Original Article

Effects of Multiple Cleaning and Disinfection Interventions on Infectious Diseases in Children: A Group Randomized Trial in China*

BAN Hai Qun[1,^], LI Tao[1,^], SHEN Jin[1], LI Jin[2], PENG Pin Zhang[2], YE Heng Ping[2], and ZHANG Liu Bo[1,#]

1. Institute of Environment Health and Related Product Safety, Center for Disease Control and Prevention of China, Beijing 100021, China; 2. Center for Disease Control and Prevention of Xiantao city, Xiantao 433000, Hubei, China

Abstract

Objective To assess the effectiveness of multiple cleaning and disinfection interventions in the homes and kindergartens, in reducing gastrointestinal and respiratory illnesses of children.

Methods From October 2010 to September 2011, we performed a prospective, controlled study in China. 408 children under 5 years old were recruited and group randomized into intervention and control groups. Families and kindergartens in the intervention group were provided with antibacterial products for hand hygiene and surface cleaning or disinfection for one year. Each child's illness symptoms and sick leave were recorded every day.

Results A total of 393 children completed the study, with similar baseline demographics in each of the 2 groups. Except for abdominal pain, the odds of symptoms (fever, cough and expectoration, runny nose and nasal congestion, diarrhea), illness (acute respiratory illness and gastrointestinal illness), and sick leave per person each month were significantly reduced by interventions. The rates of fever, diarrhea, acute respiratory illness, gastrointestinal illness and sick leave per person per year were significantly decreased as well.

Conclusion Not only the acute respiratory and gastrointestinal illness but the sick leave rate in children were significantly reduced by multiple interventions.

Key words: Communicable disease control; Child daycare centers; Sick leave; Antibacterial agents; Hand hygiene; Domestic hygiene; Surface cleaning; Surface disinfection

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INTRODUCTION

Acute infectious respiratory and gastrointestinal diseases are the leading causes of child mortality. The World Health Organization estimated that more than 3.5 million children under the age of 5 died of diarrhea and acute respiratory-related infectious diseases each year in WHO regions from 2000-2003[1]. Diarrhea and respiratory diseases are caused by a variety of pathogens transmitted by the fecal-oral route, including protozoa, bacteria, fungi, and viruses. Contaminated surfaces or hands play key roles in the route of contact transmission of these

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^These authors contributed equally to this work.

#Correspondence should be addressed to ZHANG Liu Bo, Tel: 86-10-50930190, E-mail: zlbxj@263.com

Biographical notes of the first authors: BAN Hai Qun, male, born in 1979, PhD candidate, majoring in disinfection and infection control; LI Tao, female, born in 1969, professor, majoring in disinfection technology.

infectious diseases[2]. During the past few decades, research on the epidemiology of infectious disease has focused on hand hygiene in hospitals, day care facilities, schools and homes. In contrast to hand hygiene, surface cleaning or disinfection has recently begun to gain a better insight in healthcare settings[3], but contaminated surfaces and integrated interventions in community and non-acute settings remain to be little studied[4-6]. Does hand hygiene and surface cleaning or disinfection through multiple interventions affect the risk of infectious disease transmission more efficiently? Therefore, in order to assess the effects of multiple interventions on the prevention of infectious disease, we selected children (under 5 years old) from kindergartens in central China, carried out multiple interventions (hand hygiene and surface cleaning or disinfection) in the kindergartens and homes, and monitored infectious illnesses for the course of one year.

MATERIALS AND METHODS

Ethics Statement and study Population

This study involved a prospective, group randomized, controlled design. Two kindergartens were identified from Xiantao city, Hubei province of China. Both of them are located in the downtown area, and managed by the same committee. The distance between the two kindergartens is 3 km. One of the kindergartens has 14 classes (589 children), the other has 16 classes (660 children). Due to the third grade children generally more than 5 years, from the grade one and grade two classes, we randomly selected 5 classes (221 children) and 6 classes (244 children) respectively at the two kindergartens. Questionnaires requesting the basic information of the children and the families involved, along with the informed consent forms, were distributed to parents or guardians before the study began, and all forms were required to be filled out and signed by the parents or guardians. All the families declared their written consent to participate in the study. Considering that the children played together in the same kindergartens, shared the same transmission routes, we did not adopt the use of individual randomized design. Randomization was based on the kindergarten, 221 children from one kindergarten as the intervention group, and 245 children from the other kindergarten as the control group. At the data analysis phase, 48 children were excluded because their families already had antibacterial products or their guardians didn't complete the questionnaire, 9 children were excluded because of above 5 years old, 15 children were excluded because of losing to follow-up (Figure 1).

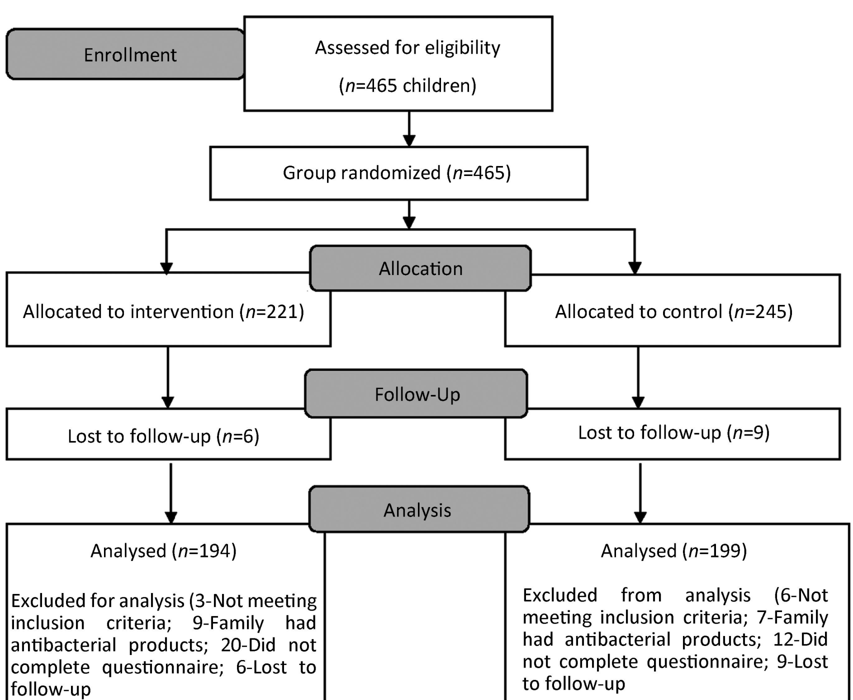

Figure 1. Participant Flow Diagram.

Interventions

The study started in October 2010 and lasted until September 2011. Families and kindergartens in the intervention group were provided with antibacterial products for hand hygiene and surface cleaning or disinfection produced by the Whealthfields Lohmann (Guangzhou) Company Ltd. Items distributed included Liquid Antimicrobial Soap for hand-washing (active ingredient: 0.2%-0.3% parachlorometaxylenol), Instant Hand Sanitizer for hand disinfecting (active ingredient: 72%-75% ethanol), Antiseptic-Germicide (active ingredient: 4.5%-5.5% parachlorometaxylenol, diluting before use) and Bleach (active ingredient: 4.5%-5.0% sodium hypochlorite, diluting before use) for surface disinfecting.

Parents or guardians and teachers in the intervention group were instructed, in person on proper hand-hygiene techniques and how to use all of the antibacterial products which were distributed. Children, their family members and teachers were advised to wash their hands daily using Liquid Antimicrobial Soap, especially before eating, after using the bathroom, after blowing their nose, and after outdoor activities. Instant Hand Sanitizer was instructed to be carried daily and used without running water. Hard surfaces in kindergartens were to be cleaned or disinfected every day using Antiseptic-Germicide or Bleach, in homes were to be cleaned or disinfected at least twice every week. Items such as children's toys, house furnishings, frequently touched objects (doorknobs, tables or desks), kitchen surfaces (utensils, cutlery, countertops, chopping boards, sinks, floors, etc.), bathroom surfaces (toilet, sink, floor, etc.), and so forth were also included in the weekly cleaning or disinfecting practices.

Families and kindergartens in the control group were not provided with any antibacterial products. Hand hygiene of children, their family members and teachers remained unchanged. Routine surface cleaning and disinfection practices in the homes and kindergartens also remain unchanged.

Data Collection

A 'Children's Daily Health Calendar' was sent to families of both groups to collect daily data on illness symptoms (fever, cough and expectoration, runny nose and nasal congestion, diarrhea, abdominal pain). Fever was defined as when the axillary temperature is higher than 37.3 °C or the range of temperature fluctuation is more than 1 °C. Cough and expectoration were defined as three or more coughs in a single hour and lasting for 4 or more hours in a single day, with or without expectoration. Runny nose and nasal congestion were defined as a runny nose lasting for 4 or more hours in one day, with or without nasal congestion. Diarrhea was defined as three or more bowel movements in one day, watery or loose stools, with or without blood in the stool. Abdominal pain was defined as an ache or pain in the stomach lasting for 1 hour or more.

Definitions of symptoms were printed on the Calendar and given to the parents or guardians at the beginning of the study. The symptom 'fever' required objective measurements using thermometers, which were provided for by the study team. All of the symptoms of illness were diagnosed and filled out by the parents or guardians based on the stated definitions. Every month upon completion, the Calendars were collected by the teachers of each classroom. The teachers checked the completeness and accuracy of the Calendars and made corrections with the parents or guardians according to the children's morning checking and medicine taking log.

A 'Children's Daily Sick Leave Calendar' was sent to the classroom teachers of both groups to collect daily data on sick leave (SL), and were filled out by the teachers.

During the whole year of this study, close contact was maintained with parents or guardians and teachers of both groups, including unscheduled parents' meetings, quarterly home visits, phone interviews, and monthly cell phone messages. All families and teachers were provided with contact details and could contact the study's management at any time. Furthermore, compliance with interventions was assessed every month by way of surveying the consumption of products. If the products provided became empty, the empty bottles could be exchanged for new ones at any time.

Statistical Analyses

All data were collected in a database (EpiData 3.1, EpiData Association, Odense, Denmark) and analyzed in SPSS 11.5 (SPSS Chicago Inc.). Baseline demographic characteristics of the intervention and control groups were compared using the χ^2-Test for categorical variables and the Wilcoxon rank sum test for continuous variables. Acute respiratory illness (RI) was classified as the appearance of two or more of the following symptoms: fever, cough and expectoration, runny nose and nasal congestion. Gastrointestinal illness (GI) was classified as the appearance of diarrheal symptoms or two or more of the following symptoms: diarrhea, fever, and abdominal pain.

In order to analyze the number of RI, GI and SL, the number of person months with and without symptoms or SL were determined. The odds ratio (OR) and ±95% Confidence Intervals (CI) between the two groups were calculated and the χ^2-Test was used to detect any statistically significant differences between the groups. To analyze the frequency of symptoms, illness and SL, during all 12 months, illnesses or absences occurring 0, 1, 2, 3 or more times were determined for each child. The χ^2-Test was used to detect statistically significant differences between groups. To assess the preventive effect of interventions, the protective rate (*PR*) and ±95% CI were calculated and a non-parametric Mann-Whitney Test used to detect statistically significant differences between groups.

$$PR = \frac{p_1 - p_2}{p_1} \times 100\% \quad (1)$$

$$95\%CI = PR \pm 1.96 \sqrt{\frac{1}{p_1^2} \times \frac{p_2 \times q_2}{n_2} + \frac{p_2^2}{p_1^4} \times \frac{p_1 \times q_1}{n_1}} \times 100\% \quad (2)$$

p_1 and p_2 means the incidence rate of control and intervention groups, respectively; q_1=1-p_1, q_2=1-p_2; n_1 and n_2 means the number of children in the control and intervention group, respectively.

RESULTS

Description of Sample Population

Before completion of the one year timeframe, a total of 15 children (6 and 9 from the intervention and control group, respectively) withdrew, because of transferring to other classrooms or kindergartens. The percentage of participants withdrawing from the study was less than 5% per group, and did not significantly affect the outcome of the study (*P*=0.60, χ^2-Test).

The data of 393 children and their families were analyzed in this study. There were no significant differences in the baseline demographic characteristics between the control and intervention group, except for the number of smoker families (Table 1). 61.8% of the children are boys. 86.8% of mothers have at least a senior middle school education. 84.4% of families have an annual household income between ¥10,000-¥100,000. 29.0% of families have smoker, the control group have more smoker families (*P*=0.004).

Table 1. Baseline Demographic Characteristics of Enrolled Families, Xiantao city, Hubei Province of China, 2010-2011

Demographic Variable	Control (*n*=199)	Intervention (*n*=194)	*P* value*
Age, Mean (SD)	3.7 (0.5)	3.7 (0.4)	0.721
Size of household, Mean (SD)	4.2 (1.2)	4.1 (1.2)	0.341
Sex, *n* (%)			
Male	119 (59.8)	124 (63.9)	0.408
Female	80 (40.2)	70 (36.1)	
Education level of mother, *n* (%)			
≤Junior middle school	33 (16.6)	19 (9.8)	0.138
Senior middle school	77 (38.7)	80 (41.2)	
≥Junior college	89 (44.7)	95 (49.0)	
Smoker, *n* (%)			
Yes	71 (35.7)	43 (22.2)	0.004
No	128 (64.3)	151 (77.8)	
Household income per year, *n* (%)			
<¥10,000	9 (4.5)	8 (4.1)	0.278
¥10,000–¥50,000	105 (52.8)	121 (62.4)	
¥50,000–¥100,000	64 (32.2)	50 (25.8)	
≥¥100,000	21 (10.6)	15 (7.7)	

Note. *Analyses were performed with Chi-square or Fisher Exact test where appropriate for categorical variables and Wilcoxon rank-sum test for continuous variables.

Compliance with Interventions

We surveyed the monthly consumption of antibacterial products to evaluate compliance with guidelines set forth for the intervention group. Table 2 displays the volume of every antibacterial product used by the participants of the intervention group from 20th September 2010 to 28th September 2011. Intervention group has 194 families and 5 classrooms, has 800 family members including children and 15 teachers.

$$PU = \frac{V \times TU}{\mathrm{FMT} \times \mathrm{D}} \quad (3)$$

PU (person usage, mL/person day) means the everyday consumption of antibacterial products by person; *V* (volume, mL/bottle) means the size of the antibacterial products; *TU* (total usage, bottle) means the number of antibacterial products used by intervention group; *FMT*=815, means the number of family members including children and teachers; D=373, means the number of the days that the study last.

Based on the consumption of antibacterial products, the parents' meetings, home visits and phone interviews, we have concluded that compliance with interventions was high during the study.

Effect on the Prevalence of Illness or SL

Effect on the Number of Person Month for Illness or SL Every month for each person was counted as one person month. There were 4,728 person months for 393 children. Table 3 displays the number of person month for symptoms, illness or SL. The odds ratio (OR) and confidence intervals between the two groups were calculated. Except for abdominal pain, interventions reduced the odds of symptoms, illness or SL. There were statistically significant differences between the two groups for fever [OR=0.42 (CI: 0.3-0.5), *P*=0.000], cough and expectoration [OR=0.56 (CI: 0.48-0.52), *P*=0.000], runny nose and nasal congestion [OR=0.51 (CI: 0.43-0.60), *P*=0.000], RI [OR=0.47 (CI: 0.38-0.59), *P*=0.000], diarrhea [OR=0.37 (CI: 0.22-0.60), *P*=0.000], GI [OR=0.42 (CI: 0.26-0.67), *P*=0.000], and SL [OR=0.61 (CI: 0.45-0.82), *P*=0.001].

Table 2. The Consumption of Antibacterial Products by Person Day

Products	Volume (mL/bottle)	Total Usage (bottle)	Person Usage (mL/person day)
Liquid antimicrobial soap*	525	4124	7.7
	5000	33	
Instant hand sanitizer	20	20600	1.4
Bleach	3000	2,537	25.0
Antiseptic-germicide	1800	2116	12.5

Note. *Liquid antimicrobial soap has two size specifications which were 525 mL/bottle and 5000 mL/bottle.

Table 3. Number of Person Month for Illness or SL, OR, and 95% CI

Illness or SL	Control (*n*=2388)			Intervention (*n*=2328)			OR (95% CI)
	No	Yes	Odds	No	Yes	Odds	
Fever	2113	275	0.13	2208	120	0.05	0.42 (0.34-0.52)*
CAE#	1829	559	0.31	1989	339	0.17	0.56 (0.48-0.65)*
RNANC&	1951	437	0.22	2091	237	0.11	0.51 (0.43-0.60)*
RI	2154	234	0.11	2214	114	0.05	0.47 (0.38-0.59)*
Diarrhea	2333	55	0.02	2308	20	0.01	0.37 (0.22-0.60)*
Abdominal Pain	2368	20	0.01	2312	16	0.01	0.82 (0.42-1.58)
GI	2330	58	0.02	2304	24	0.01	0.42 (0.26-0.67)*
SL**	1873	117	0.06	1869	71	0.04	0.61 (0.45-0.82)*

Note. #CAE-cough and expectoration; &RNANC- runny nose and nasal congestion; *Statistically significant result (χ^2-Test, $P<0.05$); **Because of summer holiday, SL has 3930 person months.

Effect on the Month Incidence Rate of Illness or Absence The incidence rates per month of the control group for fever (0-26.1%), RI (0-27.6%) and GI (0-7.0%) shown two seasonal peaks, which were autumn (October) and spring (April) for fever, autumn (October) and spring (March) for RI, autumn (November) and summer (August) for GI (Figure 2A-2C). Overall, the incidence rates of the intervention group decreased compared to the control group, especially for the seasonal peaks. The range of incidence rates in the intervention group per month were 0-17.0% (fever), 0-21.6% (RI), 0-4.6% (GI), respectively. There was only one seasonal peak at the beginning of the study, and a decline of incidence rates could be seen.

The incidence rates for SL of the intervention group (4.1%-9.5%) decreased compared to the control group (0.5%-11.9%), although the intervention group was higher than the control group at the beginning of the study (Figure 2D). A decline of incidence rates could be seen in the intervention group.

Effect on the Frequency of Illness or Absence in 12 Months The frequency (occurring 0, 1, 2, 3 or more times) of fever, diarrhea, RI, GI, and SL were determined for each child (Table 4). The constitution ratios of 1, 2, 3 or more times for fever, diarrhea, RI and GI in intervention group are higher than control group. The constitution ratios of 1, 2 for SL in intervention group are higher than control group. There are statistically significant differences between the two groups. Interventions reduced the frequency of fever, diarrhea, RI, GI and SL.

Preventive effect on the prevalence of illness or absence The rates of fever, diarrhea, RI, GI, and SL per person year in control group were 1.41, 0.28, 1.21, 0.29, and 0.59, in intervention group were 0.62, 0.11, 0.59, 0.13, and 0.37, respectively (Table 5). Interventions reduced the rates of fever, diarrhea, RI, GI, and SL. There were statistically significant differences between two groups. The protection rates of multiple interventions on fever, diarrhea, RI and GI is more than 50%. The protection rate of multiple interventions on SL is almost 40%.

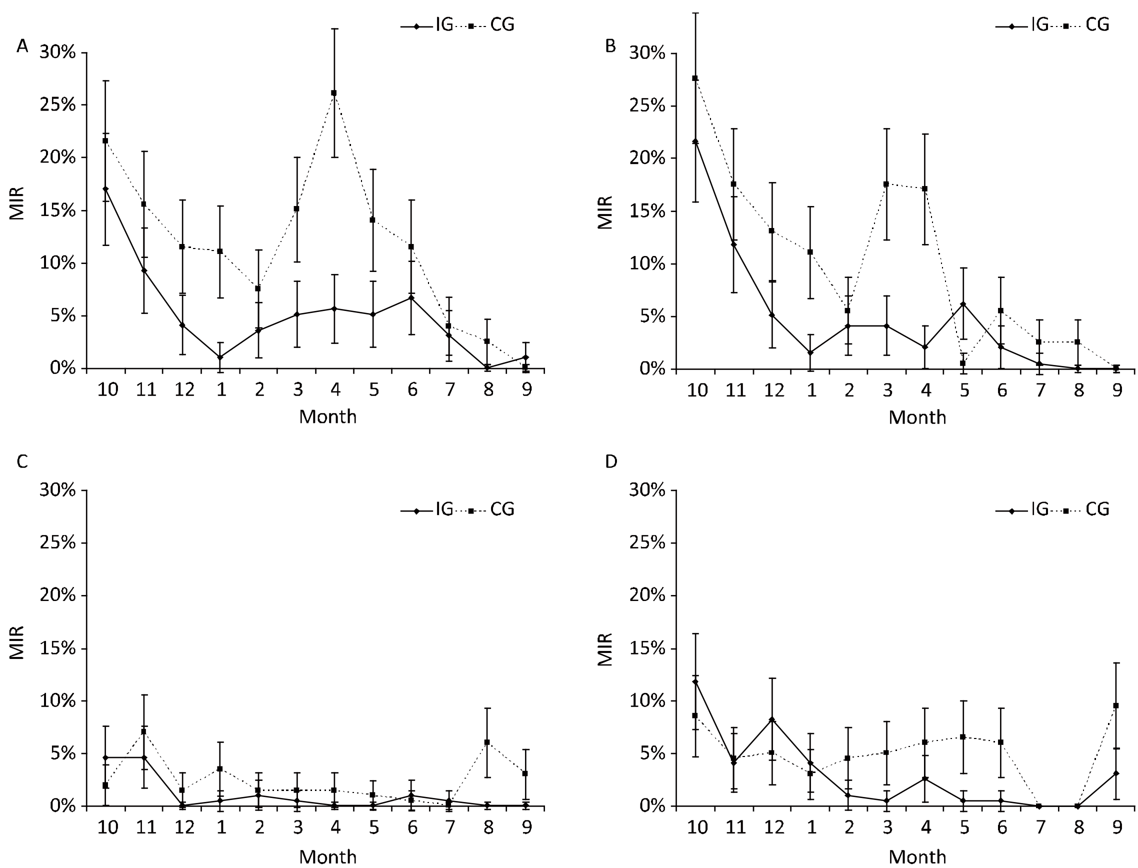

Figure 2. Month incidence rates (95% CI) for fever, RI, GI, and SL. MIR, Month incidence rate; IG, Intervention group; CG, Control group. (A) Fever; (B) RI; (C) GI; (D) SL. The horizontal axis started in Oct 2010 and lasted until Sep 2011. Jul and Aug was summer holiday.

Table 4. Effect on the Frequency of Fever, Diarrhea, RI, GI, and SL in 12 Months

Illness or SL	Frequency	Control		Intervention		*P* value
		n=199	%	*n*=194	%	
Fever	0	60	30.2	110	56.7	0.000
	1	58	29.1	58	29.9	
	2	45	22.6	17	8.8	
	≥3	36	18.1	9	4.6	
Diarrhea	0	154	77.4	175	90.2	0.004
	1	36	18.1	17	8.8	
	2	8	4.0	2	1.0	
	≥3	1	0.5	0	0.0	
RI	0	79	39.7	123	63.4	0.000
	1	59	29.6	41	21.1	
	2	22	11.1	20	10.3	
	≥3	39	19.6	10	5.2	
GI	0	152	76.4	172	88.7	0.009
	1	37	18.6	19	9.8	
	2	9	4.5	3	1.5	
	≥3	1	0.5	0	0.0	
SL	0	109	54.8	141	72.7	0.002
	1	65	32.7	38	19.6	
	2	23	11.6	12	6.2	
	≥3	2	1.0	3	1.5	

Table 5. Preventive Effect on the Rates of Fever, Diarrhea, RI, GI, and SL per Person Year

Illness or Absence	Control	Intervention	*PR* (95% CI)
Fever	1.41	0.62	56.04 (52.64,59.62)*
Diarrhea	0.28	0.11	60.83 (42.73,78.94)*
RI	1.21	0.59	50.85 (45.86,55.84)*
GI	0.29	0.13	55.79 (36.99,74.59)*
SL	0.59	0.37	37.75 (24.14,51.37)*

Note. *Statistically significant result (*P*<0.005). *PR*, protection rates.

DISCUSSION

This study is one of the first investigations on the effectiveness of multiple interventions, consisting of children and their family members, hand hygiene and the cleanliness of the environment and surfaces in their homes and kindergartens. We found that multiple interventions reduced the acute respiratory and gastrointestinal illness and the sick leave in children.

Environmental surfaces are always contaminated by bacteria, fungi and viruses, some of them may be able to survive for extended periods of time[7-10]. Pathogens can transfer from surfaces to hands, then to the respiratory tract or digestive tract. Patricia Rusin reported that under simulated laboratory conditions, surface-to-hand transfer rates of gram-positive bacteria, gram-negative bacteria, and phage were 27.59%-65.80%, fingertip-to-mouth transfer rates were 33.90%-40.99%[11]. Therefore, hand hygiene and surface disinfection could theoretically eliminate pathogens, break the transmission route, and furthermore reduce the frequency and effect of infectious diseases. During the past few decades, most of the research has paid attention to the effects of hand hygiene on infectious diseases in hospitals, day care centers, and schools. A lot of researches has shown that hand hygiene, consisting of hand washing or disinfection, could reduce nosocomial infections in hospitals[12-13], reduce the acute respiratory and gastrointestinal illness and the sick leave rate in day care facilities, schools and workplaces[14-17], as well as help to reduce the amount of acute respiratory and gastrointestinal illnesses spread between family members[18-19]. Based on papers published from January 1960 through May 2007, a Meta-Analysis showed that improvements in hand hygiene resulted in reductions in gastrointestinal illness by 31% [(CI) 19%, 42%] and reductions in respiratory illness by 21% [(CI) 5%, 34%]. Hand hygiene is clearly effective against gastrointestinal and, to a lesser extent, respiratory infections[19]. Sandora et al[4] had taken a study placed over an 8-week period (March to May 2006). A multifactorial intervention including hand sanitizer and surface disinfection reduced absenteeism caused by gastrointestinal illness in elementary school students. The absenteeism rate for respiratory illness was not reduced by this intervention which is different from our study. Our study showed that multiple interventions not only reduced gastrointestinal illness, but also reduced acute respiratory illness, the protection rate is 55.79% [(CI) 36.99%, 74.59%] and 50.85% [(CI) 45.86%, 55.84%], which illustrated that contaminated surfaces may play an important role in infectious disease transmission, especially for children. Children spend most of their time indoors such as homes, day care centers, kindergartens and schools. Because children under 5 years old likely have not developed good hand hygiene habits, contaminated surfaces threaten their health more than adults. Poorly sanitized surfaces don't only allow for the transference of infectious disease to one child but also between children and family members. Field and laboratory studies have repeatedly shown the importance of environmental disinfection as part of an integrated approach to infectious disease control[2]. And we think that multiple interventions are more effective than isolated intervention. Multiple interventions (hand hygiene and surface cleaning or disinfection) should be taken at homes, day care centers, kindergartens and schools.

Our study may have several limitations. We did not adopt the use of individual randomized design. The symptoms of illnesses were diagnosed by the parents or guardians (based on the provided definitions) rather than a clinical diagnosis or microbiologic confirmation. Sick leave was due to any of the illnesses rather than just infectious diseases. Neither the participants nor the investigators were blinded. However, keeping these limitations in mind we attempted to reduce ascertainment bias, through the use of Daily Record Calendars for both the homes and kindergartens while maintaining close contact with the parents, or guardians, and teachers from both groups.

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