A randomised controlled trial of a school-based intervention to prevent tobacco use among children and adolescents in Italy

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Abstract: AIM A randomised field trial was conducted to evaluate a school-based programme to
prevent tobacco use in children and adolescents.
SUBJECT AND METHODS Five hundred and thirty-four children and three hundred and eight
adolescents were randomly select to receive or not receive the prevention programme. The prevention
programme included: a) health facts and the effect of smoking; b) analysis of the mechanisms to start
smoking; c) refusal skills training to deal with the social pressures to smoke. A questionnaire was
administered before the intervention programme and two years later.
RESULTS The prevalence rates of smoking in both group of children and adolescents resulted to be
increased at the end of the study. Anyway, the difference of smoking prevalence between intervention
and control group was statistically significant only for children group (from 18.3% to 18.8% for the
intervention group, and from 17.8 % to 26.9% in the control group) (p = 0.035). As regards reasons
that induced to start smoking, there was a significant increase of the issue "Because smokers are fool"
(p = 0.004 for children; p < 0.001 for adolescents) and "Because smokers are irresponsible" (p ≤ 0.001
for both children and adolescents) in the experimental groups.
CONCLUSION The results suggest that a school-based intervention programme on children and
adolescent tobacco use, based on the development of cognitive and behavioural aspects, can be
effective. After one year of intervention, smoking prevalence was significantly lower in children
belonging to intervention group than in children not randomised to intervention. Targeting young
children before they begin to smoke can be a successful way of prevention.

Response to Reviewers: see attached file

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Abstract

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CONCLUSION The results suggest that a school-based intervention programme on children and adolescent tobacco use, based on the development of cognitive and behavioural aspects, can be effective. After one year of intervention, smoking prevalence was significantly lower in children belonging to intervention group than in children not randomised to intervention. Targeting young children before they begin to smoke can be a successful way of prevention.

Keywords: tobacco, smoking, school-based, prevention program.

Introduction

It is definitively demonstrated that smoking represents the most important preventable cause of different diseases and premature death. Smoking causes 5 million deaths worldwide per year, and if present trends continue, by 2025 10 million smokers per year is projected to die (Hatsukami 2008). Anyway, cigarette smoking is actually the most spread addictive behaviour in Italy, such as in all developed Countries, and this is particularly true among young people (Evans 1976; Pampel and Aguilar 2008; Ferketich et al. 2008).

An efficacious fight against smoking could be based on three factors: 1) ban of direct and in direct advertising; 2) smoking prohibition in public rooms; 3) health education and promotion.

Most people start smoking during adolescence. The etiologic model is based on psychological and environmental pressure, especially due to parents and peers, and on smoking advertising, that are responsible of inducing and perpetuating smoking habit (Farrelly 2009).

The essential elements of smoking prevention interventions, as suggested by Centres for Disease Control and Prevention (CDC), include: 1) information about social influences, including media, peer and parents; 2) information about short-term physiological effects of tobacco use; 3) training in refusal skills. In fact, there is sufficient body of evidence indicating that the most efficacious preventive approach must be based, not only on information, but on developing and reinforcement of refusal skills training for dealing with the social pressures to smoke (Centres for Disease Control and Prevention 1994; Ayzen and Fishbein 1980; Botvin and Griffin 2007; Peters et al. 2009).

As far as concerns the best age period to start tobacco smoking prevention programmes, many researchers agree to initiate them at elementary schools, because programmes started at high schools resulted to be less effective.

In literature there are many studies focused on smoking prevention programmes in adolescent populations (Puska et al. 1980; Clarke et al. 1986; Errecart et al. 1991; Perry et al. 1992; Adelman et al. 2001; La Torre et al. 2004; Resnicow 2008; Campbell et al. 2008; Johnson et al. 2009), while

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very few studies on interventions in children have been conducted (Best et al. 1988; Rasmussen et al. 2002; ; Thomas and Perera 2006; Hiemstra et al. 2009).

In order to assess the effectiveness of a smoking prevention program in children and adolescents (grade 4-9), we conducted a school-based prevention trial in three different towns of Central and Southern Italy: in Cassino and Pontecorvo (Lazio Region), and Capodrise (Campania Region). This study, taking into account both adolescents and children, gives the possibility to analyze the differences between the results obtained by two similar interventions administered to both groups. Moreover, the intervention focalize - in addition to information of health facts - on refusal skills training to make the children and the adolescents able to dealing with the social pressures to smoke.

Methods

Setting and questionnaire

The trial was conducted in three cities (Cassino, Pontecorvo and Capodirise), the first two in Lazio and the latter in Campania regions. However, despite the different regions, the cities are very close (10 Km between Cassino and Pontecorvo, and 75 Km between Cassino and Capodrise), without major socio-demographical differences able to influence differently the results of the trials.

Adolescent trial

On February 1999 an anonymous questionnaire was administered to adolescents attending high schools in grade 9 (ages 14-15) to evaluate the prevalence of smoking and attitude towards tobacco. 15 classes of Classical and Scientific Licea of Cassino (Province of Frosinone, Lazio) were selected to be enrolled in the study.

Children trial

Moreover, the same questionnaire was administered to children attending schools in 4 to 6 grades

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(ages 9-11) in Pontecorvo (Province of Frosinone, Lazio) and Capodrise (Province of Caserta, Campania) on May 2002.

Questionnaire

The questionnaire, validated in previous cross-sectional studies was designed to collect socio-demographic information about students and their parents, habits and attitudes towards tobacco and passive smoking (La Torre 1998). The main outcome variable was represented by the following question: *"Have you ever smoked a cigarette?"*, indicating the status of current or ex-smoker. The questionnaire was submitted twice: before the intervention programme and two years later.

The participation in the trial was accepted by each school Health Promotion Committee and a written consent was obtained by students' parents. The trial was conducted following the criteria of the Helsinki Declaration.

Health education intervention

The tobacco smoking prevention programme was designed as a school-based intervention focused on avoiding students' use of tobacco trough a clarification of facts. The curriculum consists of three levels of instruction: a) health facts and the effect of smoking on health; b) analysis of the mechanisms that lead children and adolescent to start smoking; c) refusal skills training for dealing with the social pressures to smoke.

The intervention was scheduled on a basis of five appointments, the first and the last ones delivered by the schools' teachers involved in the project. These teachers were trained through a tobacco prevention course, organised one month before the starting of the intervention by the scientific responsible of the project. From the second to the fourth appointments, the participants in the experimental groups underwent to the intervention that lasted for two hours each. Finally, the teachers of the involved schools reinforced the intervention in a last appointment.

In the intervention group, effects of smoking on short-term period, more than on long-term, were emphasised, and students were allowed to clarify their opinions regarding tobacco use. Moreover,

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peer led discussions and skills practice activities were performed.

The curriculum underlined psycho-social themes, such as relational stress within peers and family, that can influence and perpetuate the attitude toward tobacco, as well as economic aspect related to the cultivation of tobacco plant (the intervention was conducted in a tobacco production zone). The intervention was aimed to develop the capability of children to firmly and politely refuse cigarette offered by peers and to maintain a conversation in order to sustain adequately their refusal position. The participants followed the programme for one year. One more year later, the questionnaire was administered again to both students that received and do not receive the intervention programme, in order to assess differences in the prevalence of smoking in the intervention and in the control groups.

At the end of the intervention, students in the experimental arm were asked to fill a questionnaire on the quality of the intervention, considering the following items:

- Interests towards the issues covered in the intervention

- Comprehensiveness of the intervention

- Availability of the intervention teaching staff to answer questions

- Usefulness of the intervention

Thanks to a strong collaboration with teachers responsible for health education in the selected schools, it was possible to follow students' career in order to avoid lost to follow-up in the trial.

Sample size and Randomisation

Sample size calculations, with a sensitivity of 90% and a power of 80%, an expected frequency of smoking of 30% and an estimated OR of smoking equal to 0.70 for students participating in the intervention groups, suggested to sample 778 individuals. We do not calculate the number of classes to accrue, since the outcome of the trial was at the individual level, and not at the class level. So, considering an average class composed by 20 students, we estimated that a total of 39 classes were

needed for the trials. On the basis of the total number of classes in the selected schools, and considering the proportion of children and adolescents at schools in the cities involved, we randomised 24 elementary classes and 15 high school classes to both intervention or control groups. The randomisation process gave the scheme shown in Figure 1: in children group, 242 pupils were randomised to the experimental group and 292 to the control group; in adolescent group, 162 and 146 students were respectively randomised to intervention and control groups.

[Figure 1 here]

Sample size calculations were made using the program Statcalc in EpiInfo statistical package.

Statistical analysis

Chi-square test, with Yates' correction where applicable, and Fisher exact test were used to assess statistical significant differences between questionnaire answers at the beginning and at the end of the trial in the two groups.

In order to estimate the influence of socio-demographic factors on both children and adolescents cigarette smoking attitudes, multiple logistic regression analyses were performed, using the backward elimination procedure described by Hosmer and Lemeshow (Hosmer and Lemeshow 1989).

The covariates considered in the models were: gender (males as reference group), age of children, parents' smoking habits (no smokers as reference group), father's job activity (managerial status as reference group). The results are expressed as Odds Ratio (OR) and 95% Confidence Interval (95% CI). The goodness of fit was assessed using the Hosmer-Lemeshow test. The level of statistical significance was fixed at $p=0.05$.

To evaluate the effectiveness of the smoking prevention programme, it has been calculated, for each subgroup and globally, the percentage of the outcome variable (smoking status) variation in the intervention group (experimental event rate, EER) and in the control group (control event rate,

CER). Finally, the absolute risk reduction (ARR), the relative risk reduction (RRR), and the number needed to prevent an event (NNT = 1/ARR) were calculated.

Moreover, a different analysis was conducted in order to take into account cluster randomization. We followed the methods suggested by Donner and Klar (2000), using adjustments for chi-square test and generalized estimating equations (GEE) in order to construct an extension of standard logistic regression which adjusts for the effect of clustering, without requiring parametric assumptions.

The statistical analyses was conducted using SPSS for Windows (release 12.0) and Stata 9.

Results

Children trial

Two hundred and fourty-two (242) students were enrolled in the study in the intervention group (125 males; mean age 11.03 years, SD = 1.07), and two hundred and ninety-two (292) students were enrolled in the control group (146 males; mean age 11.01 years, SD = 0.96).

Table 1 shows socio-demographic characteristics of pupils, indicating no differences existed between the two groups at baseline.

[table 1 here]

In table 2 the prevalence of smoking in the two groups at the beginning and at the end of the trial are shown. The prevalence of smoking in the intervention group resulted to be quite constant, going from 18.3% to 18.8%, while a relevant increase was observed in the control group, raising from 17.8 % to 26.9% (p= 0.035; cluster randomised analysis p = 0.042).

[table 2 here]

Table 3 shows data relative to changes on knowledge and attitude towards tobacco smoking, both in

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the experimental and control groups. It is interesting to note that smoking prevention programme is considered to be useful mostly in the experimental group (p = 0.019; cluster randomised analysis p = 0.026).

As regards reasons that induced to start smoking, in the experimental group there is a significant increase regarding the issue *"Because smokers are fool"* (p = 0.004; cluster randomised analysis p = 0.012) and *"Because smokers are irresponsible"* (p = 0.001; cluster randomised analysis p = 0.019).

[table 3 here]

In Italy, advertising of tobacco products are banned since 1962 but remains forms of indirect advertising, like the brand related to sponsorship, particularly of sporting events. In both groups the prevalence of children remembering cigarette indirect advertising is very high (almost 40% at the end of the trial), mostly related to Formula 1 Ferrari-Marlboro Team.

As far as concerns effectiveness of the community intervention to prevent children tobacco use, after 2 years, the experimental event rate (EER) is 0.5%, while the control event rate (CER) is 9.1% and the relative risk reduction (RRR) of being smokers for children randomised to the intervention group is 94.5%. An interesting indicator for assessing the intervention effectiveness is the number needed to prevent an event (NNT), that in our experience is 11.6. I.e. we need to treat 11-12 children (equivalent to half a class) in order to have a children that remains a no smoker in one year. Significant predictors of tobacco smoking in the children trial were age (OR = 1.32 for one unit increase) and belonging to the control group (risk almost double with respect to intervention group; cluster randomised analysis OR = 0.76; p = 0.023) (Table 4).

[table 4 here]

Adolescents trial

One hundred and sixty-two adolescents (162) were enrolled in the intervention group (77 males;

mean age 14.39 years, SD = 0.7), and one hundred and fourty-six (146) adolescents were enrolled in the control group (70 males; mean age 14.33 years, SD = 0.69).

In table 1 socio-demographic characteristics of participants of the trial are shown, indicating no differences existed between intervention and control groups at baseline.

In table 2 the prevalence rates of smoking at the beginning and at the end of the study are shown. It is remarkable that in the second year of the trial the prevalence rates of smoking increased in both groups: in the intervention group went from 16.9% to 29.4%, while in the control group from 18.5 % to 33.4%, even if increases were not statistically significant. Since within-cluster correlation was near 0, we considered Pearson chi-square test as appropriate.

Table 5 presents data regarding variations on knowledge and attitude towards tobacco smoking in the two periods, both in the experimental and control groups. Among reasons that induced to start smoking, in the experimental group there is a significant increase regarding the issue *"To be part of a group with peers"* (p = 0.001), *"Because parents smoke"* (p< 0.001), *"Because smokers are fool" (*p < 0.001*)* and *"Because smokers are irresponsible"*(p < 0.001).

[table 5 here]

In the intervention group there has been a significant increase of thinking that the passive smoking was harmful (p = 0.015; cluster randomised analysis p = 0.053) and of knowledge about direct advertising in Italy (p = 0.005; cluster randomised analysis p = 0.037). The prevalence of adolescents remembering cigarette indirect advertising significantly increased in both groups.

Moreover, also the prevalence of adolescents that felt themselves uncomfortable when someone smokes in their presence significantly increased in both groups.

As far as concerns effectiveness of the community intervention to prevent adolescents tobacco use, it should be underlined that the experimental event rate (EER) is 12.5%, while the control event rate (CER) is 14.9%. The relative risk reduction (RRR) of being smokers for adolescents randomised to the intervention group is 16.1%. The number needed to prevent an event (NNT) is 41.7, i.e. we need to treat 42 adolescents (equivalent to approximately two classes) in order to have an individual that

remains a no smoker in one year.

Significant predictors of tobacco smoking in the adolescents trial were age (OR = 2.01 for one unit increase) and the status of current smoker of the father (OR = 1.88) (Table 4). Considering the cluster randomised analysis, the OR were 1.89 and 1.73, respectively.

Both children and adolescent

Considering all participants in the trial, the experimental event rate (EER) is 5.6%, while the control event rate (CER) is 10.9%. The number needed to prevent an event (NNT) is 18.9, i.e. we need to treat 19 individuals (equivalent to approximately one class) in order to have an individual that remains a no smoker in one year. At the end of the intervention trial the following judgment were found in the intervention group:

- Interests towards the issues covered in the intervention: 95%

- Comprehensiveness of the intervention: 97%

- Availability of the intervention teaching staff to answer questions: 99%

- Usefulness of the intervention: 91%

The logistic regression (Table 4) showed that cigarette smoking among children was significantly associated to the status of current smoker of the father (OR= 1.90; IC 95%: 1.33 – 2.70), and increasing age (OR= 1.18 for one unit increase; IC 95%: 1.11 – 1.26).

Discussion

The results suggest that a school-based intervention on children tobacco use, based on the development of cognitive and behavioural aspects, can be effective in the Italian setting, especially for children. After one year of intervention, smoking prevalence was significantly lower in children

who received the community intervention programme than in children not randomised to intervention. The adolescents trial had not the same results, ==and this result is in line with a systematic review of controlled trials for adolescent smoking cessation (Garrison et al, 2003) that demonstrated there is very limited evidence of efficacy of smoking-cessation interventions in adolescents, and no evidence on the long-term effectiveness of these interventions.== Despite similar intervention and social characteristics of the two settings, the prevention doesn't work at the same way. The deepest differences between the two groups of intervention are likely imputable to the age of participants. If the onset of smoking occurs predominantly during adolescence, maybe this age is too late to start effective prevention program, and targeting young children before they begin to smoke can be a successful way of prevention.

In this trial the high prevalence of ever smoking among children and adolescents at baseline must not be surprising, since the chosen towns are located in areas of tobacco production, and this is witnessed mainly by the prevalence of smoking in parents, very high with respect the Italian average where smoke the 24,5% of population (32,4% men and 17,1% women) (Istat 2000).

The findings are consistent with other studies of community interventions to prevent children and adolescent tobacco use (Clarke et al. 1986; Perry et al. 1992; Resnicow 2008; Campbell et al. 2008; Rasmussen et al. 2002; Faggiano et al. 2008; Perry et al. 2009). Recent review of the scientific literature underlines the need to reinforce smoking prevention programmes even at very young ages (elementary school) and the need to use the school environment as a fundamental place where preventing smoking (La Torre et al. 2005; Sherman and Primack 2009).

Many systematic reviews demonstrate that school-based smoking prevention programmes are effective in reducing smoking habits, if conducted in a methodologically rigorous way (Rundall and Bruvold 1988; Bruvold 1993; Rooney and Murray 1996; Thomas 2002; Sowden et al. 2003; Hwang et al. 2004; Thomas and Perera 2009; Richardson 2009).

They show evidence of a decreased prevalence of smoking among students exposed to the social influence programmes compared to students in control groups, with the mean difference between treated and nontreated groups (schools or classrooms) ranging from 5% to 60%, with a duration of 1-4 years.

In this context, the Control of Adolescent Smoking Study (CAS) is an interesting survey that investigated the relationships between national tobacco policies, school smoking policies and adolescent smoking in eight European countries (Austria, French-speaking Belgium, Denmark, Finland, Germany, Norway, Scotland and Wales). The CAS study suggest that prevalence of smoking among students was related to the strength and enforcement of policies to control smoking and good teacher support for students was correlated with lower smoking rates in students; therefore the main recommendation from the CAS study is to aim for smoke-free schools and support this aim with comprehensive national tobacco control policies (Wold et al. 2004). On the other hand, it would be necessary to act at different levels in the community, also implementing training programs among healthcare personnel in order to develop ability in smoking cessation techniques for providing an active support to smokers (Gianti et al. 2007).

It is evident that school programmes designed to prevent tobacco use in children and adolescents could become one of the most effective strategies available to reduce tobacco use all over the world, especially if the programme comprehends the involvement of communities.

The present trial has some limitations. First of all, the trial was designed having the class as the randomisation unit. In this way, the effect of the intervention could have been diluted for the impossibility of taking completely separated the participants in the trial within the same school. Anyway, if this happened, the results suggest the positive influence of the intervention. Another critical point is the duration of follow-up. Our trial was designed to study the effect of the intervention in the short-medium term, and obviously we were not able to show long term effect of the same intervention. Moreover, a possible selection bias could have occurred since we recruited the

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participants in two different periods (1999 and 2002), but it is difficult that time trends could have affect the results, due to the short period, and no new tobacco control measures were implemented in Italy during that period. We were not able to apply the same standardised intervention to children in the same grade due to logistic reasons. Finally, a possible dilution of the effect could have not been avoided at all, especially in the adolescent trial, due to the objective difficulty (or even impossibility) to avoid communication between adolescents that belongs to different classes (involved and not in the experimental groups).

The major strength of this trial was the possibility to fully follow-up the participants, due to the collaboration of the selected schools. Our intervention was greatly appreciated by the school personnel, and demonstrates once again the school as one of the best environment in which an educational intervention could be implemented.

Conflict of interests

The Authors declared they have not any conflict of interests

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Table

Table 1– Socio-demographic characteristics of the participants of the trial.

Characteristics	Number (%) or mean (Standard Deviation)			Number (%) or mean (Standard Deviation)		
	Children trial			Adolescents trial		
	Experimental group	Control group	p	Experimental group 162	Control group 146	p
Age (at the beginning of the trial)mean (SD)	11.03 (1.07)	11.01 (0.96)	0.965	14.39 (0.70)	14.33 (0.69)	1.000
Gender of students						
Males	125 (51.5)	146 (50)	0.738	77 (47.5)	70 (47.9)	0.942
Females	117 (48.5)	146 (50)		85 (52.5)	76 (52.1)	
Father's work activity						
Managerial/professional	19 (8.2)	28 (9.7)		14 (8.6)	12 (8.2)	
Non manual (blue collar)	56 (24.2)	66 (22.8)		38 (23.5)	33 (22.6)	
Skilled Manual	109 (47.2)	140 (48.3)	0.955	78 (48.1)	68 (46.6)	0.959
Not skilled Manual	42 (18.2)	51 (17.6)		26 (16.1)	24 (16.4)	
Unemployed	4 (1.7)	3 (1.0)		2 (1.2)	3 (2.1)	
Retired from work	1 (0.4)	2 (0.6)		4 (2.5)	6 (4.1)	
Smoking Status of the father	114 (47.3)	132 (45.5)	0.681	67 (41.4)	63 (43.2)	0.698

Mother's work activity						
Managerial/professional	7 (2.9)	6 (2.1)		7 (4.3)	5 (3.4)	
Non manual (blue collar)	35 (14.5)	50 (17.1)		27 (16.7)	25 (17.1)	
Skilled Manual	10 (4.1)	19 (6.5)	0.576	11 (7.5)	9 (6.2)	0.993
Not skilled Manual	39 (16.2)	49 (16.8)		20 (12.3)	18 (12.4)	
Housewife	150 (62.3)	167 (57.4)		97 (59.9)	89 (61.0)	
Smoking Status of the mother	76 (31.5)	82 (28.2)	0.399	53 (32.7)	46 (31.5)	0.820

Table 2 - Prevalence rates at the beginning of the trial and after 2 years in the experimental and control groups in children and adolescents trials.

Trial	Experimental group			Control group			
	Ever Smokers (%)	*No smokers (%)*	*Total*	*Ever Smokers (%)*	*No smokers (%)*	*Total*	*p*
Children trial							
Prevalence rate at the beginning of the trial	44 (18.3)	197 (81.7)	241	52 (17.8)	240 (82.2)	292	0.893
Prevalence rate after 2 years	45 (18.8)	194 (81.2)	239	78 (26.9)	216 (73.1)	292	0.035
Adolescents trial							
Prevalence rate at the beginning of the trial	27 (16.9)	135 (83.1)	162	27 (18.5)	119 (81.5)	146	0.673
Prevalence rate after 2 years	47 (29.4)	113 (70.6)	160	48 (33.4)	96 (66.7)	144	0.457
Total trial							
Prevalence rate at the beginning of the trial	71 (17.6)	332 (82.4)	403	79 (18)	359 (82)	438	0.874
Prevalence rate after 2 years	92 (23.1)	307 (76.9)	399	126 (28.9)	312 (71.1)	436	0.060

Table 3 – Differences in attitude and knowledge toward tabacco in the experimental and control groups in children trial

Attitude/knowledge	Children trial					
	Experimental group			Control group		
	Baseline n° (%) [242]	After 2 years n° (%) [239]	p	Baseline n° (%) [292]	After 2 years n° (%) [292]	P
It is important to prevent smoking at school	203 (84.2)	218 (91.2)	0.019	248 (84.9)	251 (86)	0.725
Smoking is unhealthy	238 (99.1)	235 (98.3)	0.695	287 (98.3)	290 (99.3)	0.450
Reasons that induce to start smoking						
• *To imitate others*	123 (51.0)	113(47.3)	0.437	160 (54.8)	163(55.8)	0.802
• *To be part of a group with peers*	70 (29.0)	69(28.9)	0.093	96 (32.9)	94(32.2)	0.860
• *To feel older*	161 (66.8)	160 (67.0)	0.923	202 (69.2)	207 (70.9)	0.651
• *Because parents smoke*	34 (14.1)	32 (13.4)	0.376	36 (12.3)	31 (10.6)	0.516
• *Because in some place smoking is not allowed*	15 (6.2)	12 (5.0)	0.097	11 (3.8)	14 (4.8)	0.539
• *Because smokers are fool*	81 (33.5)	112 (38.8)	0.004	93 (31.8)	88 (30.1)	0.654
• *Because smokers are irresponsible*	110 (45.6)	148 (61.2)	0.001	126 (43.2)	110 (46)	0.173
Do you remember an advertising related to cigarette	36 (14.9)	95 (39.7)	< 0.001	41(14.0)	108 (37)	< 0.001

smoking?						
Do you know direct advertising of cigarette is forbidden in Italy?	133 (55.2)	179 (74.9)	< 0.001	170 (58.2)	174 (59.6)	0.736
Passive smoking is harmful	216 (89.6)	231 (94.5)	0.01	257 (88.0)	264 (90.4)	0.248
Do you feel uncomfortable when someone smokes in your presence?	194 (80.5)	186 (77.8)	0.197	241 (82.5)	239 (81.8)	0.829

Table 4 - Logistic regression of the predictors of tobacco smoking post-intervention

independent variables: smoking at baseline, age, SES, gender, group (intervention vs control)

Variables	Children trial OR (95% CI)	p	Adolescent trial OR (95% CI)	P	All OR (95% CI)	p
Gender						
Male (reference)	1		1		1	
Female	0.81 (0.49-1.34)	0.410	0.66 (0.39 – 1.14)	0.134	0.85 (0.62 – 1.16)	0.301
Father smoke						
No (reference)	1		1		1	
Yes	1.53 (0.91 – 2.58)	0.108	1.88 (1.05 – 3.36)	0.034	1.90 (1.33 – 2.70)	< 0.001
Mother smoke						
No (reference)	1		1			
Yes	1.08 (0.63- 1.85)	0.772	1.58 (0.84 – 3.00)	0.159	1.27 (0.85 – 1.88)	0.243
Socio-economic status						
Very high (reference)	1		1		1	
High	1.03 (0.29 – 3.65)	0.966	1.07 (0.31 – 3.87)		1.04 (0.30 – 3.73)	
Medium	1.08 (0.32 – 3.67)	0.900	1.02 (0.30 – 3.29)		1.07 (0.32 – 3.79)	
Low	0.90 (0.28 – 2.87)	0.853	0.95 (0.34 – 3.05)		0.91 (0.27 – 2.68)	

Age	1.32 (1.05 – 1.66)	0.016	2.01 (1.26 – 3.20)	0.003	1.18 (1.11 – 1.26)	< 0.001
Smoking at baseline						
No (reference)	1		1		1	
Yes	1.12 (0.35 – 3.58)	0.853	1.20 (0.72 – 2.01)	0.488	1.35 (0.98 – 1.86)	0.066
Group						
Control group	1		1		1	
Experimental group	0.54 (0.31 – 0.93)	0.026	0.88 (0.63 – 1.23)	0.39	0.72 (0.50 – 1.03)	0.071
Hosmer and Lemeshow						
Goodness of fit test	10.807	0.147	3.241	0.862	3.641	0.888

Table 5 – Differences in attitude and knowledge toward tabacco in the experimental and control groups in adolescents trial.

	Adolescents trial					
	Experimental group			**Control group**		
	Baseline	**After 2 years**	**p**	**Baseline**	**After 2 years**	**p**
	n° (%)	**n° (%)**		**n° (%)**	**n° (%)**	
Attitude/knowledge	**[162]**	**[160]**		**[146]**	**[144]**	
It is important to prevent smoking at school	145 (89.5)	149 (93.1)	0.249	131 (89.7)	127 (88.2)	0.677
Smoking is unhealthy	155 (95.7)	155 (96.9)	0.785	139 (95.2)	142 (98.6)	0.173
Reasons which induce to start smoking						
• *To imitate others*	70 (43.2)	81 (50.6)	0.182	66 (45.2)	71 (49.3)	0.484
• *To be part of a group with peers*	49 (30.2)	76 (47.5)	0.001	46 (31.5)	47(32.6)	0.836
• *To feel older*	102 (62.7)	109 (68.1)	0.329	89 (61.0)	99 (68.8)	0.165
• *Because parents smoke*	20 (12.3)	46 (28.8)	< 0.001	16 (11.0)	19 (13.2)	0.559
• *Because in some place smoking is not allowed*	11 (6.8)	13 (8.1)	0.648	13 (8.9)	11 (7.6)	0.695
• *Because smokers are fool*	29 (17.9)	71 (44.4)	< 0.001	26 (17.8)	29 (20.1)	0.612
• *Because smokers are irresponsible*	49 (30.2)	101 (61.2)	< 0.001	51 (34.9)	58 (40.3)	0.347

Do you remember an advertising related to cigarette smoking?	27 (16.7)	62 (39.7)	< 0.001	26 (17.8)	50 (34.7)	0.001
Do you know direct advertising of cigarette is forbidden in Italy?	101 (62.3)	123 (76.9)	0.041	93 (63.7)	95 (66.0)	0.685
Passive smoking is harmful	143 (88.3)	153 (95.6)	0.015	131 (89.7)	131 (91.0)	0.719
Do you feel unconfortable when someone smokes in your presence?	105 (64.8)	126 (78.8)	0.005	98 (67.1)	113 (78.5)	0.029

Figure 1 – Randomisation scheme of the children and adolescents trials on smoking prevention.
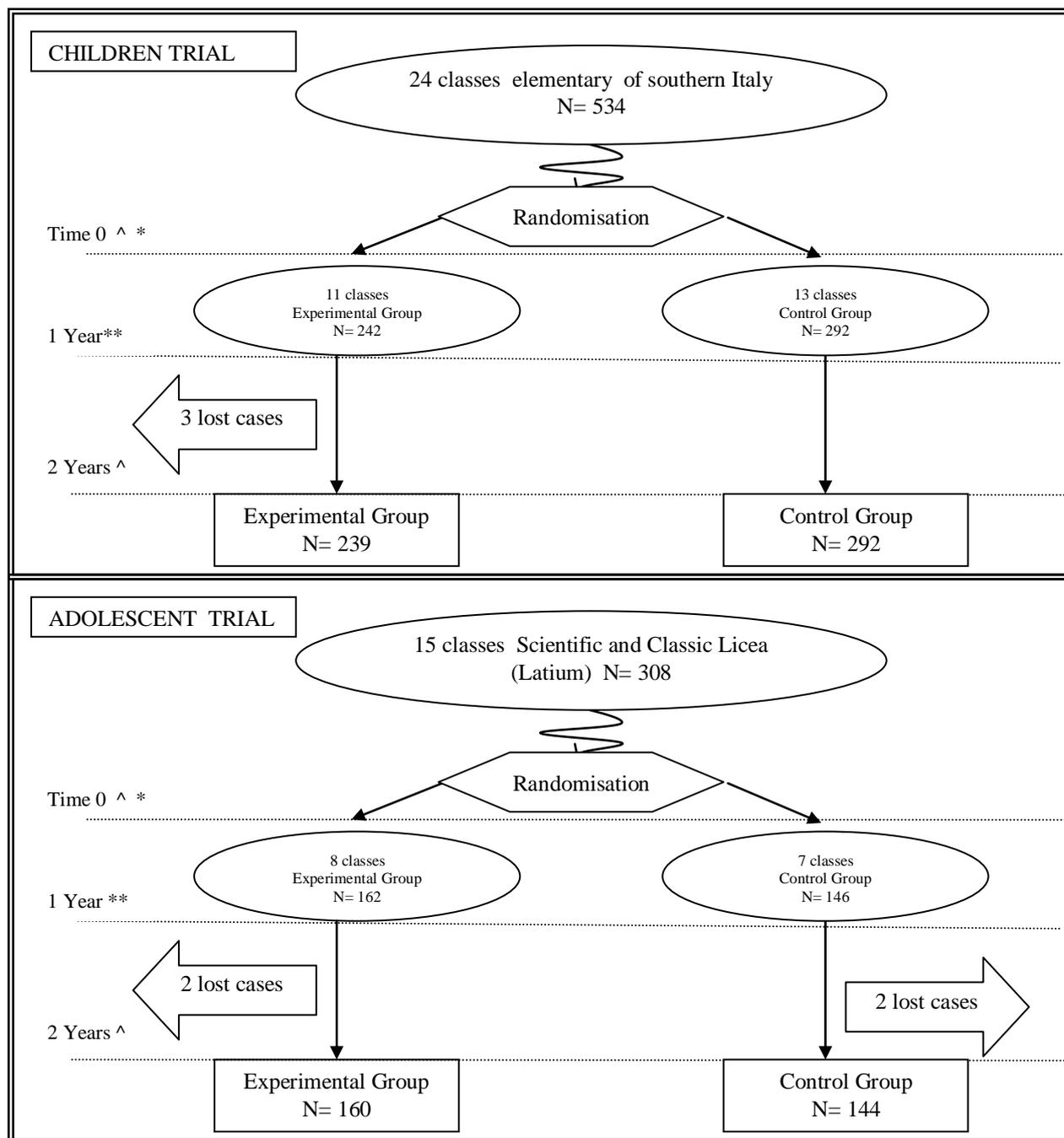
^ Questionnaire administered

* Beginning of intervention programme

** Conclusion of intervention programme.

Answer to reviewer 1 – R2

We thank very much the reviewer for his/her valuable suggestions, and we hope that the manuscript has been improved in this revised version.

1.While an appropriate citation is given now, the two sentences added taht highlight the specificity of the study are inconclusive. Comparing the same intervention in 2 age groups seems not an assett, knowing that cognitive, emotional and social factors differ between these age groups. The results between the two groupsps must be different, and in deed that is what is discussed in the discussion section. I still can not see the advantage of combining the two age groups and would recommend focussing on the children trial only. This would require a major revison.

Answer: the reviewer stated that the results between the two groups should have been different, but this was just what we intended to demonstrate with the trial. One of the major points that arise from this study was that an early exposure to the intervention group can be efficient to better face with tobacco prevention issue in the school environment. Another point is that we are not combining the two age groups, and as a matter of fact we presented methods and results considering them separately. We are not in agreement with the reviewer to focus on the children trial only, since we are firmly convinced that one researcher must publish paper with negative results , as we found for the "adolescent " trial. We reinforced the discussion concerning this critical point, giving a new citation (Garrison) concerning the adolescent trials.

2. By focussing on the children class this criticism would disappear. Otherwise, the added comments are not "deeply" describing the problem, 3 years, between 1999 and 2002 can pose a significant impact, perhaps there were tobacco control measures implemented in Italy during that time? I can just guess, because the authors don´t illsutrate thoughts about time effects others than 3 years is short. More detail and thought is needed.

Answer: We thanks the reviewer for the specification and we now added a new sentence indicating that "no new tobacco control measures were implemented in Italy during that period".

3. The information added is sufficient

OK

4.My comments about the power analysis, the number needed and the randomization by classes were not considered at all. Please consider these.

Answer: **We are in agreement with the reviewer, since in the last revision we forgot to insert an explanation in the methods section. We apologize for that. In this revision we specify that "We do not calculate the number of classes to accrue, since the outcome of the trial was at the individual level, and not at the class level. So, considering an average class composed by 20 students, we estimated that a total of 39 classes were needed for the trials". Moreover, we added why there were differences between children and adolescent classes, explaining that we selected 24 and 15 classes, respectively, "considering the proportion of children and adolescents at schools in the cities involved".**

5. Well done, but do not call it Cluster analysis since this term is used for parsimony method that combines variables to different clusters

Answer: **we agree with the reviewer, and now indicate the cluster randomised analysis, as appropriate**