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Impact of a website based educational program for increasing vaccination coverage among adolescents

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ABSTRACT

Data regarding the use of technology to improve adolescent knowledge on vaccines are scarce. The main aim of this study was to evaluate whether different web-based educational programmes for adolescents might increase their vaccination coverage. Overall, 917 unvaccinated adolescents (389 males, 42.4%; mean age ± standard deviation, 14.0 ± 2.2 years) were randomized 1:1:1 into the following groups: no intervention (n = 334), website educational program only (n = 281), or website plus face to face lesson (n = 302) groups. The use of the website plus the lesson significantly increased the overall knowledge of various aspects of vaccine-preventable disease and reduced the fear of vaccines ($p < 0.001$). A significant increase in vaccination coverage was observed for tetanus, diphtheria, acellular pertussis and conjugated meningococcal ACYW vaccines in the 2 groups using the website ($p < 0.001$), and better results were observed in the group that had also received the lesson; in this last group, significant results were observed in the increase in vaccination coverage for meningococcal B vaccine ($p < 0.001$). Overall, the majority of the participants liked the experience of the website, although they considered it important to further discuss vaccines with parents, experts and teachers. This study is the first to evaluate website based education of adolescents while considering all of the vaccines recommended for this age group. Our results demonstrate the possibility of increasing vaccination coverage by using a website based educational program with tailored information. However, to be most effective, this program should be supplemented with face-to-face discussions of vaccines at school and at home. Thus, specific education should also include teachers and parents so that they will be prepared to discuss with adolescents what is true and false in the vaccination field.

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Introduction

For many years, immunization of adolescents had been limited to the administration of a booster dose of diphtheria and tetanus vaccines.[1] Recently, it has been shown that protection evoked by the pertussis vaccine progressively weakens, and a booster dose is needed during adolescence to avoid an increased risk of pertussis in previously vaccinated subjects and in unvaccinated or incompletely vaccinated infants.[2,3] Moreover, new vaccines for the prevention of illnesses that typically occur during adolescence, such as human papillomavirus (HPV) and meningococcal infections, have been developed.[4-6] All these findings have raised particular concern regarding the immunization of adolescents, and in most countries, the immunization schedules for these subjects have been updated, although with varying recommendations.[7,8]

However, compliance with recommendations from health authorities regarding vaccination in adolescence is poor worldwide. In the USA, in 2015, vaccination coverage was satisfactory among 13–17 y old adolescents for only the trivalent tetanus/diphtheria, acellular pertussis (TdaP) vaccine (i.e., 86.4 ± 1.0%).[9] However, coverage was very poor for both the HPV and tetravalent conjugate A, C, Y, W135 meningococcal (MenACYW) vaccines. Only 41.9% (± 1.8%) of females and 28.1% (± 1.6%) of males 13–17 y old had received ≥ 3 doses of HPV, and only 33.3% (± 2.7%) of 17 y old adolescents had received ≥ 2 doses of the MenACYW vaccine.[9] In Europe, where the HPV vaccine has been recommended in most countries since 2007/2008, it has been estimated that the mean immunization coverage among females aged 10–20 y was only 31.1% as of October 2014.[10]

Several studies have shown that for adolescents, as for younger children, barriers to vaccination may be increased by health authorities, providers and parents having poor knowledge of the immunization schedule, of vaccine efficacy and of vaccine-related adverse events.[11] However, adolescents' knowledge of immunization has been found to be even lower than that of providers and parents, thus suggesting that education may be essential to improve compliance with recommendations.[12] School is considered to be a potentially appropriate location for both vaccine administration to and education of adolescents.[13,14] School-based educational programmes have been found to be effective in increasing HPV and influenza vaccination in adolescents.[15,16] Usually, school-based education about vaccines is delivered by face-to-face structured information,

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brochures or presentations. Technology can significantly promote vaccine use. It has been reported that health information technology interventions can facilitate rapid or real-time identification of children in need of vaccination and provide a foundation for vaccine-oriented parental communication or clinical alerts in a flexible and tailored manner.[17] However, data regarding the use of technology to improve adolescent knowledge on vaccines are scarce.

The main aim of this study was to evaluate whether different web-based educational programmes for adolescents might increase their vaccination coverage.

Results

We conducted a prospective, randomized controlled trial over one school year to analyze whether different web-based educational programmes for adolescents might increase their vaccination coverage. Table 1 summarizes the baseline characteristics of the study population according to the randomization groups. The age was slightly but significantly higher among subjects randomized to the no intervention arm ($p = 0.02$). Moreover, in the group randomized to the website and the lesson, there were significantly more females than in the other 2 groups ($p = 0.02$). Nationality and underlying chronic diseases were observed with a similar prevalence in the 3 groups. The majority of the participants in the 3 groups completed the questionnaire presented at the end of the school year. Only 14.4%, 20.3%, and 21.2% of students included in the group of no intervention, only internet intervention and internet plus oral lesson, respectively, were no more available at final evaluation. Table 2 describes personal knowledge and attitudes toward vaccination before and after intervention according to randomization groups in subjects who completed the study. The results showed that the use of the website plus the lesson significantly increased the overall awareness of the benefits of vaccinations against diseases ($p < 0.01$), knowledge on vaccine-preventable disease (i.e., potential severity, $p = 0.001$; transmission route of meningitis, $p < 0.01$) and to reduce the fear of vaccines ($p < 0.001$).

Table 3 shows the frequency of specific vaccinations after presentation of the project at school, for subjects who completed the study. A significant increase in vaccination coverage was observed for TdaP and menACYW in the 2 groups using the website ($p < 0.001$), and the results were better in the group that had also participated in the lesson; in this last group, a significant increase in vaccination coverage was also observed for meningococcal B vaccine ($p < 0.001$). Table 4 summarizes the association between vaccination and the randomization group after intervention. Interestingly, the website alone or combined with the lesson always had a significant effect on increasing vaccination coverage regardless of age and gender ($p < 0.001$), although the website plus the lesson educational program appeared to be the most effective intervention.

Table 5 describes the satisfaction of subjects with the website educational program in the 2 intervention groups according to sex and age. Overall, the website was appreciated mainly for its clarity of language and easy navigation. The majority of the subjects spent a few minutes reading the website, although a significantly higher percentage of males spent more than 16 minutes ($p = 0.01$). Interestingly, the mechanism of action of vaccines and vaccine safety were the sections for which further details were requested, and there were differences according to the type of educational program, gender and age group. Approximately 20% of parents visited the website at least once, and there were no differences among the groups. The majority of the participants liked the experience of the website, although they considered it important to discuss vaccines with parents, experts and teachers.

Table 1. Baseline characteristics of the study population according to randomized group.

Characteristic	No intervention (n = 334)	Web-site only (n = 281)	Web-site + lesson (n = 302)	p-value
Age				
Mean ± SD	14.1 ± 2.3	13.8 ± 2.3	13.6 ± 2.0	**0.02**
Sex				
Male	150 (44.9)	131 (46.6)	108 (35.8)	
Female	184 (55.1)	150 (53.4)	194 (64.2)	**0.02**
Nationality [a]				
Italian	275 (83.1)	243 (86.8)	246 (81.7)	
Other	56 (16.9)	37 (13.2)	55 (18.3)	0.23
Chronic diseases				
No	318 (95.2)	268 (95.4)	285 (94.4)	
Yes	16 (4.8)	13 (4.6)	17 (5.6)	0.83
Available at final evaluation				
No	48 (14.4)	57 (20.3)	64 (21.2)	
Yes	286 (85.6)	224 (79.7)	238 (78.8)	0.054

[a]The numbers do not add up to the total because of several missing values

Discussion

The need for higher vaccination coverage among adolescents has led to the development of several strategies to improve vaccination in this demographic group. Implementing vaccination requirements before adolescents enter school, sending reminders, and issuing national recommendations for adolescent vaccination have been found to be effective in this regard.[18] Moreover, educational interventions for adolescents, parents, and health care workers can further increase vaccination coverage.[19] The widespread use of the new media by the general population, including adolescents, has led to the use of internet-based interventions to improve education and the community demand for immunization. In some cases, the impacts of specific immunization campaign websites and personalized portals has been explored and found to have positive results.[20-24] However, in most of these cases, young adults such as medical students or parents were the main target of these programmes, and adolescents were rarely involved. Moreover, the effects on vaccination rates for only single vaccines, typically either the HPV or influenza vaccine, have been evaluated.

To the best of our knowledge, our study is the first internet-based intervention study including adolescents and all vaccines recommended for this age group. Moreover, our study was based on a clear and easy to navigate website providing information tailored to the users, because individualization of educational materials to reflect the unique experiences, beliefs, and concerns of each user has been found to be an effective strategy for improving compliance with a variety of preventive health behaviors in many diverse populations.[25] However, educational programmes based on tailored information conveyed through

Table 2. Personal knowledge and attitude toward vaccinations before and after intervention according to randomization group in subjects who completed the study.[a]

Knowledge and attitude	No intervention (n = 286)			Web-site only (n = 224)			Web-site + lesson (n = 238)		
	Answer at baseline	Answer after intervention	p-value [b]	Answer at baseline	Answer after intervention	p-value [b]	Answer at baseline	Answer after intervention	p-value [b]
Do you think that you could die from infectious diseases that can be prevented by vaccines?									
Yes	189 (66.1)	194 (68.3)		139 (62.0)	158 (70.8)		142 (59.7)	169 (71.9)	
No/Only those having chronic diseases/Don't know	97 (33.9)	90 (31.7)	0.54	85 (38.0)	65 (29.2)	**0.02**	96 (40.3)	66 (28.1)	**0.001**
Do you think that vaccinations are useful?									
They are useful to prevent diseases in vaccinated and non-vaccinated people	224 (79.1)	241 (84.6)		169 (75.8)	174 (78.0)		184 (77.3)	203 (86.4)	
Other answers/Don't know	59 (20.9)	44 (15.4)	**0.03**	54 (24.2)	49 (22.0)	0.43	54 (22.7)	32 (13.6)	**0.002**
How is meningitis transmitted?									
Airborne route	196 (68.5)	181 (63.5)		160 (71.4)	159 (71.0)		156 (65.5)	179 (76.2)	
Other answers/Don't know	90 (31.5)	104 (36.5)	0.08	64 (28.6)	65 (29.0)	0.90	82 (34.5)	56 (23.8)	**0.005**
How is diphtheria transmitted?									
Airborne route	149 (52.1)	128 (44.9)		115 (51.6)	105 (46.9)		126 (53.2)	134 (57.5)	
Other answers/Don't know	137 (47.9)	157 (55.1)	**0.03**	108 (48.4)	119 (53.1)	0.27	111 (46.8)	99 (42.5)	0.32
How is tetanus transmitted?									
Through skin wounds, animal bites or injections	236 (82.5)	233 (81.7)		188 (83.9)	181 (80.8)		201 (84.4)	203 (86.7)	
Other answers/Don't know	50 (17.5)	52 (18.3)	0.78	36 (16.1)	43 (19.2)	0.24	37 (15.6)	31 (13.3)	0.46
How is pertussis transmitted?									
Airborne route	228 (79.7)	215 (76.0)		181 (80.8)	175 (78.5)		190 (79.8)	192 (82.4)	
Other answers/Don't know	58 (20.3)	68 (24.0)	0.18	43 (19.2)	48 (21.5)	0.49	48 (20.2)	41 (17.6)	0.48
How is papillomavirus transmitted?									
Sexual route	232 (82.3)	201 (71.0)		187 (83.9)	176 (78.6)		194 (82.5)	203 (86.4)	
Other answers/Don't know	50 (17.7)	82 (29.0)	<**0.001**	36 (16.1)	48 (21.4)	0.12	41 (17.5)	32 (13.6)	0.22
Are you afraid of vaccinations?									
No	194 (68.1)	214 (75.1)		147 (65.6)	164 (73.2)		152 (63.9)	181 (77.0)	
Yes/Only some of them/I don't know	91 (31.9)	71 (24.9)	**0.006**	77 (34.4)	60 (26.8)	**0.02**	86 (36.1)	54 (23.0)	<**0.001**
Do you recommend that acquaintances/friends get vaccinated?									
Yes	240 (84.2)	246 (86.6)		180 (80.4)	195 (87.0)		198 (83.2)	205 (87.2)	
No/Just some/I don't know	45 (15.8)	38 (13.4)	0.31	44 (19.6)	29 (13.0)	**0.02**	40 (16.8)	30 (12.8)	0.11

[a]The numbers may not add up to the total because of several missing values.
[b]p-values from McNemar's test for paired data.

websites to improve vaccination coverage has been only recently tested in small groups of adults and have had conflicting results. Gerend et al. have evaluated the impact of a message individually tailored to address the perceived barriers to HPV vaccine uptake on the intention of participants to receive that vaccine.[26] The authors found that participants in the tailored condition reported greater increases in intention than did participants in the non-tailored condition. In contrast, no effect on the intention to vaccinate or vaccine uptake was found by Dempsey et al., who provided tailored educational material to parents via iPads in clinic waiting rooms.[27] Our results suggest that an educational website program based on tailored information can significantly increase vaccination coverage in adolescents, independently of age and gender. Interestingly, increased was also the coverage for vaccines such as the menACWY and men B that are not presently recommended by health authorities in Italy. However, the improvement in vaccination outcomes was far greater when the website program was preceded

Table 3. Frequency of specific vaccinations after presentation of the project at school in 748 subjects who completed the study, according to randomization group.[a]

Vaccination	Overall (n = 748) n (%)	No intervention (n = 284) n (%)	Web-site only (n = 224) n (%)	Web-site + lesson (n = 238) n (%)	p-value
Tdap booster	262 (35.1)	15 (5.3)	99 (44.2)	148 (62.2)	<**0.001**
MenACYW vaccine	182 (24.4)	3 (1.1)	52 (23.2)	127 (53.4)	<**0.001**
HPV vaccine	44 (5.9)	17 (6.0)	9 (4.0)	18 (7.6)	0.27
MenB vaccine	41 (5.5)	0 (0.0)	0 (0.0)	41 (17.2)	<**0.001**
MenC vaccine	9 (1.2)	1 (0.3)	4 (1.8)	4 (1.7)	NE
Chickenpox vaccine	2 (0.3)	0 (0.0)	0 (0.0)	2 (0.8)	NE
Influenza vaccine	2 (0.3)	1 (0.3)	0 (0.0)	1 (0.4)	NE

[a]Two subjects (in group A) had follow-up contact but did not answer questions on vaccinations performed during follow-up
HPV: human papillomavirus; MenACYW: conjugated meningococcal ACYW vaccine; MenB: meningococcal B vaccine; Tdap: tetanus, diphtheria, acellular pertussis; and NE: not estimable because of the small number of vaccinated subjects.

Table 4. Association between vaccination and randomization group after intervention.

Vaccination	OR (95% CI)	p-value
Vaccination (any) after presentation of the project at school		
No intervention	1 (reference)	—
Web-site only	**7.3 (4.7–11.3)**	**<0.001**
Web-site + lesson	**17.4 (11.1–27.5)**	**<0.001**
Same analysis, subgroup <14 y		
No intervention	1 (reference)	—
Web-site only	**6.4 (3.3–12.4)**	**<0.001**
Web-site + lesson	**23.8 (11.8–47.9)**	**<0.001**
Same analysis, subgroup ≥ 14 y		
No intervention	1 (reference)	—
Web-site only	**9.6 (5.1–18.0)**	**<0.001**
Web-site + lesson	**18.3 (9.4–35.7)**	**<0.001**
Same analysis, males only		
No intervention	1 (reference)	—
Web-site only	**13.3 (6.2–28.4)**	**<0.001**
Web-site + lesson	**46.8 (19.9–110.0)**	**<0.001**
Same analysis, females only		
No intervention	1 (reference)	—
Web-site only	**5.5 (3.1–9.7)**	**<0.001**
Web-site + lesson	**12.3 (7.0–21.7)**	**<0.001**

ORs adjusted for age, sex, nationality, and presence of chronic diseases.
95% CI: 95% confidence interval; OR: odds ratio.

by a presentation on the subject held by an expert, during which adolescents had had the opportunity to ask questions about immunization and to obtain straightforward answers. However, in the final questionnaire, the adolescents highlighted their need to discuss vaccines with parents, experts, and teachers. This result is not surprising, because school-based, face-to-face educational interventions delivered by authoritative experts have been reported to play a significant role in improving the acceptance of health intervention by adolescents.[28] It is highly likely that the beliefs of adolescents who have already received information regarding vaccines from the face-to-face discussion may be strengthened with the website program, and the adolescents might readily accept the idea of being vaccinated with at least some of the recommended vaccines.

However, in our study, both the interventions had a positive effect on the immunization rates for only TdaP, Men ACYW and MenB vaccines, and the effect on HPV and influenza vaccination was marginal. Although adolescents stated that approximately 20% of their parents visited the website at least once in the 2 intervention arms, the parents were not directly involved in the educational program and only authorized their children to participate. This finding may at least partly explain why uptake of only some vaccines was increased. Gargano et al. have reported that methods to improve vaccine uptake by adolescents are more effective when the cultural needs of parents are met.[29] In this study, adolescents who had been persuaded by the educational intervention to be vaccinated had to ask permission from their parents, who gave consent only for those vaccines that they knew. The TdaP vaccine is generally well known by Italian parents because it has been recommended by official health authorities for several years and is given repeatedly during the first years of life. Meningococcal vaccines have been recently marketed in Italy, and a sustained information campaign for their use has been made by experts through mass media to inform parents of their potential effectiveness against very severe diseases such as meningitis. In contrast, Italian parents do not know the clinical relevance of the influenza vaccine and have some difficulties accepting the HPV vaccine. In Italy, despite recommendations of scientific societies that for some years have supported influenza immunization for all the pediatric population,[30] the Ministry of Health and the health authorities of the Italian regions include only children at risk of influenza-related complications due to a severe chronic underlying disease on the list of subjects for whom influenza vaccination must be provided free of charge and administered annually.[31] No campaign for healthy children is planned, and the lack of prevention of influenza through vaccination remains an unrecognized problem. It seems unlikely that a single educational program may cause adolescents and parents to consider influenza vaccination.

Regarding HPV vaccination in Italy, the poor effectiveness of both educational programmes studied appears to be related to the tendency of both students and parents to underestimate the likelihood of HPV infection, which in turn is associated with a lower propensity for vaccination.[32,33] The positive effects of the internet based educational programs used in this study have been achieved although in Italy there are no school-based vaccination programs and recommended vaccines are given to adolescents only when they are accompanied by parents to the regional vaccination centers. Distance in time and geography between education and vaccine administration is a limit to vaccine acceptance. It is highly likely that these programs may induce even greater improvement of vaccination coverage rates if they are implemented in those countries where the school plays a relevant role in adolescent health education and vaccine administration.

This study has some limitations. First of all, educational programs did not directly involve parents. This has probably increased difference between the 2 groups of adolescents who received web education because it is likely that those students who have received also the lesson by an expert had more attention to vaccines and had more frequently informed parents and obtained consent for vaccination. Secondly, randomization of enrolled adolescents took place at the class level. Probably, there was clustering by class and most adolescents have talked to each other leading to some bleed-over between groups. This could have led to reduce differences among groups. In addition, nearly 1/3 of the students invited to participate in this research did not provide parental consent and, although minimized by randomization, this could have impacted the results because only those parents most interested in vaccination were willing to have their adolescent in the study. Furthermore, the loss to follow-up could have partially impacted the results, although findings from per-protocol and intent-to-treat analyses were the same. Despite these limitations, this study shows the possibility of increasing vaccination coverage in adolescents by using a website-based educational program with tailored information. However, for this program to be best effective, it should be supplemented with face-to-face discussions regarding vaccines at school and at home. Thus, education should specifically include teachers and parents so that they can have adequate knowledge to discuss what is true and false in the vaccination field with adolescents.

Table 5. Satisfaction of subjects in the 2 intervention groups regarding the website educational program, according to sex and age.

	Web-site only group (n = 281)	Web-site + lesson (n = 302)	p-value	Males (n = 239)	Females (n = 344)	p-value	Age <14 (n = 275)	Age 14+ (n = 307)	p-value
Satisfaction with the website, regarding the following features: (0 = min; 5 = max)	**mean ± SDn = 80**	**mean ± SDn = 89**		**mean ± SDn = 71**	**mean ± SDn = 98**		**mean ± SDn = 47**	**mean ± SDn = 122**	
Clarity of language	4.0 ± 1.1	4.0 ± 0.9	0.98	4.0 ± 1.2	4.0 ± 0.8	0.39	3.7 ± 1.3	4.1 ± 0.8	0.08
Clarity of contents	3.9 ± 1.1	4.1 ± 1.0	0.32	3.9 ± 1.2	4.1 ± 0.9	0.99	3.7 ± 1.3	4.1 ± 0.9	0.12
Easy navigation	4.0 ± 1.1	3.9 ± 1.0	0.82	3.9 ± 1.2	4.0 ± 0.9	0.52	3.7 ± 1.3	4.1 ± 0.9	0.16
Web design	3.8 ± 1.2	3.9 ± 1.1	0.42	3.8 ± 1.3	3.9 ± 1.0	0.86	3.7 ± 1.3	3.9 ± 1.1	0.53
Overall satisfaction	3.8 ± 1.1	4.0 ± 1.0	0.43	3.8 ± 1.2	4.0 ± 0.8	0.94	3.7 ± 1.2	4.0 ± 0.9	0.22
On average, how long did you spend reading the website when you accessed it?	**n (%) n = 81**	**n (%) n = 104**		**n (%) n = 81**	**n (%) n = 104**		**n (%) n = 65**	**n (%) n = 120**	
Less than 1 minute	12 (14.8)	17 (16.3)		17 (21.0)	12 (11.5)		20 (30.8)	9 (7.5)	
2 to 4 minutes	24 (29.6)	23 (22.1)		22 (27.2)	25 (24.0)		8 (12.3)	39 (32.5)	
5 to 15 minutes	37 (45.7)	52 (50.0)		29 (35.8)	60 (57.7)		26 (40.0)	63 (52.5)	
16 minutes or more	8 (9.9)	12 (11.5)	0.71	13 (16.0)	7 (6.7)	**0.01**	11 (16.9)	9 (7.5)	**<0.001**
What topic did you most enjoy?	**n (%) n = 74**	**n (%) n = 85**		**n (%) n = 66**	**n (%) n = 93**		**n (%) n = 41**	**n (%) n = 118**	
Immune system	18 (24.3)	24 (28.2)		21 (31.8)	21 (22.6)		10 (24.4)	32 (27.1)	
Response against pathogen	6 (8.1)	11 (12.9)		5 (7.6)	12 (12.9)		3 (7.3)	14 (11.9)	
Vaccines	24 (32.4)	24 (28.2)		21 (31.8)	27 (29.0)		13 (31.7)	35 (29.7)	
Risk and protective factors for infectious disease	10 (13.5)	12 (14.1)		9 (13.6)	13 (14.0)		7 (17.1)	15 (12.7)	
Vaccine-preventable diseases	13 (17.6)	10 (11.8)		8 (12.1)	15 (16.1)		6 (14.6)	17 (14.4)	
Other	3 (4.0)	4 (4.7)	0.81	2 (3.0)	5 (5.4)	0.66	2 (4.9)	5 (4.2)	0.95
What topic would you have liked to be more discussed? (multiple answers allowed)	**n yes (%) n = 75**	**n yes (%) n = 82**		**n yes (%) n = 64**	**n yes (%) n = 93**		**n yes (%) n = 40**	**n yes (%) n = 117**	
Vaccine mechanism of action	14 (18.7)	5 (6.1)	**0.02**	8 (12.5)	11 (11.8)	0.90	10 (25.0)	9 (7.7)	**0.004**
Vaccine safety	17 (22.7)	20 (24.4)	0.80	21 (32.8)	16 (17.2)	**0.02**	19 (47.5)	18 (15.4)	**<0.001**
The body's defense mechanisms	6 (8.0)	7 (8.5)	0.9	4 (6.2)	9 (9.7)	0.44	2 (5.0)	11 (9.4)	0.52
Infectious diseases	11 (14.7)	22 (26.8)	0.06	15 (23.4)	18 (19.3)	0.54	8 (20.0)	25 (21.4)	0.85
Advice for infectious disease prevention	20 (26.7)	13 (15.8)	0.10	12 (18.7)	21 (22.6)	0.56	4 (10.0)	29 (24.8)	**0.048**
Vaccine scepticism	19 (25.3)	17 (20.7)	0.49	10 (15.6)	26 (28.0)	0.07	6 (15.0)	30 (25.6)	0.17
Other	5 (6.7)	6 (7.3)	0.87	5 (7.8)	6 (6.4)	0.74	1 (2.5)	10 (8.5)	0.29
Did your parents visit the website at least once?	**n (%) n = 137**	**n (%) n = 145**		**n (%) n = 122**	**n (%) n = 160**		**n (%) n = 106**	**n (%) n = 176**	
No	104 (75.9)	111 (76.5)		96 (78.7)	119 (74.4)		81 (76.4)	134 (76.1)	
Yes	33 (24.1)	34 (23.5)	0.90	26 (21.3)	41 (25.6)	0.40	25 (23.6)	42 (23.9)	0.96
Have you discussed the website at school with your teachers?	**n (%) n = 122**	**n (%) n = 138**		**n (%) n = 108**	**n (%) n = 152**		**n (%) n = 92**	**n (%) n = 168**	
No	97 (79.5)	112 (81.2)		87 (80.6)	122 (80.3)		68 (73.9)	141 (83.9)	
Yes	25 (20.5)	26 (18.8)	0.74	21 (19.4)	30 (19.7)	0.95	24 (26.1)	27 (16.1)	0.052
Which of these statements do you agree with most?	**n (%) n = 75**	**n (%) n = 88**		**n (%) n = 66**	**n (%) n = 97**		**n (%) n = 45**	**n (%) n = 118**	
I didn't like my experience with this website, and I considered it useless	10 (13.3)	4 (4.5)		8 (12.1)	6 (6.2)		0 (0.0)	14 (11.9)	
I liked my experience with this website, but I would like to meet again with people who recommended it to me, to discuss specific questions	11 (14.7)	8 (9.1)		9 (13.6)	10 (10.3)		2 (4.4)	17 (14.4)	
I liked my experience with this website, but I would like to discuss it further with my parents	6 (8.0)	19 (21.6)		6 (9.1)	19 (19.6)		7 (15.6)	18 (15.2)	
I liked my experience with this website, but I would like to discuss it further with my teachers	11 (14.7)	13 (14.8)		8 (12.1)	16 (16.5)		5 (11.1)	19 (16.1)	
I'm really satisfied with my experience with this website	37 (49.3)	44 (50.0)	**0.047**	35 (53.0)	46 (47.4)	0.23	31 (68.9)	50 (42.4)	**0.01**

Materials and methods

Study design

This was a prospective, randomized controlled trial taking place over one school year, involving 4 secondary schools for adolescents 11–13 y old and 8 schools for adolescents 14–18 y old in Milan, Italy. Each class was randomized 1:1:1 on the basis of a computerized randomization list that included 3 arms: 1) registration of vaccination coverage and attitudes toward vaccination at the beginning and at the end of the school year, but no intervention; 2) registration of vaccination coverage and attitudes toward vaccination at the beginning and at the end of the school year plus participation in a presentation and access to a specific website dedicated to vaccines and vaccination; and 3) the procedures described in arm 2 plus participation in a lecture on vaccines and vaccination from medical experts in classrooms. The study was conducted over the course of one school year between November 2015 and June 2016. The adolescents' vaccination status was established by consulting the official vaccination chart issued by the Vaccination Service of the Lombardy Region, the Region in which they lived. All the students had an official vaccination chart and data were obtained from this record.

The study was approved by the Ethics Committee of Milan Area B and by the Direction of each of the 12 participating schools. Students were enrolled after written consent of both parents and written consent from students were provided.

Study population

Inclusion criteria included an age between 11 and 18 years, no receipt of vaccination recommended by the Italian Vaccination Plan for the adolescents (i.e., diphtheria, tetanus, pertussis, HPV vaccines),[31] and written informed consent signed by both the parents and written consent signed by the adolescents. In agreement with the Italian Vaccination Plan and the recommendations of the Lombardy Region (i.e., where Milan is located), the HPV vaccine was considered to be recommended only for females. The absence of meningococcal vaccinations was not included among inclusion criteria because in the Lombardy Region, according to the Italian Vaccination Plan, only meningococcal C conjugate vaccine with one dose between 1 and 18 y was recommended when the study was performed, although families sometimes requested MenACYW vaccine and were also interested in meningococcal B vaccine. Influenza vaccination, which was recommended only for adolescents with underlying chronic disease at risk of influenza complications, and varicella vaccination, which was recommended only for adolescents with a negative history of varicella, were not included among the inclusion criteria. All the vaccines in Italy are administered in vaccination centers during school days and not at school.

Of the 4,453 students who attended the 12 schools, 1,710 (38.4%) had already been vaccinated with one or more of the vaccines recommended for adolescents, 1,380 (31.0%) were excluded because of the absence of written consent and/or assent, and 446 (10.0%) were excluded because they were not aged 11–18 y. Overall, 917 (20.6%) unvaccinated adolescents were enrolled, and 334 were randomized to no intervention, 281 were randomized to the website educational program only, and 302 were randomized to the website educational program plus the face to face lesson.

Methods

Between November 1, 2015, and December 20, 2015, all the adolescents who met the inclusion criteria and did not fulfil the exclusion criteria were enrolled. At enrolment, all the students completed a survey regarding their vaccination status (adding a copy of their personal vaccination chart) and their personal knowledge and attitudes toward infectious diseases and vaccination.

After enrolment, to reduce risk of contamination, passwords for access to a website providing explanations through multiple choice questions on how the immune system works, details on vaccine-preventable diseases, and information on vaccines were given only to subjects randomized to arms 2 and 3.

Subjects randomized to arm 3 also participated in a lecture on vaccines and vaccination regarding the same topics included in the internet presentation from medical experts in classrooms.

In all the enrolled subjects, the same questionnaire presented at enrolment was completed at the end of the school year by a blind researcher (i.e., between May and June 2016). A total of 748 out of 917 (81.6%) students completed the study: 284/334 (85.0%) in the group no intervention, 224/281 (79.7%) in the group web only and 238/302 (78.8%) in the group web + lesson.

Statistical analysis

Assuming a proportion of 10% of subjects in the non-intervention group vaccinated during the year, a sample size of 265 subjects in each group achieved a 90% power (with $\alpha = 0.05$) to detect a difference in the group proportions of 10%, i.e., a proportion of vaccinated subjects in the intervention group during the year equal to 20%. Sample size calculation was performed using PASS v.11 software (NCSS, LLC. Kaysville, Utah, USA).

Each class in the 12 schools was randomized to the 3 study groups by using a block randomization according to the class level, through the PLAN procedure in SAS.

Due to absence of differences between intent-to-treat and per-protocol analyses, per-protocol results were presented. Categorical variables were presented in the descriptive tables as numbers and percentages, and continuous variables through mean values $\pm$ standard deviation (SD). Analyses included only those who completed the follow-up. For categorical data, comparisons among groups were performed by using the contingency table analysis with the χ^2 or Fisher's exact test, when appropriate. The McNemar's test for paired data were used to compare the within-group frequency distribution of (correct) answers to the same question before and after intervention. Continuous data were compared using an analysis of variance or the corresponding non-parametric Kruskall-Wallis test when the 3 study groups were analyzed together; when comparisons involved 2 groups, a 2-sided Student's t-test or the corresponding non-parametric 2-sided Wilcoxon's rank-sum test were used. Odds ratios (OR) and 95% confidence intervals (CI) were calculated to measure the association between the randomization group and vaccination received after intervention. ORs were obtained using unconditional multiple logistic regression, adjusted for age, sex, nationality and presence of chronic diseases. The analyses were also conducted in subgroups of age (< 14 / ≥ 14 y old) and sex. All of the analyses were 2 tailed, and p-values of 0.05 or less were considered to be statistically significant. Statistical analyses were conducted using SAS version 9.2 (Cary, NC, USA).

Disclosure of potential conflicts of interest

None to declare.

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