sinks (n=22), followed by surfaces near the patient (n=10), and least common surfaces often touched by staff within the room (n=6).

On multivariable logistic regression, naïve to clustering by patient, recent receipt of a proton pump inhibitor (OR 2.35, 95% CI 1.00 – 5.52, P=0.049) and presence of one or more wounds (OR 2.56, 95% CI 1.05 – 6.26, P=0.038) were significantly associated with environmental transmission (OR 1.56, 95% CI 1.01 – 2.43, P=0.046) (Table 1).

TABLE 1. Logistic regression for detection of patient to environment transmission of multi-drug resistant organisms

Variable	Bivariable OR (95% CI)	P-Value	Multivariable OR (95% CI)	P-Value
Patient characteristics				
Sedated	1.02 (0.41 – 2.55)	0.96		
Wound present	2.71 (1.19 – 6.17)	0.02	2.56 (1.05 – 6.26)	0.04
Bedfast[a]	2.35 (0.82 – 6.69)	0.11		
Diarrhea[b]	0.79 (0.37 – 1.71)	0.56		
Invasive devices present				
Mechanical ventilation	1.67 (0.80 – 3.46)	0.17		
Central venous catheter	1.86 (0.85 – 24.05)	0.12		
Urinary catheter	1.09 (0.52 – 2.28)	0.82		
Rectal tube	2.44 (1.07 – 5.56)	0.03		
Medication use				
Broad-spectrum antibiotic use[c]	1.09 (0.97 – 1.05)	0.64		
Laxative[d]	1.18 (0.49 – 2.86)	0.71		
Proton pump inhibitor[d]	2.59 (1.21 – 5.53)	0.01	2.35 (1.03 – 5.52)	0.049

NOTE. Model developed naïve to clustering by patient; OR, odds ratio, CI; confidence interval

[a]Bedfast determined by a mobility score of 1 on daily Braden score assessment

[b]As documented by medical staff

[c]Number of anti-pseudomonal antibiotic days within the prior 30 days

[d]Within 3 days

Conclusion: MDRO contamination of patient rooms is common with detection of organisms attributed to, and foreign to, the occupant.

Disclosures: Michael Z. David, MD PhD, GSK (Consultant)

## 158. Intra- and Inter-hospital Epidemiology of Carbapenem-resistant *klebsiella Pneumoniae* in US Hospitals

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Session: O-30. MDRO Epidemiology and Transmission

Background: Carbapenem-resistant Enterobacterales (CRE) and specifically *Klebsiella pneumoniae* (CRKp) are a global threat. CRE rapidly spreading in a healthcare network may infect a distinct patient cohort or have higher virulence. We determined the impact of cluster assignment of CRKp on transmission dynamics and clinical outcomes.

Methods: CRACKLE-2 is a multi-site, prospective, observational cohort study of hospitalized patients with a clinical CRE culture from any anatomic site. We analyzed 351 patients enrolled 4/30/2016–8/31/2017 in 42 US hospitals with clonal group 258 CRKp. Static clusters were set as ≤ 21 core single nucleotide polymorphisms (SNPs), identified by Snippy, and sharing a recent common ancestor, using a maximum likelihood phylogeny (RAxML v8.2.4). Dynamic clusters were set as > 80% probability of being within 3 transmissions by the R program transcluster (λ = 4, β = 1.6). Clinical outcome was assessed by desirability of outcome ranking with best outcome as alive without events and worst outcome as death. Events were no clinical response, unsuccessful discharge, and adverse events. We compared patients in and out of clusters. For patients in clusters, we also compared intra- vs inter-hospital clusters.

Results: In total, there were 49 static (median: 5, IQR: 2, 8) and 45 dynamic clusters (median: 5, IQR: 2, 20). For static clusters, 176 patients (50%) were in clusters with 82 (47%) patients in intra-hospital clusters. A higher proportion of patients in clusters, vs not in clusters, had a CRKp culture > 3 days from admission (P = 0.037). More patients in inter-hospital, vs intra-hospital, clusters had diabetes (P = 0.02). For dynamic clusters, 179 patients (51%) were in clusters with 69 (39%) patients in intra-hospital clusters. A lower proportion of patients in clusters, vs not in clusters, had CRKp isolated from urine (P = 0.04). More patients in inter-hospital, vs intra-hospital, clusters had a CRKp culture 3 days from admission (P = 0.04). Clinical outcomes were the same for patients in clusters vs not in clusters for static and dynamic clusters.
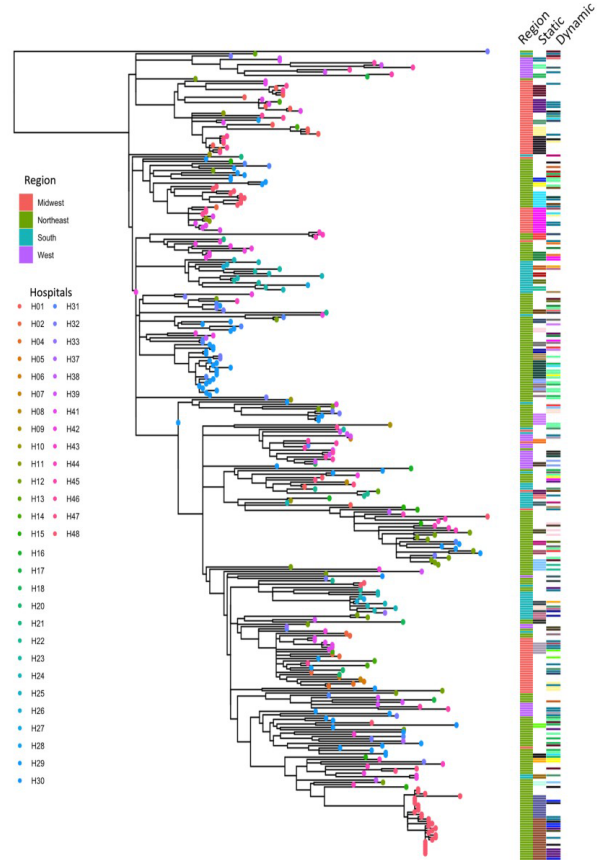
Figure 1. Phylogenetic population structure of *K. pneumoniae* CG258 strains. Panels from left to right indicate core SNP maximum likelihood phylogenetic tree, region of isolation, static CRKp clusters and dynamic CRKp clusters. Hospitals of isolation are colored at the nodes of the tree. For static clusters, each color represents a group of *K. pneumoniae* CG258 genomes differing by ≤ 21 core SNPs and sharing a recent common ancestor. For dynamic clusters, each color represent a group of *K. pneumoniae* CG258 genomes with >80% probability of being within 3 transmission.
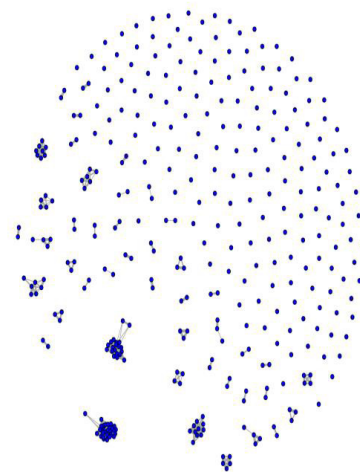
Figure 2. Dynamic cluster structure of *K. pneumoniae* CG258 strains. Individual CRKp strains (circles) were clustered based on SNPs and date of culture isolation with the edges between nodes indicating a > 80% probability of being within 3 transmissions. Edge thickness represents the number of likely transmissions between isolates with the thinnest edge representing 3 transmissions.

Conclusion: This analysis shows that clinical outcomes are independent of clustering assignment. Static clustering better represented nosocomial spread, based on a higher proportion of patients in clusters having a later CRKp culture.

159. efficacy of CD377, a Novel Antiviral Fc-conjugate, Against Seasonal Influenza in Lethal Mouse Infection Models

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Session: O-31. Novel Vaccines and Antibodies

Background: Cidara's AVCs (antiviral Fc-conjugates) are novel conjugates of potent, antiviral agents with the Fc domain of human IgG1. CD377 is an AVC development candidate for prevention and treatment of influenza that has broad anti-neuraminidase activity in both enzymatic and cell-based assays and the potential to engage the immune system, as well as a long half-life.

Methods: Efficacy studies were conducted in BALB/c mice lethally challenged intranasally at 3x the LD_{95} with influenza A (H1N1, H3N2) and influenza B (both lineages). CD377 was administered as a single dose subcutaneously (SC) 2 hours after viral challenge. Body weights (BW) and health scores were monitored daily, with 20% BW loss recorded as a mortality.

Results: In mice challenged with a lethal dose of an H1N1 strain (A/California/12/2012), a single 0.3 mg/kg dose of CD377 administered 2 hours post-challenge was fully protective (P=0.0015 relative to vehicle) (Fig 1A). In a similar study against a mouse-adapted H3N2 subtype (A/Hong Kong/1/1968), a single dose of CD377 at 0.1 mg/kg was fully protective (P=0.0025) (Fig 1B). In both studies, only a transient loss of BW was observed before mice began recovering weight.

The activity of CD377 was also evaluated against both lineages of influenza B (Fig 1C, 1D). Against influenza B/Colorado/06/2017 (Victoria), a single CD377 dose of 0.3 mg/kg was fully protective (P=0.0035) while the Fc-only control dosed at 1 mg/kg was not, as expected. Against the Yamagata lineage (B/Florida/4/2006), CD377 demonstrated full protection at a dose of only 0.03 mg/kg (P=0.0023).

Conclusion: A single dose of CD377 (0.3 mg/kg or less) was protective against lethal challenge with several seasonal influenza A/B subtypes. The exceptional PK profile of CD377 combined with potent broad-spectrum activity highlight its potential for use as a long-term preventative against seasonal influenza.

Seasonal influenza efficacy

Figure 1. Activity of CD377 against H1N1 (A), H3N2 (B), Yamagata lineage (C), Victoria lineage (D)
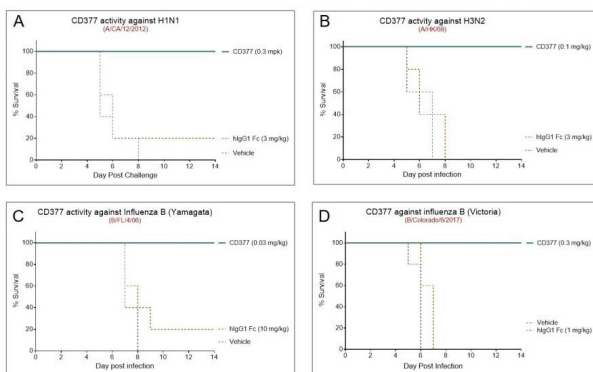
160. Safety and Immunogenicity of Escalating Dose Formulations of High-dose Quadrivalent Influenza Vaccine in Children 6 Months Through < 18 Years of Age

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QHD04 Study Team

Session: O-31. Novel Vaccines and Antibodies

Background: Children do not respond immunologically as well as adults to standard-dose (SD) influenza vaccination and remain at increased risk of influenza and its complications. A method to improve efficacy in children may be to increase antigen amount per dose, a successful strategy used in older adults. Trivalent high-dose (HD) influenza vaccine (60ug hemagglutinin/strain) showed significantly improved effectiveness for prevention of clinical outcomes related to influenza in adults ≥65 years; moreover, a quadrivalent HD formulation was approved by US FDA (2019) for use in this group.

Methods: A Phase 2, randomized, modified double blind study (NCT03698279) was conducted in US and Canadian children to evaluate safety and immunogenicity of IIV4-HD compared to an IIV4-SD and adjuvanted trivalent influenza vaccine (aIIV3). Children (n=661, 6 months through < 18 years) were assigned to receive intramuscularly 1 of 3 formulations of IIV4-HD (30, 45, or 60 μg HA/strain/dose), a licensed IIV4-SD, or a licensed aIIV3. Depending on child's previous influenza vaccination status and age, they received 1 or 2 doses of study vaccine 28 days apart. Post-vaccination (28 days after each vaccination) geometric mean titers (GMTs) and seroconversion rates were measured using hemagglutinin inhibition (HAI) assay. Reactogenicity data were collected through 1 week; safety data were collected through 6 months post-vaccination.

Results: IIV4-HD was more reactogenic than IIV4-SD, but unsolicited related adverse events were similar (Table 1). No related serious adverse events or deaths occurred. A dose-related increase in HAI GMT ratio was observed across the age range for A/H3N2 but only in children 6 months through < 3 years for A/H1N1 and the 2 B strains (Table 2). Compared with IIV4-SD, the 60 μg HA/strain/dose formulation of IIV4-HD generated highest HAI GMT ratios and high seroconversion rates for all 4 strains in US children 6 months through < 3 years. Canadian children receiving IIV4-HD generated HAI titers incongruent to those of US children receiving IIV4-HD, limiting direct comparison against aIIV3.

Safety Overview (US and Canadian subjects 6 months through <18 years)

Subject experiencing at least one	US				Canada	
N = number of subjects	IIV4-HD 30μg N= 122	IIV4-HD 45μg N= 121	IIV4-HD 60μg N= 158	IIV4-SD pooled N= 234	IIV4-HD 60μg N= 13	aIIV3 N= 13
Immediate unsolicited AE	0 (0%)	0 (0%)	1 (0.6%)	0 (0%)	0 (0%)	0 (0%)
Solicited reaction	95 (77.9%)	94 (78.3%)	111 (70.3%)	146 (62.9%)	13 (100%)	13 (100%)
Injection site reaction	89 (73.0%)	89 (74.8%)	101 (63.9%)	128 (55.2%)	9 (69.2%)	9 (69.2%)
Systemic reaction	62 (50.8%)	62 (51.7%)	71 (44.9%)	97 (41.8%)	13 (100%)	13 (100%)
Unsolicited AE	46 (37.7%)	46 (38.0%)	53 (33.5%)	80 (34.2%)	11 (84.6%)	12 (92.3%)
SAE (within 28 days post vaccination)	0 (0%)	0 (0%)	2 (1.3%)	0 (0%)	0 (0%)	0 (0%)
AE of special interest	0 (0%)	0 (0%)	1 (0.6%)	0 (0%)	0 (0%)	0 (0%)
SAE (during the entire study)	0 (0%)	0 (0%)	2 (1.3%)	0 (0%)	0 (0%)	1 (7.7%)
AE of special interest	0 (0%)	0 (0%)	1 (0.6%)	0 (0%)	0 (0%)	0 (0%)

*No related SAEs were reported in the study. The two SAEs in the IIV4-HD 60μg group were a febrile seizure (also defined as an AESI) and an RSV infection. The SAE in the aIIV3 group was severe bilateral otitis.

HAI GMT Ratios (QIV-HD/QIV-SD) at 28 days After the Last Vaccination (US subjects 6 months through <18 years)

Age Group	Dose	Influenza Virus Strain			
		A/H1N1	A/H3N2	B/Victoria	B/Yamagata
6 months to <3 years	30μg	**2.13**	0.93	1.23	1.10
	45μg	**1.75**	1.49	1.38	1.18
	60μg	**4.24**	**3.14**	**2.04**	**1.92**
3 to < 5 years	30μg	0.54	**1.56**	0.80	0.96
	45μg	0.57	**2.97**	0.84	0.91
	60μg	0.50	**2.37**	1.05	1.27
5 to <9 years	30μg	0.61	**2.09**	1.01	1.06
	45μg	0.69	**2.60**	1.38	1.15
	60μg	0.88	**2.99**	**1.89**	**1.52**
9 to <18 years	30μg	0.98	1.38	1.21	1.16
	45μg	1.02	**1.86**	1.23	0.99
	60μg	1.28	**1.54**	1.43	1.15

*GMT ratios > 1.5 are in bold.

Conclusion: The favorable safety profile and the HAI GMT ratios support pediatric dose selection of 60μg HA/strain/dose as most appropriate to evaluate in Phase 3.