	Unclear	Yes	Yes	No	No
Kim[73]	6	Yes	Yes	Yes	No	Unclear	Yes	Yes	No	Yes
Soeters[74]	5	Yes	Unclear	Unclear	Yes	Unclear	Yes	Yes	No	Yes
McNamara[75]	5	Yes	Yes	Unclear	Yes	Unclear	Yes	Yes	No	Unclear
Bali[76]	3	Unclear	Yes	Unclear	Yes	Unclear	Yes	Unclear	No	Unclear
Van Ravenhorst[21]	8	Yes	Yes	Yes	Yes	Unclear	Yes	Yes	Yes	Yes
Oldfield[77]	3	Yes	Unclear	Unclear	No	Unclear	Yes	Unclear	Yes	Unclear
Breakwell[78]	5	Yes	Yes	Unclear	Yes	Unclear	Yes	Yes	No	Unclear

Gilca[3]	3	Yes	Unclear	Unclear	No	Unclear	Yes	Yes	No	No
McMillan[79]	5	Yes	Unclear	Unclear	Yes	Unclear	Yes	Yes	Yes	No
Marshall[2]	9	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Table 4 continued

Watle[80]	8	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes
He[81]	8	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes
Choi[82]	6	Yes	Yes	Unclear	Yes	Unclear	Yes	Yes	Yes	Unclear

Studies highlighted in "green" had a high quality score (9—6 yes). Studies highlighted in "yellow" had a medium quality score (5—3 yes). Studies highlighted in "red" had a low quality score (0—2 yes).

Questions on the checklist are: 1. Was the sample frame appropriate to address the target population? 2. Were study participants sampled in an appropriate way? 3. Was the sample size adequate? 4. Were the study subjects and the setting described in detail? 5. Was the data analysis conducted with sufficient coverage of the identified sample? 6. Were valid methods used for the identification of the condition? 7. Was the condition measured in a standard, reliable way for all participants? 8. Was there appropriate statistical analysis? 9. Was the response rate adequate, and if not, was the low response rate managed appropriately?

3.1.4 Results

Of the 27 articles selected for this *N. meningitidis* carriage in high-risk settings literature review, 10 examined university residential college populations, eight examined general university populations, and nine examined general adolescent populations, in universities and secondary schools, or just secondary schools. Eleven studies were cross sectional[62,66,68,69,71–73,76,80,81,83] and a further 11 were repeat cross sectional studies, following up with students at more than one timepoint.[4,21,22,57,65,74,75,77,79,82,84] Three studies were cohort studies[3,63,64] and two studies were randomised control trials.[2,67] The studies ranged in size from 158 to 34,000 participants, with ages ranging from 17 – 25 years.

3.1.4.1 Studies set in residential colleges

The 10 *N. meningitidis* carriage studies that focused solely on residential student populations included six repeat cross sectional studies[57,65,74,77,82,84], two cross sectional studies[64,76], and two cohort studies[3,63]. Six studies had fewer than 340 participants[3,63–65,76,82], while four had between 1,400 and 2,500 participants.[57,74,77,84] The smaller studies were located in Korea (n=2)[65,82], New Zealand (n=1)[63], India (n=1)[76], Canada (n=1)[3] and the United Kingdom (n=1)[64], while the larger studies were located in either the United Kingdom (n=2)[57,77] or the United States (n=2).[74,78] The studies were carried out at varying times during the academic calendar. Only one study occurred following an outbreak.[74] Age of participants from all studies ranged from 17—25. One study that included

vaccination excluded people who had previous meningococcal vaccines, previous meningococcal disease, were pregnant, had previously experienced hypersensitivity to vaccines, had an acute or chronic illness, or were on immune suppressive therapy or had recently received blood products or antibiotics.[63] Of the eight remaining studies, two excluded participants who had one or more previous meningococcal vaccinations, had recently had antibiotics, or had an illness or immunosuppression.[76,82] The remaining seven studies did not document any exclusion criteria.[3,57,64,65,74,77,78] While six studies did not describe recruitment methods[3,63–65,76,77], in four studies recruitment occurred either during attendance at university health centres for routine college induction (n=1)[57] or for vaccination (n=1)[74], or by invitation at residence entry ways (n=1)[82], or in university common spaces (n=1).[78]

While all 10 studies examined carriage prevalence in residential college populations, four also examined the impact of vaccination on carriage[63,74,77,84], one examined risk factors for acquisition[63], and five examined risk factors for carriage.[57,65,74,82,84] Data on risk factors was collected from survey tools that were completed by participants. Of the five studies that used vaccination data, two relied on participants self-reporting[57,74], two used immunisation records from Student Health Services or from other sources such as family GP[84,85], and two recorded vaccinations as part of the study.[63,74] Risk factors for carriage that were examined by more than one study included: gender[57,74,82,84]; attendance at parties, bars and social gatherings[57,65,74,82,84]; intimate kissing[57,65,82]; smoking[57,65,74,82,84]; passive smoking[57,74,82,84]; vaccination[74,77,84]; recent upper respiratory tract infection[65,74,82,84]; recent antibiotics[65,74,82,84]; impact of living quarters[57,74,82,84]. Risk factors that were examined only by single studies included: alcohol consumption[82]; international travel[65]; and cup or cigarette sharing.[82] None of the studies from residential college settings examined electronic cigarette use as a risk factor. Two studies evaluated the effect of vaccines administered during the studies[63,74], and three examined the effect of vaccines that were administered to participants some time prior to the studies.[57,84,85] Vaccinations evaluated were MeNZB[63], MenB-fHbp[74], MCV4[74,77], MenACWY[84], and MenC.[63]

3.1.4.1.1 Laboratory methods in studies set in residential colleges

Sample collection and laboratory techniques varied according to the date of the study. Seven studies describe plating swabs immediately[57,64,65,74,77,84,86], while three state swabs were plated at the laboratory.[63,76,82] Of studies that plated swabs at the laboratory, one stated swabs were delivered to the laboratory within three hours[76], but two omitted this information.[63,82] Eight of the 10 studies used polymerase chain reaction (PCR) to identify isolate serogroups. [22,65,74,76,77,82,84,86] Three studies used additional techniques, either to elicit further information on isolates (n=1)[74] or to compare

methods (n=2).[84,86] Additional laboratory techniques used included slide agglutination serogrouping (SASG)[74,84,86], whole genome sequencing (WGS)[74] and direct PCR.[86]

3.1.4.1.2 Statistical methods studies set in residential colleges

Of the six studies that examined risk factors for carriage one used chi-square test to identify relationships between risk factors and carriage[65], and five used multi-variable analysis to identify relationships and estimate the scale of the relationships.[57,63,74,82,84] Four studies did not examine risk factors, instead describing carriage prevalence.[64,76,77,86]

3.1.4.2 Studies set in general university populations

Studies set among general university populations have the benefit of a larger population from which to sample. Many of the demographic characteristics, and most of the potential risk factors for *N. meningitidis*, are shared with students residing in residential colleges. Eight such studies were included in the literature review. Studies that focused solely on general university populations included three repeat cross sectional studies[22,75,79], four cross sectional studies[66,69,71,72], and one randomised control trial[67]. Five studies had fewer than 602 participants, while three had between 2,500—3,500 participants. The smaller studies were located in Australia (n=1), Brazil (n=1), Chile (n=1), Greece (n=1) and Portugal (n=1), while the larger studies were again located in either the United States (n=1) or the United Kingdom (n=2). The studies were carried out at varying times during the academic calendar. One study took place after an outbreak, and another study had several cases of disease during the study period. The age of participants ranged from 17—32, with most participants being aged 18—22 years. Two studies documented exclusion criteria, which included previous meningococcal disease, chronic ailments (not further defined), immunodeficiency, and recent antibiotic use. One study only included medical students. Recruitment occurred on campus for all but one study, which examined students from all over Turkey at a national conference. Specific campus locations for recruitment included in a medical centre during the wait time post vaccination (n=1), in halls and libraries (n=1), at the end of lectures (n=1), and during orientation week (n=1). While all eight studies aimed to examine carriage prevalence, four studies also examined a range of risk factors, two studies were designed to measure the effect of vaccination on carriage, and two studies examined laboratory methods. Again, data on risk factors was collected from survey tools that were completed by participants. Of the two studies assessing the effect of vaccination, one study verified self-reported vaccination history via university health records and a state-run immunisation register, while the other excluded those that had previously

been vaccinated but did not state how they obtained vaccination history. Risk factors for carriage that were examined by more than one study included: age; gender; attendance at parties, bars and social gatherings; intimate kissing; smoking; passive smoking; vaccination; recent upper respiratory tract infection; recent antibiotics; impact of living quarters. Risk factors that were examined only by single studies included: ethnicity; and water pipe smoking. None of the studies from general university settings describe examining electronic cigarette use as a risk factor. One study was a randomised control trial of MenACWY-CRM and 4CMenB vaccines, and another took place following an outbreak and evaluated the impact of MenB-4C and MenB-fHbp on carriage. Other meningococcal vaccinations included in studies were MCV4 and MenC.

3.1.4.2.1 Laboratory methods in studies of general university populations

Sample collection and laboratory techniques varied between studies. Four studies described plating swabs immediately, while one study stated swabs were plated at the laboratory, and one study used both methods and compared the results. Of studies that plated swabs at the laboratory, one stated that swabs were delivered to the laboratory within five hours, while the other omitted information on length of time taken to deliver swabs to the laboratory. Six of the eight studies used PCR to identify isolate serogroups, usually in combination with either SASG (n=1) or WGS (n=2) or both (n=1). One study used SASG alone, and another did not describe the laboratory techniques used.

3.1.4.2.2 Statistical methods in studies of general university populations

Of the five studies that examined risk factors for carriage one used chi-square test to identify relationships between risk factors and carriage, one used univariable analysis, and three used multi-variable analysis to identify relationships and estimate the scale of those relationships. Three studies did not examine risk factors, focusing instead on carriage prevalence.

3.1.4.3 Studies set in general adolescent populations

Studies set among general adolescent populations have the benefit of an even larger population from which to sample. Again, many of the demographic characteristics, and some of the potential risk factors for *N. meningitidis*, are shared with students residing in residential colleges. Others, however, are not, and allow for additional analysis and comparison. Examples are age, and attendance at bars. Nine studies set in general adolescent populations were included in the literature review. Studies of general adolescent populations included two repeat cross sectional studies[4,21], six cross sectional studies[62,68,73,80,81,83], and one randomised control trial[2].

Two studies had fewer than 1,000 participants, while five had between 1,200—2,300 participants. Two large studies had 14,000 and 34,000 participants. The smaller studies were in China (n=1) and the UK (n=1). Mid-sized studies were based in Brazil (n=1), Korea (n=1), the Netherlands (n=1), Norway (n=1) and the UK (n=1). The largest studies were based in the United Kingdom and Australia. The studies were carried out at varying times during the school year. Only one study reported taking place after an outbreak. One study included university, secondary and primary school students, one study included university and secondary students, one study included students from primary and secondary schools, and six studies included secondary school students only. Three studies included primary school students, and one of these included pre-schoolers. Consequently, the age of participants ranged from 1—25 years, however most studies examined ages 13—19 years. Only three studies documented exclusion criteria, which included previous meningococcal B vaccination (n=3), recent antibiotic use (n=1), participation in clinical trials involving medications (n=1), pregnancy or lactation (n=1), and previous anaphylaxis with vaccination (n=1). Recruitment is reported as occurring in schools for all studies, and in universities where applicable. Four studies describe sending individual invitations home with students who were selected randomly.

All nine studies examined carriage prevalence and at least one risk factor for carriage, with one study designed to measure the effect of vaccination on carriage, and two studies examining laboratory methods. Of the six studies assessing the effect of vaccination, four studies relied on self-reported vaccination history, one study verified self-reported vaccination history via a national immunisation record, and one study documented vaccinations that were given as part of the study. Risk factors for carriage that were examined by more than one study included: age; gender; attendance at parties, bars and social gatherings; intimate kissing; smoking; passive smoking; vaccination; living quarters; recent upper respiratory tract infection; recent antibiotics; impact of living quarters. Risk factors that were examined only by single studies included: ethnicity; socio-economic status; level of education; level of parental education; smokeless tobacco; water pipe use; electronic cigarette use; Norwegian Russefeiring celebration (a weeklong social event similar to a university orientation week). One study was a large, randomised control trial of 4CMenB vaccines. Another study examined carriage pre and post vaccination with MenC vaccine, and two studies took place following widespread administration of vaccinations, one MenC vaccine and the other MenACWY vaccine.

3.1.4.3.1 Laboratory methods general adolescent populations

Sample collection and laboratory techniques varied between studies. Four studies describe plating swabs immediately, three studies delivered swabs to the lab for plating (in under six, five, or four hours in respectively), and one large study compared a variety of methods. One study did not

describe their sample collection methods. Two studies solely used PCR to identify isolate serogroups, while other studies used additional techniques including WGS (n=5), SASG (n=1), direct PCR (n=1), and Ouchterlony serological technique (n=1). Two studies reported on their comparison of laboratory methods, and two studies did not describe the laboratory techniques used.

3.1.4.3.2 Statistical methods general adolescent populations

Of the eight studies that examined risk factors for carriage two used univariable analysis, and six used multivariable analysis to identify relationships and estimate the scale of those relationships. One study did not examine any risk factors, focusing instead on carriage prevalence and analysis of laboratory methods.

3.1.4.4 Carriage of *n. Meningitidis*

Carriage varied significantly according to setting and geographic location. Four studies that included primary and secondary school children and university students demonstrated that adolescents experienced higher carriage than children.[4,68,70,81] Geographic location, or differing cultural values and behaviours between geographic locations, appear to account for a wide variation in adolescent carriage, with higher carriage in the UK (range 31.0—47.0%), New Zealand (24.8%), Canada (21.9%) and the USA (range 14.6—24.0%). Carriage was lower in European countries of Norway (16.0%), Portugal (13.3%) and Greece (10.4%), and in Korea (range 12.7—14.0%). Low carriage in South American were demonstrated in Brazil (12.1%) and Chile (4.0%), and in Australia (8.6%) and India (1.5%). Eight studies conducted within the UK show variation of carriage over time, within school (range 32.8% in 2006 —13.9% in 2015) and residential college populations (range 34.2% in 1997—46% in 2016), however there was less variation over time between studies of adolescent carriage in Korea (range 14% in 2009—12.7% in 2018). From the studies included within this review the most prevalent result from serogroup analysis was capsule null locus and non-groupable (15 studies), followed by serogroup B (6 studies) and Y (5 studies). Serogroup B was most frequently reported as the second most prevalent serogroup (14 studies). One study from Brazil reported serogroup C being the most prevalent.

3.1.4.5 Laboratory methods

Seven studies compared different specimen collection and sampling techniques. Variables considered included anatomical location specimens were collected from, time and location for

plating samples, use of a plate compared with use of enrichment broth or transport medium, and various test methods for identifying isolates and serogroups.

3.1.4.5.1 Swab site

As *N. meningitidis* colonises the pharynx, swabs were taken from either the nasopharynx or the oropharynx. No studies compared collecting specimens from the two sites, nor did any provide any evidence that nasopharyngeal or oropharyngeal was preferable to the other. One cohort study that involved repeat visits used nasopharyngeal swabbing[63], and noted a high incidence of loss to follow up compared to repeat cross sectional studies that used oropharyngeal swabbing.[21,75,77,78] It is possible that the more invasive nature and discomfort of nasopharyngeal swab collection increased loss to follow up. One recent study compared genomic analysis of saliva with genomic analysis of oropharyngeal swabs.[79] The same transport medium (skim milk, tryptone, glucose and glycerol or STGG) were used for both saliva and swabs. Following genomic analysis, it was found that swabbing identified 6.2% carriage, whereas saliva identified 5.4% carriage. Of the nine participants that were positive for *N. meningitidis* in both swab and saliva, isolates were grown from six saliva specimens, compared with seven swab specimens. The author reported that saliva offered few benefits and involved more resource to process at the time of collection, however, is undoubtedly less invasive.

3.1.4.5.2 Time to plate

Conflicting evidence has previously been published regarding the significance of time taken to plate specimens, with opposing studies advocating for either immediate plating on site[87] or using transport medium to delay plating until the laboratory.[88] The majority of the 27 studies plated specimens onsite (n=13) as opposed to in the lab (n=8). Of the eight studies that plated samples in the laboratory, samples were delivered within either six (n=1), five (n=2) four (n=2) or three (n=1) hours of collection, with two studies not specifying the timeframe. Two additional studies used a combination of methods, with one study reporting results of investigating time delay prior to freezing samples.[79] The authors transported swabs in STGG, then compared results of rt-PCR carried out prior to freezing, with isolates that could be cultured after freezing, following time delay from collection to freezing of 6 hours (23/26, 88.5%) or 16 hours (24/26, 92.3% of isolates grew) or 48 hours (14/26, 53.9%). The authors surmise that use of an appropriate transport media successfully enabled a delay to processing or freezing in the laboratory, however a delay of more than 16 hours was detrimental.[79]

3.1.4.5.3 Laboratory methods.

Once specimens had been plated, plates incubated, and *N. meningitidis* isolates identified, studies used a variety of analytical laboratory methods to identify serogroup and other distinguishing characteristics. Laboratory methods used by studies included WGS, PCR/rt-PCR, SASG and serogrouping by the Ouchterlony method.

Six studies compared different laboratory methods. Van Ravenhorst et al found that of serogroup B isolates characterised by WGS (n=72), isolate PCR and the Ouchterlony method correctly identified the serogroup in 65 (76%) and 37 (51%) respectively, providing a hierarchy of effectiveness for laboratory methods in their study.[21] Van Ravenhorst et al. found 10 isolates that were identified by PCR, which were not identified by WGS. Of the 10 additional isolates identified by PCR, 9/10 did not grow in culture, and 1/10 grew but lacked capsule locus when WGS was carried out. They concluded that WGS was the current gold standard for laboratory analysis. However, currently WGS is an expensive process and is hard to access, with few New Zealand facilities offering WGS.

More accessible technologies include isolate PCR and SASG. Isolate PCR was found by all studies to be either as reliable[69] or more reliable than SASG.[4,78,86] Gilca et al. and Jeppesen et al. found that SASG identified only 60% and 48% of the serogroup B isolates identified by isolate PCR in their respective studies.[4,86] Breakwell et al. found that SASG identified 0.7% of isolates as serogroup B in both rounds of their study whereas isolate PCR identified 1.8% and 2.6%.[78] Similar results were found for overall carriage, with isolate SASG identifying 0.0—0.2% carriage, compared to isolate PCR identifying 0.9—1.0% carriage. In addition, isolate PCR had the advantage of classifying fewer *N. meningitidis* isolates as non-groupable (n=188/248) when compared with isolate SASG (n=230/248). Rodrigues et al. also noted that PCR led to fewer non-groupable results, with 10% more serogroups identified via PCR when compared to SASG, despite both methods identifying the same number of isolates.[69]

While the majority of studies plated specimens, either on-site or at the laboratory, and used PCR to test isolates, four studies examined the effect of directly testing swabs (without plating them) or directly testing the medium in which swabs have been placed. Gilca et al. collected two swabs simultaneously then plated one and placed the other in Digene transport medium.[86] Specimens from university students resulted in 58 serogroup B positive results (defined as positive by at least one method), of which 53 were identified by PCR of plated isolates, and 35 were identified by PCR directly from a swab. Gilca et al. also noted that although samples taken directly from swabs enabled a positive or negative result, the lack of an isolate for further analysis was a disadvantage. PCR of isolates was also more effective at identifying carriage than direct PCR for Van Ravenhorst et al. and

Jeppesen et al., who found direct PCR only identified 76% and 69% of serogroup B isolates in their respective studies. Rizek was the only author who found that direct PCR test of swabs identified more *N. meningitidis* carriage (n=132/190, 69.5%) than PCR of isolates (n=23/190, 12.1%) following analysis of dual samples from 190 medical students.[72] Rizek et al. point out that while having an isolate to test for antibiotic susceptibilities is important for guiding treatment following IMD, for carriage studies retaining a culture is of less concern. They suggest that direct PCR may be more effective because there are more variables involved in culturing on a plate, including sampling and plating technique, transportation, storage and bacterial autolysis. However they also acknowledge that PCR has limitations, including a propensity to identify non-viable micro-organisms.

3.1.4.6 Risk and protective factors for carriage of *n. Meningitidis*

Several risk factors have been associated with higher prevalence of carriage of *N. meningitidis*, including adolescence, male gender, attending clubs and parties at least once a week, and smoking, while other factors have been found to have a protective effect, such as recent anti-biotic use and vaccination with a conjugate meningococcal vaccine.[2] This chapter outlines the findings of my literature review in relation to risk and protective factors for carriage of *N. meningitidis* among students residing in residential colleges.

3.1.4.6.1 Age

Although age within residential colleges is not a variable that will differ greatly, the age at which most residents arrive at residential colleges is the age at which carriage is most prevalent. In a 2010 meta-analysis of 89 carriage studies, Christensen et al. found that the relationship between carriage and age was non-linear, increasing through childhood from 4·5% in infants to 7·7% in 10-year olds and peaking at 23·7% in 19-year olds before decreasing into older adulthood (13·1% in 30-year olds and 7·8% in 50-year olds).[5] Several studies note the association between age and carriage in observational or univariable analysis.[4,68,79,81,86] The extent to which age acts an independent variable is investigated by five studies.

McNamara et al. carried out a repeat cross-sectional study with 3,802 university students aged 18 upwards at a single university in Oregon, United States, during a meningococcal vaccination campaign in 2015.[75] Multivariable analysis of baseline carriage data showed of participants ages 18—22, age 20 had the highest prevalence of carriage (adjusted OR for 20 years vs 18 years, 1.6; 95% CI, 1.1—2.3, *P*=.02). Tryfinopoulou et al. carried out a cross-sectional study of 680 military

recruits and 740 university students, 18—26 years of age, from various locations in Greece during 2015.[71] Multivariable analysis was reported as showing that being 18—21 years of age was an independent risk factor (adjusted OR 1.81, p=0.001), compared to being 22—26 years of age. Unfortunately, Tryfinopoulou did not report which risk factors were adjusted for. Marshall et al. studied carriage in 34,000 South Australian secondary school students aged 15-18 years during a randomised control trial (RCT) in 2017.[2] Year of schooling was used as a proxy for age, and following multivariable analysis, the later the year of schooling, the higher the risk of carriage (adjusted OR for year 12 vs. year 10, 2.75; 95% CI, 2.03 to 3.73).

In contrast to the above studies, Van Ravenhort et al. carried out a repeat cross-sectional study of 1,715 Dutch adolescents aged 13—23 years in 2013—2014.[21] Carriage prevalence rose from 4.7% for age 13—14 years, to 22.6% for age 17—18 years, and univariable analysis showed a strong correlation between age and carriage (unadjusted OR 5.88, 95% CI 3.36-10.29, p<0.001) however once adjusted for other risk factors, the association weakened (adjusted OR 1.89, 95% CI 0.96-3.70, *P*=.07). Watle et al. carried out a cross-sectional study that included 2,159 Norwegian teenagers aged 13—19 years, in 2018, and found carriage was highest among 18 year olds (16.4% carriage rate) when compared to 13 year olds (unadjusted OR 9.99, 95% CI 4.10–24.33, p< 0.001). However following multivariable analysis this association disappeared (adjusted OR 0.96, 95% CI 0.31–3.02, *P*=.950).[80] Watle made the point that their results showed carriage increasing above 5% at 16 years (6% carriage prevalence), before reducing at 19 years, and suggested vaccination at age 15 year should be considered.

On balance, it appears likely that while carriage varies with age, it is most likely to be an artefact of increasing exposure to various other risk factors, including risk factors that may not be included in surveys. A limitation of relying on self-reported data are the possibility of under reporting of activities that are deemed undesirable or illegal, such as smoking water pipes, which might in turn confound results. Regardless, all studies included in this review showed a peak of carriage between ages 18—20 years, followed by a decline in participants who were older.

3.1.4.6.2 Gender

Male gender has a strong association with higher prevalence of *N. meningitidis* carriage in all carriage studies in this review, regardless of geographical location and cultural variation. Eight studies used multivariable analysis to assess whether the association between gender and carriage remains once other risk factors are accounted for. Six studies, including all four set in residential

colleges, found that the relationship persisted, with adjusted OR ranging from 1.2 (95% CI 1.0—1.5, *P*=.03) to 2.8 (95% CI 1.18—5.90, *P*=.022).[57,74,75,81,82,84] The two remaining studies were both set in schools, examining carriage in 15—18 and 13—18 year olds in Australia and Norway respectively. Marshall et al.'s study of 34,459 secondary students in 2017, of whom 668 were positive for *N. meningitidis* carriage, found the adjusted OR for males vs females was 1.09 (95% CI 0.92—1.29), with the confidence interval containing the null hypothesis value of one, and therefore not achieving statistical significance.[2] Watle et al.'s study of 2,159 Norwegian teenagers in 2018, of whom 159 were positive for carriage, found being female was a protective factor, however following multivariable analysis the result was not statistically significant (adjusted OR 0.79; 95% CI 0.53—1.17 *P*=.235).[80] These two results are less applicable to residential college settings, as the studies were based in school settings, and in populations with relatively low carriage prevalence (1.8—7.8%). The evidence presented in the studies suggest that during adolescence there are cultural or behavioural aspects that make male gender an independent risk factor for carriage of *N. meningitidis*.

3.1.4.6.3 Ethnicity

The role that ethnicity has as a risk or protective factor for carriage does not appear to have been widely studied, despite differences in carriage prevalence between countries with different cultures. Three studies enable us to assess the role ethnicity has as a risk factor. Durey et al. carried out a repeat cross-sectional study of 158 university students in South Korea in 2009 and found a relatively low carriage prevalence (14.1%) compared with carriage prevalence reported in the UK, North America and New Zealand. While Durey et al. did not include ethnicity as a risk factor, perhaps due to the low level of ethnic diversity in their small sample, McMillan et al. and Marshall et al. were able to include ethnicity in their risk factor analysis for their Australian based studies. In 2019, during university orientation week, McMillan et al. carried out a repeat cross-sectional study of 421 South Australian university students, including Caucasian (65.1%) and Asian (26.9%) ethnicities among others, and found that although carriage prevalence were lower among Asian participants (2.7% compared to 7.4% for Caucasian and 9.1% for ethnicities categorised as other) the unadjusted OR of 0.36 (with Caucasian as reference) was not statistically significant (95% CI 0.10—1.88, *P*=.09). The aforementioned RCT of secondary school students by Marshall et al. had a much larger sample and does report a statistically significant adjusted OR 0.50 (95% CI 0.31—0.80) for Asian ethnicity, with White as the reference (White is the terminology used in the paper). In addition, Marshall et al. found OR 1.34 (95% CI 0.90—2.01) for Aboriginal and Torres Strait Islander ethnicity in their sample. The results for Aboriginal and Torres Strait Islander ethnicity were adjusted for risk factors that

include the Index of Community Socio-educational Advantage (ICSEA), which is a scale of socio-educational advantage that is computed for each school, however there may be other confounding risk factors that were not adjusted for that contribute to the impact ethnicity appears to have on carriage.[89] The findings of these three studies suggest that ethnicity can be either a risk or protective factor for the general population. It is likely that cultural attitudes and behaviours mediate other risk factors, in the same manner that age and gender do. It is also possible that the effect of ethnicity may change with age and social circumstances, therefore future carriage studies in residential colleges should collect data on the ethnicity of students to further explore the impact ethnicity has on carriage in this group.

3.1.4.6.4 Vaccination

Vaccination provides protection against IMD, however the impact various meningococcal vaccinations have on carriage is less certain. Four studies were designed specifically to measure the impact vaccination programmes had on carriage of *N. meningitidis*, and four other studies estimate the impact of vaccination as one of several risk factors. Vaccines examined included meningococcal serogroup B recombinant vaccines, meningococcal group C conjugate vaccine, and quadrivalent meningococcal conjugate vaccines.

3.1.4.6.5 Recombinant *N. meningitidis* serogroup B vaccines

Meningococcal serogroup B vaccines from around the world, including 4CMenB, MenB-4C, and MenB-FHbp, protect against IMD caused by serogroup B. Four studies examined the relationship between recombinant serogroup B vaccines and carriage of *N. meningitidis*. In 2010 Read et al. carried out a randomised control trial on 2,954 18-24 year olds in England, comparing a control group (Japanese Encephalitis vaccine, n=984) to participants who either received recombinant (4CMenB, n=974) or conjugate (MenACWY-CRM, n=983) meningococcal vaccines.[67] Although there was no difference in carriage at one month, after three months the 4CMenB vaccine group experienced a broad reduction in carriage of all serogroups. However, the study was unable to show a specific effect of the vaccine on serogroup B carriage. While the authors adjusted for many variables, they acknowledge that the timing of the study might have been a confounding factor, as it coincided with the start of the university year, when carriage acquisition is highest, and the carriage recorded was similar to those of other carriage studies. Soeters et al. examined the impact of recombinant meningococcal B vaccine (MenB-FHbp) as part of a cross-sectional study of 2,014

Rhode Island university students during a vaccination campaign that was initiated in response to a IMD serogroup B outbreak in 2015—2016.[74] The majority of students, 73% to 91% per round, reported living on campus. Students were given up to three doses and followed up at four intervals over twelve months. Following multivariable analysis they found MenB-FHbp vaccine did not have a relationship with carriage following one dose (adjusted PR 1.5, 95% CI 1.0—2.4, *P=*.074), two doses (adjusted PR 1.4, 95% CI 1.0—2.1, *P=*.082) and three doses (adjusted PR 1.6, 95% CI 0.9—2.7, *P=*.124). The aforementioned study by McNamara et al. also examined the impact of both the MenB-FHbp and MenB-4C vaccines during a vaccination campaign, enrolling 3,802 university students, and carrying out four surveys over 11 months.[75] Few students completed the full course of vaccinations, limiting analytical power of the study, however following multivariable analysis there was no evidence of a protective effect on carriage for either MenB-FHbp (3 doses, adjusted OR 1.3, 95% CI 0.7—2.2, *P=*.4) or MenB-4C (2 doses, adjusted OR 1.5, 95% CI 1.0—2.3, *P=*.08). Finally, the RCT carried out by Marshall et al. provides perhaps the most compelling evidence, having studied 34,489 students in school years 10—12 (ages ~15—18), over 12 months.[90] Students were vaccinated either at the beginning of the study, or at the end (controls). There was little difference in carriage between the control group (2.52%) and the vaccinated group (2.55%), with the adjusted OR 1.02 (95% CI 0.80—1.31, *P=*.85).

3.1.4.6.6 Conjugate vaccines

Conjugate meningococcal vaccines include quadrivalent MCV4, MenACWY-T, MenACWY-CRM and MenACWY-D, which all protect against IMD from serogroup A, C, W, and Y. The monovalent group C conjugate vaccine MenC protects against IMD caused by serogroup C. Eight studies within this literature review evaluated the relationship between conjugate vaccines and carriage of *N. meningitidis*, comprising three that examine MenC vaccine, and five that examine MenACWY vaccines.

Three authors provided observational data suggesting that previous MenC vaccination campaigns have been responsible for low carriage prevalence of serogroup C. All lack pre-vaccination baseline data. Rodrigues et al. carried out a cross-sectional study on 601 Portuguese university students in 2012, and noted high MenC vaccine coverage in Portugal since the vaccine was introduced in 2006, and suggested this was responsible for the low carriage prevalence of 0.3% for serogroup C.[69] Tryfinopoulou noted of 740 participants from a university, 76.2% self-reported receiving a MenC vaccine, which was a scheduled immunisation in Greece from 2001, and proposed that this may account for the zero carriage of serogroup C detected in their study carried out in 2015.[71] Van

Ravenhorst et al. studied 1,715 adolescents in the Netherlands during 2017 and identified only six isolates with serogroup C loci, but expression of capsule was not detected in any.[21] The authors speculate that the low carriage prevalence may have been attributable to high MenC vaccine uptake (with coverage >90% in the Netherlands), however, like all the aforementioned studies, they had no pre-vaccine baseline to compare MenC carriage prevalence to. Moving beyond the full text articles included in this literature review, there is evidence from a letter published in 2002 that prevalence of serogroup C carriage has been low prior to extensive vaccination campaigns, and periods with relatively high prevalence of IMD C, suggesting that serogroup C carriage may be transient and hard to detect.[91] Therefore it is hard to conclude from the above three studies that the MenC vaccine is responsible for the low prevalence of carriage encountered.

The five studies that examined MenACWY vaccines were able to collect baseline data prior to vaccine administration, strengthening confidence in their findings. Only two were able to access medical records or immunisation databases, while the rest relied on self-reported vaccination history which is less reliable. In 2010 Read et al. found that although MenACWY-CRM had not reduced carriage one month after administration (adjusted OR 0.9, 95% CI 0.6—1.3), when measured at 12 months a reduction in carriage of 36.2% (95% CI 15.6—51.7) was observed for serogroups C,W, and Y.[67] In 2015 Breakwell et al. carried out a repeat cross-sectional study of 1,837 undergraduate students aged 19—21 years in the United States, 1,609 (87.6%) of whom had evidence of MenACWY vaccination on their medical record.[78] Following bi-variable analysis the prevalence ratio (PR) for carriage of any *N. meningitidis* following one or two doses of MenACWY was 1.33 (95% CI 0.90—1.98, *P=.*15) and 1.23 (95% CI 0.80—1.89, *P=.*35) respectively, relative to baseline carriage pre vaccination. These results suggest an absence of a statistically significant relationship. However, the study found few serogroup C or Y isolates, and no serogroup W isolates, suggesting that MenACWY may have had some impact on carriage of these serogroups. Soeters et al. reported 95% of participants in their study self-reported receiving MenACWY at least two weeks prior to specimen collection, and found that MenACWY was not associated with carriage of *N. meningitidis* (bivariable prevalence ratio 1.1, 95% CI 0.8—1.6, *P=.*633).[74] The authors noted that a limitation of their study was that it spanned two academic years, and was broken by a summer break in between. The subsequent disruption in social-mixing, and the intake of new students, may have resulted in a lower carriage prevalence, which may have underestimated the effect of the vaccines examined (both MenACWY and MenB-FHbp). Oldfield et al. noted a substantial increase in serogroup W carriage during their repeat cross-sectional study of 1,410 first year students residing in residential colleges in the United Kingdom in 2016.[74] Vaccination levels went from 30% on enrolment in the study to ~70% following induction to the university. Baseline specimens were collected on

enrolment in September 2015 from 769 students, revealing a carriage prevalence of 14% for serogroups combined, and 0.7% for serogroup W. Follow up specimens collected during March 2016, from 288 students, revealed a carriage prevalence of 46% for serogroups combined, and 8.0% for serogroup W. Of note, the follow up specimens were not necessarily from the original participants, and all follow up participants resided in residential colleges, although the authors report that the demographics of the two groups were similar. While the authors do not report any risk factor analysis, it seems logical to conclude that such a high rate of acquisition in a well vaccinated population suggests MenACWY vaccine may not protect against carriage. Watle et al. found no statistically significant association between vaccination with MCV4 (a meningococcal ACWY conjugate vaccine) and carriage of all serogroups (adjusted OR 0.86, 95% CI 0.59—1.26, *P=.*442) among Norwegian teenagers.[80] This finding is particularly credible as they were able to access the Norwegian immunisation database to verify vaccination history of participants, rather than rely on self-report.

3.1.4.6.7 Close living arrangements

The association between close living arrangements in dormitory type accommodation and carriage of *N. meningitidis* appears in literature as far back as 1918, when Captain Glover identified increased carriage in overcrowded barracks during World War One (carriage of 25% in severely overcrowded barracks, as opposed to 5% in barracks with no overcrowding).[33] In New Zealand Baker et al. carried out a case control study of 202 cases of confirmed or probable meningococcal disease between 1997—1999.[34] Although not focused on carriage per se, the study highlighted the increased risk of transmission associated with overcrowded living conditions, with those living in households with more people aged over ten years per room having a higher likelihood of disease than households with fewer people (OR 10.7, 95% CI 3.9-29.5). Ten of the studies included in this literature review examined the role of close living arrangements, in either dormitories (shared rooms) or residential colleges (single rooms or shared rooms with other shared facilities). In 1997 Neal et al. carried out a repeat cross-sectional study on 2,507 first year United Kingdom university students, the majority of whom (2,284/2,507) were students residing in residential colleges. The study found that more time off campus was protective (adjusted OR 0.64, 95% CI 0.5—0.9, *P=.*01) and that catered halls, where presumably students had more frequent mixing, had higher prevalence of carriage than self-catered halls (12.9% vs 10.3%).[57] Tryfinopoulou et al.'s 2015 study of Greek university students and military recruits found that living in crowded conditions was an independent risk factor for carriage (adjusted OR 1.45, *P=.*04, no confidence intervals published by the author), however it is unclear how many of

those living in crowded conditions were students.[71] In 2017 He et al. carried out a cross-sectional study of 663 Chinese students aged 15—19 years, after noticing a spike in carriage of *N. meningitidis* during annual surveillance.[81] They found an association between density of students in classrooms and carriage, with >1 persons/m² resulting in adjusted OR 2.12 (95% CI 1.50—3.00, *P*=.007). They also found that increased time spent in classrooms (14 hours in class) resulted in adjusted OR 3.70 (95% CI 1.42—9.63, *P*=.007). While the results from He et al. support the likelihood that increased transmission is associated with crowding and increased time of exposure, it is unclear from their study if any of the students lived in dormitories, and they only adjusted for four variables (classroom density, time in class, gender, and recent antibiotics), making it possible that other confounding factors may be influencing the strength of the relationship.

Several studies indicate there is no relationship between carriage and close living arrangements in adolescents and university students. Breakwell et al. examined living arrangements in their repeat cross-sectional study of university students from the USA, and found that among the 77% of participants that resided in residential halls, the adjusted prevalence ratio for carriage of 0.85 (95% CI 0.66—1.10, *P*=.23) was not statistically significant.[78] McNamara's study of university students, 37% (1,398/3,809) of whom lived in residential halls, reported that residence type (hall/house/fraternity) nor the number of room-mates (0—>3) had a statistically significant relationship with carriage prevalence.[75] In 2015 Kim et al. carried out a cross-sectional survey of 1,460 Korean 16 year olds, of whom 4.5% (66/1460) resided in dormitory accommodation. Kim et al. reported those in dormitories had an adjusted OR 0.9 (95% CI 0.21-3.77, *P*=.88) for carriage. In their large RCT of South Australian students, Marshall et al. did not find that being a boarding student was a statistically significant independent risk factor for carriage (adjusted OR 1.33, 95% CI 0.72—2.43).[2] Soeters et al. found that living on campus was not a statistically significant risk factor (bivariable prevalence ratio 0.9, 95% CI 0.8—1.1, *P*=.544)[74], and McMillan et al. found that living with 5 or more others was not a statistically significant risk factor (unadjusted OR 1.08, 95% CI 0.45—2.54, *P*=.85).[79] Finally, Choi et al.'s 2018 repeat-cross sectional study of 332 South Korean students residing in residential colleges living in dorms found no statistically significant association between having three or more room mates and carriage (unadjusted OR 1.21, 95% CI 0.59—2.46, *P*=.724).[82]

3.1.4.6.8 Recent Illness

Whether recent illness is an independent risk factor for carriage of *N. meningitidis* has been studied by several authors. Breakwell et al.'s study of 1,478 students residing in residential colleges in the United States found that a self-reported upper respiratory tract infection (URTI) in the past 14 days

was associated with carriage, with an adjusted OR 1.23 (95% CI 1.00—1.51, *P*=.049).[78] Marshall et al. also found that there was an independent association, with 7,213/34,172 secondary students self-reporting URTI and having an adjusted OR 1.35 (95% CI 1.12-1.63).[90]

Kim et al. found that URTI was not associated with carriage in their study of South Korean 16 year olds (unadjusted OR 0.47, 95% CI 0.15—1.54, *P*=.203).[73] McNamara et al. also failed to find a statistically significant relationship between URTI in the previous 30 days and carriage (adjusted OR 1.1, 95% CI 0.9—1.3, *P*=.2)[75], as did Soeters et al. (unadjusted prevalence ratio 1.1, 95% CI 1.0—1.2, *P*=.064)[74] and Tryfinopoulou et al. (unadjusted OR 0.74, 95% CI 0.48—1.14, *P*=.168).[71] Watle et al. and Choi et al. both reported UTRI in the past week was not independently associated with carriage, with adjusted OR 0.88 (95% CI 0.61—1.26, *P*=.486)[80] and adjusted OR 1.86 (95% CI 0.73—4.72, *P*=.194)[82] respectively. Lastly, McMillan collected self-reported data on participants who had a cold or sore throat at the time of specimen collection, and found no relationship with carriage (unadjusted OR 2.17, 95% CI 0.83—5.67, *P*=.11).[79] Other authors examined recent illness but did not report their results[70] or had too few participants to provide a statistically reliable result.[65]

The results from Breakwell's high quality study of students residing in residential colleges are particularly relevant to the subjects of this study. Marshall's large study from Australia is also very applicable to New Zealand, given the cultural and therefore behavioural similarities. The studies that found no statistically significant association were smaller, or not based in residential colleges, or less culturally and behaviourally aligned, suggesting that on the balance of evidence, recent respiratory illness may be an independent risk factor for university students residing in residential colleges in New Zealand.

3.1.4.6.9 Antibiotic use

While several studies excluded participants who reported recent antibiotic use, other studies examined the impact of recent antibiotic use as a risk or protective factor for carriage. MacLennan et al.'s study of 14,000 UK 15—19 year olds provided evidence that self-reported recent or current antibiotic use is protective against *N. meningitidis* carriage (adjusted OR 0.66 (95% CI 0.52—0.83, p<0.001).[62] This finding was supported by Breakwell et al., McNamara et al. and Soeters et al., who reported adjusted OR 0.42 (95% CI 0.27—0.65, p<0.01)[84], adjusted PR 0.4 (95% CI 0.3—0.7, p<0.0001) [75] and adjusted PR 0.4 (95% CI 0.3—0.6, p<0.001) respectively.[74] Two studies that examined antibiotic use found that antibiotics were neither protective nor a risk factor for carriage. Choi et al. reported that among their sample of Korean university students antibiotic use in the

previous two weeks had an unadjusted OR 1.32 (95% CI 0.48—3.63, *P*=.781)[82], and McMillan et al. reported antibiotic use in the previous month had an unadjusted OR 0.80 (95% CI 0.18—3.55, *P*=.78).[79] Both studies had fewer than 500 participants. It is likely that antibiotic use is protective against carriage for students in residential colleges.

3.1.4.6.10 Smoking

Cigarette smoking has long been linked to increased carriage of *N. meningitidis*, and almost all studies in this review report smoking as an independent risk factor. However, the strength of the relationship follows a general downwards trend over time, and the most recent studies found smoking was not a statistically significant independent risk factor. This may be related to a decrease in the number of smokers in society, and consequently study participants. In 2000 Neal et al. studied 2,507 students residing in residential colleges and found smokers had an adjusted OR of 2.4 (95% CI 1.6—3.7, *P*=.0001).[57] In 2006 MacLennan et al. studied 14,000 UK adolescents 15—19 years of age, and found that smoking 6-10 cigarettes per day led to an adjusted OR 1.69 (95% CI 1.43-2.00, p<0.001), and established a dose dependant relationship, with the higher the number of cigarettes smoked per day, the higher the OR.[62] US students residing in residential colleges were studied by Breakwell et al. in 2015, and Soeters in 2017, and they found an adjusted OR 1.53 (95% CI 1.21—1.94, p<0.01)[84] and adjusted PR 1.3 (95% CI 1.1-1.5, *P*=.003)[74] respectively. Marshall et al.'s large RCT in South Australia in 2017 found that any self-reported smoking in the past week resulted in an adjusted OR 1.91 (95% CI 1.29-2.83). From the above evidence it is clear that there is an independent relationship between smoking and carriage of *N. meningitidis*. Two recent studies found smoking was not associated with carriage. Watle et al.'s study of Norwegian adolescents found an adjusted OR 1.35 (95% CI 0.92—2.00, *P*=.126) for any smoking, and McMillan et al.'s study of South Australian university students found an unadjusted OR 2.22 (95% CI 0.26—18.73, *P*=.47). However, while Watle et al. had 295/2159 smokers in their study sample, only 9/295 smoked daily, with the rest being categorised under 'Occasionally'. Similarly, McMillan et al. only had 8/421 smokers in their sample. These low numbers is the likely reason for the lack of statistically significant associations. The mechanism by which smoking influences carriage is unclear, however Watle et al. found that Swedish Snus, a moist form of smokeless tobacco that is placed under the upper lip, was an independent risk factor for carriage (adjusted OR 1.56, 95% CI 1.07—2.27, *P*=.02)[80], suggesting that the components of tobacco itself may make individuals more susceptible, as opposed to other variables associated with smoking.

3.1.4.6.11 Exposure to cigarette smoke

While there is strong evidence for the relationship between smoking and carriage of *N. meningitidis*, there is little evidence from the literature in this review that confirms exposure to cigarette smoke, or passive smoking, is an independent risk factor for carriage of *N. meningitidis*. Nine studies examined the exposure to cigarette smoke, with only two providing some evidence of an association. In 2000, Neal et al. compared days of exposure to cigarette smoke (1—7 days), and results indicate a dose dependent relationship, with increasing days of exposure resulting in increasing OR.[57] Using zero to two days exposure as the reference point, Neal et al. found that three to six days exposure lacked statistical significance, but 7 days of exposure was associated with carriage of *N. meningitidis* (adjusted OR 2.03, 95% CI 1.3—3.1, *P*=.001). In their 2006 study MacLennan et al. do not measure days of exposure to cigarette smoke, however they found that living in a house with others who smoke was associated with an adjusted OR 1.17 (95% CI 1.05—1.30, *P*=.004) when compared to not living in a house with others who smoke. None of the other studies found a statistically significant relationship between exposure to cigarette smoke and carriage of *N. meningitidis*. An influencing factor may be reduction in smoking over time, and amendments to legislation that have reduced smoking in enclosed spaces.

3.1.4.6.12 Electronic cigarette use

Literature on the impact that e-cigarette use has on carriage of *N. meningitidis* does not appear to have been published prior to 2020. Two studies included analyses of the role of e-cigarettes as risk factor for carriage. Marshall et al. included 370 participants who reported smoking an e-cigarette in the previous week, from a total of 34,132 Australian secondary school students used for risk factor analysis.[2] E-cigarette use does not feature in the table of multi-variable results, but there is a footnote stating that it was included in the multivariable model. The author kindly supplied the results of their analysis, which showed that while e-cigarette users had a higher prevalence of carriage (10.5% carriage vs 3.4% for no e-cigarette use), and univariable analysis showed OR 3.31 (95% CI 2.31—4.74, p<0.0001) for those that used e-cigarettes compared to those who did not, following multivariable analysis the results lost statistical significance (adjusted OR 1.17; 95% CI 0.74—1.85, *P*=.5051).[90] The second study was carried out by Watle et al., and included 75 occasional and 9 daily users of e-cigarettes among 2,159 12—24 year old Norwegian adolescents.[80] Again, e-cigarette users had higher prevalence of carriage (19.1% compared to 6.8% for non-users), and unadjusted OR 3.11 (95% CI 1.79—5.39, p< 0.001), but following multivariable analysis the results

lost statistical significance (adjusted OR 1.63; 95% CI 0.92—2.88, *P*=.092). The conclusion from these studies was that e-cigarette use does not appear to be an independent risk factor following multivariable analysis. However, Watle et al. had only 9/1,277 daily e-cigarette users and 286/1,277 occasional users. Without further detail on how occasional is defined, it may be that the actual exposure to e-cigarettes was low, and subsequently underrepresented. The same may hold true for Marshal et al., who did not define the degree of exposure to e-cigarette use in their 370 e-cigarette users. It is possible that the degree of exposure secondary students had was lower than the exposure students residing in residential colleges had, particularly in South Australia, where e-cigarette use under the age of 18 is illegal.[92] For this reason, and due to the growing popularity of e-cigarette use, and with over 50% of New Zealand 18—24 year olds experimenting with e-cigarette use, further investigation of the effect e-cigarette use has on carriage among university and students residing in residential colleges may be beneficial.[93]

3.1.4.6.13 Attendance at clubs, bars, and parties

Attendance at crowded noisy venues, such as pubs, bars and parties is a recognised risk factor for meningococcal carriage. Such events often occur at the intersection of other risk factors, such as smoking and kissing, but evidence from 12 studies in this literature review shows that parties, bars, night clubs or crowded places are independent risk factors for carriage. Four of those studies demonstrated a dose dependant relationship, with more times attended increasing the OR. Neal et al. studied students in a residential college in 1997, and found 1-4 visits to a pub resulted in an adjusted OR 1.74 (95% CI 1.1—2.8, *P*=.03) and >5 visits resulted in OR 2.71 (95% CI 1.5—4.8, *P*=.0005), while visits to nightclubs resulted in adjusted OR 1.25 (95% CI 1.0-1.6, *P*=.05).[57] Other studies set in residential colleges include those by Breakwell et al. in 2015[78], Soeters et al. in 2017[74], and Choi et al. in 2018[82] found visits to crowded venues more than once a week resulted in adjusted OR 2.03 (95% CI 1.52—2.72, p<0.01), adjusted OR 1.8 (95% CI 1.5-2.1, p<0.001) and adjusted OR 3.70 (95% CI 1.54-8.92, *P*=.004) respectively. Studies in general university settings include those by McNamara and McMillan. McNamara found attending one bar, club or party per week resulted in adjusted PR 2.0 (95% CI 1.6-2.5, p<0.0001), and attending 2-3 times per week resulted in adjusted PR 2.8 (95% CI 2.2—3.6, p<0.0001).[75] McMillan et al. found attending two or more parties or bars in the week prior to specimen collection resulted in an unadjusted OR 7.29 (95% CI 2.51—21.18, p<0.001).[79] Among the six studies in general adolescent populations that examined this risk factor, those by MacLennan and Marshall have particular significance due to their size and the similarity of cultural behaviours with New Zealand. MacLennan et al. examined 14,000 adolescents in the UK in

2006 and found that one night attending pubs or clubs in the week prior to specimen collection resulted in OR 1.52 (95% CI 1.33—1.75, p<0.001), and that the adjusted OR increased incrementally up to 2.27 (95% CI 1.79—2.87, p<0.001) for five to seven nights.[62] In 2017 Marshall et al. examined 34,290 South Australian 15-18 year old students and found that one or more days out in public bar or club in the week prior to specimen collection resulted in adjusted OR 1.54 (95% CI 1.28—1.86).[2]

3.1.4.6.14 Intimate kissing

Nine studies included in the literature review examined the association between kissing and carriage of *N. meningitidis*. Unfortunately, there was little consistency between studies in terms of the definition used for kissing, meaning comparison is difficult. Neal et al. examined the relationship between number of persons intimately kissed and carriage, reporting that kissing one other person increased the odds of carriage (adjusted OR 1.4, 95% CI 1.0—1.8, *P*=.04) among students residing in residential colleges.[67] In 2006 MacLennan et al. carried out a cross-sectional study on 14,000 United Kingdom school students, 15—19 years of age, and found an association between kissing and carriage, with the adjusted OR increasing from 1.49 (95% CI 1.34—1.66) for one person kissed, to 2.00 (95% CI 1.44—2.78, p<0.001) for three persons kissed in the last week.[62] In 2012 Rodriguez et al. carried out a cross-sectional carriage study with 500 Chilean 18—24 year old university students, and following univariable analysis did not find a statistically significant relationship between carriage and the number of people kissed in the last month (unadjusted OR 1.43, 95% CI 1.0—2.1, *P*=.05).[66] Van Ravenhorst et al.'s study of 1715 Dutch 13—23 year olds, in 2013, found that the number of people kissed in the previous week did have a relationship with carriage, with the adjusted OR 1.99 (95% CI 1.48-2.67, p<0.001).[21] In 2019 McMillan et al. studied 421 South Australian university students during their orientation week, and found that despite a surprisingly low carriage prevalence (n=26/421, 6%) kissing one or more persons in the last week had an adjusted OR 4.13 (95% CI 1.63—10.45, *P*=.0014).[79] In 2020 Marshall et al.'s large study in South Australian teenagers found intimate kissing was related to carriage, with an adjusted OR of 1.65 (95% CI 1.33—2.05)[90], and Watle et al.'s study of Norwegian teenagers found kissing more than two people had an adjusted OR 2.76 (95% CI 1.49—5.10).[80] The only study that did not find a statistically significant connection between intimate kissing and carriage was published by Choi et al. in 2021, who found that those South Korean students residing in residential colleges who had intimate contact with another person in the previous four weeks had an adjusted OR 1.31 (95% CI 0.63—2.7, *P*=.47). This result may be influenced by the small number of participants who experienced intimate contact (n=77), a lack of

definition of what intimate contact constituted, but may also reflect cultural differences between western and Asian cultures.[82]

3.1.4.6.15 Other possible risk factors:

The association between several other possible risk factors and carriage of *N. meningitidis* were examined, but often only by one or two studies.

3.1.4.6.16 Deprivation

Deprivation was studied in 2011 by Cleary et al., who conducted a cross-sectional study of 469 UK 5—18 year olds, and used the UK Index of Multiple Deprivation 2010 score which is based on postcode.[68] Cleary et al. noted that carriage was higher in deprived areas, at 17.7%, compared with least deprived areas, at 5.6%, and drew the conclusion that deprivation is one of the most important predictors of carriage. However, the degree of association between various Index of Multiple Deprivation scores and carriage prevalence was not consistent, and the four unadjusted ORs for each Index of Multiple Deprivation score lacked statistical significance, indicating that deprivation may not be an independent risk factor.

3.1.4.6.17 Level of parental education

In 2012 De Moraes et al. found that among 1,208 Brazil students, 11—19 years of age, having parents with a lower level of education was independently associated with a higher risk of carriage (adjusted OR 2.14, 95% CI 1.11—4.12, *P*=.022).[70]

3.1.4.6.18 Water pipe use

In their large RCT in South Australian 15—18 year olds Marshall et al. found that water pipe use in the week preceding specimen collection was an independent risk factor for carriage (adjusted OR 1.82, 95% CI 1.30—2.54).[2] Because smoking, particularly smoking of illicit substances, is illegal for 15—18 year olds in South Australia the risk factor may have been under reported, which may have under estimated Marshal et al.'s finding. McMillan also examined water pipe use, but with only 14 participants reporting use of water pipes, lacked numbers required for a statistically reliable result.[79]

3.1.4.6.19 Alcohol

In 2017 Van Ravenhorst et al.'s study of Norwegian teens aged 13—23 found an independent association between drinking alcohol and carriage (adjusted OR 2.42, 95% CI 1.54—3.81, p<0.001).[21]

However Choi et al. studied this association and did not find a statistically significant result, with adjusted OR 1.91 (95% CI 0.23—15.73, *P*=.546).[82] While van Ravenhorst et al.'s study was larger, a comparison between the two results is problematic due to unknown variables, such as the type of alcohol, the setting in which alcohol was consumed, and other factors that may be influenced by cultural differences between the Netherlands and Korea. It is surprising that alcohol has not been investigated more frequently, given the association between crowded venues and carriage of *N. meningitidis*.

3.1.4.6.20 Russ/orientation week celebrations

The inclusion of the Russ celebration in Watle et al.'s 2018—2019 carriage study has particular significance for studies of carriage among university students. Russ is a week-long event that celebrates the end of schooling for adolescents in Norway, and involves drinking and social mixing. This event is similar to university orientation weeks. Watle et al. found attendance at Russ was an independent risk factor for carriage of *N. meningitidis* (adjusted OR 2.85, 95% CI 1.62—5.02, p<0.001).[80] While other studies have noted the rapid increase in carriage of *N. meningitidis* at the beginning of the university year, this is the only study in this literature review to include an orientation week type event as an independent risk factor.

3.1.5 Conclusion

There is strong evidence that adolescence, male gender, attendance at clubs/bars/parties, intimate kissing, smoking, water pipe use, recent illness and close living arrangements are independent risk factors for carriage of *N. meningitidis.*

There is some evidence, from studies of varying quality, that smokeless tobacco use, deprivation, ethnicity, alcohol use, and large communal events targeting young people (such as university orientation week events) are risk factors for carriage, but further investigation would be beneficial.

The evidence suggests that recombinant *N. meningitidis* serogroup B vaccines do not protect against carriage of *N. meningitidis*, and that while historical evidence suggests conjugate MenC vaccination programmes have resulted in a reduction of *N. meningitidis* serogroup C carriage, more recent studies on conjugate MenACWY vaccines have not identified this protective effect against carriage.

There is some evidence that antibiotic use is protective against carriage.

3.2 2018 *N. meningitidis* Carriage Study - Methods

3.2.1 Design

As discussed in Chapter Two, numerous *N. meningitidis* carriage studies have been carried out overseas. Carriage studies are predominantly cross sectional prevalence studies[22,23,62,68,69,74,75,77,84,94,95], although some carriage studies use repeat cross-sectional methodology to observe carriage acquisition or persistence over time.[2–4,21,63,79,82] The 2018 carriage study and risk factor survey were cross sectional, without a longitudinal component.

To ensure the study samples were representative of students residing in residential colleges, all 14 of University of Otago Dunedin's residential colleges that had first year students were included. Efforts were made to recruit at least 50% of students from each college.

The carriage study involved both collecting specimens, to identify *N. meningitidis*, and administering a risk factor survey. Participation was voluntary. Information on the carriage study and risk factor survey were provided to all potential participants. All participants who consented were recruited. The expectation was that participants would be a representative sample of the broader first year residential college population, with diversity of gender, ethnicity, social, educational, and income status.

The carriage study also enabled an assessment of the impact that mass administration of antibiotics has on carriage rates in a residential college setting. Because antibiotics were administered in a residential college, with clinical urgency, in response to meningococcal disease cases, no specimen collection occurred prior to antibiotic administration. Instead, other residential colleges, where students did not receive antibiotics', were used as a control group for comparison.

3.2.2 Study setting

The study was carried out in University of Otago residential colleges, in Dunedin, New Zealand. In total 14 colleges, with a total first year student population of 2,804 students, agreed to host the study. The carriage survey was carried out face to face.

3.2.3 Ethics approval.

The lead investigators, Dr Susan Jack and Dr James Ussher gained approval to undertake the carriage survey from the heads of the University of Otago residential colleges, and ethics approval was granted by the University of Otago Human Ethics Committee (Health). The Ethics Committee reference code was HE18/008. All students in their first year at a residential college who attended their residential college dining hall during the lunch hours that the carriage study and risk factor surveys were running, received an information sheet and were invited to participate in the study. Participants had to sign the consent form before participating. The consent form included name and date of birth, was separated from the study data, and was stored securely.

An amendment to the ethics approval was obtained to collect immunisation records from University of Otago Student Health records, as discussed below under Immunisation Records. The amended ethics approval retained the same reference code HE18/008.

3.2.4 Recruitment

Students were informed of the survey by their residential college administration, via email, Facebook posts, and posters in common areas prior to the recruitment.

Students were not offered any monetary enticement to participate. On the day of the carriage study and risk factor survey students were engaged face to face at the entrance to their dining area, by a member of the data collection team. Students were given an information sheet, a consent form and the risk factor survey instrument to complete during their lunch break, and students who agreed to participate were swabbed after their lunch. Following swabbing, students submitted their completed risk factor survey.

3.2.5 Survey instruments

A paper-based risk factor survey was constructed to collect data on the demographics of participants and on their exposure to known and suspected risk factors for *N. meningitidis* (Appendix 1). Questions on demographics and established risk factors included: age; gender; ethnicity; residential college; antibiotic use in the two weeks prior to swabbing; cigarette smoking; exposure to cigarette smoke; attendance at parties; and intimate kissing. The survey also enquired about e-cigarette use, which at the time of the survey was a potential risk factor that did not appear to have been

examined in the literature on carriage of *N. meningitidis*. For cigarette smoking, attendance at parties, intimate kissing, and e-cigarette use the survey sought data on quantity and frequency.

No pre-existing survey instrument was uncovered during the literature review, hence the survey instrument was designed by the principal investigators in accordance with best practice recommendations[96]. Questions were succinct, to avoid ambiguity and make the survey as easy as possible to complete. The survey was restricted to one page, but with sufficient spacing between questions to ensure clarity. Questions were clearly numbered to provide a navigational path. Paper forms enabled participant compliance in completing the forms.

On the survey instrument, identifying information was collected first, in a section that would enable identifying information to be separated from the main form. This separation was clearly visible to participants, to engender trust that their identifying information would be separated, hence anonymising their responses. Demographic information followed. To reduce variability in answers participants were asked to tick yes or no or enter numerals to all but three questions (name, date of birth and residential college). Ethnicity was listed as a) Māori, followed by; b) Pacific Peoples; c) Asian; d) Middle Eastern; Latin American, African; e) NZ European; f) other (with space for a free text entry), with participants able to record multiple ethnicities. Although this is not entirely in keeping with the MOH guidelines for prioritised ethnicity, the six recommended categories were used, participants self-determined their ethnicity, and were able to record more than one ethnicity, and had space to add free text in the 'other' categroy.[97] For quantity and frequency, the survey instrument grouped continuous data into three categories, such as: 1-5; 6-10; >10. The question on intimate kissing included a definition of intimate kissing to reduce the risk of variability in interpretation.

The risk factor survey tool was pretested on members of the study team to identify and correct problems with questionnaire design and logic, and to ensure that the questions would be clearly understood by study participants. Due to time and resource constraints, and the simplicity of the survey instrument, the survey was not pretested on a subgroup of the population of interest.

3.2.6 Specimen and survey collection training

Staff from the local Public Health Unit, including health protection officers, administration workers and registered nurses, performed the swabbing and administration roles. Swab collectors attended a theoretical and practical training session prior to commencement. Swabbing technique consisted of swabbing the oropharynx[98], and was taught and assessed by a medical microbiologist and

principal investigator. Administration staff agreed on a standardised process for allocating study identification numbers and reviewing returned forms for completeness. All staff had prior experience and adhered to Southern District Health Board requirements for handling confidential patient data.

3.2.7 Laboratory methods

After throat swabs were collected, they were delivered to the laboratory for processing within an hour. Southern Community Laboratories' staff plated samples on chocolate agar plates. Plates were incubated overnight at 37°C in 5% CO_2. Colonies with a morphology consistent with *N. meningitidis* were then identified using MALDI-TOF-MS (Bruker) and with Remel™ BactiCard™ Neisseria (Thermo Scientific). Isolates were sent to the University of Melbourne for WGS and in silico sero-grouping.

3.2.8 Genomic DNA extraction and next-generation sequencing

Staff from University of Melbourne report that genomic DNA of isolates was extracted from a single colony using a QIAsymphony™ DSP DNA Mini Kit (Qiagen) according to manufacturer's instructions, and next-generation sequencing was performed on an Illumina NextSeq 500 instrument with 150 bp paired-end reads using Illumina libraries and protocols (Illumina, San Diego, CA, USA). DNA extraction and sequencing of study isolates was performed at Microbiological Diagnostic Unit Public Health Laboratory (MDU PHL). The resulting data, including MLST, ctrA, serogroup, PorA VR type, and FetA VR type was supplied to me by University of Melbourne. The data were later reanalysed and developed into figures (Appendix 2) by Dr George Taiaroa, with the intention of inclusion in a published paper on the study results. ESR, the national reference laboratory for New Zealand, has been approached for WGS data from the original four invasive meningococcal cases. The WGS data from ESR will be compared to the WGS data from the carriage survey isolates, to determine how closely related they are.

3.2.9 Accessing immunisation records

The immunisation status of participants was collected to examine the association between meningococcal immunisation and carriage, and to evaluate the impact that funding of meningococcal vaccine has on uptake of immunisation. Permission was sought from participating students to access their meningococcal immunisation records. Administration staff involved in the

carriage study and risk factor survey were given training on the use of the online NIR. Administration staff then used the names and dates of birth of participants to search the NIR.

While many students had childhood immunisations recorded on the NIR, including doses of MeNZB, very few had recent meningococcal immunisations recorded. To verify that NIR data were correct, access to University of Otago Student Health records was sought. A further ethics amendment was obtained, granting approval to include this new source of data for the risk factor survey. Carriage study administration staff rematched name and date of birth to the study identification number, which enabled Student Health to search student records and provide the meningococcal immunisation details for participants. The data from Student Health confirmed that the NIR was an incomplete and unreliable source of immunisation history for students. Subsequently, all data on immunisation history was collected from both the NIR and Student Health records.

3.2.10 Data management

Data was transcribed from paper survey forms into the REDCap computer platform, by a third-year medical student, during a summer studentship. During transcription 10 percent of the paper forms were double entered to check the quality of the transcription. Once transcription was complete the data were exported from REDCap into a password protected Excel spreadsheet which was held on the secure Southern DHB IT system, and on the author's password protected laptop.

Risk factor survey data were merged with data from the specimen results (initial laboratory analysis from Dunedin), from the WGS results (subsequent laboratory analysis from Melbourne), from the NIR, and from Student Health records, and was combined in a master spreadsheet.

Separately, data were obtained from the University of Otago on the demographics of first year residential college occupants. This data enabled assessment of the representativeness of participants in relation to the residential college population.

3.2.11 Missing data

For the 2018 carriage study and risk factor survey, missing data were identified during transcription from the paper forms to Excel spreadsheet. Where survey responses were either missing, illegible or non-sensical, the response was entered into the Excel spread sheet as "Missing". A separate record was kept of all answers categorised as missing.

3.2.12 Data analysis

To understand how representative the study participants were of the underlying study population, demographic data on all first-year students in residential colleges was obtained from the University. Demographic data included age, gender, ethnicity, residential college and residency status. For the 2018 carriage and risk factor study, the University data were collected 8 months prior to the study commencing, therefore date of birth was used to backdate the age of study participants. This enabled a comparison of participants' ages with the age of the total population of first year students living in University of Otago residential colleges. Both data sets included students with multiple ethnicities. In the original 2018 survey data set ethnicity was prioritised as a) Māori, followed by; b) Pacific; c) Asian; d) NZ European; e) Middle Eastern, Latin American, African; f) Other. This prioritisation occurred prior to the commencement of this thesis, and although it is inconsistent with the MOH Ethnicity Data Protocols, the small number of entries effected was deemed unlikely to significantly effect the results in a meaningful way.[97] For consistency and to enable accurate comparison the same prioritisation was applied to subsequent data sets, including that obtained from the University. Proportions were calculated for all demographic variables for both the study sample and the broader population, and these proportions were compared to assess how well the study sample represented the underlying study population. Residential colleges were coded (1-14) for anonymity. Participants without an NIR record were divided into those with a National Health Index (NHI) number (very likely to be domestic students, or New Zealand citizens), and those without (likely to be international students).

Carriage and risk factor data from 2018 were imported into StataMP v13 for analysis. Chi-square test was used to test the null-hypothesis that there was no association between the various risk factors and carriage of *N. meningitidis*. Columns contained the number of participants with carriage of *N. meningitidis* present, the number with carriage absent, the percentage of participants with carriage present, and the 95% confidence interval for the percentage with carriage present. Rows included all risk factors included in the study. Univariable logistic regression analysis followed and was carried out to establish the odds ratio of the dependant variable, carriage of *N. meningitidis*, being associated with each independent variables, the various risk factors. Risk factors included as independent variables in univariable analysis included age; gender; ethnicity; residential college; residency status; antibiotic use in prior two weeks; meningococcal vaccination – self report; meningococcal vaccination – primary health records; recent respiratory illness; cigarette smoking (frequency and number per day); exposure to cigarette smoke; vaping; attendance at

clubs/bars/parties; and intimate kissing. 95% confidence intervals were calculated to provide a range within which the odds ratios fell, thus providing an indication of precision.

Then, multivariable logistic regression analysis was undertaken with the same outcome and predictor variables to assess the independent effect of risk factors. Risk factors that were not included in this multivariable model due to low statistical significance (*P*>.05) in the univariable analysis were residency status; meningococcal vaccination – self report; and meningococcal vaccination – primary health records. Risk factors that were deemed clinically important a priori despite low statistical significance in univariable analysis (antibiotics in prior two weeks; residency status; intimate kissing; recent respiratory illness; ethnicity), and those statistically significant in univariable analysis due to a *P* value threshold ≤ 0.05 (gender, cigarette smoking, exposure to cigarettes; attendance at parties, residential college) were used in a stepwise backward procedure to build a multivariable logistic regression model variable. A *P* value threshold of 0.05 was used to identify risk factors that are having significant independent associations with the outcome after adjusting for other risk factors. Antibiotic use, ethnicity, cigarette smoking and vaping were retained in the model as adjusting variables irrespective of their *P* values as they were deemed considered clinically important. Risk factors that were eliminated during backwards stepwise logistic regression included recent respiratory illness; exposure to cigarettes; intimate kissing; and residency status.

3.3 2018 *N. meningitidis* Carriage Study - Results

This section describes the results of the 2018 carriage study and risk factor analysis. Specimens and survey responses were collected from participants at their residential colleges between 25 September 2018 and 12 October 2018. All 14 Dunedin residential colleges that host University of Otago students were visited once. A total of 1,145 students consented to participate and were swabbed, and 1,143 survey forms were collected. Immunisation status was collected from the New Zealand NIR between 12 October 2018 and 1 December 2018. Student Health records were accessed in November 2019, to verify Immunisation status. Analysis was undertaken in 2020, using StataMP v13. *P* values are reported as per the Journal of Medical Internet Research recommendations.[99]

3.3.1 Characteristics of study population and participants

Anonymised demographic data on all 2018 first year students residing in residential colleges was obtained from the University of Otago in 2019, which enabled the representativeness of the sample to be gauged. The only available data on age of the population was age at March 2018, the start of the academic year in New Zealand. Therefore, solely for the purposes of comparison with the population, the age of study participants was back-dated to March 2018, using birth date. For all other analysis age at time of data collection is used. The demographics of participants closely represented the broader population (Table 5). Participants made up 41% (1145/2804) of eligible students residing in residential colleges. Mean age of participants was 18.6 years, and 715/1145 (64.5%) were female. Following prioritisation of ethnicity, New Zealand European ethnicity was most prevalent (801/1145, 70%), followed by Asian (166/1145, 14.5%), and Māori (124/1145, 10.8%). The prioritisation used resulted in 5/1145 participants (0.4%) who would have been classified as Middle Eastern, Latin American or African under the MOH Ethnicity Data Protocols, and 2/1145 participants (0.2%) who would have been classified as Other Ethnicity, being categorised as New Zealand European. Only 34/1145 (3%) were international students. Participants who received clearance antibiotics seven weeks prior to the study, due to residing in the residential college that experienced cases of IMD totalled 118/1145 (10.3%).

Table 5: Characteristics of Participants

	All first-year students residing in residential colleges (n=2804)	**Participants (n=1145)**
Age	(At March 2018)	(At March 2018)*
17	244 (8.7%)	122 (10.7%)
18	2266 (80.8%)	909 (79.4%)
19	247 (8.8%)	91 (7.9%)
≥20	47 (2.6%)	21 (1.8%)
Missing	0	2 (0.2%)
Gender		
Female	1787 (63.7%)	715 (64.5%)
Male	1017 (36.3%)	421 (36.8%)
Gender Diverse	NA	<5^
Missing	0	7 (0.6%)
Ethnicity		
Māori	335 (11.9%)	124 (10.8%)
Pacific peoples	98 (3.5%)	22 (1.9%)
Asian	434 (15.5%)	166 (14.5%)
New Zealand European/Pakeha	1895 (67.6%)	801 (70.0%)
Middle Eastern, Latin American, African	33 (1.2%)	23 (2.0%)
Other	9 (0.3%)	7 (0.6%)
Missing	0	2 (0.2%)
Residency Status		
Domestic Student	2703 (96.4%)	1109 (96.9%)
International Student	101 (3.6%)	34 (3.0%)
Missing	0	2 (0.2%)

* Age of participants backdated to enable comparison with broader population. For the rest of the paper Age refers to participants' age at the time of the study.

^ Groupings with fewer than five participants do not have the exact number listed to protect the privacy of participants.

The majority of international students identified as being of Asian ethnicity (23/34), followed by those identifying as New Zealand European/Pakeha (6/34), Middle Eastern, Latin American or African (<5/34) and Māori (<5/34). The majority of Asian participants (143/166) were domestic students, with New Zealand residency or citizenship (Table 6).

Table 6: Characteristics of Ethnicity and Residency Status

Ethnicity	Domestic Student	International Student
Māori	123	<5^
Pacific Peoples	22	0
Asian	143	23
New Zealand European/Pakeha	795	6
Middle Eastern, Latin American, African	26	<5^

^ Groupings with fewer than five participants do not have the exact number listed to protect the privacy of participants.

3.3.2 Missing data

During transcription from paper survey forms to the electronic database, all anomalies were noted. There were two people who had missing survey forms, for which only the swab result was available. These two swab results were included in the carriage survey but were missing risk factor survey data were excluded from the risk factor analysis (36 individual data values missing). A further 46 of 20,610 (0.2%) individual data values, from 36 participants (3.1% of all participants), were either missing, illegible, or nonsensical. Of the 36 participants, seven were positive for carriage (2.5% of participants who were positive for carriage), and most were only missing one or two variables. The missing values were spread across all variables, including recent respiratory illness, and exposure to smoke (n=11), gender, vaping, and frequency of vaping (n=7), cigarette use, frequency of use, and gender (n=5), antibiotic use (n=4), attendance at parties, and frequency of attendance at parties (n=3). This very low number of missing values was deemed unlikely to influence results to a considerable extent, whereas excluding the 36 participants, including seven who were positive for carriage, would reduce the power of analysis. Therefore, missing values have been omitted, with no statistical methods, such as imputations, used to account for them.

3.3.3 Carriage prevalence

This section addresses objective A, detailing the carriage and serogroup prevalence of isolates. After incubation of specimens, 283 isolates were cultured from 282/1145 participants, with two isolates being cultured from one sample (Table 7). Excluding participants who received clearance antibiotics (n=118), the overall carriage prevalence was 26.8% (95% CI 24.1—29.6%). Participants from the residential college that received clearance antibiotics seven weeks prior to sampling had a carriage prevalence of 5.9% (95% CI 2.4—11.8%), and WGS carried out by University of Melbourne confirmed there was no carriage of the disease-causing strain of serogroup B. Following WGS of all isolates

(N=283), the most prevalent serogroups were Y (21.9%, 95% CI 17.2—27.2) and W (21.2%, 95% CI 16.6—26.4%), followed by B (15.2, 95% CI 11.2—19.9) and C (2.1%, 95% CI 0.7—4.6%). Other (39.6%, 95% CI 33.8—45.5%) isolates were non-groupable. Of the 171 groupable isolates, B accounted for 25.1% (95% CI 18.8—32.3%). WGS identified the strain of *N. meningitidis* serogroup B that was associated with the three cases of IMD in 2018 in seven isolates collected from five different colleges.

Table 7: Serogroup of isolates from students residing in residential colleges, Dunedin, 2018.

	Carriage	*N. meningitidis* serogroup from WGS					
	Overall	A	B	C	W	Y	Non-groupable
Outbreak college (IMD cases)	—	—	3‡	—	—	—	—
Outbreak college, 7 weeks post antibiotics	7 of 118 participants (5.9%)	0	0	0	0	5	2
All other colleges	275 of 1,027 participants (26.8%)	0	43*	6	60	57	110*

*one participant positive for both serogroup B and non-groupable.

‡data supplied by ESR (Institute of Environmental Science and Research).

3.3.4 Prevalence of known risk and protective factors for carriage of *N. meningitidis*.

This section addresses objective B, by detailing the prevalence of known risk factors for carriage of *N. meningitidis* among University of Otago students residing in residential colleges (Table 8). Our study found that, among the 1,145 Otago students residing in residential colleges who participated, as expected there was little variation in age, with only 6 (0.5%) participants aged 17, 567 (49.5%) aged 18, 510 (44.5%) aged 19, and 60 (5.2%) aged 20 years or over. 421 (36.3%) were male. Two participants self-reported being gender diverse on their survey response. 571 (49.9%) reported attending at least one party or bar in the week prior to specimen collection, with 392 (34.2%) only attending a party or bar on one occasion, 135 (11.8%) on two occasions, and 44 (3.8%) on three or more occasions. A total of 393 (34.3%) reported intimate kissing in the week prior to specimen collection, either with one partner (364, 31.8%), two partners (21, 1.8%), or more (8, 0.7%). 125 (10.9%) smoked one or more cigarette in the week prior to specimen collection, with 105 (9.2%)

smoking on one to three days, and 12 (1.0%) smoking on a daily basis. Participants reported the number of cigarettes they smoked per day, with most smoking one to five cigarettes per day (101, 8.8%), and some smoking either six to 10 (10, 0.9%) or more than 10 (14, 1.2%). Despite the relatively low prevalence of smoking, 376 (32.8%) participants reported exposure to cigarette smoke. 70 (6.1%) participants reported vaping in the week prior to specimen collection, with 45 (3.9%) vaping on one to three days, 8 (0.7%) on four to six days, and 17 (1.5%) on a daily basis. Most participants, 801 (70%), were of NZ European ethnicity. 166 (14.5%) were Asian, 124 (10.8%) were Māori, 23 (2%) were Middle Eastern, Latin American or African, 22 (1.9%) were Pacific Peoples, and seven (0.6%) people recorded their ethnicity as Other. Only 34 (3%) participants were international students, the majority of whom (23, or 2%) were of Asian ethnicity. In total 51 (4.5%) self-reported antibiotic use in the two weeks prior to specimen collection. 856 (73.8%) participants had a documented MeNZB vaccination on the NIR, but only three had a recorded MenACWY-D or MenACWY-T vaccination. Investigation revealed that the NIR did not have an accurate or complete record of participants recent meningococcal vaccinations. Student Health records revealed that 1.3% of participants had received a MenACWY vaccine, 25.2% of participants had received no meningococcal vaccinations, and 74.8% had received a MeNZB vaccine in childhood. For comparison, participants were asked to self-report their vaccination status, and 549 (47.9%) reported having ever been given a vaccine for meningococcal disease, 86 (7.5%) reported never having a vaccine for meningococcal disease, and 508 (44.4%) reported being unsure.

Table 8: Prevalence of known and potential risk factors

Age (years)	N	Proportion (%)	95% CI
17-18	573	50.0	47.1—53.0
19	510	44.5	41.6—47.5
20+	60	5.2	4.0—6.7
Missing	2	0.2	0.0—0.6
Gender			
Male	421	36.8	34.0—40.0
Female	715	62.4	59.6—65.3
Gender diverse	<5^	-	0.0—0.6
Missing	7	0.6	0.2—1.2

Table 8 continued

Ethnicity (prioritised)			
Māori	124	10.8	9.1—12.8
Pacific Peoples	22	1.9	1.2—2.9
Asian	166	14.5	12.5—16.7
New Zealand European/Pakeha	801	70.0	67.2—72.6
Middle Eastern, Latin American, African	23	2.0	1.3—3.0
Other	7	0.6	0.2—1.2
Missing	2	0.2	0.0—0.6
Receiving clearance antibiotics seven weeks prior to specimen collection			
Received clearance antibiotics	118	10.3%	8.6—12.2%
Other	1027	89.7%	87.8—91.4%
Missing	2	0.2%	0.0-0.6%
Other antibiotic use in the two weeks prior to specimen collection			
No	1092	95.4%	94.0—96.5%
Yes	51	4.5%	3.3—5.8%
Missing	2	0.2%	0.0—0.6%
Domestic/International student			
Domestic	1109	96.9%	95.7—97.8%
International	34	3.0%	2.1—4.1%
Missing	2	0.2%	0.0—0.6%
Self-reported meningococcal vaccine			
Previous meningococcal vaccine	549	47.9%	45.0—50.9%
No previous meningococcal vaccine	86	7.5%	6.1—9.2%
Unsure	508	44.4%	41.5—47.3%
Missing	2	0.2%	0.0—0.6%
Documented meningococcal vaccine			
Unvaccinated	289	25.2%	22.7—27.9%
MeNZB	856	74.8%	72.1—77.3%
MenACWY (with or without MeNZB)	15	1.3%	0.7—2.2%
Missing	2	0.2%	0.0—0.6%

Table 8 continued

Respiratory illness in the week prior to specimen collection			
No	659	57.6%	54.6—60.4%
Yes	475	41.5%	38.6—44.4%
Missing	11	1.0%	0.4—1.7%
Cigarette smoking in the week prior to specimen collection			
No	1015	88.6%	86.7—90.4%
Yes	125	10.9%	9.2—12.9%
Missing	5	0.4%	0.1—1.0%
If Yes: Frequency of cigarette smoking **			
1-3 days per week	105	84.0%	76.4—89.9%
4-6 days per week	8	6.4%	2.8—12.2%
Daily	12	9.6%	5.1—16.2%
Quantity of cigarettes smoked per day **			
1-5 cigarettes	101	80.8%	72.8—87.3%
6-10 cigarettes	10	8.0%	3.9—14.2%
> 10 cigarettes	14	11.2%	6.3—18.1%
Exposure to cigarette smoke in the week prior to specimen collection			
No	758	66.2%	63.4—68.9%
Yes	376	32.8%	30.1—35.6%
Missing	11	1.0%	0.5—1.7%
E-cigarette use in the week prior to specimen collection			
No	1068	93.3%	91.7—94.7%
Yes	70	6.1%	4.8—7.7%
Missing	7	0.6%	0.2—1.3%
If Yes: Frequency of e-cigarette use in the week prior to specimen collection Ψ			
1-3 days	45	64.3%	51.9—75.4%
4-6 days	8	11.4%	5.1—21.3%
Daily	17	24.3%	14.8—36.0%
Attendance at parties, clubs or bars in the week prior to specimen collection			
No	571	49.9%	46.9—52.8%
Yes	571	49.9%	46.9—52.8%
Missing	3	0.3%	0.0—0.8%

Table 8 continued

If Yes:	**Frequency of attendance at parties, clubs or bars in the week prior to specimen collection**			
	One time	392	68.7%	64.7—72.4%
	Two times	135	23.6%	20.2—27.3%
	Three times	34	6.0%	4.2—8.2%
	Four times	7	1.2%	0.5—2.5%
	Five times	2	0.4%	0.0—1.3%
	Six or more times	1	0.2%	0.0—1.0%
Intimate kissing in the week prior to specimen collection				
No		750	65.5%	62.7—68.3%
Yes		393	34.3%	31.6—37.2%
Missing		2	0.2%	0.0—0.6%
If Yes:	**Number of partners intimately kissed in the week prior to specimen collection** Φ			
	1	364	92.6%	89.6—95.0%
	2	21	5.3%	3.3—8.1%
	3	4	1.0%	0.3—2.6%
	4	2	0.5%	0.1—1.8%
	>5	2	0.5%	0.1—1.8%

** Denominator 125 participants who smoked any amount of cigarettes.

Ψ Denominator 77 participants who used e-cigarettes.

Φ Denominator 393 participants who kissed.

3.3.5 Characteristics of individuals with carriage compared with individuals without carriage

To further address objective B, and to address objective C, we assessed the association between known and potential risk factors and carriage of *N. meningitidis* (Table 9). Chi square test confirmed a statistically significant association between *N. meningitidis* carriage and gender (*P*<.001), ethnicity (*P*=.04), cigarette smoking (*P*<.001), exposure to cigarette smoke (*P*<.001), vaping (*P*<.001), attendance at parties, bars or clubs (*P*<.001), and receiving clearance antibiotics 7 weeks prior to specimen collection (*P*<.001). Chi square test did not find a statistically significant association between *N. meningitidis* and age (*P*=.91), residency status (*P*=.08), antibiotic use in the two weeks prior to specimen collection (*P*=.13), self-reported meningococcal vaccination status (*P*=.38), recorded vaccination status (*P*=.26), recent respiratory illness (*P*=.56), and intimate kissing (*P*=.07).

Table 9: Association between carriage of *N. meningitidis* and potential risk factors.

	Present (N=280)	Absent (N=863)	% present	95% CI for % present	Chi square *P*=value
Age					
≤18	141	432	24.6	(21.1 - 28.3)	
19	123	387	24.1	(20.4 - 28.0)	*P*=.91
≥20	16	44	26.7	(16.1 - 39.7)	
Missing	2	0			
Gender					
Male	138	283	32.8	(28.3 - 37.5)	
Female	142	573	19.9	(17.0 - 23.0)	*P*<.001
Other/Missing	2	7			
Ethnicity					
Māori	35	89	28.2	(20.5 - 37.0)	
Pacific Peoples	7	15	31.8	(13.9 - 54.9)	
Asian	26	140	15.7	(10.5 - 22.1)	*P*=.04
Middle Eastern, Latin American, African and Other	10	20	33.3	(17.2 - 52.8)	
New Zealand European, Pakeha	202	599	25.2	(22.2 - 28.4)	
Missing	2	0			
Receiving clearance antibiotics seven weeks prior to specimen collection					
Received clearance antibiotics	9	109	7.6	(3.5 - 14.0)	*P*<.001
Other	271	754	26.4	(23.8 - 29.3)	
Missing	2	0			
Other antibiotic use in the two weeks prior to specimen collection					
No antibiotic	272	820	24.9	(24.9 - 1.3)	*P*=.13
Antibiotic	8	43	15.7	(7.0 - 28.6)	
Missing	2	0			
Domestic/International student					
Domestic Student	276	833	24.9	(22.3 - 27.5)	*P*=.08
International Student	4	30	11.8	(3.3 - 27.5)	
Missing	2	0			

Table 9 continued

Self-reported meningococcal vaccination					
Unvaccinated	17	69	19.8	(12.0 - 29.8)	*P*=.38
Vaccinated	143	406	26.0	(22.4 - 29.9)	
Unsure	120	388	23.6	(20.0 - 27.6)	
Missing	2	0			
Documented meningococcal vaccination					
Unvaccinated	62	225	21.6	(16.9 - 26.8)	*P*=.26
MeNZB only	215	626	25.5	(22.6 - 28.7)	
Menactra only	1	1	50.0	(1.3 - 98.7)	
Menactra and MeNZB	2	11	15.4	(1.9 - 45.4)	
Missing	2	0			
Respiratory illness in the week prior to specimen collection					
No illness	158	501	24.0	(20.8 - 27.4)	*P*=.56
Illness	121	354	25.5	(21.6 - 30.0)	
Missing	3	8			
Cigarette smoking in the week prior to specimen collection					
No	226	789	22.3	(19.7 - 25.0)	*P*<.001
Yes	54	71	43.2	(34.4 - 52.4)	
Missing	2	3			
Frequency of cigarette smoking in the week prior to specimen collection					
No	226	789	22.3	(19.7 - 25.0)	*P*<.001
4-7 days a week	11	9	55.0	(31.5 - 76.9)	
1-3 days a week	43	62	41.0	(31.5 - 51.0)	
Missing	2	3			
Quantity of cigarettes smoked per day					
No	226	789	22.3	(19.7 - 25.0)	*P*<.001
1-5 per day	40	61	39.6	(30.0 - 49.8)	
>6 per day	14	10	58.3	(36.6 - 77.9)	
Missing	2	3			

Table 9 continued

Exposure to cigarette smoke in the week prior to specimen collection					
No	159	599	21.0	(18.1 - 24.1)	*P*<.001
Yes	119	257	31.6	(27.0 - 36.6)	
Missing	4	7			
E-cigarette use in the week prior to specimen collection					
No	247	821	23.1	(20.6 - 25.8)	*P*<.001
Yes	32	38	45.7	(33.7 - 58.1)	
Missing	3	4			
Frequency of e-cigarette use in the week prior to specimen collection					
No	247	821	23.1	(20.6 - 25.8)	*P*<.001
4-7 days per week	12	13	48.0	(27.8 - 68.7)	
1-3 days per week	20	25	44.4	(29.6 - 60.0)	
Attendance at parties, clubs or bars in the week prior to specimen collection					
No	94	477	16.5	(13.5 - 19.8)	*P*<.001
Yes	185	386	32.4	(28.6 - 36.4)	
Missing	3	0			
Frequency of attendance at clubs/bars/parties in the week prior to specimen collection					
No	94	477	16.5	(13.5 - 19.8)	*P*<.001
1 per week	109	283	27.8	(23.4 - 32.5)	
2 per week	56	79	41.5	(33.1 - 50.3)	
3 or more per week	20	24	45.5	(30.4 - 61.2)	
Intimate kissing in the week prior to specimen collection					
No	171	579	22.8	(19.8 - 26.0)	*P*=.07
Yes (any number of people)	109	284	27.7	(23.4 - 32.4)	
Missing	2	0			

3.3.6 Association between Risk Factors and Carriage

To further address objectives B and C, univariate logistic regression was used to find associations between the presence of carriage of *N. meningitidis* and various demographic and behavioural characteristics (Table 10). The odds of having carriage among females was half of that of males (OR 0.50, 95% CI 0.39 to 0.67, *P*<.001). Compared to Māori ethnicity, Asians are less likely to have carriage (OR 0.47, 95% CI 0.27 to 0.84, *P*<.001). However, a statistically significant difference was not

observed between Māori ethnicity and any of the other ethnic groups. Having antibiotics to clear carriage seven weeks prior to specimen collection significantly reduced the odds of having carriage (OR 0.22, 95% CI 0.11—0.46, *P*<.001). There was a dose response to the frequency of smoking, with the odds ratio increasing as smoking frequency increased from smoking one to three days per week (OR 2.42, 95% CI 1.60—3.67, *P*<.001) to smoking four to seven days a week (OR 4.27, 95% CI 1.75—10.42, *P*<.001). There was also a dose response to the number of cigarettes smoked with prevalence odds ratio increasing with the more cigarettes smoked, with OR 2.29 (95% CI 1.50—3.50, *P*<.001) for one to five cigarettes per day increasing to OR 4.89 (95% CI 2.14—11.15, *P*<.001) for more than six cigarettes smoked per day. Exposure to cigarette smoke was also associated with higher odds of carriage (OR 1.74, 95% CI 1.32—2.31, *P*<.001), as was vaping (OR 2.80 95% CI 1.71—4.58, *P*<.001). Similar to cigarette smoking there was a dose response seen for vaping with more frequent vaping associate with higher odds of carriage, from odds ratio of 2.66 (95% CI 1.45—4.87, *P*<.001) for vaping one to three days to odds ratio of 3.07 (95% CI 1.38—6.81, *P*<.001) for vaping four to seven days per week. Attendance at clubs, bars or parties resulted in odds ratio of 2.43 (95% CI 1.83—3.23, *P*<.001), with the odds increased with increasing days per week of attendance, from one per week (OR 1.95, 95% CI 1.43—2.67, *P*<.001) to two per week (OR 3.60, 2.39—5.41, *P*<.001) to three or more per week (OR 4.23, 95% CI 2.24—7.97, *P*<.001).

We found no evidence of a statistically significant difference in odds of having carriage versus not having carriage between domestic and international students (OR 0.40, 95% CI 0.14—1.15, *P*=.09), having antibiotics in the prior two weeks (OR 0.56, 95% CI 0.26—1.21, *P*=.14), having had a documented MeNZB vaccine (OR 1.18, 95% CI 0.86—1.63, *P*=.29), having had a previous MenACWY-D vaccine (OR 0.76, 95% CI 0.21—2.72, *P*=.68), having had a recent respiratory illness (OR 1.08, 95% CI 0.83—1.42, *P*=.56), or intimate kissing (OR 1.30, 95% CI 0.98—1.72, *P*=.07).

3.3.7 Independent Risk Factors for carriage

Univariate odds ratios cannot be used to identify risk factors with independent effect because they were unadjusted for other risk factors. Hence, the last step in addressing objectives B and C was to identify risk factors with independent effects, using a multivariable logistic regression model as described in Chapter Three (section 3.2.12). This model included seven variables, four of which retained an independent effect after adjusting for each other variables. Independent risk factors for carriage of *N. meningitidis* (Table 10) include attending clubs or bars or parties (adjusted OR 2.12, 95% CI 1.56—2.87, *P*<.001). Protective factors included being of female gender (adjusted OR 0.55, 95% CI 0.41—0.73, *P*<.001), Asian ethnicity (adjusted OR 0.50, 95% CI 0.27—0.92, *P*=.03) or having received clearance antibiotics seven weeks prior (adjusted OR 0.18, 95% CI 0.09—0.36, *P*<.001). In

the study smoking (adjusted OR 1.54, 95% CI 0.99—2.41, *P*=.06), antibiotics in the previous two weeks (adjusted OR 0.54, 95% CI 0.24—1.20, *P*=.13) and e-cigarette use (adjusted OR 1.51, 95% CI 0.86—2.64, *P*=.15) were not significant independent risk factors.

Table 10: Risk factors for carriage of *N. meningitidis* identified using univariable and multivariable logistic analyses.

	Participants	**Univariable**		**Multivariable**	
	Carriers/total (%)	**Odds Ratio (95% CI)**	***P***	**Odds Ratio (95% CI)**	***P***
Age *					
≤18	141 / 573 (24.6)	Ref			
19	123 / 510 (24.1)	0.97 (0.74—1.29)	*P*=.85		
≥20	16 / 60 (26.7)	1.11 (0.61—2.04)	*P*=.73		
Gender					
Male	138 / 421 (32.8)	Ref		1	
Female	142 / 715 (19.9)	**0.50 (0.39 - 0.67)**	***P*<.001**	**0.55 (0.41 - 0.73)**	***P*<.001**
Other/Missing	2 / 9				
Ethnicity *					
Māori	35 / 124 (28.2)	Ref		1	
Pacific Peoples	7 / 22 (31.8)	1.19 (0.45 - 3.16)	*P*=.73	1.32 (0.44 - 3.96)	*P*=.62
Asian	26 / 166 (15.9)	**0.47 (0.27 - 0.84)**	***P*<.001**	**0.50 (0.27 - 0.92)**	***P*=.03**
Middle Eastern, Latin American, African and Other	10 / 30 (33.3)	0.86 (0.56 - 1.31)	*P*=.48	0.82 (0.52 - 1.28)	*P*=.38
New Zealand European/ Pakeha	202 / 801 (25.2)	1.27 (0.54 - 2.99)	*P*=.58	1.28 (0.52 - 3.13)	*P*=.60
Receiving clearance antibiotics seven weeks prior to specimen collection*					
Outbreak/received clearance Abs	9 / 118 (7.6)	**0.22 (0.11—0.46)**	***P*<.001**	**0.18 (0.09—0.36)**	***P*<.001**
Other	271 / 1025 (26.4)	Ref		Ref	

Table 10 continued

Other antibiotic use in the two weeks prior to specimen collection *					
No antibiotic	272 / 1092 (24.9)	Ref		1	
Antibiotic	8 / 51 (15.7)	0.56 (0.26—1.21)	*P*=.14	0.54 (0.24—1.20)	*P*=.13
Domestic/international student *					
Domestic Student	276 / 1109 (24.9)	Ref			
International	4 / 34 (11.8)	0.40 (0.14—1.15)	*P*=.09		
Documented meningococcal vaccination					
Unvaccinated	64 / 289 (22.2)	Ref			
MeNZB	218 / 856 (25.5)	1.18 (0.86—1.63)	*P*=.29		
Menactra	3 / 15 (20.0)	0.76 (0.21—2.72)	*P*=.68		
Respiratory illness in the week prior to specimen collection Δ					
No illness	158 / 659 (24.0)	Ref			
Illness	121 / 475 (25.5)	1.08 (0.83—1.42)	*P*=.56		
Cigarette smoking in the week prior to specimen collection - frequency †					
No	226 / 1015 (22.3)	Ref		1	
Yes (any frequency)	54 / 125 (43.2)	**2.66 (1.81—3.90)**	***P*<.001**	1.54 (0.99—2.41)	*P*=.06
1-3 days a week	43 / 105 (41.0)	**2.42 (1.60—3.67)**	***P*<.001**		
4-7 days a week	11 / 20 (55.0)	**4.27 (1.75—10.42)**	***P*<.001**		
Quantity of cigarettes smoked per day †					
No	226 / 1015 (22.3)	Ref			
1-5 per day	40 / 101 (39.6)	**2.29 (1.50—3.50)**	***P*<.001**		
>6 per day	14 / 24 (58.3)	**4.89 (2.14—11.15)**	***P*<.001**		
Exposure to cigarette smoke in the week prior to specimen collection Δ					
No	159 / 758 (21.0)	Ref			
Yes	119 / 376 (31.7)	**1.74 (1.32—2.31)**	***P*<.001**		

Table 10 continued

E-cigarette use in the week prior to specimen collection ∞					
No	247 / 1068 (23.1)	Ref		Ref	
Yes (any frequency)	32 / 70 (45.7)	**2.80 (1.71—4.58)**	***P*<.001**	1.51 (0.86—2.64)	*P*=.15
1-3 days per week	20 / 45 (44.4)	**2.66 (1.45—4.87)**	***P*<.001**		
4-7 days per week	12 / 25 (48.0)	**3.07 (1.38—6.81)**	***P*<.001**		
Attendance at parties, clubs or bars in the week prior to specimen collection ‡					
No	94 / 571 (16.5)	Ref		Ref	
Yes (any number)	185 / 571 (32.4)	**2.43 (1.83—3.23)**	***P*<.001**	**2.12 (1.56—2.87)**	***P*<.001**
1 per week	109 / 392 (27.8)	**1.95 (1.43—2.67)**	***P*<.001**		
2 per week	56 / 135 (41.5)	**3.60 (2.39—5.41)**	***P*<.001**		
3 or more per week	20 / 44 (45.5)	**4.23 (2.24—7.97)**	***P*<.001**		
Intimate kissing in the week prior to specimen collection *					
No	171 / 750 (22.8)	Ref			
Yes	109 / 393 (27.7)	1.30 (0.98—1.72)	*P*=.07		

* Missing 2; ‡ Missing 3; † Missing 5; ∞ Missing 7; Δ Missing 11

3.3.8 Association between *N. meningitidis* serogroups carriage and risk factors

Multivariable analysis was carried out for individual *N. meningitidis* serogroup carriage and independent risk factors using the multivariable logistic regression model as described in Chapter Three (section 3.1.12). As displayed in Table 11, for serogroup Y, the protective effect of female gender (adjusted OR 0.43, 95% CI 0.25—0.75, *P*<.001) and Asian ethnicity (adjusted OR 0.24, 95% CI 0.07—0.78, *P*=.02) remained, but other risk factors were not statistically significant. For serogroup W, attendance at pubs, clubs and parties remained an independent risk factor (adjusted OR 2.45, 95% CI 1.36—4.42, *P*<.001), but other risk factors were not statistically significant. Generally, limiting analysis to a single serogroup reduced the statistical significance of results, likely due to the lower number of isolates used in analysis.

Table 11: Serogroup specific risk factor analysis.

	Adjusted Odds Ratio (95% Confidence Interval) *P*= Value				
Risk factor	**Combined**	**Non-groupable**	**Serogroup Y**	**Serogroup W**	**Serogroup B**
	N=277	N=112	N=62	N=60	N=43
Parties, Bars, Clubs	**2.12 (1.56—2.87) *P*<.001**	**2.24 (1.38—3.63) *P*=.001**	1.17 (0.66—2.07) *P*=.58	**2.45 (1.36—4.42) *P*=.003**	1.09 (0.57—2.10) *P*=.79
E-cigarette Use	1.51 (0.86—2.64) *P*=.15	**2.11 (1.07—4.18) *P*=.03**	1.61 (0.67—3.86) *P*=.28	0.70 (0.20—2.48) *P*=.58	0.53 (0.11—2.46) *P*=.42
Cigarette Smoking	1.54 (0.99—2.41) *P*=.06	1.77 (0.93—3.39) *P*=.08	1.45 (0.68—3.11) *P*=.34	0.66 (0.26—1.68) *P*=.39	1.21 (0.45—3.20) *P*=.71
Female Gender	**0.55 (0.41—0.73) *P*<.001**	0.74 (0.48—1.14) *P*=.08	**0.43 (0.25—0.75) *P*=.003**	0.85 (0.49—1.47) *P*=.56	0.63 (0.33—1.20) *P*=.16
Asian Ethnicity	**0.50 (0.27—0.92) *P*=.03**	0.93 (0.38—2.29) *P*=.88	**0.24 (0.07—0.78) *P*=.018**	1.22 (0.38—3.92) *P*=.74	0.23 (0.43—1.24) *P*=.09
Clearance Antibiotics	**0.18 (0.09—0.36) *P*<.001**	**0.12 (0.03—0.51) *P*=.004**	0.62 (0.24—1.63) *P*=.34	1	1
Other Antibiotics	0.54 (0.24—1.20) *P*=.13	0.54 (0.16—1.84) *P*=.33	0.31 (0.04—2.36) *P*=.34	2.25 (0.84—6.07) *P*=.11	0.52 (0.07—3.91) *P*=.53

Chapter 4: 2019 and 2020 Vaccine Hesitancy Surveys

This chapter describes the vaccine hesitancy surveys carried out by the author in 2019 and 2020. The chapter includes a literature review, methods and results of the two vaccine hesitancy surveys. The chapter aims to address the following objective:

Objective D:

> To identify factors influencing uptake of meningococcal vaccination by University of Otago first year students living in residential halls.

4.1 Vaccine hesitancy surveys - literature review

4.1.1 Introduction

Literature investigating vaccine hesitancy among students residing in residential colleges, particularly in relation to meningococcal vaccines and COVID-19 vaccines, appears scant. Indeed, between 2010 and 2020 there is little published literature on vaccine hesitancy in older adolescents, with the exception of studies into HPV vaccine hesitancy in secondary school students.[100–103] However, during the course of this study, interest in vaccine hesitancy intensified, as COVID-19 vaccines were developed in response to the global COVID-19 pandemic. Many studies have recently been published on the topic of vaccine hesitancy in relation to COVID-19, and these were included in the literature review due to the paucity of evidence relating to meningococcal vaccines. While limited by the constraints of the master's thesis format, this brief literature review seeks to understand vaccine hesitancy among students living in residential colleges. This chapter outlines the objective of the literature review, and the strategy used. Following selection of articles, the body of literature will be assessed as a whole, before evidence underpinning each risk factor is appraised.

4.1.2 Objectives

The objectives of this review are:

To review studies on meningococcal and COVID-19 vaccine hesitancy among students residing in residential colleges, in terms of their core components and methodological strengths and weaknesses; and

To identify gaps in the literature on the topic, and to summarise the evidence on vaccine hesitancy among students residing in residential colleges.

4.1.3 Methods

4.1.3.1 Search strategy

The aim of the search strategy was to identify peer reviewed journal articles describing studies on vaccine hesitancy among university students living in residential colleges. The search strategy was restricted to full text articles from 2010 onwards, and articles published in English language. Grey literature, including reports from governmental and non-governmental organisations were excluded.

4.1.3.2 Literature search

Ovid Medline, PubMed and Scopus databases were accessed via the University of Otago Library website and searched on 10 April 2019, then repeated on 1 October 2021. An initial scan of the literature was performed using the key terms “vaccine hesitancy” in conjunction with “university” and their truncations. Once additional key words were gained the search terms were extended to include the following terms:

Vaccin* or immuni*

AND

Hesitan* or Refus*

AND

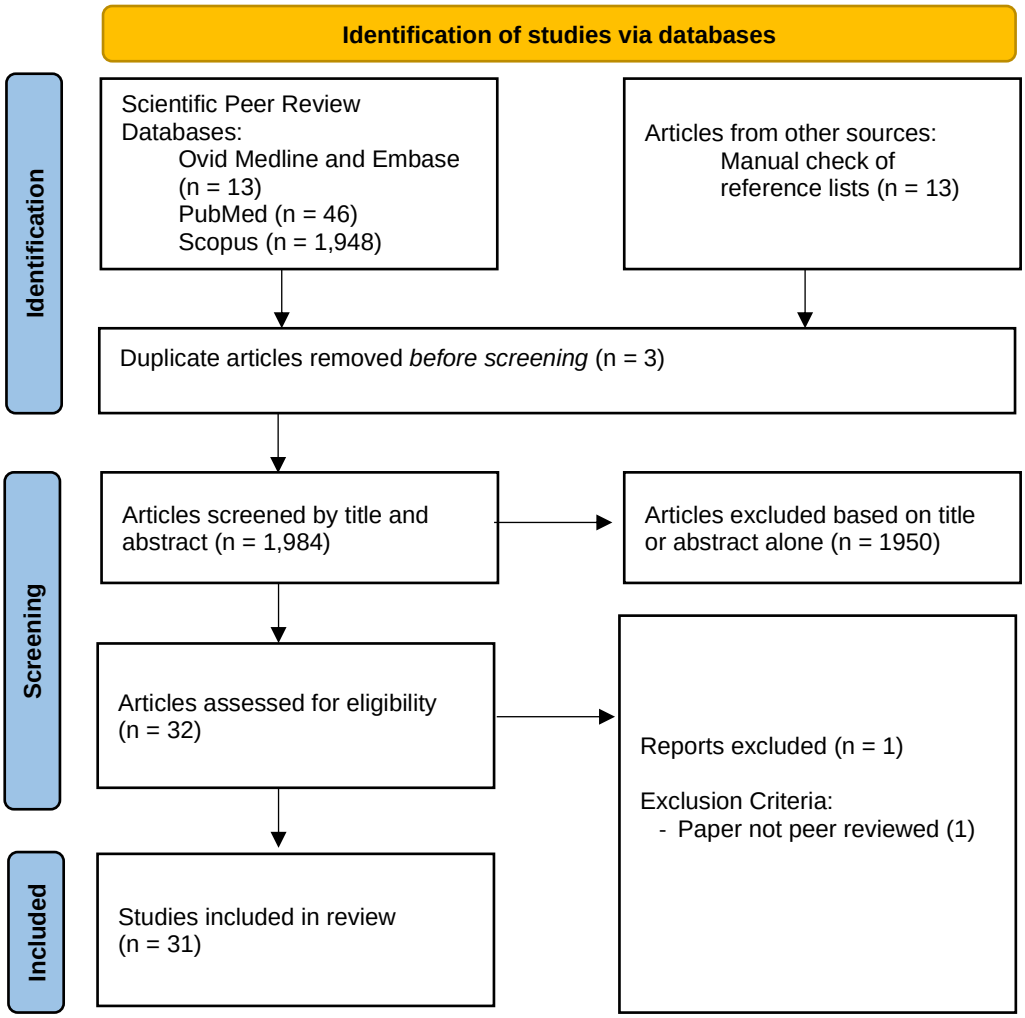
college or dorm* or student* or university or varsity or institut* or undergraduate or polytech*

PubMed (life sciences and biomedical), Ovid Medline (life sciences and biomedical) and Scopus (life sciences, social sciences, physical sciences and health sciences) databases were chosen for their relevance to the topic and to ensure adequate coverage of the literature. The search strategy was reviewed by the subject librarian at the University of Otago Library. The PubMed search was limited to articles that were full text, from 1/1/2010—1/10/2021, on humans, from Medline and Embase or Nursing Journals, encompassing adolescents (13–18 years) or young adults (19–24 years), and either clinical trial, meta-analysis, randomised controlled trial, review, or systematic review. Due to the small number of articles returned, no limits were used in Ovid. The Scopus search was limited to

published articles from subject areas medical, immunology, sociology, human vaccines and immunotherapeutics, vaccine, vaccines and BMC public health; and exact key words "Human", "Humans", "Vaccination", "Vaccines", "Vaccine", "Immunization", "Adolescent", "COVID-19", "Vaccine Hesitancy", "Young Adult", "Coronavirus Disease 2019", "Vaccination Refusal", "COVID-19 Vaccines" and "SARS-CoV-2 Vaccine".

Once the searches had been completed abstracts from PubMed (n=46), Ovid Medline and Embase (n=13) and Scopus (n=1,948) were imported into Mendeley v1.19.8 and duplicates were removed (n=3). Once duplicates had been removed titles and abstracts were screened. During screening, articles with a focus on disease, animals, children, secondary students, adults, vaccines other than meningococcal or COVID-19, and the studies on the process of developing vaccines were excluded (n=1,950). Following screening of titles and abstracts 19 articles remained. Reference lists of these 19 articles were manually screened to identify additional studies, resulting in 13 additional articles being included. At the end of the literature search 31 articles remained (Figure 3).

Figure 3: PRISMA flow diagram[58] for literature review of studies on vaccine hesitancy in University Students



4.1.3.3 Appraising literature

Due to the constraints of this master's thesis literature was not formally appraised with a standardised tool, however consideration was given to the limitations of individual studies when assessing the contribution of each study.

4.1.4 Results

Of the 31 articles selected for this literature review of vaccine hesitancy, one study was carried out in 2015, three in 2018, eight in 2020, and 19 in 2021 (see Table 12). One study examined meningococcal vaccine uptake[104], another examined general vaccine uptake[105], and the rest examined COVID-19 vaccine uptake. Of the studies on COVID-19 vaccine, 17 took place prior to the COVID-19 vaccine being widely available[104,106–121], and 13 took place afterwards.[122–134] 30 studies were cross sectional online surveys, and one was a pre-test–post-test study evaluating an initiative to boost meningococcal vaccination uptake.[105] While no studies took place exclusively in residential colleges, one study included students residing in residential colleges, and provided comparison between general university students and students residing in residential colleges.[128] 14 studies took place in general university populations[104–106,109,111,114,116,117,121,122,126,127,132,133], five took place in medical schools[113,118,128,131,134], three took place in nursing schools[119,124,129], three took place in dental schools[107,108,125], and six took place in a combination of the above.[110,112,115,120,123,130] Studies were from around the globe, with seven from the United States of America[105,108,116,118,119,123,132], four from Italy[111,114,115,122], three from China[121,130,134], three from Poland[113,120,129], and one each from Cyprus[117], Czech Republic[109], Egypt[110], France[126], India[131], Jordan[112], Palestine[107], Saudi Arabia[127], Slovakia[128], United Kingdom[104] and Vietnam.[133] Two studies included multiple European countries[106,124], and one was global.[125] All studies report recruiting participants via email, with some also recruiting via other University channels, such as in lectures[113,124] or face to face on campus.[105] Two studies used 'snowball technique' to recruit through existing participants social media networks.[109,127] While most studies did not report whether or not they used exclusion criteria, six studies specified that they did not have exclusion criteria[104,116,117,120,125,130] and six stated their exclusion criteria, which varied from students employed in healthcare settings[114], to those already vaccinated[109,111], to anyone over 23[105] or 25 years.[126,127] Survey tools varied, with the majority being constructed specifically for individual studies. All followed the themes outlined in the WHO SAGE document; confidence, complacency and convenience.[135] Broadly, questionnaires included sections on: demographics, health status, general attitude to vaccinations, experience of COVID-19, knowledge of COVID-19, source of knowledge on COVID-19 vaccines, and attitude towards COVID-19 vaccines. Individual studies also included tools to assess depression and anxiety, academic achievement, and vaccine conspiracy belief scale.[112] Platforms included Google forms, REDCaps, etc. A variety of statistical methods were used, with some studies relying on proportions alone, and others also using Chi2 test, univariable and multivariable analysis. Twenty-six studies measured students' intention to vaccinate, while five assessed intention and vaccines that had been given.[122,123,128,129,132] All studies appear to rely on self-reported vaccination status.

4.1.4.1 Proportion of students who are vaccine hesitant

Although the proportion of vaccine hesitant students is likely to fluctuate over time, it is none-the-less useful to be aware of what proportion of a given population is vaccine hesitant. A summary of vaccine hesitancy by country is presented below in Table 12.

Table 12: Vaccine hesitancy among university students by country, date of survey and setting.

Location	Author	Date	Subjects	University Course	Vaccine Refusal %	Vaccine Hesitant %	Vaccine Acceptance %
China	Walker[130]	2021	330	General	14.6	38.2	45.8
China	Li[134]	2021	2,196	Medical	8.2	34.5	58.8
China	Bai[121]	2021	2,881	General	–	–	76.3
Cyprus	Guzoglu[117]	2020	327	General	14.9	24.5	60.6
Czech Republic	Riad[109]	2021	1,351	General	19.3	7.4	73.3
Egypt	Saied[110]	2021	2,133	Health	19.0	46.0	35.0
Europe	Patelarou[124]	2021	2,249	Nursing	22.2	34.0	43.8
France	Tavolacci[126]	2021	3,089	General	17.0	25.0	58.0
Global	Riad[125]	2021	6,639	Dental	13.9	22.5	63.5
India	Jain[131]	2021	1,068	Medical	4.0	6.6	89.4
Italy	Giuseppe[114]	2020	1,518	General	–	–	84.1
Italy	Galle[122]	2021	3,226	General	1.9	6.1	91.9
Italy	Salerno[111]	2021	2,667	General	mRNA 1.0	mRNA 7.2	mRNA 91.8
Italy	Barello[115]	2020	735	General	–	13.9	86.1
Italy and Belgium	Ilogu[106]	2018	2,079	General	–	49.2	–
Jordan	Sallam[112]	2021	1,106	General	39.6	25.5	34.9
Palestine	Kateeb[107]	2021	417	Dental	14.9	27.0	57.8
Poland	Szmyd[120]	2020	1,971	General	15.6	13.6	70.8
Poland	Talarek[113]	2020	675	Medical	5.4	–	94.6
Poland	Gotlib[129]	2021	793	Nursing	7.4	4.4	85.8
Saudi Arabia	Almalki[127]	2021	407	General	6.1	–	93.9
Slovakia	Sovicova[128]	2021	1,228	Medical	–	28.6	71.7
UK	Landowska[104]+	2015	177	General	–	51.7	48.3
USA	Graupensperger[116]	2020	647	General	–	–	91.6
USA	Richardson[105] *	2018	1,083	General	–	–	–
USA	Lucia[118]	2020	168	Medical	23.0	–	77.0
USA	Manning[119]	2020	1,029	Nursing	12.3	27.4	60.3
USA	Mascarenhas[108]	2021	248	Dental	–	44.0	56.0

USA	Kecojevic[132]	2021	457	General	–	36.3	63.7
USA	Kelekar[123]	2020	415	Med and Dental	–	23 (M) 45 (D)	–
Vietnam	Khuc[133]	2021	398	General	0.5	16.1	83.4

+ Landowska studied general vaccination uptake among University Students, pre COVID-19.

* Richardson evaluated an initiative to increase meningococcal vaccination uptake, pre COVID-19.

4.1.4.2 Factors associated with vaccine hesitancy

Understanding factors associated with vaccine hesitancy can help guide attempts to increase vaccination rates via health promotion and other public health measures. A range of variables have been investigated in the literature, and a summary is provided below. This literature review has been constrained by the limitations of my thesis, and subsequently only select variables are considered.

4.1.4.2.1 Childhood vaccinations complete

Two studies examined the relationship between childhood vaccination and vaccine hesitancy. Szmyd et al's study of 1,971 Polish medical students did not find a statistically significant relationship following binary logistic regression modelling (OR 1.08, 95% CI 0.66—1.77, *P*=.751)[120], but in their study of 177 UK university students Landowska et al found odds of vaccine acceptance increased in those whose childhood vaccinations were complete (OR 3.57; 95% CI 1.21 to 10.59; p=0.02).[104]

4.1.4.2.2 Influenza vaccination

Two studies demonstrate an association between having had an influenza vaccine and increased likelihood of vaccine acceptance for COVID-19. Talarek et al's study of 675 Polish medical students provided an unadjusted OR 6.1 (95% CI 1.4–26.6, *P*=.006)[113], and Patelarou et al's study of 2,249 nursing students from across Europe provided an adjusted OR 2.38 (95% CI 1.57—3.59, *P*<.001) for being vaccinated for COVID-19 if participants had an influenza vaccine.[124]

4.1.4.2.3 Gender

Males consistently have lower vaccine hesitancy, including in Giuseppe et al's study of 1,518 university students and faculty members, with the adjusted odds for males being vaccine hesitant being 0.67 (95% CI 0.48–0.92, *P*=.015).[114] Using faculty members was a limitation of Giuseppe's study, as was using face to face interviews for some participants, which resulted in a higher proportion of vaccine acceptance. Patelarou et al, mentioned above, found males had an adjusted

OR 1.41 (95% CI 1.09—1.82, *P*=.008) for vaccine acceptance.[124] Studies by Walker et al and Landowska et al present unadjusted results that show a higher proportion of females are vaccine hesitant.[104,130]

4.1.4.2.4 Socio-economic Status

Two studies examined socio-economic status in relation to vaccine hesitancy. Riad et al studied 6,639 dental students from 22 countries, and describes participants from lower socioeconomic areas being more likely to be vaccine hesitant. The proportion of vaccine hesitant participants from lower socioeconomic status areas was 37.2%, compared to 27.8% in low-middle, and 25.2% in middle-high 25.2%, and 11.1% in high socioeconomic areas.[125] Landowska et al found an unadjusted OR 1.11 (95% CI 1—1.23, *P*=.06), with lower socio-economic status resulting in greater odds of being vaccine hesitant, but not meeting the statistical threshold of *P*=.05.[104]

4.1.4.2.5 Educational achievement

Li et al studied 2,196 medical students in South China and found that those with higher educational achievement had a higher likelihood of vaccine hesitancy, with an unadjusted OR 1.72 (95% CI 1.11–2.67).[134]

4.1.4.2.6 Students enrolled on health courses

Several studies compared vaccine hesitancy among students studying to be healthcare workers with non-healthcare students. Tavolacci et al found non-healthcare students were less likely to be vaccine hesitant (adjusted OR 2.92, 95% CI 2.39–3.59, p<.001).[126] Following binary logistic regression Bai et al found that among their sample of 2,881 university students, those from health-related courses were more willing to have a COVID-19 vaccine (OR 1.58, 95% CI 1.29—1.94, *P*<.001). Szmyd et al found that among Medical students, those in a later year of study were more likely to want to be vaccinated as soon as possible, compared with earlier year of study (adjusted OR 1.27, 95% CI 1.11—1.45, p<.001)[120], and Li et al found that those with a requirement to be vaccinated for their placement, or place of work, were more likely to be vaccinated (OR 0.38, 95% CI 0.25–0.57).[134]

4.1.4.2.7 Prior infection with COVID-19

The proportion of students who had been infected with COVID-19 varied with every study, depending on geographical location and phase of the epidemic. Proportion of students with prior infection varied from 9.3% in Southern Italy in February–April 2021[122], to 11.1% in Saudi Arabia in April 2021[127], to 17.4% in France in January 2021[126], to 29.6% in Czech Republic in April–June 2021[109], to 36.4% in Poland in March–April 2021.[129] In their global study of 6,639 Dental students Riad et al

found 16.6% of students had prior infection, and they were more resistant (20.4% vs 12.6%) and hesitant (24.1% vs 22.2%) to be vaccinated than participants who had not been infected.[125] In their study of 1,351 university students Riad et al found students who had not been infected had lesser odds of hesitancy (adjusted OR 0.61, 95% CI 0.40–0.92).[109]

4.1.4.2.8 Relative or friend infected with COVID-19

The proportion of students who knew a relative or friend who had COVID-19 also varied, from 29.4% in Southern Italy in February–April 2021[122], to between 72.0%[129]–98.8%[109] in other studies from a similar time period. Szmyd et al found that there was no statistically significant difference in the odds of vaccine hesitancy between medical students who had a relative with COVID-19, and those that did not (adjusted OR 0.995, 95% CI 0.62–1.59, *P*=.98)[120], however Salerno's study of 2,667 Italian university students found those with a relative who had had COVID-19 were less likely to be vaccine hesitant (adjusted OR 0.65, 95% CI 0.46–0.93).[111] Conversely, two studies showed no statistically significant difference in vaccine hesitancy between students who had been exposed to COVID-19 deaths and those that had not.[109,120]

4.1.4.2.9 Other factors

In Landowska et al's study, participants with a fear of needles had higher odds of vaccine hesitancy (adjusted OR 2.44; 95% CI 1.12 to 5.36, *P*=026), but previous negative experience of vaccination did not make a statistically significant difference (adjusted OR 3.53 95% CI 0.92 to 13.53, *P*=066).[104]

In surveys that considered motivation for having a COVID-19 vaccine, 'personal benefit' was the most frequently reported motivation across surveys. Li et al reported those reporting their motivation was personal benefit were less likely to be vaccine hesitant (adjusted OR 0.519, 95% CI 0.25–0.67).[134] Those who reported a desire to protect loved ones had a higher likelihood of vaccine acceptance (adjusted OR 1.26, 95% CI 1.11--1.41, *P*<.001) in Szmyd et al's study.[120]

There was no evidence for a statistically significant difference between various religions[104] or ethnicities.[104]

4.2 Conclusion

Comparing the articles is difficult, as they are from different countries, and each country will have had a different experience of the pandemic.

There is strong evidence that individuals who have had an influenza vaccine, and males, are less likely to be vaccine hesitant. A particularly large study found that lower socio-economic status increased the likelihood of vaccine hesitancy.

There is some evidence that having a higher educational qualification increases the likelihood of vaccine hesitancy. The evidence is unclear in regard to the extent to which completion of recommended childhood vaccinations influences vaccine hesitancy during adolesence.

There is no evidence in the reviewed literature that religion or ethnicity contribute to vaccine hesitancy.

4.3 2019 and 2020 Vaccine Hesitancy Surveys - Methods

4.3.1 Design

To identify factors influencing uptake of meningococcal vaccination (objective D) annual sequential follow up online surveys were carried out in 2019 and 2020. These follow up surveys, combined with data from the original 2018 carriage and risk factor study, each targeting students in their first year, formed three years of sequential cross-sectional studies, with different study participants in each year's cohort. Analysis focused on two aspects. The first compared the different health education, immunisation promotion, and funding for the MenACYW-D meningococcal immunisation that the three cohorts experienced, to evaluate the outcome variable of documented vaccinations. The second was examining participants' responses to gauge the outcome variable of vaccine hesitancy.

To ensure the study samples were representative of students residing in residential colleges all 14 of the Dunedin University of Otago residential colleges that take first year students were included in the study.

Participation in the surveys was voluntary, with the entire population of students in their first year in a residential college being invited to participate. The expectation was that participants would be a representative sample of the broader first year residential college population, with diversity of gender, ethnicity, social, educational, and income status.

4.3.2 Setting

All 14 colleges agreed to participate, giving a total student population size of 2853 students in 2019, and 2887 students in 2020. The surveys were carried out entirely online.

4.3.3 Ethics

Prior to the 2019 and 2020 surveys, amendments to the original ethics approval (reference code was HE18/008) were gained from the University of Otago Human Ethics Committee (Health), Dunedin, for the two additional surveys. All participants received an information sheet on the study and consented to participate.

4.3.4 Recruitment

Invitations to participate in the survey were given to all first-year students residing in the 14 residential colleges, by their residential college, via email, Facebook posts, and posters in common areas. The first email about the study was sent to students a week before the questionnaire opened. Students then received a further four emails during the survey period, with one week between each email. The survey period ran for five to six weeks, from 13 August to 26 September in 2019, and from 7 September to 9 October in 2020.

Students were offered the chance to win groceries vouchers in exchange for participation (ten $100 vouchers available for the 2019 survey, five $100 vouchers available for the 2020 survey).

4.3.5 Survey instruments

The questionnaires used for data collection were developed in accordance with recommendations from the 2014 report of the WHO SAGE working group on vaccine hesitancy.[49] The report recommends using questions to gauge the level of confidence, convenience and complacency associated with the vaccines of interest. Questions were taken from WHO SAGE sample questions and the working group's Determinants of Vaccine Hesitancy Matrix. The 2019 questionnaire (Appendix 3) began with a page of information on the survey, followed by a requirement for participants to confirm they consented to participate. Following consent, participants were required to enter demographic information, including: name; date of birth; gender, ethnicity, residential college, parental occupations, parental qualification status. Ethnicity options were listed in the same order as the preceding 2018 survey, for consistency and comparability, despite being contrary to the MOH Ethnicity Data Guidelines. Next, participants answered questions on: belief in ability of immunisations to protect from illness; childhood vaccination status; hesitancy to get a vaccination; refusal to get an immunisation; which immunisations were refused, and for what reason. Then there were questions on: whether the participant has ever had a meningococcal vaccination; which meningococcal vaccinations the participant has had; why they have, or have not, had a meningococcal immunisation; whether cost has been a barrier to having a meningococcal immunisation (with an explanation on the cost); barriers to getting a meningococcal immunisation. Next the participants were given questions on whether they believed people should not be vaccinated; what sources they get information about immunisation from; whether they receive negative information about immunisation, and from what source. Finally, participants had the option of providing contact details for the prize draw. The REDcap platform was used to record and

collate responses. Only the author, and the University of Otago REDCap administrator, had access to the REDCap account and the survey responses stored within REDCaps.

The 2020 questionnaire replicated the 2019 questionnaire but included additional questions on attitudes towards a (at the time hypothetical) COVID-19 vaccine. The additional questions were: whether participants would have a COVID-19 vaccination if one were available; why or why not.

Questionnaires used a variety of answer formats as best suited the question, including single answer check box, multiple answer check boxes, free text, and a rating scale (1-100). Some questions gave participants up to 20 responses to choose from. This made the questionnaire long and increased the risk of participants clicking randomly to hurry through sections. However, retaining the questions ensured the questionnaire was consistent with the SAGE Report recommendations, and would ensure consistency with other studies that used the tool. There were free text options for the category of 'other' in each section and for parental occupation. Parental occupation was translated into socio-economic status using the 2018 New Zealand Socioeconomic Index (NZSEI). Once each parent's occupation was given a NZSEI score, scores were combined to give a total NZSEI score between 0–200 for each participant. For analysis scores were allocated into one of eight categories, 0-25, 26-50, 51-75, etc up to 200. For parental educational achievement a single highest level of education, from either parent, was used. A rating scale (0-100) was used for students to indicate the degree of protection they think vaccines confer. For analysis responses were categorised into 10 categories, 0-10, 11-20, 21-30, etc up to 100.

Once constructed the questionnaires were pretested on a selection of individuals not associated with the research, to check design and logic. The pretesting group included three undergraduate students. Following this, the questionnaire was distributed to the eligible population by email via their residential college administration.

4.3.6 Accessing immunisation records

The immunisation status of participants was collected in 2019 and 2020, as it had been in 2018. Permission was sought from participating students to access their meningococcal immunisation records. NIR was checked by the author, to ensure consistency, with supplementary data again being sought from, and supplied by, University of Otago Student Health.

4.3.7 Data management

The 2019 and 2020 questionnaire data were collated in REDcap and was only accessible to the author and the University of Otago REDcap administrator. The data were exported into a password protected spreadsheet and held on the author's password protected laptop.

As in 2018, data were obtained from University of Otago on the demographics of the 2019 and 2020 first year residential college occupants. This data enabled analysis of how representative the study participants were of the underlying study population.

4.3.8 Missing data

For the 2019 and 2020 vaccine hesitancy study, the amount of missing data were likely to be higher than the 2018 carriage survey, as the questionnaire was longer, there was no form of oversight of participants' responses, and the incentive of a prize may have attracted participants who were undertaking the questionnaire with little regard for the accuracy of their answers. Participants with all questionnaire fields missing were deleted from the dataset. Those with only some missing values were kept, with the data included in observational analysis for specific variables.

4.3.9 Data analysis

To understand how representative study participants were of the broader residential college first year population, summary demographic data on all students in their first year at residential colleges was obtained from the University for each year of the study. The University data were collected 8 months prior to the study commencing, therefore, solely for the purpose of comparison, date of birth was used to backdate the age of study participants. This enabled a comparison of participants ages with the age of the broader population. When multiple ethnicities were recorded, they were prioritised. As discussed in section 3.2.12, the original dataset from the 2018 survey did not prioritise ethnicity according to the MOH Ethnicity Data Protocols, but instead as a) Māori, followed by; b) Pacific; c) Asian; d) NZ European e) Middle Eastern; Latin American, African; f) Other.[97] For consistency, the same prioritisation was applied to analysis in 2019 and 2020. Once prioritised, Māori ethnicity was used as the reference ethnicity for analysis. Proportions were calculated for age, gender and ethnicity for both the study sample and the broader population, and these proportions were compared to assess how well the study sample represented the underlying study population.

In preparation for further analysis parental occupation was converted into a NZSEI ranking, as per the University of Auckland's 2018 NZSEI Brief Technical Summary.[136] Each parents' occupation was ranked, then joined, to give a final ranking between 0-200. Residential colleges were coded, 1—14, for anonymity.

Data from the 2019 and 2020 questionnaires were imported into StataMP v13 for analysis. The characteristics of the study samples were compared with the population data for all 2019 and 2020 University of Otago students residing in residential colleges using percentages. Questions which allowed multiple responses per individual were used to elicit factors that contribute to participants vaccine acceptance or hesitancy. Responses to these questions were presented at person level, describing the proportion of people who choose the answer of interest, as opposed to response level (or the proportion of answers chosen). Consequently, the total percentage for these answers will be more than 100%.

In all analysis of vaccination history, the documented vaccination status was used. To understand the impact that government funding had on vaccine uptake, participant specific data from the NIR and from Student Health were used to describe which participants had received a meningococcal vaccine, how many doses they received, and in which year. In addition, Student Health provided the total number of meningococcal vaccines given in each year to all university students (eg; including students not included in the study). Finally for this section, self-reported immunisation status is presented to gauge participants' understanding of their own vaccination status.

Variables with multiple response options were presented as proportions. Chi-square test was used to test the null-hypothesis that there was no association between independent variables of interest and vaccine hesitancy. For Chi-square test columns contained the number of participants with and without vaccine hesitancy, the percentage of participants with vaccine hesitancy. Rows included all variables from the questionnaires with single answer options. Univariable logistic regression analysis was carried out to establish the odds ratio of the dependant variable, vaccine hesitancy, being associated with each independent variable. Factors included as independent variables in univariable analysis included age; gender; ethnicity; residential college; combined parental NZSEI ranking; parental educational achievement; meningococcal vaccination – self report; meningococcal vaccination – primary health records; opinion on how protective vaccination is; presence or absence in NIR; self-reported childhood vaccination status; previous vaccine refusal; exposure to negative information on meningococcal vaccination. For the analysis of opinion on how protective vaccination is rankings 10—60 were combined to a single group to avoid very small frequencies. Desire to have a COVID-19 vaccine was also included for participants from the 2020 cohort. 95% Confidence intervals

were calculated to provide a range within which the odds ratios fell, thus providing an indication of precision.

Then, multivariable logistic regression analysis was undertaken with the same outcome and predictor variables to assess the independent effect the factors listed above. Independent variables that were not included in this multivariable model due to low statistical significance (*P*>.05) in the univariable analysis were age and parental educational achievement. Risk factors that were deemed clinically important a priori despite low statistical significance in univariable analysis (NZSEI ranking and presence in NIR), and those statistically significant in univariable analysis due to a P value threshold ≤ 0.05 (gender, ethnicity, residential college, opinion on how protective vaccines are, childhood vaccination status, previously refusing a vaccine and having received negative information on meningococcal vaccines) were used in a stepwise backward procedure to build multivariable logistic regression models seperately for both the 2019 and 2020 studies. A *P* value threshold of 0.05 was used to identify variables that have a significant independent association with the outcome after adjusting for other independent variables. Risk factors that were eliminated during backwards stepwise logistic regression included having received negative information on meningococcal vaccines, gender, and NZSEI score in the 2019 cohort, and residential college, ethnicity, presence in NIR, gender, and NZSEI score in the 2020 cohort.

4.4 2019 and 2020 Vaccine Hesitancy Surveys - Results

This section addresses objective D, which is to identify factors influencing uptake of meningococcal vaccination by University of Otago first year students living in residential halls. Meningococcal vaccination data from 2018, 2019 and 2020 will be presented, as will data from the 2019 and 2020 vaccine hesitancy surveys. Where values such as percentages, odds ratios, and confidence intervals are provided, they are given in the order of 2019, 2020, unless otherwise stated.

Survey responses were collected online during September and October in 2019 and 2020. All 14 Dunedin residential colleges that host University of Otago students shared the surveys with their students via internal emails and on Facebook pages, and several also displayed posters and promoted it on digital screens. In total 1,040 and 1,243 students consented to participate in 2019 and 2020 respectively, giving response rates of 36.45% and 43.06%. Immunisation status was collected from the New Zealand NIR between October 2019 and January 2021. Student Health provided immunisation data on consenting participants in June 2021, to verify their immunisation status. Analysis was undertaken in 2021, using StataMP v13.

4.4.1 Missing data

Responses were examined for completeness, and for duplicate email addresses, surname, date of birth and first name. Some participants left the questionnaire at the questions regarding immunisation history, then completed another questionnaire form at a later time. When this occurred responses were merged, with data from the later survey always given priority. Other participants completed more than one survey, perhaps to gain multiple entries to the prize draw. In total 69 and 84 incomplete or duplicate responses were removed in 2019 and 2020 respectively.

Because not all questions were mandatory, and some questions allowed multiple answers, the remaining surveys included a varying amount of missing data. The 2019 survey had 338 of 161,700 (0.2%) individual data values coded as missing. The 2020 survey had 1,064 of 244,871 (0.4%) individual data values coded as missing. In both surveys the missing values were distributed across many variables and were considered unlikely to have a significant effect on results. Consequently, no statistical methods were used to account for missing values.

4.4.2 Characteristics of study population and participants

Anonymised summary data on all 2019 and 2020 first year students residing in residential colleges was obtained from the University of Otago in 2020, which enabled the representativeness of the sample to be gauged. The only available data on age of the population was age as at March (the start of the academic year in New Zealand), so for the purposes of comparison with the population, and solely for this purpose, study participants birth date was used to back-dated age. Participants aged 18 years or under were over represented (91.6% in 2019, 88.9% in 2020) relative to the population (73.1%, 74.4%). Participants aged 19 years were under represented (5.9%, 8.0%) relative to the population (24.0%, 22.8%). Participants of female gender were over represented with 71.6% of the sample being female in both years, compared to 59.4% and 62.7% of the population being female. Male gender was under represented, with 28.0% and 26.1% of participants being male, compared to 40.6% and 37.2% of the population being male. Following prioritisation of ethnicity, New Zealand European ethnicity was most prevalent in both years, accounting for 68.8% (703 of 1020) and 69.7% (866 of 1243) in 2019 and 2020 respectively, followed by Asian at 14.2% (145 of 1020) and 11.7% (145 of 1243), Māori at 11.8% (120 of 1020) and 10.3% (128 of 1243), only 3.3% (34 of 1020) and 4.7% (58 of 1243) Pacific Peoples, and 1.5% (15 of 1020) and 1.8% (22 of 1243) categorised as Middle Eastern, Latin American, African. The prioritisation used resulted in 1/1020 participants (0.1%) in 2019 and 3/1243 participants (0.2%) in 2020, who would have been classified as Middle Eastern, Latin American or African under the MOH Ethnicity Data Protocols, being categorised as New Zealand European. It also resulted in 2/1243 participants (0.2%) who would have been classified as Other under the MOH Ethnicity Data Protocols, being categorised as New Zealand European in 2020.

Table 13: Study Sample Compared to Population at March, 2019 and 2020.

	March 2019		March 2020	
	Participants N (%)	**All first-year students residing in residential colleges** N (%)	**Participants** N (%)	**All first-year students residing in residential colleges** N (%)
	N=1,020	N=2,853	N=1,243	N=2,887
Age at March*				
18 and younger	934 (91.6)	2,083 (73.1)	1,106 (88.9)	2,147 (74.4)
19	60 (5.9)	686 (24.0)	100 (8.0)	659 (22.8)
20 and older	26 (2.5)	84 (2.9)	37 (3.0)	81 (2.8)
Gender				
Male	286 (28)	1,158 (40.6)	325 (26.1)	1,073 (37.2)
Female	730 (71.6)	1,694 (59.4)	890 (71.6)	1,810 (62.7)
Gender Diverse	<5	<5	7 (0.6)	<5

Missing	–	–	21 (1.7)	–
Prioritised Ethnicity				
Māori	120 (11.8)	378 (13.2)	128 (10.3)	383 (13.3)
Pacific peoples	34 (3.3)	120 (4.2)	58 (4.7)	143 (5.0)
Asian	145 (14.2)	453 (15.9)	145 (11.7)	418 (14.5)
New Zealand European	703 (68.9)	1,875 (67.5)	866 (69.7)	1,895 (65.6)
Middle Eastern, Latin American, African	15 (1.5)	18 (0.6)	22 (1.8)	34 (1.2)
Other	–	9 (0.3)	–	14 (0.5)
Missing	3 (0.3)	–	24 (1.9)	–

* Age at March is used for the purposes of comparison with sample data. This is different to age at the time of the study, which was conducted during the latter part of each year.
^ Groupings with fewer than five participants do not have the exact number listed to protect the privacy of participants.

4.4.3 Characteristics of the study sample.

This section details the prevalence of factors that may influence vaccine hesitancy among University of Otago students residing in residential colleges. All percentages describe the proportion of total participants (Table 14).

Among participants there was little variance in age, with only 1.9% and 6.4% of participants aged 20 or over, 32.4% and 44.2% aged 19, and 65.8% and 49.3% aged 18 or under. Gender varied little between 2019 and 2020, with 28.0% and 26.1% male. Parental employment was converted to socio-economic status using NZSEI rankings from 0 (lowest) to 200 (highest). After both parents' rankings were combined, most participants were in the 126–150 bracket (28.0%, 27.7%), followed by the 101–125 (19.9%, 19.2%), 76–100 (14.6%, 12.6%), 51–75 (13.7%—12.4%) and 151–175 (6.5%, 8.2%) brackets. Parental educational achievement was categorised according to the highest level of educational achievement of either parent. Most participants had at least one parent with a bachelor's degree or higher (58.4%, 56.4%), followed by tertiary diplomas/certificate (22.4%, 21.6%), high school qualification (12.2%, 13.0%) and lastly no qualification (2.8%, 3.1%). Nearly all participants were on NIR (96.6%, 97.4%) as opposed to not on NIR (3.4%, 2.6%). Most participants self-reported "yes" when asked if they had received all recommended childhood vaccines (89.5%, 88.7%), with the rest responding unsure (6.3%, 4.5%) or no (3.9%, 4.3%), while a small proportion were missing (0.3%, 2.5%). In response to the question have you ever been hesitant to get a vaccine, most responded "no" (77.5%, 77.1%), with fewer responding "yes" (22.4%, 20.4%). Fewer participants reported ever refusing a vaccine (11.4%, 10.7%) compared to not ever refusing a vaccine (88.4%, 86.6%). Most participants had not received negative information about meningococcal vaccines (73.4%, 77.6%) although a sizable number had (23.4%, 16.8%).

Table 14: Description of Study Sample

	2019 (N=1,020)			2020 (N=1,243)		
	Participants	**%**	**95% CI**	**Participants**	**%**	**95% CI**
Age						
18 and younger	671	65.8	62.8–68.7	613	49.3	46.5–52.1
19	330	32.4	29.5–35.3	550	44.2	41.5–47.1
20 and older	19	1.9	1.1–2.9	80	6.4	5.1–7.9
Gender						
Male	286	28.0	25.3–30.9	325	26.1	23.7–28.7
Female	730	71.6	68.7–74.3	890	71.6	69.0–74.1
Gender Diverse	<5^	–	0.0–0.1	7	0.6	0.2–1.2
Missing	0	–	–	21	1.7	1.0–2.6
Prioritised ethnicity						
Māori	120	11.8	9.9–13.9	128	10.3	8.7–12.1
Pacific peoples	34	3.3	2.3–4.6	58	4.7	3.6–6.0
Asian	145	14.2	12.1–16.5	145	11.7	9.9–13.6
New Zealand European	703	68.9	66.0–71.8	866	69.7	67.0–72.2
Middle Eastern, Latin American, African	15	1.5	0.8–2.4	22	1.8	1.1–2.7
Other	0	–	–	0	0.0	–
Missing	3	0.3	0.1–0.9	24	1.9	1.2–2.9
College						
1	81	7.9	6.4–9.8	82	6.6	5.3–8.1
2	37	3.6	2.6–5.0	61	4.9	3.8–6.3
3	36	3.5	2.5–4.9	182	14.6	12.7–16.7
4	79	7.7	6.2–9.6	97	7.8	6.4–9.4
5	108	10.6	8.8-12.6	115	9.3	7.7–11.0
6	127	12.5	10.5–14.6	132	10.6	9.0–12.5
7	110	10.8	8.9–12.9	86	6.9	5.6–8.5
8	66	6.5	5.0–8.2	56	4.5	3.4–5.8
9	23	2.3	1.4–3.4	37	2.9	2.1–4.1

Table 14 continued

10	39	3.8	2.7–5.2	11	0.9	0.4–1.6
11	81	7.9	6.4–9.8	68	5.5	4.3–6.9
12	56	5.5	4.2–7.1	52	4.2	3.1–5.5
13	48	4.7	3.5–6.2	66	5.3	4.1–6.7
14	129	12.6	10.7–14.8	177	14.2	12.3–16.3
Missing	0	–	–	21	1.7	1.0–2.6
Combined parental NZSEI ranking						
0-25	21	2.1	1.3–3.1	34	2.7	1.9–3.8
26-50	45	4.4	3.2–5.9	58	4.7	3.6–6.0
51-75	140	13.7	11.7–16.0	154	12.4	10.6–14.4
76-100	149	14.6	12.5–16.9	151	12.6	10.4–14.1
101-125	203	19.9	17.5–22.5	239	19.2	17.1–21.5
126-150	286	28.0	25.3–30.9	344	27.7	25.2–30.3
151-175	66	6.5	5.0–8.2	102	8.2	6.7–9.9
176-200	17	1.7	1.0–2.7	18	1.5	0.8–2.3
Missing	93	9.1	7.4–11.1	143	11.5	9.8–13.4
Parental educational achievement						
No qualification	29	2.8	1.9–4.1	38	3.1	2.2–4.2
High School qualification	124	12.2	10.2–14.3	161	13.0	11.1–14.9
Tertiary diplomas/certificates	228	22.4	19.8–25.0	269	21.6	19.4–24.0
Bachelor’s degree or higher	596	58.4	55.3–61.5	701	56.4	53.6–59.2
Missing	43	4.2	3.1–5.6	74	6.0	4.7–7.4
Opinion on how protective vaccines are						
0–9 (not protective)	1	0.1	0.0–0.5	0	–	–
10–19	1	0.1	0.0–0.5	1	0.1	0.0–0.4
20–29	7	0.7	0.3–1.4	2	0.2	0.0–0.6
30–39	5	0.5	0.2–1.1	1	0.1	0.0–0.4
40–49	3	0.3	0.1–0.9	2	0.2	0.0–0.6
50–59	9	0.9	0.4–1.7	12	1.0	0.5–1.7

Table 14 continued

60–69	34	3.3	2.3–4.6	37	3.0	2.1–4.1
70–79	143	14.0	11.9–16.3	105	8.5	7.0–10.1
80–89	256	25.1	22.5–27.9	285	22.9	20.6–25.4
90–100 (very protective)	546	53.5	50.4–56.6	753	60.6	57.8–63.3
Missing	15	1.5	0.8–2.4	45	3.6	2.7–4.8
Experience of Vaccination						
National Immunisation Register						
On NIR, has NHI	985	96.6	95.3–97.6	1,211	97.4	96.4–98.2
Not on NIR, has NHI	35	3.4	2.4–4.7	26	2.1	1.4–3.0
Not on NIR, no NHI	0	–	–	6	0.5	0.2–1.0
Did you receive all the recommended childhood vaccines?						
No	40	3.9	2.8–5.3	54	4.3	3.3–5.6
Yes	913	89.5	87.4–91.3	1,102	88.7	86.8–90.4
Unsure	64	6.3	4.9–7.9	56	4.5	3.4–5.8
Missing	3	0.3	0.1–0.9	31	2.5	1.7–3.5
Have you ever been hesitant to get a vaccine?						
No	790	77.5	74.7–80.0	958	77.1	74.6–79.4
Yes	228	22.4	19.8–25.0	253	20.4	18.1–22.7
Missing	2	0.2	0.0–0.7	32	2.6	1.8–3.6
Have you ever refused a vaccine?						
No	902	88.4	86.3–90.3	1,076	86.6	84.5–88.4
Yes	116	11.4	9.5–13.5	133	10.7	9.0–12.6
Missing	2	0.2	0.0–0.7	34	2.7	1.9–3.8
Would you have a COVID-19 vaccine if available?						
No	–	–	–	19	1.5	0.9–2.4
Yes	–	–	–	1,022	82.2	80.0–84.3
Unsure	–	–	–	139	11.2	9.5–13.1
Missing	–	–	–	63	5.1	3.9–6.4

Table 14 continued

Sources of Information for meningococcal vaccines						
Have you received negative information on meningococcal vaccines?						
Yes	239	23.4	20.9–26.2	209	16.8	14.8–19.0
No	749	73.4	70.6–76.1	964	77.6	75.1–79.8
Missing	32	3.1	2.2–4.4	70	5.6	4.4–7.1

^ Groupings with fewer than five participants do not have the exact number listed to protect the privacy of participants.

4.4.4 Attitudes and beliefs regarding vaccination

Participants were asked questions relating to their attitudes towards vaccination in general (Table 15). In response to the question 'Are there any reasons why you think people should not be vaccinated?' 84.0% (95% CI 81.6–86.3) and 82.2% (95% CI 79.9–84.4) of respondents indicated there were no reasons why people should not be vaccinated. Of responses suggesting there were reasons why people should not be vaccinated, the most common reasons were fear of side effects (7.0%, 95% CI 5.5–8.7; 8.1%, 95% CI 6.6–9.8), low risk of getting a vaccine preventable disease (6.6%, 95% CI 5.1–8.3; 4.8%, 95% CI 3.7–6.3) and belief that even after vaccination people might get sick (6.5%, 95% CI 5.0–8.2; 6.6%, 95% CI 5.2—8.2). Less than three percent of people responded that vaccines are not natural (2.6%, 95% CI 1.7–3.8; 2.9%, 95% CI 2.0–4.1), lacked trust in vaccine manufacturers (1.5%, 95% CI 0.9–2.5; 2.5%, 95% CI 1.6–3.5) and vaccine preventable disease is not a problem for their community (1.6%, 95% CI 0.9–2.6; 1.3%, 95% CI 0.7–2.2). 3.6% and 3.7% of participants selected 'other' and included free text that have been grouped into themes for analysis. Free text comments from one individual can include more than one theme. The most expressed reasons why people should not vaccinate in free text answers were pre-existing health conditions (25.7%, 38.6%), allergy (22.9%, 18.2%), personal preference (14.3%, 6.8%) and parental disapproval (8.6%, 49.1%).

To further explore beliefs and motivations in relation to vaccination refusal, the 116 (2019) and 133 (2020) participants who had ever refused a vaccination were asked why they had refused (Table 16). Fifty-six percent (65/247, 95% CI 46.5—65.2) and 50.4% (67/282, 95% CI 41.6—59.2) of responses were that vaccines are not needed. A smaller proportion responded that negative media (26.7%, 95% CI 18.9—35.7; 27.1%, 95% CI 19.7—35.5), vaccines having side effects (24.1%, 95% CI 16.7—33.0; 28.6%, 95% CI 21.1—37.0) and vaccines not being effective (20.7%, 95% CI 13.7—29.2; 18.0%, 95% CI 11.9—25.6) were reasons for refusal. Only 4.0% and 2.8% responded that vaccines are too expensive. With regards free text responses, a third (29.4%, 31.0%) indicated that parental disapproval was the reason for vaccine refusal, and over a quarter refused HPV vaccination due to a belief they were too young.

Table 15: Attitudes and beliefs regarding vaccination

Are there reasons why you think people shouldn't be vaccinated?	2019 1,106 responses from 976 participants			2020 1,274 responses from 1,136 participants		
	n	%*	95% CI	n	%*	95% CI
None of the above, people should be vaccinated	820	84.0	81.6–86.3	934	82.2	79.9–84.4
I fear the side effects of vaccines	68	7.0	5.5–8.7	92	8.1	6.6–9.8
Even after vaccination I might get sick from the disease	63	6.5	5.0–8.2	75	6.6	5.2–8.2
Low risk of getting a vaccine preventable disease	64	6.6	5.1–8.3	55	4.8	3.7–6.3
Vaccines are not natural	25	2.6	1.7–3.8	33	2.9	2.0–4.1
I do not trust the manufacturers	15	1.5	0.9–2.5	28	2.5	1.6–3.5
Vaccine preventable disease is not a problem for my community	16	1.6	0.9–2.6	15	1.3	0.7–2.2
Other (free text categories):	35 (35)	3.6	2.5–5.0	42 (42)	3.7	2.7–5.0
	n	%Ψ		n	%Ψ	
Pre-existing health conditions	9	25.7		17	38.6	
Allergy	8	22.9		8	18.2	
Personal Preference	5	14.3		3	6.8	
Parents disapprove	3	8.6		4	9.1	
Religious or Cultural reasons	1	2.9		3	6.8	
If vaccines are too new	1	2.9		3	6.8	
Vaccines are harmful	2	5.7		2	4.5	
Links to Autism and "ITP"	–	–		2	4.5	
Don't have enough information	2	5.7		–	–	
Not needed for healthy people	1	2.9		1	2.3	
Fear of needles	1	2.9		1	2.3	
Cost	1	2.9		–	–	
Animal exploitation	1	2.9		–	–	

* proportion of people who choose the answer of interest Ψ proportion of free text answers

Table 16: Reasons given by participants who have refused any vaccine.

Reasons for ever refusing any vaccine?	2019 247 responses from 116 participants			2020 282 responses from 133 participants		
	N	%*	95% CI	N	%*	95% CI
Vaccines not needed	65	56.0	46.5—65.2	67	50.4	41.6—59.2
Negative media	31	26.7	18.9—35.7	36	27.1	19.7—35.5
Vaccines have side effects	28	24.1	16.7—33.0	38	28.6	21.1—37.0
Didn't know enough about vaccine	28	24.1	16.7—33.0	35	26.3	19.1—34.7
Vaccines are not effective	24	20.7	13.7—29.2	24	18.0	11.9—25.6
Someone else had a bad experience of vaccination	9	7.8	3.6—14.2	11	8.3	4.2—14.3
Vaccines are too expensive	10	8.6	4.2—15.3	8	6.0	2.6—11.5
Vaccines are not safe	8	6.9	3.0—13.1	10	7.5	3.7—13.4
Fear of needles	8	6.9	3.0—13.1	8	6.0	2.6—11.5
I had a bad experience of vaccination	7	6.0	2.5—12.1	9	6.8	3.1—12.5
Didn't know where to get info	3	2.6	0.5—7.4	11	8.3	4.2—14.3
Cultural reasons	3	2.6	0.5—7.4	3	2.3	4.7—6.5
Religious reasons	4	3.4	0.9—8.6	1	0.8	0.0—4.1
Prior bad experience at a clinic	2	1.7	0.2—6.1	3	2.3	4.7—6.5
Didn't know where to get a vaccine	0	–	–	1	0.8	0.0—4.1
Unable to leave my workplace	0	–	–	0	–	–
Other (free text responses):	16 (16)	13.8	8.1—21.4	17 (17)	12.8	7.6—19.5
	N	%ᵠ		N	%ᵠ	
Parents disapprove	5	29.4		9	31.0	
Too young for HPV at the time	4	23.5		8	27.6	
Vaccine too new	2	11.8		2	6.9	
Personal Preference	1	5.9		2	6.9	
Pre-existing health conditions	0	–		2	6.9	
Reaction to a prior vaccine	1	5.9		1	3.4	
Religious or Cultural reasons	0	–		1	3.4	
Vaccine not needed	1	5.9		0	–	
Cost	0	–		1	3.4	
Don’t have enough information	0	–		1	3.4	
Cost	0	–		1	3.4	
Unable to get an appointment	0	–		1	3.4	
Invalid free text	3	17.6		0	–	

* proportion of people who choose the answer of interest ᵠ proportion of free text answers

4.4.5 Meningococcal vaccination status

Participants were asked to self-report their meningococcal vaccination history (Table 20) and their immunisation status was also checked on the NHI and Student Health Records (Table 22). Comparing self-reported vaccination status with documented vaccination status enables us to gauge participants' understanding of their vaccination status. Most participants stated they had received a meningococcal vaccination (70.2%, 72.7%), with the rest unsure (14.9%, 17.0%) or stating they had not (12.5%, 5.5%). Participants were also asked to self-report which meningococcal vaccinations they thought they had received (Table 21). In 2019 the most common response was 4CMenB (24.7%), followed by MenACWY-D (23.3%), MeNZB (22.7%), MenACWY-T (11.6%) and MenC (5.1%), with 37.5% of participants being unsure. In 2020 the most common response was MenACWY-D (29.0%), followed by MeNZB (24.2%), 4CMenB (21.1%), MenACWY-T (6.5%) and MenC (4.0%), with 38.3% unsure.

The NIR and Student Health records showed that 87.5% and 87.8% of students had received a meningococcal vaccination of some description in their lifetime, but there was no record of meningococcal vaccination for the remaining 12.5% and 12.2%. With regard to documented meningococcal vaccinations, 77.5% and 75.6% of participants had received MeNZB vaccines, with 19.5% and 19.6% not having had a MeNZB vaccine for an unknown reason, and 3.0% and 4.9% had 'declined' documented in their NIR record for MeNZB. At the time of the study, the NIR did not differentiate between MenACWY-B and MenACWY-T vaccines, but instead referred only to MenACWY vaccine. As displayed in Table 17 MenACWY vaccines were only documented for 11.8% of participants in 2019, however this jumped to 44.0% in 2020. Conversely, 4CMenB vaccines were documented for 29.9% of participants in 2019, but only 12.6% of participants in 2020.

Table 17: Proportion of participants with documented MenACWY and 4CMenB vaccines.

MenACWY		**2018 Sample (%)**	**2019 Sample (%)**	**2020 Sample (%)**	Total per year
Date Given	2018	15 (100%)	34 (28.3%)	22 (4.0%)	71
	2019		86 (71.7%)	76 (13.9%)	162
	2020			448 (82.1%)	448
Total per Sample		15	120	546	

4CMenB		**2018 Sample (%)**	**2019 Sample (%)**	**2020 Sample (%)**	Total per year
Date Given	2018	–	9 (2.9%)	2 (1.3%)	11
	2019		297 (97.1%)	16 (10.3%)	131
	2020			138 (88.4%)	138
Total per Sample		0	306	156	

Key: Colour coding according to degree of health promotion and cost of vaccines.

MenACWY $138 | 4CMenB $240	Available
MenACWY $100 | 4CMenB $240	Available and promoted
MenACWY Free	Available and promoted and funded

The correct two-dose course of 4CMenB was documented for 20.0% and 5.5% of participants in 2019 and 2020 respectively, while 9.9% and 7.1% only received one dose by the end of 2020. As displayed in Table 18, this equates to one third (33.3%) of participants from the 2019 sample who received 4CMenB and over half (56.4%) of participants from the 2020 sample only receiving one dose instead of two.

Table 18: Proportion of participants who completed the full course of two dose of 4CMenB.

	2018 Sample	**2019 Sample**	**2020 Sample**	**Total**
Single Dose	–	102 (33.3%)	88 (56.4%)	190 (41.1%)
Two Doses	–	204 (66.7%)	68 (43.6%)	272 (58.9%)

In addition to supplying data for study participants, Student Health supplied data on the total number of MenACWY and 4CMenB vaccines administered from their clinics to all university students (Table 19). The additional information confirms that Student Health administered significantly more MenACWY in 2020 (n=525) than 2019 (n=9), including non-funded vaccine to university students not residing in residential colleges. Conversely, fewer 4CMenB vaccines were administered in 2020 (n=495) compared to 2019 (n=1,296). Student Health administered more second 4CMenB doses than first doses in both 2019 (n=738 vs 558) and 2020 (n=252 vs 243).

Table 19: Meningococcal vaccinations administered by Student Health to all students, including students that are not enrolled in the study.

	2019	**2020**
MenACWY Funded	1	459
MenACWY Non-funded	8	66
4CMenB dose 1	558	243
4CMenB dose 2	738	252

Table 20: Self-reported meningococcal vaccination status.

	2019			2020		
	Participants	**%**	**95% CI**	**Participants**	**%**	**95% CI**
Self-Reported Meningococcal Vaccines						
Have you ever had a meningococcal vaccination						
No	127	12.5	10.4–14.6	68	5.5	4.3–6.9
Yes	716	70.2	67.3–73.0	904	72.7	70.2–75.2
Unsure	152	14.9	12.8–17.2	211	17.0	14.9–19.2
Missing	25	2.5	1.6–3.6	60	4.8	3.7–6.2

Table 21: Self-reported meningococcal vaccines received.

	2019			2020		
	Participants	**%***	**95% CI**	**Participants**	**%***	**95% CI**
Menactra (MenACWY-D)	238	23.3	20.8–26.1	361	29.0%	26.5–31.7
Nimenrix (MenACWY-T)	118	11.6	9.7–13.7	81	6.5%	5.2–8.0
Neisvac (MenC)	52	5.1	3.8–6.6	50	4.0%	3.0–5.3
Bexsero (4CMenB)	252	24.7	22.1–27.5	262	21.1%	18.8–23.5
MeNZB	232	22.7	20.2–25.4	301	24.2%	21.9–26.7
Unsure	383	37.5	34.6–40.6	476	38.3%	35.6–41.1

* percentage of total responses.

Table 22: Documented Meningococcal Vaccination Status

	2019 (N=1,020)			2020 (N=1,243)		
	Participants	**%**	**95% CI**	**Participants**	**%**	**95% CI**
Documented Meningococcal Vaccines						
MeNZB Doses						
0	199	19.5	17.1–22.1	243	19.6	17.4–21.9
1	6	0.6	0.2–1.3	5	0.4	1.3–0.9
2	3	0.3	0.0–0.9	11	0.9	0.4–1.6
3	781	76.6	73.8–79.1	923	74.3	71.7–76.7
Declined	31	3.0	2.1–4.3	61	4.9	3.8–6.3
Menactra Doses						
0	900	88.2	86.1–90.1	697	56.1	53.3–58.9
1	119	11.7	9.8–13.8	544	43.8	41.0–46.6
2	1	0.1	0.0–0.5	2	0.2	0.0–0.6
Menactra Date Given						
2018 or prior	34	3.3	2.3–4.6	22	4.0	2.5–6.0
2019	86	8.4	6.8–10.3	76	13.9	11.1–17.1
2020	–	–	–	446	81.7	78.2–84.8
2021	–	–	–	2	0.4	0.0–1.3
Bexsero Doses						
0 Doses	715	70.1	67.2–72.9	1087	87.5	85.5–89.2
1 Dose	102	9.9	8.1–11.9	88	7.1	5.7–8.6
2 Doses	204	20.0	17.6–22.6	68	5.5	4.3–6.9
Bexsero Date Given						
2018	9	0.9	0.4–1.7	2	1.3	0.2–4.6
2019	297	29.1	26.3–32.0	16	10.3	6.0--16.1
2020	–	–	–	138	88.5	82.4–93.0
Any Documented Meningococcal Vaccine						
No	127	12.5	10.2–14.2	152	12.2	10.5–14.2
Yes	893	87.5	82.7–87.2	1,091	87.8	85.8–89.5

4.4.6 Motivations for meningococcal vaccination

Participants were asked whether they had received a meningococcal vaccination, and were then asked to explain why, or why not. Participants who were unsure of their meningococcal vaccination status were asked to answer both questions. The main motivations for having a meningococcal vaccination (Table 23) were for personal (91.1%, 95% CI 88.9–93.0; 88.3%, 95% CI 86.2–90.2) and community (54.0%, 95% CI 50.5–57.4; 61.2%, 95% CI 58.1–64.2) benefit. This was supported by a high proportion of free text responses referencing acquaintances who had died following IMD (38.9%, 47.1% of free text responses). 61.3% (95% CI 57.8–64.6) and 57.7% (95% CI 54.6–60.7) of respondents indicated that vaccines being effective, and safe (54.0%, 95% CI 50.5–57.4; 52.4%, 95% CI 49.3–55.5), were reasons for being vaccinated. 58.7% (95% CI 55.2–62.1) and 54.2% (95% CI 51.1–57.3) of respondents identified that the vaccine being recommended was a reason for being vaccinated, and recommendation and requirement was referenced in multiple free text answers (combined 61.2%, 47.1%). Ranking of reasons for having a meningococcal vaccine was consistent between 2019 and 2020, except for cost (3.7%, 8.3%), which was ranked higher in 2020.

In contrast, a high proportion of participants who had not received a meningococcal vaccination (Table 24) indicated that expense was a reason for not having a vaccine (59.8%, 95% CI 52.1–67.1; 29.0%, 95% CI 25.5–32.7). Lack of knowledge about the vaccine being available (13.8%, 95% CI 9.0–19.8; 28.5%, 95% CI 25.0–32.2) and about the vaccine generally (16.7%, 95% CI 11.5–23.1; 12.4%, 95% CI 9.9–15.2) ranked highly, and free text comments supported this with participants referencing not being sure which vaccines they had already had (30.6% of free text comments in 2020), and not knowing if it was recommended for them (10.5%, 18.1% of free text comments). Participants also indicated a belief that the vaccine was not needed (16.1%, 95% CI 11.0–22.4; 22.8%, 19.6–26.3%). Few respondents indicated a lack of confidence in vaccine, evidenced by low ranking for vaccines are not safe (2.9%, 95% CI 0.9–6.6; 2.1%, 95% CI 1.1–3.5) and not effective (4.0%, 95% CI 1.6–8.1; 1.1% 95% CI 0.4–2.3), and fewer referred to negative media (1.7%, 95% CI 0.3–5.0; 1.3%, 95% CI 0.5–2.5) or others (2.3%, 95% CI 0.6–5.8; 1.1%, 95% CI 0.4–2.3) being a reason not to vaccinate. Free text responses indicated inconvenience was a barrier, citing not getting around to it (47.4%, 23.6%) and being too busy to wait at the clinic (10.5%, 6.9%). Free text respondents were unsure which vaccines they had already received (27.5% in 2020) and whether meningococcal vaccines were recommended for them (12.5%, 16.63%).

All participants were asked to identify any barriers to receiving a meningococcal vaccination (Table 25), and the majority indicated there were no barriers (72.0%, 77.1%). For those that did perceive

barriers, cost was the main barrier (68.8%, 54.2%) with the small remainder selecting inconvenience (7.2%, 9.9%).

Table 23: Reasons for accepting a meningococcal vaccine.

Reasons for having a meningococcal vaccine*	2019 4,028 responses from 808 participants			2020 5807 responses from 1033 participants		
	N	%*	95% CI	N	%*	95% CI
Personal benefit	736	91.1	88.9–93.0	912	88.3	86.2–90.2
Vaccines are effective	495	61.3	57.8–64.6	596	57.7	54.6–60.7
Community benefit	436	54.0	50.5–57.4	632	61.2	58.1–64.2
Vaccine was recommended	474	58.7	55.2–62.1	560	54.2	51.1–57.3
Vaccines are safe	436	54.0	50.5–57.4	541	52.4	49.3–55.5
No cost	150	18.6	15.9–21.4	486	47.0	44.0–50.1
No concerns about side effects	266	32.9	30.0–36.3	355	34.4	31.5–37.4
Access to good information	229	28.3	25.3–31.6	332	32.1	29.3–35.1
Being offered the vaccine	168	20.8	18.0–23.8	373	36.1	33.2–39.1
Prior good vaccination experience	204	25.2	22.3–28.4	321	31.1	28.3–34.0
Prior good clinic experience	208	25.7	22.8–28.9	301	29.1	26.3–32.0
Someone else told me they're safe	93	11.5	9.4–13.9	142	13.7	11.7–16.0
Positive media	78	9.7	7.7–11.9	134	13.0	11.0–15.2
Convenient to leave work	37	4.6	3.2–6.3	73	7.1	5.6–8.8
Someone else had a good experience of vaccination	17	2.1	1.2–3.3	48	4.6	3.4–6.1
Religious reasons	1	0.1	0.0–0.7	1	0.1	0.0–0.5
Other (free text responses):	23(22)	2.8	1.8–4.2	28(17)	2.7	1.8–3.9
	N	%ᴪ		N	%ᴪ	
Acquaintance died of IMD	7	31.8		8	47.1	
Recommended by College	7	31.8		3	17.6	
Professional requirement	2	9.1		1	5.9	
Recommended for travel	1	4.5		1	5.9	
Encouraged at school	1	4.5		1	5.9	
Compulsory in country of origin	0	–		2	11.8	
Due to a health issue	0	–		1	5.9	
Invalid free text	4	18.2		0	–	

* proportion of people who choose the answer of interest ᴪ proportion of free text answers

Table 24: Reasons for declining a meningococcal vaccine.

Reasons for not having a meningococcal vaccine*	2019 292 responses from 174 participants			2020 956 responses from 631 participants		
	N	%*	95% CI	N	%*	95% CI
Vaccines too expensive	104	59.8	52.1–67.1	183	29.0	25.5–32.7
Didn't know vaccines available	24	13.8	9.0–19.8	180	28.5	25.0–32.2
Meningococcal vaccines are not needed	28	16.1	11.0–22.4	144	22.8	19.6–26.3
Didn't know enough about vaccines	29	16.7	11.5–23.1	78	12.4	9.9–15.2
Vaccine not recommended to me	14	8.0	4.5–13.1	74	11.7	9.3–14.5
Fear of needles	12	6.9	3.6–11.7	47	7.4	5.5–9.8
Didn't know where to get a vaccine	11	6.3	3.2–11.0	37	5.9	4.2–8.0
Unable to leave the workplace	9	5.2	2.4–9.6	27	4.3	2.8–6.2
Vaccines have side effects	10	5.7	2.8–10.3	18	2.9	1.7–4.5
Didn't know where to get information on a vaccine	8	4.6	2.0–8.9	18	2.9	1.7–4.5
Prior bad experience of vaccination	4	2.3	0.6–5.8	20	3.2	1.9–4.9
Vaccines are not safe	5	2.9	0.9–6.6	13	2.1	1.1–3.5
Vaccines are not effective	7	4.0	1.6–8.1	7	1.1	0.4–2.3
Negative media	3	1.7	0.3–5.0	8	1.3	0.5–2.5
Someone else told me vaccines are not safe	4	2.3	0.6–5.8	7	1.1	0.4–2.3
Someone else had a bad experience of vaccination	2	1.1	0.1–4.1	5	0.8	0.3–1.8
Prior bad experience of a health clinic	1	0.6	0.0–3.1	5	0.8	0.3–1.8
Religious reasons	1	0.6	0.0–3.1	2	0.3	0.0–1.1
Cultural reasons	0	–	–	3	0.5	0.1–1.4
Other (free text responses):	16 (16)	9.2	5.3–14.5	80 (72)	12.7	10.2–15.5

Table 24 continued

	N	%ᵠ		N	%ᵠ	
Didn't get around to it	9	56.3		17	21.3	
Not sure which vaccines I've had	0	–		22	27.5	
Didn't know if it was recommended for me	2	12.5		13	16.3	
Too busy/didn't want to go back and wait at the clinic	2	12.5		5	6.3	
Not needed for me	1	6.3		5	6.3	
Fear of pain or fainting	2	12.5		2	2.5	
Intended to but forgot	1	6.3		3	3.8	
I was unwell the day it was due	1	6.3		1	1.3	
Pre-existing health condition	0	0.0		2	2.5	
Parents disapproved	1	6.3		0	–	
GP didn't know about it	0	–		1	1.3	
Only gives short term protection	0	–		1	1.3	

* proportion of people who choose the answer of interest ᵠ proportion of free text answers

Table 25: Barriers to meningococcal vaccination

Perceived barriers to meningococcal vaccination*	2019 1,461 responses from 987 participants			2020 1,712 responses from 1,148 participants		
	N	%*	95% CI	N	%*	95% CI
No barriers	711	72.0	69.1–74.8	885	77.1	74.5–79.5
Cost	501	50.8	47.6–53.9	481	41.9	39.0–44.8
Cost of accessing clinic	178	18.0	15.7–20.6	141	12.3	10.4–14.3
Time required to get to a clinic	51	5.2	3.9–6.7	74	6.4	5.1–8.0
Distance to a clinic	20	2.0	1.2–3.1	40	3.5	2.5–4.7
Other	0	–	–	91	7.9	6.4–9.6

* proportion of people who choose the answer of interest

4.4.7 Sources of information on meningococcal vaccination

When asked which sources they had accessed for information on meningococcal vaccines(Table 26), 69.8% (95% CI 66.9–72.7) and 74.2% (95% CI 71.5–76.8) or respondents selected 'parents', 62.6% (95% CI 59.4–65.6) and 63.1% (95% CI 60.2–66.0) selected 'residential college' and 52.1% (95% CI 49.0–55.3) and 63.8% (95% CI 60.8–66.6) selected 'family GP'. A smaller proportion of students accessed information from non-authoritative sources such as Google search (21.0%, 95% CI 18.5–23.6; 20.1%, 95% CI 17.8–22.6), Advertising (13.2%, 95% CI 11.1–15.4; 12.9%, 95% CI 10.9–15.0) and Facebook (6.4%, 95% CI 4.9–8.1; 3.4%, 95% CI 2.4–4.7). The high number of responses (3,754 and 4,410) compared to participants (1,020 and 1,243) indicates that participants access information from more than one source.

Table 26: Sources of information for meningococcal vaccinations

What sources have you accessed for information on meningococcal vaccines?	2019 3,754 responses from 988 participants			2020 4,419 responses from 1079 participants		
	N	%*	95% CI	N	%*	95% CI
Parents	690	69.8	66.9–72.7	801	74.2	71.5–76.8
Residential College	618	62.6	59.4–65.6	681	63.1	60.2–66.0
Family GP	515	52.1	49.0–55.3	688	63.8	60.8–66.6
University enrolment material	398	40.3	37.2–43.4	387	35.9	33.0–38.8
Friends	327	33.1	30.2–36.1	410	38.0	35.1–41.0
Student Health staff	281	28.4	25.6–31.4	325	30.1	27.4–33.0
MOH or IMAC websites	202	20.4	18.0–23.1	324	30.0	27.3–32.9
Student Health website	202	20.4	18.0–23.1	257	23.8	21.3–26.5
Google search	207	21.0	18.5–23.6	217	20.1	17.8–22.6
Advertising	130	13.2	11.1–15.4	139	12.9	10.9–15.0
I haven't looked for or received information	68	6.9	5.4–8.6	97	9.0	7.4–10.9
Facebook	63	6.4	4.9–8.1	37	3.4	2.4–4.7
Other	27	2.7	1.8–4.0	28	2.6	1.7–3.7
Vaccine manufacturers	26	2.6	1.7–3.8	28	2.6	1.7–3.7

* proportion of people who choose the answer of interest

Among the 239 (23.4%, 95% CI 20.9–26.2) and 209 (16.8%, 95% CI 14.8–19.0) participants that had received negative information about meningococcal vaccines (Table 27), the majority received that information from Facebook (49.0%, 95% CI 42.4–55.5; 42.1%, 95% CI 35.3–49.1), Friends (41.8%, 95% CI 35.5–48.4; 46.4%, 95% CI 39.5–53.4) and Websites (not further defined) (44.4%, 95% CI 37.9–50.9; 39.7%, 95% CI 33.0–46.7). Surprisingly 9.6% (95% CI 6.2–14.1) and 13.9% (95% CI 9.5–19.3) of respondents nominated Health Professionals as the source of negative information.

Table 27: Sources of negative information on meningococcal vaccinations

What was the source of negative information?	2019 479 responses from 239 participants			2020 394 responses from 209 participants		
	N	%*	95% CI	N	%*	95% CI
Facebook	117	49.0	42.4–55.5	88	42.1	35.3–49.1
Friends	100	41.8	35.5–48.4	97	46.4	39.5–53.4
Websites	106	44.4	37.9–50.9	83	39.7	33.0–46.7
TV or Radio	44	18.4	13.7–23.9	21	10.0	6.3–14.9
Health Professionals	23	9.6	6.2–14.1	29	13.9	9.5–19.3
Parents	25	10.5	6.9–15.1	24	11.5	7.5–16.6
Magazines	24	10.0	6.5–14.6	18	8.6	5.2–13.3
Podcasts of Vlogs	27	11.3	7.6–16.0	14	6.7	3.7–11.0
Other	9	3.8	1.7–7.0	11	5.3	2.7–9.2
Vaccine manufacturer data sheets	4	1.7	0.5–4.2	9	4.3	2.0–8.0

* proportion of people who choose the answer of interest

4.4.8 Willingness to accept a hypothetical COVID-19 vaccine

The 2020 questionnaire asked participants if they would have a hypothetical vaccine for COVID-19. Among participants 82.2% (95% CI 80.0–84.3) stated ‘yes’, 11.2% (95% CI 9.5–13.1) were ‘unsure’, and 1.5% (95% CI 0.9–2.4%) stated ‘no’. When asked why they wanted a COVID-19 vaccine(Table 28), the most common answers were for personal benefit (84.3%, 95% CI 82.0–86.3) and community benefit (81.4%, 95% CI 79.0–83.6). 58.3% (95% CI 55.4–61.2) stated vaccines being effective was a reason, and 50.3% (95% CI 47.4–53.2) stated vaccines being safe was a reason. Having the vaccine recommended or offered to them was a reason for 42.5% (95% CI 39.6–45.5) and 40.7% (95% CI 37.8–43.6) respectively.

Table 28: Reasons for having a COVID-19 vaccine*

Reasons for having a COVID-19 vaccine*	2020 6,625 responses from 1145 participants		
	N	%*	95% CI
Personal benefit	965	84.3	82.0–86.3
Community benefit	932	81.4	79.0–83.6
Vaccines are effective	668	58.3	55.4–61.2
Vaccines are safe	576	50.3	47.4–53.2
Vaccine was recommended	487	42.5	39.6–45.5
Being offered the vaccine	466	40.7	37.8–43.6
Prior good vaccination experience	422	36.9	34.1–39.7
Access to good information on the vaccine	381	33.3	30.4–36.1
Prior good clinic experience	342	29.9	27.2–32.6
No cost	297	25.9	23.4–28.6
Someone else told me they're safe	266	23.2	20.8–25.8
No concerns about side effects	258	22.5	20.1–25.1
Positive media	258	22.5	20.1–25.1
Someone else had a good experience of vaccination	154	13.4	11.5–15.6
Convenient to leave work	128	11.2	9.4–13.1
Religious reasons	4	0.3	0.1–0.9
Other (free text responses):	21	1.8	1.1–2.8

* proportion of people who choose the answer of interest Ψ proportion of free text answers

For participants that indicated they were unsure, or would not have a COVID-19 vaccine (Table 29), the most frequently chosen reasons were the vaccine not being safe (40.9%, 95% CI 32.6–49.6) or having side effects (38.0%, 95% CI 29.8–46.7). Among other reasons for not having a vaccine, 32.1% (95% CI 24.4–40.6) of respondents selected negative media, 31.4% (95% CI 23.7–39.9) selected vaccines being too expensive, and 30.7% (95% CI 23.1–39.1) selected not knowing enough to decide.

Table 29: Reasons for not having a COVID-19 vaccine

Reasons for not having a COVID-19 vaccine*	2020 439 responses from 137 participants		
	N	%*	95% CI
Vaccine is not safe	56	40.9	32.6–49.6
Vaccine has side effects	52	38.0	29.8–46.7
Negative media	44	32.1	24.4–40.6
Vaccine too expensive	43	31.4	23.7–39.9
Don't know where to get information on a vaccine	43	31.4	23.7–39.9
Didn't know enough about vaccine	42	30.7	23.1–39.1
Vaccine not recommended to me	29	21.2	14.7–29.0
Someone else told me vaccine is not safe	27	19.7	13.4–27.4
Vaccine not needed	20	14.6	9.2–21.6
Someone else had a bad experience of vaccination	16	11.7	6.8–18.2
Fear of needles	14	10.2	5.7–16.6
Vaccine is not effective	9	6.6	3.0–12.1
No community benefit	6	4.4	1.6–9.3
Don't know where to get a vaccine	6	4.4	1.6–9.3
Unable to leave the workplace	6	4.4	1.6–9.3
Prior bad experience of vaccination	5	3.6	1.2–8.3
Cultural reasons	5	3.6	1.2–8.3
Prior bad experience of a health clinic	0	–	–
Religious reasons	0	–	–
Other reasons	16	11.7	6.8–18.3

* proportion of people who choose the answer of interest Ψ proportion of free text answers

4.4.9 Characteristics of vaccine hesitant individuals compared with non-vaccine hesitant individuals

To further address objective D the association of known and potential factors with vaccine hesitancy were assessed (Table 30). Vaccine hesitancy is defined by a yes or no response to the question "have you ever been hesitant to get a vaccination". Chi square test confirmed a statistically significant association between vaccine hesitancy and both gender (*P*=.003) and ethnicity (*P*=.001) in 2019, but not in 2020 (gender *P*=.41, ethnicity *P*=.82). In both 2019 and 2020 there was a statistically significant association between combined parental NZSEI category (*P*=.001, *P*<.001), opinion on how protective vaccines are, receiving childhood vaccines, ever having refused a vaccine, self-reported meningococcal vaccination status (all *P*<.001 for 2019 and 2020) and having received negative information on meningococcal vaccines (*P*=.002, *P*<.001). Chi square test did not find a statistically significant association between vaccine hesitancy and age (*P*=.71, *P*=.12), college (*P*=.85, *P*=.11), parental educational achievement (*P*=.23, *P*=.82), being on the NIR (*P*=.37, *P*=.69) and documented meningococcal vaccination status (*P*=.14, *P*=.10).

Table 30: Characteristics of vaccine hesitant individuals compared with non-vaccine hesitant individuals

	2019 (N=1,020)					2020 (N=1,243)				
	Hesitant	Not Hesitant	% Hesitant	95% CI	Chisquare *P* value	Hesitant	Not Hesitant	% Hesitant	95% CI	Chisquare *P* value
Demographic Information										
Age										
18 and younger	145	524	21.7	18.6–25.0		130	468	21.7	18.5–25.3	
19	79	251	23.9	19.4–28.9	*P*=.71	103	435	19.1	15.9–22.7	*P*=.12
20 and older	<5^	15	21.1	6.1–45.6		20	55	26.7	17.1–38.1	
Gender										
Male	45	241	15.7	11.7–20.5		187	686	21.4	18.7–24.3	
Female	183	545	25.1	22.0–28.5	*P*=.003	58	256	18.5	14.3–23.2	*P*=.41
Gender Diverse	0	<5^	0.0	–		<5^	5	28.6	3.7–71.0	
Prioritised Ethnicity										
Māori	33	87	27.5	19.7–36.4		25	100	20.0	13.4–28.1	
Pacific peoples	16	18	47.1	29.8–64.9		9	48	15.8	7.5–27.9	
Asian	23	122	15.9	10.3–22.8	*P*=.001	32	107	23.0	16.3–30.9	*P*=.82
New Zealand European	153	548	21.8	18.8–25.1		174	674	20.5	17.8–23.4	

Table 30 continued

Middle Eastern, Latin American, African	>5^	13	13.3	1.7–40.5		5	17	22.7	7.8–45.4	
Other	0	0	–	–		0	0	–	–	
College										
1	15	66	18.5	10.8–40.5		24	57	29.6	20.0–40.8	
2	10	27	27.0	13.8–44.1		17	44	27.9	17.1–40.8	
3	7	29	19.4	8.2–36.0		30	143	17.3	12.0–23.8	
4	22	57	27.8	18.3–39.1		12	83	12.6	6.7–21.0	
5	28	79	26.2	18.1–35.6		28	85	24.8	17.1–33.8	
6	27	100	21.3	14.5–29.4		19	110	14.7	9.1–22.0	
7	27	83	24.5	16.8–33.7		15	71	17.4	10.1–27.1	
8	10	56	15.2	7.5–26.1	*P*=.85	13	40	24.5	13.8–38.3	*P*=.11
9	5	18	21.7	7.5–43.7		7	30	18.9	8.0–35.2	
10	11	28	28.2	15.0–44.9		2	9	18.2	2.3–51.8	
11	20	61	24.7	15.8–35.5		14	52	21.2	12.1–33.0	
12	11	45	19.6	10.2–32.4		9	40	18.4	8.8–32.0	
13	10	38	20.8	10.5–35.0		14	51	21.5	12.3–33.5	
14	25	103	19.5	13.1–27.5		43	132	24.6	18.4–31.6	

Table 30 continued

Combined Parental NZSEI Ranking										
0-25	5	16	23.8	8.2–47.2		9	25	26.5	12.9–44.4	
26-50	13	32	28.9	16.4–44.3		19	39	32.8	21.0–46.3	
51-75	33	107	23.6	16.8–31.5		32	121	20.9	14.7–28.2	
76-100	46	103	30.9	23.6–39.0	*P*=.01	28	122	18.7	12.8–25.8	*P*<.001
101-125	37	166	18.2	13.2–24.2		45	192	19.0	14.2–24.6	
126-150	63	223	22.0	17.4–27.3		80	263	23.3	18.9–28.2	
151-175	8	58	12.1	5.4–22.5		15	87	14.7	8.4–23.1	
176-200	0	17	0.0	0–19.5		1	14	6.7	0.2–31.9	
Parental Educational Achievement										
No qualification	7	22	24.1	10.3–43.5		9	29	23.7	11.4–40.2	
High School qualification	35	89	28.2	20.5–37.0		35	124	22.0	15.8–29.3	
Tertiary diplomas or certificates	51	176	22.5	17.2–28.5	*P*=.23	58	208	21.8	17.0–27.3	*P*=.82
Bachelor's degree or higher	119	476	20.0	16.9–23.4		143	555	20.5	17.6–23.7	

^ Groupings with fewer than five participants do not have the exact number listed to protect the privacy of participants.

Table 30 continued

Beliefs Regarding Vaccination										
Opinion on How Protective Vaccines Are (Scale 0–100)										
0–69	36	24	60.0	46.5–72.4		28	26	51.9	37.8–65.7	
70–79	47	96	32.9	25.2–41.2	*P*<.001	42	62	40.4	30.9–50.5	*P*<.001
80–89	63	192	24.7	19.5–30.5		62	223	21.8	17.1–27.0	
90–100	81	465	14.8	12.0–18.1		114	638	15.2	12.7–17.9	
Experience of Vaccination										
NIR										
On NIR, has NHI	218	765	22.2	19.6–24.9		244	936	20.7	18.4–23.1	
Not on NIR has NHI	10	25	28.6	14.6–46.3	*P*=.37	8	17	32.0	14.9–53.5	*P*=.69
Not on NIR no NHI	–	–	–	–		1	5	16.7	0.4–64.1	
Childhood vaccines complete										
No	24	15	61.5	44.6–76.6		38	16	70.4	56.4–82.0	
Yes	177	736	19.4	16.9–22.1	*P*<.001	196	905	17.8	15.6–20.2	*P*<.001
Unsure	26	38	40.6	28.5–53.6		19	37	33.9	21.8–47.8	
Refused a vaccine										
No	153	749	17.0	14.6–19.6		178	897	16.6	14.4–18.9	
Yes	74	41	64.3	54.9–73.1	*P*<.001	74	59	55.6	46.8–64.2	*P*<.001

Table 30 continued

Documented Meningococcal Vaccine Received (one or more of any vaccine)										
No	35	92	27.6	20.0–36.2	*P*=.14	39	107	26.7	19.7–34.7	*P*=.10
Yes	193	698	21.7	19.0–24.5		214	851	20.1	17.7–22.6	
Self-reported Meningococcal Vaccine Received (one or more of any vaccine)										
No	47	80	37.0	28.6–46.0	*P*<.001	31	37	45.6	33.5–58.1	*P*<.001
Yes	132	584	18.4	15.7–21.5		162	741	17.9	15.5–20.6	
Unsure	41	111	27.0	20.1–34.8		55	156	26.1	20.3–32.5	
Have you received negative information on meningococcal vaccines?										
Yes	70	169	29.3	23.6–35.5	*P*=.002	66	142	31.7	25.5–38.5	*P*<.001
No	149	600	19.9	17.1–22.9		181	782	18.8	16.4–21.4	
Would you have a COVID-19 vaccine if available										
No	–	–	–	–	–	10	9	52.6	28.9–75.6	*P*<.001
Yes	–	–	–	–		180	841	17.6	15.3–20.1	
Unsure	–	–	–	–		58	81	41.7	33.4–50.4	

* one-sided, 97.5% confidence interval

4.4.10 Association between independent variables and vaccine hesitancy

To further address objective D, univariate logistic regression was used to find associations between vaccine hesitancy and other variables included in the survey (Table 31). In 2019 male participants were nearly half as likely to be vaccine hesitant as female participants (OR 0.56, 95% CI 0.39–0.80, *P*=.001), but there was no statistically significant difference between genders in 2020 (OR 0.91, 95% CI 0.67–1.23, *P*=.53). In 2019 the odds of participants who were Pacific Peoples being vaccine hesitant (OR 2.34, 95% CI 1.07–5.13, *P*=.03) were greater than those for Māori (reference group), while odds of hesitance among participants of Asian ethnicity was half of that of among Māori (OR 0.50, 95% CI 0.27–0.90, *P*=.02). For other ethnicities, and for all ethnicities in 2020, there was no statistically significant difference in odds of vaccine hesitance between ethnicities. The difference in odds of vaccine hesitancy between colleges were not statistically significant, with the exception of two colleges in 2020. Colleges coded four (OR 0.38, 95% CI 0.18–0.80, *P*=.01) and six (OR 0.46, 95% CI 0.24–0.88, P=.02) were less than half as likely to have participants who were vaccine hesitant when compared to the college used as the reference. Participants from both 2019 and 2020 who ranked vaccines as less protective had higher odds of vaccine hesitancy. In 2019, odds of vaccine hesitancy for a ranking of 80—89 (OR 1.88, CI 1.30–2.72, *P*=.001) rose incrementally until ranking of 0—69 (OR 8.61, 95% CI 4.88–15.19, *P*<.001). In 2020 odds followed a similar trend, from rankings 80—89 (OR 1.54, 95% CI 1.09–2.18, *P*=.01) to 0—69 (OR 6.19, 95% CI 3.52–10.89, *P*<.001). Participants from both years who reported receiving all their childhood vaccines were less likely to be vaccine hesitant (2019: OR 0.15, 95% CI 0.08–0.29, *P*<.001; 2020: OR 0.09, 95% CI 0.05–0.17, *P*<.001), as were those who were unsure of their childhood vaccination status (2019: OR 0.43, 95% CI 0.19–0.97, *P*=.04; 2020: OR 0.22, 95% CI 0.10–0.48, *P*<.001) when compared to participants who reported not receiving all their childhood vaccinations (reference group). Participants who had ever refused any vaccine were over six times more likely to be vaccine hesitant (2019: OR 8.84, 95% CI 5.81–13.44, *P*<.001; 2020: OR 6.29, 95% CI 4.31–9.17, *P*<.001). Participants from 2019 were less likely to be vaccine hesitant if they had received the MeNZB vaccine in childhood (OR 0.64, 95% CI 0.45–0.90, *P*=.01), but there was no statistically significant difference in odds for the 2020 cohort (OR 0.89, 95% CI 0.64–1.23, *P*=.47). In both years participants who self-reported receiving one or more dose of any meningococcal vaccine were less than half as likely to be vaccine hesitant (2019: OR 0.38, 95% CI 0.26–0.58, *P*<.001; 2020: OR 0.26, 95% CI 0.16–0.44, *P*<.001), and the same was true for participants who unsure of their meningococcal vaccination history in 2020 (OR 0.42, 95% CI 0.24–0.74, *P*=.003), but not in 2019 (OR 0.63, 95% CI 0.38–1.04, *P*=.07). Participants who reported receiving negative information on meningococcal vaccines were more likely to be vaccine hesitant (2019: OR 1.67, 95% CI 1.20–2.32, *P*=.02; 2020: OR 2.03, 95% CI 1.45–2.83, *P*<.001). Finally,

participants from the 2020 cohort were five times less likely to be vaccine hesitant if they reported being willing to have a hypothetical vaccine for COVID-19 (OR 0.19, 95% CI 0.08–0.48, *P*<.001). There was no evidence of a statistically significant difference in odds of having vaccine hesitance between the participants of different age, between Māori, New Zealand European and Middle Eastern, Latin American, African ethnic groups, between most colleges, between various parental NZSEI categories, between participants who parents had differing levels of educational achievement, between participants who were and were not on the NIR, and between participants who had a documented receiving one or more dose of a 4CMenB or MenACWY vaccine.

Table 31: Univariable analysis of factors associated with vaccine hesitancy

	2019			2020		
	Odds Ratio	95% CI	*P* value	Odds Ratio	95% CI	*P* value
Demographic Information						
Age						
18 and younger	1	–	–	1	–	–
19	1.14	0.83–1.55	*P*=.42	0.85	0.65–1.13	*P*=.26
20 and older	0.96	0.32–2.95	*P*=.95	1.47	0.88–2.44	*P*=.14
Gender						
female	1			1		
male	**0.56**	**0.39–0.80**	***P*=.001**	0.91	0.67–1.23	*P*=.53
gender diverse	1.00	–	–	1.35	0.26–6.98	*P*=.72
Ethnicity						
Māori	1	–	–	1	–	–
Pacific peoples	**2.34**	**1.07–5.13**	***P*=.03**	0.74	0.33–1.66	*P*=.47
Asian	**0.50**	**0.27–0.90**	***P*=.02**	1.27	0.73–2.22	*P*=.41
New Zealand European	0.74	0.47–1.14	*P*=.17	1.02	0.65–1.59	*P*=.94
Middle Eastern, Latin American, African	0.41	0.08–1.90	*P*=.25	1.05	0.36–3.10	*P*=.93
College						
1	1	–	–	1	–	–
2	1.63	0.65–4.08	*P*=.30	0.88	0.42–1.83	*P*=.73
3	1.06	0.39–2.88	*P*=.91	0.62	0.35–1.12	*P*=.11

Table 31 continued

4	1.70	0.81–3.58	*P*=.16	**0.38**	**0.18–0.80**	***P*=.01**
5	1.56	0.77–3.16	*P*=.22	0.80	0.43–1.51	*P*=.50
6	1.19	0.59–2.40	*P*=.63	**0.46**	**0.24–0.88**	***P*=.02**
7	1.43	0.70–2.91	*P*=.32	0.48	0.23–1.00	*P*=.05
8	0.79	0.33–1.89	*P*=.59	0.91	0.43–1.92	*P*=.81
9	1.22	0.39–3.82	*P*=.73	0.53	0.21–1.37	*P*=.19
10	1.73	0.71–4.23	*P*=.23	0.51	0.10–2.52	*P*=.41
11	1.44	0.68–3.07	*P*=.34	0.70	0.34–1.46	*P*=.34
12	1.08	0.45–2.56	*P*=.87	0.68	0.31–1.52	*P*=.35
13	1.16	0.47–2.83	*P*=.75	0.67	0.32–1.41	*P*=.29
14	1.07	0.52–2.17	*P*=.86	0.78	0.44–1.39	*P*=.39
Combined Parental NZSEI Ranking						
0-25	1	–	–	1	–	–
26-50	1.30	0.39–4.29	*P*=.67	1.35	0.53–3.46	*P*=.53
51-75	0.99	0.34–2.90	*P*=.98	0.76	0.32–1.78	*P*=.52
76-100	1.43	0.49–4.14	*P*=.51	0.66	0.28–1.56	*P*=.35
101-125	0.71	0.25–2.07	*P*=.53	0.68	0.30–1.55	*P*=.36
126-150	0.90	0.32–2.56	*P*=.85	0.86	0.38–1.91	*P*=.70
151-175	0.44	0.13–1.54	*P*=.20	0.48	0.19–1.22	*P*=.12
176-200	1.00	–	–	0.79	0.21–3.05	*P*=.74

Table 31 continued

Parental Educational Achievement						
No qualification	1	–	–	1	–	–
High School qualification	1.24	0.48–3.15	*P*=.66	0.96	0.42–2.21	*P*=.93
Tertiary diplomas/certificates	0.91	0.37–2.25	*P*=.84	0.94	0.42–2.10	*P*=.89
Bachelor's degree or higher	0.79	0.33–1.88	*P*=.59	0.85	0.39–1.83	*P*=.67
Beliefs Regarding Vaccination						
Opinion on How Protective Vaccines Are (Scale 0–100)						
0–69	**8.61**	**4.88–15.19**	***P*<.001**	**6.19**	**3.52–10.89**	***P*<.001**
70–79	**2.81**	**1.84–4.28**	***P*<.001**	**3.85**	**2.49–5.95**	***P*<.001**
80–89	**1.88**	**1.30–2.72**	***P*=.001**	**1.54**	**1.09–2.18**	***P*=.01**
90–100	1	–	–	1	–	–
Experience of Vaccination						
NIR						
On NIR, has NHI	1	–	–	1	–	–
Not on NIR, has NHI	1.40	0.66–2.97	*P*=.38	1.8	0.79–4.09	*P*=.16
Not on NIR, no NHI	–	–	–	0.68	0.08–5.85	*P*=.73
Childhood vaccines complete						
No	1	–	–	1	–	–
Yes	**0.15**	**0.08–0.29**	***P*<.001**	**0.09**	**0.05–0.17**	***P*<.001**
Unsure	**0.43**	**0.19–0.97**	***P*=.04**	**0.22**	**0.10–0.48**	***P*<.001**

Table 31 continued

Refused a vaccine						
No	1	–	–	1	–	–
Yes	**8.84**	**5.81–13.44**	***P*<.001**	**6.29**	**4.31–9.17**	***P*<.001**
Documented Meningococcal Vaccines						
MeNZB Doses						
No	1	–	–	1	–	–
Yes	0.64	0.45–0.90	*P*=.01	0.89	0.64–1.23	*P*=.47
4CMenB or MenACWY						
No	1	–	–	1	–	–
Yes	0.79	0.58–1.07	*P*=.13	0.95	0.73–1.23	*P*=.68
Self-reported Meningococcal Vaccine Received (one or more of any vaccine)						
No	1	–	–	1	–	–
Yes	**0.38**	**0.26–0.58**	***P*<.001**	**0.26**	**0.16–0.44**	***P*<.001**
Unsure	0.63	0.38–1.04	*P*=.07	**0.42**	**0.24–0.74**	***P*=.003**
Have you received negative information on meningococcal vaccines?						
No	1	–	–	1	–	–
Yes	**1.67**	**1.20–2.32**	***P*=.02**	**2.03**	**1.45–2.83**	***P*<.001**
Would you have a COVID-19 vaccine if available						
No	–	–	–	1	–	–
Yes	–	–	–	**0.19**	**0.08–0.48**	***p*<.001**
Unsure	–	–	–	0.64	0.25–1.69	0.37

4.4.11 Independent variables associated with vaccine hesitancy

To identify variables with an independent effect on vaccine hesitancy two multivariable logistic regression models were used, as described in chapter 4.3.9. The models included six variables, five in one model and four in the other (Table 32). Independent variables associated with vaccine hesitancy included belief on vaccine effectiveness. In both 2019 and 2020 the less effective the vaccine was perceived to be, the higher the adjusted odds of vaccine hesitancy. Relative to a rating of 90—100, a rating of 70-80/100 had an adjusted OR 2.33 (95% CI 1.36–3.98, *P*=.002) and 3.05 (95% CI 1.87–4.96, *P*<.001), and a rating of 0—69/100 had an adjusted OR 4.72 (95% CI 2.20–10.12, *P*<.001) and 3.89 (95% CI 2.05–7.40, *P*<.001). Self-reported completion of childhood vaccinations had an adjusted OR 0.36 (95% CI 0.14–0.96, *P*=.04) and 0.25 (95% CI 0.12–0.51, P<.001) when compared to self-reported incomplete childhood vaccinations. In 2020 being unsure of childhood vaccination status was associated with an adjusted OR 0.28 (95% CI 0.11—0.71, *P*=.01), however this effect was not seen in 2019. Ever having declined a vaccine had an adjusted OR 6.44 (95% CI 3.71–11.20, *P*<.001) and 4.18 (95% CI 2.68–6.52, *P*<.001). In 2019 ethnicity Pacific Peoples had an adjusted OR 3.18 (95% CI 1.11–9.11, *P*=0.03) relative to Māori ethnicity. Despite Asian ethnicity reducing the odds of vaccine hesitancy in univariable analysis, this effect no longer has statistical significance following multivariable analysis, with an adjusted OR 0.47 (95% CI 0.20–1.08, *P*=0.07). Residing in residential colleges with the code 4, 5, 7, 11, 13 had adjusted OR 3.33 (95% CI 1.11–9.99, *P*=.03), 4.27 (95% CI 1.51–12.09, *P*=.01), 3.06 (95% CI 1.05–8.91, *P*=.04), 5.76 (95% CI 1.83–18.12, *P*=.003) and 1.65 (95% CI 0.45–6.08, *P*<.001) respectively. Finally, in 2020 having received negative information on meningococcal vaccines had an adjusted OR 1.76 (95% CI 1.21—2.56, *P*<.001) relative to not receiving negative information.

Table 32: Multivariable analysis of factors associated with vaccine hesitancy

	2019			2020		
	AOR	95% CI	P value	AOR	95% CI	P value
Ethnicity						
Māori	1	–	–	–	–	–
Pacific peoples	**3.18**	**1.11–9.11**	**0.03**	–	–	–
Asian	0.47	0.20–1.08	0.07	–	–	–
New Zealand European	0.74	0.40–1.36	0.34	–	–	–
Middle Eastern, Latin American, African	0.19	0.02–1.77	0.15	–	–	–

Table 32 continued

College						
1	1	–	–	–	–	–
2	3.26	0.84–12.65	*P*=.09	–	–	–
3	2.03	0.51–8.04	*P*=.31	–	–	–
4	**3.33**	**1.11–9.99**	***P*=.03**	–	–	–
5	**4.27**	**1.51–12.09**	***P*=.01**	–	–	–
6	2.33	0.83–6.56	*P*=.11	–	–	–
7	**3.06**	**1.05–8.91**	***P*=.04**	–	–	–
8	1.51	0.45–5.07	*P*=.50	–	–	–
9	4.21	0.93–19.10	*P*=.06	–	–	–
10	2.99	0.86–10.40	*P*=.09	–	–	–
11	**5.76**	**1.83–18.12**	***P*=.003**	–	–	–
12	0.62	0.15–2.51	*P*=1.00	–	–	–
13	**1.65**	**0.45–6.08**	***P*<.001**	–	–	–
14	2.14	0.74–6.12	*P*=.16	–	–	–
Opinion on How Protective Vaccines Are (Rating Scale 0-100)						
0–69	**4.72**	**2.20–10.12**	***P*<.001**	**3.89**	**2.05–7.40**	***P*<.001**
70—79	**2.33**	**1.36–3.98**	***P*=.002**	**3.05**	**1.87–4.96**	***P*<.001**
80—89	1.28	0.79–2.09	*P*=.32	1.43	0.99–2.07	*P*=.56
90—100	1	–	–	1	–	–
Childhood vaccines complete						
No	1	–	–	1	–	–
Yes	**0.36**	**0.14–0.96**	***P*=.04**	**0.25**	**0.12–0.51**	***P*<.001**
Unsure	1.37	0.42–4.45	*P*=.60	**0.28**	**0.11–0.71**	***P*=.01**
Refused a vaccine						
No	1	–	–	1	–	–
Yes	**6.44**	**3.71–11.20**	***P*<.001**	**4.18**	**2.68–6.52**	***P*<.001**
Have you received negative information on meningococcal vaccines?						
No	–	–	–	1	–	–
Yes	**–**	**–**	**–**	**1.76**	**1.21–2.56**	***P*<.001**

Chapter 5: Discussion

This chapter discusses the results of the carriage study, risk factor survey, and vaccine hesitancy surveys in relation to the objective of the thesis.

5.1 Objective A

Objective A was to estimate the prevalence of *N. meningitidis* carriage among University of Otago students in their first year living in residential halls, including prevalence in a residential college seven weeks post *N. meningitidis* eradication therapy. Carriage prevalence of *N. meningitidis* among students in their first year in a residential college, was 26.8% (275/1027), with a margin of error of 2.75%. This is higher than estimates for carriage in the broader community[14], however is consistent with carriage prevalence reported by a paper examining University of Otago students residing in residential colleges in 2008.[63] It is also consistent with other studies of students residing in residential colleges from western cultures[3,74], but is lower than prevalence reported by some studies from England and United States of America.[64,77,137] Previous studies have found that individual carriage of *N. meningitidis* has a duration of a few months[20,57], therefore prevalence in large groups such as residential colleges can be expected to fluctuate over the duration of living in a residential college.[137] Carriage prevalence is influenced by exposure to risk factors, including crowded social events like Orientation Week, and Re-orientation Week.[80] Given the study took place late in the academic year, seven to eight months after the mass crowded social events of Orientation Week, it is likely to be an underrepresentation of peak carriage in the early part of the academic year. The most prevalent serogroup was non-groupable, which is not usually associated with IMD. The next most prevalent serogroup was Y, followed by W, and B. Serogroup Y, W and B are associated with IMD, and a strain of serogroup B was associated with the three IMD cases in 2018. WGS carried out on all study isolates enabled genomic linking of isolates and revealed that the strain of serogroup B that caused the three IMD cases was also being carried by seven students who resided in five other residential colleges (see Appendix 2). This demonstrates the transmissibility and potential for *N. meningitidis* to spread, and the associated risk to students.

The carriage prevalence for students that received clearance antibiotics seven weeks prior to specimen collection was 5.9%. Of seven isolates, five were serogroup Y and two were ungroupable. WGS showed the serogroup Y isolates were linked to each other and to one other participant in another other college, demonstrating that reacquisition of *N. meningitidis* carriage may occur relatively quickly among students who mix socially within and between residential colleges.

The clearance antibiotic used was a single 500mg dose of Ciprofloxacin, as recommended by the MOH Communicable Disease Manual.[1] There is a previous study from the United Kingdom, with 570 participants, that demonstrated Ciprofloxacin single dose treatment was successful in clearing carriage from 97% of participants. The study detailed that side effects included headache (4%), diarrhoea (4%), nausea (3%), abdominal pain (3%), arthralgia (2%), vomiting (1%) and rash (1%). Resistance to Ciprofloxacin is rare but has been described. A meningococcal C outbreak in 2018 in Fiji was shown to be resistant to ciprofloxacin. If such a strain is suspected, ciprofloxacin should not be used for antibiotic prophylaxis.

5.2 Objective B

Objective B was to estimate the prevalence of known risk (and protective) factors of *N. meningitidis* throat carriage and any associations with the various serogroups among University of Otago first year students living in residential halls. The literature review identified adolescence, male gender, attendance at clubs/bars/parties, intimate kissing, smoking, water pipe use, recent illness and close living arrangements as independent risk factors for carriage of N. meningitidis. There is some evidence, from studies of varying quality, that smokeless tobacco use, deprivation, ethnicity, alcohol use, and large communal events targeting young people (such as university orientation week events) are risk factors for carriage, but further investigation would be beneficial.

Among participants 10.9% smoke, 49.9% attended parties, 34.3% kissed someone intimately and 41.5% has had a recent respiratory illness. While students residing in residential colleges cannot modify adolescence nor gender, health promotion interventions could target modifiable risk factors, to minimise risk of transmission, and to achieve other health benefits. Health promoting polices for residential colleges could focus on minimising smoking and having robust policies on illness within colleges.

In addition to looking at prevalence of risk factors we analysed the relationship between carriage of N. meningitidis and the presence of risk factors. Multivariable risk factor analysis found that female gender is protective, as is Asian ethnicity. Prior to this study ethnicity had rarely been examined as a risk factor, however our finding that Asian ethnicity is protective supports the same findings from Marshall et al, and is consistent with lower prevalence of *N. meningitidis* found by carriage studies from Asian countries.[65,73,76,82] It seems likely that Asian cultural values and behaviours may have a protective effect. In the 2018 carriage study most participants of Asian ethnicity were domestic students, with a minority being international students, suggesting that the protective effect is not constrained to students of Asian ethnicity raised overseas. Data from the 2018 population census

reveals that the proportion of the population that identifies as Asian is 15.1%[11], however data from ESR shows that in 2019 only 5% of all IMD cases were experienced by people of Asian ethnicity, which may be consistent with the findings regarding reduced carriage prevalence[6].

The majority of studies on risk factors for carriage have confirmed smoking is an independent risk factor, however our study did not find a statistically significant result confirming this. While the mechanism by which risk to smokers is increased is unclear, others have noted increased carriage among Snus tobacco (smokeless) users as well.[80] A recent review highlights the increased risk of IMD among smokers.[138] Coen et al, conducted a case control study that found smokers exposed to cigarette smoke are at higher risk of transmission due to interpersonal contact with smokers, rather than to a direct effect of tobacco smoke on susceptibility.[139] It is likely that the results of this carriage study were affected by low numbers of participants who smoke more than 3 days per week (12/1145) and more than 10 cigarettes per day (14/1145). Most participants who smoked did so infrequently, on 1-3 days per week (105/1145) and smoked only 1-5 cigarettes per day (101/1145). Our findings are consistent with other carriage studies with low numbers of smokers, such as Durey et al., who found no statistically significant association, with 4% of participants smoking.[65] Our study also failed to find an association between exposure to cigarette smoke and carriage once exposure to cigarette smoking was included in the multivariable model. Our results may also be due to smoking and exposure to smoke have reducing over time, with increasingly restrictive legislation limiting where people can smoke, who can smoke, and advertising of smoking. We did not attempt to measure degrees of exposure to smoke, but it is likely that any exposure experienced by study participants is at a lower intensity and frequency than it would have been 20—30 years ago, as awareness of the harm caused by smoking has increased, and legislation like the Smokefree Environments Act have been progressively strengthened.[140] Future studies should include data on the degree to which people smoke, and should aim to capture a larger number of frequent smokers, to enable a more accurate assessment of the dose dependant relationship between carriage and smoking.

Attendance at pubs, bars and clubs was confirmed to be an independent risk factor. This is consistent with the findings of previous studies. One study found that the Russ celebration, a month-long celebration centred on drinking and partying for school leavers, was an independent risk factor, and it is likely that similar events, such as university orientation weeks are also independent risk factors. This information can be used for targeted health promotion and education and should inform timing of vaccination, to ensure that optimum immunity is acquired before attending Orientation Week.

5.3 Objective C:

Objective C was to assess electronic cigarette (e-cigarette) use as a risk factor for *N. meningitidis* throat carriage among University of Otago first year students living in residential halls. E-cigarette use is being promoted as a cigarette smoking cessation tool in New Zealand and is noted to be less harmful than cigarette smoking. However, uptake of e-cigarette use is increasing especially among youth and young adults.[93] In this context, understanding the relationship between e-cigarette use and *N. meningitidis* carriage is important. When this study was designed there was no literature examining the relationship between e-cigarette use and carriage of *N. meningitidis*, however two Australian studies have since evaluated the relationship. McMillan et al included e-cigarette use in their survey of 421 university students in 2017, but only one participant was an e-cigarette user. Marshall et al included e-cigarette use in their large study of 24,269 secondary school students aged 15.6±1.2, however the results are less transferable to the residential college setting, where e-cigarette use is likely to increase because university students are legally allowed to purchase e-cigarettes from age 18 years, and because students residing in residential colleges appear to indulge in risk taking behaviours to a greater extent. The 2018 carriage survey included 70 participants who had used e-cigarettes in the week prior to specimen collection, however only 25 had used e-cigarettes on more than three days, suggesting the remaining 50 may be casual users. Univariable analysis showed that those who use e-cigarettes have higher odds of carriage, with a dose response for those who use e-cigarettes more frequently. While this study found that e-cigarette use was not an independent risk factor for carriage, further investigation of the relationship between frequent e-cigarette use and carriage would be beneficial given the growing popularity of e-cigarette use, and with over 50% of New Zealand 18—24 year olds experimenting with e-cigarette use.(92)

5.4 Objective D

Objective D was to identify factors influencing uptake of meningococcal vaccination by University of Otago students in their first year living in residential halls. Multiple influencing factors were revealed by the vaccine hesitancy surveys. A key factor of interest was the impact government funding would have on vaccination. There was an increase in Meningococcal vaccination uptake from 2018—2019 following promotion alone, however the data from 2019 and 2020 showed that the funding of MenACWY vaccine coincided with an increase in MenACWY uptake but a significant decrease in uptake and completion of 4CMenB. Given serogroup B is most frequently associated with IMD in New Zealand, it is concerning that uptake of 4CMenB reduced. Although some students may have

received a MenACWY as part of the Public Health response to the localised meningococcal W outbreak in Northland in 2019, the number of these students in the sample is likely to be small.

Data on self-reported vaccination status did not reflect data on documented vaccination status, indicating that students may have poor recall of vaccination status, or an inability to distinguish between meningococcal vaccinations. A lack of knowledge about the meningococcal vaccines could contribute to failure to complete a full course of meningococcal vaccinations. Most participants indicated that when making a decision about accepting or rejecting a vaccination, they sought information on vaccinations from parents, which suggests childhood vaccination status, which is also determined by parents, may be an indicator of meningococcal vaccine hesitancy. Social media has previously been associated with vaccine hesitancy.[108] Among participants Facebook was low on the list of sources of information access by participants. However, for participants that did receive negative information Facebook was the most common source, followed by friends, and websites. Health professionals were a source of negative information for some participants.

Survey responses from participants revealed that they while the majority (>80%) supported vaccination in general, a minority feared the side effects of vaccines in general, or believed vaccines in general were ineffective, or that vaccine preventable diseases present low risk. Among those that had ever refused any vaccine, the majority did so because they felt vaccines they refused was not needed. Similarly, those that declined a meningococcal vaccine did so because the vaccines were too expensive, or were not needed, or they did not know about them. These responses suggest that convenience is the primary concern, and that confidence in vaccine safety is not a concern for established vaccines, or vaccines for established diseases. In contrast, those that were hesitant about a hypothetical COVID-19 vaccine indicated concern about safety and side effects.

For those who are not vaccine hesitant in relation to meningococcal and COVID-19 vaccines, reasons for vaccination were for personal and community benefit, and because vaccines were perceived as safe.

5.5 Clearance Antibiotics

After the administration of clearance antibiotics, no further cases of IMD were notified to Public Health South, and the serogroup that caused the IMD was no longer being carried in the nasopharynx among students that received antibiotics. WGS demonstrated that seven other students, residing in five other residential colleges (who therefore did not receive antibiotics) were genomically linked isolates were present in other colleges. Students from the college that received

clearance antibiotics as expected had a much lower carriage of *N. meningitidis* at 5.9% seven weeks after clearance antibiotics. The isolates recovered from these participants were all serogroup Y and were all genomically linked. While previous evidence suggests that acquisition rate of *N. meningitidis* is high during the first week in a residential college[64], it is probable that reacquisition of *N. meningitidis* carriage post clearance occurred at a slower rate later in the year, due to lower levels of social mixing in the lead up to exams. The risk of recolonisation with the serogroup associated with IMD exists, which supports the current MOH guidelines that in addition to receiving clearance antibiotics, close contacts should receive vaccination against IMD.

There are unfavourable side-effects of antibiotic administration. Clearance antibiotics are only given to close contacts as unnecessary use of antibiotics may contribute to the proliferation of antibiotic resistant organisms[40], and can have unpleasant physiological effects, such as *Clostridioides difficile* infection[41]. Antibiotic use may also lead to variation in the upper respiratory tract microbiome, creating conditions that are more or less favourable for *N. meningitidis* carriage.[42]

5.6 NIR

The NIR was an unreliable data source at the time this research was undertaken. There appeared to be no option for general practices to record 4CMenB vaccines. This was raised with the NIR administration team at the time.

5.7 Strengths

Strengths of the study include the relatively high number of participants for a study of students residing in residential colleges. The carriage study is the largest in New Zealand with the specific aim of examining carriage prevalence in students residing in residential colleges. It appears to be the only study to examine the prevalence of carriage seven weeks after the mass administration of clearance antibiotics (specifically, ciprofloxacin). The vaccine hesitancy surveys appear to be the only studies on the topic in a residential college setting. Finally, being able to compare vaccine hesitancy with data on actual vaccination, as opposed to relying solely on intent to vaccinate, adds strength to the findings in this study. The study is generalisable to other residential college settings in New Zealand, and other countries with a similar culture, such as Australia and the United Kingdom.

5.8 Limitations

Limitations of the carriage study and risk factor survey include the reliance on good swab collection, transport, and storage. Although data were anonymised, forms were filled in with peers during lunch, and were scanned for completeness by admin staff, so social desirability bias may have affected responses. A limitation of the single cross-sectional methodology used by the carriage study was that, unlike repeat cross sectional studies, it did not allow for the study of rate of acquisition, point of acquisition, nor any indication of duration of carriage. The carriage study also omitted alcohol consumption, which has previously been shown to be associated with carriage[141], and is a common risk factor among students residing in residential colleges. However, attendance at parties, pubs and clubs is likely to be a reasonable proxy for alcohol consumption among the students. The survey may have had fewer missing responses if an online survey tool was used. Having an online survey tool would have reduced unintelligible answers and may have been faster for participants, however, would have involved additional cost and complexity. With regard to laboratory techniques, by relying on culturing isolates as opposed to direct PCR testing, the carriage study may have missed some false negatives.[82,142] The storage of isolates for several months may also have played a part in reducing bacterial viability.[142] The use of WGS for determining isolates was not initially intended, but future studies may consider collecting more epidemiological data, which when paired with WGS results, would allow examination of mode and location of transmission.

Limitations of our research on vaccine hesitancy includes the fact we did not further categorise participants that expressed vaccine hesitancy into vaccine hesitant and vaccine refusal. Self-selection bias may occur, due to voluntary participation. In relation to COVID-19 vaccines, the survey was carried out while vaccines were still in trial phase (except for Russia's Sputnik vaccine), and many months before the start of vaccination in New Zealand. Being a cross sectional study, no control group was used, and results are specific to the time and location of the study, with attitudes likely to change. Intention may not reflect behaviour, and results cannot be generalised to populations other than residential college settings within societies with a similar culture.

The literature review and the univariable analysis of the pre-COVID-19 sample (participants from 2019) found that females were more likely to be vaccine hesitant. The proportion of females was observed to be higher in the pre-COVID-19 sample than in the population. It is therefore possible the prevalence of vaccine hesitance estimated from the sample is an over estimation of the prevalence in the population for this period. However, in the post-COVID-19 sample (year 2020), univariable analysis did not find a statistically significant association between vaccine hesitancy and gender. This implies, overrepresentation of the sample by one gender was unlikely to influence the overall

estimate of the prevalence of hesitance in the post-COVID19 period. It may be that vaccine hesitancy has been influenced by the COVID-19 experience, however this is beyond the scope of this thesis.

COVID-19 turned a spotlight on vaccination, and may have affected participants attitude to vaccine hesitancy during the study, however, Student Health do not believe COVID-19 impacted their meningococcal vaccination programme. Similarity of results from the 2019 and 2020 cohorts supports the argument that COVID-19 had little effect on the surveys.

5.9 Implications for Practice, Policy and Future Research.

Carriage rate of *N. meningitidis* was high among first year Otago University students in residential colleges in 2019, and is likely to remain high in subsequent years. During outbreaks of IMD in residential college settings, clearance antibiotics can effectively eliminate carriage of *N. meningitidis*, although recolonisation is likely to occur in following weeks or months. During outbreaks in residential colleges it is likely that outbreak strains will be found in peripheral groups, as WGS associated with this research found, so health practitioners should remain vigilant despite the use of clearance antibiotics.

Vaccine hesitancy among residential college students towards meningococcal vaccines appears to be based on factors that can be categorised as convenience factors. Cost was the primary barrier, therefore funding vaccines that protect against Meningococcal serogroup B, which is the serogroup associated with the highest number of IMD cases in New Zealand, is likely to dramatically increase vaccine uptake. Residential college students appear to have a poor understanding of both recommendations regarding meningococcal vaccines, and their own meningococcal vaccination history. Students' parents and their residential colleges are their main sources of information on vaccination. Therefore, an education campaign targeting residential college students and their parents, delivered in collaboration with the residential colleges is advisable. During COVID-19, universities in New Zealand mandated COVID-19 vaccines for students entering residential colleges. Mandating a full course of meningococcal vaccines for students entering residential colleges should be considered, particularly if vaccines are free. The NIR was found to be an unreliable data source, and should be upgraded to ensure vaccinations are accurately recorded. Vaccination rates could then be monitored, and in the event of IMD cases in the residential college community, efforts to increase vaccination coverage can be targeted at unvaccinated students.

Carriage studies can and should be carried out among residential college populations, to inform practice and policy. Carriage studies should be repeated if vaccination rates increase, to detect any impact that vaccination has on carriage rates. Research using whole genome sequencing has the

potential to increase understanding of dynamics of transmission. Ongoing research monitoring of vaccine hesitancy, and drivers of vaccine hesitancy, should be carried out, particularly in the wake of COVID-19. Research on vaccine hesitancy enables vaccination providers to understand and overcome barriers to vaccine uptake.

Chapter 6: Conclusion

The prevalence of *N. meningitidis* carriage among students residing in residential colleges was found to be 26·8%. Non-modifiable independent risk factors such as adolescence and male gender are part of the residential college population, as are modifiable independent risk factors such as attending parties and social events. It is therefore likely that carriage prevalence will remain high in the residential college population, and sporadic cases of IMD will continue. This study found that carriage of serogroup B accounted for 25% of identifiable isolates. Serogroup B strains have been responsible for between 40-60% of IMD cases in the past five years. Recent funding for the MenACWY vaccine increased uptake of MenACWY vaccine, but appears to have resulted in a decrease in uptake of the 4CMenB vaccine. Students residing in residential colleges do not appear to have a good understanding of the various meningococcal vaccines on offer. Uptake of the 4CMenB vaccine may be improved by funding the vaccine, as might providing education on the various meningococcal vaccines available. When cases of IMD occur within residential college settings treating close contacts with Ciprofloxacin results in a significant decrease in *N. meningitidis* carriage seven weeks after administration, however WGS has shown that recolonisation occurs, which emphasises the importance of the protection offered by meningococcal vaccines.

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Appendix 1: 2018 Risk Factor Survey

Study ID Sticker

Questionnaire for 2018 Meningococcal Carriage Survey among First Year University of Otago Students Living in Residential Halls.

1. Full Name (first names & surname):_____

2. Date of birth:_____

Please note: Name and date of birth will be removed from all data following check from the National Immunisation Register for meningococcal vaccination history

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Questionnaire for 2018 Meningococcal Carriage Survey among First Year University of Otago Students Living in Residential Halls.

PLEASE TICK or FILL IN AS APPROPRIATE

Study ID Sticker

3. Age ☐ (years)

4. Residential college name:_____ Confirm First Year Student Yes ☐

5. Gender: Female ☐ Male ☐ Other ☐

6. Ethnicity: Please tick as many as apply.
   - a. Māori ☐ b. Pacific ☐ c. Asian ☐
   - d. NZ European ☐ e. Middle Eastern, Latin American, African ☐
   - f. Other: ☐ If other please specify:_____

7. Domestic (NZ) Student ☐ OR International Student ☐

8. Any antibiotic use in the past two weeks?
   No ☐ Yes ☐ If yes, antibiotic name:_____

9. Any meningococcal vaccinations received at any age? Yes ☐ No ☐ Unsure ☐

10. Any respiratory illness (cough, runny nose) in the past two weeks? Yes ☐ No ☐

11. Any cigarette smoking in the past week? Yes ☐ No ☐
    If yes, how often? Daily ☐ 4-6 days per week ☐ 1-3 days per week ☐
    Number of cigarettes smoked in the past week? 1-5 ☐ 6-10 ☐ >10 ☐

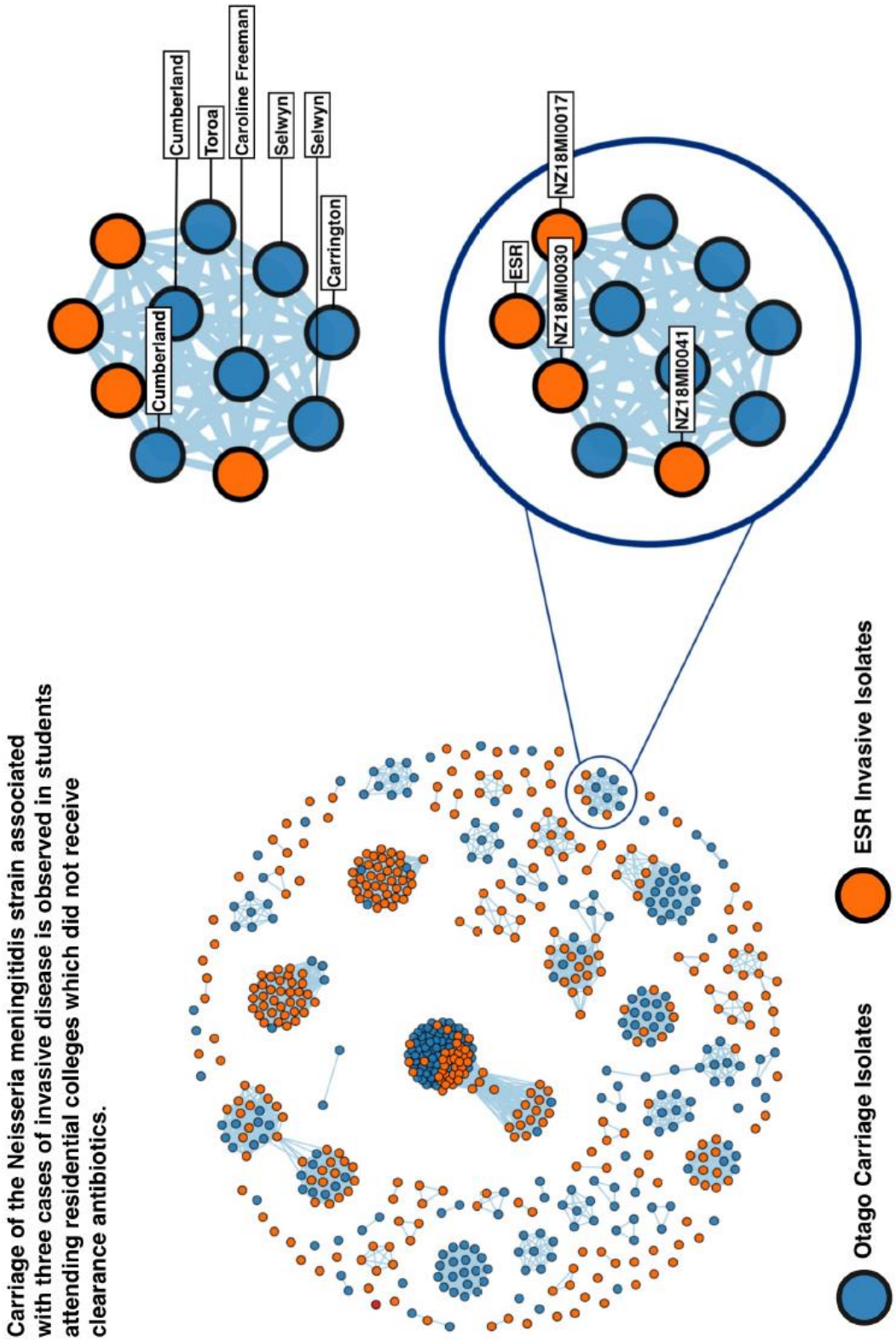
12. Any exposure to cigarette smoke in the past week? Yes ☐ No ☐

13. Any vaping in the past week? Yes ☐ No ☐
    If yes, how often? Daily ☐ 4-6 days per week ☐ 1-3 days per week ☐

14. Any attendance at pubs/nightclubs/bars/parties in the past week?
    No ☐ Yes ☐ If yes, how many times? ☐

15. Any intimate kissing (open mouth more than 3 seconds) in the past week?
    No ☐ Yes ☐ If yes, number of persons intimately kissed in the past week? ☐

Appendix 2: Figure displaying whole genome sequence results



Appendix 3: Vaccine Hesitancy Questions for REDCaps

2020 Survey Form:

Changes from 2019 highlighted

	Consent	
	Information page	Change source of vaccine history from NIR to Primary Health record (Student Health) as agreed with SH.
	First name	
	Last name	
	Date of birth	
	Check box for consent	
	Demographics	
1	Age	- 17 - 18 - 19 - 20 - 21 - Other (free text)
	If Other please specify:	
2	Gender	- Male - Female - Gender Diverse
3	Ethnicity	Please tick all boxes that apply: - Māori - Pacific - Asian - NZ European/Pakeha - Middle Eastern, Latin American, African - Other (please specify)
	If Other please specify:	
4	Residential College	- Aquinas - Arana - Carrington - Caroline Freeman - Cumberland - Hayward - Knox - St Margaret's - Salmond - Selwyn - Studholme - Te Rangi Hiroa - Toroa - Unicol
5	Mother/carer's occupation	Free text
6	Father/carer's occupation	Free text
7	Mother/carer's highest educational attainment	- No qualification - High School qualification

		- Tertiary diplomas/certificates - Bachelors degree or higher
8	Father/carer's highest educational attainment	- No qualification - High School qualification - Tertiary diplomas/certificates - Bachelors degree or higher
	Determinants –Vaccine Specific	
9	Do you believe that vaccines can protect people from serious illnesses?	Likert scale 1–5 1 no protection– 5 full protection
10	Do you think that you had all the recommended vaccines available as a child?	Y/N/unsure
11	Have you ever been reluctant or hesitated to get a vaccination?	Y/N
12	Have you or your parents ever refused a vaccination for you?	Y/N
13	(If yes to 12) Which vaccines?	Free text
14	(If yes to 12) What was the reason?	Tick all that apply: - My parents or I did not think it was needed - My parents or I did not know enough about it - Too expensive - Heard or read negative media - Did not know where to get vaccination - Had a bad experience or reaction with previous vaccination - Did not know where to get good/reliable information - Had a bad experience with previous vaccinator/health clinic - Not possible to leave my work/study - Someone else told me they/their child had a bad reaction - Did not think the vaccine was effective - Someone else told me that the vaccine was not safe - Did not think the vaccine was safe/concerned about side effects - Fear of needles - Religious reasons - Other beliefs/traditional medicine - Other (specify)
	If Other please specify:	
15	Have you ever had any vaccinations to protect you against meningococcal disease?	Y/N/unsure
16	(If yes to 15) What vaccine/s do you think you have had?	- Menactra (MCV4-D, quadrivalent meningococcal conjugate vaccine for protection against meningococcal disease caused by *Neisseria meningitidis* groups A, C, Y and W)

		- Nimenrix (MCV4-T, quadrivalent meningococcal conjugate vaccine for protection against meningococcal disease caused by *Neisseria meningitidis* groups A, C, Y and W) - NeisVac-C (MenCCV, monovalent meningococcal conjugate vaccine for protection against meningococcal disease caused by *Neisseria meningitidis* group C) - Bexsero (4CMenB, meningococcal B vaccine for protection against meningococcal disease caused by *Neisseria meningitidis* group B) - MeNZB (meningococcal B vaccine used in the New Zealand immunisation programme between 2004 and 2006, offered free to anyone under the age of 20. Routine immunisation for babies and preschoolers continued until June 2008) - Unsure
17	(If yes to 15) If you had a meningococcal vaccine, what was the reason?	Tick all that apply: - My parents or I thought they were needed for my personal benefit - My parents or I thought they were needed to benefit my community - They were free for me - I heard or read positive media - I was offered the vaccinations - The meningococcal vaccination was recommended to me - I had good experiences with previous vaccination - My parents or I knew where to get good/reliable information - I had good experiences with previous vaccinator/health clinic - It was convenient to leave work/study during the day - Someone else told me they/their child had a good experience - I do think the vaccines are effective - Someone else told me that the vaccines are safe - I do think the vaccines are safe - I have no concerns about side effects - Religious reasons - Other (specify)
	If Other please specify:	
18	(If no to 15) If you did not have a meningococcal vaccine, what was the reason?	Tick all that apply: - My parents or I did not think they were needed - My parents or I did not know enough about them - I did not know the vaccines were available - Too expensive - I heard or read negative media - I did not know where to get vaccinated

		- I had a bad experience or reaction with previous vaccination - I did not know where to get good/reliable information - The meningococcal vaccination was not recommended to me - I had a bad experience with previous vaccinator/health clinic - It was not possible to leave my work/study during the day - Someone else told me they/their child had a bad reaction - I do not think the vaccines are effective - Someone else told me that the vaccines are not safe - I or my parents think the vaccines are not safe - I'm concerned about side effects - I have a fear of needles - Religious reasons - Other beliefs/traditional medicine - Other (specify)
	If Other please specify:	
19	Has cost of a meningococcal vaccine prevented you from getting a meningococcal vaccine?	Y/N
20	Have any of these factors prevented you from getting a meningococcal vaccine?	- Distance - Timing of clinic - Time needed to get to clinic or wait at a clinic - Costs in getting to a clinic
21	Would you have a vaccine to protect you against Covid-19 if one becomes available?	Y/N/unsure
22	(If yes to 21) If you would have a Covid-19 vaccine, what is the reason?	Tick all that apply: - My parents or I think it is needed for my personal benefit - My parents or I think it is needed to benefit my community - Because it would be free for me - Because of hearing or reading positive media - Because I was offered the vaccination - Because it was recommended for me - Because of good experiences with previous vaccinations - My parents or I would know where to get good/reliable information - I have had good experiences with previous vaccinator/health clinic appointments - If it was convenient to leave work/study during the day - If someone else told me they/their child had a good experience

		- I do think that vaccines are effective - If someone else told me that the vaccine is safe - I do think that vaccines are safe - I have no concerns about side effects - Religious reasons - Other (specify)
	If Other please specify:	
18	(If no to 15) If you do not think you would have a Covid-19 vaccine, what is the reason?	Tick all that apply: - My parents or I do not think it is needed for me - My parents or I do not think it is needed for the community - My parents or I do not know enough about them - Too expensive - Hearing or reading negative media - Not knowing where to get vaccinated - I have had a bad experience or reaction with previous vaccination - Not knowing where to get good/reliable information - The Covid-19 vaccination not being recommended to me - I had a bad experience with previous vaccinator/health clinic - Not being able to leave my work/study during the day - Someone else telling me they/their child had a bad reaction - I do not think the vaccines are effective - Someone else telling me that the vaccine is not safe - I or my parents thinking the vaccine is not safe - I'm concerned about side effects - I have a fear of needles - Religious reasons - Other beliefs/traditional medicine - Other (specify)
	If Other please specify:	
21	Are there any reasons you (or your parents) think that generally people should not be vaccinated?	- I do not think there is much risk of getting a vaccine preventable disease - I do not see vaccine preventable diseases as a problem for my community - I do not trust the companies that manufacture vaccines - I fear the side effects of vaccines - Vaccines are not natural - Even if I have the vaccine I might still get sick from the disease - Other (specify)
	If Other please specify:	-

22	From what sources have you looked for or received information on the meningococcal vaccine?	Please tick all that apply: - Parents - Friends - Residential college mail/email - University enrolment material - Student Health - Family GP - Ministry of Health or Immunisation Advisory Centre website - Advertising - Google search - Vaccine manufacturer - Facebook - Other
	If Other please specify:	
23	Have you ever received or heard negative information about meningococcal vaccines?	Y/N
24	(If yes to 23) What was the source of the information?	Please tick all boxes that apply: - Parents - Friends - Health professionals - Facebook - Websites - TV/radio - Podcasts/vlogs - Magazines - Vaccine manufacturer data sheets - Other
	If Other please specify:	
	Competition	
	Thank you for your time. If you would like to go in the draw for one of ten $100 grocery vouchers, please enter you email address here. We will only use your email address to contact you if you win. Once the draw is complete all records of your email address will be destroyed.	Free text
	Details on where to get further information on Mens vacs and MMR and on study/survey.	
	END	

Appendix 4: Submission to Pharmac

Public Health South

Dunedin: Private Bag 1921, Dunedin 9054
Ph: 03 476 9800 Fax: 03 476 9858

Invercargill: PO Box 1601, Invercargill 9840
Ph: 03 211 8500 Fax: 03 214 9070

Queenstown: PO Box 2180, Wakatipu, Queenstown 9349
Ph: 03 450 9156 Fax: 03 450 9169

SUBMISSION ON:	**Proposal to fund 4CMenB meningococcal vaccine for close contacts of cases and people at higher risk of meningococcal disease**
To:	**PHARMAC** **vaccines@pharmac.govt.nz**
Details of Submitter:	**The Southern District Health Board**
Address for Service:	**Public Health South** **Southern District Health Board** **PO Box 1601 / Private Bag 1921 / PO Box 2180** **INVERCARGILL 9840 / DUNEDIN 9054 / QUEENSTOWN 9349**
Contact Person:	**Dr Susan Jack**
Our Reference:	**21May04**
Date:	**21 May 2021**

Introduction

Thank you for the opportunity to submit on the proposed funding of the 4CMenB (Bexsero) meningococcal vaccine.

Southern District Health Board (Southern DHB) presents this submission through its public health service, Public Health South. Southern DHB delivers health services to a population of 335,990 and has responsibility under the New Zealand Public Health and Disability Act 2000 to improve, promote and protect the health of people and communities. It seeks to promote equity and to reduce adverse social and environmental effects on the wellbeing of people and communities.

This submission is intended to provide general commentary to PHARMAC relating to the proposal to fund meningococcal B vaccine for close contacts of cases and people at higher risk of meningococcal disease. In this submission we present unpublished data from a Meningococcal Study on Otago University students residing in residential colleges.

General Comments

We **support** the proposal to fund 4CMenB (Bexsero) for people who are close contacts of meningococcal cases of any meningococcal group (e.g. A, C, W, Y or B), or are at higher risk of Invasive Meningococcal Disease (IMD) because they are pre- or post-splenectomy, have functional or anatomic asplenia, HIV, complement deficiency, are pre- or post-solid organ transplant, following bone marrow transplant or following immunosuppression.

However, we recommend that 4CMenB be listed with a high priority for adolescents (aged 13-19 years) in close-living situations and be funded in the same manner as the ACWY-D (Menactra) meningococcal vaccine is listed.

Rationale for recommendations:

1) IMD is hard to treat and has a high case fatality rate of 8%, so vaccination for prevention is the best strategy.
2) IMD disproportionately effects Māori and Pacific peoples, creating an inequity that broadening funding would help address.
3) Proportion of IMD Cases that are Serogroup B is 51%.
4) Carriage Rate among students residing in residential colleges is 27%, confirming students residing in residential colleges are at high risk of carriage and therefore infection. Risk factors for carriage are not easily modifiable.
5) 4CMenB vaccine is effective.
6) Cost is barrier to uptake of vaccines for students residing in residential colleges.
7) Ethical considerations, including consistency with funding for MenACYW-D vaccine, Te Tiriti obligations, and health promotion actions, all support our recommendation.
8) Evidence of cross protection against Gonorrhoea provides additional benefit.
9) Implementation will be carried out by Student Health Services, minimising burden on other primary services.

Summary

1) Invasive Meningococcal Disease

The 4CMenB vaccine (Bexsero) protects against invasive meningococcal disease (IMD). IMD can be difficult to diagnose, and progresses rapidly, often in otherwise healthy young people. During 2020 IMD had a case-fatality ratio of 8.6% in all ages groups in New Zealand.[143] These factors highlight the need to reduce incidence through vaccination, rather than relying on detection and treatment of cases.

2) Incidence of IMD in New Zealand

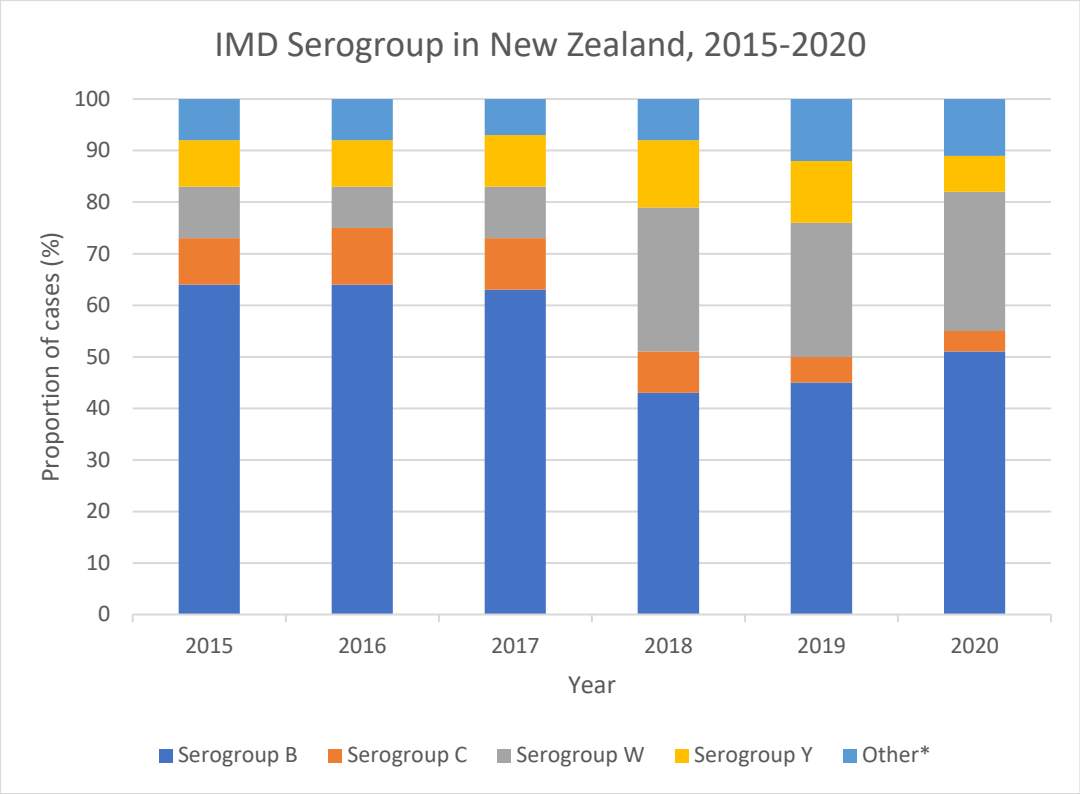
Between 2013 and 2017, there were between 26 and 70 annual cases of IMD each year in New Zealand, and between 2 and 9 deaths, with an overall upward trend since 2014.[12] In 2018, there were 120 reported cases and in 2019 there were 139 cases. In both 2018 and 2019 there were 10 deaths.[6] In 2020 New Zealand experienced 35 cases, despite the COVID-19 lockdowns, and 3 deaths. IMD disproportionately effects young children under 5 years of age, and Māori and Pacific peoples.[6] The increasing incidence of IMD in New Zealand pre-

COVID-19 underscore the importance of a vaccination strategy to protect those at highest risk of IMD.

3) Proportion of IMD Cases that are Serogroup B

ESR data shows that of the 35 cases of IMD in New Zealand in 2020, over half (18/35, 51%) were caused by Serogroup B *N. meningitidis*.[143] This is consistent with previous years, which have seen Serogroup B responsible for 43-63% of IMD cases.[6]

Chart 1: Annual IMD in New Zealand, 2015–2020.



4) Carriage of *N. meningitidis*

Carriage of *N. meningitidis* is a precursor for IMD. Studies have shown carriage lasts for 15 to 23 weeks in the majority of cases[20], but can persist for 8 months or more, and that during the course of carriage the bacteria can evolve, potentially becoming better adapted to its host.[21] Carriage of serogroups B and W have been shown to persist for longer than other serogroups.[21] Carriage rates of *N. meningitidis* vary over time and differ by country, with international carriage rates varying from 3 to 35% in the general population[14] and from 2.5%[2] to 60%[22] in adolescent populations. Adolescents in their first year attending university have the highest carriage rates of all age groups, with an increase in carriage following admission[22] and following social mixing at university orientation type events.[23] Consequently, adolescents in their first year attending university are at increased risk of IMD.

In 2018 we carried out a cross sectional carriage study examining carriage of *N. meningitidis* among Otago University students in their first year in a residential college, and risk factors associated with carriage. The study took place across 14 residential colleges, and 1145 of 2084 eligible students participated. The distribution of demographics of participants (age,

gender, ethnicity) largely matched the distribution of demographics of those eligible. The work has not been published yet, but the findings are relevant to this PHARMAC decision. We found that 275 of 1027 (27%) participants carried N. meningitidis. Isolates were sent to Melbourne for whole genome sequencing. Most of the isolates (110/275) were not serogroupable. 43 were serogroup B. Full results are in Table 1.

Table 1: *N. meningitidis* carriage in Otago University students during their first year in a Residential College, 2018.

***N. meningitidis* serogroup**	Any *N. meningitidis*	A	B	C	W	Y	Non-groupable
Number of participants	275 of 1027 (26·8%)	0	43*	6	60	57	110*

*one participant positive for both serogroup B and non-groupable.

International carriage studies have provided evidence that risk factors for carriage include male gender, adolescence, cigarette smoking, smoking of water pipes, attendance in pubs or night clubs, and intimate kissing[2,23,57,71,73–75,79,82,84,144]. All these risk factors are experienced by a high proportion of university students and reflect increased risk of transmission of *N. meningitidis* in this group. Our study examined prevalence of these risk factors among participants, and the association between these risk factors and carriage with our study sample. Following univariate analysis, protective factors included female gender and Asian whereas risk factors included cigarette smoking, exposure to cigarette smoke, vaping, attendance at parties, bars, or clubs. Our multivariate model included vaping, gender, cigarette smoking, exposure to cigarette smoke, intimate kissing, attendance at parties, bars or clubs, respiratory illness in the prior two weeks, ethnicity, international student. The multivariate model used backward elimination to establish independent risk factors. Gender and attendance at parties, bars and clubs are independent risk factors for carriage of *N. meningitidis*.

The study found no relationship between carriage and the following variables: age; residency; antibiotic use in the previous two weeks; meningococcal vaccination – primary health record; meningococcal vaccination – self report; recent respiratory illness.

Our data on New Zealand students living in residential colleges highlights that risk factors for carriage for this high-risk group are present and are not easily modifiable. In addition, carriage rates of *N. meningitidis* are high among students. Both these findings support our position that the 4CMenB vaccine should be funded for students residing in residential colleges.

5) The 4CMenB Vaccine is Effective

As was noted in the Committee minutes from the Pharmacology and Therapeutics Advisory Committee meeting on 21-22 February 2019, there is good evidence of the effectiveness of the 4CMenB vaccination for young children. A recent publication notes that "five years of 4CMenB use post-licensure confirms the clinical benefit of vaccination as predicted during development. Preliminary evidence suggests an extended impact on other meningococcal serogroups and *Neisseria gonorrhoea".*[145]

6) Cost as a Barrier to Vaccination

In 2019 and 2020 an additional study was undertaken, investigating vaccine hesitancy. The study involved an online survey of students in their first year in residential colleges. The

questions followed the recommendations of the WHO Strategic Advisory Group of Experts (SAGE) on Immunisation recommendations.[49] Again, 14 colleges were involved in these cross-sectional surveys. REDCap surveys were emailed to eligible participants (2804). Of the barriers investigated in the survey, cost of vaccination was the most common barrier. Relevant results are included in Table 2 below. Anecdotal reports from the Otago University Student Health Service suggest that after low uptake in 2018 and 2019, when the MenACYW-D was not funded, uptake increased significantly in 2020, when MenACYW-D became funded for students living in residential colleges. Using both measures, it is evident that cost is a barrier to vaccine uptake. This supports our recommendation that 4CMenB should be expanded to include students in close living arrangements.

Table 2: Proportion of students who stated financial barriers would prevent them from getting a vaccination against meningococcal.

	2019	2020
Participants	1103/2804	1349/2804
If you did not have a meningococcal vaccine, what was the reason?	Too expensive (107/172, 59.8%)	Too expensive (187/646, 28.9%)
Has the cost of a meningococcal vaccine prevented you from getting one, or is it likely to prevent you from getting one in the future?	NB: a full course of meningococcal vaccines is approximately $340 at student health or $415 privately. Yes (515/1009, 51.0%)	NB: a full course of meningococcal vaccines includes the Menactra vaccine (free) and two Bexsero vaccines ($240 at Student Health). Yes (492/1224, 40.2%)
Have any of these factors prevented you from getting a meningococcal vaccine?	Distance from a clinic (23/973, 2.4%), Timing of clinic (54/973, 5.5%), Time needed to get to clinic or wait at a clinic (84/973, 8.6%), Costs in getting to a clinic (187/973, 19.2%), None of the above (725/973, 74.5%)	Distance from a clinic (43/1169, 3.7%), Timing of clinic (77/1169, 6.6%), Time needed to get to clinic or wait at a clinic (94/1169, 8.0%), Costs in getting to a clinic (147/1169, 12.6%), None of the above (921/1169, 78.8%)

7) Ethical considerations

There are three ethical drivers that compel PHARMAC to fund 4CMenB.

Firstly, PHARMAC has acknowledged the benefit the 4CMenB vaccine will provide. In 2019 PHARMAC funded MenACYW-D (Menactra) vaccine for individuals aged 13 to 25 years in close-living situations. Given that over half of IMD cases are caused by serogroup B *N. meningitidis*, PHARMAC should be consistent, and fund 4CMenB in the same manner they have funded MenACYW-D.

Secondly, on their website PHARMAC have acknowledged the higher burden Māori and Pacific peoples bear in relation to IMD.[146] While PHARMAC is correct that their proposed limited funding of 4CMenB would "improve access to meningococcal vaccination for Māori and Pacific peoples in the groups proposed for funding", by not funding the vaccine for other high risk groups, such as students residing in residential colleges, PHARMAC will be exacerbating inequalities for Māori and Pacific people in those high risk groups. Māori and Pacific people experience lower income, and experience more barriers accessing health services, so are less likely to access a non-funded vaccine. For PHARMAC, the inequitable access to the 4CMenB for Māori should be of particular concern. PHARMAC has the following statement on its website:

> "The text of Te Tiriti o Waitangi, including the preamble and the three articles, along with the Ritenga Māori declaration ("Te Tiriti"), is the enduring foundation of PHARMAC's commitment to achieving best health outcomes for Māori in its work. PHARMAC is committed to and upholds the articles of Te Tiriti across all its work."[147]

The Ministry of Health states that the intent of Te Tiriti in relation to health is ensuring equity.[148] By expanding funding of 4CMenB PHARMAC will move closer to ensuring equitable availability of 4CMenB for Māori, and potentially reduce the inequitable burden of IMD that Māori currently endure.

Finally, when viewing IMD through a health promotion lens, PHARMAC should prioritise funding for vaccination. Health promotion is the process of enabling people to increase control over, and to improve, their health. The World Health Organisations (WHO) Ottawa Charter laid out the priorities for health promotion, and prioritise the actions of 'health public policy' and 'creating supportive environments'.[149] In relation to accessing a vaccination, and reducing disease incidence, these two actions suggest expanding the availability of vaccines should be prioritised.

8) Potential Cross Protection

There is evidence that previous serogroup B vaccines have provided cross protection against gonorrhoea, both in New Zealand[150] and internationally.[151] The disease gonorrhoea is caused by *Neisseria gonorrhoeae* which is of the same genus as *N. meningitidis*. This added benefit

9) Implementation

It is noted that on the PHARMAC website there is a reference to the disruption that a vaccine roll out could potentially cause for GP practices.[146] We would like to note that for students residing in residential colleges, Student Health Services would deliver most vaccines, which is a service they already have processes and expertise for.

We do not wish to be heard in regards to this submission.

Yours sincerely,

Dr Susan Jack (Medical Officer of Health, Clinical Director, Public Health South)

Mike O'Brien (RN, Clinical Nurse Specialist, Infection, Prevention & Control, Southern District Health Board)

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