

Findings of a cluster randomized controlled trial of face masks and hand hygiene to prevent influenza transmission in households

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Hong Kong NPI study



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- Trial coordination – Calvin Cheng, Vicky Fang, Rita Fung, Conrad Lam, Winnie Lim, Joey Sin, Eileen Yeung.
- GPs, HCAs and study nurses facilitating and conducting fieldwork.

Background – NPIs



Physical interventions to interrupt or reduce the spread of respiratory viruses: systematic review

Tom Jefferson, coordinator,¹ Ruth Foxlee, trials search coordinator,² Chris Del Mar, dean,³ Liz Dooley, review group coordinator,⁴ Eliana Ferroni, researcher,⁵ Bill Hewak, medical student,³ Adi Prabhala, medical student,³ Sree Nair, professor of biostatistics,⁶ Alex Rivetti, trials search coordinator¹

Source: BMJ 2008; 336:77-80.

Using physical barriers to reduce the spread of respiratory viruses

Handwashing and wearing masks, gloves, and gowns are highly effective

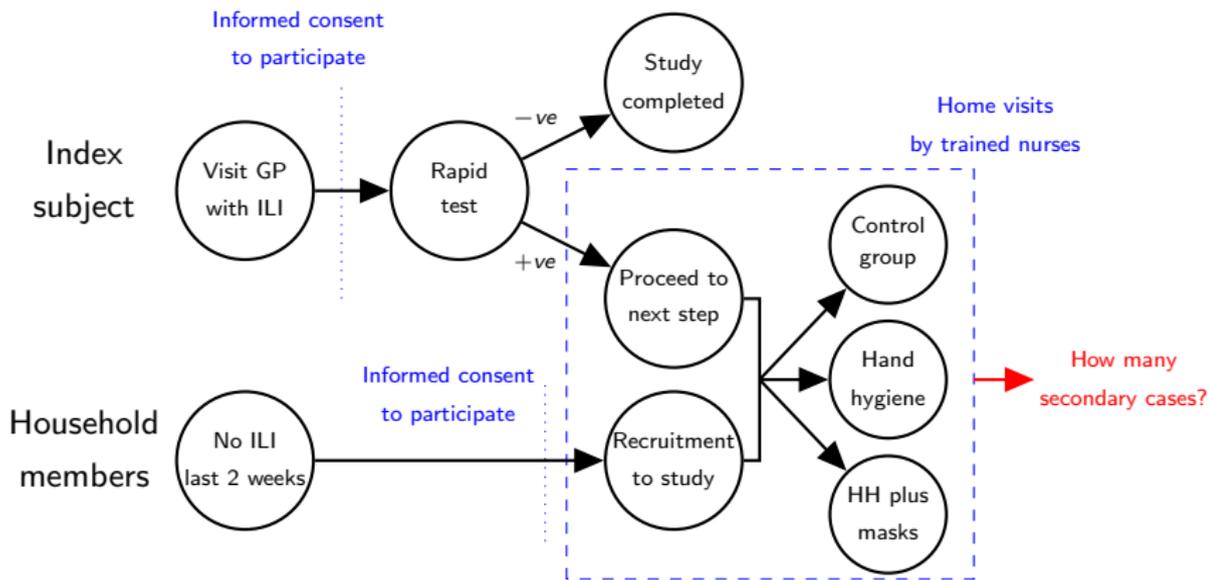
Source: Dawes M. et al; BMJ 2008; 336:55-6.

Hong Kong NPI RCT – Inclusion criteria

Case-ascertainment design – index cases with influenza-like illness recruited from outpatient clinics

- Any 2+ ILI symptoms or signs (broad definition).
- Onset of symptoms within the last 48 hours.
- Live with at least 2 other people.
- No other household members have had ILIs within the past 2 weeks.

NPI RCT – Study design



306 households successfully followed up with lab-confirmed index case; in compliance with the protocol 47 households with RT-PCR-confirmed co-index cases at the time of the intervention were excluded from subsequent analyses.

Data collection

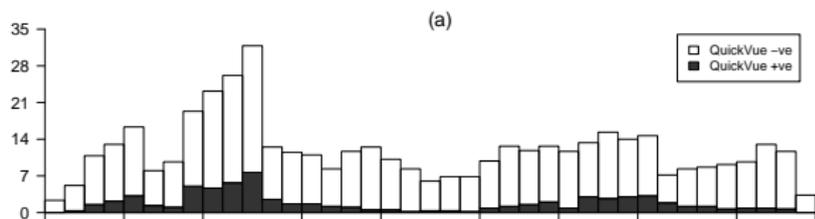
- Initial rapid diagnostic test (and additional nose/throat swab for validation by RT-PCR).
- Nose/throat swabs collected from index cases and household contacts in home visits at baseline, and after 3 and 6 days.
- Detailed baseline questionnaire.
- Daily self-reported symptom diaries during follow-up period.
- Final visit review adherence to interventions.

Interventions

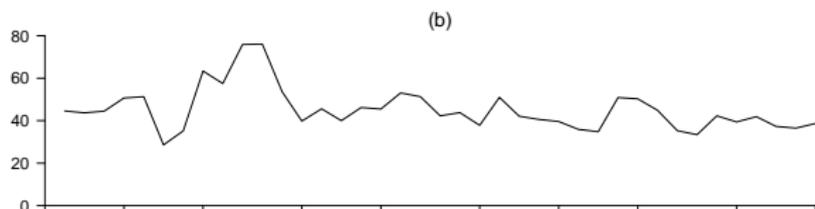
- **Control** arm. Index case and all household contacts receive education on self care for ILI, and the benefits of a healthy lifestyle and diet.
- Control plus **hand-hygiene** arm. Index case and all household contacts are provided with **soap dispensers** and **alcohol hand rub** and educated on their use.
- Control plus hand-hygiene plus **face mask** arm. Index case and all household contacts are provided with **surgical masks** and educated on their proper use and hygienic disposal.

Recruitment vs flu activity

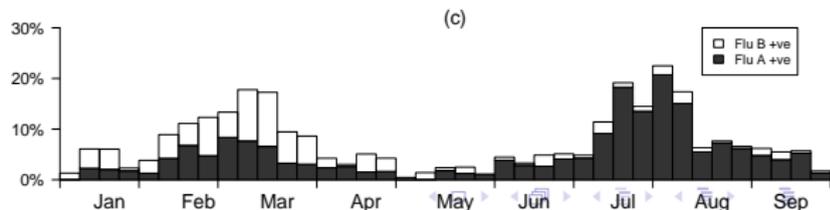
Study recruitment rate
(subjects per day)



Community ILI circulation
(ILI cases per 1,000 GP consultations)



Positive laboratory
isolates (QMH)



Hong Kong NPI study

Main results (I.T.T.) – secondary attack ratios

Table: Secondary attack ratios in the contacts of 259 analyzed households.

	Secondary attack ratio (95% CI)*						p-value [†]
	Control (<i>n</i> =279)		Hand hygiene (<i>n</i> =257)		Mask+HH (<i>n</i> =258)		
Lab-confirmed influenza	0.10	(0.06, 0.14)	0.05	(0.03, 0.09)	0.07	(0.04, 0.11)	0.22
Clinical influenza ⁽¹⁾	0.19	(0.14, 0.24)	0.16	(0.12, 0.21)	0.21	(0.16, 0.27)	0.40
Clinical influenza ⁽²⁾	0.05	(0.02, 0.08)	0.04	(0.02, 0.06)	0.07	(0.04, 0.11)	0.28

* By a cluster bootstrap method.

† By Pearson chi-square test adjusted for within-household correlation.

- (1) is at least 2 of fever $\geq 37.8^{\circ}\text{C}$, cough, headache, sore throat, aches or pains in muscles or joints.
- (2) is fever $\geq 37.8^{\circ}\text{C}$ plus cough or sore throat.

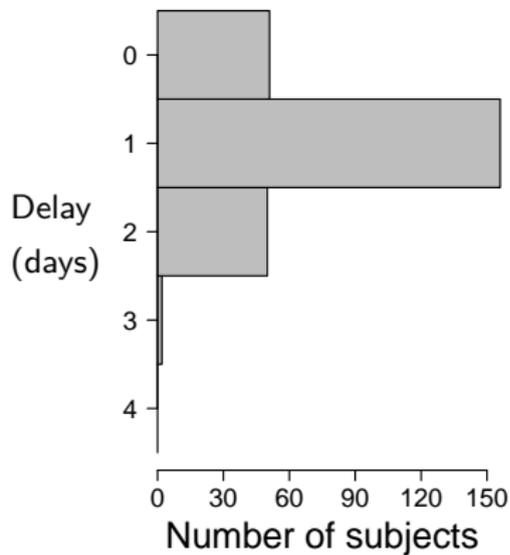
RT-PCR confirmed secondary cases (I.T.T.)

Characteristic	<i>n</i>	Adjusted OR*	95% CI for OR
Control arm	279	1.00	
Hand hygiene arm	257	0.57	(0.26, 1.22)
Mask+HH arm	258	0.77	(0.38, 1.55)
Adult (aged 16+)	662	1.00	
Child (aged 6-15)	88	2.87	(1.42, 5.78)
Child (aged ≤5)	44	1.91	(0.69, 5.30)
Not vaccinated	688	1.00	
Vaccinated in past 1 year	106	0.33	(0.12, 0.91)
Adult (aged 16+) index	71	1.00	
Child (aged 6-15) index	144	2.74	(0.95, 7.90)
Child (aged ≤5) index	44	2.82	(0.87, 9.14)
Index not prescribed antiviral	191	1.00	
Index prescribed antiviral	68	0.70	(0.33, 1.45)

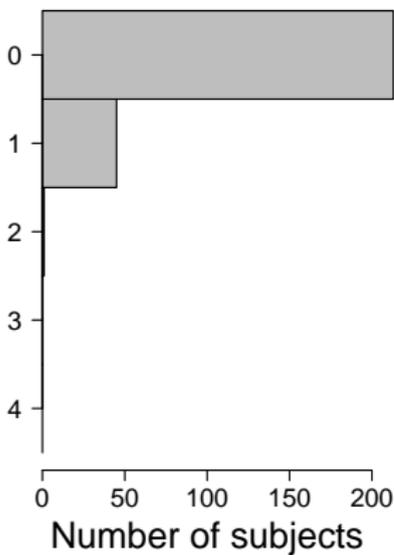
- * *Adjusted odds ratios of infection of household contacts estimated under a multivariable logistic regression model also adjusting for sex of household contact, sex of corresponding index case, and allowing for within-household clustering.*

Delays between index onset and intervention

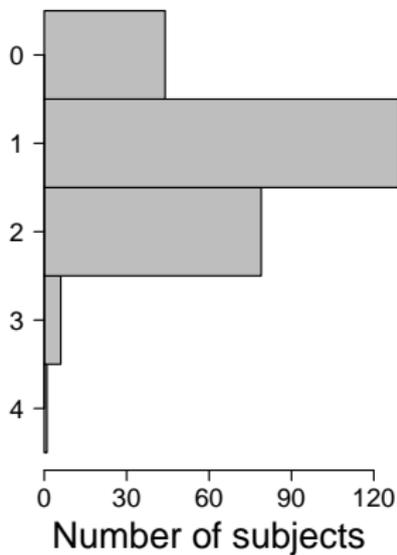
Delay from symptom onset
to recruitment



Delay from recruitment to
intervention



Delay from symptom onset
to intervention



SARs for timely intervention

Table: Secondary attack ratios in the contacts of 154 analyzed households where the intervention was applied within 36 hours of symptom onset in the index case.

	Secondary attack ratio (95% CI)*						<i>p</i> -value [†]
	Control (<i>n</i> =183)		Hand hygiene (<i>n</i> =130)		Mask+HH (<i>n</i> =149)		
RT-PCR-confirmed influenza	0.12	(0.07, 0.18)	0.05	(0.01, 0.11)	0.04	(0.01, 0.07)	0.04
Clinical influenza ⁽¹⁾	0.23	(0.16, 0.30)	0.11	(0.05, 0.17)	0.18	(0.12, 0.24)	0.03
Clinical influenza ⁽²⁾	0.07	(0.03, 0.11)	0.04	(0.01, 0.07)	0.07	(0.03, 0.12)	0.52

* By a cluster bootstrap method.

† By Pearson chi-square test adjusted for within-household correlation.

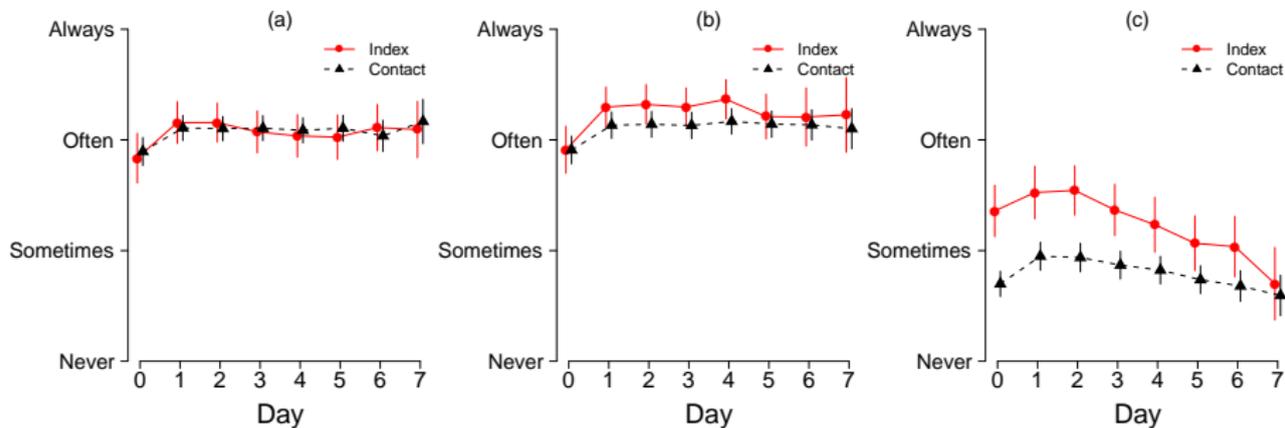
- (1) is at least 2 of fever $\geq 37.8^{\circ}\text{C}$, cough, headache, sore throat, aches or pains in muscles or joints.
- (2) is fever $\geq 37.8^{\circ}\text{C}$ plus cough or sore throat.

RT-PCR-confirmed 2nd cases for timely intervention

Characteristic	<i>n</i>	Adjusted OR*	95% CI for OR
Control arm	183	1.00	
Hand hygiene arm	130	0.46	(0.15, 1.43)
Mask+HH arm	149	0.33	(0.13, 0.87)
Adult (aged 16+)	386	1.00	
Child (aged 6-15)	51	3.02	(1.16, 7.85)
Child (aged ≤5)	25	2.45	(0.75, 8.01)
Not vaccinated	401	1.00	
Vaccinated in past 1 year	61	0.40	(0.12, 1.33)
Adult (aged 16+) index	39	1.00	
Child (aged 6-15) index	85	1.17	(0.33, 4.23)
Child (aged ≤5) index	30	1.55	(0.37, 6.45)
Index not prescribed antiviral	109	1.00	
Index prescribed antiviral	45	0.81	(0.32, 2.04)

- * Adjusted odds ratios of infection of household contacts estimated under a multivariable logistic regression model also adjusting for sex of household contact, sex of corresponding index case, and allowing for within-household clustering.

Adherence to interventions



(a) Reported frequency of hand washing with liquid hand soap/alcohol hand rub in the hand hygiene arm;

(b) Reported frequency of hand washing with liquid hand soap/alcohol hand rub in the mask+HH arm;

(c) Reported frequency of face mask use in the mask+HH arm.

Discussion

- Substantial and significant benefits of face masks and hand hygiene if implemented within 36 hours of index case symptom onset.
- Cannot distinguish relative contributions of each intervention and both may be important.
- Moderate adherence to the interventions, especially the reported use of the surgical mask in household contacts.

Limitations

- Potential bias due to recruiting symptomatic index cases.
 - Preferentially recruit index cases with higher viral shedding.
 - Delay between symptom onset and intervention may lead us to underestimate the true effectiveness of the interventions.
 - Bias towards including household contacts with pre-existing immunity.
- Primary outcome is RT-PCR-confirmed influenza virus infections.
 - Some infections may be missed if peak viral shedding occurred between home visits
 - or if specimens were poor quality or degenerated during transport or freezing.

Part II

Appendix

Characteristics of index cases

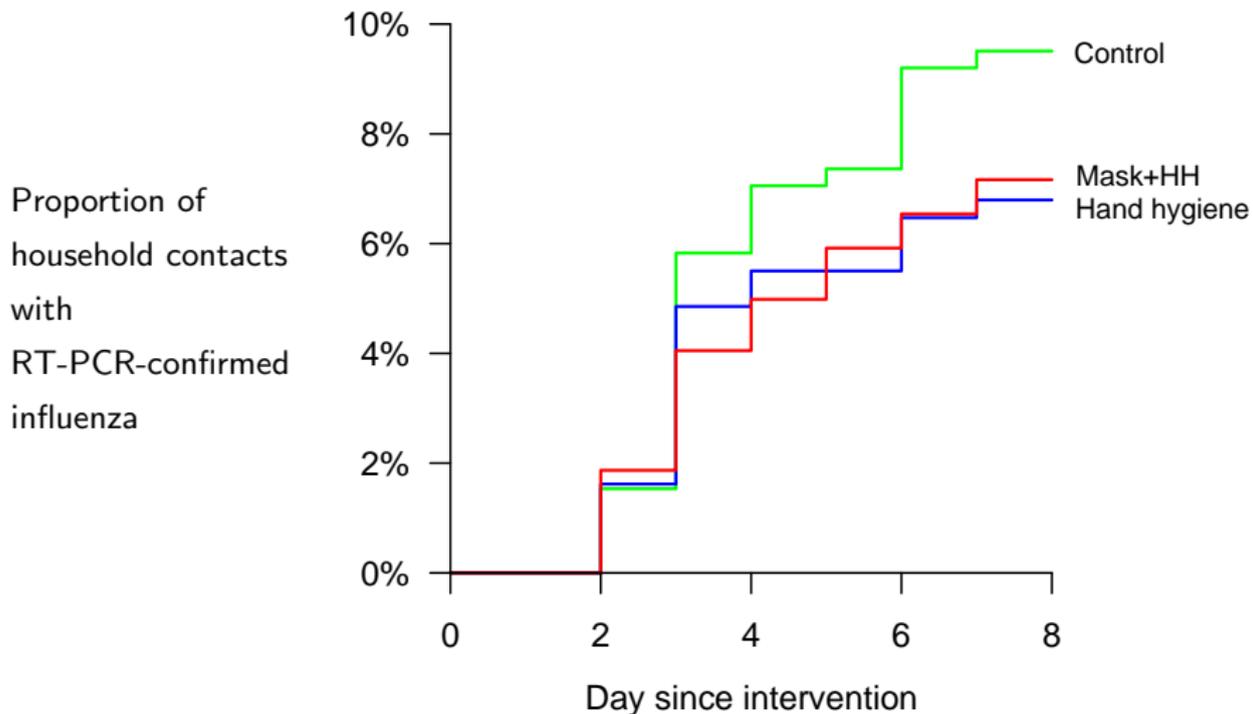
	Control				Hand hygiene				Mask+HH			
	Randomized (<i>n</i> = 134)		Analyzed* (<i>n</i> = 91)		Randomized (<i>n</i> = 136)		Analyzed* (<i>n</i> = 85)		Randomized (<i>n</i> = 137)		Analyzed* (<i>n</i> = 83)	
Age group (%)												
0 – 5 yrs	26	(19%)	20	(22%)	19	(14%)	10	(12%)	25	(18%)	14	(17%)
6 – 15 yrs	70	(52%)	54	(59%)	66	(49%)	46	(54%)	67	(49%)	45	(54%)
16 – 30 yrs	17	(13%)	5	(5%)	24	(18%)	12	(14%)	22	(16%)	11	(13%)
31 – 50 yrs	15	(11%)	11	(12%)	23	(17%)	15	(18%)	18	(13%)	9	(11%)
50+ yrs	6	(4%)	1	(1%)	4	(3%)	2	(2%)	5	(4%)	4	(5%)
Male sex (%)	63	(47%)	44	(48%)	76	(56%)	41	(48%)	62	(45%)	33	(40%)

*Excluding 85 households who dropped out, 16 households where the index did not have RT-PCR-confirmed infection at the first home visit, and 47 households with 1+ household contacts with RT-PCR-confirmed influenza (co-index cases).

Characteristics of household contacts

	Control (<i>n</i> = 279)	Hand hygiene (<i>n</i> = 257)	Mask+HH (<i>n</i> = 258)
Age group (%)			
≤ 5 yrs	20 (7%)	9 (4%)	15 (6%)
6 – 15 yrs	29 (10%)	32 (12%)	25 (10%)
16 – 30 yrs	37 (13%)	27 (11%)	36 (14%)
31 – 50 yrs	157 (56%)	125 (49%)	131 (51%)
50+ yrs	34 (12%)	53 (21%)	50 (19%)
Unknown age	2 (1%)	11 (4%)	1 (0%)
Male sex (%)	105 (38%)	103 (40%)	98 (38%)
Vaccinated in past year	30 (11%)	32 (12%)	44 (17%)

Time to RT-PCR-confirmed influenza



Implications for future studies

- Case-ascertained recruitment versus a cohort design
 - Case ascertainment driven by influenza seasonality and may be particularly challenging in temperate locations.
 - Much larger cohort study would be needed given low annual influenza attack rate.
- Challenging to obtain longitudinal laboratory specimens.
 - But reliance on clinical symptoms may not allow results specific to influenza virus.
 - Paired serology could be compared to determine influenza infections.

Clinical (1) secondary cases for timely intervention

Characteristic	<i>n</i>	Adjusted OR*	95% CI for OR
Control arm	183	1.00	
Hand hygiene arm	130	0.46	(0.22, 0.96)
Mask+HH arm	149	0.86	(0.48, 1.53)
Adult (aged 16+)	386	1.00	
Child (aged 6-15)	51	2.09	(1.01, 4.32)
Child (aged ≤5)	25	2.16	(0.87, 5.34)
Not vaccinated	401	1.00	
Vaccinated in past 1 year	61	1.33	(0.71, 2.49)
Adult (aged 16+) index	39	1.00	
Child (aged 6-15) index	85	1.57	(0.66, 3.74)
Child (aged ≤5) index	30	2.26	(0.86, 5.95)
Index not prescribed antiviral	109	1.00	
Index prescribed antiviral	45	0.76	(0.42, 1.38)

(1) *is at least 2 of fever $\geq 37.8^{\circ}$ C, cough, headache, sore throat, aches or pains in muscles or joints.*

- * *Adjusted odds ratios of infection of household contacts estimated under a multivariable logistic regression model also adjusting for sex of household contact, sex of corresponding index case, and allowing for within-household clustering.*

Clinical (2) secondary cases for timely intervention

Characteristic	<i>n</i>	Adjusted OR*	95% CI for OR
Control arm	183	1.00	
Hand hygiene arm	130	0.64	(0.20, 2.02)
Mask+HH arm	149	1.45	(0.49, 4.24)
Adult (aged 16+)	386	1.00	
Child (aged 6-15)	51	7.57	(2.79, 20.6)
Child (aged ≤5)	25	7.20	(1.92, 27.0)
Not vaccinated	401	1.00	
Vaccinated in past 1 year	61	1.10	(0.31, 3.91)
Adult (aged 16+) index	39	1.00	
Child (aged 6-15) index	85	0.79	(0.20, 3.19)
Child (aged ≤5) index	30	2.36	(0.46, 12.3)
Index not prescribed antiviral	109	1.00	
Index prescribed antiviral	45	0.66	(0.21, 2.06)

(2) is the standard CDC classification of fever $\geq 37.8^{\circ}\text{C}$ plus cough or sore throat.

- * Adjusted odds ratios of infection of household contacts estimated under a multivariable logistic regression model also adjusting for sex of household contact, sex of corresponding index case, and allowing for within-household clustering.