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Major Article

Effectiveness of a hand hygiene program to reduce acute gastroenteritis at child care centers: A cluster randomized trial

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Key Words:
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A B S T R A C T

We aimed to assess the effectiveness of an educational and hand hygiene program in daycare centers (DCCs) and homes on acute gastroenteritis (AGE) incidence in children attending DCCs.

METHODS: A randomized, controlled, and open study of 911 children aged 0-3 years attending 24 DCCs in Almería (Spain) with an 8-month follow-up was employed. Two intervention groups of DCCs families performed educational and hand hygiene measures, 1 with soap and water (soap and water group; n = 274), another with hand sanitizer (hand sanitizer group [HSG]; n = 339), and the control group (CG; n = 298) followed usual handwashing procedures. We compared AGE episode rates with Poisson regression model.

RESULTS: seven hundred fourteen AGE episodes were registered, significant differences between HSG and CG children were found during December and January. A multivariate model was applied and the adjusted incidence rate ratios by rotavirus vaccination found significant differences when children were previously vaccinated, the children in the soap and water group had a higher risk of AGE episodes (incidence rate ratio: 1.28, 95% confidence interval:1.0-1.64), compared with those in the HSG.

CONCLUSIONS: This study demonstrated that hand hygiene programs that included hand sanitizer were most effective in the winter months. Further, the largest reduction of AGE episodes occurred in the children that followed hand hygiene programs including hand sanitizer and educational measures for DCC staff, parents, and children, and were vaccinated for rotavirus.

Acute gastroenteritis (AGE) is a leading cause of morbidity and mortality in children under 5 years worldwide.[1,2] In developed countries, it is an important cause of primary care and emergency visits, hospitalization, and medication prescription, especially in children attending daycare centers (DCCs).[3-10] Diarrhea incidence ranges from 0.5 to 2 episodes/y in children under three years in the European Union,[11] with rotavirus being the most frequent cause of severe diarrhea.[6,11,12] Rotavirus vaccines have been available in Spain since 2006 and have had a great impact on severe AGE prevention and rotavirus disease burden reduction.[13-19]

Handwashing is the most important and effective measure to prevent infection transmission.[20,21] Hydroalcoholic gels or hand sanitizers are virucides and bactericides against gastrointestinal and respiratory pathogens.[22-26]

Meta-analyses and systematic reviews[27-29] found that handwashing can reduce the risk of diarrhea by 31%-47%. Handwashing

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promotion (education activities, sometimes with the provision of soap) at DCCs or schools prevents approximately 30% of diarrhea episodes in high-income countries.[30]

There are studies that assess the impact of hand hygiene programs on infectious disease transmission reduction in schools[31-35] and households.[36,37] However, there are few recent studies that evaluate their effectiveness in DCCs,[38-40] specifically, those examining the importance of hand hygiene health education for DCC-staff and parents to reduce infection transmission in DCCs.[37,41,42]

Few randomized studies regarding the effectiveness of hand hygiene programs (hand sanitizer vs handwashing vs control) linked to a decrease in AGE in DCCs in developed countries have been published. We aimed to assess the effectiveness of an educational and hand hygiene program in DCCs and homes on AGE incidence in children at the individual level, and the association of sociodemographic characteristics and personal background with incidence AGE in children.

METHODS

Design

An 8-month (November 2013-June 2014) cluster, randomized, controlled, and open study of 3 cohorts of families with children aged 0-3 years attending 25 state DCCs in the Almeria metropolitan area (Spain) was designed. The Delegation of Education provided the information for 52 state DCCs. These were randomized after each administration agreed to participate; 25 DCCs were randomly selected, and after DCCs were assigned to one of the intervention groups (IG) or the control group (CG) by using statistical software (Epidat 4.0, Coselleria de Sanidad de Xunta de Galicia, Spain) for a 1:1:1 ratio randomization. The 25 randomized DCC administrations informed parents by mail with the following documents: a study information sheet, an authorization form, and a questionnaire about AGE risk factors (Table 1). Before starting the study, parents authorized their children's participation and knew which group their children belonged to.

Inclusion criteria: Children between 0 and 3 years old enrolled in the aforementioned DCCs and attending at least 15 hours per week whose parents and/or guardians had signed an informed consent document were included.

Exclusion criteria: Children with chronic illnesses or taking medication that could affect their likelihood of contracting an infection were excluded.

Sample size

A cluster sampling design[44] was used, with proportional allocation to the size of the cluster. The clusters were the DCCs for children in Almeria.

There were 52 DCCs, with 50 children per DCC on average. As in another study[11] for an incidence rate of 1.6, we assumed a 20% reduction in AGE incidence rate in the experimental groups with respect to the CG during the study period. Minimum selections of 6 DCCs per group were needed for a statistical power of 80% and a 5% significance level. A 10% variation coefficient was considered, and the average sample size was 30 children per cluster, to account for families that may decline study participation. Furthermore, an increase of 2 DCCs per group were randomly selected for the CG and soap and water group (SWG); and 3 DCCs for hand sanitizer group (HSG), with at least 240 children per group, for possible follow-up losses. The expected loss to follow-up was higher in the HSG because of parents' possible refusal to use hand sanitizer on their children's hands.

Table 1
Risk factors for acute gastroenteritis included in the multilevel model

Child
Age at the beginning of the study
Age at start of DCC attendance
Hours per week in DCC
Sex (female, male)
Country of origin
Chronic illness
Duration of breastfeeding (months)
Rotavirus vaccine
Sleeping arrangements (private, shared bedroom)
Siblings at home (0, 1-2, ≥3)
Home
Family size (≤3, 4-5, ≥6)
Mother's age
Father's age
Mother's profession* (I, II, III, IV, V, VI, VII, VIII, IX, X)
Father's profession* (I, II, III, IV, V, VI, VII, VIII, IX, X)
Mother's educational level (low, middle, high)
Father's educational level (low, middle, high)
Housing (flat, house, semi-detached house, other)
Shared bedroom
Season
Month of infection
DCC factors
Meals at DCC
Hygiene intervention group at the DCC (none, soap, hand sanitizer)
Average number classrooms per DCC
Average space per child in classroom (Children per square meter)
Number of children per staff

*Professions are according to the European Socioeconomic classification: I - managers and professionals of high level; II - managers and professionals of a low level; III - white-collar employees of high level; IV - small employers and self-employed nonagricultural workers; V - self-employed agricultural workers; VI - supervisors and technicians of lower rank; VII - workers of services and commerce of lower rank; VIII - skilled manual workers; IX - unskilled workers; X - excluded labor market and long-term unemployed.[43]

Intervention

One month before study initiation (October 1-3, 2013) parents and DCC-staff assigned to intervention groups (IGs) (HSG and SWG) and the CG attended 1-hour hand hygiene workshops, which were designed and taught by the researchers. All participating families and DCC-staff attended. The content included education about handwashing practices and hand sanitizers use, possible side effects, and precautionary measures (only for the HSG).

Researchers instructed both IGs' children/parents and DCC-staff to maintain usual handwashing procedures after using the toilet and when their hands were visibly dirty. Both IGs followed protocol in these circumstances: after coming into the classroom; before and after lunch; after playing outside; when they went home; and after coughing; sneezing or blowing their noses; after diapering. In the HSG and SWG classrooms, hand sanitizer and liquid soap dispensers were installed, respectively, and informational brochures about when and how to perform hand hygiene were available. IG families were provided the same informational brochure and supplies of hand sanitizer (HSG) or liquid soap (SWG) for home use during the study period by the research assistant in the DCCs. The HSG children were supervised by DCC-staff and parents when using hand sanitizer, and for young children, it was administered by DCC-staff and parents. The CG followed usual handwashing procedures. Hand sanitizer characteristics: ethyl alcohol 70%, pH = 7.0-7.5. The liquid soaps used for handwashing in the SWG did not contain specific antibacterial components (pH = 5.5).

During the follow-up, researchers organized 2 identical training sessions per DCC for parents and/or DCC staff in the IGs that were given 1 month apart, the first 3 on respiratory infections and AGE and their treatments, the second 3 on fever. Those who were unable

to attend training in their own DCC were invited to attend sessions in other centers. The workshop content was sent by e-mail to the IGs.

Every 2 weeks, the research assistant and DCC-staff performed the same activities (stories, songs, and posters in the classrooms and DCCs) regarding hand hygiene and infection transmission.

Data collection and illness definitions

During October 2013, parents completed the baseline questionnaire and gave it to the DCC staff. Information about DCCs was provided by the staff (Table 1). Beginning on November 1, 2013, DCC-staff collected parent-completed AGE episode (with or without DCC absenteeism) sheets, which reported AGE symptoms, treatments, contact with medical services, and complementary analyses. The research assistant collected the episode sheets weekly and telephoned absent children's parents to inquire about the absence causes. The DCC staff and/or parents in the IGs were asked if the hand sanitizer or soap caused any side effects in the children.

AGE was defined as a decrease in stool consistency (loose or liquid) and/or an increase in frequency (typically ≥3 in 24 hours), with or without fever or vomiting, according to the ESPGHAN definition.[11]

During follow-up, the research pediatricians extracted AGE episode medical data and checked rotavirus vaccination status from the Department of Health's electronic records. International Classification of Diseases, Ninth Revision, Clinical Modification[45] diagnosis codes were used: diarrhea (787.91), or gastroenteritis (558.9).

In 2010, the Spanish Agency of Medicine suspended the commercialization of both rotavirus vaccines (not funded by the government) for 5 months in the case of the pentavalent vaccine (June-November 2010), and for 6 years for the monovalent vaccine (June 2010-June 2016). From 2011 to 2014, only the pentavalent rotavirus vaccine was available in Spain, and the vaccination schedule was at 2-4-6 months old.

The medical researchers made the final diagnosis based on the symptoms described above and a review of the medical history of children with AGE.

In this study, a DCC absenteeism episode was defined as when a child fails to attend a DCC because of AGE. We also recorded AGE episodes without DCC absenteeism. A new AGE episode was considered to be the occurrence of AGE after a period of 3 symptom-free days, as in other studies.[36,39] The duration of absenteeism was defined as the number of DCC days missed due to AGE, excluding weekends and holidays.

Outcome measures

The AGE incidence rate was calculated by the number of AGE episodes divided by the number of children during the study period. The incidence rate ratio (IRR) was defined as the ratio of AGE between 2 groups. Percentage of AGE absenteeism days in the 3 groups calculated as the ratio of AGE absenteeism days to all possible study period attendance days. The total possible days of attendance was calculated as the total number of children multiplied by the possible attendance days.

Statistical analysis

Children's socio-demographic and DCC characteristics in the 3 study groups were compared by using χ^2 tests, Fisher-Snedecor distribution from analysis of variance, Welch test, and Brown-Forsythe test with a 95% confidence intervals (CIs)

A multilevel Poisson regression model was applied to fit the number of AGE events. Two levels were considered: children grouped into classrooms by age (0-1, 1-2, and 2-3 years) and DCC random effect level. In addition, infant random effect was included to take into account overdispersion in the Poisson mode.[46-48] We used observation-level random effects to model overdispersion in counting data for ecology and evolution. First, an unadjusted covariate model was applied to check the IRR of AGE for each covariate of study applied. Thus, adjustment for variables in Table 1 was calculated. Finally, a full multivariate model with all variables under study was applied, and model reduction was conducted by using a backward procedure. Covariates were removed if no significant association with the parameter was detected, if no interaction effect with group was found, and when no change in the rest of parameters was observed after removal (considering a 30% of change as a possible confounder).[49,50] Goodness of fit of the model in each step was performed by checking residuals and the Bayesian information criteria. The adjusted IRR from the multivariate model is provided along with its 95% CI. The percentage of days absent from a DCC was compared with Poisson exact test results.

The statistical tests were performed at a 5% significance level by using SPSS version 19.0 (SPSS, Inc., Chicago, IL) and R version 3.1.3 (R Foundation, Austria).

This study was reviewed and approved by the ethical review board for clinical trials at Hospital Torrecardenas (Almeria, Spain), and permission to review medical records was also granted.

RESULTS

Fifty-two DCCs were initially contacted, of which 25 were randomized with 1176 children, and 960 (81.63%) had parental participation authorization. Approximately 95% of parents returned the completed questionnaire and AGE data collection notebook, so the final sample size was 911 children. Approximately 5% of the children did not complete the study; this did not affect the results as confirmed by nonreported analyses. One child in the HSG showed worsening of localized atopic dermatitis due to hand sanitizer gel use and was excluded during the follow-up (Fig 1).

Table 2 includes the 3 groups' sociodemographic and DCC characteristics. Significant between-group differences were found including more SWG families had immigrant status, and the parents had lower social class and educational level. All DCCs met the requirements regarding facilities, material conditions, square meters per child, number of courses per DCC, and the number of children per staff member stipulated by the government.[51] The potential biases were controlled by including these variables in the multilevel analysis, adjusting the incidence rates of AGE by them (Table 1).

During the study period, 714 AGE episodes occurred (242 CG, 231 SWG, 241 HSG); a doctor confirmed diagnoses in 79.3% of episodes. Figure 2 shows AGE incidence per child and per month. Significant differences between the HSG versus CG were found when children had more AGE episodes, in December and January, $P < .05$.

Table 3 includes the final adjusted multivariate model. The adjusted incidence rate ratios by rotavirus vaccination show significant differences when children had been previously vaccinated. For children with rotavirus vaccination, the risk of AGE when using soap and water was significantly higher than when using hand sanitizer (IRR: 1.28, 95% CI: 1.0-1.64). Note that male sex and child age at DCC initiation were also significantly associated with AGE. No other variables were significant.

Pupils missed 1781 DCC days due to AGE (CG = 584, SWG = 594, HSG = 603). The total possible days of attendance were 44,998 (CG), 41,374 (SWG), and 51,189 (HSG). The percentage of AGE absenteeism days was not significantly lower in the HSG (1.17%, 95% CI: 1.08-1.27) compared to SWG (1.43%, 95% CI: 1.32-1.55), $P = .051$ and CG (1.29%, 95% CI: 1.19-1.41), $P = .098$; and SWG versus CG $P = .086$.

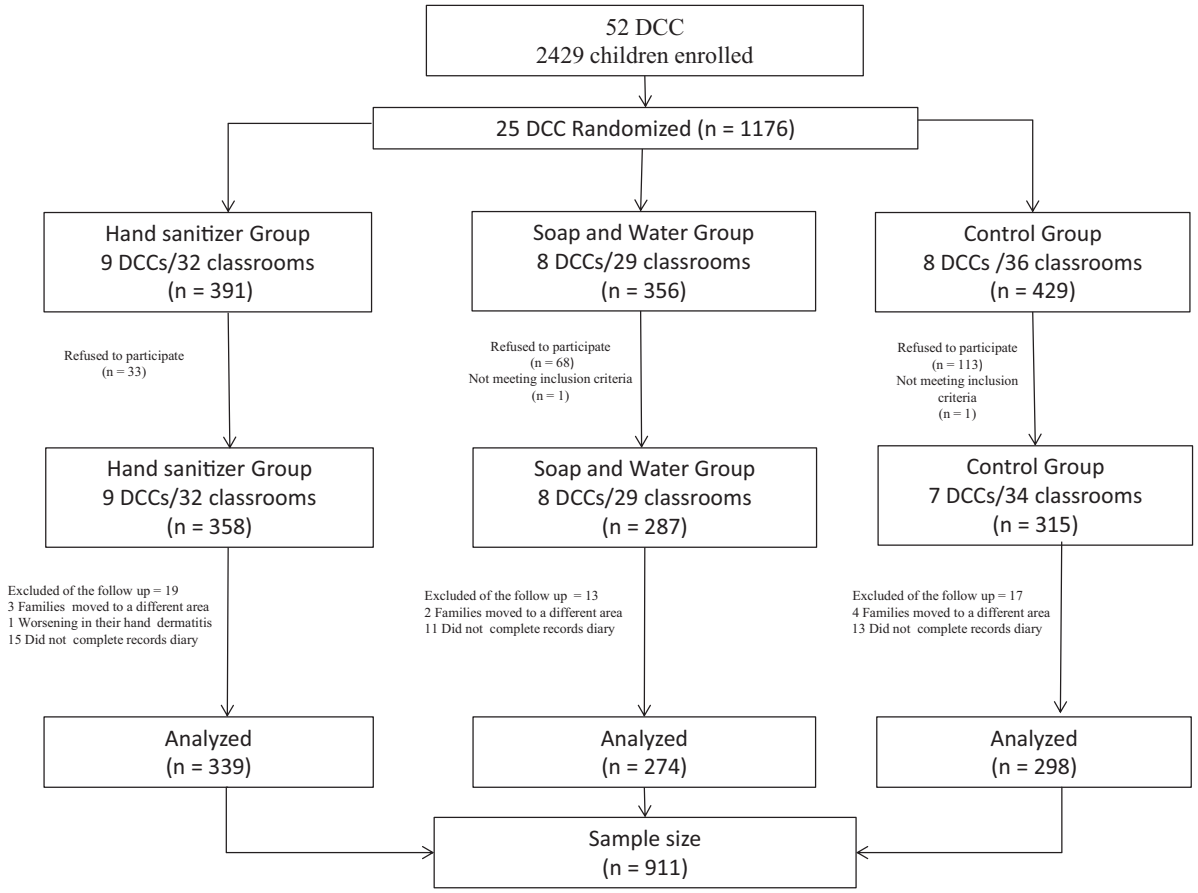


Fig 1. Participant flow diagram.

DISCUSSION

To our knowledge, this is the first paper that studies the effectiveness of educational and hand hygiene programs (hand sanitizer vs hand-washing vs control) in DCCs and homes on AGE incidence in children attending DCCs. Significant differences regarding AGE episodes between HSG and CG were found during the months of December and January. A randomized study[39] observed a 50% reduction in AGE episodes in children over 24 months of age attending DCCs who followed a hand hygiene intervention with hand sanitizers. We found significant differences in the winter months, this may be because these months had an increase of AGE episodes and this is when the intervention may be more effective (Fig 2). A similar winter peak seasonal influence has been reported in other industrialized countries[9,52,53] and it suggests contributions of rotavirus and norovirus to the increased AGE incidence in children at DCCs.[9]

For children with rotavirus vaccination, we found a 28% higher risk of AGE, when belonging to the SWG instead of the HSG. Lennell et al[40] separately measure both interventions and found a 12% reduction of absenteeism due to infections in the HSG compared with using soap. Our results of a lower incidence of AGE in HSG versus SWG (0.72/child/study period vs 0.93/child/study period) were in part due to an increase in rotavirus vaccine coverage in the HSG (77.9%) compared with SWG (59.5%), according to others studies,[15,17,54,55] and in part due to the herd effect of rotavirus vaccination.[56] In addition, the virucidal effect[22,23] and greater adherence to the hand hygiene program with hand sanitizer than to the soap-and-water program may explain the results, as educational measures were the same in both groups in our study. Families and/or DCC staff used 1660 L of hand sanitizer during the study period; with the expected use of 1-2 mL of hand sanitizer per disinfection, we estimated that each child used hand sanitizer between 6 and 8 times per day. Families and/or DCC staff used 890 L of liquid soap during the study period; with the expected use of 1-1,5 mL of soap per washing, we estimated that each child washed their hands with soap between 3 and 5 times per day.

Other studies,[57,58] did not observe a significant reduction in AGE episodes in children attending DCCs following hand hygiene interventions. However, comparing our results with previous studies is difficult for several reasons: the differences in design, most of the studies conducted at DCCs were prior to the availability of rotavirus vaccines,[38,39,59] and others do not analyze its influence on the gastroenteritis incidence.[57,58] Hand hygiene is known to be an effective measure to prevent the transmission of AGE.[27-30] However, the best way to prevent rotavirus diarrhea is rotavirus vaccination.[17,19,60]

The children in the HSG had fewer DCC absence days due to AGE than those in the SWG and CG, and there was near statistical significance between the HSG and SWG. This was in line with another study,[40] and indicates a possible reduction in the use of medical resources and parent work absenteeism.

Previous studies found different results regarding the association of gender with infectious diseases.[39,53,61,62] In our study girls had a lower risk of AGE than boys.

Children who were older at DCC initiation were less at risk of gastroenteritis than younger children, in line with other studies[7,53,61] it is probably due to greater maturity of the immune system.

Families from different socioeconomic levels and countries of origin, as well as children who used public and private health services, took part in our study, so our findings are likely representative of the AGE episodes in children at DCCs in our area. These could be

Table 2
Sociodemographic and DCC characteristics in intervention and control groups

	CG (N = 298)	SWG (N = 274)	HSG (N = 339)	*P*
Age at the beginning of the study in months, mean (SD)	20.67 (7.94)	21.10 (7.73)	21.59 (8.21)	.13*
Age at start of DCC attendance in months, mean (SD)	11.32 (5.56)	11.91 (5.79)	12.63 (6.31)	. 02†
Hours per week in DCC, mean (SD)	27.6 (7)	29.6 (7.7)	28.2 (7.1)	.05†
Duration of breastfeeding in months, mean (SD)	5.85 (6.45)	6.38 (6.14)	5.83 (6.28)	.81*
Sex female, n (%)	126 (42.28)	146 (53.28)	149 (43.95)	.018‡
Immigrant status, n (%)	20 (6.71)	43 (15.69)	20 (5.90)	.001‡
Chronic illness n (%)	2 (0.7%)	7 (2.6)	13 (3.8)	.034‡
Pentavalent rotavirus vaccine, n (%)	227 (76.2)	163 (59.5)	264 (77.9)	<.001‡
Family size				.050‡
≤3	124 (41.61)	108 (39.42)	123 (36.28)	
>3-≤5	161 (54.03)	137 (50)	187 (55.16)	
>5	13 (4.36)	29 (10.58)	29 (8.55)	
Siblings at home n (%)				.017‡
0	135 (45.30)	117 (42.70)	128 (37.76)	
1-2	158(53.02)	139 (50.73)	191 (56.34)	
≥3	5 (1.68)	18 (6.57)	20 (5.90)	
Father's age, mean (SD)	35.4 (6.6)	34.3 (6.7)	35.5 (5.7)	.06*
Mother's age, mean (SD)	33.1 (5.7)	31.2 (5.7)	33.3 (5.2)	.21*
Father's educational level, n (%)				<.001‡
Low	91 (30.06)	108 (40.00)	91 (27.16)	
Middle	162 (52.29)	114 (42.22)	151 (45.07)	
High	40 (13.65)	48 (17.78)	93 (27.76)	
Mother's educational level, n (%)				0.002‡
Low	69 (23.15)	87 (31.75)	78 (23.01)	
Middle	146 (48.99)	117 (42.70)	134 (39.53)	
High	83 (27.85)	70 (25.55)	127 (37.46)	
Father's profession[d], n (%)				.002‡
I-III, VI	74 (25.26)	59 (21.85)	107 (31.94)	
IV-V	53(18.09)	43 (15.93)	71 (21.19)	
VII, X	95 (32.42)	76 (28.15)	74 (22.09)	
VIII, IX	71 (24.23)	92 (34.07)	83 (24.78)	
Mother's profession[d], n (%)				0.001‡
I-III, VI	93 (31.21)	72 (26.28)	136 (4.12)	
IV-V	47 (15.77)	34 (12.41)	40 (11.80)	
VII, X	43 (14.43)	29 (10.58)	44 (12.98)	
VIII, IX	115 (38.59)	139 (50.73)	119 (35.10)	
Type of dwelling, n (%)				<.001‡
Flat	226(75.84)	161 (58.76)	204 (60.18)	
House	33 (11.07)	68 (24.82)	59 (17.40)	
Semidetached houses	35 (11.74)	44 (16.06)	69 (20.35)	
Other	4 (1.34)	1 (0.36)	7 (2.06)	
Shared bedroom, n (%)	206 (69.13)	190 (69.34)	214 (63.13)	.166‡
Meals at DCC, n (%)	284 (95.3)	259 (94.5)	320 (94.4)	.86‡
DCCs characteristics	N = 7	N = 8	N = 9	
Number classrooms per DCC, mean (SD)	4.9 (3.2)	3.6 (1.9)	3.6 (1.4)	.035†
Children/m^2 space in classroom, mean (SD)	3.7 (1.7)	3.1 (1.1)	2.8 (1.4)	.452*
Number of children per staff, mean (SD)	6.6(1.8)	7.2 (2.1)	7.7(3.1)	.029*

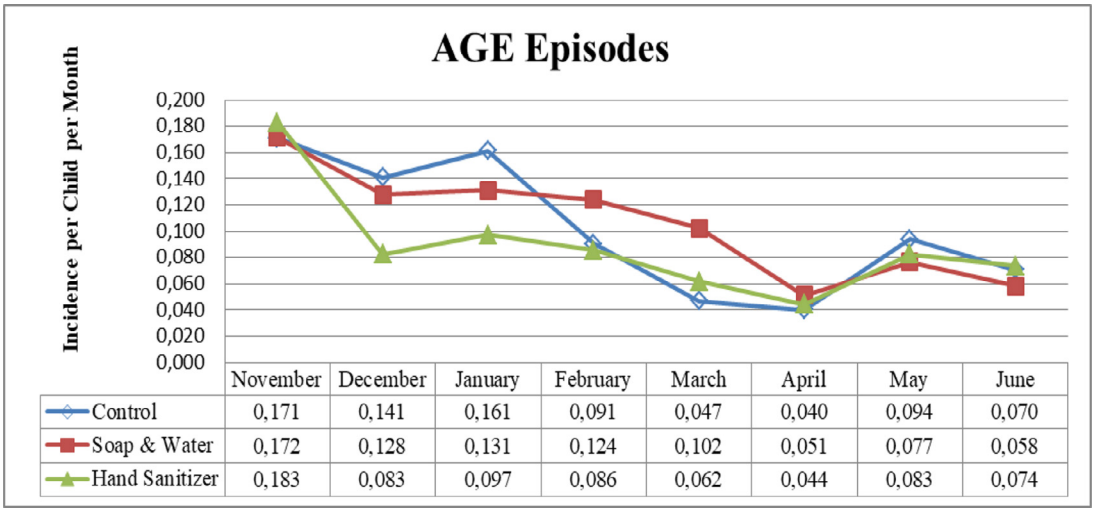
SD, standard deviation.
*F-Snedecor.
†Welch Test.
‡Chi-square test (χ^2).
¶Professions are according to the European Socioeconomic classification (see Table 1).

generalized in similar DCCs in Spain and with similar vaccination coverages against rotavirus because most of the AGE episodes were diagnosed by a doctor. As other authors indicate[53,63] the risk and protective factors of infections in children at DCCs are difficult to identify, and their importance may vary between societies and countries. Therefore, these results may not be generalizable to DCCs where sociodemographic factors, infrastructure, and rotavirus vaccination coverages are substantially different.

Future studies are needed to assess which factors of multicomponent interventions may be most effective in reducing infections in children attending DCCs.

Limitations

Although 79.3% of AGE episodes had medical diagnoses, there was not microbiological confirmation in all cases (it was requested in 7.69%) as its diagnosis is clinical in most cases. Approximately 90% of children under 3 years old in Almeria attend state and state-subsidized, privately run DCCs, but we did not have access to exclusively private centers. The number of parents who did not authorize the study was greater in the CG, however, this did not affect the sample size. Masking both participants and researchers was not feasible given the study characteristics, so the statistical analyses were masked until completion. We did not monitor the IGs program compliance through continuous hand hygiene behavior observation as in most DCC intervention studies;[40,57,59] however previous researchers[64-66] found that individuals might change their behavior when aware of observation. Nevertheless, we monitor the IGs hand hygiene material consumption. Only the IGs received educational intervention making the relative contributions of education versus hand hygiene in the reduction of AGE episodes unattainable in this study. Another potential limitation is that we do not know if the families of CG used hand sanitizer during the study period.



	November	December	January	February	March	April	May	June
Control	0,171	0,141	0,161	0,091	0,047	0,040	0,094	0,070
Soap & Water	0,172	0,128	0,131	0,124	0,102	0,051	0,077	0,058
Hand Sanitizer	0,183	0,083	0,097	0,086	0,062	0,044	0,083	0,074

Fig 2. AGE episodes in the CG, SWG, and HSG per child per month at DCCs in Almeria (Spain), November 2013 to June 2014.

Table 3
Multivariate adjusted IRR for episodes due to AGE in children at DCCs

	Groups	IRR	95% CI	*P*
Rotavirus vaccination (RV)	CG vs SWG	0.96	0.76-1.23	.77
	CG vs HSG	1.24	0.99-1.55	.07
	SWG vs HSG	1.28	1.0-1.64	.04
No Rotavirus vaccination (Non-RV)	CG vs SWG	0.86	0.58-1.26	.44
	CG vs HSG	0.93	0.60-1.42	.73
	SWG vs HSG	1.08	0.74-1.57	.69
Age at the start of DCC attendance		0.98	0.97-0.99	.01 .02
Sex (male vs female)		1.22	1.03-1.44	.02

The final multilevel analysis was adjusted by age at start of DCC attendance, sex (female vs male) and rotavirus vaccine (interaction effect between rotavirus vaccination and group). The DCC characteristics considered were hygiene intervention groups at the DCC (none, soap, or hand sanitizer)
CG, control group; CI, confidence interval; HSG, hand sanitizer group; IRR, incidence rate ratio; RV, rotavirus vaccine; SWG soap and water group.

However, randomization was performed by DCC (all children in each DCC belonged to the same group) so there would be no contamination between groups.

CONCLUSIONS

This study demonstrated that hand hygiene programs that included hand sanitizer were most effective in the winter months with the highest incidence of AGE in children at DCCs. Further, the largest reduction of AGE episodes occurred in the children that followed hand hygiene programs including hand sanitizer and educational measures for DCC staff, parents, and children, and were vaccinated for rotavirus.

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References

1. Bryce J1, Boschi-Pinto C, Shibuya K, Black RE. WHO estimates of the causes of death in children. *Lancet*. 2005;365:1147–1152.
2. Walker CLF, Rudan I, Liu L, et al. Global burden of childhood pneumonia and diarrhoea. *Lancet*. 2013;381:1405–1416.
3. Zutavern A, Rzehak P, Brockow I, et al. Day care in relation to respiratory tract and gastrointestinal infections in a German birth cohort study. *Acta Paediatr*. 2007;96:1494–1499.
4. Ochoa C, Barajas MV, Muñoz B. Relación de la asistencia a guarderías y enfermedad infecciosa aguda en la infancia. Una revisión sistemática. *Rev Esp Salud Pública*. 2007;81:113–129.
5. Van der Wielen M, Giaquinto C, Gothefors L, et al. Impact of community-acquired paediatric rotavirus gastroenteritis on family life: data from the REVEAL study. *BMC Fam Pract*. 2010;11:22.
6. Ogilvie I, Khoury H, Goetghebeur MM, El Khoury AC, Giaquinto C. Burden of community-acquired and nosocomial rotavirus gastroenteritis in the pediatric population of Western Europe: a scoping review. *BMC Infect Dis*. 2012;12:62.
7. Enserink R, Ypma R, Donker GA, Smit HA, van Pelt W. Infectious disease burden related to child day care in the Netherlands. *Pediatr Infect Dis J*. 2013;32:e334–e340.
8. Enserink R, Scholts R, Bruijning-Verhagen P, et al. High detection rates of enteropathogens in asymptomatic children attending day care. *PLoS One*. 2014;9:e89496.
9. Hullegie S, Bruijning-Verhagen P, Uiterwaal CS, van der Ent CK, Smit HA, de Hoog ML. First-year daycare and incidence of acute gastroenteritis. *Pediatrics*. 2016;137:e20153356.
10. Del Castillo-Aguas G, Gallego-Iborra A, Gutiérrez-Olid M, Pérez-González O, Moreno-Muñoz G, Ledesma-Albarrán JM. Infectious morbidity and resource use in children under 2 years old at childcare centres. *J Paediatr Child Health*. 2017;53:116–122.
11. Guarino A, Ashkenazi S, Gendrel D, Lo Vecchio A, Shamir R, Szajewska H. European Society for Pediatric Gastroenterology, Hepatology, and Nutrition/EuropeanSociety for Pediatric Infectious Diseases evidence-based guidelines for the management of acute gastroenteritis in children in Europe: update 2014. *J Pediatr Gastroenterol Nutr*. 2014;59:132–152.
12. Giaquinto C, van Damme P, Group RS. Age distribution of paediatric rotavirus gastroenteritis cases in Europe: the REVEAL study. *Scand J Infect Dis*. 2010;42:142–147.

13. Akikusa JD, Hopper SM, Kelly JJ, Kirkwood CD, Kirkwood CD, Buttery JP. Changes in the epidemiology of gastroenteritis in a paediatric short stay unit following the introduction of rotavirus immunisation. *J Paediatr Child Health*. 2013;49:120–124.
14. Gil-Prieto R, Gonzalez-Escalada A, Alvaro-Meca A, et al. Impact of non-routine rotavirus vaccination on hospitalizations for diarrhoea and rotavirus infections in Spain. *Vaccine*. 2013;31:5000–5004.
15. Rha B, Tate JE, Payne DC, et al. Effectiveness and impact of rotavirus vaccines in the United States - 2006-2012. *Expert Rev Vaccines*. 2014;13:365–376.
16. Atchison CJ, Stowe J, Andrews N. Rapid declines in age group-specific rotavirus infection and acute gastroenteritis among vaccinated and unvaccinated individuals within 1 year of rotavirus vaccine introduction in England and wales. *J Infect Dis*. 2016;213:243–249.
17. Karafillakis E, Hassounah S, Atchison C. Effectiveness and impact of rotavirus vaccines in Europe, 2006-2014. *Vaccine*. 2015;33:2097–2107.
18. Pindyck T, Tate JE, Parashar UD. A decade of experience with rotavirus vaccination in the United States - vaccine uptake, effectiveness, and impact. *Expert Rev Vaccines*. 2018;17:593–606.
19. Díez-Domingo J, Garces-Sanchez M, Gimenez-Sanchez F, Colomina-Rodríguez J, Martinón-Torres F. Qué hemos aprendido sobre rotavirus en España en los últimos 10 años [e-pub ahead of print]. *An Pediatr (Barc)*. 2019. https://doi.org/10.1016/j.anpedi.2019.01.024. Accessed April 8, 2020.
20. Boyce JM, Pittet D, Healthcare Infection Control Practices Advisory Committee. HICPAC/SHEA/APIC/IDSA Hand Hygiene Task Force. Guideline for hand hygiene in health-care settings. Recommendations of the Healthcare Infection Control Practices Advisory Committee and the HICPAC/SHEA/APIC/IDSA Hand Hygiene Task Force. Society for Healthcare Epidemiology of America/Association for Professionals in Infection Control/Infectious Diseases Society of America. *MMWR Recomm Rep*. 2002;51(RR-16):1–45. quiz CE1–CE4.
21. World Health Organization. *WHO guidelines on hand hygiene in health care*. 2009.. Available at: http://apps.who.int/iris/bitstream/handle/10665/44102/9789241597906_eng.pdf . jsessionid= 7B49BB6C8F91C1E194FA2A843F05871F? sequence= 1. Accessed November 14, 2013.
22. Sattar SA, Abebe M, Bueti AJ, Jampani H, Newman J, Hua S. Activity of an alcohol-based hand gel against human adenovirus, rhinovirus, and rotavirus using de fingerpad method. *Infect Control Hosp Epidemiol*. 2000;21:516–519.
23. Sattar SA1, Ansari SA. The fingerpad protocol to assess hygienic hand antiseptics against viruses. *J Virol Methods*. 2002;103:171–181.
24. Fendler EJ, Hammond BS, Lyons MK, Kelley MB, Vowell NA. The impact of alcohol hand sanitizer use on infection rates in an extended care facility. *Am J Infect Control*. 2002;30:226–233.
25. Kampf G, Kramer A. Epidemiologic background of the most important agents for scrubs and rubs. *Clin Microbiol Rev*. 2004;17:863–893.
26. Tamimi AH, Carlino S, Edmonds S, Gerba CP. Impact of an alcohol based hand sanitizer intervention on the spread of viruses in homes. *Food Environ Virol*. 2014;6:140–144.
27. Curtis V, Cairncross S. Effect of washing hands with soap on diarrhoea risk in the community: a systematic review. *Lancet Infect Dis*. 2003;3:275–281.
28. Aiello AE, Coulborn RM, Perez V, Larson EL. Effect of hand hygiene on infectious disease risk in the community setting: a meta-analysis. *Am J Public Health*. 2008;98:1372–1381.
29. Willmott M, Nicholson A, Busse H, MacArthur GJ, Brookes S, Campbell R. Effectiveness of hand hygiene interventions in reducing illness absence among children in educational settings: a systematic review and meta-analysis. *Arch Dis Child*. 2016;101:42–50.
30. Ejemot-Nwadiaro RI, Ehiri JE, Arikpo D, Meremikwu MM, Critchley JA. Hand washing promotion for preventing diarrhoea. *Cochrane Database Syst Rev*. 2015 CD004265.
31. White CG, Shinder FS, Shinder AL, Dyer DL. Reduction of illness absenteeism in elementary schools using an alcohol-free instant hand sanitizer. *J Sch Nurs*. 2001;17:258–265.
32. Bowen A, Ma H, Ou J, et al. A cluster-randomized controlled trial evaluating the effect of a handwashing-promotion program in Chinese primary schools. *Am J Trop Med Hyg*. 2007;76:1166–1173.
33. Sandora TJ, Shih MC, Goldmann DA. Reducing absenteeism from gastrointestinal and respiratory illness in elementary school students: a randomized, controlled trial of an infection-control intervention. *Pediatrics*. 2008;121:e1555–e1562.
34. Azor-Martínez E, Cobos-Carrascosa E, Gimenez-Sanchez F, et al. A. Effectiveness of a multifactorial handwashing program to reduce school absenteeism due to acute gastroenteritis. *Pediatr Infect Dis J*. 2014;33:e34–e39.
35. Azor-Martínez E, Gonzalez-Jimenez Y, Seijas-Vazquez ML, et al. The impact of common infections on school absenteeism during an academic year. *Am J Infect Control*. 2014;42:632–637.
36. Lee GM, Salomon JA, Friedman JF, et al. Illness transmission in the home: a possible role for alcohol-based hand gels. *Pediatrics*. 2005;115:852–860.
37. Sandora T, Taveras E, Shih MC, et al. A randomized, controlled trial of a multifaceted intevention including alcohol-based hand-hygiene education to reduce illness transmission in the home. *Pediatrics*. 2005;116:587–594.
38. Carabin H, Gyorkos TW, Soto JC, Joseph L, Payment P, Collet JP. Effectiveness of a training program in reducing infections in toddlers attending day care centers. *Epidemiology*. 1999;10:219–227.
39. Roberts L, Jorm L, Patel M, Smith W, Douglas RM, McGilchrist C. Effect of infection control measures on the frequency of diarrheal episodes in child care: a randomized, controlled trial. *Pediatrics*. 2000;105(4 Pt 1):743–746.
40. Lennel A, Kühlmann-Berenzon S, Geli P, et al. Alcohol-based hand-disinfection reduced children's absence from Swedish day care centres. *Acta Paediatr*. 2008;97:1672–1680.
41. Rosen L, Manor O, Engelhard D, et al. Can a handwashing intervention make a difference? Results from a randomized controlled trial in Jerusalem preschools. *Prev Med*. 2006;42:27–32.
42. Zomer TP, Erasmus V, van Empelen P, et al. Sociocognitive determinants of observed and self-reported compliance to hand hygiene guidelines in child day care centers. *Am J Infect Control*. 2013;41:862–867.
43. Segura del Pozo J. Social classes in 21st century Spain (I): the European Socioeconomic Classification (ESeC). Available at:www.madrimasd.org/blogs/salud_publica/2012/02/12/133091. Accessed November 14, 2013.
44. Manatunga AK, Hudgens MG, Chen SD. Sample size estimation in cluster randomized studies with varying cluster size. *Biometric J*. 2001;43:75–86.
45. Centers for Disease Control and Prevention. International classification of diseases, Ninth revision, clinical modification [ICD-9-CM]. Available at:https://www.cdc.gov/nchs/icd/icd9cm.htm. Accessed December 5, 2014.
46. Gelman A, Hill J. Data analysis using regression and multilevel/hierarchical models. *JEM*. 2007;45:94–97.
47. Gardiner J, Luo Z, Roman LA. Fixed effects, random effects and GEE: what are the differences? *Stat Med*. 2009;28:221–239.
48. Harrison XA. Using observation-level random effects to model overdispersion in count data in ecology and evolution. *Peer J*. 2014;2:e616.
49. Miettinen OS, Cook EF. Confounding: essence and detection. *Am J Epidemiol*. 1981;114:593–603.
50. Hak E, Verhaij M, Grobbee DE, Nichol KL, Hoes AW. Confounding by indication in non-experimental evaluations of vaccine effectiveness: the example of prevention of influenza complication. *J Epidemiol Commun Health*. 2002;56:951–955.
51. BOJA. Decreto 149/2009 de 12 de mayo, por el que se regulan los centros que imparten el primer ciclo de educación infantil. Available at:www.juntadeandalucia.es/boja/2009/92/boletin.92.pdf. Accessed June 15, 2012.
52. Van Damme P, Giaquinto C, Huet F, et al. Multicenter prospective study of the burden of rotavirus acute gastroenteritis in Europe, 2004-2005: the REVEAL study. *J Infect Dis*. 2007;195(Suppl 1):S4–S16.
53. Gudnason T, Hrafnkelsson B, Laxdal B, Kristinsson KG. Can risk factors for infectious illnesses in children at day care centres be identified. *Scand J Infect Dis*. 2012;44:149–156.
54. Payne DC, Selvarangan R, Azimi PH, et al. Long-term consistency in rotavirus vaccine protection: RV5 and RV1 vaccine effectiveness in US children, 2012-2013. *Clin Infect Dis*. 2015;61:1792–1799.
55. Thomas SL, Walker JL, Fenty J, et al. Impact of the national rotavirus vaccination programme on acute gastroenteritis in England and associated costs averted. *Vaccine*. 2017;35:680–686.
56. Mast TC, Wang FT, Su S, Seeger JD. Evidence of herd immunity and sustained impact of rotavirus vaccination on the reduction of related medical encounters among infant from 2006-2011 in the United States. *Pediatr Infect Dis J*. 2015;34:615–620.
57. Gudnason T, Hrafnkelsson B, Laxdal B, Kristinsson KG. Does hygiene intervention at day care centres reduce infectious illnesses in children? An intervention cohort study. *Scand J Infect Dis*. 2013;45:397–403.
58. Zomer TP, Erasmus V, Looman CW, et al. A hand hygiene intervention to reduce infections in child daycare: a randomized controlled trial. *Epidemiol Infect*. 2015;143:2494–2502.
59. Pönkä A, Poussa T, Laosmaa M. The effect of enhanced hygiene practices on absences due to infectious diseases among children in day care centers in Helsinki. *Infection*. 2004;32:2–7.
60. Soares-Weiser K, Bergman H, Henschke N, Pitan F, Cunliffe N. Vaccines for preventing rotavirus diarrhoea: vaccines in use. *Cochrane Database Syst Rev*. 2019;3:CD008521.
61. Lu N, Samuels ME, Shi L, Baker SL, Glover SH, Sanders JM. Child day care risks of common infectious diseases revisited. *Child Care Health Dev*. 2004;30:361–368.
62. Chen Y, Williams E, Kirk M. Risk factors for acute respiratory infection in the Australian community. *PLoS One*. 2014;9: e101440.
63. Enserink R, Mughini-Gras L, Duizer E, Kortbeek T, Van Pelt W. Risk factors for gastroenteritis in child day care. *Epidemiol Infect*. 2015;143:2707–2720.
64. Sax H, Allegranzi B, Chraiti MN, Boyce J, Larson E, Pittet D. The World Health Organization hand hygiene observation method. *Am J Infect Control*. 2009;37:827–834.
65. Zomer TP, Erasmus V, Looman CW, et al. Improving hand hygiene compliance in child daycare centres: a randomized controlled trial. *Epidemiol Infect*. 2016;144:2552–2560.
66. Van Beeck AH, Zomer TP, Van Beeck EF, Richardus JH, Voeten HA, Erasmus V. Children's hand hygiene behaviour and available facilities: an observational study in Dutch day care centres. *Eur J Public Health*. 2016;26:297–300.