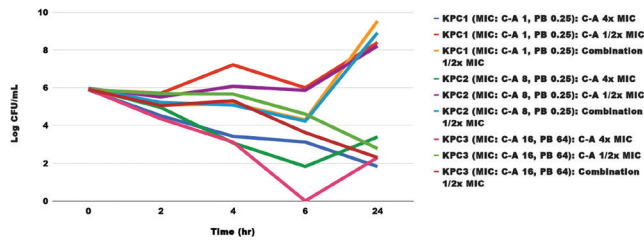


Figure 1. Time-kill Analyses of C-A Alone and in Combination With PB.



Disclosures. E. Wenzler, Melinta Therapeutics: Speaker's Bureau, Speaker honorarium.

2452. Treatment and Outcomes of Daptomycin-Nonsusceptible Methicillin-Resistant *Staphylococcus aureus* Bloodstream Infections

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Background. Daptomycin (dap) is approved as an alternative to vancomycin (van) for therapy of methicillin-resistant *Staphylococcus aureus* (MRSA) bloodstream infection (BSI). Cases of therapy failure associated with the emergence of daptomycin-nonsusceptible (DNS) MRSA strains have been documented. Information on the treatment and outcome of DNS MRSA BSI is scarce. This study describes the treatment and outcome of patients with DNS MRSA BSI at our healthcare center.

Methods. This is a retrospective review of patients with DNS (E-test MIC >1.0 µg/mL) MRSA BSI at a tertiary healthcare center in Detroit, Michigan between September 24, 2005 and March 31, 2018. The variables collected were: BSI source, inpatient and discharge antibiotic therapy, BSI duration, in-hospital and 90-day mortality, and 90-day MRSA BSI recurrence. Inpatient therapy was defined as the treatment used for the most consecutive days from index DNS MRSA blood culture during hospitalization. Discharge therapy is the treatment used post-discharge or on the expiration date. Antibiotics used for ≤2 days were excluded.

Results. A total of 32 nonduplicate patients with DNS MRSA BSI were identified. One patient with an inaccessible chart was excluded. The source of BSI was endovascular in 9 (29%) patients, secondary BSI in 14 (45%), central-line associated in 3 (10%), and unknown in 5 (16%). A total of 24 different antibiotic regimens were used to treat DNS MRSA BSI. Van monotherapy was the most commonly used regimen for inpatient and discharge therapy, followed by dap + ceftaroline (cef). Table 1 is a summary of the results.

Table 1: Treatment and Outcomes of Patients with DNS MRSA BSI

Inpatient Therapy	Discharge Therapy (n)	In-Hospital Mortality, n(%)	90-Day Mortality, n(%)	Mean BSI Duration (days)	90-Day BSI Recurrence, n(%)
van (10)	van (8) cef (1) dap + cef (1)	3(30)	4(40)	2.9	3(30)*
dap + cef (5)	cef + dap (3) cef + van (1) van (1)	0(0)	0(0)*	4.4	1(20)**
lin ± gen ± rif (5)	lin (3) van + sxt (1) quin/dal (1)	1(20)	3(60)	6.8	1(20)
other (11)		4(36)	4(36)	3.5	2(22)*
Totals		6(26)	11(35)	4.4	7(23)

gen = gentamycin; rif = rifampin; lin = linezolid; sxt = TMP-SMX; quin/dal = quinupristin/dalfopristin.

*1 pt with unknown status.

** 3 patients with unknown status.

Conclusion. A variety of therapeutic regimens was used to treat DNS MRSA BSI in our cohort. However, van monotherapy was the most common inpatient and discharge regimen.

Disclosures. All authors: No reported disclosures.

2453. Repeated Exposures to Minocycline/Rifampin and + Chlorhexidine Combination Used to Coat Catheters Fails to Induce Antimicrobial Resistance

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Background. Central venous catheters (CVC) impregnated with minocycline and rifampin (M/R) are recommended for use in high-risk patients to reduce catheter related bloodstream infections (CRBSI). We developed a second generation antimicrobial CVC with addition of chlorhexidine (CHD) for extended spectrum activity against virulent Gram-positive and Gram-negative bacteria as well as yeast. In this study we examined the potential for induced resistance with repeated exposure to M/R+CHD.

Methods. Potential to induce resistance was evaluated by exposing a broad-spectrum of CRBSI pathogens to serial passages of sub-inhibitory concentrations of M/R+CHD and retesting MICs following each passage. Susceptibility to individual agents in the combination were assessed, to identify organisms that were originally resistant to the individual agents in the combination. A total of 24 Gram-positive, Gram-negative, and yeast pathogens were evaluated for baseline MICs following standard CLSI procedures. Subsequently, organisms that were exposed to one half the MIC were cultured and MICs retested. This process was carried out for a total of 21 passages to assess trends in MICs and potential for induction of resistance. Any organism with ≥4 fold increase in MIC were then passed in broth alone to assess phenotypic adaptation.

Results. Synergy in the triple combination of M/R + CHD was detected for several resistant organisms that had low susceptibilities to the individual components but were highly susceptible to the combination. After a series of 21 passages, the organisms maintained the same MIC values as baseline with no clinically significant increases. One strain of Enterobacter showed a 4-fold MIC increase; however, the MIC returned to baseline after culturing in broth alone.

Conclusion. Repeated exposure of M/R + CHD failed to show induced antimicrobial resistance among a large number of pathogens with both low and high susceptibilities. Furthermore, any increase in MIC returned to baseline with the removal of the stressor (M/R + CHD), indicating that the increase in MIC was a phenotypic adaptation rather than induced resistance. Surveillance studies assessing development of resistance will need to be conducted in a clinical setting.

Disclosures. I. Raad, The University of Texas MD Anderson Cancer Center: Shareholder, Licensing agreement or royalty. The University of Texas MD Anderson Cancer Center: Shareholder, Dr. Raad is a co-inventor of the Nitroglycerin-Citrate-Ethanol catheter lock solution technology which is owned by the University of Texas MD Anderson Cancer Center (UTMDACC) and has been licensed to Novel Anti-Infective Technologies LLC, in which UTMDACC and Licensing agreement or royalty.

2454. Pertussis Vaccine Effectiveness and Waning Immunity in Alberta, Canada: 2004–2015

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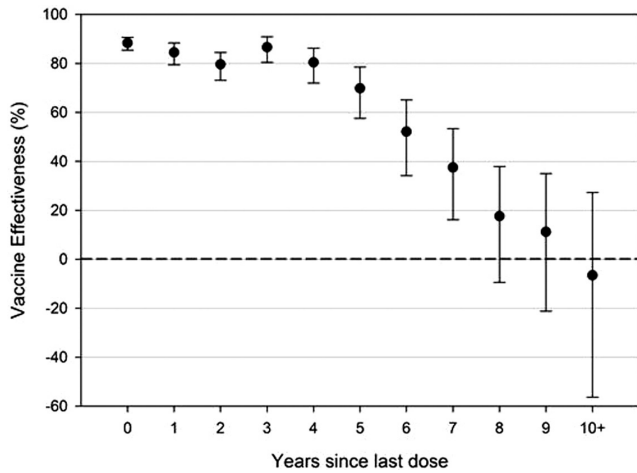
Background. Despite childhood vaccination coverage rates exceeding 75%, pertussis is still frequently reported in Canada. In Alberta, pertussis incidence ranged from 1.8 to 20.5 cases per 100,000 persons for 2004–2015. Most cases occurred in those aged < 15 years. We investigated pertussis vaccine effectiveness (VE) using a test-negative designed (TND) study.

Methods. All individuals who had undergone a real-time PCR laboratory test for *Bordetella pertussis* between January 1, 2004 and August 31, 2015, in the province of Alberta, Canada were included. Vaccination history was obtained from Alberta's immunization repository. Vaccination status was classified as complete, incomplete, or not vaccinated, based on the province's vaccination schedule. Multivariable logistic regression models were used to estimate adjusted odds ratios (aOR) and 95% confidence intervals (95% CI) for pertussis infection by time since last vaccination, comparing those with complete or incomplete vaccination to those not vaccinated. We adjusted for age, sex, income, urban/rural status, and the presence of a co-morbid condition. Vaccine effectiveness (VE) was calculated as [(1-aOR)*100].

Results. Of 28,154 individuals tested, 2,297 (12.3%) tested positive for *B. pertussis*. Among those with complete vs. no vaccination, VE was 88% (95% CI 85–91%) at 1 year, 83% (95% CI 79–86%) at 1 to 3 years, 70% (95% CI 63–76%) at 4 to 6 years, 28% (95% CI 12–42%) at 7 to 9 years, and -4% (95% CI -53 to 29%) at 10 or more years since a last dose of a pertussis vaccine (Figure 1). VE was similar but attenuated in the incompletely vaccinated group, with a comparable waning of immunity.

Conclusion. Pertussis VE was high in the first year after vaccination, then declined noticeably after 5 years. Our results suggest there is a large number of adolescents and adults susceptible to pertussis. Regular boosters throughout childhood, adolescence, and during pregnancy are critical to protect those at greatest risk of infection and complications. Further validation of the strengths and weaknesses of the TND for assessing pertussis VE is needed.

Figure 1. Pertussis VE by year since last vaccination in those with complete vaccination status.



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2455. Is Category B Working? Uptake Patterns of Meningococcal Group B Vaccine Among US Adolescents and Young Adults

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Background. In October 2015, ACIP recommended that serogroup B meningococcal (MenB) vaccine may be administered to persons aged 16–23 years (age 16–18 preferentially) as Category B (individual clinical decision-making), in addition to the Category A recommendation made in June 2015 for at-risk individuals aged ≥10 years. Currently, MenB vaccine coverage among adolescents and young adults (AYAs), including whether disparities exist, is not well-described.

Methods. We performed a cross-sectional analysis of claims data collected by IQVIA and linked to sociodemographic data collected by Experian to estimate overall and subpopulation-level uptake of MenB vaccine (≥1 dose) among AYAs aged 10–25 years as of May 31, 2017.

Results. Among 2,501,188 AYAs aged 10–25 years, MenB vaccine uptake was only 1.4% at the end of May 2017. MenB vaccination varied by age, with uptake of 0.2%, 2.5%, 1.6%, and 0.2% among individuals aged 10–15, 16–18, 19–23, and 24–25 years ($P < 0.01$), respectively. Lower uptake was observed for non-Hispanic blacks (1.0% vs. 1.4% among non-Hispanic whites, $P < 0.01$), AYAs in lower income households (1.0% vs. 2.2% among lowest vs. highest income deciles, $P < 0.01$), and those living in rural (0.6%) or urban/inner-city (0.9%) areas (vs. 1.5% in suburban areas, $P < 0.01$). The strongest predictors of MenB vaccination were previously receiving quadrivalent meningococcal (MenACWY) or human papillomavirus (HPV) vaccines. These AYAs were 36.1 and 5.1 times more likely to have received MenB vaccine and had MenB uptake of 9.8% and 5.1%, respectively.

Conclusion. As of May 2017, MenB vaccine uptake among AYAs aged 10–25 years was low (<2%). Even though absolute differences were small, significant disparities in MenB uptake existed. Uptake was notably higher for AYAs who had received ≥1 dose of MenACWY or HPV vaccine. This suggests MenB vaccination is occurring primarily among AYAs who have received other Category A vaccines, and that conversations between clinicians and patients about MenB vaccination—which are at the heart of a Category B recommendation—are limited outside of this context. Given the real-world inadequacies of a Category B recommendation highlighted by our study, future efforts should improve the AYA vaccination platform to ensure adequate immunization of AYAs, especially in underserved communities.

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2456. Immunogenicity and Safety of a MenACWY-CRM Booster Dose 4–6 Years After Primary Quadrivalent Meningococcal Conjugate Vaccination in Healthy US Adolescents and Adults

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Background. *Neisseria meningitidis* serogroups A, B, C, W, and Y are a leading cause of bacterial meningitis and sepsis worldwide. Infants <1 year, adolescents and young adults are at the highest risk. The US Advisory Committee on Immunization Practices (ACIP) recommends routine MenACWY conjugate vaccination for adolescents at 11–12 years of age, with a booster dose 5 years later. We examined responses to a booster dose of MenACWY-CRM given 4–6 years after primary vaccination with a licensed quadrivalent meningococcal conjugate vaccine (NCT02986854).

Methods. 602 adolescents and adults aged 15–55 years who had received either MenACWY-CRM ($N = 301$) or MenACWY-D ($N = 301$) 4–6 years earlier, and a control group of vaccine-naïve participants ($N = 102$) were enrolled at 37 centers across the US and 701 overall received a single dose of MenACWY-CRM at Day 1, across study groups. Immunogenicity was evaluated pre-vaccination, either 4 or 6 days post-vaccination (sampling subgroups) and 29 days post-vaccination by serum bactericidal activity assay using human complement (hSBA). After vaccination, all participants were to be monitored for 7 days for reactivity, 29 days for unsolicited adverse events (AEs), and 6 months for occurrence of medically attended events, AEs leading to withdrawal and serious AEs.

Results. Sufficiency of the immune response to a booster dose of MenACWY-CRM was demonstrated as the lower limit of the 1-sided 97.5% confidence interval for percentages of participants with hSBA seroresponse for each serogroup at 29 days post-vaccination was >75%, both in participants primed with MenACWY-CRM and MenACWY-D. Independent of quadrivalent meningococcal vaccine priming, >93% of participants achieved a seroresponse at day 29 post-booster. By day 6 post-booster, >47% of primed participants achieved hSBA titers ≥1:8 for MenA, >87% for MenC, >93% for MenW and >85% for MenY, and by day 29 almost all primed participants had seroprotective titers across all serogroups. Overall, the vaccine was well tolerated across participants in all 3 groups and no safety concerns were raised.

Conclusion. MenACWY-CRM induced robust boosting in adolescents and adults primed with a quadrivalent meningococcal conjugate vaccine 4–6 years earlier, with an acceptable clinical safety profile.

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Disclosures. S. L. Block, GSK: Research Contractor, Research support. P. Keshavan, GSK Vaccines: Employee, Salary. T. Mzolo, GSK Vaccines: Employee, Salary. M. Pellegrini, GSK Vaccines S.r.l.: Employee and Shareholder, Salary.

2457. Multivariate Analyses of Socio-Economic Inequities in Parental Awareness and Utilization of Meningococcal Serogroup B Vaccines

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Background. In 2015, the US Advisory Committee on Immunization Practices (ACIP) made a Category B recommendation for serogroup B meningococcal (MenB) vaccines for adolescents 16–18 years. In 2016, MenB caused ~60% of invasive meningococcal disease among US individuals 16–23 years old; however, utilization of MenB vaccines was much lower than other vaccines with Category A recommendations. Therefore, we examined factors associated with awareness and utilization of MenB vaccines.

Methods. An online quantitative survey was fielded among 619 US parents of adolescents aged 16–19 years, recruited from GfK's KnowledgePanel[®] in December 2016. Demographics, access to care, decision making, and vaccine use were collected. A population-based weighting method was applied. Four logistic regressions and Classification And Regression Trees (CART) were conducted to examination most influential factors associated with MenB vaccine awareness and utilization.

Results. Of the weighted sample, 57% were unaware of MenB vaccines (Figure 1). Results from logistic regression models (Table 1) revealed that awareness was likely associated with gender and race. Parents who obtained a recommendation from HCPs were 4.8 (95% CI: 2.5–9.4) times more likely to vaccinate or intend to vaccinate their adolescent children and 5.7 (95% CI: 2.5–12.9) times more likely have adolescents already vaccinated than those parents who did not receive the recommendation from HCP. Race/ethnicity and insurance type were associated with awareness and vaccine utilization. The results from CART verified that HCPs' recommendation is the most influential factor to predict the vaccination status. Parents' socio-economic status and their relationship with HCPs were among the most influential predictors of awareness of MenB vaccines or interest in learning about MenB vaccines if they were unaware.

Conclusion. MenB awareness and vaccination are associated with parents' socio-economic status and HCPs' recommendation. Even among those unaware, there was a willingness to vaccinate when recommended by an HCP. These data underscore the critical need for robust understanding and consistent implementation of ACIP's Category B recommendation to reduce inequities in MenB vaccine awareness and utilization.