

Portugal meningococcal B vaccine (menB) effectiveness study

Submission date 15/05/2019	Recruitment status No longer recruiting	<input type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
Registration date 21/05/2019	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
Last Edited 02/12/2020	Condition category Nervous System Diseases	<input type="checkbox"/> Individual participant data

Plain English summary of protocol

Background and study aims

Meningococcal group B bacteria are a serious cause of life-threatening infections worldwide, including meningitis and blood poisoning. Developing a vaccine against the most common cause (type B) has been a priority but technically very difficult. Because the disease is so rare it has not been possible to carry out the standard type of study (randomised controlled trial) to prove that these vaccines actually protect people against the disease, instead licensure was based on the pattern of antibodies produced and predicted coverage of the commonest strains of Meningococcal disease.

Who can participate?

All children and adolescents diagnosed with invasive meningococcal disease in Portugal between October 2014 and March 2019 inclusive will be eligible for inclusion. For each case, 2 - 4 age and location matched controls will be identified.

What does the study involve?

Examination of medical records including immunisation history of cases and matched controls

What are the possible benefits and risks of participating?

None

Where is the study run from?

Coimbra, Portugal with participation of multiple hospitals in Portugal

When is the study starting and how long is it expected to run for?

April 2018 to September 2019

Who is funding the study?

The investigators and clinicians providing data are undertaking the study as part of their professional duties. No external funding has been sought or obtained.

Who is the main contact?

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Contact information

Type(s)

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Additional identifiers

EudraCT/CTIS number

Nil known

IRAS number

ClinicalTrials.gov number

Nil known

Secondary identifying numbers

1.3

Study information

Scientific Title

Case control study to evaluate the effectiveness of the 4CMenB vaccine for protection against invasive meningococcal disease caused by group B *Neisseria meningitidis* in Portugal

Acronym

PT-BEST

Study objectives

Current study hypothesis as of 03/07/2019:

That rates of full immunisation per licensed schedule for age with Bexsero among children presenting with culture and/or PCR-proven meningococcus group B invasive disease will be significantly lower than among age and gender-matched controls presenting at the same hospitals at around the same time with conditions unrelated to meningococcal infection.

Previous study hypothesis:

That rates of full immunisation per licensed schedule for age with Bexsero will be significantly higher among children presenting with culture and/or PCR-proven meningococcus group B invasive disease will be significantly lower than among age and gender-matched controls presenting at the same hospitals at around the same time with conditions unrelated to meningococcal infection.

Ethics approval required

Old ethics approval format

Ethics approval(s)

Approved 14/05/2018, Ethics Committee from Centro Hospitalar e Universitário de Coimbra (Centro Hospitalar Universitário de Coimbra, Serviço de Doenças Infecciosas, Praceta Mota Pinto, 3000-075 Coimbra, Portugal; +351 239 400 402; jscunha@fmed.uc.pt), ref: CHUC-099-17
National Data Protection authorisation number 306/ 2018

Study design

Multi-centre density case-control study

Primary study design

Observational

Secondary study design

Case-control study

Study setting(s)

Hospital

Study type(s)

Treatment

Participant information sheet

No participant information sheet available

Health condition(s) or problem(s) studied

Neisseria meningitidis

Interventions

All children and adolescents diagnosed with invasive meningococcal disease in Portugal between October 2014 and March 2019 inclusive will be eligible for inclusion. For each case, 2-4 age and location matched controls will be identified.

The study involves examination of medical records and extraction of anonymised information.

Intervention Type

Biological/Vaccine

Phase

Phase IV

Drug/device/biological/vaccine name(s)

4CMenB (Bexsero®)

Primary outcome measure

Effectiveness of the 4CMenB vaccine for protection against invasive meningococcal disease caused by group B Nm in Portugal (partially immunized children considered unvaccinated). Data are extracted from the medical records of cases and matched controls including immunisation history.

Secondary outcome measures

1. Effectiveness of the 4CMenB vaccine for protection against invasive meningococcal disease caused by group B Nm in Portugal when partially vaccinated children are excluded from analysis.
 2. Effectiveness of one or more doses of 4CMenB vaccine for protection against invasive meningococcal disease caused by group B Nm in Portugal (i.e. partially vaccinated children included in analysis but considered to be vaccinated).
 3. Effectiveness of the 4CMenB vaccine, using the 3 approaches summarized above, for protection against all-cause invasive meningococcal disease in Portugal.
- Standardised data are extracted from the medical records of cases and matched controls including immunisation history.

Overall study start date

01/01/2017

Completion date

01/09/2019

Eligibility

Key inclusion criteria

Case participant inclusion criteria:

1. Age > 2 months and 14 days and < 18 years
2. Meningococcal invasive disease confirmed by culture or PCR in a normally-sterile biological sample (blood, CSF, pleural fluid, joint fluid, other)
3. Resident in Portugal at time of presentation
4. Eligible to have received and responded to 4CMenB (age at least 2 months and 14 days, absence of vaccine contraindication)
5. Available information about vaccine status for 4CMenB, MenC and MenACWY from central immunisation records database.

Control participant inclusion criteria:

6. Born within specified time period of matched case participant. If case is less than < 2 years old, controls have to have been born +/- 14 days (minimum age of 2 months and 14 days); if cases are aged 2-5 years, controls have to have been born +/- 60 days, if cases are aged \geq 5 years or more, controls have to have been born +/-90 days
7. Eligible to have received and responded to 4CMenB (aged at least \geq 2 months and 14 days, absence of vaccine contraindication)
8. Living in the same district as the case
9. Same gender as the case
10. Presenting to the same hospital, within the same week of the case (up to 14 days before or after the day when the case was observed), with an illness that was clearly not invasive meningococcal disease (i.e. not meningitis, septicaemia or pyrexia of unknown origin)
11. Available information about vaccine status for 4CMenB, MenC and MenACWY from central immunisation records database

Vaccination status:

For the primary analysis, children who have received the appropriate number of vaccine doses for their age will be considered vaccinated – i.e. those aged 4 to 15 months who have had 2 or more vaccine doses with the second dose at least 14 days before presentation and those aged 16 months or more who have had either 2 or 3 doses before 1 year of age and one dose after 1 year of age (with the booster dose at least 14 days before presentation) or who have had at least 2 vaccine doses after the first birthday (with the second dose at least 14 days before

presentation). All children who have received fewer than the appropriate number of doses as defined above will be considered unvaccinated. Children too young to have received two priming doses with the second at least 14 days before presentation (i.e. less than 4 months and 14 days old) will not be included in this analysis.

Participant type(s)

Mixed

Age group

Child

Lower age limit

2 Months

Upper age limit

18 Years

Sex

Both

Target number of participants

At an estimated 30% vaccine coverage for 80% power at a 5% level of significance, we require a minimum of 36 cases and 72 controls. If the vaccine uptake in controls is 20% these number rise to 54 cases and 108 controls.

Total final enrolment

98

Key exclusion criteria

1. Unknown vaccine status from centralised immunisation records database
2. Belonging to a risk group for meningococcal invasive disease: asplenia, immunodeficiency including but not restricted to complement deficiency or on treatment with Eculizumab
3. History of invasive meningococcal disease
4. Recent known or suspected contact with a case of meningococcal invasive disease

Date of first enrolment

01/04/2019

Date of final enrolment

01/09/2019

Locations**Countries of recruitment**

Portugal

Study participating centre

Hospital Pediátrico - Centro Hospitalar e Universitário de Coimbra
Av. Afonso Romão

Coimbra
Portugal
3000-602

Study participating centre

Centro Materno Infantil do Norte
Largo da Maternidade de Júlio Dinis
Porto
Portugal
4050-651

Study participating centre

Hospital S. Pedro - Centro Hospitalar Trás-os-Montes e Alto Douro
R. dos Lagoeiros 43
Vila Real
Portugal
5000-508

Study participating centre

Centro Hospitalar da Póvoa do Varzim/Vila do Conde
Largo da Misericórdia
Póvoa do Varzim
Portugal
4490-421

Study participating centre

Centro Hospitalar de Vila Nova de Gaia
Rua Conceição Fernandes, s/n
Vila Nova de Gaia
Portugal
4434-502

Study participating centre

Centro Hospitalar Barreiro Montijo
Av. Movimento das Forças Armadas 79C
Barreiro
Portugal
2830-003

Study participating centre
Centro Hospitalar de S. João
Alameda Prof. Hernâni Monteiro
Porto
Portugal
4200-319

Study participating centre
Hospital de Faro - Centro Hospitalar do Algarve
R. Leão Penedo
Faro
Portugal
8000-386

Study participating centre
Hospital de Aveiro - Centro Hospitalar do Baixo Vouga
Avenida Doutor Artur Ralara
Aveiro
Portugal
3810-193

Study participating centre
Hospital D. Estefânia - Centro Hospitalar Lisboa Central
R. Jacinta Marto
Lisboa
Portugal
1169-045

Study participating centre
H. Santa Maria - Centro Hospitalar Lisboa Norte
Av. Prof. Egas Moniz
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Portugal
1649-035

Study participating centre
Hospital Padre Américo - Centro Hospitalar Tâmega e Sousa
Avenida do Hospital Padre Américo 210
Penafiel
Portugal
4564-007

Study participating centre
Centro Hospitalar da Cova da Beira
Quinta do Alvito
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Portugal
6200-251

Study participating centre
Hospital de Torres Novas - Centro Hospitalar do Médio Tejo
R. Xanana Gusmão, 45
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2350-754

Study participating centre
Hospital Beatriz Angelo
Av. Carlos Teixeira, 514
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Study participating centre
Hospital Cuf Descobertas
R. Mário Botas
Lisboa
Portugal
1998-018

Study participating centre
Hospital CUF Porto
Estrada da Circunvalação, 14341
Porto
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4100-180

Study participating centre
Hospital de Braga
Sete Fontes - São Victor

Braga
Portugal
4710-243

Study participating centre
Hospital de Cascais
Av. Brigadeiro Victor Novais Gonçalves
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2755-009

Study participating centre
Hospital de S. Teotónio - Centro Hospitalar Tondela Viseu
Av. Rei Dom Duarte
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Study participating centre
Hospital de Santarém
Av. Bernardo Santareno, 3737B
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Study participating centre
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Ponta Delgada
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9500-370

Study participating centre

Hospital Espírito Santo

Largo do Sr. da Pobreza

Évora

Portugal

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Study participating centre

Hospital Fernando da Fonseca

IC 19

Amadora

Portugal

2720-276

Study participating centre

Hospital Garcia de Orta

Av. Torrado da Silva

Almada

Portugal

2805-267

Study participating centre

Hospital S. Bernardo

R. Camilo Castelo Branco 175

Setúbal

Portugal

2910-549

Study participating centre

Hospital Senhora da Oliveira

R. dos Cutileiros 114, Creixomil

Guimarães

Portugal

4835-044

Study participating centre

ULS Baixo Alentejo - Hospital de Beja

R. Dr. Antonio Fernando Covas Lima

Beja

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7801-849

Study participating centre**Unidade Local de Saúde Alto Minho - Hospital de S. Luzia**

Estr. de Santa Luzia 50

Viana do Castelo

Portugal

4901-858

Study participating centre**Hospital de S. André - Centro Hospitalar de Leiria**

R. de Santo André

Leiria

Portugal

2410-197

Study participating centre**Hospital Privado Algarve**

Urbanização Casal de Gambelas

Faro

Portugal

8005-226

Study participating centre**Hospital Nélío Mendonça**

Av. Luís de Camões 6180

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Sponsor information

Organisation

Sociedade Portuguesa de Pediatria

Sponsor details

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Sponsor type

Other

Website

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Funder(s)

Funder type

Other

Funder Name

Investigator initiated and funded.

Results and Publications

Publication and dissemination plan

It is anticipated that this research will lead to publications in one or more journals covering the areas of paediatric infectious disease or vaccine research. Initial results will be presented at The European Meningococcal Disease Society 27/05/2019.

Intention to publish date

01/10/2019

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study will be stored in a publicly available repository

University of Bristol Research Data Repository
[data.bris](https://data.bris.ac.uk/)

<https://www.bristol.ac.uk/staff/researchers/data/accessing-research-data/>

Anonymised dataset used to calculate effectiveness (both primary and secondary endpoints) including age in months, date of presentation and immunisation history of cases and controls. Data will become available when study is published and will be available indefinitely.

Data will be open access and users will be able to download and analyse it in whatever way they wish.

This study was a case-control study involving access to personally identifiable information only by managing clinical teams and no identifiers were provided to researchers running the study and undertaking the analysis.

It was not feasible nor deemed necessary by the ethical committee and data protection regulators to obtain consent from cases or controls.

There are no ethical or legal restrictions.

IPD sharing plan summary

Stored in repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/12/2020	02/12/2020	Yes	No