Infection Control in Settings of Respiratory Viruses

Allison McGeer, MSc MD, FRCPC
Mount Sinai Hospital
University of Toronto

Day	Events	Illness
Day 0	Patient admitted to hospital #1 with pneumonia -A	1 CAP
Day 2	Transmission to roommate – dialysis patient – B	
Day 6	Transmission to ICU roommate – C	
Day 6,8	Patient B febrile – dialysis unit transmission to D,E,F,G,H,I	1 febrile dialysis pt
Day 10/11	P	1 VAP
Day 11	P P	1 pneumonia, dialysis pt
Day 15	ICU pt (J) repatriated to hospital #2 – transmits to pts (N,O) Patients D-I transmit to 3 dialysis patient (P,Q,R)	fever in ICU pt
Day 16/17	Patients D-H admitted to hospital – transmission to hospital visitor (S) , family member (T), nurse (U)	
Day 17	Patients D and E criticalled to hospital #3 ICU - transmission to intubating MD (V)	Dialysis cluster
Day 18	Hospital #1 recognizes cluster of dialysis patients with pneumonia (5 admitted over weekend)	Dialysis cluster recognized
Day 18	Family member (L) admitted to hospital #4	

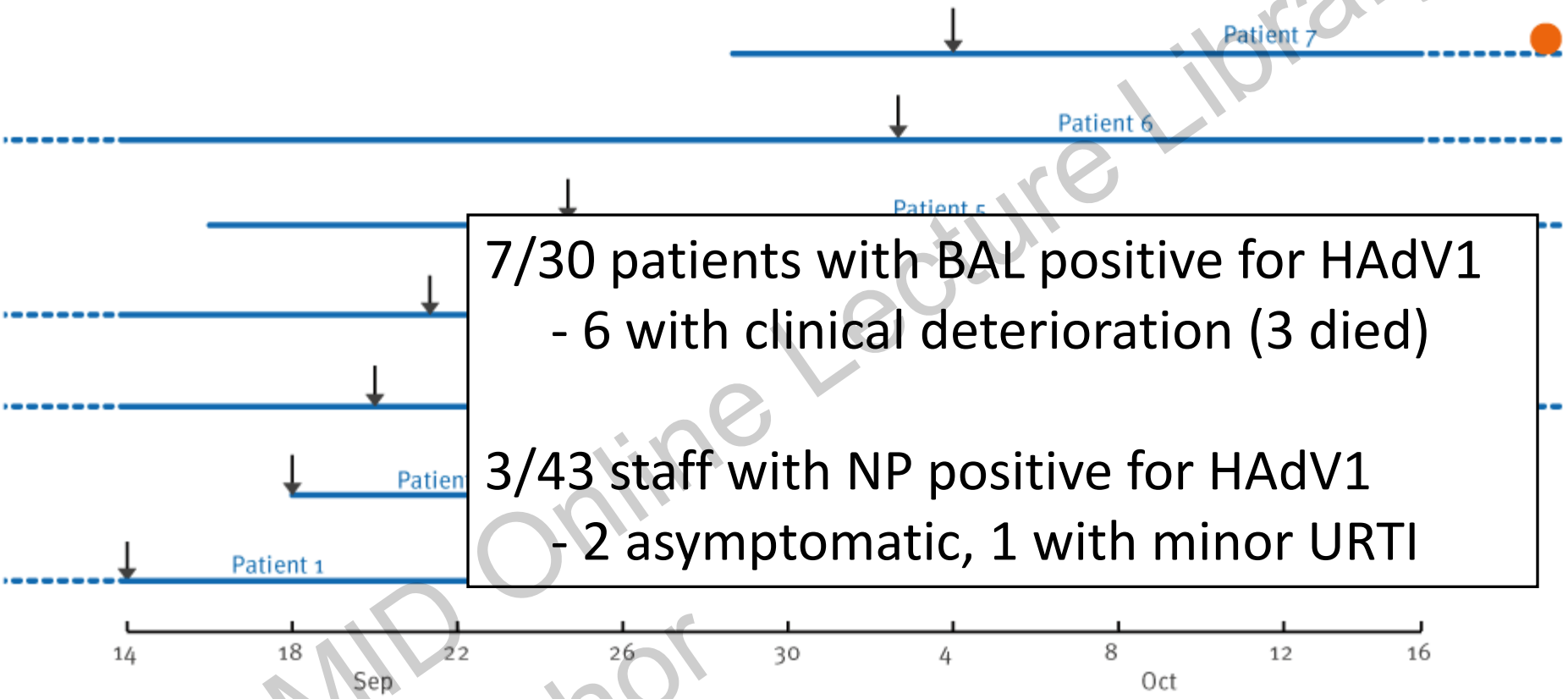
18 days: 22 patients (3 HCWs)
4 hospitals

Epidemiology of respiratory viruses in healthcare institutions

- Infection is equal opportunity (patients, staff, visitors)
  - Severity of illness is patients>>>>visitors

FIGURE

Timeline of diagnosis and outcomes for patients with human adenovirus type 1 severe pneumonia during their stay in the intensive care unit, human adenovirus type 1 outbreak, Marseille, France, September–October 2012 (n=7)



7/30 patients with BAL positive for HAdV1
- 6 with clinical deterioration (3 died)

3/43 staff with NP positive for HAdV1
- 2 asymptomatic, 1 with minor URTI

Cassir Eurosurv 2014;19(39)

Case fatality in SARS outbreak, 2003

Hong Kong

Category	CFR
Non-HCW	21.8%
HCW	2%

Toronto (index hospital)

	CFR
Hospital/ED patients	50%
HCW	0

Singapore

Category	CFR
Non-HCW	11%
HCW	5%

Epidemiology of respiratory viruses in healthcare institutions

- Infection is equal opportunity (patients, staff, visitors)
  - Severity of illness is patients>>>>visitors
- Transmission is heterogeneous

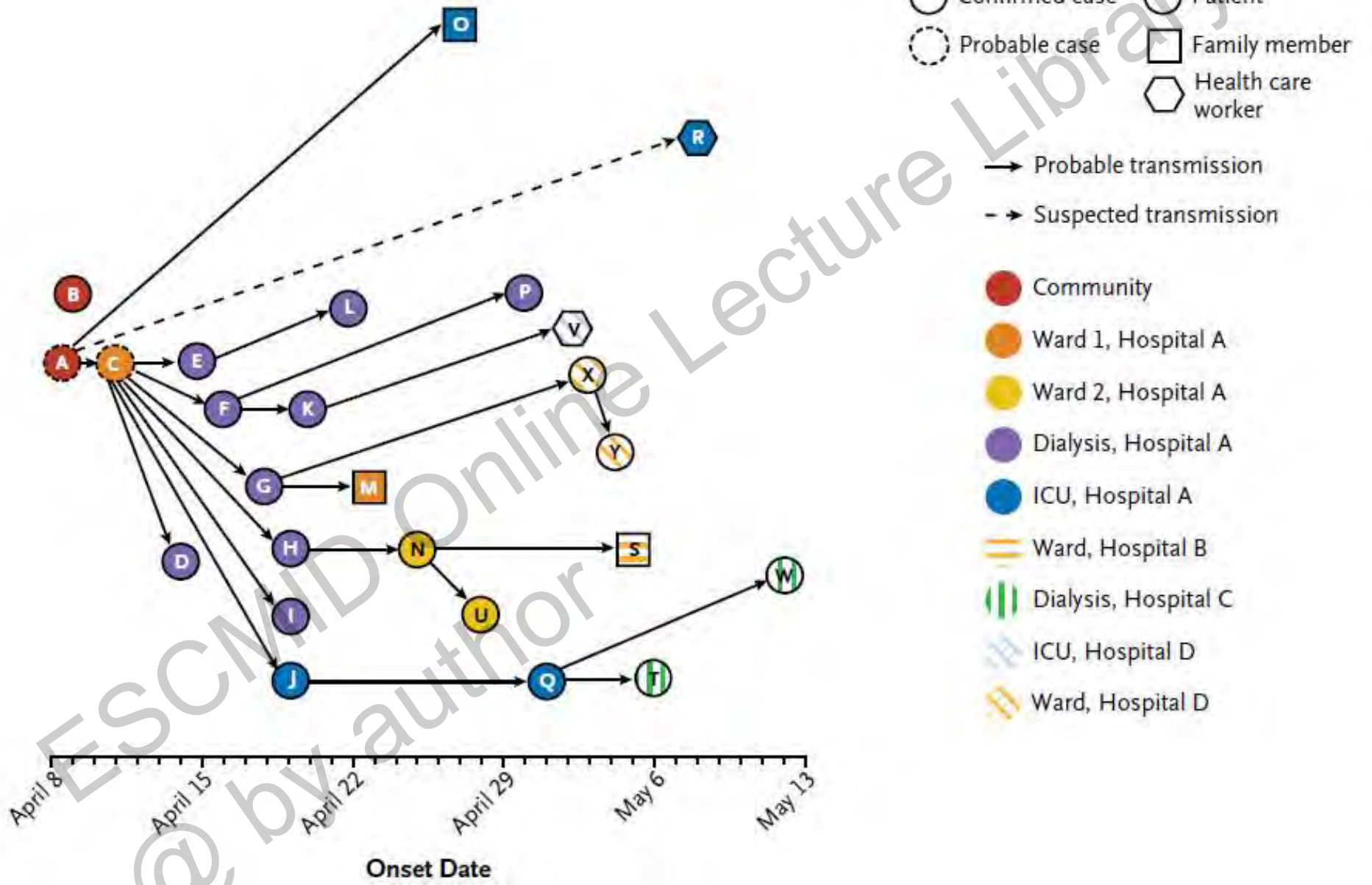
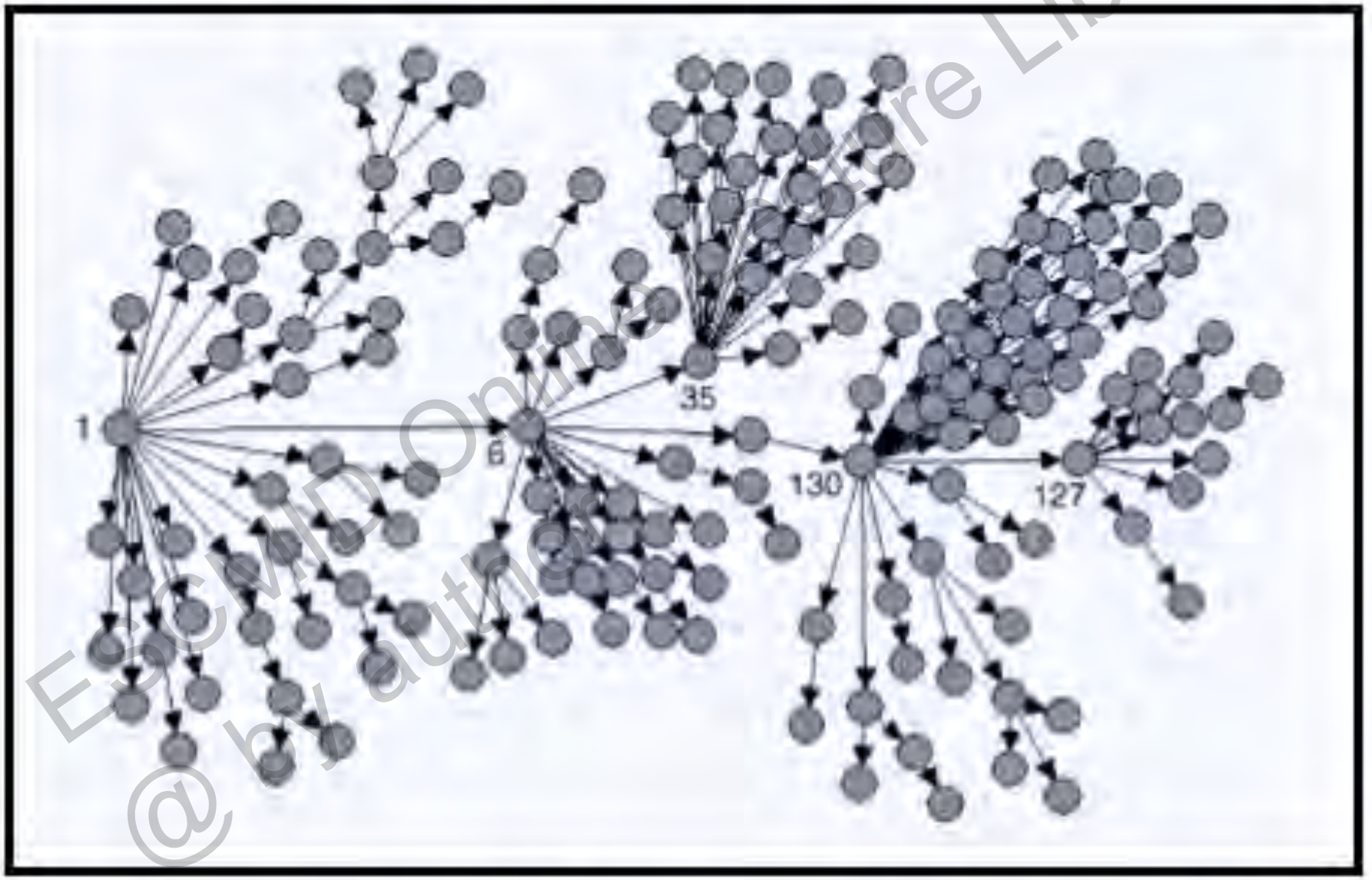


FIGURE 2. Probable cases of severe acute respiratory syndrome, by reported source of infection* — Singapore, February 25–April 30, 2003



What contributed to superspreading events (SSE) in SARS?

- 127 wards in 26 hospitals in HK/Guangzhou
  - Included all wards with at least one case of SARS
  - Pediatric wards, and designated SARS wards excluded
- SSE= ≥3 new cases occurring within 8 days on one ward
- Data collection: host, administrative and environmental factors

Sung HK Med J 2009;15(Suppl 8):S29

Factors associated with SSEs SARS, HK, 2003

Factor	OR (95% CL)
≤1m between beds	6.9 (1.7-29)
Presence of washing/changing facilities for staff	0.12 (0.02-0.97)
Staff working with symptoms	10.6 (2.3-49)
Performance of resuscitation	3.8 (1.0-14)
Resorting to oxygen therapy	4.3 (1.0-18)
Use of BIPAP	12 (2.0-71)

Sung HK Med J 2009;15(Suppl 8):S29

Epidemiology of respiratory viruses in healthcare institutions

- Infection is equal opportunity (patients, staff, visitors)
  - Severity of illness is patients>>>>visitors
- Transmission is heterogeneous
  - ~20% of patients responsible for 70-75% of transmission
- Distribution of mechanisms of transmission is not known, and likely differs between viruses

Modes of transmission of respiratory viruses

Direct contact with droplets

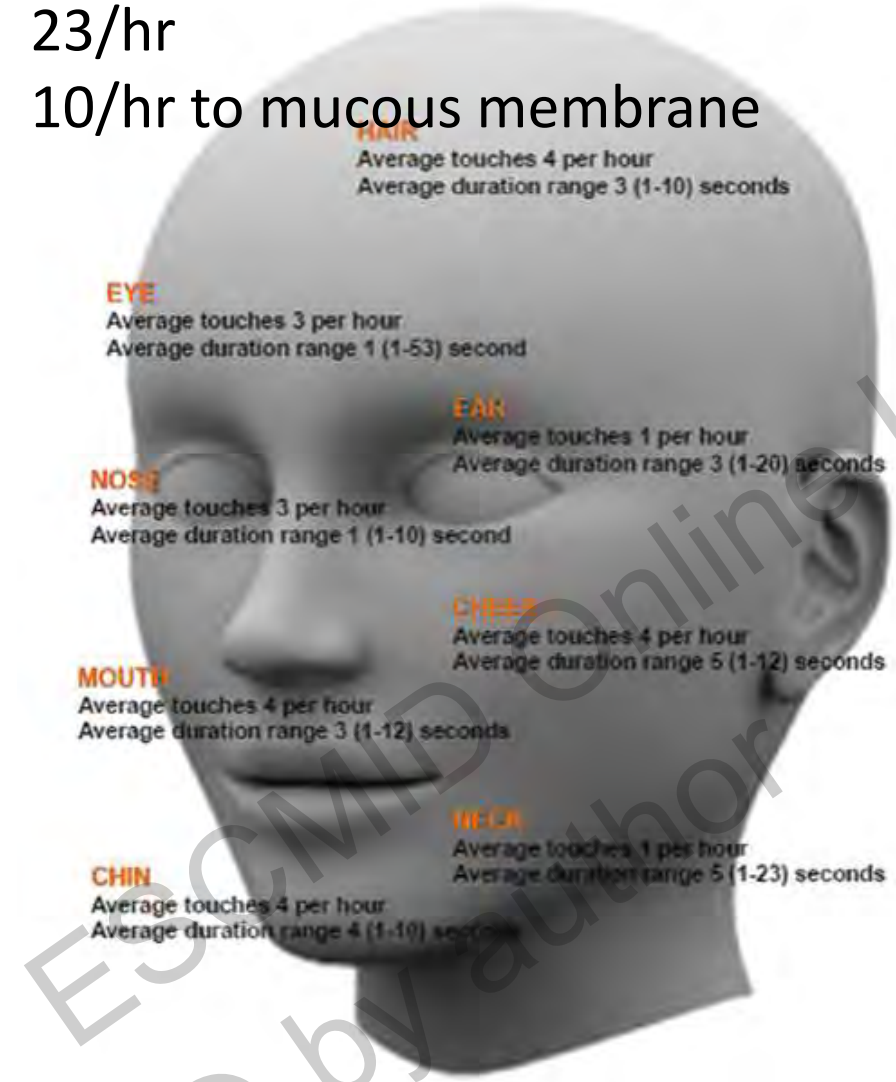
Inhale small particles

Droplet deposition on to hands or fomites

Hands to face

Medical students listening to 2 hr IPC lecture

- 23/hr
- 10/hr to mucous membrane



Kwok AJIC 2015;43:112

Students working alone in office cubicle x 3 hrs

- 15.7/hr to mucous membrane

Nicas JOEH 2008;5:347

Family medicine workers x 2 hrs

- 9.5/hr to mucous membrane
  - 5 MD/NP
  - 8 nurses
  - 16 other staff

Elder JABFM 214;27:339

Transmission of RSV

Volunteers	*Cuddlers**	*Touchers†*	*Sitters‡*
No. exposed	7	10	14
No infected	5	4	0
Afebrile URI§	3	3	–
Febrile URI	2	0	–
Asymptomatic	0	1	–
Incubation	4 days	5.5 days	

Sitters: sat >6 feet away from children; no touching
Touchers: touched surfaces in room when children were away, then self-inoculated eyes and nose
Cuddlers: cared for infants fro 2-4 hours, including feeding, diapering, playing

Breese Hall J Peds 1981;99:100

Rhinoviruses

- Recovered from the hands of 40% of infected persons from a single sampling
  - Only found in saliva in 50% infected person
- Only 2/25 with positive cultures from coughs or sneezes into petri dishes
- No rhinovirus recovered in small particle aerosols
- Transfer hand to hand occurred in 20 of 28 10 second exposures
  - Then touching eyes/nose resulted in infection 8/9 times
- 1 in 12 susceptibles infected across table

Gwaltney Trans Am Clin Climatol Assoc. 1978;89:194-200

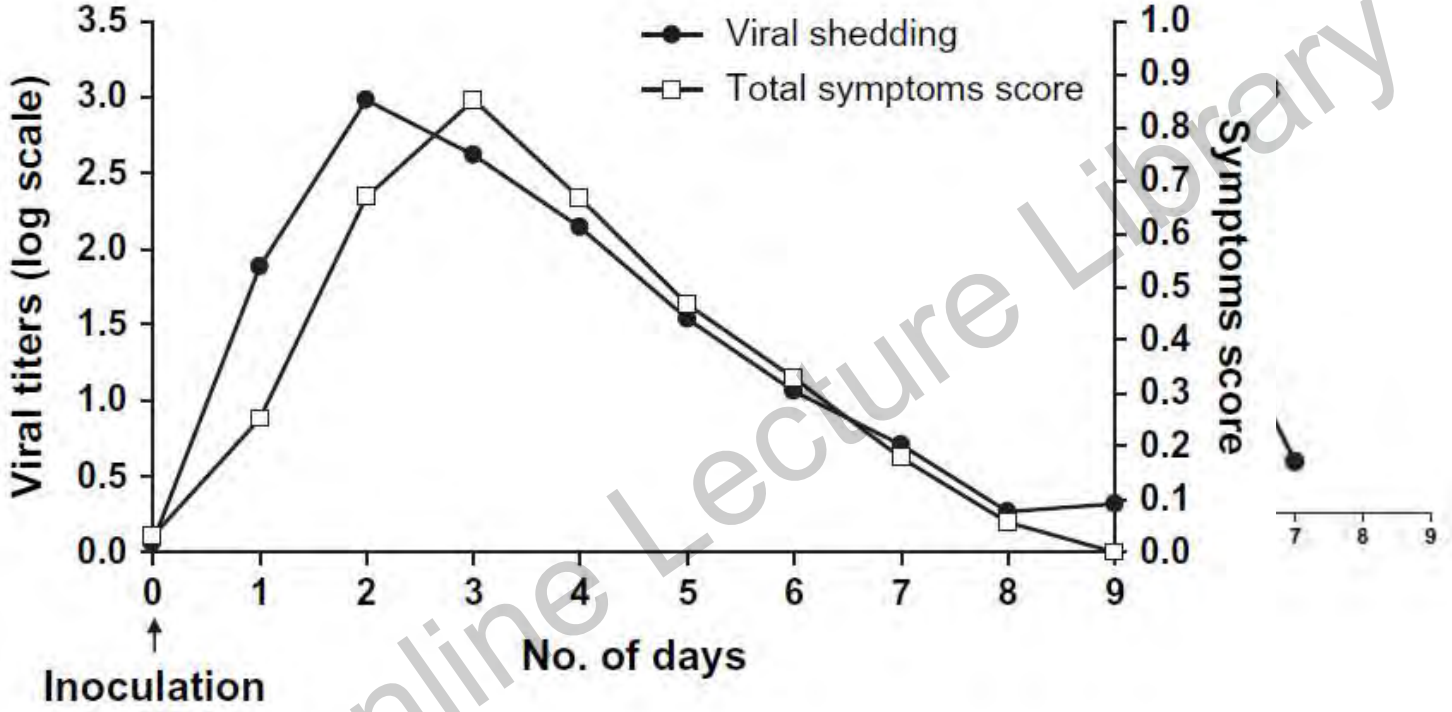
Influenza

- Recovered from:
  - 17% (PCR) and 1% (culture) from hands of infected children
  - 4/6 (PCR) hands of adult inpatients
- 7 of 9 with positive PCR from coughing into petri dishes
- Virus survival on hands measured in minutes
- Virus detectable in 2/21 (by culture) and 26/61 (by PCR) aerosols from infected patients
- Majority of exhaled influenza virus is in particles in the respirable range
  - 8.8 more in particles ≤5 vs. >5µm; 65% in particles <5µm; 89% in particles <5µm

Simmerman CID 2010;51:1053; Lindsley PLoS One 2010;5:315100; Johnson CID 2009;49:275
Milton PLoS Pathogens 2013:e1003205Bischoff JID 2013;207:1037.; Macias JHI2009;73:280

Epidemiology of respiratory viruses in healthcare institutions

- Infection is equal opportunity (patients, staff, visitors)
  - Severity of illness is patients>>>>visitors
- Transmission is heterogeneous
  - ~20% of patients responsible for 70-75% of transmission
- Distribution of mechanisms of transmission is not known, and likely differs between viruses
- Viral shedding patterns differ for MERS and SARS

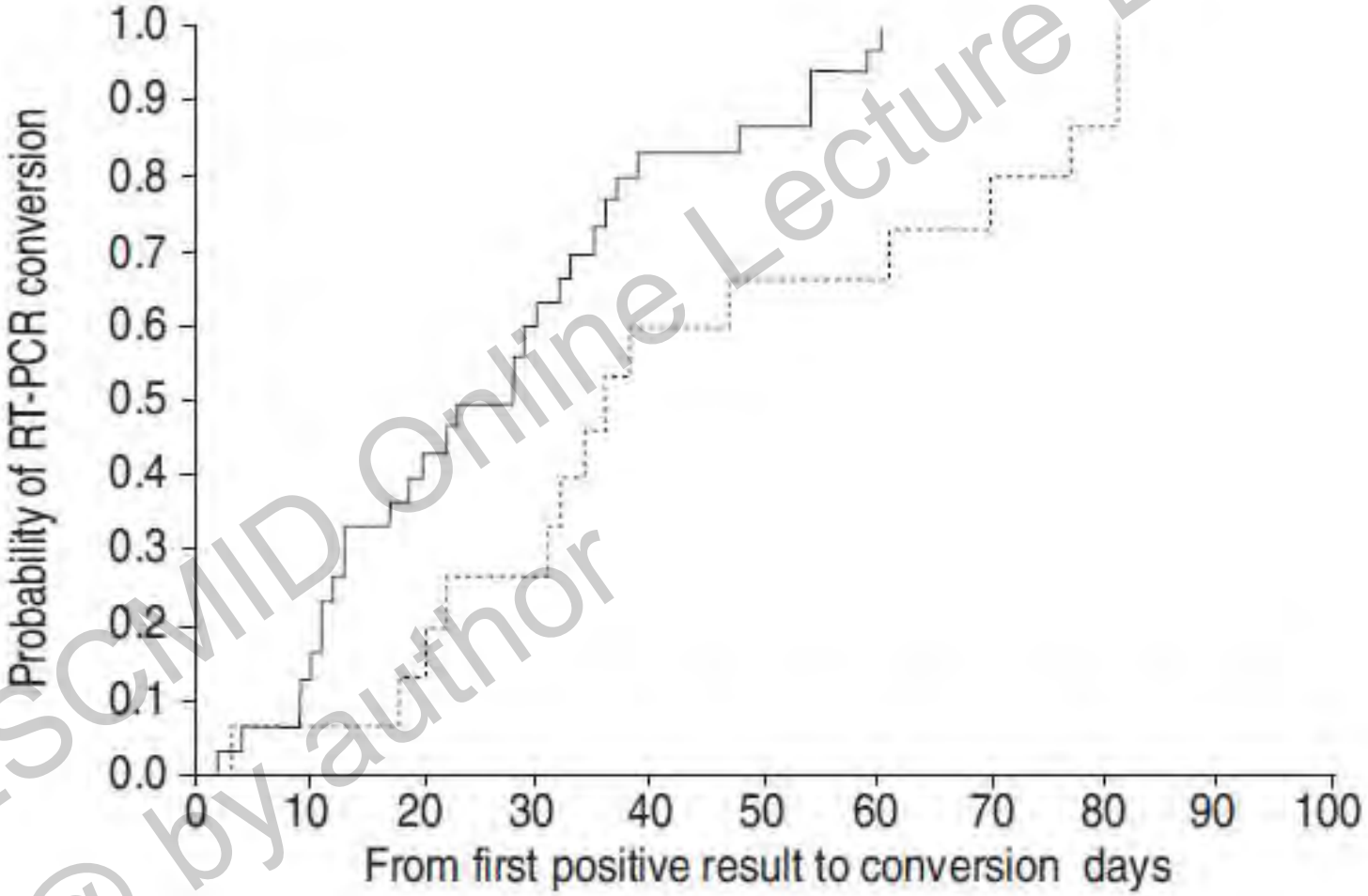


Viral shedding:

- Significant prior to symptoms
- Peaks early in illness
- Higher with more severe symptoms
- Self-limited (ex. severe IS/neonate)
- Limited to respiratory tract

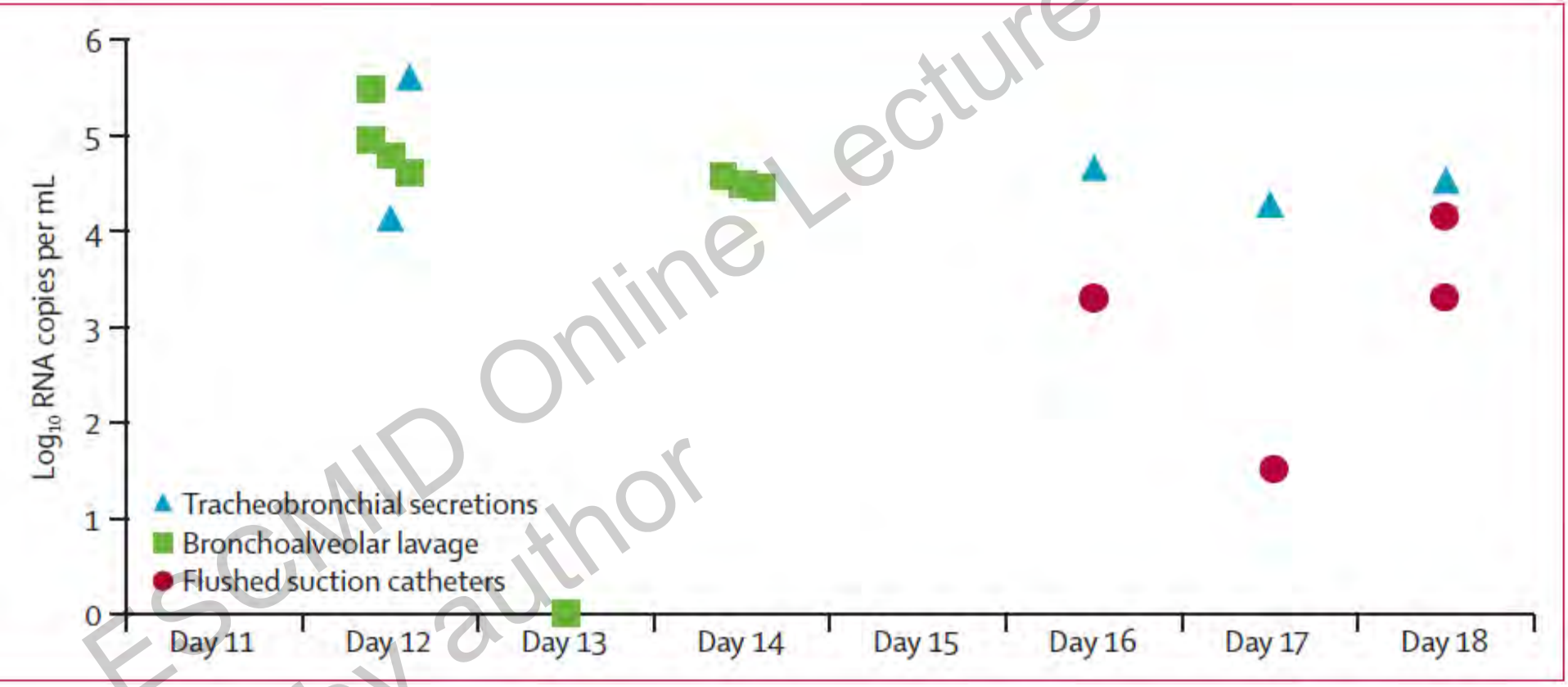
Carrat

Time to first negative PCR for SARs in NP by whether urine PCR for SAS positive



Chu ERJ 2005;25:12

Viral load in the respiratory tract of a patient with MERS CoV



Drosten Lancet ID 2013;13:745

Viral load/shedding during illness

Non MERS/SARS

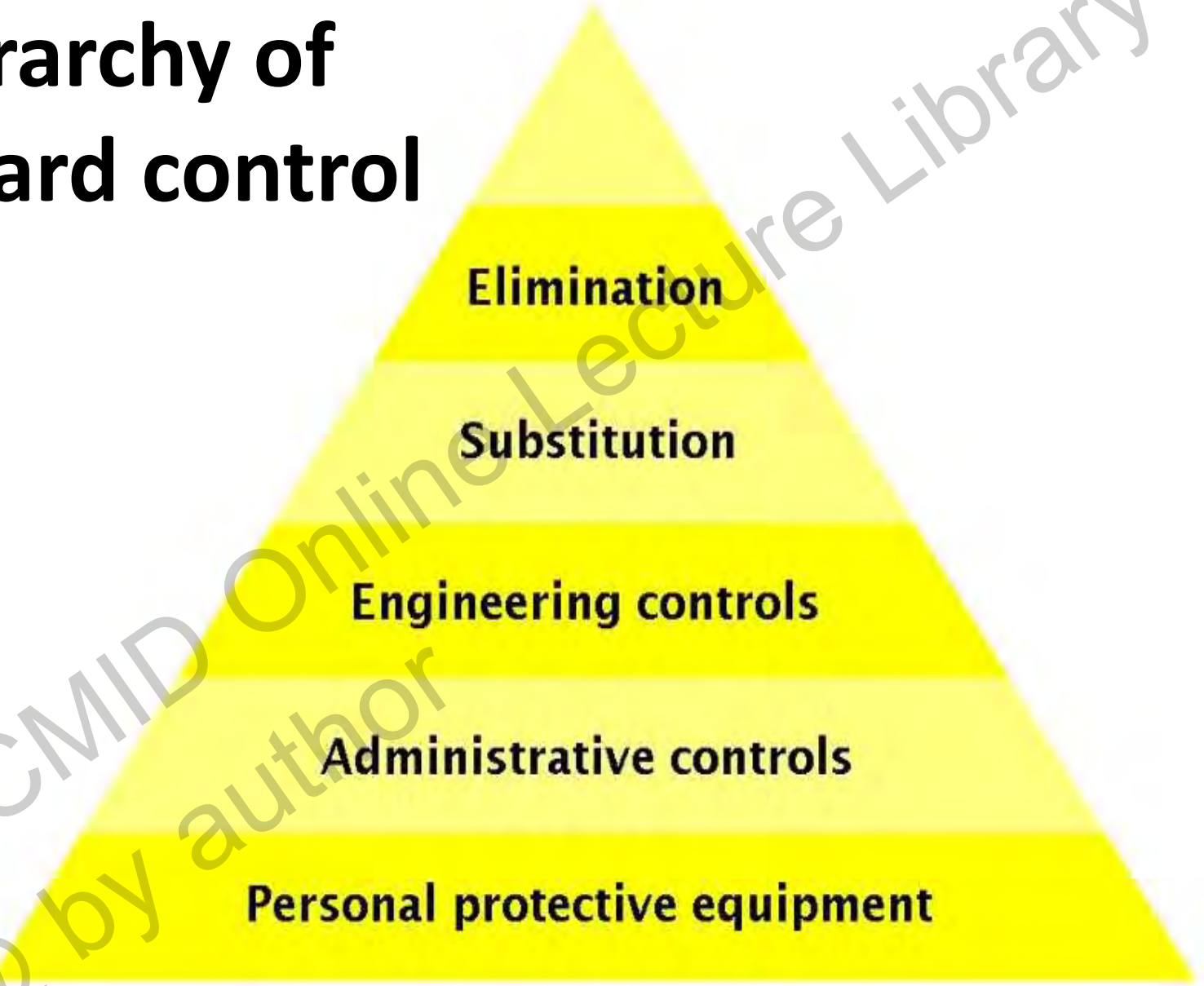
- Significant prior to symptoms
- Peaks early in illness

- Higher with more severe symptoms
- Self-limited (ex. severe IS/neonate)
- Limited to respiratory tract

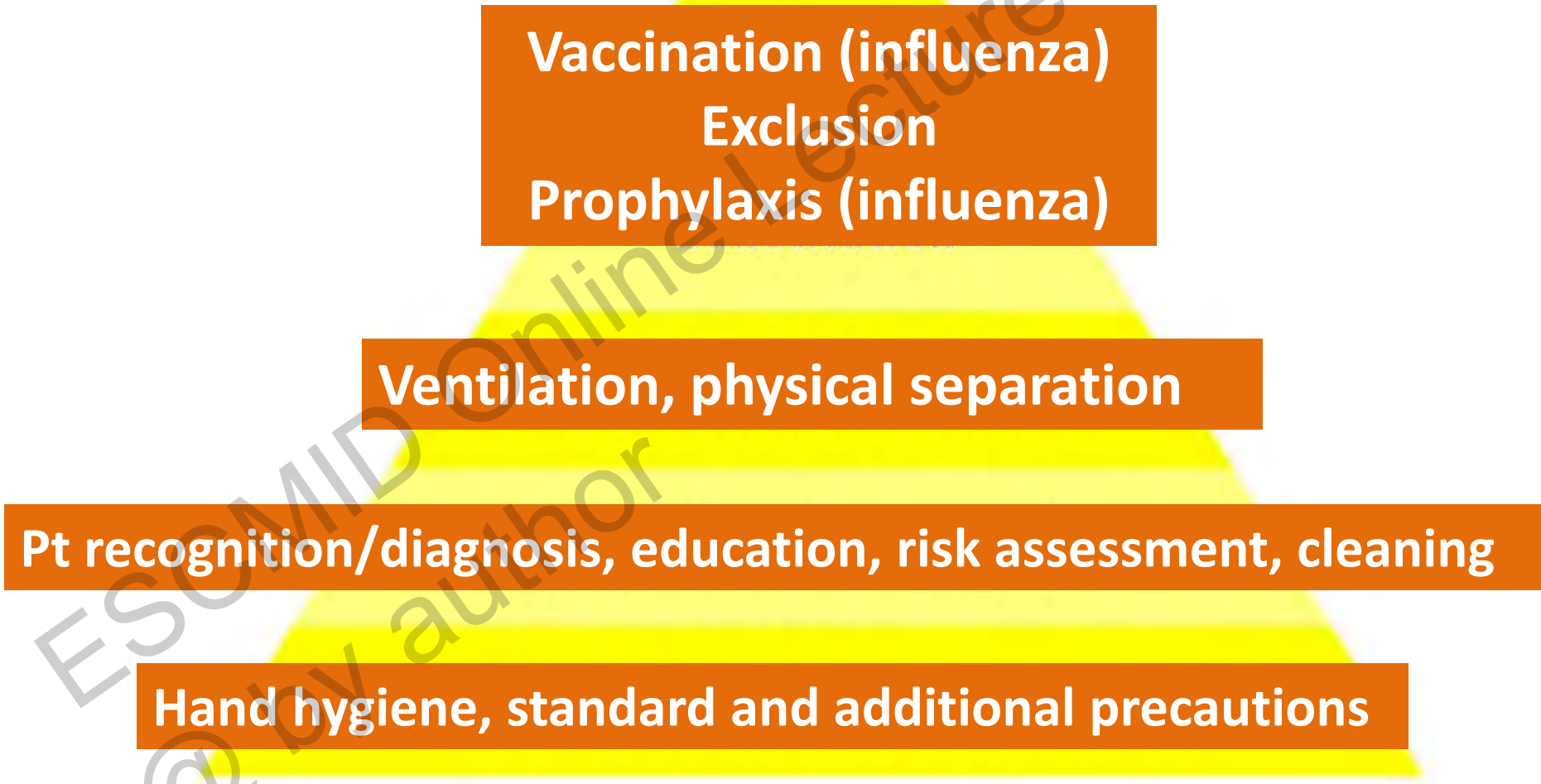
MERS/SARS

- **Low prior to symptoms**
- **Increases/persists during illness**
- Higher with more severe symptoms
- Self-limited **but prolonged**
- **Widespread viral shedding (stool, urine, kidney, liver**

Hierarchy of hazard control

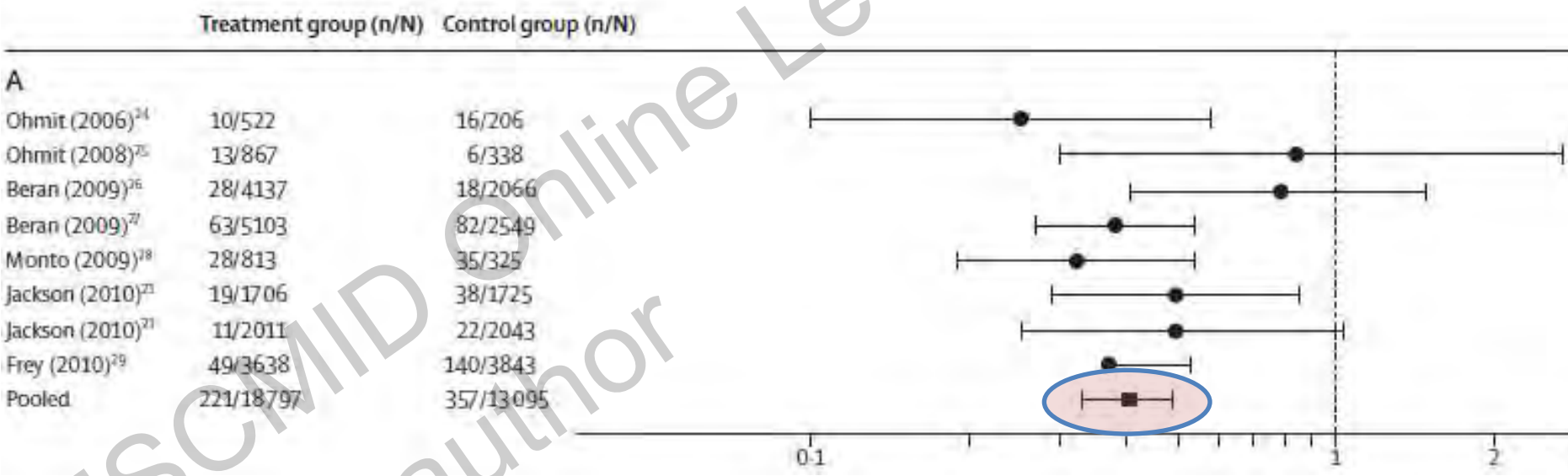


Hierarchy of hazard control



Efficacy of influenza vaccine healthy adults

- 59% reduction in PCR confirmed, symptomatic influenza infection



  - "breakthrough" illness less severe

Osterholm Lancet ID 2012;12:36

Outcomes associated with influenza vaccination of HCWs, meta-analyses of RCTs in long term/chronic care

		Cochrane review	CDC review
Outcome	**No. Pts**	**Adjusted pooled OR (95% CL)**	**Adjusted pooled OR (95% CL)**
Mortality	8468	0.68 (0.55, 0.84)*	0.71 (0.59, 0.85)*
Influenza-like illness (ILI)	7031	0.71 (0.58, 0.88)*	0.58 (0.46, 0,73)*
GP consult for ILI	2572	0.48 (0.33, 0.69)*	
Death from ILI	2572	0.72 ().31, 1.70)	
Lab confirmed influenza	752	0.87 (0.38, 1.99)	0.80 (0.31, 2,1)
Pneumonia	1059	0.71 (0.29, 1.71)	
Deaths from pneumonia	4459	0.87 (0.47, 1.64)	
Hospital admission	5972	0.90 (0.66, 1.21)	0.90 (0.69, 1,2)

*=statistically significant result

Additional data

- PRO vaccine effect:
  - Carman (Lancet 2000)
    - As HCW vaccination rates increased, patient mortality decreased
  - Hayward (BMJ 2006)
    - Effect of reduced mortality was shown ONLY during influenza season, and ONLY during year with active influenza
- CON vaccine effect
  - In Potter and Lemaitre, reduction in mortality appeared to precede influenza season

Risk factors for hospital acquired influenza

Characteristic	Adjusted OR (95% CI)
Age, per year older	1.03 (0.99-1.07)
Influenza source (patient or HCW) on unit	5.22 (1.08-25.2)
Proportion of HCW vaccinated above median (35%)	0.07 (0.005-0.98)

Benet BMCID 2012;12:30

Cluster randomized trial of hospital HCW vaccination

	Control	Intervention	P value
Percent HCWs vaccinated	17.8%	28.6%	<.001
Influenza or pneumonia during hospitalization			
Adults	9.6%	3.9%	0.015
Children	1.9%	3.6%	0.19
Pneumonia during hospitalization	8.5%	1.4%	0.03
Adults	1.1%	1.3%	0.65
Children			

Riphagen-Dalhuisen et al. Eurosurveillance 2013;18(26)

Work exclusion

- 36% reduction in self-reported ILI among individuals who could work from home; 28% reduction in those who could stay home from work for 7-10 days
- Quasi cRCT: workplace policy enabling remaining home on full pay reduced employee risk of pH1N1 (OR 0.8, 05% CL 0.66-0.97)
- Teleworking arrangements reduced number of employees working with severe ILI by 30%

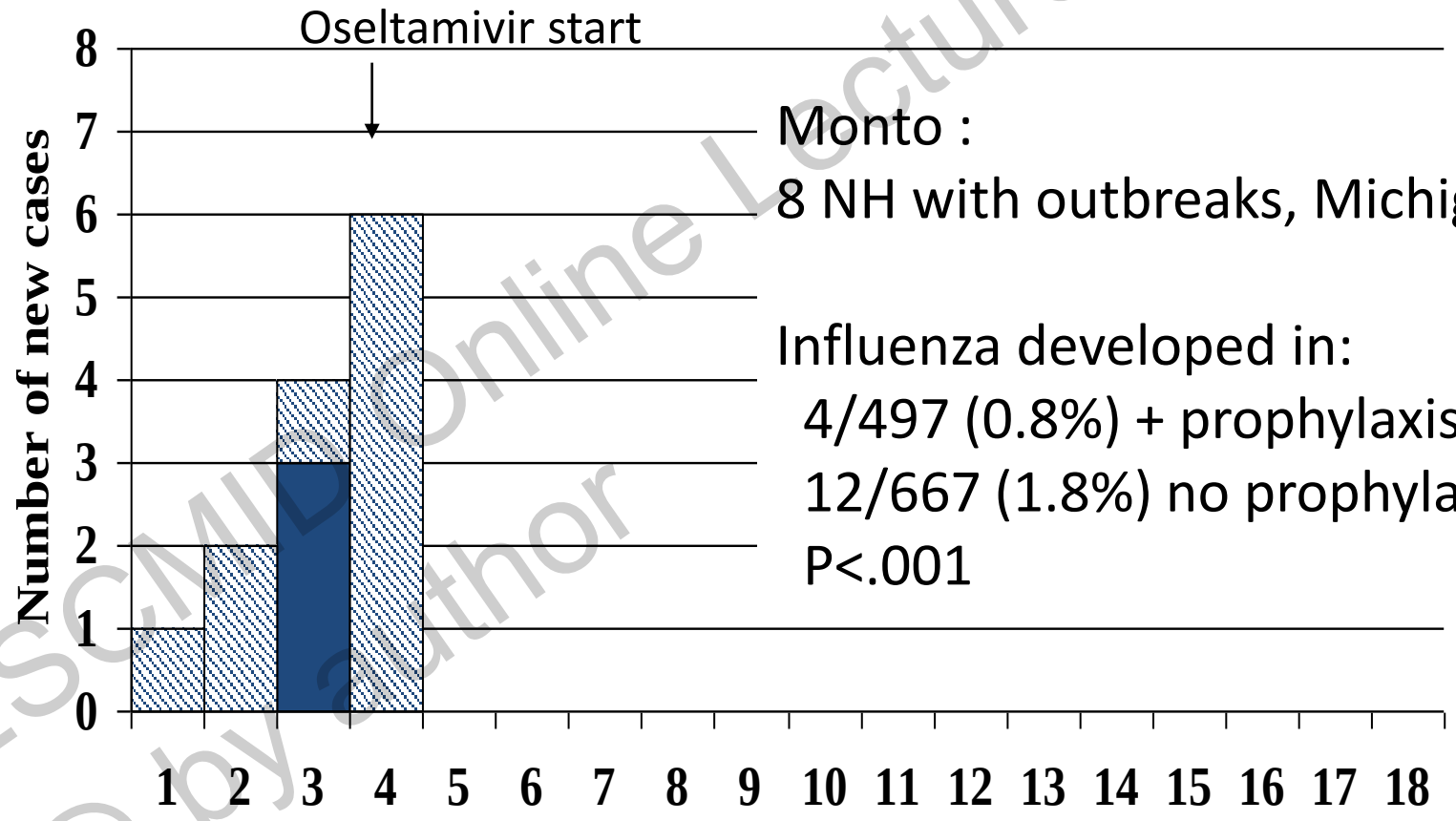
Kumar AJPH 2012;102:134; Miyaki JOH 2011;53:287; Rousculp JOEM 2010;52:1009-13
Rashid PedRespRev 2015;16:119

Working while ill

- During the 2009 pandemic, only27 (6.4%) of 423 students and 5 (8.6%) of 58 faculty with ARI reported staying home while ill
- Among on-duty HCWs, 35/119 symptomatic and 7-200 asymptomatic workers were shedding respiratory viruses
  - 47% of nurses and 80% physicians reported working with ILI
- 60% of HCWs reported not taking sick leave during ILI

Mitchell CID 2011 ;52:S138; Esbenshade ICHE 2013;34:373; Turnberg AJIC 2010;38:486.

Oseltamivir compassionate use program, Ontario, 2000 (outbreak B4)



Monto :
8 NH with outbreaks, Michigan

Influenza developed in:
4/497 (0.8%) + prophylaxis
12/667 (1.8%) no prophylaxis
P<.001

Bowles, JAGS 2002

“Exclusion” versus prophylaxis

- Continuous universal school closure was less cost-effective than stockpiling antiviral drugs or pre-pandemic vaccines
  - School closure 14-21 x more costly for equivalent morbidity and mortality benefits

Sander Value Health 2009; 12:226

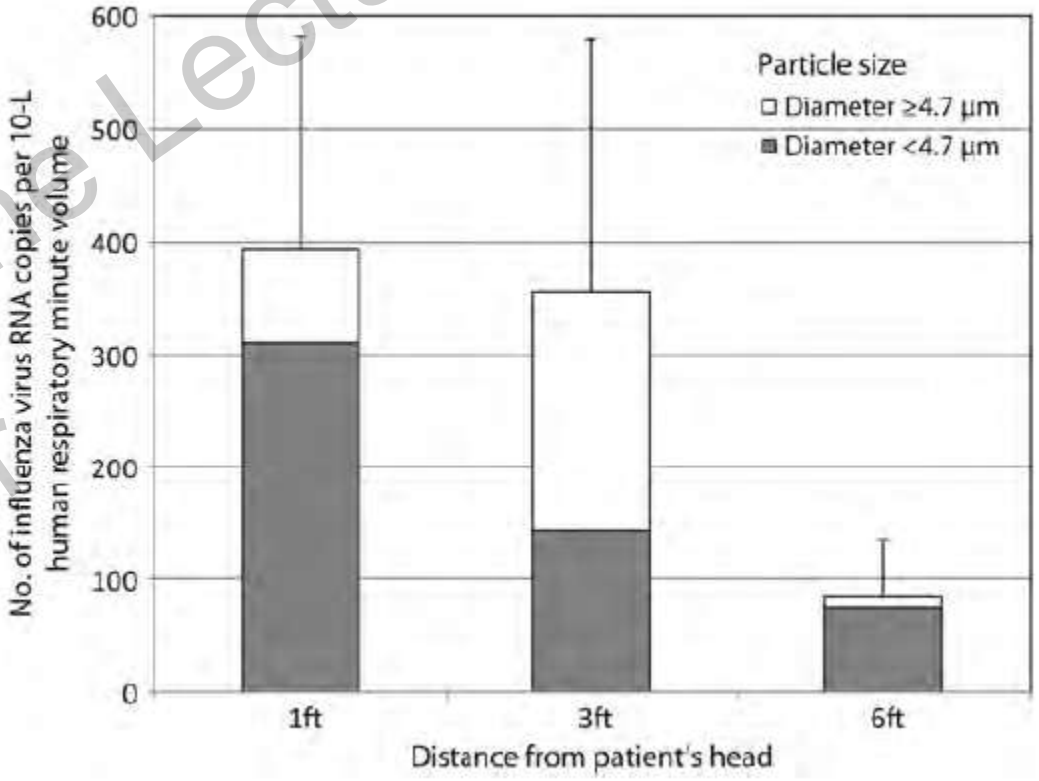
Engineering

"There is strong and sufficient evidence to demonstrate the association between ventilation, air movements in buildings and the transmission/spread of infectious disease such as measles, tuberculosis, chickenpox, influenza, smallpox and SARS."

Li Indoor Air 2007;17:2

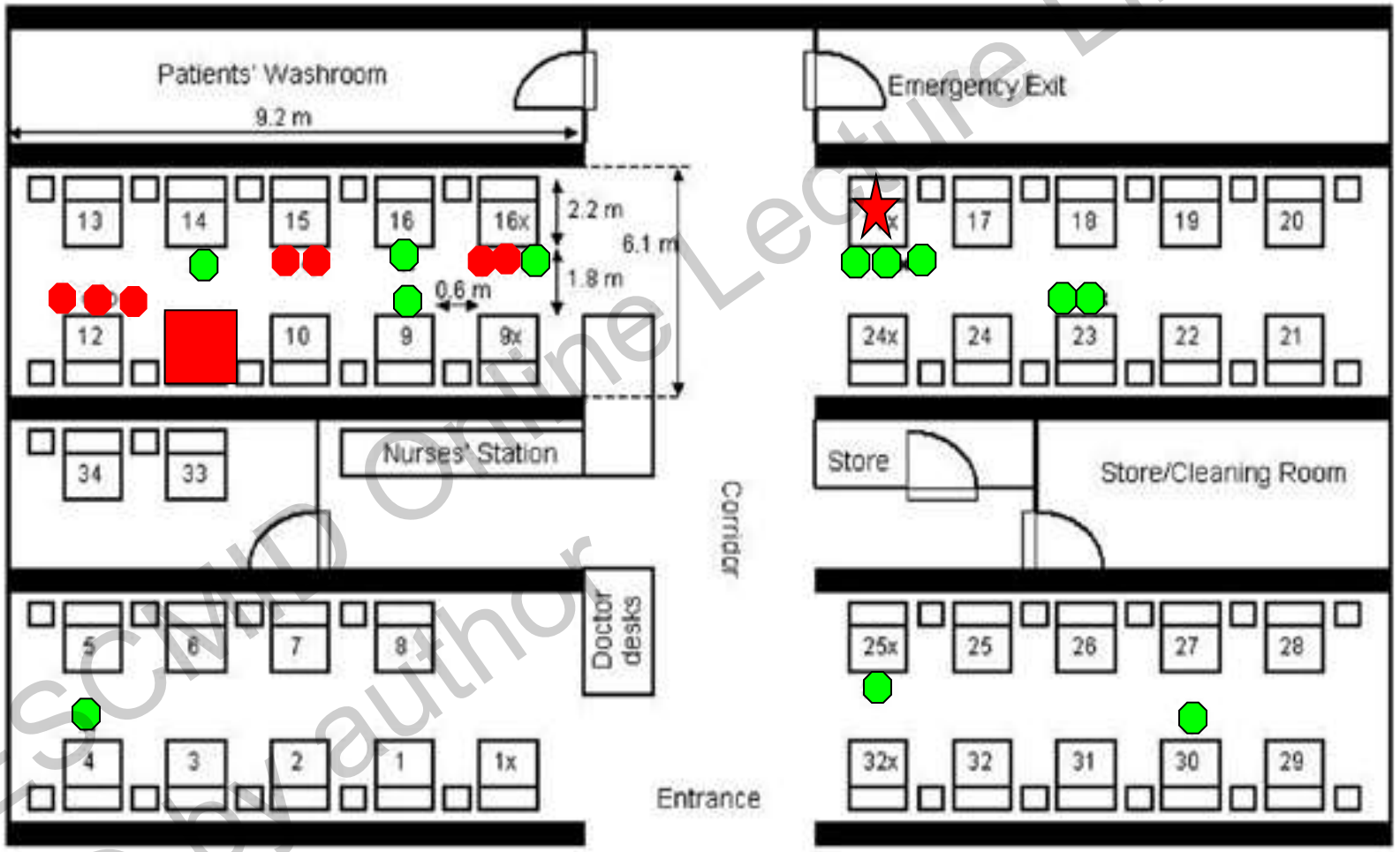
Physical separation

- Evidence of reduced acquisition of both GAS and *N. meningiti*
  >1m feet apart
- RSV and influenz
  detected at >2m
- SARS SSE less fre

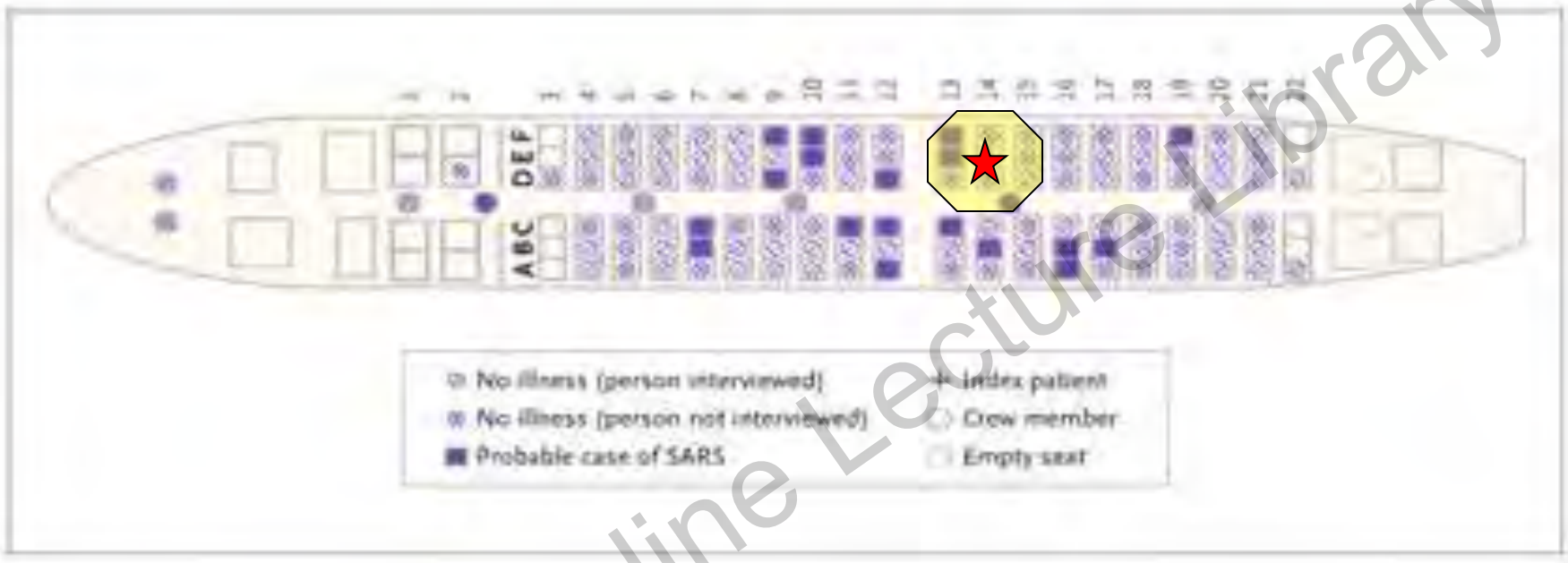


New Engl J Med 1982;307:1255-7; Am J Med 1948;4:690; Sung HK Med 2009;15(Suppl 8):S29;

SARS in medical students exposed to a single unrecognized patient, Hong Kong



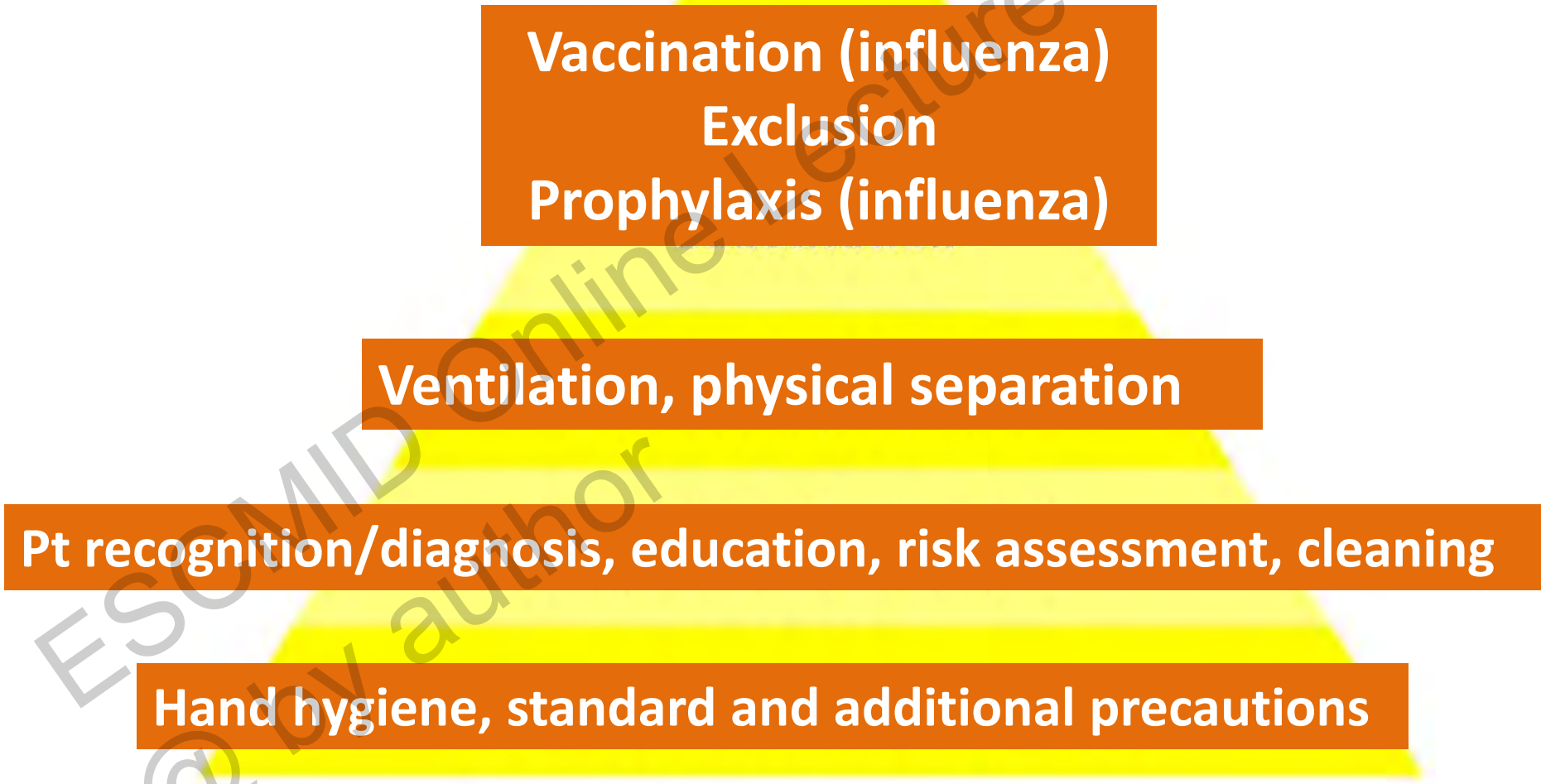
Wong, EID Feb2004 http://www.cdc.gov/ncidod/EID/vol10no2/03-0452.htm



Increased risk associated with sitting closer
BUT 90% of infected not within 3 feet

Olsen NEJM 2003:349:2416

Hierarchy of hazard control



Cohort studies of factors associated with SARS transmission despite precautions

	Infection control education	P value
Lau	(<2 hrs) 0.47	0.1
	(>=2 hrs) 0.03	<.001
Shigayeva	0.27	0.03

Cleaning

- Single case/control study from in community in Hong Kong
- In multivariable analysis, OR for SARS-CoV infection associated with “thorough disinfection of living quarters” 0.41 (95% CL 0.29-0.58)

Lau 2004

Hand hygiene

- 6/8 trials of interventions to increase hand hygiene in schools or households found significant reductions (10-50%) in ARI/ILI

- 5/7 case control studies of SARS found that adherence to hand hygiene was associated with a reduced risk of infection (pooled OR 0.54, 95% CL 0.44-0.67)

Jefferson Cochrane 2011: CD006207. DOI: 10.1002/14651858

Effect of hand hygiene on influenza transmission in the community

Study or Subgroup	Hand hygiene Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Hand hygiene only							
Cowling BJ (2008)	5	84	12	205	4.0%	1.02 [0.37, 2.80]	2008
Cowling BJ (2009)	14	257	28	279	10.7%	0.54 [0.29, 1.01]	2009
Larson EL (2010)	31	946	26	904	15.5%	1.14 [0.68, 1.90]	2010
Stebbins S (2011)	51	1695	53	1665	28.5%	0.95 [0.65, 1.38]	2011
Subtotal (95% CI)		**2982**		**3053**	**58.6%**	**0.90 [0.67, 1.20]**	
Total events	101		119				

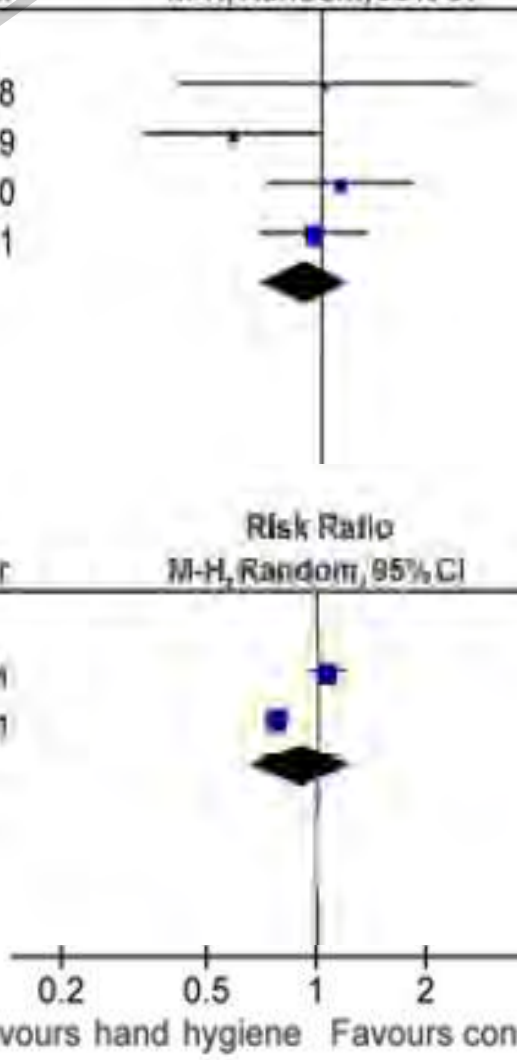
Heterogeneity: $\tau^2 = 0.01$; $\chi^2 = 3.50$, D.F. = 3 ($P = 0.32$); $I^2 = 14\%$

Test for overall effect: $Z = 0.73$ ($P = 0.47$)

Study or Subgroup	Hand hygiene Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Hand hygiene only							
Simmerman JM (2011)	66	292	58	302	32.8%	1.18 [0.86, 1.61]	2011
Talaat M (2011)	125	20882	281	23596	34.4%	0.50 [0.41, 0.62]	2011
Subtotal (95% CI)		**21174**		**23898**	**67.2%**	**0.76 [0.33, 1.77]**	
Total events	191		339				

Heterogeneity: $Tau^2 = 0.35$; $Chi^2 = 19.80$, $df = 1$ ($P < 0.00001$); $I^2 = 95\%$

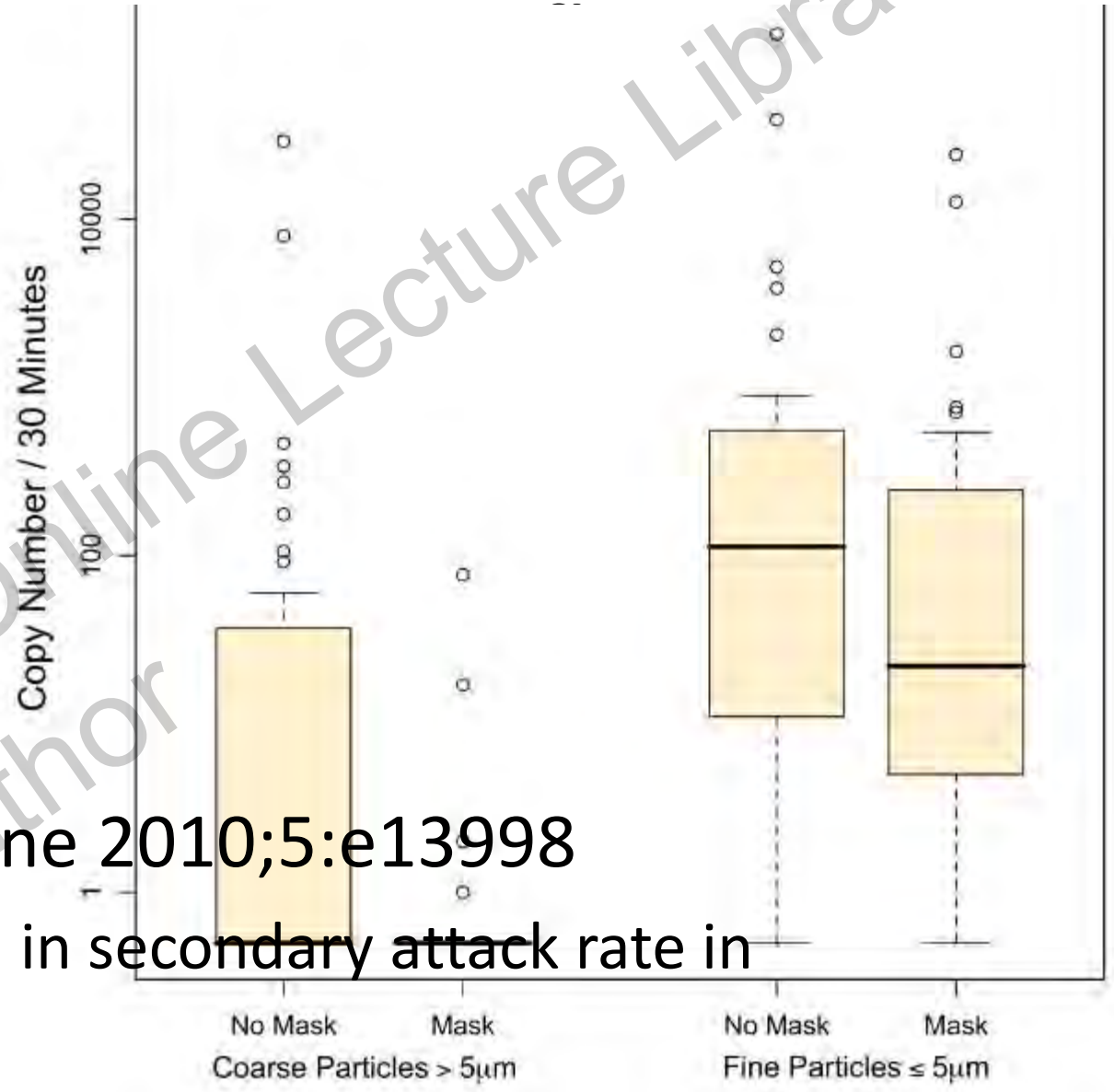
Test for overall effect: $Z = 0.68$ ($P = 0.53$)



Wong Epidemiol Infect 2014;142:922

Do masks worn by infected persons reduce e

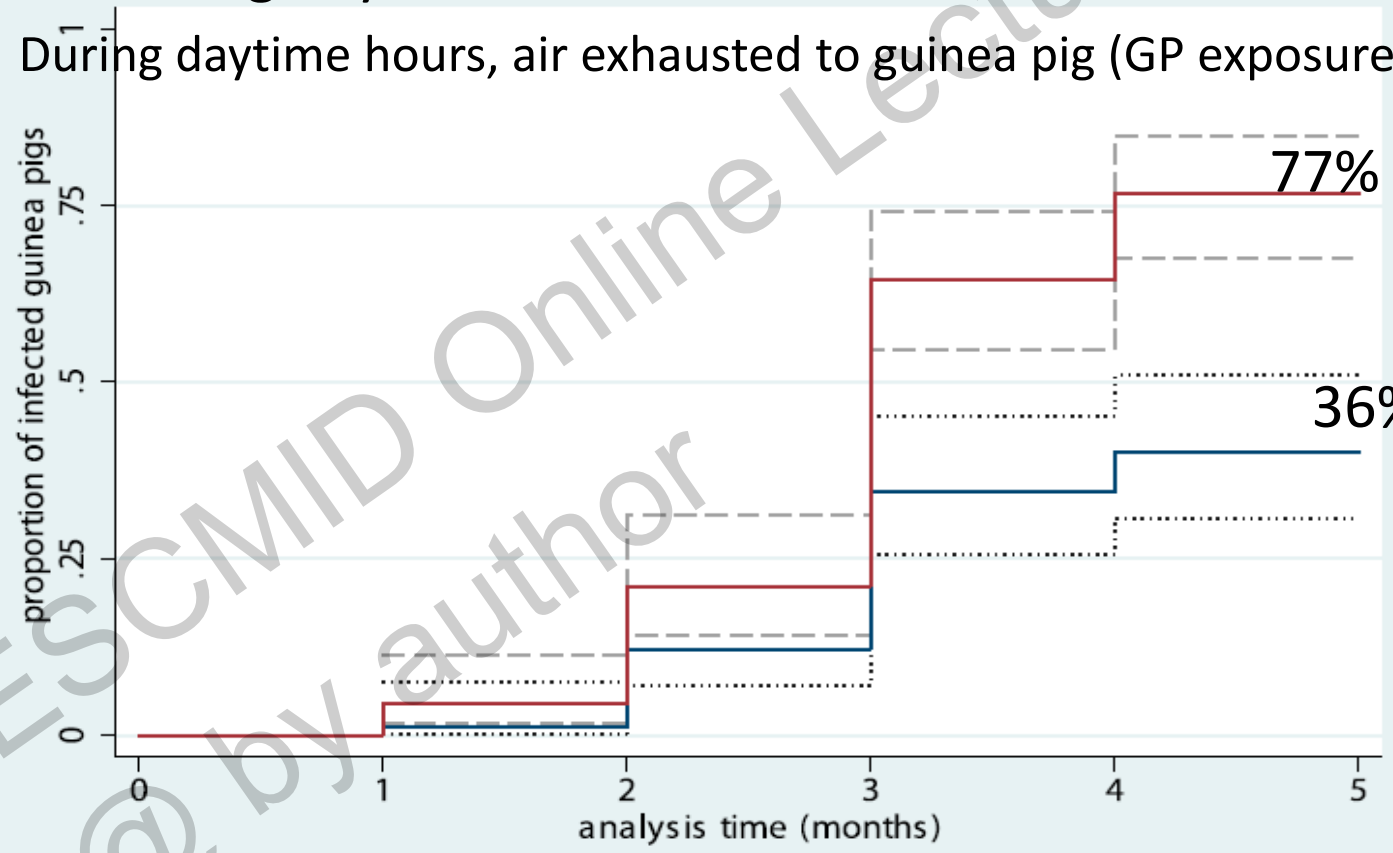
- Johnson CID 2
  - Either mask
    influenza to
- Milton PLoS P
  - Masks produ
    shedding
- Canini PLoS One 2010;5:e13998
  - No reduction in secondary attack rate in households



Surgical Face Masks Worn by Patients with Multidrug-Resistant Tuberculosis

Impact on Infectivity of Air on a Hospital Ward

- 17 patients with MTB alternated wearing masks and not wearing masks during daytime hours x 12 weeks
  - During daytime hours, air exhausted to guinea pig (GP exposure chambers)



Dharmadhikar AJRCCM 2012;185:1104i

Experimental data: masks, respirators and protection from influenza aerosols

- Noti et al. CID 2012;54:1569
  - Reductions in influenza virus penetration
    - Sealed mask (silicone seal) – 94.8%
    - Sealed N95 respirator (silicone seal) – 99.5%
    - Mask, no seal – 57%
    - N95 respirator (poor fit) – 67%
- Makison-Booth JHI 2012;84:22
  - Influenza plaque reduction factor 1.1-55 with different surgical masks

Masks plus hand hygiene to prevent influenza (I)

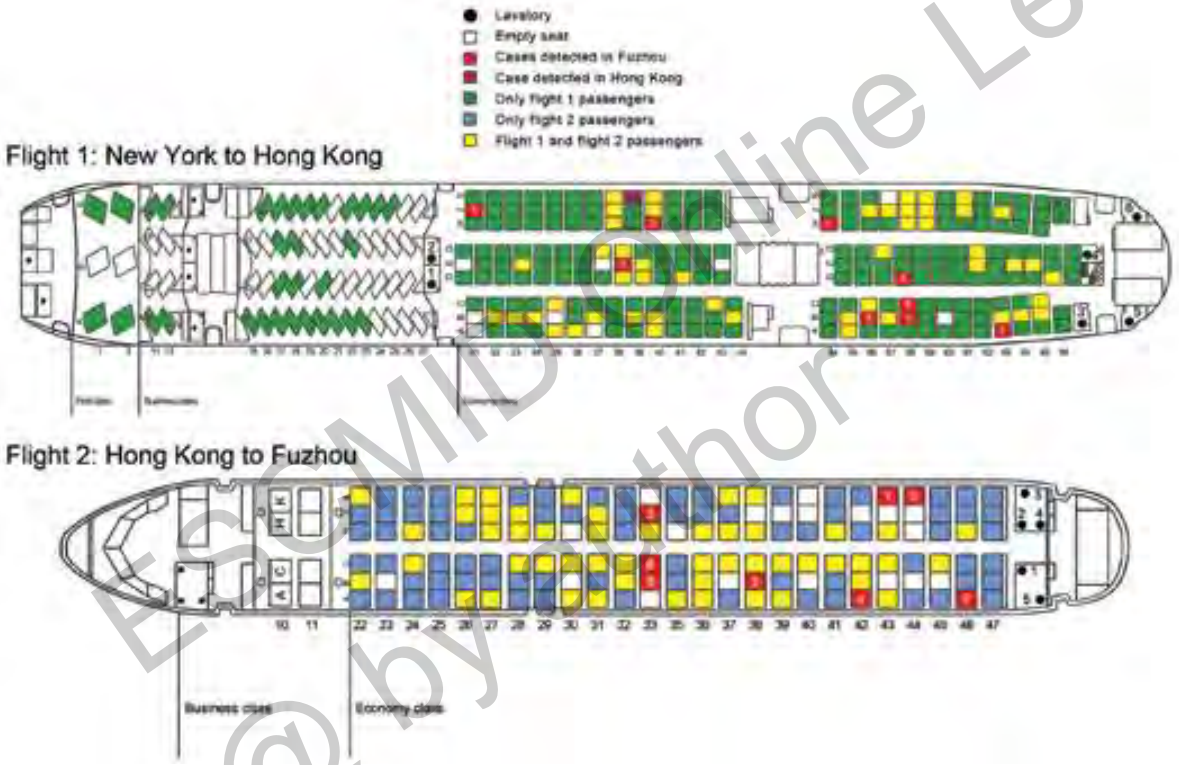
Study	Primary outcome	Secondary outcome
MacIntyre; household RCT: control vs.mask vs. P2 Outcome: ILI	No difference	74% reduced risk of ILI with adherent use of mask/P2 (P=0.02)
Cowling: household RCT: control vs. hand hygiene (HH) vs. mask+HH Outcome: influenza	No difference	In households implementing mask+HH within 36 hours of index case onset, 66% reduction in secondary influenza cases (P<0.05)
Simmerman: household RCT: control vs. handwashing vs. HW + paper mask Outcome: influenza	No difference	

Masks plus hand hygiene to prevent influenza (II)

Study	Primary outcome	Secondary outcome
Seuss: household (104) **RCT: control vs. mask vs. mask+HH** **Outcome: influenza**	No difference	In households with mask+HH <36h after index case onset, 84% reduction in 2° influenza cases (P=.04). In fully adherent households in mask only group, 70% reduction in 2^0 influenza (P=.04)
Larson: household (105) **RCT: education vs HH vs HH+mask** **Outcomes: URI/ILI/LCflu**	No difference	Some evidence that adherence to mask use reduced risk of secondary upper respiratory tract infection
Aiello: university residence (106) **RCT: control vs. HH vs. HH+mask** **Outcome: ILI**	No difference	After week 4, significant reduction in ILI in hand hygiene plus mask group

Protection by Face Masks against Influenza A(H1N1)pdm09 Virus on Trans-Pacific Passenger Aircraft, 2009

Lijie Zhang,[1] Zhibin Peng,[1] Jianming Ou,[1] Guang Zeng,[1] Robert E. Fontaine, Mingbin Liu, Fuqiang Cui, Rongtao Hong, Hang Zhou, Yang Huai, Shuk-Kwan Chuang, Yiu-Hong Leung, Yunxia Feng, Yuan Luo, Tao Shen, Bao-Ping Zhu, Marc-Alain Widdowson, and Hongjie Yu



- Wore a face mask for entire flight:
  - 0/9 cases
  - 15/32 controls
  - (P=.02)

Administrative controls

- Education: precautions and recognition of disease
- Empiric additional precautions for symptomatic patients AND/OR Additional precautions for patients with confirmed disease
- (Single room accommodation for patients in precautions)
- (Restriction of ill visitors)
- (Monitoring/evaluation of process/outcomes)
- (Masking/exclusion of ill staff)

RSV control - I

All children tested on admission,
Plus weekly and at onset respiratory symptoms

Control measure	RSV infection rate
None	6/23 (26%)
Cohort nursing alone	7/36 (19%)
Gowns/gloves alone	10/36 (28%)
Cohort nursing plus gowns/gloves	1/33 (3%) 10/105 (9%)

Madge Lancet 1992;340:1079

RSV control - II

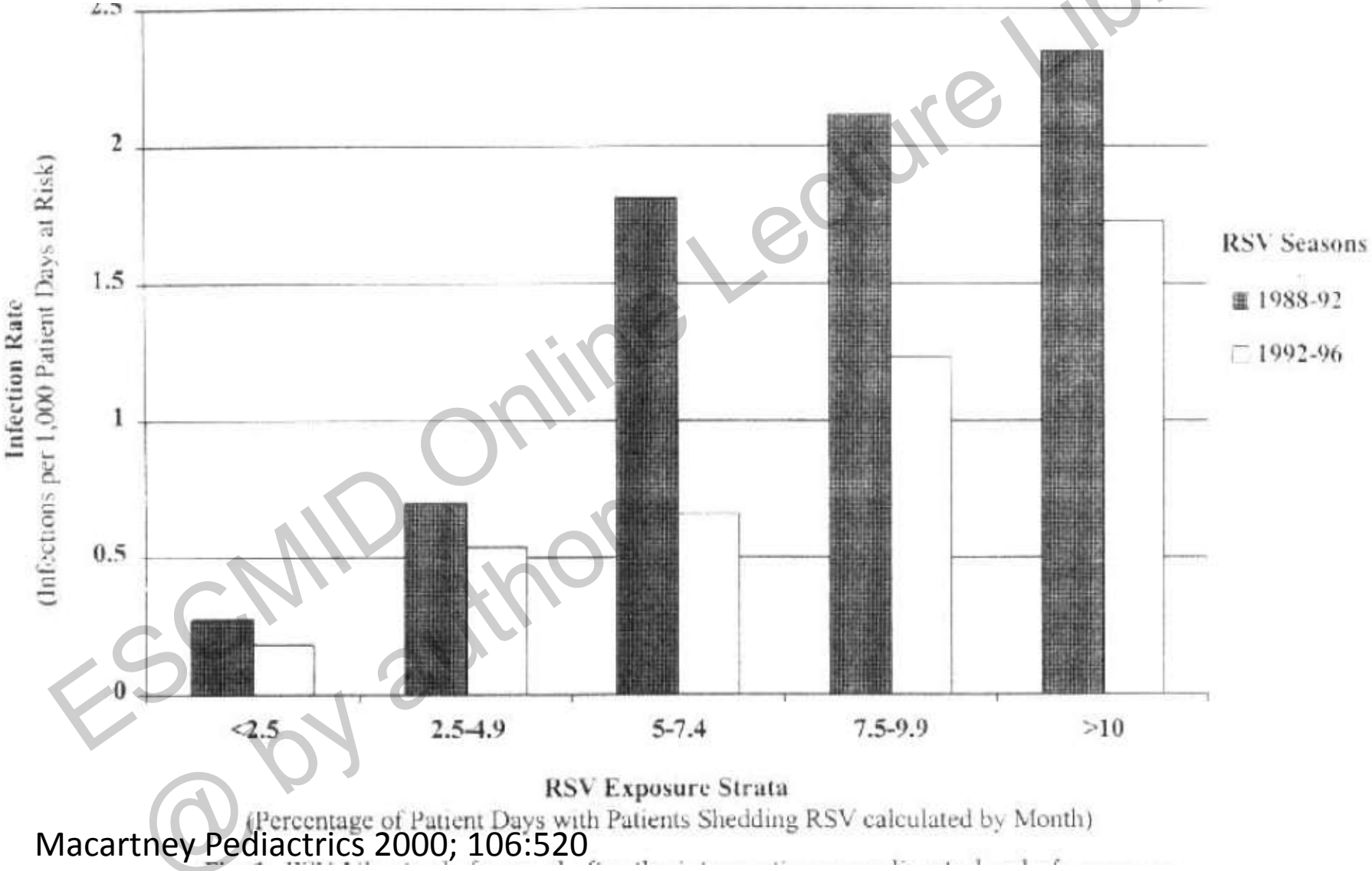
Table 2. Unit location of RSV cases by year: Number of nosocomial cases and total

Year	Other units nosocomial	Total other units (% nosocomial)	Infant unit nosocomial	Total infant unit (% nosocomial)	Total nosocomial	Total cases	Percentage	Odds ratio†
Preintervention								
1989-1990	3	38 (5.3)	6	36 (16.7)	9	74	12.2	1*
1990-1991	3	40 (7.5)	14	44 (46.7)	17	84	20.2	
Postintervention								
1991-1992	6	75 (7.9)	5	73 (7.4)	11	148	7.4	.41
1992-1993	2	39 (5.1)	7	92 (7.6)	9	131	6.9	.37
1993-1994	5	48 (10.4)	8	87 (9.2)	13	135	9.6	.46
1994-1995	4	106 (3.8)	0	134 (0)	4	240	1.7	.09
1995-1996	5	48 (10.4)	8	131 (6.1)	13	179	7.3	.40
1996-1997	0	21 (0)	2	88 (2.3)	2	109	1.8	.09

*Average of both years.
†χ^2 test for trends.

Karanfil AJIC 1999;27:91

RSV control III



Macartney Pediactrics 2000; 106:520

SARS/MERS control

- SARS hospital outbreaks terminated in
  - China, Hong Kong, Taiwan, Singapore, Toronto

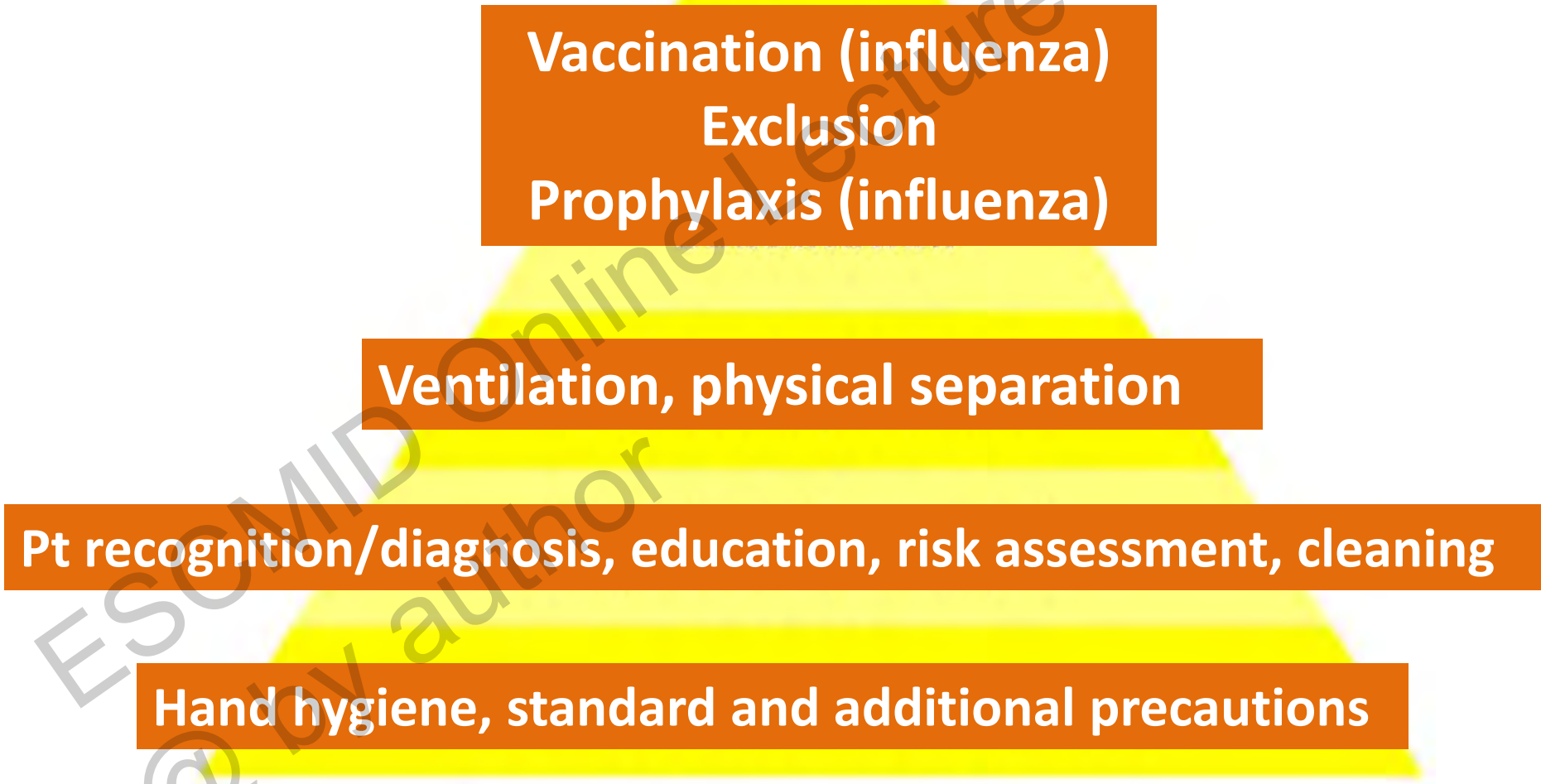
- MERS hospital outbreaks terminated in Al-Hasa in 2013 and in other cities in KSA in 2014

Influenza

- No evidence on effect of control programs on reducing the risk of sporadic nosocomial disease, or outbreaks

- Substantial, but anecdotal evidence of inability to control influenza outbreaks once established

Hierarchy of hazard control



In sum

- Transmission of respiratory viruses continues in our healthcare facilities
  - In outbreaks, for viruses other than influenza, administrative controls are effective in controlling transmission
  - In non-outbreak situations, control programs are either not tested or partially effective
  - Diagnostic capacity is a critical component of administrative controls
- Continued research in control measures in healthcare institutions is needed