

Influenza Disease Burden

Summary of SAGE Influenza Vaccine Working Group Discussions

**SAGE meeting
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Overview

- SAGE WG reviewed influenza epidemiology and disease burden data at each meeting
- 6 presentations on DB provided to WG members
 - WG focused on recent data relevant to discussions of targeted vaccination, and data from LIC and MIC settings
- Additional documents shared with the WG
- This presentation intended to be a summary of WG discussions
 - Not a complete review of influenza-associated disease burden
 - Data presented are illustrative, not meant to represent the totality of the data considered



Summary plan

- Pregnant women
- Health care workers
- Young children
- Elderly
- Persons with high risk conditions



Substantial morbidity and mortality from influenza on pregnant women

- Neuzil, K. et al; Am J Epidemiol 1998;148:1094-102
 - Women in 3rd trimester w/o other risk factors had 21.7 events per 10,000 women-months during flu season; half attributable to influenza.
 - Compared with 1.91 (1.51-2.31) and 1.16 (-0.09 to 2.42) per 10,000 women months rates in non-pregnant and postpartum were, respectively.
 - Women with other risk factors had higher risk of admission
- Risk of hospitalization among pregnant women with asthma higher than among pregnant women with no other risk factors (OR= 10.6). (Hartert, et al., American J Obstet Gynecol 2003;189:1705-12)
- Excess mortality attributed to influenza observed among pregnant women from 1998-2005 in the US, particularly in the 3rd trimester. (Callaghan, Obstetric Gynecol 2010; 115: 919-23.)
 - Increased influenza-associated mortality confirmed in multiple studies during 2009 pandemic (Louie 2010; Archer 2010; Jamieson 2009)



Case-Control Study of Risk Factors for Hospitalization Caused by Pandemic (H1N1) 2009

Ward KA. EID Vo. 17, No.8 Aug. 2011

Table 3. Risk factors for mechanical ventilation because of pandemic (H1N1) 2009 infection, Sydney, Australia, 2009*

Patient characteristic	No. (%) case-patients, n = 37	No. (%) controls, n = 603	OR (95% CI)	p value	Adjusted OR (95% CI)	p value
Health condition†						
Asthma	13 (65)	93 (15)				
No regular medication	5 (14)	48 (8)	2.2 (0.8–6.1)	0.0061		
Regular medication	8 (22)	45 (7)	3.8 (1.6–8.9)			
Heart disease§	3 (9)	41 (7)	1.3 (0.4–4.3)	0.7136		
Kidney disease¶	1 (3)	8 (1)	2.1 (0.3–16.9)	0.5013		
Mental health problem	6 (16)	49 (8)	2.2 (0.9–5.5)	0.0958		
Neurologic problem	3 (8)	42 (7)	1.2 (0.3–4.0)	0.792		
Immunosuppression	1 (3)	22 (4)	0.7 (0.1–5.6)	0.7655		
Obstructive sleep apnea	2 (5)	23 (4)	1.4 (0.3–6.4)	0.6296		
Lung disease	6 (16)	31 (5)	3.6 (1.4–9.2)	0.0084	8.6 (2.6–28.5)	0.0005
Diabetes	5 (14)	38 (6)	2.3 (0.9–6.3)	0.0977	4.4 (1.2–15.6)	0.0383
Liver disease	2 (5)	20 (3)	1.7 (0.4–7.4)	0.503		
Pregnancy	8 (22)	7 (1)	23.4 (8.0–69.2)	<0.001	40.5 (9.7–168.1)	<0.0001

Data: Sydney Australia admission records, random community controls

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Effect of respiratory hospitalization during pregnancy on infant outcomes in Nova Scotia

McNeil, et al., AJOG Supplement to JUNE 2011

Neonatal outcomes

Outcome	Any influenza-season hospital admission during the pregnancy		Unadjusted relative risk (95% CI)	Adjusted relative risk (95% CI)
	Yes ^a (n = 208)	No (n = 132,099)		
Low birthweight: <2500 g, n (%)	13 (6.3)	6035 (4.6)	1.39 (0.80–2.45)	1.30 (0.59–2.86) ^b
Small for gestational age, n (%)	31 (15.3)	12594 (9.7)	1.68 (1.14–2.46)	1.66 (1.11–2.49) ^c
Preterm: <37 weeks' gestation, n (%)	15 (7.2)	7159 (5.4)	1.36 (0.80–2.30)	1.20 (0.71–2.04) ^d
Neonatal morbidity, n (%) ^e	14 (6.7)	6488 (4.9)	1.40 (0.81–2.41)	1.13 (0.61–2.08) ^b
Mean birthweight, g ^f	3360.3 ± 634.7	3468.3 ± 583.8	$\beta = -108.01$ ($P = .008$)	$\beta = -86.14^b$ ($P = .009$)
Mean birthweight, g ^{f,g}	3448.5 ± 498.2	3531.3 ± 504.1	$\beta = -82.79$ ($P = .02$)	$\beta = -86.67^b$ ($P = .009$)

Evidence that influenza vaccination of pregnant women can result in higher birth weight (Omer, et al 2012; Steinhoff, et al 2012).



Health care workers

- Healthcare workers are at increased risk of infection with influenza compared to the general adult population.
- Risk of infection is not evenly distributed to all HCWs
Higher in Emergency Departments, other clinical settings, nurses
- HCWs frequently come to work despite being sick, which can result in nosocomial transmission of influenza to patients.
- Evidence of transmission of influenza viruses from healthcare workers to patients.
- More likely exposed to high risk persons



Young children

- The global disease burden associated with influenza in children <5 years of age is substantial.
- Rates of severe disease may be much higher in LICs compared with developed countries.
- Rates of complications highest in youngest children
 - Highest hospitalizations among children < 2 years – comparable to elderly rates
- Children shed virus longer than adults, so are important for community outbreak initiation and spread



Influenza in young children

Nair et al., Lancet 2011; 378: 1917–30

- Influenza-associated outcomes among children 0-59 months
 - 20.5 (95% CI- 13, 32) million cases of influenza associated ALRI (13% paediatric ALRI)
 - 1 (95% CI- 0.7, 1.5) million cases of influenza associated severe ALRI (7% paediatric ALRI)
 - 28,000 to 111,000 deaths (2 to 7% of paediatric ALRI deaths)
- These estimates do not consider bacterial co-infection – increased burden
- As pneumococcal and Hib immunization included in EPI in developing countries, proportion of viral ALRI likely to rise



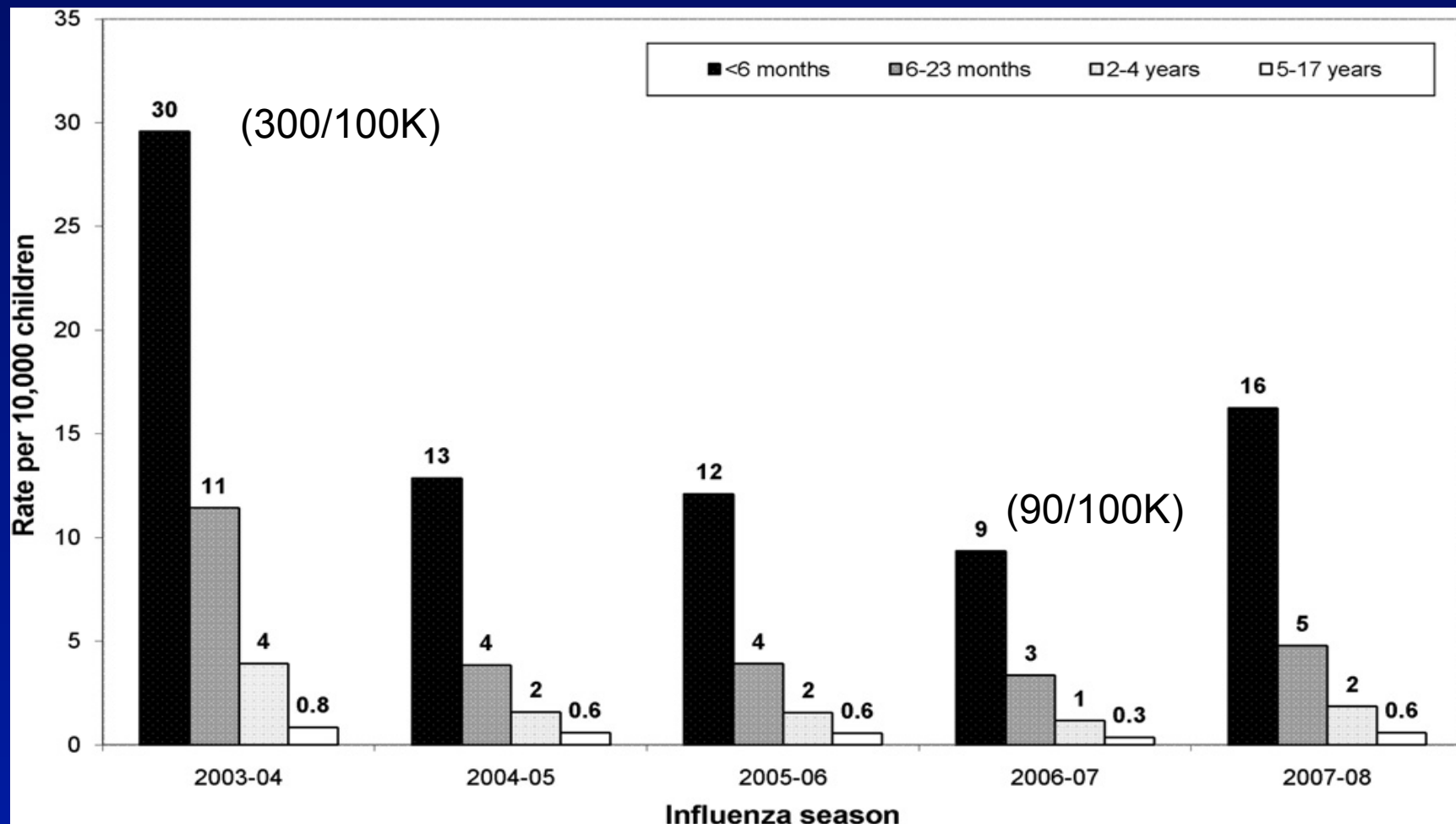
Global annual incidence of severe influenza in children

Nair et al., Lancet 2011; 378: 1917–30

	Incidence/100K ALRI (95%CI)	Incidence/100K Severe ALRI (95%CI)
Developing countries		
<6 mo. old		290(200 - 410)
0-11 mo. old	2260 (890 - 5720)	280 (190 - 410)
0-59 mo. old	3500 (2200 -5500)	170 (110 - 250)
Industrialized countries		
<6 mo. old		340 (230 - 500)
0 – 11 mo. old	1470 (1380, 1570)	230 (180 - 300)
0 – 59 mo. old	1160 (750 - 1800)	120 (90 - 170)



Annual variation in Incidence of Lab Confirmed Influenza in Hospitalized Children, U.S. EIP Network, 2003-7/8



Dawood, et al. J Pediatr 2010;157:808-14

www.cdc.gov/flu



Annual Rates (per 1000 children) of laboratory confirmed influenza related SARI in 2 Kenyan refugee camps, 2007-9

		Flu A (95 % CI ¹)	Flu B (95 % CI ¹)
Kakuma	<1 yr	12.3 (7.7 -19.5)	1.2 (0.3 -5.3)
	1 to 5 yrs	4.2 (2.9 – 6.1)	1.4 (0.8 – 2.7)
	<5 yrs	5.6 (4.2 – 7.5)	1.4 (0.8 – 2.5)
Dadaab	<1 yr	10.3 (6.8 – 15.6)	2.9 (1.3 – 6.3)
	1 to 5 yrs	2.9 (2.1 – 4.2)	0.7 (0.3 – 1.4)
	<5 yrs	4.2(3.2 – 5.5)	1.1 (0.6 – 1.8)
Overall	<1 yr	11.1 (8.2 – 15.1)	2.2 (1.1 – 4.4)
	1 to 5 yrs	3.4 (2.7 – 4.4)	1.0 (0.6 – 1.6)
	<5 yrs	4.8 (3.9 – 5.8)	1.2 (0.8 – 1.8)

¹95% confidence Interval

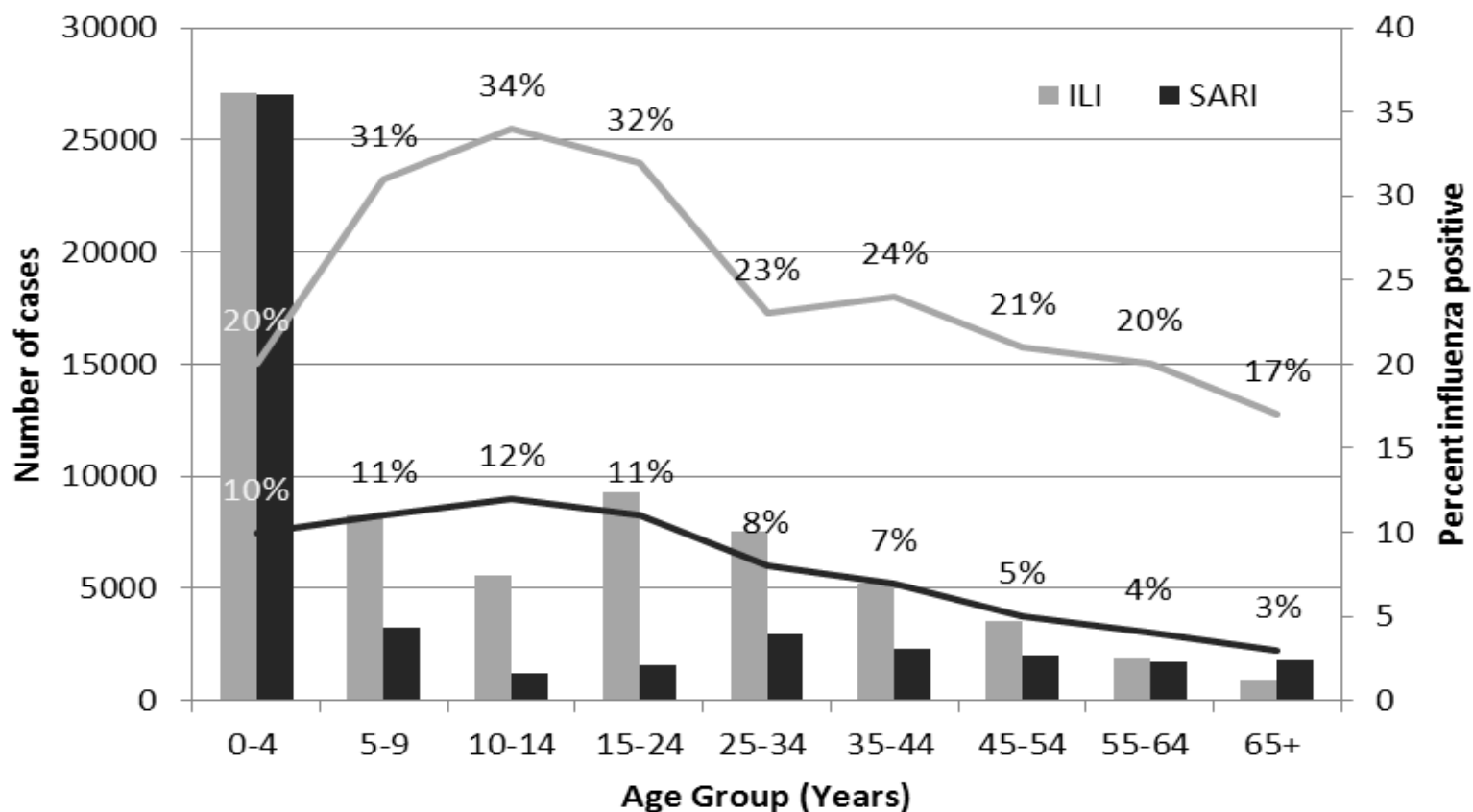
Ahmed, et al. BMC Infectious Diseases 2012, 12:7



African Network of Influenza Surveillance and Epidemiology (ANISE)

Severe Acute Respiratory Disease (SARI)

15 countries, 2006-2010



Elderly persons

- Influenza is a key contributor to mortality in the elderly.
 - They have the highest rate of influenza-associated deaths of any defined high-risk group
- The majority of influenza-associated deaths during seasonal epidemics occur in persons ≥ 65 years
- Elderly at greater risk of hospitalization compared with non-elderly adults
- Limited data indicate that rates of severe disease in elderly in developed countries are substantially higher than similar age groups in industrialized countries



Comparing rates of influenza-related all-cause mortality in different settings (per 100,000 person-years)

Country	>65 years	All Ages	Reference
United States	133	20	Thompson et al*
Hong Kong	136	16	Wong et al†
Singapore	168	15	Chow et al‡
Australia	116	Not done	Newall et al
China, South	151	18	Feng et al**
China, North	75	11	

* Thompson et al JAMA 2003

† Wong et al Clin Infect Dis 2004

‡ Chow et al Emerg Inf Dis 2006

|| Newall et al Epidem Infect 2008

** Feng et al. WHO Bull 2012



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China, North	75	11	
South Africa	545	Not done	Cohen et al§

* Thompson et al JAMA 2003

† Wong et al Clin Infect Dis 2004

‡ Chow et al Emerg Inf Dis 2006

|| Newall et al Epidem Infect 2008

**Feng et al. WHO Bull 2012

§ Cohen et al Clin Infect Dis 2011



Persons with underlying health conditions

- Individuals with specific underlying health conditions are more likely to develop severe or fatal disease due to influenza infection compared with healthy individuals.
 - Even after controlling for age
- Significant proportion of hospitalizations and deaths are among persons with underlying health conditions
 - Proportion increases with increasing severity of outcome (e.g. hospitalizations vs. ICU)
- Risk groups identified during seasonal epidemics and pandemics
- Recently appreciated risk groups include morbid obesity and indigenous populations



Groups of persons with underlying health conditions considered by SAGE WGIV

Respiratory disease

- a. Asthma
- b. Chronic bronchitis and emphysema
- c. Other pulmonary diseases

Cardiac disease

- a. Atherosclerotic heart disease
- b. Cardiomyopathy/chronic congestive heart failure
- c. Congenital heart disease

Neurodevelopmental disorders

- a. cerebral palsy
- b. musculodystrophy
- c. cognitive disorders

Metabolic disorders

- a. Diabetes

Immunocompetency disorders

- a. HIV/AIDS
- b. Chemotherapy
- c. Transplant patients on immunosuppressive agents
- d. Chronic corticosteroid therapy

Chronic renal insufficiency on dialysis

Chronic liver disease especially with cirrhosis.

Morbid obesity

Hematological diseases

- a. Sickle cell anemia
- b. Thalassemia major

Chronic aspirin therapy in children (risk of Reye's syndrome)

Other groups to consider (not necessarily with a chronic illness):

Members of socially disadvantaged minority groups.

Residents of long term care facilities.



Risk Factors for Severe Disease

- UK: 69% of 480 fatal cases with available information had one clinical risk for vaccination.
 - 23% with respiratory disease including asthma
 - 19% with immunosuppression
 - 8 (2%) cases were pregnant
 - 72% of 178 were NOT vaccinated with seasonal vaccine this season



Risk Factors for Severe Outcomes following 2009 Influenza A (H1N1) Infection: A Global Pooled Analysis

PLoS Medicine | July 2011 | Volume 8 | Issue 7 | e1001053

Risk Factor ^a	Severity Level ^b						RR of Severe Disease (IQR) ^c			
	<i>n</i> ^d	Hospitalized Cases	<i>n</i> ^d	ICU-Admitted Cases	<i>n</i> ^d	Fatal Cases	<i>n</i> ^d	RR _{hosp}	<i>n</i> ^d	RR _{death}
Age	14	19.0 (14.8–27.5)	9	42.0 (35.0–45.0)	13	46.0 (37.0–52.0)	— ^e	— ^e		
Gender (percent female)	12	49.8 (46.2–51.5)	11	47.0 (41.9–50.5)	14	44.7 (41.5–48.7)	12	1.0 (0.8–1.1)	14	0.8 (0.7–1.0)
Chronic medical illness										
Respiratory disease	12	10.3 (5.0–21.7)	11	17.2 (10.5–29.9)	16	20.4 (9.3–29.5)	5	3.3 (2.0–5.8)	8	7.8 (4.9–26.6)
Asthma	11	17.6 (10.0–20.4)	9	9.8 (5.6–14.3)	15	5.3 (4.0–10.6)	3	1.8 (1.2–2.6)	6	1.7 (1.5–2.1)
Diabetes	14	9.0 (3.5–12.6)	12	13.6 (9.3–17.3)	17	14.4 (13.0–18.0)	7	0.9 (0.5–1.7)	10	4.0 (3.1–6.9)
Cardiac disease	12	7.1 (3.7–10.9)	11	10.9 (8.8–15.0)	15	12.1 (10.0–16.4)	6	2.0 (1.5–2.2)	8	9.2 (5.4–10.7)
Renal disease	13	4.0 (2.0–5.1)	11	6.3 (3.5–8.4)	16	7.1 (5.0–8.1)	2	4.4 (4.2–4.5)	3	22.7 (21.0–25.4)
Liver disease	9	1.1 (0.3–2.0)	9	2.4 (0.9–5.0)	12	4.9 (2.7–6.0)	3	5.7 (3.2–15.7)	4	17.4 (11.6–28.0)
Neurological disease	11	4.0 (2.5–7.5)	11	7.0 (3.5–9.5)	14	13.9 (5.5–18.4)	2	1.1 (0.9–1.3)	3	13.1 (8.4–32.4)
Immune compromised	13	5.0 (2.0–7.2)	11	6.7 (3.2–18.4)	15	12.5 (7.9–18.4)	2	24.3 (16.1–32.6)	4	27.7 (14.0–66.5)
Cases with ≥1 chronic medical illnesses	14	31.1 (19.0–47.1)	10	52.3 (41.1–58.7)	16	61.8 (48.5–67.9)	NA	NA		
Pregnancy^f										
First trimester	7	2.0 (1.0–3.5)	6	2.0 (1.5–2.5)	5	0.9 (0.0–2.5)				
Second trimester	7	7.0 (3.9–9.3)	7	5.0 (1.7–6.2)	5	2.5 (0.0–14.1)				
Third trimester	7	9.5 (7.6–21.3)	8	8.0 (4.0–14.6)	6	16.9 (5.1–32.0)				
Unknown trimester	8	6.0 (1.9–9.3)	6	2.8 (1.7–3.2)	7	0.0 (0.0–2.1)				
Total (any trimester)	10	17.4 (13.5–30.2)	9	15.0 (9.4–24.2)	11	6.9 (0.0–9.1)	10	6.8 (4.5–12.3)	11	1.9 (0.0–2.6)

Thank you



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