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Effectiveness of hand hygiene and provision of information in preventing influenza cases requiring hospitalization ☆,☆☆,★

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ABSTRACT

Background. The objective of the study was to investigate the effectiveness of non-pharmacological interventions in preventing cases of influenza requiring hospitalization.

Methods. We performed a multicenter case-control study in 36 hospitals, in 2010 in Spain. Hospitalized influenza cases confirmed by reverse-transcription polymerase chain reaction and three matched controls (two hospital and one community control) per case were selected. The use of non-pharmacological measures seven days before the onset of symptoms (frequency of hand washing, use of alcohol-based hand sanitizers and handwashing after touching contaminated surfaces) was collected.

Results. We studied 813 cases hospitalized for influenza and 2274 controls. The frequency of hand washing 5-10 times (adjusted odds ratio [aOR] = 0.65) and >10 times (aOR = 0.59) and handwashing after contact with contaminated surfaces (aOR = 0.65) were protective factors and were dose-responsive ($p<0.001$). Alcohol-based hand sanitizers were associated with marginal benefits (aOR = 0.82).

Conclusions. Frequent handwashing should be recommended to prevent influenza cases requiring hospitalization.

Introduction

The influenza A (H1N1) pdm09 virus pandemic and the late availability of the specific vaccine have highlighted the importance of identifying non-pharmacological measures to reduce transmission of the virus. Following the recommendations of the World Health Organization (WHO), many countries have made recommendations on non-pharmacological measures, especially during the beginning of the pandemic, such as improving hand and respiratory hygiene, the use of surgical facemasks, barrier nursing and quarantine of contacts, social distancing measures and travel restrictions (Bell and World Health Organization Writing Group, 2006a; Ferguson et al., 2006; Nicoll, 2006). Some authors (Bootsma and Ferguson, 2007; Hatchett et al., 2007; Longini et al., 2005) also report that these measures prolong the epidemic period and reduce the attack rate at the peak of the epidemic wave, thus reducing the burden of care and providing significant benefits during a period of increased demand for health services.

Studies have underlined the importance of influenza transmission by respiratory secretions and contact between hands and contaminated surfaces (Weber and Stilianakis, 2008). In Spain, as in other countries, measures to reduce the transmission of pandemic influenza and other respiratory viruses include the promotion of hand hygiene and the provision of information on respiratory and hand hygiene. The generalized use of face masks is not recommended.

Some of these measures were also used to mitigate the 2003 outbreak of severe acute respiratory syndrome (SARS) (Fung and Cairncross, 2006). The effectiveness of hand and respiratory hygiene has been shown in various studies in health centres (Harrington et al., 2007; Hilburn et al., 2003; Pittet et al., 2000). Studies have also been made in various institutions including kindergartens, schools, university campuses and military facilities, but the results of compliance and effectiveness of these interventions in open communities is less well known (Roberts et al., 2000; Ryan et al., 2001; Falsey et al., 1999; Larson et al., 2003; Luby et al., 2005; White et al., 2003, Falsey et al., 1999).

More recently, specific studies have been carried out on the effectiveness of information on influenza protection measures (respiratory and hand hygiene), and the application of hand hygiene and/or the use of face masks. Stebbins et al. found that education and hand hygiene was highly effective in reducing school absences and confirmed cases of influenza A (but not influenza B) (Stebbins et al., 2011) while studies in households in New York(Larson et al., 2010), Berlin(Suess et al., 2012) and Bangkok (Simmerman et al., 2011) also suggest, though not conclusively, that these measures are effective.

The hypothesis of this study was that hand hygiene and the provision of information on influenza prevention are associated with a lower risk of hospitalization due to influenza. The objective of the study was to investigate the effectiveness of non-pharmacological community interventions (hand hygiene, alcohol-based hand sanitizers and the provision of information on influenza prevention) in preventing hospitalization for influenza A (H1N1) pdm09.

Methods

Study design

We performed a multicenter matched case-control study in 36 Spanish hospitals from seven Spanish regions (Andalusia, the Basque Country, Castile and Leon, Catalonia, Madrid, Navarre, and Valencia Community). All hospitals were public reference hospitals located in the main cities of each community and all provided free-at-the-point-of-delivery healthcare under the auspices of the Spanish National Health Service. Cases admitted to participating hospitals between July 2009 and February 2010 and the corresponding controls were recruited.

Selection of cases and controls

Patients hospitalized for influenza syndrome, acute respiratory infection, septic shock or multiple organ failure in whom influenza A (H1N1) pdm09 virus infection was confirmed by real time–polymerase chain reaction (RT-PCR) were selected. Patients with nosocomial infection, defined as influenza virus infection appearing ≥ 48 hours after admission for other reasons, were excluded.

In order to control for selection bias and to compare estimates of the effectiveness of the measures in different groups of controls, we selected three matched controls for each case. Two controls were patients with unplanned hospital admission for reasons other than acute respiratory infection, influenza syndrome, septic shock or multiple organ failure. A third outpatient control was selected from patients attending primary health care centres (PHC) for any reason other than influenza-like illness or acute respiratory infection. Inpatient and outpatient controls were matched for each case according to age (± 3 years in patients aged <18 years and ± 5 years in patients aged ≥ 18 years), date of hospitalization of the case (± 10 days) and the province of residence.

Sociodemographic and clinical data

The following demographic variables and pre-existing medical conditions were collected for all study participants: age, sex, ethnicity, educational level, smoking, alcohol consumption, pregnancy in women aged 15- 49 years, history of pneumonia in the last two years, chronic obstructive pulmonary disease (COPD), asthma, cardiovascular disease, renal failure, diabetes, HIV infection, disabling neurological disease, neoplasia, transplantation, morbid obesity (body mass index [BMI] ≥ 40), treatment with systemic corticosteroids and inhaled corticosteroids, and antibiotic treatment within 90 days prior to admission.

Table 1
Distribution of sociodemographic variables in cases and controls, Spain 2010.

Features	Cases n = 813 (%)	Controls n = 2274 (%)
Age: mean (SD)	38.48 (22.79)	39.13 (22.68)
Age group (years)		
0-17	195 (24.0)	517 (22.7)
18-65	517 (63.6)	1458 (64.2)
≥ 65	101 (12.4)	299 (13.1)
Female	410 (50.4)	1170 (51.5)
Ethnicity		
White	698 (86.9)	2082 (92.8)
Romany	19 (2.4)	16 (0.7)
Amerindian	53 (6.6)	84 (3.7)
Arab or North African	22 (2.7)	24 (1.1)
Other	11 (1.4)	38 (1.7)
Educational level		
Secondary or higher	436 (56.9)	1388 (63.2)
Pregnant	49 (14.0)	58 (6.1)
Smoker	306 (42.0)	829 (41.2)
Excess alcohol	44 (5.6)	151 (7.0)

Information on and use of non-pharmacological measures

A structured interview was used to determine whether study participants had received information on preventing the transmission of pandemic influenza: washing or sanitizing hands often; staying at home when sick; avoiding touching eyes, nose, and mouth; covering coughs and sneezes; and, keeping your distance from sick people. In addition, participants were asked about the use of non-pharmacological measures (frequent hand washing, use of alcohol-based hand sanitizers and handwashing at home after touching potentially contaminated surfaces on public transport or in shops, for example) in the seven days before the onset of symptoms in cases and the seven days before the onset of symptoms in the matched case in controls.

Statistical analysis

A bivariate comparison was made between cases and controls for demographic variables and pre-existing medical conditions using the McNemar test for categorical variables and the paired *t* test for continuous variables. Unadjusted matched odds ratios [OR] were estimated using the McNemar test.

A multivariate analysis was performed using conditional logistic regression to estimate the adjusted OR (aOR) and including those variables associated with hospitalization and the independent variables with a p value <0.2 in the bivariate analysis. In the different regression models, the aOR for all controls considered together and for hospital and ambulatory controls separately were calculated in order to evaluate possible differences and discard selection bias. Missing data were<2% and were excluded from the analysis. The analysis was performed using SPSS version 18.

Data confidentiality and ethical aspects

All information collected was treated as confidential in strict observance of legislation on observational studies. The study was approved by the Ethics Committees of the participating hospitals. Written informed consent was obtained from patients included before interviews were carried out.

Results

A total of 813 cases hospitalized due to influenza A (H1N1) pdm09 virus infection confirmed by RT-PCR and 2274 matched controls (1570 hospital and 704 PHC) were included.

Cases had a mean age of 38.5 years (SD = 22.7), 50.4% were female, 84.9% were white, 56.9% had secondary or higher education, 42% were smokers or former smokers and 5.6% reported excessive alcohol consumption. Controls had similar characteristics with the only significant differences being in educational levels, ethnicity and pregnancy (Table 1).

Cases presented a higher frequency of risk factors and risk medical conditions for influenza compared with controls: specifically, cases had a higher frequency of pneumonia in the previous two years, COPD, asthma, HIV infection, disabling neurological disease, neoplasia, transplantation, morbid obesity, treatment with systemic corticosteroids and inhaled corticosteroids, and antibiotic treatment in the 90 days prior to admission (Table 2).

Cases also had a lower frequency of factors that may protect against influenza infection and hospitalization. Cases reported having received less information on preventing pandemic influenza (OR = 0.49; 95%CI 0.38-0.63) and a lower frequency of hand washing 5-10 times (OR = 0.73; 95%CI 0.60-0.89) and > 10 times (OR = 0.58; 95%CI 0.46-0.73) daily, the use of alcohol-based hand sanitizers (OR = 0.83; 95%CI 0.68-1.01) and washing after touching potentially contaminated surfaces (OR = 0.58; 95%CI 0.46-0.73) in the seven days before the onset of symptoms (Table 3).

All the demographic and clinical variables associated with the risk of hospitalization (Tables 1 and 2) were introduced in the logistic regression model. In the multivariate analysis, receiving information on preventing influenza (OR = 0.44; 95% CI 0.33-0.60), and a higher frequency of hand washing and hand washing after contact with contaminated surfaces were protective factors against hospitalization due to influenza. In addition, they were dose-responsive. Hand

Table 2
Influenza risk factors and medical conditions in cases and controls, Spain 2010.

Features	Cases n = 813 (%)	Controls n = 2274 (%)	OR (95% CI)	p-value
Pneumonia in previous 2 years	85 (15.1)	108 (4.8)	3.25 (2.34 - 4.52)	<0.001
COPD	76 (9.4)	85 (3.8)	2.81 (2.00 - 3.95)	<0.001
Asthma	135 (16.7)	140 (6.3)	3.06 (2.35 - 3.97)	<0.001
Chronic cardiovascular disease	81 (10.0)	200 (9.0)	1.12 (0.83 - 1.50)	0.46
Renal failure or nephrotic syndrome	44 (5.4)	127 (5.7)	0.89 (0.62 - 1.29)	0.54
Diabetes	98 (12.1)	225 (10.1)	1.22 (0.93 - 1.59)	0.15
AIDS / HIV infection	21 (2.6)	24 (1.1)	2.28 (1.23 - 4.21)	0.01
Disabling neurological disease	34 (4.2)	39 (1.8)	2.71 (1.65 - 4.44)	<0.001
Neoplasms	69 (8.6)	197 (8.9)	0.95 (0.71 - 1.28)	0.75
Transplantation	36 (4.5)	49 (2.2)	2.15 (1.37 - 3.37)	0001
Obesity (BMI ≥ 40)	24 (4.8)	33 (2.1)	2.03 (1.12 - 3.67)	0.01
Previous antibiotics	207 (25.7)	408 (18.4)	1.53 (1.25 - 1.86)	<0.001
Systemic corticosteroids	72 (8.9)	113 (5.1)	1.79 (1.31 - 2.45)	<0.001
Inhaled corticosteroids	174 (21.5)	154 (7.0)	3.94 (3.07 - 5.06)	<0.001
≥ 2 risk factors	215 (26.4)	430 (18.9%)	1.58 (1.30 - 1.93)	<0.001

COPD, chronic obstructive pulmonary disease
BMI, body mass index
OR, odds ratio
CI, Confidence interval

Table 3
Health information and non-pharmacological measures for the prevention of influenza requiring hospitalization (cases and all controls), Spain 2010.

Characteristics	Cases n = 813 (%)	Controls n = 2274 (%)	Crude OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Received information on influenza prevention[a]						
No	132 (16.5)	211 (9.04)	1		1	
Yes	670 (83.5)	2043 (90.6)	0.49 (0.38 - 0.63)	<0.001	0.44 (0.33 - 0.60)	<0.001
Frequency of daily handwashing[b]						
1-4 times	320 (40.7)	736 (32.7)	1		1	
5-10 times	285 (36.3)	871 (38.7)	0.73 (0.60 - 0.89)	0.002	0.65 (0.52 - 0.84)	0.001
> 10 times	181 (23.0)	644 (28.6)	0.58 (0.46 - 0.73)	<0.001	0.59 (0.44 - 0.79)	<0.001
Use of alcohol-based hand sanitizers[c]						
Never	553 (70.5)	1516 (67.1)	1		1	
Sometimes	231 (29.5)	742 (32.9)	0.83 (0.68 - 1.01)	0.06	0.82 (0.65 - 1.02)	0.08
Handwashing after touching contaminated surfaces[d]						
Never	196 (24.6)	403 (17.9)	1		1	
Occasionally/Always	600 (75.4)	1852 (82.1)	0.58 (0.46 - 0.73)	<0.001	0.65 (0.50 - 0.84)	0.001

OR, odds ratio.
CI, Confidence interval.
[a] Adjusted OR for: Ethnicity, Educational level, COPD, Diabetes, AIDS, Inhaled corticosteroids and non-pharmacological measures.
[b] Adjusted OR for: Ethnicity, Educational level, COPD, Asthma, AIDS, Previous antibiotics and non-pharmacological measures.
[c] Adjusted OR for: Educational level, COPD, Asthma, Diabetes, Disabling neurological disease, Systemic corticosteroids and non-pharmacological measures.
[d] Adjusted OR for: Educational level, COPD, Diabetes, Transplantation, Previous antibiotics, Systemic corticosteroids, Inhaled corticosteroids and non-pharmacological measures.

washing 5-10 times had an aOR of 0.65 (95% CI 0.52 to 0.84) and hand washing > 10 times an aOR of 0.59 (95% CI 0.44 to 0.79) compared to hand washing 1-4 times daily (Table 3). Using the same variables and models, when hospital and PHC controls were analysed separately, very similar aOR were observed (Tables 4 and 5) for information on the prevention of influenza (0.44 versus 0.44) hand washing 5-10 times (0.68 versus 0.72) and more than 10 times (0.60 versus 0.57) and washing after touching surfaces (0.64 versus 0.61).

Discussion

This study has demonstrated the effectiveness of hand washing and the provision of information on influenza prevention in the community in preventing hospitalization due to influenza A (H1N1) pdm09. We also found that hand washing after contact with potentially contaminated surfaces was also effective. The use of alcohol-based hand sanitizers was associated with marginal benefits

The notable protective effect of handwashing was observed during the study period, which coincided with the period of greatest intensity of pandemic influenza in Spain, and is also consistent with the period in which it was determined (7 days before the onset of symptoms in cases and an equivalent period in controls) and with the information released by health authorities on the prevention of pandemic influenza, which focused on hand washing, and the fact that the cases reported a lower level of information on preventive measures compared with controls (OR = 0.44, 95% CI 0.33 - 0.60). In addition, hand washing after contact with potentially contaminated surfaces had a similar effect. This strength of this protective effect was also dose-responsive association, with the OR being greater in persons who washed their hands 5-10 times and >10 times daily compared with 1-4 times. The protective role of hand hygiene (and the dose-response effect) was also observed when hospital and PHC controls were analysed separately. This corresponds with studies that document the survivability of the influenza virus on nonporous surfaces for at least 24 hours and the possibility of contaminating hands and generating new infections(Ansari et al., 1989; Bean et al., 1982; Bell and World Health Organization Writing Group, 2006b), and also with studies that show that hand washing with soap and water is effective in removing pathogens from the surface of the hands (Larson et al., 2003; Luby et al., 2001).

Receiving information on preventing pandemic influenza was a protective factor against hospitalization due to influenza. This suggests that mass information and education of the community can protect against influenza, as suggested by other studies carried out in schools (Stebbins et al., 2010, 2011) and urban households (Larson et al., 2010). These studies suggest, but not conclusively, that information results in a reduction both in school absence and cases of influenza. Our results support policies of providing information on

Table 4
Health information and non-pharmacological measures for the prevention of influenza requiring hospitalization (cases and hospital controls), Spain 2010.

Characteristics	Cases n = 813 (%)	Hospital controls n = 1570 (%)	Crude OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Received information on prevention[a]	670 (83.5)	1400 (89.6)	0.54 (0.42 - 0.70)	<0.001	0.44 (0.32 - 0.60)	<0.001
Frequency of daily hand washing[b]						
1-4 times	320 (40.7)	522 (33.6)	1		1	
5-10 times	285 (36.3)	614 (39.5)	0.73 (0.60 – 0.90)	0.003	0.68 (0.53 - 0.57)	0.002
> 10 times	181 (23.0)	417 (26.9)	0.64 (0.50 – 0.83)	0.001	0.60 (0.45 - 0.81)	0.001
Use of alcohol-based hand sanitizers[c]						
Never	553 (70.5)	1067 (68.4)	1		1	
Sometimes	231 (29.5)	494 (31.6)	0.87 (0.71 – 1.08)	0,22	0.79 (0.62 - 1.01)	0.06
Hand washing after touching contaminated surfaces[d]						
Never	196 (24.6)	295 (18.9)	1		1	
Occasionally/Always	600 (75.4)	1264 (81.1)	0.63 (0.49 – 0.80)	<0.001	0.64 (0.49 - 0.85)	0.002

OR, odds ratio.
CI, Confidence interval.
[a] Adjusted OR for: Ethnicity, Educational level, COPD, AIDS, Transplantation, Inhaled corticosteroids and non-pharmacological measures.
[b] Adjusted OR for: Ethnicity, Educational level, COPD, Asthma, AIDS, Previous antibiotics and non-pharmacological measures.
[c] Adjusted OR for: Educational level, COPD, Asthma, Previous antibiotics, Systemic corticosteroids and non-pharmacological measures.
[d] Adjusted OR for: Educational level, COPD, Transplantation, Previous antibiotics, Systemic corticosteroids, Inhaled corticosteroids and non-pharmacological measures.

Table 5
Health information and non-pharmacological measures for the prevention of influenza requiring hospitalization (cases and community controls), Spain 2010.

Features	Cases n = 702 (%)	Outpatient controls n = 704 (%)	Crude OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Received information on prevention[a]	584 (93.9)	643 (92.9)	0.34 (0.23 - 0.51)	<0.001	0.44 (0.26-0.72)	0.001
Frequency of daily hand washing[b]						
1-4 times	282 (41.2)	215 (30.7)	1		1	
5-10 times	247 (36.1)	257 (36.8)	0.71 (0.54-0.92)	0.01	0.72 (0.52 - 0.99)	0.04
> 10 times	155 (22.7)	227 (32.5)	0.45 (0.33 - 0.61)	<0.001	0.57 (0.39-0.82)	0.003
Use of alcohol-based hand sanitizers[c]						
Never	475 (69.9)	449 (64.4)	1		1	
Sometimes	205 (30.1)	248 (35.6)	0.74 (0.57 - 0.95)	0,02	0.76 (0.57 - 1.02)	0.06
Handwashing after touching contaminated surfaces[d]						
Never	166 (24.0)	108 (15.5)	1		1	
Occasionally/Always	526 (76.0)	588 (84.5)	0.51 (0.38 - 0.69)	<0.001	0.61 (0.42 - 0.88)	0.01

OR, odds ratio.
CI, Confidence interval.
[a] Adjusted OR for: Ethnicity, Educational level, Chronic cardiovascular disease, Diabetes, AIDS, Inhaled corticosteroids and non-pharmacological measures.
[b] Adjusted OR for: Educational level, Asthma, Diabetes, AIDS and non-pharmacological mesures.
[c] Adjusted OR for: Educational level, COPD, Asthma, Previous antibiotics, Systemic corticosteroids and non-pharmacological measures.
[d] Adjusted OR for: Educational level, COPD, Chronic cardiovascular disease, AIDS, Transplantation, Previous antibiotics, Systemic corticosteroids, Inhaled corticosteroids and non-pharmacological measures.

influenza and the currently recommended respiratory and hand hygiene measures for seasonal and pandemic influenza.

The multivariate analysis found no protective effect of using alcohol-based hand sanitizers. It is known that these products are effective in inactivating a wide range of viruses, including the influenza virus (Kampf and Kramer, 2004; Sattar et al., 2002). The protective effect of alcohol-based hand sanitizers is only observed when the hands are not visibly dirty and, therefore, they are recommended for use by health workers only when this is the case (Siegel and Centers for Disease Control (US), 2007; Widmer et al., 2007). In lay people with insufficient instruction in this respect, such as the participants in this study, the measure may not always have been used correctly.

This observational study is one of the first to provide evidence on the effectiveness of handwashing and the provision of information on influenza prevention in the community in preventing influenza cases requiring hospitalization. Other case-control studies have shown the effectiveness of handwashing in preventing the transmission of SARS. A case-control study in Hong Kong (Lau et al., 2004) found a very similar effectiveness of handwashing >10 times a day in the community in preventing the transmission of SARS (OR = 0.58). Another case-control study in Beijing (Wu et al., 2004) found that handwashing after returning home had a protective effect (OR = 0.3). More recently, a meta-analysis of 6 case-control studies (Jefferson et al., 2008), found that handwashing > 10 times daily was remarkably effective in preventing SARS (OR = 0.45, CI 0.36-0.57).

Randomized trials of interventions in specific communities have also found that handwashing is effective in reducing the transmission of ILI. An intervention trial in universities (Aiello et al., 2010) found an effectiveness of 35%-51% in reducing ILI in university students when improved handwashing was combined with the wearing of masks, but not when only masks were used. A clinical trial (Cowling et al., 2009) that evaluated the effectiveness of measures to reduce home transmission of the influenza A and B viruses found that hand hygiene and wearing facemasks were effective but only when applied in the 36 hours after the onset of symptoms in the index case: the study could not analyse the effect of each intervention separately. A clinical trial (MacIntyre et al., 2009) that assessed the effectiveness of wearing facemasks in reducing the transmission of ILI in home contacts found no effect. The study found an adherence rate of <50%, and suggested that facemasks are not useful in reducing seasonal influenza infections in the community due to their low acceptance, although they could be effective in those who wore them. In contrast, information on influenza prevention, improving general hygiene, including hand hygiene, and avoiding touching mucosal surfaces with the hands are well-accepted socially (MacIntyre, et al., 2009; Stebbins et al., 2009).

In Spain, influenza causes a large number of hospitalizations and excess mortality (Godoy et al., 2011a, 2011b; López-Cuadrado et al., 2012). Handwashing and the provision of information on influenza prevention (respiratory and hand hygiene) in the community may have a notable impact in Spain by reducing the number of severe cases requiring hospitalization and the pressure on hospital services caused during the epidemic influenza period.

Our study has some limitations. Information on risk factors, medical conditions and vaccination were collected from medical records, but questions on the use of non-pharmacological measures were collected by personal interview and interviewers were not blinded to the status of cases and controls. However, the questionnaire was constructed with closed questions, the interviewers were trained and the questions related to a period of seven days before the onset of symptoms of patients hospitalized for influenza. Due to the rapid decline of the pandemic wave, most interviews were conducted retrospectively and the answers may have been affected by selective recall, although if this did not occur differentially, it should not have affected the results. Another possible limitation was that while only confirmed influenza infections were included in the case definition, some controls could have been misclassified due to lack of testing, false negative tests or the exclusion of other influenza virus strains. However, the exclusion criteria for controls were to have symptoms of either influenza-like illness or respiratory infection at hospital admission and hospital admission due to influenza later than April 2009. Therefore, there was probably no misclassification.

The effectiveness of the measures may also have been underestimated, since the questions referred to the use of protective measures in general without referring to specific exposures, although the seven-day period corresponds to the influenza incubation period. In addition, the fact that the results were broadly similar in both hospital and PHC controls supports the consistency of the study.

Conclusions

Our results suggest that provision of information on influenza prevention (respiratory and hand hygiene) and hand washing at least 5 times a day and, if possible, > 10 times a day, should be recommended at the community level in order to prevent severe or complicated cases of influenza requiring hospitalization. The use of alcohol-based hand sanitizers was associated with marginal benefits

Conflict of interest statement

The author declare that there are no conflict of interest.

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