in recent years. However, limited data exist addressing the mortality associated with HCV infection since the advent of DAAs. This study examines multiple-cause-of-death (MCOD) data from 2014 to 2017 to describe changes in HCV-associated mortality in the United States.

Methods. HCV infection since the advent of DAAs. This study examines multiple-cause-of-death (MCOD) data from 2014 to 2017 to describe changes in HCV-associated mortality in the United States.

Methods. We examined death certificate information from public use MCOD data obtained from the National Center for Health Statistics. All-cause mortality associated with HCV, as defined by ICD-10 codes (B17.1 and B18.8, was evaluated. The age-adjusted crude mortality rate was calculated. Overall HCV-associated mortality, stratified by race and gender, was analyzed.

Results. From 2014 to 2017, the number of deaths associated with HCV, as listed in death certificates decreased from 19,613 to 17,253. This represents an average of 4% decrease in mortality each year. Crude age-adjusted mortality decreased from 5.01 (95% CI 4.93–5.08) deaths per 100,000 people in 2014 to 4.13 (95% CI 4.07–4.20) deaths per 100,000 people in 2017. Males had age-adjusted mortality of 6.82 (95% CI 6.76–6.88) and females had age-adjusted mortality of 2.59 (95% CI 2.55–2.63). African Americans had age-adjusted mortality of 7.50 (95% CI 7.37–7.63), and whites had age-adjusted mortality of 4.39 (95% CI 4.35–4.42) during the three-year period.

Conclusion. After the introduction of DAAs in 2014, mortality associated with HCV significantly decreased in the United States. There were differences in mortality rates by gender and race, which may reflect differences in HCV seroprevalence. With the availability of effective, well-tolerated HCV treatment, aggressive HCV screening and testing is essential to improve outcomes for patients with HCV.

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2900. High Rates of Experienced and Witnessed Opioid Overdose in PWID Receiving HCV Treatment: Data From the ANCHOR Study

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Session: 310. Hepatitis C: Progress on Elimination and Treatment
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Background. People who inject drugs (PWID) have significant morbidity and mortality associated with hepatitis C (HCV); however, harms associated with ongoing injecting drug use (IDU)—such as opioid overdose—may pose a more imminent risk, especially in high-risk populations. Receiving HCV treatment is an important intervention, but data are lacking on how this strategy impacts per- treatment mortality levels in high cohorts of PWID.

Methods. We collected paired maternal delivery-cord sera from infants of women who received Tdap ≥7 days before birth. IgG to pertussis toxin (PT), filamentous hemagglutinin ( FHA), fimbrial proteins (FIM) and pertactin (PRN) was quantified by Luminex assay (AU/mL). Mean geometric concentrations (GM) with 95% confidence intervals (95% CI) for pertussis antibodies were calculated. Four infant groups were compared by weeks of gestation: very (<32), moderate (32–33) and late preterm (34–36), and term (≥37).

Results. 344 preterm and 688 term mother-infant pairs were included. Among preterm infants, mean gestational age was 31.2 weeks (range 15.1–39.3); 37% were white, 37% Hispanic, 17% Black, 8% Asian and 1% other. Fifty-six were very preterm infants (16%, mean gestation 30.5 weeks), 82 moderate (24%, 31.1 weeks), and 206 late (60%, 35.4 weeks); 17% were born ≥37 weeks. For preterm infants, Tdap was administered at a mean gestation of 29.9 weeks (very 27.9; moderate 29.7; late 30.3; [P < .001]), and 34% of Tdap vaccinated preterm infants were vaccinated before 36 weeks of gestation (very 17.9; moderate 24.4; late 34.5; [P < .001]). Eleven (3%) women received Tdap during the second trimester (very 8, very 2, moderate 1, late 1), GMCs (95% CI) of pertussis-specific IgG by birth gestation (table). Infant antibody levels as a proportion of maternal antibodies increased from 24 to 32%, 65% to 117 to 132% in those <37 weeks gestation.

Conclusion. Although levels are lower than in term infants, maternal immunization with Tdap results in substantial pertussis-specific antibodies in most preterm infants, especially late preterm infants.

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Session: 311. Vaccination II - Other
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Background. PCV13 implementation in children resulted in a substantial decline in carriage of and disease by vaccine serotypes (VT13). However, disease caused by non-PCV13 serotypes (NVT) is still relatively prevalent and even increasing, leading to an effort to develop a 20-valent vaccine (PCV20), containing the additional 7 serotypes: 8, 10A, 11A, 12F, 15B/C, 22F, 33F (VT20-13). We assessed dynamics of VT13, VT20-13, and non-PCV20 (NVT20) in nasopharyngeal carriage, respiratory infections, and IPD in children < 2 years following PCV13 implementation.

Methods. Multiple prospective, population-based surveillance projects, conducted in Israel between 2009 and 2017 were used. We studied isolates from IPD, otitis media (OM); conjunctivitis; carriage in healthy children; carriage during lower respiratory tract infections with chest radiography examination (LRI); and carriage during non-LRI illnesses. We added data from healthy children in the community since 2011. Prevalence rate ratios were calculated, comparing VT13, VT20-13 and NVT20 rates in late-PCV13 (2015–2017) vs. early-PCV (2009–2011) periods.

Results. Overall, 9,089 episodes were recorded. VT13 declined significantly in all 6 groups by 75–86% (Figures 1 and 2). Proportions of VT20-13 significantly increased in all groups, excluding conjunctivitis. The highest increases were observed in IPD, OM, and carriage during LRI. In 2015–2017, VT20-13 consisted 24%, 23%, and 19% of carriage in healthy children, carriage in non-LRI illness, and conjunctivitis, respectively, vs. 51%, 33%, and 32% in IPD, OM, and carriage during LRI. VT20-13 rapidly became the leading fraction in IPD. NVT20 proportions increased in all groups.

Conclusion. (1) PCV13 implementation resulted in a substantial increase in NVT carriage and disease; (2) In IPD, VT20-13 became the dominant group; (3) The increases in the proportion of VT20-13 seen in OM and carriage during LRI was significantly higher than in conjunctivitis and in carriage without LRI.

Figure 1: Dynamics of nasopharyngeal carriage, conjunctivitis, otitis media (OM) and IPD (proportion of VT13, VT20-13 and NVT20 of all nasopharyngeal isolates) in children < 24 months, Israel, October 2009 through June 2017

Figure 2: Prevalence rate ratios of VT13, VT20-13 and NVT20 of all nasopharyngeal isolates in carriage, conjunctivitis, otitis media (OM) and IPD in children < 24 months, Israel; comparing July 2015 – June 2017 vs. October 2009 – June 2011

2904. Protective Efficacy of Nucleic Acid Vaccines Against Transmission of Zika Virus During Pregnancy in Mice

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Session: 311. Vaccination II - Other
Saturday, October 5, 2019: 4:00 PM

Background. Zika virus (ZIKV) caused an epidemic of microcephaly and congenital malformations in 2015–2016, prompting the development of ZIKV vaccines. Plasmid DNA and modified mRNA lipid nanoparticle-encapsulated (mRNA-LNP) vaccines were among the first to reach human clinical trials, where their evaluation is ongoing. Few studies have evaluated vaccine efficacy in the setting of infection during pregnancy, and there is an open question around antibody-dependent enhancement (ADE) of flaviviral disease due to cross-reactive fusion loop epitope (FLE) antibodies.

Methods. Female C57BL/6J mice and human STAT2 knock-in (hSTAT2-KI) mice were immunized with plasmid DNA (VRCS283) or mRNA-LNP (Moderna Inc.) vaccines encoding the ZIKV preM-E genes. Antibody responses were assayed, and immunized mice were mated and WT mice were transiently immunocompromised by administration of interferon blocking antibody, followed by ZIKV challenge. 1 week post-infection, ZIKV burden was measured via qRT-PCR. ZIKV-specific memory B cell (MBC), long-lived plasma cell (LLPC), and CD8+ T cell vaccine responses were also assayed.

Results. VRCS283 and mRNA-LNP vaccines were highly immunogenic, eliciting serum neutralizing EC50 responses >110,000, and markedly reduced placental ZIKV burden and fetal transmission. An improved mRNA-LNP construct with higher immunogenicity correlated with reduced placental viral burden. Significantly, an FLE-mutant mRNA-LNP vaccine yielded comparable EC50 responses without compromising vaccine efficacy; sera from these mice did not enhance dengue virus infection in vitro. Both VRCS283 and mRNA-LNP vaccines elicited MBC, LLPC, and CD8+ T cell responses, although MBC and LLPC responses were greater after mRNA-LNP immunization. Surprisingly, low-level ZIKV infection of the placenta and a minority of fetal hairs were observed despite robust neutralizing antibody responses, which was not seen in the immunocompetent hSTAT2-KI model.

Conclusion. Nucleic acid vaccines were highly immunogenic and protective against vertical ZIKV transmission during pregnancy in mice. These data support and inform the ongoing clinical development of these vaccines in humans.

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2905. Long-term Immunological Persistence of the Adjuvanted Recombinant Zoster Vaccine: Clinical Data and Mathematical Modeling

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Background. The adjuvanted recombinant zoster vaccine (RZV, GSK), administered to adults ≥ 50 years of age (YOA) demonstrated ≥ 90% efficacy against herpes zoster across all age cohorts. Vaccine-specific immune responses elicited by two RZV doses in adults ≥ 60 YOA have been shown to persist above pre-vaccination levels at least up to 9 years after initial vaccination. Here we present persistence of the humoral and cellular immunity and safety up to 10 years after initial vaccination as well as data from mathematical modeling, performed to predict immune persistence up to 15 years.

Methods. This phase IIIB, open-label extension trial (NCT02735915) included 70 participants who had received two RZV doses in the initial trial (NCT00434577) and built on a previous extension trial (NCT01295310). Cellular and humoral immune responses up to year 10 after an initial 2-dose vaccination schedule are presented here. Additionally, prediction of immunological persistence at year 15 was assessed by mathematical modeling (Piecewise, Power-law, Fraser), using the individual subject values for available data up to year 10.

Results. The median frequency of varicella-zoster virus glycoprotein E (gE)-specific CD4+ T-cells expressing ≥ 2 activation markers plateaued at 3.3-fold above pre-vaccination levels starting around year 4 up to year 10 post-initial vaccination. Anti-gE antibody concentrations plateaued starting around year 2 up to year 10 post-initial vaccination. Ten years after initial vaccination, humoral responses remained 5.9-fold higher as compared with pre-initial vaccination levels (Figure 1). No relevant safety events were identified during the study (year 9–10 post-initial vaccination).