#DefeatingMeningitis

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Poster abstract book

Contents

Prevention and epidemic control

#P2 The Value of Invasive Meningococcal Disease Combination Vaccine – a Qualitative Study of Adolescents and Parents/Caregivers' Preferences in the US

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Keywords: Meningococcal Infection; Vaccine; Infection Prevention And Control Programs; Combination vaccine; Adolescent

Background
MenACWY and MenB are commonly used vaccines to prevent invasive meningococcal disease (IMD), targeting serogroups A, B, C, W, Y. MenABCWY combination vaccines are under development and could provide increased vaccine coverage of serogroups. This qualitative study aimed to identify concepts affecting preferences in adolescents (Ado) and parents/caregivers (P/C) decision making towards combination vaccine in the US.

Methods
Two focus group discussions (FGD), 90-minutes with Ado (16-23 years) and P/C of adolescents (16-18 years) were conducted (Table 1). Guides were developed based on a targeted literature review to investigate preferences for potential features of a combination vaccine. Participants were presented with IMD and vaccines information. Important/least important factors for decision-making were transcribed in response to open-ended/probes questions. FGDs were coded to apply thematic assessment. Results were synthesized separately by moderator-probed and spontaneously mentioned themes. Percentages were calculated on participant numbers contributing to a theme.

Results
Thirteen participants were included in FGDs (6 Ado, 7 P/C, 57% P/C with college or lower degree, Table 2). Ado preferred a combination vaccine which provided time saving (100%) and convenience (83%) by reducing the number of injections in the immunization series (100%) and number of visits (100%). P/C considered injection site discomfort (71%) as an important decision factor for a combination vaccine, however Ado considered this as least important (100%). Both groups considered impact on healthcare system and environment as least important for a combination vaccine (55%) (Table 3). Cross-protection against other infectious disease (55%, probed) and spontaneous themes (e.g. duration of protection, effectiveness, side effects and dosing interval) emerged (Table 4). These concepts were considered relevant for combination vaccine decision-making, although could be applicable to IMD vaccination more generally.

Conclusion
The findings suggest vaccine-receivers preferred a combination vaccine covering serogroups A, B, C, W, Y, with simplified schedules (e.g. fewer visits and injections) and potential cross-protection against other infectious diseases

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#P3 In hospital death among under five years children hospitalized with meningitis in the eastern of the Democratic Republic of Congo

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Keywords: Children, Meningitis, Cerebrospinal Fluid, Mortality

Background: Meningitis is a major public health problem needing timely diagnosis, appropriate treatment, prevention and control. Despite the advances in diagnosis and treatment of infectious diseases, meningitis is still considered as an important cause of mortality and morbidity, especially in the paediatric population of lower income countries such as the Democratic Republic of the Congo (DR Congo). In this study, we aimed to analyse the fatality aspect of suspected meningitis among children under five years.

Materials and Methods: A prospective, descriptive study was carried out in the Paediatrics departments of four hospitals in the South-Kivu province in the Eastern part of the DR Congo from April 2021 to March 2022. Of the 1386 children enrolled, 251 children were suspected of meningitis. This study captures data generated in the framework of routine medical practice, which includes medical history, clinical diagnosis and results of locally conducted laboratory tests.

Results: Throughout the study period, a total of 251 patients (18.1%) aged 1 month to 59 months with suspected meningitis were recruited out of 1386 children hospitalized in the Paediatrics. The fatality among hospitalized children with suspected meningitis during the study period was 27.9%, however the mortality linked to meningitis decreases with age, ranging from 37.5% among children under 2 years to 19.4% among those over 2 years old. Children hospitalized for meningitis with malnutrition as an underlying conditions, had a 3.5 times greater risk of dying. The case fatality rate was higher in transferred and not vaccinated children respectively (2.3 and 2.5 times).
We observe that the death occurs early within the first 3 days.

Conclusion: Our study noted a higher fatality rate in children with suspected meningitis that could probably be linked to the gape in vaccination and malnutrition as underline condition

Funding Source: CHILDREN'S PRIZE 2020

#P4 Safety and immunogenicity of quadrivalent meningococcal polysaccharide vaccine (MPV ACYW135) compared with quadrivalent meningococcal conjugate vaccine (Menactra®) in Malian Children

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Five Keywords: meningococcal polysaccharide vaccines, meningococcal conjugate vaccines, Mali, meningococcal disease prevention, meningitis belt

Affordable, polyvalent meningococcal vaccines are needed for use in emergency reactive immunization campaigns. A phase IV randomized, observer-blind, controlled study compared the safety and immunogenicity of a quadrivalent meningococcal polysaccharide vaccine (MPV-4, MPV ACYW135) and quadrivalent meningococcal ACWY conjugate vaccine (MCV-4, Menactra®). Healthy, 2- to 10-year-old children in Bamako, Mali were randomized 1:1 to receive one dose of MPV-4 or MCV-4. Safety outcomes were evaluated for 6 months post-immunization. Immunogenicity for all serogroups was assessed for non-inferiority between MPV-4 and MCV-4 30 days post immunization by serum bactericidal antibody assay using baby rabbit complement (rSBA). From December 2020 to July 2021, 260 healthy subjects were consented and randomized. At Day 30 post-immunization, the proportions of subjects with rSBA titers ≥128 for all serogroups in the MPV-4 group were non-inferior to those in MCV-4 group. The proportions of subjects with rSBA ≥ 4-fold increase and rSBA titers ≥ 8 for all serogroups were similar among vaccine groups (P>0.05). Geometric Mean Titers and Geometric Mean Fold Increases for all serogroups in both vaccine groups were similar (P>0.05). Few local and systemic post-immunization reactions of similar severity and duration were observed within 7 days and were similar in both groups (P>0.05). All resolved without sequelae. Unsolicited adverse events were similar in both groups regarding relationship to study vaccine, severity and duration. No serious adverse events were reported during the study period. MPV ACYW135 showed a non-inferior immunogenicity profile and a comparable reactogenicity profile to MCV-4 in Malian children aged 2-10 years.

Funding source: This work was supported by Yuxi Walvax Biotechnology Co., Ltd., Yuxi, Yunnan, China.

#P5 The Value of Invasive Meningococcal Disease Combination Vaccine – A Qualitative Study of Healthcare Providers' Preferences in the United States (US)

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Five Keywords: Meningococcal Infection; Vaccine; Healthcare provider; prevention; combination vaccine

Background
Invasive meningococcal disease (IMD) is a severe infection caused by different serogroups (e.g., A, B, C, W and Y) that are currently prevented by separate vaccines (e.g., MenACWY and MenB) for 11–23 year olds. MenABCWY combination vaccine candidates could provide increased serogroup coverage. This qualitative study identified concepts affecting healthcare provider (HCP) preferences in decision-making towards a combination vaccine.

Methods
A 90-minute focus group (FG) and 45-minute phone interviews (IW) were conducted with HCPs in the US (Table 1). A targeted literature review informed the FG discussion guide. Emerging themes were explored in IWs. HCP-related factors and what HCPs considered most/least important for vaccine-receivers were recorded in response to open-ended and probed questions. Transcripts were coded and synthesized for thematic assessment. Percentages were calculated based on participant number contributing to a theme.

Results
Eight HCPs were included in the study (5 in FG, 3 in IW) with 8–32 years of experience (Table 2). HCPs valued a combination vaccine covering serogroups A, B, C, W and Y, and representing 95% of serogroup B strains in the US (Table 3). HCPs viewed reducing the burden on adolescents/parents was important to increase uptake and compliance for a combination vaccine. Important attributes included decreasing the number of injections in the immunization series (80% FG, 100% IWs) leading to increased convenience (80% FG, 33% IWs), less injection site discomforts (40% FG), less healthcare visits for vaccine administration (40% FG) and increased time saving (33% IWs). The least important attributes included impact on the healthcare system (60% FG) (e.g., reduced storage, staff time, dosing schedule changes), environment (60% FG) (e.g., reduced packaging, carbon footprint), financial cost to adolescent/parent (33% IWs) for informing HCPs' preferences for a combination vaccine (Table 4).

Conclusion
HCPs prefer a combination vaccine with broad serogroup coverage. Increased time saving, fewer injections and visits to boost convenience and reduce burden on adolescents/parents were valued by HCPs. This suggests simplification of current recommendations for prescribing vaccines was acceptable by HCPs.

Funding source: GlaxoSmithKline Biologicals SA funded this study (GSK study identifier: 219275) and was involved in all stages of study conduct, including analysis of the data. GlaxoSmithKline Biologicals SA also took in charge all costs associated with the development and publication of this abstract.

#P7 Invasive meningococcal disease vaccination – a targeted literature review of adolescents and parents/caregivers' preferences

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Five keywords: Meningococcal Infection, Vaccination, Prevention, Attitudes and preferences

Background: Invasive meningococcal disease (IMD) serogroups A, B, C, W, Y are commonly prevented by MenACWY and MenB vaccines. MenABCWY candidate vaccines could potentially provide benefits as less injections, simplified schedules, and increased uptake. However, there is limited insight on factors influencing preferences for IMD vaccines/vaccination (Vax). This targeted literature review synthesized evidence of factors influencing IMD Vax preferences in 16–23-year-old adolescents/young adults (Ado/YA) and parents/caregivers (P/CG) of 16-18 year-old adolescents.

Methods: PubMed and Google Scholar were searched globally to identify publications on IMD Vax attitudes and preferences (**Table 1**). Studies were restricted to English and published between 2005-2022. Data were extracted and synthesized from full text reviews to list IMD Vax preference attributes.

Results: From the 77 abstracts screened, 19 publications were extracted (**Table 2**) and 17 relevant for Ado/YA and P/CG. Knowledge of disease severity (20% of Ado/YA articles) and vaccine (29% of P/CG articles) were the most reported factors influencing Vax preference. Severity of disease increased Vax preference for both groups (14%), while low disease awareness limited P/CGs' willingness to vaccinate children (14% of P/CG articles). Some Ado/YA preferred fewer injections in the immunization series due to reduced injection site discomforts (13%). P/CG preferred less injections due to less time and less physician visits, as it may reduce vaccine preparation/injection/administration and indirect costs associated with parental work loss (7%). However, their concerns over injection-related pain were a Vax barrier (14%). IMD vaccine effectiveness was recognized by Ado/YA (13%). Longer duration of protection was important for P/CG (14%), whilst herd immunity and direct protection was preferred in Ado/YA (13%).

Conclusions: Findings highlight IMD Vax characteristics as key considerations among Ado/YA and P/CG when making Vax decisions. To improve vaccination coverage and protection, the evidence supports preferences for vaccinations offering benefits such as fewer injections. Trade-offs between factors relevant for a IMD combination vaccine need further research.

Funding Source: GlaxoSmithKline Biologicals SA funded this study (GSK study identifier: 219275) and was involved in all stages of study conduct, including analysis of the data. GlaxoSmithKline Biologicals SA also took in charge all costs associated with the development and publication of this abstract.

Table 1: TLR broad search inclusion/exclusion criteria (PICOS)[1]

Parameter	Inclusion criteria	Exclusion criteria
Population of interest	Healthcare providers, paediatricians, family physicians, nurse practitioners, physician assistants, internal medicine, parents / caregivers of adolescents, adolescents, young and adult population (aged 16-23 years)	Parents/caregivers of individuals <16 years and >18 years old and population <16 years and >23 years old
Interventions of interest	Meningococcal vaccine Invasive meningococcal disease vaccine IMD vaccine Combination vaccine Multivalent vaccine Pentavalent vaccine	
Comparators of interest[1]	Meningococcal conjugate vaccine (MCV4) – MenACWY (Menactra, MenHibrix, Menveo, Nimenrix, MenQuadfi) Serogroup B meningococcal vaccine-MenB vaccine, 4CMenB, MenB-FHbp (Bexsero, Trumenba) MenC vaccine	
Outcomes of interest	Concepts such as but not limited to features, characteristics, attributes benefits, impacts, experiences, cost, willingness to pay, monetary value(s) safety, effectiveness, attitudes, acceptability, preferences	Literature not including an outcome of interest
Study design of interest	Qualitative studies involving patient/parent/caregiver interviews/focus groups exploring preferences Studies eliciting preferences from HCPs, parents or caregivers of adolescents, and adolescents and adults Quantitative studies (preference studies such as but not limited to discrete choice experiment, time trade off, swing weighting, best worst scaling) Real-world evidence (observational) studies associated with these vaccines Clinical trial literature Targeted literature reviews or systematic literature reviews on meningococcal disease vaccination (with focus on preference)	

[1] Table includes a broader literature search including healthcare professionals' preferences, however they are not included in this analysis.

Table 2: Studies characteristics and results in the TLR full text review[1]

Study Type	N=19	%[3]
1. Discrete Choice Experiment & Conjoint analysis	7	37%
2. Real-world evidence (observational study)	1	5%
3. Survey[2]	6	32%
4. Mixed methods study	2	11%
5. Literature review	2	11%
6. Individual and group interviews[2]	1	5%
Country	N=19	%[3]
United States	5	26%
Multiple locations (>2 locations)	3	16%
Australia	2	11%
England	2	11%
Italy	2	11%
France	1	5%
France and Germany	1	5%
Germany	1	5%
The Netherlands	1	5%
Uganda	1	5%
Study Population	N=19	%
Parents of teens/adolescents	4	21%
University students / US college students (age 18-28)	4	21%
Paediatricians / healthcare workers	2	11%
Parents of children young children	2	11%
N/A (Real-world evidence study and review on value of childhood combination vaccines)	2	11%
Adolescents (aged 15-19)	1	5%
Adults (mean age 43 years) and adolescents (mean age 16 years)	1	5%
Adults / parents	1	5%
Parents of adolescents (aged 11-21) & healthcare workers	1	5%
Parents, children, adolescents and healthcare providers	1	5%
Indication / Type of vaccine	N=19	%[3]
Non-specific (multiple indications)	7	37%
Meningitis B	7	37%
Meningococcal disease (general)	4	21%
Meningococcal serogroup C meningitis or measles	1	5%
Concept/Attributes for Adolescents/Young Adults	N=15[5]	%
Knowledge about disease severity	3	20%
Number of injections in the immunization series[4]	2	13%
Vaccine effectiveness	2	13%
Knowledge about vaccine and its administration[6]	2	13%
Potential for indirect protection / herd effect	2	13%
Vaccine risks/safety profile	1	7%
Vaccine cost (out-of-pocket cost)	1	7%
Duration of protection	1	7%
Vaccine broader protection / cross protection	1	7%
Time saving (convenience)	0	0%
Concept/Attributes for Parents and Caregiver	N= 14[5]	%
Knowledge about vaccine and its administration[6]	4	29%
Number of injections in the immunization series[4]	2	14%
Vaccine risks/safety profile	2	14%
Duration of protection	2	14%
Vaccine effectiveness	1	7%
Time saving (convenience)	1	7%
Vaccine cost (out-of-pocket cost)	1	7%
Knowledge about disease severity	1	7%
Potential for indirect protection / herd effect	0	0%
Vaccine broader protection	0	0%
Concept/Attributes for Adolescents/Young Adults and Caregiver	N=29[5]	%
Knowledge about vaccine and its administration[6]	6	21%
Number of injections in the immunization series[4]	4	14%
Knowledge about disease severity	4	14%
Vaccine risks/safety profile	3	10%
Vaccine effectiveness	3	10%
Duration of protection	3	10%
Vaccine cost (out-of-pocket cost)	2	7%
Potential for indirect protection / herd effect	2	7%
Time saving (convenience)	1	3%
Vaccine broader protection	1	3%

[1]Two articles that did not meet the inclusion criteria were included for extraction due to the insights around combination vaccines (assessing preferences relevant for a combination vaccine)

[2]The surveys and individual and group interview studies includes the 2 articles that did not meet the inclusion criteria (population = parents of infants/children aged <2), however, they were included for extraction upon GSKs request due to the insights around the combination vaccines

[3]Categories are not mutually exclusive

[4]Reducing injection site-related discomfort and resource/time use and costs

[5] Categories are not mutually exclusive, one literature can cover different attributes

[6]Including disease awareness and preference for location to receive vaccination

#P8 A Systematic Literature Review of Disparities That May Influence Health Equity in Invasive Meningococcal Disease Prevention in the US

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Five keywords: Meningococcal Infection, Vaccination, Health Inequity, equality, prevention

Background: Meningococcal serogroup A, C, W, Y (MenACWY) and B (MenB) vaccines are recommended in the US to prevent invasive meningococcal disease (IMD), a rare but life-threatening disease. Yet the suboptimal uptake of and adherence to these vaccines may relate to inequities for healthcare access. This systematic literature review (SLR) synthesized the US evidence on disparities associated with IMD prevention.

Methods: Embase, MEDLINE and six conferences were searched and handpicked studies included from 01/01/2012 to 23/08/2022. Studies were screened twice against inclusion criteria (Table 1) via a standardised form. Newcastle Ottawa Scale was used for quality assessment. Synthesis findings reported here were from a broader SLR on IMD risk, prevention and control.

Results: The SLR found 26 studies, 14 relevant for prevention (Table 2-3). MenACWY series completion had higher odds for adolescents with a family annual income >$75,000 vs. ≤$30,000. Individuals from families below poverty status (annual income ≤$75,000 in 2021) had lower MenB vaccination coverage rates. MenACWY booster compliance was lower in uninsured vs. insured adolescents. Higher odds for ≥1 dose of MenB vaccine were observed if individuals had Medicaid vs. private insurance. For parents/guardians of ≥1 dependent of 16-19 years old, with some insurance was significantly associated with MenB vaccine initiation vs. no insurance. Adolescents living outside a metropolitan statistical area had lower vaccination coverage with ≥1 MenACWY than adolescents in MSA principal cities. MenB series completion rates were lower in rural vs. urban areas in commercial insured populations. Non-Hispanic Black and Hispanic population were more likely to be vaccinated for MenB compared to non-Hispanic Whites, however one study found the opposite. MenB series completion were lower in the Black versus White Medicaid populations.

Conclusions:
Disparities in IMD prevention were reported for race/ethnicity, geographical factors, income/poverty level and health insurance status. Simplification of current recommendation (e.g., combination vaccine with increased convenience and reduced injections in the IMD vaccination schedule) could improve low uptake and adherence in disadvantaged groups.

Funding Sources: GlaxoSmithKline Biologicals SA funded this study (GSK study identifier: VEO-000436) and was involved in all stages of study conduct, including analysis of the data. GlaxoSmithKline Biologicals SA also took in charge all costs associated with the development and publication of this abstract.

Table 1: SLR broad search inclusion/exclusion criteria (PECOS Selection Criteria)[1]

	Study Inclusion			**Study Exclusion**
	IMD Risk	**IMD Prevention (Engagement in Preventive Practices)**	**IMD Control (Disease Control)**	
Population	**IMD cases or carriers and controls (susceptible or not infected) of all ages**	**IMD cases or carriers and controls (susceptible or not infected) of all ages**	**IMD cases, long-term survivors of IMD, caregivers of IMD cases and long-term survivors of all ages**	Populations not related to IMD or at-risk of IMD Patients with influenza/bacterial infections caused by Haemophilus influenzae Patients with pneumonia/bacterial infections caused by Streptococcus pneumoniae Patients with viral meningitis
	IMD cases/carriers/IMD patient population would include adults/adolescents/children/infants with one or more of the following descriptions: Patients with meningococcal disease/meningitis/ bacterial meningitis/meningococcaemia/septicaemia meningococcal sepsis/Waterhouse–Friderichsen syndrome Patients with bacterial infections caused by Neisseria meningitidis Patients with IMD caused by all serogroups	**IMD cases/carriers/IMD patient** population would include adults/adolescents/children/infants with one or more of the following descriptions: Patients with meningococcal disease/meningitis/ bacterial meningitis/meningococcaemia/septicaemia meningococcal sepsis/Waterhouse–Friderichsen syndrome Patients with bacterial infections caused by Neisseria meningitidis Patients with IMD caused by all serogroups	**IMD cases/carriers/IMD patient** population would include adults/adolescents/children/infants with one or more of the following descriptions: Patients with meningococcal disease/meningitis/ bacterial meningitis/meningococcaemia/septicaemia meningococcal sepsis/Waterhouse–Friderichsen syndrome Patients with bacterial infections caused by Neisseria meningitidis Patients with IMD caused by all serogroups	
Exposure* **	Exposures may have included, but were not limited to: social, economic, environmental, and other factors of health including the following: Person's individual characteristics and behaviours: ○ Ethnicity ○ Sex/sexual orientation ○ Religion ○ Physical disability ○ Mental health ○ Age			Exposures that were not considered as factors that attribute to inequalities of health

	Study Inclusion			Study Exclusion
	IMD Risk	**IMD Prevention (Engagement in Preventive Practices)**	**IMD Control (Disease Control)**	
	○ Exposure to crime and violence Social and economic factors: ○ Social deprivation ○ Wealth ○ Socioeconomic status ○ Insurance status and type ○ Education level ○ Occupation ○ Working life conditions ○ Basic amenities ○ Unemployment and job security ○ Food security ○ Early childhood development ○ Structural conflict ○ Access to affordable health services of decent quality Physical environment: ○ Geographic location/region ○ Housing and household size			
Comparator	Alternative levels within each exposure (e.g., rural/urban or differing levels of education). A "no comparator" was also to be used if applicable (e.g., employed vs. not employed)			NA
Outcomes	Studies reporting on the association between exposures and IMD risk for any of the following outcomes: IMD incidence IMD prevalence Carriage Mortality Sequelae HRQoL	Studies reporting on differences in exposures in relation to the following outcomes: Vaccine uptake Vaccine adherence/ Compliance Series completion	Studies reporting on differences in exposures in relation to the following outcomes: HCRU due to complications during acute phase and due to long-term sequelae ○ Hospitalisations ○ ICU visits ○ ER visits ○ Outpatient care ○ Specialist visits Differences in access to healthcare services for survivors and caregivers including, but not	Publications that report the following type of outcomes Clinical efficacy Safety Effectiveness of treatments /vaccines Clinical burden

	Study Inclusion			Study Exclusion
	IMD Risk	**IMD Prevention (Engagement in Preventive Practices)**	**IMD Control (Disease Control)**	
			limited to, the following: ○ Age-specific ○ Sex-related ○ Racial and ethnic ○ Cost and affordability ○ Geography/location related ○ Insurance status and insurance type Economic costs due to sequelae treatment for survivors and caregivers ○ All direct costs including: - Treatment costs - Medication costs - Hospitalisation costs - Other medical services costs ○ All indirect costs including: - Special education costs - Productivity losses for survivors and caregivers (absenteeism, presenteeism, income loss)	
Study type	Observational studies (i.e., cohort, case control, cross-sectional, case series) Database studies Modelling studies Economic evaluations SLRs or TLRs (for reference chasing only)			RCTs Non-randomised and single-armed designs

	Study Inclusion			Study Exclusion
	IMD Risk	**IMD Prevention (Engagement in Preventive Practices)**	**IMD Control (Disease Control)**	
				In vitro/ex vivo/animal/pharmacokinetic studies Narrative reviews
Sub-analysis and subgroups of interest	Based on the following countries/Country specific subgroups in adults/adolescents/children: ○ US* ○ EU5 (France, Germany, Italy, Spain and the United Kingdom) ○ Japan ○ Other high-income countries ○ Latin America^ COVID-19 Exposure as per Dahlgren model Outcomes (based on IMD risk, prevention and control) Age-based subgroups (e.g., infants vs. children vs. adolescents vs. adults vs. older adults, etc.) Different serogroups Study type-based subgroups			African region/Sub-Sahara Africa Middle and low-income countries**
Publication type	Full-text publications Conference abstracts and posters (2020–present)			Conference abstracts published prior to 2020 Editorials Erratum Trial protocols Guidelines Narrative reviews Systematic reviewsμ
Limits				
Time Period	2012–present			Studies published prior to 2012
Language	English, French, Spanish, Italian, Portuguese			Studies in other languages will be tagged but not extracted

	Study Inclusion			Study Exclusion
	IMD Risk	**IMD Prevention (Engagement in Preventive Practices)**	**IMD Control (Disease Control)**	
Countries	High-income countries including US, EU5 (France, Germany, Italy, Spain and the United Kingdom), Latin America^#			African region/Sub-Sahara Africa Middle- and low-income countries*
[1] This table shows the PECOS criteria for the complete study scope (i.e., including risk and control besides of prevention) *** Focus of this abstract is on US only** **** As defined by the World Bank World Bank Country and Lending Groups https://datatopics.worldbank.org/world-development-indicators/the-world-by-income-and-region.html** **^ Including Central America and Caribbean** **µ Only used for citation chasing** **Abbreviations: ER = emergency room; EU = European Union; HCRU = healthcare resource utilisation; HRQoL = health-related quality of life; ICU = intensive care unit; IMD = invasive meningococcal disease; NA = not applicable; PECOS = population, exposures and comparators, outcomes and study design criteria; RCT = randomised controlled trial; SLR = systematic literature review; TLR = total literature review; US = United States**				

Table 2: Study Characteristics

Study Name Author, Year	Country	Brief Patient Description	Study Design	Sample Size	Data Source	Data Collection Years
Basta, 2019	US (Minnesota)	Parents of teens attending high school in 2017-2018	Cross-sectional study	445	University of Minnesota's Driven to Discover research facility	2017
Cheng, 2020	US (all locations)	Adolescents aged 17 years	Cross-sectional study	Unweighted: 22,928 Weighted: 3,948,025	NIS-Teen	2011-2016
Ghaswalla, 2022	US (Multicentre, from a variety of geographic regions)	People with a new diagnosis of HIV who were eligible for MenACWY vaccine	Retrospective cohort study	1,208	Optum Research Database	2016-2018
Ghaswalla, 2021	US (all locations)	Patients with newly diagnosed asplenia and eligible for MenACWY or MenB vaccination	Retrospective cohort study	MenACWY: 2,273 MenB: 741	Optum Research Database	2005-2018
Hansen, 2021	US (all locations)	Adolescents aged 17 years	Cross-sectional study	7,288	NIS-Teen	2017-2018
Holloway, 2018	US (Los Angeles County)	MSM who might or might not have received the MenACWY vaccine	Cross-sectional study	368	NR	2016-2017
Huang, 2020	US (Multicentre, Lightspeed/ All Global panel of >55,600 US HCPs)	Patients who received or did not receive MenB vaccine within the	Retrospective cohort study	1,521	Patient chart review conducted by HCPs	2017

Study Name Author, Year	Country	Brief Patient Description	Study Design	Sample Size	Data Source	Data Collection Years
		previous 6 months				
Kempe, 2018	US (all locations)	Paediatricians and family physicians	Cross-sectional study	660	University of Colorado Denver	2016
Kurosky, 2019	US (all locations)	Younger adolescents aged 10.5 through 13 years and older adolescents aged 15.5 years through 18 years	Retrospective cohort study	Commercial Claims and Encounters Younger adolescents: 376,825 Older adolescents: 419,814 Medicaid Younger adolescents: 310,383 Older adolescents: 206,301	Commercial Claims and Encounters and Medicaid MarketScan Databases	2011-2016
La, 2021	US (all locations)	Adolescents aged 17 years	Cross-sectional study	7,288	NIS-Teen	2017-2018
Marshall, 2022	US (all locations)	Patients with complement component deficiencies and eligible for MenACWY or MenB vaccination	Retrospective cohort study	MenACWY: 1,470 MenB: 396	Optum Research Database	2005-2018
Packnett, 2022	US (all locations)	Adolescents and young adults with private (Commercial) and Medicaid insurance who initiated MenB vaccination	Retrospective cohort study	Commercial: 156,080 Medicaid: 57,082	IBM MarketScan Commercial Claims and Encounters databases; IBM MarketScan Multi-State Medicaid Database	2014-2020
Pingali, 2021	US (all locations)	Adolescents aged 13-17 years	Cross-sectional study	NR	NIS-Teen	2020

Study Name Author, Year	Country	Brief Patient Description	Study Design	Sample Size	Data Source	Data Collection Years
Srivastava, 2020	US (all locations)	Adult parents or guardians (aged within the range of 35 to ≥65 years) of ≥1 dependent aged 16 to 19 years	Cross-sectional study	619	Survey (participants were identified through the Ipsos Knowledge Panel®)	2016

Abbreviations: HCP = healthcare provider; MenACWY = quadrivalent meningococcal conjugate vaccine (serogroups A, C, W, Y); MenB = meningococcal serogroup B; MSM = men who have sex with men; NIS-Teen = National Immunization Survey-Teen; NR = not reported; US = United States

Table 3: Quality Assessment Scores Using Newcastle Ottawa Scales[1] and Study Types

Author, Year	Total Score[2]
NOS - Cohort (n=6)	
Ghaswalla, 2021	9
Ghaswalla, 2022	8
Huang, 2020	5
Kurosky, 2019	6
Marshall, 2022	7
Packnett, 2022	9
NOS - Cross-sectional (n=8)	
Basta, 2019	6
Cheng, 2020	8
Hansen, 2021	8
Holloway, 2018	9
Kempe, 2018	5
La, 2021	8
Pingali, 2021	7
Srivastava, 2020	7
Study Design	**Total (N=14)**
Cross-sectional study	8 (57%)
Retrospective cohort study	6 (43%)

Abbreviations: NOS = Newcastle Ottawa Scale

[1] The Newcastle Ottawa Scale is used to evaluate non-randomised studies' quality including their study groups selection, their group comparability and their ascertainment of either the exposure or outcome of interest for case-control or cohort studies. (Source: Wells GA, Shea B, O'Connell D, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp. Published 2000. Accessed August 5, 2022.

[2] 9 = very high quality, 0 = very low quality. The Newcastle Ottawa Scale evaluates the risk of bias in the findings of observational studies by considering three domains of potential bias: the selection domain (four questions), the comparability domain (one question) and the exposure domain (three questions) or outcome domain (three or two questions). The scale has different versions depending on the type of observational study. Each question was assessed and the score was recorded in the form of 0, 1 or 2, as per the criteria defined in the tool. The maximum possible score was nine in all three version.

#P9 Investigation into the Potential of two conserved recombinant proteins as Group B Streptococcus Vaccine Candidates

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Five Keywords: Group B strep, sublingual delivery, Protein antigen, Mucosal vaccine, Opsonophagocytic assay

Background: The development of a Group B streptococcus (GBS) vaccine that elicits both mucosal and systemic immunity would be an advantage for the effective prevention and control of GBS infections. Mucosal immunity plays a crucial role in eliminating GBS colonisation, the main risk factor for GBS transmission from the mother to the foetus, thereby contributing to herd immunity. Despite the ongoing development of conjugated capsular polysaccharide (CPS) vaccines, their focus on systemic immunity to ensure maternal IgG placental transfer against limited vaccine serotypes leaves a gap. This research investigates the viability of two conserved GBS recombinant proteins, FbsC and EsxA, important in vaginal tract adhesion, invasion, and colonization, as potential mucosal GBS vaccines.

Methods: Recombinant expression of FbsC and EsxA proteins was performed to obtain purified vaccine candidates. Balb/c mice were immunised subcutaneously with the individual proteins with and without Alum adjuvant to evaluate their immunogenicity and the resulting serum was used in an OpkA assay to determine the ability of the antibodies to mediate the killing of GBS.

Results: Immunization with FbsC generated a significant immune response, both with and without the adjuvant, indicating its potential as an effective vaccine candidate. On the other hand, EsxA demonstrated the ability to generate antibodies but only in the presence of an adjuvant. In addition, results from the opsonophagocytic assay demonstrated that immune sera from the proteins mediated substantial killing of GBS serotype III.

Conclusion: These findings show the potential of FbsC and EsxA as GBS vaccine candidates. Future investigations will focus on evaluating the opsonophagocytic ability of the induced response against other GBS serotypes and the potential of these two proteins to be used as carriers to conjugate to GBS polysaccharides, using our mouse-sublingual delivery model that demonstrated promising results with TT-based GBS glycoconjugates. In summary, this study aims to advance the GBS vaccine landscape by considering both mucosal and systemic immunity. FbsC and EsxA's potential, evident in their immunogenicity or opsonophagocytic activity, highlights a promising avenue for comprehensive GBS prevention.

Funding source: MHRA

#P10 Invasive Meningococcal Disease In Older Adults – Current Perspectives And Call For Action

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Five keywords: Invasive meningococcal disease, older adults, atypical presentations, mortality, immunisation

Background: Invasive meningococcal disease (IMD) is considered an important global public health concern, resulting in high mortality and often life-long sequelae in survivors. IMD affects all age groups. Routine child and adolescent immunisation programmes have substantially reduced IMD in targeted populations. A significant proportion of IMD cases are observed in older adult population (≥60 years age) and there no specific recommendations for prevention of IMD in this group.

Methods: In this context, an international multidisciplinary expert working group (EWG) was established to evaluate the existing knowledge on meningococcal disease in older adults and discuss evidence gaps.

Results: The burden of IMD in older adults, typically due to serogroups W and Y, is yet underestimated as atypical presentations (bacteremic pneumonia, gastrointestinal symptoms, and septic arthritis) may impact the accuracy of IMD surveillance and are frequently observed in older adults. These can result in diagnostic and therapeutic delay. Mortality rates and direct medical costs are substantially higher for meningococcal disease in older adults when compared with young individuals. Routine meningococcal immunisation in adults is not recommended except those considered at high-risk. Common medical co-morbidities reported in older adults, including diabetes, chronic pulmonary and renal disease are a risk factor in meningococcal pneumonia with most often insufficient vaccine coverage.

Conclusions: IMD in older adults remains overlooked. A greater awareness is required (at clinical and public level). Clinicians and immunisation policy makers should reconsider opinion that IMD is a childhood disease and rectify the existing inequity in older adult access to protective meningococcal immunisation

Funding Source: The EWG meetings were funded by Sanofi

#P12 Can some childhood mental health disorders be prevented? Long-term risk of psychiatric disorders following neonatal, invasive Group-B Streptococcus disease. A population-based cohort study from Denmark.

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Five Keywords: Group B Streptococcus disease, risk of neurodevelopmental disorder, Epidemiology, Population-based study, Denmark

Background/ hypothesis
Invasive group B Streptococcus disease (iGBS) is the most common infection in early childhood, annually affecting approximately 500,000 newborns globally. iGBS disease can lead to several neurodevelopmental impairments such as intellectual and/or motor, vision, or hearing impairment. However, the risk of psychiatric disorders has not been investigated in infants with iGBS, especially iGBS sepsis. We aim to examine the association between infant iGBS (sepsis or meningitis) and the risk of psychiatric disorders from early childhood until adolescence.
Methods
We conducted a population-based cohort study using national health care data from 1997 through 2018 in Denmark. Exposed children had hospital-diagnosed iGBS during the first 89 days of their life. A general population comparison cohort was randomly sampled and matched 10:1 to the exposed cohort by sex, year of birth and gestational age. Psychiatric disorders were defined by the International Classification of Diseases, Tenth Revision codes (ICD-10-codes). Cumulative risk (CR) of psychiatric disorder was calculated by treating death as a competing event. Cox proportional hazards regression was used to compute hazard ratios (HRs) and the associated 95% confidence intervals (CIs).
Results
The CR for the entire follow-up period (0-22 years) of any psychiatric disorder was increased in children with iGBS (22.6% (95% CI 19.4–25.9%)) compared with the comparison cohort (19.4% (95% CI 18–20.8%)). The adjusted HR for any psychiatric disorder was 1.42 (95% CI 1.22–1.66). Our findings also show an increased risk of neurotic disorders, mental developmental disorders and emotional disturbances for the iGBS cohort.
Conclusion
Our study finds an increased long-term risk of psychiatric disorders following neonatal iGBS. Our findings close another knowledge gap regarding neonatal, invasive infections and long-term mental health outcomes. Several neonatal infections, including iGBS, can be prevented with screening, antibiotic treatment or vaccines.
Our findings indicate that preventive strategies can reduce the burden of mental health disorders in the future.
Funding source: None

#P16 Genetic detoxification of an unencapsulated meningococcal vaccine strain enhances potency and cross-reactivity of outer membrane vesicle vaccine responses

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Five keywords: Vaccines, outer membrane vesicles, genetic detoxification, cross-reactivity, breadth of coverage

Outer membrane vesicle (OMV) vaccines have been used to successfully quell meningococcal serogroup B (MenB) infections in epidemic settings. However, immunodominant responses to the PorA protein limit the potential for utilization of OMV vaccines to prevent invasive disease caused by MenB strains expressing PorA serosubtypes heterologous to the vaccine strain. We previously reported that OMVs isolated from a MenB strain (ΔABR) deleted for expression of PorA and two additional major outer membrane proteins (OMPs), PorB and RmpM, elicited functional antibodies in animals that were more cross-reactive, but less potent, than those induced by wild-type (WT) OMVs.

Diminished potency was associated with a decrease in structural membrane integrity of ΔABR OMVs upon detergent detoxification, which is required to limit toxicity of lipooligosaccharide (LOS). Deletion of the acyl transferase LpxL1 has been reported to genetically detoxify LOS by preventing formation of the highly toxic hexa-acylated LOS structure, rendering detergent detoxification unnecessary. In an attempt to examine the impact of detergent detoxification on potency of OMV vaccines, we engineered a genetically-detoxified MenB strain, ΔABRL, that was deleted for expression of PorA, PorB, RmpM, and LpxL1. ΔABRL OMVs were isolated and used to immunize rabbits and mice; sera from animals were tested in human complement serum bactericidal assays (hSBAs) for functional antibody responses against a panel of up to 17 antigenically diverse MenB strains. Functional antibody responses were observed in a greater number of animals immunized with genetically-detoxified ΔABRL OMVs compared to those administered detergent-detoxified WT or ΔABRL OMVs. LpxL1 deletion was also associated with bactericidal activity against a greater number of MenB strains.

The effects of LpxL1 deletion were greatly enhanced by additional deletion of the *siaD* gene, which rendered the vaccine strain (ΔABRSL) unencapsulated. Proteomics studies demonstrated that complexes formed when OMV antigens were immunoprecipitated by anti-ΔABRSL OMV sera vs. anti-ΔABRL sera were significantly enriched for putative adhesins and OMPs, including NMB0586, NMB1125, and Opc. These studies suggest that: (1) deletion of LpxL1 and SiaD from the ΔABR vaccine strain increases OMV vaccine potency, and (2) the presence of residual capsular components in OMV vaccines diminishes serological responses to cross-reactive vaccine antigens, either by decreasing immune recognition of antigens or by dampening overall B cell responses

Funding Source: US Food and Drug Administration, Oak Ridge Institute for Science and Education, National Institute of Allergy and Infectious Diseases (NIAID) U19 grant number AI144180-01 to Ann E. Jerse NIAID grant number UC6-AI058607 to Duke Human Vaccine Institute

#P19 An evaluation of human factors surrounding the usability of a novel vial adapter system versus a traditional 2-vial vaccine reconstitution system

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Five keywords: MenABCWY; vaccination; vaccine administration; vial adapter; vaccine preparation

Objective: Many vaccines are supplied as lyophilized powders in vials that require reconstitution by a healthcare professional just before administration. Traditional reconstitution systems include 2 vials and 2 needles (2V) and can be relatively time-consuming to prepare. This study evaluated performance by, and preferences of, vaccinators with a 2V system compared with a simplified system that uses 1 needle and a novel vial adapter (VA).

Methods: The 2V system comprised a diluent vial, placebo powder vial, graduated syringe, and mixing (21-gauge) and administration (25-gauge) needles. The VA system comprised a placebo powder vial, diluent in a prefilled syringe, administration needle, and the vial adapter—a plastic assembly shaped like the bottom end of a syringe with a Luer opening on the top and a hollow spike opposite the Luer opening pointing towards the base. After removing the flip cap, the adapter is locked onto the vial by pressing it base-down over the vial top; this allows the spike to pierce the rubber stopper. The prefilled syringe is twisted onto the Luer opening and the diluent is injected.
Individuals who provide vaccinations to the public were recruited in Atlanta and Boston in March 2022. Using the quick reference guides provided, each participant attempted 2 vaccine reconstitution/administration simulations for each system. The study moderator provided no guidance or other indications of the participant's performance at any time. The systems were presented to participants in a counterbalanced order to mitigate against possible order effects. Usability was based on participants' successful, independent completion of each step of each system's workflow. After all simulations were completed, participants were interviewed to solicit subjective feedback regarding each system.

Results: Of the total participants (n=56; retail pharmacists [n=13] and nurses/vaccine coordinators [n=43]), 75% were female and 89% were right-handed. Overall success was comparable between systems (2V, 81%; VA, 76%). Most participants considered the VA system easier (89%) and faster (85%) than the 2V system; 89% expressed a preference for the VA system over the 2V system.
Conclusions: Performance data suggest that the VA system is at least as easy to use as the 2V system. Participants preferred using the VA system, citing its reduced preparation time and ease of use. These findings indicate that use of the VA system for the investigational pentavalent serogroups A, B, C, W, and Y meningococcal vaccine (MenABCWY) and other vaccines may increase convenience and save time relating to vaccine administration. Funded by Pfizer.

Funding Source: Pfizer Inc

#P20 Rationale for a pentavalent meningococcal serogroup ABCWY vaccine: a review of epidemiological and clinical data

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Five keywords: Epidemiology, Immunogenicity, Meningococcal, Pentavalent, Vaccine

Background
Invasive meningococcal disease (IMD) while unpredictable, is dominated by serogroups A, B, C, W, and Y globally; currently available vaccines target serogroups ACWY and, separately, serogroup B using different schedules. We present the potential utility of a pentavalent MenABCWY vaccine to address challenges of evolving IMD epidemiology and vaccination recommendations.

Methods
Global IMD burden was assessed through review of surveillance reports and PubMed articles published during January 2010–June 2020. Clinical data were derived from the MenABCWY clinical development program covering 3 phase I/IIb/III studies in >4000 adolescents and young adults. Immunogenicity evaluations were based on serum bactericidal antibody assays using human complement (hSBA) using serogroup A/C/W/Y strains and 4 diverse, vaccine-heterologous serogroup B strains. Proportions of participants achieving seroprotective hSBA titers (≥1:8 or ≥1:16 depending on strain) and those achieving ≥4-fold rises in hSBA titers from baseline (seroresponse) were determined. Safety was also evaluated.

Results
Data from 77 countries indicated that IMD incidence during 2010–2019 varied among countries and was generally low (<3 per 100,000) but was characterized by unpredictable shifts in disease-causing serogroups and sporadic outbreaks. Incidence peaked among infants and young children, with secondary peaks in adolescents/young adults and sometimes older adults. Serogroups A/B/C/W/Y caused most IMD; serogroup B dominated in many regions and serogroups W and Y increased in some regions.
After 2 MenABCWY vaccinations (0,6-month schedule), 93.3%–97.8% of ACWY-naive and 68.1%–95.9% of all participants achieved seroresponses for serogroups A/C/W/Y and serogroup B test strains, respectively, which were noninferior at the −10% margin to 1 MenACWY-CRM dose and 2 MenB-FHbp doses (0,6-month schedule), respectively. Most (78.3%) achieved seroprotective hSBA titers against all 4 serogroup B strains combined. A/C/W/Y seroresponses to MenABCWY were also noninferior to MenACWY-CRM in ACWY-experienced participants. One MenABCWY dose was also noninferior to one MenACWY-CRM dose in all participants. Four-year immunopersistence was similar to licensed comparators. After a 4-year booster dose, 100% of participants achieved seroprotective hSBA titers for A/C/W/Y, and percentages achieving seroprotective hSBA titers for B test strains were higher than after the primary series. Seroresponses for all 5 serogroups trended higher on a 0,12-month schedule compared to the 0,6-month schedule except for serogroup C. MenABCWY was well-tolerated. No safety concerns were identified.

Conclusions
MenABCWY was safe, well-tolerated, and highly immunogenic. It has the potential to address challenges of evolving IMD epidemiology and complex vaccination schedules by providing adolescents and young adults with comprehensive protection using a single vaccine.

Funded by Pfizer.
NCT03135834, NCT04440163, NCT04440176
Funding Source: Pfizer

#P21 A phase 3B, open-label study to evaluate the safety and immunogenicity of MenACWY-TT vaccine in healthy infants given at 3 and 12 months of age

Susanna Koski,[1] Federico Martinon-Torres,[2] Mika Rämet,[3] **Lefteris Zolotas**,[4] Ryan Newton,[4] Roger Maansson,[5] Mark Cutler,[6] Paula Peyrani,[7] Jamie Findlow,[8] Paul Balmer,[7] Luis Jodar,[7] William C. Gruber,[6] Annaliesa S. Anderson,[6] Johannes Beeslaar[4]

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Five keywords: *Neisseria meningitidis*; quadrivalent ACWY conjugate vaccines; infants; immunogenicity; safety

Objectives
Infants and young children have the highest age-related risk of invasive meningococcal disease (IMD). Meningococcal A, C, W, Y tetanus toxoid conjugate vaccine (MenACWY-TT; Nimenrix®, Pfizer Ltd, Sandwich, UK) is approved as a 2-dose schedule in infants 6 weeks to <6 months of age and a single dose in infants >6 months with a booster dose given at 1 year. This study evaluated the safety and immunogenicity of a single dose prime of MenACWY-TT in infants at 3 months of age with a booster dose at 12 months.

Methods
In this Phase 3b, multicenter, open-label, single-arm study, healthy infants 3 months of age received a single dose of MenACWY-TT followed by a booster dose at 12 months (1+1 series). Functional antibody before and 1 month after each vaccination were evaluated with serum bactericidal activity using rabbit complement (rSBA) titers ≥1:8 (threshold for seroprotection) and geometric mean titers (GMTs) for each of the MenACWY serogroups. Local reactions and systemic events occurring within 7 days were collected. Unsolicited adverse events (AEs), serious AEs, and newly diagnosed chronic medical conditions were collected.

Results
Overall, 145 and 143 infants received the first and booster MenACWY-TT doses, respectively. One month after the first dose (n=124 evaluable infants), 82.3%–91.1% achieved seroprotective rSBA titers across all serogroups. One month after the booster dose (n=128 evaluable infants), 100% of infants achieved seroprotection across all serogroups. GMTs across all serogroups were considerably higher 1 month after the booster dose (n=128; range, 1299.5–2714.1) than 1 month after the first dose (n=124; range, 54.7–202.4), indicating a strong anamnestic immune response. No new safety concerns were identified during the study. AEs were experienced by 30.3% of infants; serious AEs were reported by 6.9%. All local reactions and most systemic events were mild to moderate in severity.

Conclusions
MenACWY-TT given at 3 and 12 months of age has a favorable safety profile consistent with the well-established safety profile of MenACWY-TT in infants. The immunogenicity data indicate that a high proportion of participants are protected across the 4 serogroups following the first dose, and that the booster dose induces robust anamnestic responses across all 4 serogroups. MenACWY-TT 1+1 could be an alternative immunization schedule for infants <6 months of age, providing protection against IMD caused by serogroups ACWY and allowing flexibility in infant immunization schedules.
NCT04819113
Funding: Pfizer

Funding Source: Pfizer

#P22 Persistence of Immune Response After MenACYW-TT Vaccination in Children, Adolescents, and Adults

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Five keywords: MenACYW-TT, immune-persistence, meningococcal quadrivalent conjugate vaccine, invasive meningococcal disease, vaccination

Background: Invasive meningococcal disease (IMD) is a major cause of morbidity and mortality worldwide, with at least three incidence peaks observed throughout life: in young children, in adolescents and young adults, and in older adults ≥ 65 years of age. Here we describe immune persistence of a meningococcal quadrivalent tetanus toxoid conjugate vaccine (MenACYW-TT) in these age groups.

Methods: Three phase III randomized studies (2 modified double blind [NCT03476135 and NCT04084769] and 1 open label [NCT04142242]) included the assessment of immune persistence at least 3 years following primary vaccination with either MenACYW-TT or a comparator meningococcal vaccine (MenACWY-TT, MenACWY-CRM or MPSV4) in children, adolescents and young adults, and older adults. A serum bactericidal assay with human complement (hSBA) was performed to determine seroprotection rates (SPRs; percentages of subjects with hSBA titers ≥ 1:8) and geometric mean titers (GMTs) against the four vaccine serogroups at 3 time points: before, 30 days after, and at least 3 years after primary vaccination.

Results: At least 3 years after primary vaccination, SPRs for serogroups C, W, and Y were generally higher in MenACYW-TT-vaccinated subjects vs those who received comparator meningococcal vaccine for all age groups. Similarly, hSBA GMTs were higher for serogroups C, W, and Y in those vaccinated with MenACYW-TT vs comparator vaccines. The most substantial differences in SPRs and GMTs were observed for serogroup C while SPRs and GMTs were generally similar between MenACYW-TT and comparator vaccines for serogroup A.

Conclusion: MenACYW-TT demonstrated consistently higher antibody persistence (as assessed by hSBA titers ≥ 1:8 and GMTs) vs comparator vaccines for serogroups C, W, and Y at least 3 years after primary vaccination in toddlers, adolescents, young adults, and older adults. These data provide support for decisions around the use of meningococcal vaccines for the prevention of IMD of in persons 12 months of age and older.

Funding source: Sanofi

COI: BZ, CR, KG, SB, and MSD are employees of Sanofi and may hold company shares and/stock options. JP, MV and JJ received grants from Sanofi to conduct research on the studies at their respective sites.

Studies MET62, MET59, and MEQ00066, which are reported in this abstract, evaluated the safety and immunogenicity of a booster dose of MenACYW-TT in children, adolescents & young adults, and older adults, respectively. These studies were presented separately as posters at prior meetings: (1) MET62 was presented at ESPID 2021 (Poster #545, IMMUNOGENICITY AND SAFETY OF A QUADRIVALENT MENINGOCOCCAL CONJUGATE VACCINE ADMINISTERED AS A BOOSTER DOSE IN CHILDREN VACCINATED AGAINST MENINGOCOCCAL DISEASE 3 YEARS EARLIER AS TODDLERS). Presenter: MS. Dhingra (2) MET59 was presented at IDWeek2021 (Poster #1072402, IMMUNOGENICITY AND SAFETY OF A QUADRIVALENT MENINGOCOCCAL CONJUGATE VACCINE [MenACYW-TT] ADMINISTERED AS A BOOSTER DOSE IN ADULTS AND ADOLESCENTS VACCINATED AGAINST MENINGOCOCCAL DISEASE 3-6 YEARS EARLIER). Presenter: M. S. Dhingra (3) MEQ00066 was presented at IDWeek2021 (Poster #1046, IMMUNOGENICITY AND SAFETY OF A QUADRIVALENT MENINGOCOCCAL CONJUGATE VACCINE [MenACYW-TT] ADMINISTERED AS A BOOSTER TO ADULTS ≥ 59 YEARS OF AGE). Presenter: C. Robertson The 3 studies have also been published in the open-access peer-reviewed journals: (1) MET62: Piazza FM, Virta M, Paassilta M, Ukkonen B, Ahonen A, EstevesJaramillo A, Forsten A, Seppa I, Ding J, Neveu D, Jordanov E, Dhingra MS. Immunogenicity and safety of an investigational quadrivalent meningococcal conjugate vaccine administered as a booster dose in children vaccinated against meningococcal disease 3 years earlier as toddlers: A Phase III, openlabel, multi-center study. Hum Vaccin Immunother. 2022 Dec 31;18(1):1-10. doi: 10.1080/21645515.2021.1902701. Epub 2021 Jun 4. PMID: 34085900; PMCID: PMC8920225. (2) MEQ00066: Robertson CA, Jacqmein J, Selmani A, Galarza K, Oster P. Immunogenicity and safety of a quadrivalent meningococcal conjugate vaccine (MenACYW-TT) administered as a booster to adults aged ≥59 years: A phase III randomized study. Hum Vaccin Immunother. 2023 Jan 11;19(1):2160600. doi: 10.1080/21645515.2022.2160600. Epub ahead of print. PMID: 36632042; PMCID: PMC9980625. (3) MET59: Zambrano B, Peterson J, Deseda C, Julien K, Spiegel CA, Seyler C, Simon M, Hoki R, Anderson M, Brabec B, Áñez G, Shi J, Pan J, Hagenbach A, Von Barbier D, Varghese K, Jordanov E, Dhingra MS. Quadrivalent meningococcal tetanus toxoid-conjugate booster vaccination in adolescents and adults: phase III randomized study. Pediatr Res. 2023 Mar 10:1–9. doi: 10.1038/s41390-023-02478-5. Epub ahead of print. PMID: 36899125; PMCID: PMC10000353.

Diagnosis and Treatment

#DT1 A REVIEW ON THE COMPREHENSIVE BURDEN OF GONORRHOEA IN EUROPE

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Five keywords: Gonococcal infection, 4CMenB Vaccination, economic burden, medical burden, humanistic burden

Background:
Emerging evidence on the 4CMenB vaccine's gonorrhoea cross-protection raised hopes for targeted gonorrhoea prevention. Whilst incidence is increasing, men-having-sex-with-men (MSM) and individuals between 15-25 years are disproportionally affected, particularly in the United Kingdom (UK). This targeted literature review synthesized the burden of gonorrhoea in selected European countries to understand the comprehensive disease burden and inform decision-making on the potential delivery of the vaccine.

Methods
Findings reported here for the UK, France, Germany, Italy and Spain were part of a global search where observational, health-economic and review studies in MEDLINE were screened from 2012 to 30/06/2022. Excluding grey literature and global reviews, relevant local studies were reviewed by title/abstract and synthesised by medical, humanistic, and economic burden.

Results:
Five medical (3 German, 1 French, 1 UK) and one humanistic burden study (UK) were identified. Two German studies showed increasing azithromycin antimicrobial resistance (AMR) (5.6% of analysed samples). Another German study reported prevalence ranges (7.4-14.8%) for MSM, highest among HIV-negative pre-exposure prophylaxis users. The French study showed most patients were diagnosed symptomatic (women-having-sex-with-men 53.3%, men-having-sex-with-women 90%). MSM had the highest HIV-coinfection level (13.9%). The UK (Brighton) study found 12% of samples collected >1 year were genetically related, suggesting long-term asymptomatic carriage of gonorrhoea. No local studies assessing infections per anatomical sites, sequelae, AMR beyond MSM and co-infections beyond HIV were captured. Gaps in humanistic burden in patients and spillovers to others remain, a UK study assessed quality-of-life of only 2 patients. No economic burden studies were captured in relevant geographies. Overall, no studies were identified in Italy and Spain.

Conclusions:
To better understand the role and target of emerging prevention options against gonorrhoea, more local disease burden evidence is needed.

Funding Source: GlaxoSmithKline Biologicals SA funded this study and was involved in all stages of study conduct, including analysis of the data. GlaxoSmithKline Biologicals SA also took in charge all costs associated with the development and publication of this abstract.

#DT2 - MENINGITIS SCREENING IN YOUNG INFANTS BASED ON A NOVEL, NON-INVASIVE, TRANSFONTANELLAR ULTRASOUND DEVICE: A PROOF-OF-CONCEPT STUDY

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Five keywords: meningitis, neonatal, diagnosis, deep-learning, non-invasive

Background: Meningitis is a potentially life-threatening disease if not promptly diagnosed and treated. Clinical presentation is often unspecific, especially among young infants and newborns, justifying the need to perform lumbar punctures (LP) to obtain cerebrospinal fluid (CSF) for a laboratory-based confirmation. In high-income settings, LPs are often part of the protocolized systematic approach to screen for meningitis, but as a result, and given the relatively low incidence of meningitis, most are not confirmatory. Additionally, nearly half of LPs cause small bleeding in the puncture zone, hindering the interpretation of cellularity evaluation. The aim of this study was to validate a novel transfontanellar ultrasound-based technique to screen for meningitis, designed to non-invasively identify ranges of white blood cells(WBC) in CSF, to be used on patients with criteria for a LP.

Methods: We prospectively recruited patients under one year of age, with suspected meningitis, a permeable fontanelle and a LP performed within 24h before enrolment, from three Spanish University Hospitals (2021-2023). A total number of 6 cases and 10 controls was pre-defined for this proof-of-concept study. Images showing the backscatter pattern from CSF were obtained using a customized high-resolution ultrasonic probe. A deep-learning model (DL) was trained to classify CSF patterns according to WBC values obtained through the LP, setting a 30 cells/mm^3 threshold to differentiate controls from cases.

Results: Among 16 targeted and recruited patients, 17 LPs were performed, confirming 6 meningitis cases (one patient had a second LP to verify response to treatment) and 10 negative controls. The device showed a sensitivity of 100% and a specificity of 90%, with one control misclassified.

Conclusion: This proof-of-concept study confirmed that our device, based on ultrasound and DL, could potentially be used as an automated screening method to accurately rule in or out meningitis, thus potentially sparing up to 90% of LPs in patients without meningitis.

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#DT3 Development of a novel multiplex real-time PCR assay for detection of four main causes of bacterial meningitis

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Five Keywords: Multiplex real time PCR, sensitivity, specificity, PPV, NPV, efficiency

Context: Strengthening diagnostic capabilities and monitoring circulating pathogens are essential to effectively combat meningitis. Current multiplex assays cannot detect all four WHO priority pathogens for meningitis diagnosis. This study therefore aimed to develop multiplex real time PCR assay capable of simultaneously detecting Neisseria meningitidis, Haemophilus influenzae, Streptococcus pneumoniae and Streptococcus agalactiae.

Methods: A total of 45 DNA samples were used, including isolates from the National Collection of Type Cultures (NCTC). Specific real-time PCR primers and probes targeting porA, dmsA, SP2020, and cfb for N. meningitidis, H. influenzae, S. pneumoniae and S. agalactiae respectively were tested in vitro individually (monoplex) and simultaneously (multiplex). Standard curves were plotted using tenfold dilutions of DNA extracted from reference strains and the limit of detection (LLD), slope, intercept and R2 were determined. In addition, sensitivity, specificity, and positive/negative predictive value (PPV/NPV) of the multiplex assays were calculated.

Results: The optimised monoplex and multiplex real-time PCR assays showed the same sensitivity, specificity, PPV and NPV for each of the four bacteria, indicating that multiplexing did not alter the reagents performance. The genes sensitivities were all 100%, specificities were between 91.7% (porA) and 100%, PPVs were between 72.7% (porA) and 100% and NPVs were 100%. The multiplex assay showed high efficiency and robust amplification for each target genes. The LLD ranged from 4 (S. agalactiae) to 37.04 (H. influenzae) genome copies/µl for the tested bacteria.

Conclusion: The developed multiplex assay showed good performance for rapid and accurate detection of meningitis associated bacteria. Such a test would be useful for improved diagnosis of meningitis particularly for group B Streptococci which is still underdiagnosed in LMIC. However, further validation with patients' samples would be required before implementation.

Funding Source: The MEVacP project is funded by the Department of Health and Social Care using UK Aid funding and is managed by NIHR. Kanny Diallo was supported by a Crick African Network Fellowship and the DELTAS Africa Initiative (Afrique One-ASPIRE/DEL-15-008).

#DT4 Development of a new LAMP assay for diagnosing the main meningitis pathogens

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Five keywords: LAMP assay, diagnostic, meningitis, bacterial pathogens

Context: Meningitis is a serious disease with significant burden in low- and middle-income countries. Current diagnostic tests are expensive and difficult to use in secondary health centres where resources are limited. LAMP assays could be an alternative method to bring molecular detection closer to patients. The aim of this study was to develop LAMP tests capable of detecting the four main meningitis pathogens using improved genetic targets.

Method: Four different LAMP assays were evaluated using sodC, psaA, cfb and fuck genes targeting Neisseria meningitidis, Streptococcus pneumoniae, Streptococcus agalactiae and Haemophilus influenzae, respectively. Three published methodologies were assessed for optimisation purposes. The optimisation involved varying the temperature, the concentration of DNA polymerase; and the enzyme used. Finally, the optimised protocol was evaluated on 49 bacteria. LAMP products were analysed by visualisation of a colour change of SYBR Green I and amplifications were confirmed by UV visualisation and agarose gel electrophoresis. Sensitivity, specificity, negative predictive value (NPV) and positive predictive value (PPV) were calculated to assess the performance of the assay.

Results: LAMP assay targeting sodC, psaA and fuck genes showed a sensitivity, specificity, PPV and NPV of 100% for detection of N. meningitidis, S. pneumoniae and H. influenzae respectively while the assay targeting cfb for detection of S. agalactiae gave a sensitivity of 86%, a NPV of 97% and a specificity and PPV of 100%, as confirmed by visual, fluorescence, and agarose gel analysis methods.

Conclusion: The LAMP tests developed in this study showed efficacy and efficiency for the detection of N. meningitidis, S. pneumoniae, S. agalactiae and H. influenzae. Further development would allow the establishment of a cost efficient and portable molecular diagnosis tool for meningitis diagnosis.

Funding Source: The MEVacP project is funded by the Department of Health and Social Care using UK Aid funding and is managed by NIHR. Kanny Diallo was supported by a Crick African Network Fellowship and the DELTAS Africa Initiative (Afrique One-ASPIRE/DEL-15-008).

#DT5 APPLICATION OF SYNDROME EVALUATION SYSTEM (A MULTIPLEX PCR) IN DIAGNOSIS OF CNS INFECTIONS – DO WE NEED TO CHANGE ANY DOGMAS?

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Five keywords: Meningitis, Encephalitis, Multiplex PCR, Syndrome Evaluation System, Data science

This is a retrospective study of 6091 CSF samples that were sent to XCyton Diagnostics Pvt Ltd Bangalore for testing on their proprietary multiplex platform test called Syndrome Evaluation System (SES). This data was analyzed and visualized using 'R'- programming and other Data Science tools. All samples were tested on four different SES panels: SES tests for 11 RNA viruses, 7 DNA viruses, 17 Bacteria, 1 parasite and 4 fungi in four different panels; All CSFs were obtained from patients presenting with acute or subacute onset of CNS infections. The clinical signs, symptoms, CSF Cells, Protein & Sugar and CT / MRI results mentioned in Test Requisition Forms, were used to analyze the data. The follow up data on patients was not considered in this study. All patients received anti-infectives for > 3 days before CSF was drawn in tertiary care center.

Cases were divided as those which were sent to ***rule-in*** or ***rule out*** an infection based on the clinician's primary suspicion and the probability of discontinuation of anti-infectives if SES was negative.

Significant findings:

- Detection rate among Rule-In cases was 38.93% rate in Rule out cases was 2.37% hence SES showed very high specificity. Among cases of meningitis the detection was 51.59% while detection among encephalitis was 23.78%.
- *Streptococcus pneumoniae* and *Mycobacterium tuberculosis* presented as encephalitis in 35.06% and 26.64% of cases with seizures and altered sensorium as the primary presentations as was the case with encephalitis wherein *Herpes Simplex virus* or *Varicella zoster virus* were detected in CSF
- Hydrocephalus on MRI was associated in 50% of cases with bacteria, 28% of cases with fungi and 15% with *Mycobacterium tuberculosis*.
- Basal exudates seen on MRI were also observed 47% of the time in bacterial infections and 25% time in *Mycobacterium tuberculosis*
- MRI picture of granulomas or suspected tuberculomas was observed in some of bacterial, fungal and cysticercosis lesions in addition to the infections with Mycobacterium tuberculosis
- SES detected 13.5% of polymicrobial infections among positives. HIV, Transplants, Sepsis cases on ventilators and head injury contributed to 68% of these cases.
- Hospital acquired infections were common among cases of craniotomy, head injury, UTI, pneumonia, sepsis with or without ventilatory support, Immunosuppression, steroid therapy, autoimmune diseases on prolonged therapy, Ventricular shunts and malignancies
- Power of a multiplex detection in ruling out infections and detection of poly-microbials was thus demonstrated.

Funding Source: Self

#DT8 Non-invasive screening for meningitis via high-frequency transfontenellar ultrasound: Results from the UNITED-Meningitis study in Mozambique

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Five Keywords: Meningitis, screening, ultrasound, infants, neonates

Background: Neonatal and infant meningitis is a life-threatening disease, with significant risk of death or permanent neurologic disability if diagnosis and treatment are missed or delayed. Laboratory testing of cerebrospinal fluid (CSF) obtained via lumbar puncture (LP) for white blood cell (WBC) counts and culture is the gold standard for diagnosis. In resource-limited settings, clinicians may lack the training or material to perform LPs in young children and many health facilities lack laboratory capacity for CSF analysis. Alternative screening tools could help identify at-risk infants who need presumptive treatment and referral to centers where LP and laboratory CSF analysis are available. UNITED-Meningitis is a prospective diagnostic study evaluating a novel non-invasive, high-frequency ultrasonography (HFUS) exam for transfontanellar imaging using deep learning (DL) models for the detection of very low concentrations of WBCs in CSF.

Methods: Neonates and infants hospitalized at Hospital Central de Maputo with suspected meningitis (with/without pre-LP antibiotics) and an open anterior fontanelle were eligible for inclusion after informed consent. Known hydrocephalus and central nervous system malformations were exclusion criteria. LP was performed with CSF testing for cell counts, protein, and bacteriological exams (culture and latex agglutination). HFUS was performed at recruitment, with follow-up exams for participants with elevated WBC counts. HFUS images were processed by the DL algorithm, previously trained using a cohort of Spanish neonatal patients, and a threshold of ≥30 WBC/μL to define meningitis cases.

Results: Interim results analysis for 68 participants recruited from March 2021-June 2023 was performed. After excluding 2 participants diagnosed with hydrocephalus, 11 without CSF results, 12 with inadequate image acquisitions (due to incorrect imaging location, excessive movement, overlying blood vessels, or poor coupling) and 24 with sub-optimal acquisitions (due to signal attenuation), 19 (27.9%) participants with 20 paired CSF WBC count/HFUS were included (one participant with culture-confirmed bacterial meningitis and very high initial CSF WBC count had a repeat LP during treatment), the DL algorithm correctly identified 5/5 meningitis cases (100% sensitivity) and 13/15 controls (86.6% specificity).

Conclusions: HFUS+DL show promise as a non-invasive, quick screening tool for CSF pleocytosis suggestive of meningitis in neonates and infants. Efforts are underway to improve HFUS image quality and penetration by using methods for improved coupling for patients with dense/curly hair or thicker fontanelles, higher voltage, increased pulse frequency, and refined DL models. Follow-up images will be analyzed to assess the use of HFUS+DL to measure treatment response.

Funding source: 1. Instituto de Salud Carlos III (FIS PI16/00738); 2. Bill & Melinda Gates Foundation

#DT10 Cost-effectiveness analysis of implementing a non-invasive screening tool (Neosonics) for meningitis among newborns in Mozambique, Morocco and Spain.

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Five keywords: neonatal, screening, meningitis, cost-effectiveness, non-invasive

Introduction
Meningitis can be a devastating disease that poses a significant public health challenge, particularly in low- and middle-income countries (LMICs), which account for 98% of the estimated 5.6 million disability-adjusted life years (DALYs) attributed to the disease. Children, especially the youngest, are the most vulnerable. Underdiagnosis or delayed antimicrobial treatment exacerbate these lifelong consequences and increase mortality rates. The gold standard to diagnose meningitis is the obtention of cerebrospinal fluid (CSF) through a lumbar puncture (LP), to detect abnormally elevated counts of white blood cells (WBC) or pathogens. Neosonics, a non-invasive device using a high-frequency ultrasound system (HFUS) and a deep learning (DL) algorithm, can detect and count WBC in CSF through the permeable fontanel. The objective of this study is to compare the cost-effectiveness of implementing Neosonics with the Status quo, which involves performing an LP on all suspected cases of meningitis. We assess the cost-effectiveness of Neosonics across three countries with varying income levels and disease incidence: Spain, Morocco, and Mozambique.

Methods:
We are comparing a scenario in which the HFUS would operate as a primary screening tool, followed by a LP only in the cases with an elevated WBC count and compared it to the status quo. Data were collected from Hospital Sant Joan de Déu, Spain; Hôpital des Enfants de Rabat, Morocco; and Manhiça District Hospital, Mozambique. The model relies on a decision tree that was designed and analyzed in TreeAge. The effectiveness estimates measured in DALYs were derived from the sensitivity and specificity of the tools – 98% and 82% respectively. The model was estimated by applying deterministic, sensitivity and probabilistic analyses.

Results:
Employing the HFUS screening method (Neosonics) compared to the Status quo appears cost-effective in all three countries, including when accounting for uncertainty in the parameters. The HFUS screening method saves 19.03 USD per suspected case in Mozambique, 362.76 USD in Morocco and 3,095.46 USD in Spain. HFUS is also more effective as it averts 0.0579 DALYs per suspected case in Mozambique, 0.0138 DALYs in Morocco and 0.0055 DALYs in Spain.

Conclusion:
Neosonics dominates the status quo both in terms of costs and effectiveness in all three countries. In Spain, where medical expenses are the highest, it is the most cost-saving, while in LMICs, with a much higher incidence, it is the most effective, making the device particularly promising in outbreak or epidemic situations.

Funding Source: Newborn Solutions, S.L

Surveillance

#DS1 Meningitis caused by Streptococcus agalactiae in the Czech Republic – data of the National Reference Laboratory for Streptococcal Infections and The National Health Information System database, 2008-2022

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Five Keywords: streptococcus agalactiae, Group B Strep, meningitis, serotype, morbidity

Background
Streptococcus agalactiae (Group B Strep, GBS) is opportunistic pathogen causing non-invasive as well as invasive diseases. GBS predominantly causis neonatal sepsis and meningitis, but can also cause invasive infections in elderly patients and patients with immunodeficiency. There is no vaccine against GBS. In the Czech Republic, prevention against GBS early-onset neonatal sepsis and meningitis consists in prenatal screening for GBS in the genital and rectal area of pregnant women. In the case of positive GBS status of pregnant woman, intrapartum antibiotic profylaxis (IAP) is administered.

Methods
The data about invasive GBS diseases are recorded in the National Health Information System (ISIN, previously EpiDat). GBS isolates are sent to the National Reference Laboratory for Streptococcal Infections (NRL/STR) for confirmation of correct identification and serotyping. In the Czech Republic, surveillance of invasive infections caused by GBS is not established. This paper analyses data on meningitis caused by GBS from ISIN and NRL/STR between 2008 and 2022.

Results
Between 2008 and 2022, 90 cases of meningitis caused by GBS were recorded, 69 cases were listed in ISIN and 45 GBS isolates were sent to NRL/STR for serotyping, only 24 cases were both recorded in ISIN and GBS isolate sent to NRL/STR. 48 cases were in males, 42 cases in females.

The overall average GBS meningitis morbidity between 2008 and 2022 reached 0.057/100,000 inhabitants (the highest in 2008 – 0.096/100,000 inhabitants, the lowest in 2020 – 0.028/100,000 inhabitants). Age-specific morbidity was highest in children under one year of age – on average 3.611/100,000 inhabitants (the highest in 2010 – 7.662/100,000 inhabitants, the lowest in 2017 – 1.751/100,000 inhabitants).
Serotype was established in 45 isolates causing GBS meningitis. The most prevalent serotype was serotype III (30 cases), followed by serotype V (10) and Ia (3).

Between 2008 and 2022, 6 deaths due to GBS meningitis were recorded. Serotype was examined in 3 cases with fatal outcome and all 3 cases were due to serotype V.
Conclusions

Overall average morbidity of GBS meningitis between 2008 and 2022 was low, the highest morbidity was in children under one year of age. Serotype III was the most prevalent in our dataset. In the Czech Republic, the surveillance of GBS meningitis is not established and morbidity can be expected to be higher than reported in this paper.

Funding Source: None

#DS2 Changes in invasive meningococcal disease in England before and after the first Covid-19 lockdown

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Five keywords: Meningococcal, Covid-19, ACWY, group B

Introduction:
Meningococci that cause invasive meningococcal disease (IMD) are diverse. Strain distribution varies both geographically and temporally driven by factors such as population immunity, vaccination, introduction of novel strains, antigenic shifts in existing strains, and mass gathering events. In late March 2020 the UK went into lockdown as part of national COVID-19 restrictions leading to a dramatic and almost immediate reduction in IMD. This continued until several months after the lifting of Covid-19 restrictions in July 2021 when IMD case rates began increasing. The present study compares IMD case numbers and strain distribution in England before and after the introduction of the first lockdown.

Methods
The study includes cases confirmed by the UKHSA Meningococcal Reference Unit between April 2018 and March 2023, inclusive. Isolates underwent serogrouping and genome sequence analysis using the Illumina platform. Draft genome sequences were deposited and interrogated on the PubMLST Neisseria database. PCR-only confirmed cases underwent PCR genogrouping. All cases were followed up for information as necessary for national IMD surveillance.

Results
Prior to the first lockdown there were >500 cases per year with group B predominating (57.3%) followed by group W (22.7%), group Y (10.6%) and group C (7.7%). After the introduction of the first lockdown, the number of IMD cases decreased by >70% year on year. Following the lifting of restrictions in July 2021, IMD due to groups C, W and Y remained very low whilst group B disease increased, first in university age groups, then infants, and then all other age groups. By late 2022/early 2023, monthly group B case numbers were seen to exceed pre-pandemic levels. The main group B clonal complexes all remained in comparable proportions post-restrictions but there were sub-strain differences relating to certain sequence types including ST-485 (cc41/44) and ST-1161 (cc269).

Conclusions
The initial increase in disease post-restrictions was seen in university age groups with the return of students to full time education. This may be expected with these being the peak ages for meningococcal carriage. Subsequent increases in other age groups suggest a spreading-outwards from these age groups. The continued low levels of group C, W and Y disease are likely due to the national adolescent meningococcal ACWY vaccine programme. Sub-strain fluctuations require close monitoring; however, the current observed fluctuations are favourable from a group B vaccine coverage perspective.

Funding Source: UKHSA

#DS3 Global Meningitis Genome Library: The Power of Curation

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Five Keywords: **Meningitis, *Neisseria*, GMGL, curation, epidemiology**

The 'Global Meningitis Genome Library' (GMGL), http://pubmlst.org/gmgl, was put in place as a framework for data collection to coordinate and host publicly available, curated sets of global meningitis-causing bacterial pathogens to respond to the WHO Defeating Meningitis by 2030 global initiative. A curated genome library is defined as a coherent, preferably published, set of isolates that include isolate provenance records and annotated genome sequence data.

The database strives to include only non-personally identifiable provenance and epidemiological data linked to an isolates genome so that published analysis can be replicated and compared. The basic data (year and country of isolation, sample source, age range, and patient sex) is used to stratify the information found in the genome and offers a powerful opportunity for enhanced molecular surveillance.

The work focus is divided between four organisms: *Neisseria meningitidis*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Streptococcus agalactiae*. The surveillance of serogroup B meningococcal (MenB) disease is of particular importance, given that it is the only remaining major disease-causing meningococcal serogroup for which a polysaccharide conjugate vaccine is unavailable.

The UK GMGL isolates make up 40.4% (*n* = 5,618) of the total global *Neisseria meningitidis* database. As of August 2023, there are 13,912 curated GMGL isolate records (13,876 genome assemblies). There are 269 publications, with 12,826 (92.2%) linked isolates. There were 148 new genomes added to the GMGL in 2023.

The inclusion of basic provenance data has been at the forefront of the GMGL curation, with 11,772 (84.6%) isolates now having country data. The inclusion of epidemiological year data is detailed for 44.0% of isolates. Data for patient sex and isolation source are available for 11.6% and 23.3% of isolates, respectively. Whilst we can celebrate the success of the successful increase of some provenance data submission, the missing data not supplied is an obstacle to fulfilling the WHO Defeating Meningitis by 2030 global road map initiative. Our aim is to continue to request information from publication authors for addition to the database.

Funding Source: Meningitis Research Foundation

#DS4 Characterisation of non-meningococcal/gonococcal Neisseria strains from invasive disease cases in England

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Five keywords: Neisseria, Rare, Resistance, Vaccines, Invasive

Background: Non-meningococcal, non-gonococcal Neisseria species are predominantly commensal but can cause opportunistic disease. Disease may occur in more minor manifestations such as conjunctivitis or urethritis, but also in serious invasive presentations such as meningitis, septicaemia or endocarditis. Predisposing factors such as the creation of a surgical or similar access point for bacteria or an immunocompromised host state may increase the likelihood of infection, but disease may occur in otherwise healthy hosts.
The UK Health Security Agency's (UKHSA) Meningococcal Reference Unit (MRU) characterises and stores meningococcal isolates submitted by clinical laboratories across England, Wales and Northern Ireland. Occasionally the isolates received are non-meningococcal but have been isolated from normally sterile sites such as blood and cerebrospinal fluid, indicative of invasive disease.

Aims/Methods: The aim of the study is to determine the species and characteristics of non-meningococcal isolates from normally sterile body sites.

Invasive Neisseria isolates from English disease cases between 2010 and 2021 were phenotypically characterised including colony morphology, Gram staining, inspection of colonies and biochemical characteristics. Candidate isolates were sent for Illumina® whole-genome sequencing and the sequences uploaded to the Neisseria BIGSDb database (PubMLST.org) to determine species, antigenic profile and genetic similarity.

Results: Thirty-five unique Neisseria isolates from invasive sites were identified Neisseria including 11 N.subflava, 9 N. mucosa, 4 N. oralis, 4 N. polysaccharea, 3 N. cinerea, 2 N. elongata and 2 N. bergeri. Microbiological and clinical data (where available) are described and discussed. Penicillin and broadly cefotaxime resistance in these organisms is correlated with penA and porB amino acid sequences that have been previously shown to promote resistance in gonococci, as well as gyrA mutations which can elicit ciprofloxacin resistance in meningococci and gonococci. Ten isolates possessed alleles for one or both of the meningococcal vaccine antigens factor H binding protein (fHbp) and Neisseria heparin binding antigen (NHBA).

Conclusions: Though uncommon, infections caused by non-meningococcal, non-gonococcal Neisseria species can result in invasive disease, and these organisms should be considered in differential diagnoses, particularly where putative Neisserial organisms are isolated. Many of these species possess virulence factors found in N. meningitidis and N. gonorrhoeae and have significant potential for antibiotic resistance, possibly leading to challenges in treatment. Even commensal carriage of the organisms may confer resistance to N. meningitidis and N. gonorrhoeae through recombination.
Funding Source: N/A

#DS5 Laboratory surveillance of invasive isolates of *Neisseria meningitidis.* Argentina 2015-2022.

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Five keywords: *Neisseria meningitidis;* Meningococcal, Invasive disease; Capsular group, whole-genome sequencing

Background: invasive meningococcal disease (IMD) is a serious and potentially fatal condition. The incidence in Argentina is 0,2/100,000 inhabitants. In 2017 the Argentine National Immunisation Program (NIP) implemented MenACWY-CRM197 vaccine for 3-5-15 months and 11 y.o. Since 2020 the NIP has recommended a combined vaccination MenACWY- 4CMenB for high-risk groups. The aim of this study was to describe the clinical presentations and capsular groups distributions and characterize through Whole Genome Sequencing (WGS) invasive isolates of N. meningitidis (Men) circulating in Argentina.

Materials and methods: 444 Men isolates recovered from children and adults with IMD during 2015-2022 were received at the NRL to confirm the capsular group using PCR and characterize through WGS (344 available).

Results: the clinical presentations were meningitis 53.8%, meningococcemia 18.5%, meningitis-meningococcemia 13.3%, others 14.4%. The capsular groups distribution showed B 53,2%, W 31.8%, C 10.1%, Y 3.8%, Others 1.2%. The most frequent clonal complexes were CC11 36.9%, CC35 11.0%, CC865 11.0%, CC 41/44 10.2% and CC32 5.8%. W was mainly associated with CC11, 99.2% and B with CC865, 21.8%, CC35, 21.2%, CC 41/44, 16.5%, CC32, 11.8%. Y was mostly associated with CC167, 52.9% and C with ST-2196, 44.1%, endemic in Chaco Province, followed by CC11, 23.5%. Among W CC-11, more than 95% of the isolates exhibited the same antigenic profile: fHbp peptide 2.22, NHBA peptide 29, PorA 5,2 and NadA peptide 6 (variant 2/3 4CMenB vaccine). Regarding capsular group B, the most prevalent fHbp peptides were 2.16, 15.8% and 2.119, 10.5%, harbored mainly in CC35 and CC865 respectively. The most frequent NHBA peptides were 24, 28.1% and 21, 22.8%, mainly associated to CC865 and CC35 in that order. PorA distribution showed prevalence of 21,16-36 in CC865, 86.8% and 22-1,14 in CC35, 83.3%. Only 13.4% of isolates harbored NadA. MenDeVar analysis showed 19.3% vaccine reactivity (exact match+cross reactive) for 4CMenB and 37.4% for bivalent vaccine.

Conclusions: B was the most prevalent capsular group, associated mainly with CC865 and CC35. WGS of CC865 isolates could help clarify why these strains that are uncommon in other regions became the leading cause of IMD in Argentina. The presence of NadA peptide 6 in W strains could suggest that they exhibit cross-reactivity with 4CMenB vaccine, according to our previous study of serum bactericidal activity (hSBA). MenDeVar results must be carefully analyzed taking into account our previous hSBA assays and the same B CC distribution regarding to the precedent period.

Funding Source: Regular federal budget of the National Ministry of Health of Argentina

#DS6 Meningococcal Invasive Diseases in southern Vietnam in ten year period from 2021 to 2021.

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Five Keywords: Meningococcal invasive disease, bacterial meningitis, sepsis, antimicrobial resistance, multi-locus sequence typing.

(a) Neisseria meningitidis caused a deadly outbreak in South Vietnam in the 1970s, affecting around 3000 cases, with the incidence rate reaching up to 20 per 100,000 individuals. Serogroup C played the main role in this severe epidemic, accounting for 90% of the cases. Since then, meningococci have caused sporadic cases for decades in the country. It is worth noting to update the epidemiology of the disease, as well as to describe molecular characteristics of the pathogen.

Our aims to describe epidemiological and molecular characteristics, alonged with antimicrobial resistance (AMR) and serogroup prevalent of invasive meningococcal disease (IMD) cases in south Vietnam over 2012-2021.

(b) We used data from the notified forms to characterize IMD cases which were sent to Pasteur Institute of Ho Chi Minh City. Isolates or/and clinical specimens were confirmed using bacterial culture and/or sodC-targeted realtime PCR. Performing antimicrobial susceptibility testing determined the resistance for penicillin, ceftriaxone, ciprofloxacin, rifampicin and chloramphenicol. Sequencing was conducted to analyzing of multilocus sequence typing (MLST), porA, fetA, and antimicrobial resistant genes.

(c) The annual incidence rate of IMD averaged 0.016 per 100,000 individuals, and serogroup B was dominant accounting for over 90% of the cases (50/54). Of those, male patient showed 70%. Children under five and young adults between 10 to 24 were most
affected, occupying roundly one-third and a half, respectively. Analyzing 31 MLST profiles showed that the pathogens belonged to five different clonal-complexes, of which lineage of ST-1576, not assigned any known CC, showed most common accounting 20 over 31 profiles, and these was associated with chloramphenicol resistance. PorA subtype of P1.19,15 and fetA variant of F4-6 both accounted for more than one-third of each. ST-1576 was likely a distinct clade and they had genetically closed to those in Bangladesh when being compared to other ST of serogroup B in Asia by using whole genome data. Fourteen of 20 isolates were intermediated susceptibility to penicillin (MIC ranging 0.064 to 0.38mg/L). Six of these additionally resisted to ciprofloxacin, with MIC value ranging from 0.094 to 0.5 mg/L. These resistances correlated to the alternations of penA or gyrA in the effective sites. One isolate was non-susceptible to ceftriaxone, MIC at 0.125 mg/L, and it also resisted to both ciprofloxacin and penicillin.

(d) Ours results raised a great concern about the status of antimicrobial resistance and the widely spread across the community. ST-1576 was possible a local strain due to it was mostly detected in the country and associated with chloramphenicol resistance.

Funding Source: Internal Funding

#DS7 Defeating Meningitis in Northern Nigeria: The *Streptococcus pneumoniae* Jigsaw

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Five Keywords: Invasive Pneumococcal Diseases , Meningitis, Nasopharyngeal Carriage , Next Generation Sequencing, Pneumococcal Conjugate Vaccines

Nigeria lies in the African Meningitis Belt, and meningitis affects millions (with children less than 5 years old the worst affected) and cases from all causes of up to 200,000 per annum with case fatality rates as high as 15% have been reported. The majority of the bacterial aetiologies for meningitis in Nigeria are *Neisseria meningitidis*, *Streptococcus pneumoniae* and *Haemophilus influenzae*. Though the 10-valent pneumococcal conjugate vaccine (PCV10, Synflorix™), MenAfriVac and the pentavalent vaccines are provided routinely for protection against *S. pneumoniae, N. meningitidis* and *H. influnezae,* respectively, meningitis remains a significant public health burden in Northern Nigeria. To worsen the challenge of pneumococcal diseases burden such as meningitis, vaccine coverage for PCV10 (Synflorix™) in Northern Nigeria remains poor (at about 54% coverage) and the region has above the national average of vulnerable groups that include, internally displaced persons (IDPs), Sickle cell disease (SCD), paediatric/adult HIV/ AIDS and malnourished patients. The *S. pneumoniae* serotypes in Northern Nigeria project would be approached from two perspectives: The nasopharyngeal carriage in children and invasive pneumococcal diseases (IPDs) in all age groups. We proposed to collect (from four Federal Government of Nigeria-owned tertiary hospitals, all in Northern Nigeria, that cater for over 50 million inhabitants) detailed sociodemographic and medical history of enrolled patients, a combined total of 600 nasopharyngeal swabs from children less than 5 years in IDPs camps and at paediatric clinics for children with any of the risk factors (SCD, paediatric HIV/AIDS and malnutrition) for IPDs and 1350 blood, cerebrospinal fluids, bronchoalveolar lavage from patients of all age groups. Bacterial DNA to be extracted from minimally-processed and culture-enriched samples for molecular serotyping in multiplex-PCR to identify about 40 serotypes including all the serotypes in 20-valent pneumococcal conjugate vaccine (PCV20), antibiotic susceptibilities of recovered isolates to 10 antibiotics to be determine with automated Vitek-2 system, Next Generation Sequencing (NGS) of isolates to determine genetic relatedness, strain/ capsular type, antibiotic resistance mechanisms, virulence genes and colonization factors. Dominant serotypes, whether covered by PCV20 or non-PCV20, will be assayed for *in-vitro* biofilm properties and BOX-PCR-based genetic relatedness. The primary outcomes of the project are: *S. pneumoniae* serotypes in carriage and diseases, serotypes antibiotic susceptibilities, virulence and NGS data; while the secondary outcomes are archives of nasopharyngeal swab/IPDs samples and *S. pneumoniae* serotypes for further analyses of the upper microbiota in risk groups in Northern Nigeria.

Funding Source: TBC

#DS8 Exploiting real-time genomic surveillance data to assess 4CMenB meningococcal vaccine performance in Scotland 2015-2022

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Five Keywords: Vaccination; Bexsero; genomics; breakthrough cases; whole genome sequencing

The UK implemented the first national infant immunisation schedule for meningococcal vaccine 4CMenB ('Bexsero®') in September 2015, targeting serogroup B invasive meningococcal disease (IMD). Bexsero® contains four variable subcapsular proteins and post-implementation IMD surveillance was necessary as non-homologous protein variants can evade Bexsero®-elicited protection. We investigated post-implementation IMD cases reported in Scotland from the 1st September 2015 to 30th June 2022. Patient demographics and vaccination status were combined with genomic data from the causative meningococci, which was used to assess vaccine coverage with the Meningococcal Deduced Vaccine Reactivity (MenDeVAR) Index.

Eighty-two serogroup B IMD cases occurred in children >5 years of age, 48 (58.5%) of which were in unvaccinated children and 34 (41%) were in children who had received ≥1 Bexsero® dose. Fifteen of the 34 vaccinated children had received one dose, seventeen had received two doses and two had received three doses. For 39 cases, meningococcal sequence data were available enabling MenDeVAR Index deductions of vaccine preventable (M-VP) and nonvaccine preventable (M-NVP) meningococci. Notably, none of the 19 of the children immunised ≥2 times had IMD caused by M-VP meningococci, with 2 cases of NVP meningococci, and no deduction possible for 17. Amongst the 15 children partially vaccinated to schedule (1 dose), 7 were infected by M-VP meningococci and 2 with M-NVP meningococci, with 6 for which deductions were not possible. Of the IMD cases in unvaccinated children, 40/48 were ineligible for vaccination and 20/48 had IMD caused by M-VP meningococci, with deductions not possible for 14 meningococci.

These data are consistent with 2 and 3 doses of Bexsero®, delivered according to schedule, providing good protection against invasive disease caused by meningococci deduced from genomic data to be vaccine preventable. Single doses provide poorer protection to infants. This demonstrates the value of post-implementation genomic surveillance of vaccine preventable pathogens in providing information on real-world vaccine performance. In practical terms, these data can provide public health reassurance when vaccinated individuals develop IMD with non-vaccine preventable variants. They further indicate that additional testing is needed on variants for which no immunological data exist to improve estimates of protection, although these data suggest the uncharacterised variants are unlikely to be covered by Bexsero®. Finally, the confirmation that incomplete or absent doses in infancy lead to reduced protection supports public health and general practitioners in promoting vaccination according to schedule.

Funding Source: NHS clinical care pathways for meningococcal disease in Scotland, UK, Wellcome Trust grant 218205/Z/19/Z and Thrasher Research Fund grant 15512

#DS10 Impact of pneumococcal conjugate vaccine on childhood pneumonia in the United Kingdom (UK)

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Five Keywords: PCV13, children, pneumonia, antibiotics

Background: In April 2010, the 13-valent pneumococcal conjugate vaccine (PCV13) replaced the 7-valent pneumococcal conjugate vaccine (PCV7) in the United Kingdom (UK) in childhood immunization programmes to protect against serotypes that caused invasive pneumococcal diseases (IPDs) not covered by PCV7. Pneumonia represents the major burden of IPDs in the paediatric population. Limited evidence exists on the effect of PCV13 to prevent childhood pneumonia in community setting. In addition, the recent emerging serotype replacement has increased the burden of IPDs worldwide. This study aimed to compare the incidence of pneumonia and associated antibiotics prescribing patterns before and after the introduction of PCV13 in the UK.

Methods: A retrospective cohort study was conducted using primary care health records from the UK IQVIA Medical Research Database. The diagnosis of pneumonia was identified between 2008 and 2019 for children aged 0-18 years, using a 14-day screening period. Monthly incidence rate was calculated as the number of pneumonia episodes in each month divided by the person-months of that month. Interrupted time series analysis (ITS) was performed to assess the impact of PCV13 on monthly pneumonia incidence between the pre-PCV13 (January 2008-March 2010) and post-PCV13 periods (April 2010-December 2019). Antibiotic prescribing patterns were assessed according to the WHO AWaRe (Access, Watch and Reserve) classification.

Results: A total of 20,832 pneumonia episodes were identified during the study period. Overall, there was an immediate reduction in the monthly incidence of pneumonia shortly after the introduction of PCV13 [incidence rate ratio (IRR)=0.73 (95% CI, 0.65-0.84)] and a gradual decline in the trend of pneumonia during the post-PCV13 period (IRR=0.98; 95% CI, 0.98-0.99). The highest incidence rate was observed in children aged under 2 years (vaccine target group), followed by those aged 2-4, 5-9 and 10-18 years. In children aged under 2 years, there was an immediate decline in monthly incidence (IRR = 0.63; 95% CI, 0.53-0.76) following PCV13 introduction and no significant change in monthly incidence trend during the post PCV13 period (IRR = 0.99; 95% CI, 0.98-1.00). Access antibiotic prescriptions increased from 84.96% to 86.04%, whereas the Watch antibiotic prescriptions decreased from 15.04% to 13.83%.

Conclusion: The findings observed a 27% decrease in the overall incidence of pneumonia shortly after the introduction of PCV13. Continuous monitoring of IPDs is warranted, particularly due to decreased coverage of PCV13 vaccination during the COVID-19 pandemic and the emergence of serotype replacement.

Funding source: Queen's University Belfast

Support and care for people affected by meningitis

#S1 A UK survey to understand the experiences and support needs of adults with a recent meningitis experience

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Support services, Meningitis Now, Stroud, UK; We would like to acknowledge Picker* who have been involved in the development and implementation of this study and subsequent report.

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Five Keywords: **meningitis, adults, aftercare, support, information**

The study's aim was to develop a questionnaire to explore the experiences and support needs of the UK adult population with a recent meningitis experience.

Method

Survey development - the survey content was informed by qualitive research involving twenty participants:

- Five individual depth interviews
- Online focus group with fifteen participants

Participants were eligible if they were 16 years or older, had a UK hospital stay for bacterial or viral meningitis within the last five years, and lived in the UK.

The findings from the qualitive stage were used in conjunction with Picker's survey experience, Meningitis Now's understanding of the needs of those who had experienced meningitis, and the Picker Principles of Person-Centered Care to form a 32-question survey.

The survey was hosted online and publicised through a variety of channels by Picker and Meningitis Now. The survey ran from 15th September 2022 to 28th February 2023.

Results

Two hundred and twenty-eight responses were received. Of these 58% of respondents had suffered from bacterial meningitis, 35% viral meningitis and 7% another cause or were unsure of the cause. Fifteen percent of respondents had been admitted to hospital within the previous 3 months, 32% between 3mths and 2 years ago and 53% between 2 and 5 years ago.

Key findings:

- 98% of respondents felt that improvements could have been made to their meningitis aftercare and support.
- Only 12% of respondents were provided with helpful information about recovery expectations and management before they left hospital, however 80% reported that they did not receive this information but would have liked this.
- 94% experienced impacts of meningitis which negatively affected their home, work and social lives.
- Less than half of respondents were offered a follow-up with either a GP or hospital doctor post discharge.
- 71% were not directed to any support services (statutory or voluntary sector) but would have liked this.

Conclusions

Regardless of the cause of meningitis, analysis of the findings has highlighted gaps in follow up care and support for adults. A lack of care continuity began at discharge from hospital but extended beyond primary to secondary and tertiary care.

Respondents reported room for improvement in aftercare – both in terms of information provision and support. Viral meningitis patients were more likely to report a lack of aftercare compared to those who had suffered from bacterial meningitis.

Many respondents reported ongoing and multifaceted after-effects, which impact many aspects of their lives

Funding source: Meningitis Now

Advocacy and engagement

#A1 Development of communication tools on meningitis adapted to the African continent

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Five Keywords: Website, social network accounts, booklets, posters, cartoons

Context: Meningitis is a disease of public health concern in many countries of the world. Sub-Saharan Africa carries a large part of the burden with 26 countries included in the so-called African meningitis belt. Community awareness and sensibilization has been identified as a key pillar of the WHO roadmap to fight meningitis by 2030. Most communication tools do not reflect local realities of African countries. The Molecular Epidemiology for Vaccine Policy (MEVacP) project aimed to develop communication tools and contents adapted to an African population.

Methodology: Scenarisation work was carried out to create a comic strip telling the story of an African little boy confronted with meningitis. The main targets were children, parents and teachers. Both a French and English version of the story have been developed. These communication tools have been shared with the public on the project website and social network accounts (facebook and twitter) created to inform on meningitis. Community awareness campaigns were also organized in primary schools and health centers of three city of the country; Abidjan, Korhogo and Tengrela.

Results: Seven episodes of the comic strip have been produced in French and English, covering the most important topics identified a multidisciplinary team: i) description of the disease, Ii) the symptoms, iii) the transmission routes, iv) the consequences of the diseases, v) the attitude to have when confronted with the disease, vi) vaccination and vii) the importance of community awareness. A total of 500 booklets and 50 posters have been shared with the different communities; 140 booklets and 17 posters in Abidjan, 180 booklets and 15 posters in Korhogo and 180 booklets and 18 posters in Tengrela. The tools have been made available and the link shared with the different education and health department involved in health awareness campaign in Côte d'Ivoire for further use. The cartoons are also being finalized and will also be made available through the same channels.

Conclusion: Health communication must be adapted to the target population. It is important to create communication tools in languages and with characters that reflect local realities. The story of Kolo, available in French and English, will be a useful didactic tool in many African countries for raising awareness of meningitis, especially among children. Translations in local languages could further improve its reach.

Funding Source: The MEVacP project is funded by the Department of Health and Social Care using UK Aid funding and is managed by NIHR. Kanny Diallo was supported by a Crick African Network Fellowship and the DELTAS Africa Initiative (Afrique One-ASPIRE/DEL-15-008).

#A2 Communicating for change – Perspectives on messages and channels in the meningitis belt

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Five keywords: Communication, Engagement, Awareness, Road Map, Questionnaire

UNICEF and MRF have conducted primary research on communications about meningitis in high-burden countries in the meningitis belt; a string of 26 countries that suffer the highest burden of disease. The research was designed to assess approaches to, and the need for, communication and engagement with a range of audiences about meningitis.

This forms part of UNICEF and MRF's collaborative work to support the delivery of Pillar 5 (Advocacy and Engagement) in the WHO Defeating Meningitis by 2030 Global Road Map. This research is designed to inform and contribute to the delivery of the following strategic goals:

17: Ensure and raise awareness of communities about the impact of meningitis and available support after meningitis.

18: Ensure that people and communities know how to access meningitis vaccines, other prevention, and support after meningitis, and that they value and demand them.

19: Maintain high vaccine confidence.

The methodology consisted of a literature review and questionnaire, with responses collected from April – July 2022. Offered in English and French, the questionnaire was distributed online to communications professionals across the region. Invitations were extended to UNICEF country teams, members of the Confederation of Meningitis Organisations (CoMO) and other Road Map implementing partners. In addition to multiple choice and open text questions, respondents were invited to upload communication materials and contextual information.

Analysis of the responses revealed that funding and resourcing are key barriers to communication initiatives across the region. Consequently, nearly all respondents are more likely to adapt existing resources for communicating about meningitis and meningitis vaccination, rather than create new ones.

While respondents identified multiple audiences as targets of meningitis communications, the purposes of communications and materials/tools provided reflected outreach that was largely appropriate for caregivers or the general population.

Social media is used by all respondents, with the primary purpose of distributing information, and Facebook is the most common platform reported. That said, only half of respondents reported a policy in place to guide social media outreach.

The findings of the report will inform the development of a meningitis communication framework that can be used to deliver targeted communication and engagement activities in the meningitis belt and beyond.

Funding source: UNICEF, MRF