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A Three-Year Randomized Controlled Trial in 6-Year-Old Children on Caries-Preventive Strategies in a General Dental Practice in the Netherlands

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Key Words
Caries prevention strategies · Children · Nexø studies · Randomized controlled trial · The Netherlands

Abstract
A parallel-randomized controlled trial on caries-preventive strategies was conducted in a general dental practice with a mixed socioeconomic background patient population. The aim of this study was to test the hypothesis that, compared to regular care consisting of check-ups twice a year with professional fluoride applications and pit and fissure sealants in all permanent molars, a larger caries-preventive effect can be achieved by following a non-operative caries treatment and prevention (NOCTP) strategy or by following, in addition to regular care, an increased number of professional topical fluoride applications (IPFA). A total of 230 children (6.0 years ± 3 months of age) were randomly assigned to the two experimental groups or the control group. After 3 years, 179 participants remained in the study (54 NOCTP, 62 IPFA and 63 control). The children were examined at baseline and at 3 years by the same experienced examiner, who was blinded for the allocation of the children. Caries was scored clinically at the D_3 level. Per protocol analysis revealed a mean DMFS increment after 3 years of 0.15 (95% CI –0.05 to 0.35) for NOCTP, 0.34 (95% CI 0.11 to 0.54) for IPFA and 0.47 (95% CI 0.26 to 0.68) for the control group. To account for missing data, multiple imputation was used, after which the mean DMFS increment was 0.11 (95% CI –0.05 to 0.27) for NOCTP, 0.29 (95% CI 0.11 to 0.46) for IPFA and 0.40 (95% CI 0.21 to 0.55) for the control group. Testing the differences with independent samples t test revealed a lower caries increment in the NOCTP group compared to the control group. ANCOVA was used to correct for differences in baseline dmfs, socioeconomic status and perceived dental hygiene burden. The ΔDMFS effect size between the NOCTP and the control group dropped, losing statistical significance ($p = 0.06$). Although the results in this study are promising, it has yet to be established in a larger study whether NOCTP has the ability to be effective in regular dental practice with a mixed socioeconomic status population.

According to current standards, the daily use of fluoridated toothpaste is the most effective measure for caries prevention [Marinho et al., 2003]. Besides the use of occlusal sealants [Ahovuo-Saloranta et al., 2008], professional application of fluorides (gels, varnishes) is also considered to contribute to reduction in caries incidence

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[Marinho et al., 2002]. A meta-analysis of 14 placebo-controlled trials concluded that a higher decayed, missing or filled surfaces-prevented fraction was associated with increased frequency and intensity of application [Marinho et al., 2002]. In the Netherlands, a frequently used approach of caries prevention is to maintain a dental check-up interval of 6 months, apply 1.23% fluoride gel at these visits and routinely seal the occlusal surfaces of erupted permanent molars. Despite these continuing efforts and concomitant expenses, a large number of children still experience caries. A study in 11-year-olds in the Netherlands reported an increase in decayed, missing and filled surfaces in permanent dentition (DMFS) from 1.4 ± 2.3 in 1999 to 1.7 ± 2.8 in 2005 [Poorterman and Schuller, 2006]; this study also showed an increase in caries experience in the primary dentition (dmfs) in children aged 5 (4.0 ± 7.4 in 1999 versus 4.6 ± 8.0 in 2005).

The concept of a non-operative caries treatment and prevention (NOCTP) program has been the subject of several studies. Although results to the contrary have been found [Arrow, 2000], most studies investigating a form of NOCTP report good efficacy and effectiveness [Carvalho et al., 1992; Ekstrand et al., 2000; Ekstrand and Christiansen, 2005; Hausen et al., 2007; Evans and Dennison, 2009]. Most studies on caries prevention strategies with NOCTP are performed in high-risk populations, but also for populations with relatively low caries prevalence rates, it is important to identify the feasibility of these strategies and to determine which strategy is most effective in preventing caries.

The aim of this study was to test the hypothesis that, compared to regular care (routinely twice a year dental check-up with professional topical fluoride application and sealing of newly erupting permanent molars), a larger caries-preventive effect can be achieved by following a NOCTP strategy or by following in addition to regular care an increased number (4 times a year) of professional topical fluoride applications. All participants (from a mixed socioeconomic status population) followed the respective programs in the same general dental clinic in the Netherlands. The difference in DMFS increment was considered the main outcome measure, while the difference in levels of oral hygiene at the start and the end of the study and the difference in the number of sealants placed during the experimental period were considered secondary outcome measures.

The study was approved by the Medical Ethical Committee of the Free University Amsterdam, The Netherlands (protocol number NL13709.029.06).

Subjects and Methods

Procedure

From September 2006 to September 2008, all parents of 6-year-old children (± 3 months) – all regular patients of a large dental clinic in 's-Hertogenbosch, The Netherlands – were asked to allow their child to participate in this trial (n = 271). 's-Hertogenbosch is a city with approximately 150,000 inhabitants. This city can be considered, in terms of demographic indicators, to be representative of the Netherlands [Schuller, 2009]. The study team sent a letter to inform the parents about the study and the possibility of participation in the study, approximately 2 weeks prior to the planned dental check-up around the child's 6th birthday. After informed consent had been obtained, parents were asked to fill in a questionnaire to provide information on socioeconomic variables, oral hygiene habits, dietary habits and knowledge on dental topics. If the parent decided not to participate, the reason for non-participation was recorded and the parent was yet asked to fill in the same questionnaire. Once permission had been obtained, the children were seen by the researcher for baseline measurement. After that examination they proceeded to their own dental practitioner for regular check-up. The dental assistant, who was not familiar with the research protocols, allocated the participants to the respective research groups on the basis of the list generated by Research Randomizer [Urbaniak and Plous, 2011]. When parents decided to stop during the trial, they were considered as dropouts. Differences between non-participants and participants have been analyzed earlier [Vermaire et al., 2011].

Sample Size Estimation

The interventions aimed at the reduction of caries progression. Therefore, caries increment in permanent dentition (first 3 years after eruption) was considered the main outcome measure. A sample size of 181 was determined to be sufficient to observe a difference of 1 DMFS with 80% of power using a two-sided test at $\alpha = 0.05$. An anticipated dropout percentage of 20% was taken into account. Therefore, a total of 230 children aged 6.0 years ± 3 months were included in this study.

Interventions

Children receiving the practice's regular caries treatment and prevention served as the control group. The regular protocol comprised preventive visits (dental check-ups) twice a year, professional 1.23% fluoride gel (as NaF) application twice a year, routine sealing of pits and fissures of newly erupted molars with a resin-based material and restoration of caries at the d_3/D_3 level.

In experimental group 1, the standard protocol was abandoned and replaced by a NOCTP protocol; this individual, tailored approach was copied from the protocol used in Nexø, Denmark [Ekstrand and Christiansen, 2005] and applied to the situation in this specific dental practice. The main difference was that all children in this study started the program at the age of 6 years (and not already at 8 months). The dental personnel involved in this project followed a 1-day training course that was run by former staff of the Nexø clinic. The protocol was based on the understanding of caries being a localized process that can be prevented by toothbrushing with fluoride toothpaste. Recall intervals were individualized using the criteria described by Carvalho et al. [1992]: cooperation of the parents, activity of caries lesions within the dentition, eruption stage of permanent first molars and caries activity in the occlusal

surfaces of the first permanent molars. Each of these criteria was assigned either one (when favorable) or two (when unfavorable) points. With a maximum score, the recall interval was set at 1 month, with a minimum score at 9 months. Oral hygiene and dietary instructions were supported with written information, based on the leaflets used by the staff in the Nexø study. Professional fluoride applications were restricted to those situations where caries initiation or progression was recorded despite repeated counseling sessions. Placement of pit and fissure sealants was restricted to situations where intensified brushing with fluoride toothpaste and additional professional fluoride applications were not able to inhibit caries progression. A checklist was completed by the dental staff during each visit so that the dental staff could maintain accurate and up-to-date records of all preventive and restorative actions taken with each subject.

Children in experimental group 2 followed the same approach as the control group, but the children in this second group had two additional visits where professional fluoride treatments were given (in total 4 fluoride treatments/year). This group was called IPFA (Increased Professional Fluoride Applications). The rationale behind this was first the fact that professional fluoride gel applications gain effectiveness while increasing the frequency of applications [Marinho et al., 2002] and second to compensate for the possibility that extra visits by themselves (disregarding the content of those visits) might have a positive effect on caries prevention.

Questionnaires

Dental knowledge was scored using a dental knowledge questionnaire and perceived dental hygiene burden was scored using a questionnaire asking parents to indicate the extent to what parents felt various preventive oral health measures for the oral health of their child to be burdensome. Scores on the dental knowledge questionnaire varied from 0 to 5, with a higher score indicating higher dental knowledge. Scores on dental hygiene burden varied from 0 to 5, with higher scores indicating a higher perceived burden. A detailed description of these questionnaires is given elsewhere [Vermaire et al., 2012].

Outcome Measurements

One experienced and trained dentist, blinded to the treatment groups, carried out all clinical examinations. At baseline and after 3 years, 11 and 10% respectively of the children were re-examined by a second experienced and trained dentist. Inter-examiner agreement scores for dmfs (age 6), DMFS (age 9) and plaque scores were $\kappa = 0.89$ and $\kappa = 0.74$ for the baseline measurements, and $\kappa = 0.91$ and $\kappa = 0.80$ after 3 years, respectively. Neither of these dentists participated in the dental healthcare program of the children. The children's oral health condition was assessed clinically during a visit at the dental clinic using a mirror, light, a blunt probe and compressed air. Due to medical-ethical objections, no radiographs were taken for the purpose of this study; therefore, the incidence of caries was exclusively assessed clinically. Caries was assessed using the dmfs/DMFS index, with caries scored at the dentin threshold (d_3/D_3) [WHO, 1979]. Oral hygiene was assessed using the simplified oral hygiene index (OHI-s) [Greene and Vermillion, 1964]. Caries increment in the permanent dentition after 3 years was considered the main outcome measure. As secondary outcome measures, caries increment in the primary dentition, the level of oral hygiene and the number of professional fluoride applications and of pit and fissure sealants were also recorded.

Statistical Analysis

The sample was characterized using descriptive statistics. First data were analyzed per protocol using two-sided independent samples t tests. Second, to account for possible selective dropout between the experimental groups and the control group, missing data were substituted using multiple imputation [van Buuren, 2012] with socioeconomic status and dmfs as predicting variables. Pooled data of five drawn imputations were analyzed. Two-sided independent samples t tests were performed to identify possible differences in mean dmfs and DMFS scores between groups. ANCOVA was performed to correct for differences in socioeconomic status, dmfs, DMFS and perceived dental hygiene burden at baseline. The significance level was set at $\alpha = 0.05$. All statistical analyses were performed using IBM SPSS Statistics 20.0.

Results

After 3 years, complete data for a total of 179 children were available for per protocol analysis. A flowchart of the attrition of participants in this study is presented in figure 1. The reasons for withdrawal were the following: inconvenience to the child (n = 20), burden of traveling to the clinic (n = 20), inconvenience to the parent n = 11, of which one was seriously ill. In the IPFA group, 60% (n = 9) of the withdrawals were because of the perceived inconvenience by the child (especially gagging because of the use of fluoride gel-filled trays), while in the NOCTP group, 46% (n = 12) of the withdrawals discontinued participation in the study because of the burden of traveling. Almost 25% of the withdrawals in the NOCTP group occurred because the parents felt that they were withholding their child from receiving the regular care that they were used to.

In table 1, sample characteristics and non-clinical outcomes at 6 and 9 years of age are presented together with baseline characteristics of all participants at the age of 6. It was found that after 3 years, the NOCTP group had the greatest knowledge on dental topics and the lowest scores on oral hygiene burden questions; however, this was also the case at the age of 6 and is therefore not to be attributed to the intervention.

Table 2 shows the outcomes of the clinical measurements for each experimental group at baseline and after 3 years. After 3 years, children in the NOCTP group had developed 0.15 (95% CI –0.05 to 0.35) DMFS, while the children in the IPFA group and the control group had developed 0.34 (95% CI 0.11 to 0.54) and 0.47 (95% CI 0.26 to 0.68) DMFS, respectively. Independent samples t test showed that this difference between the NOCTP and control group was statistically significant ($t = 2.13$; $p = 0.03$).

After imputation of data to correct for the dropouts, the increment in DMFS values were 0.11 (95% CI 0.50 to

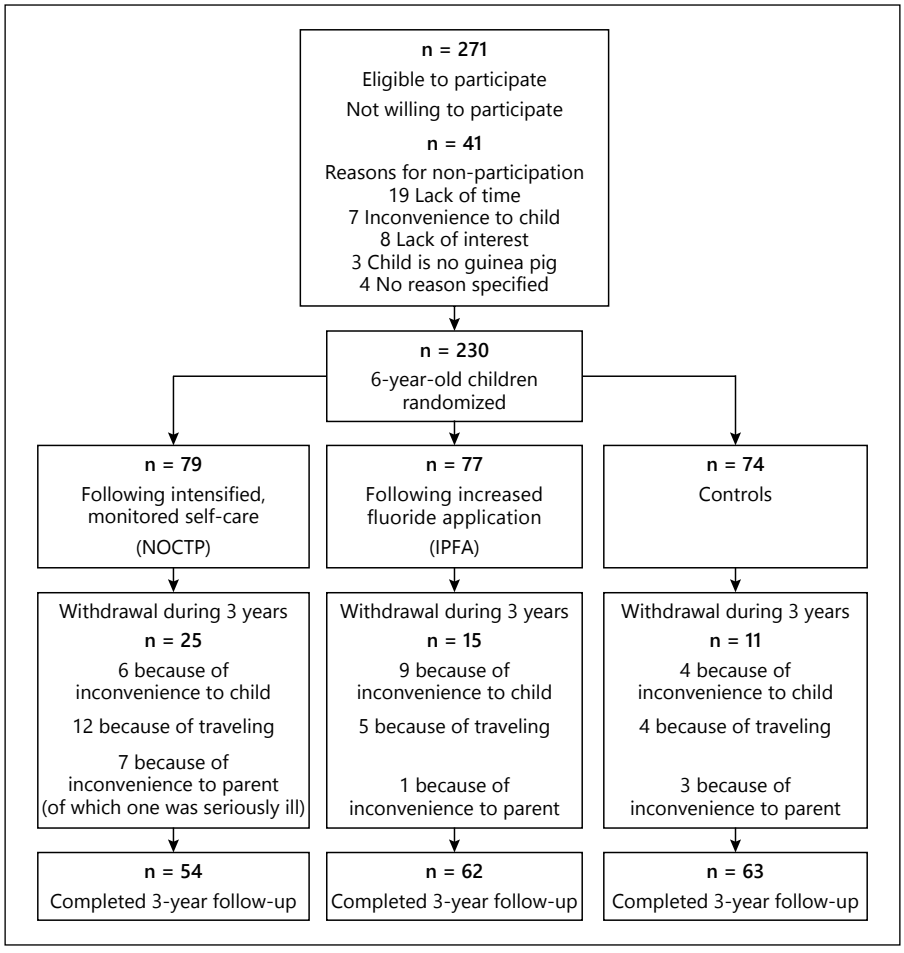

Fig. 1. Flowchart of participation in the study.

0.27), 0.29 (95% CI 0.11 to 0.46) and 0.40 (95% CI 0.26 to 0.55) for the NOCTP, IPFA and control group, respectively. Independent samples t test showed that this difference between the NOCTP and control group was statistically significant ($t = 2.56$; $p = 0.01$).

Table 3 shows the differences between the experimental groups and the control group for DMFS, oral hygiene index and number of sealants. In this table, data are presented per protocol, after multiple imputation, after multiple imputation and corrected for socioeconomic status, corrected for perceived dental hygiene burden and for dmfs at baseline. When socioeconomic status, perceived dental hygiene burden and dmfs at the age of 6 was entered as covariate, the ΔDMFS between NOCTP and control dropped from 0.32 (95% CI 0.24 to 0.39; $p = 0.03$) to 0.25 (95% CI 0.20 to 0.36), losing statistical significance ($p = 0.06$).

Table 4 shows the percentages of caries-free children and the mean caries scores of those children who developed caries during the trial in both the primary and permanent dentition for each experimental group. In the NOCTP group, 32% of the children developed on average 3.5 ± 3.4 caries lesions into dentin in their primary dentition during a period of 3 years. In the IPFA and the control group, this was 34% with on average 5.3 ± 4.6 caries lesions and 41% with on average 5.2 ± 3.8 caries lesions, respectively. For the permanent dentition, the percentages were the following: 9, 14 and 20%, with on average 1.6 ± 0.8, 2.2 ± 1.0 and 2.16 ± 1.2 dentinal lesions or fillings, respectively.

Table 5 presents an overview of all actions taken at every visit in the NOCTP group. The number of visits per year decreased during the 3 years of the experiment. The number of actions or treatments taken per visit also decreased over time. The average number of fluoride gel applications in the NOCTP group was considerably lower than in the IPFA and the control group, with 0.7 in 3 years compared to 11.2 and 5.3, respectively ($p < 0.001$). Also the number of visits for the placements of pit and fissure

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Table 1. Descriptive statistics and non-clinical outcomes

	NOCTP		IPFA		Control	
	baseline 6 years (later dropouts included) (n = 79)	baseline 6 years (later dropouts excluded) (n = 54)	baseline 6 years (later dropouts included) (n = 77)	baseline 6 years (later dropouts excluded) (n = 62)	baseline 6 years (later dropouts included) (n = 74)	baseline 6 years (later dropouts excluded) (n = 63)
Sex						
Male	41 (51.9%)	27 (50.0%)	35 (45.4%)	29 (46.7%)	37 (50.0%)	31 (49.2%)
Female	38 (48.1%)	27 (50.0%)	42 (54.6%)	33 (53.2%)	37 (50.0%)	32 (50.8%)
Socioeconomic status						
Low	18 (22.8%)	14 (25.9%)	25 (32.5%)	21 (33.9%)	24 (32.0%)	20 (31.8%)
Medium	32 (40.5%)	17 (31.5%)	30 (38.9%)	23 (37.1%)	25 (33.0%)	23 (36.4%)
High	29 (36.7%)	23 (42.6%)	22 (28.6%)	18 (29.0%)	25 (33.0%)	20 (31.8%)

	NOCTP			IPFA			Control		
	at baseline 6 years (dropouts included)	at baseline 6 years (dropouts excluded)	at follow-up 9 years (dropouts excluded)	at baseline 6 years (dropouts included)	at baseline 6 years (dropouts excluded)	at follow-up 9 years (dropouts excluded)	at baseline 6 years (dropouts included)	at baseline 6 years (dropouts excluded)	at follow-up 9 years (dropouts excluded)
Oral hygiene habits									
Only child brushes	30.9%	31.5%	64.8%	26.1%	24.2%	62.9%	28.1%	23.8%	63.5%
Only parent brushes	29.5%	29.6%	7.4%	13.3%	11.3%	4.8%	29.9%	28.6%	3.2%
Both child and parent	38.6%	38.9%	27.8%	60.6%	64.5%	32.3%	42.0%	47.6%	33.3%
Fluoride in toothpaste?									
Consciously no	3.7%	5.6%	1.8%	2.7%	3.2%	1.6%	3.9%	4.8%	3.2%
Yes, age-specific toothpaste	74.1%	75.9%	75.9%	72.1%	79.0%	67.7%	78.2%	76.2%	57.1%
Yes, adult's toothpaste	7.6%	7.4%	16.7%	9.4%	9.7%	22.6%	7.1%	6.3%	30.2%
I don't know	14.6%	11.1%	5.6%	10.8%	8.1%	8.1%	11.8%	12.7%	9.5%
Dietary habits									
Breakfast ≥6×/week	93.7%	90.5%	88.7%	90.9%	88.9%	88.9%	88.6%	89.5%	91.2%
Lunch ≥6×/week	97.5%	96.2%	90.6%	93.9%	93.3%	96.7%	90.0%	89.5%	93.4%
Dinner ≥6×/week	96.2%	96.2%	98.1%	97.0%	96.7%	98.3%	97.1%	95.1%	98.3%
Between-meal snacks									
Not every day	5.1%	3.7%	3.7%	3.8%	3.2%	3.2%	7.1%	6.3%	4.8%
1–5/day	75.9%	75.9%	83.3%	77.9%	77.4%	72.6%	72.9%	74.6%	73.0%
>5/day	19.0%	20.4%	13.0%	9.7%	19.4%	24.2%	20.0%	19.1%	22.2%
Dental knowledge score (0–10)									
<5	5.3%	7.4%	3.7%	8.5%	6.5%	14.5%	9.6%	7.9%	14.3%
5–7	33.6%	35.2%	24.1%	39.9%	37.1%	59.7%	34.6%	38.1%	33.3%
>7	61.1%	57.4%	72.2%	51.6%	56.4%	25.8%	55.8%	54.0%	52.4%
Dental hygiene burden score (0–5)									
<2	37.8%	38.9%	27.7%	28.1%	27.4%	16.1%	27.0%	23.8%	20.6%
2–4	40.1%	38.9%	55.6%	34.6%	30.6%	37.1%	39.3%	39.7%	42.9%
>4	22.2%	22.2%	16.7%	37.3%	42.0%	46.8%	33.7%	36.5%	36.5%

Fl^- in toothpastes: <5 years 500 ppm; ≥5 years 1,000–1,500 ppm.

Table 2. Mean scores of clinical variables divided by experimental group

	NOCTP (95% CI)	IPFA (95% CI)	Control (95% CI)	NOCTP vs. control		IPFA vs. control	
				t	p	t	p
Baseline measurements at age 6 years – later dropouts excluded (n = 179)							
	n = 54	n = 62	n = 63				
OHI-s (0–3)	0.85 (0.71–1.06)	0.82 (0.65–0.98)	0.90 (0.70–1.03)	0.42	0.68	0.63	0.53
Sealants	0.19 (0.08–0.45)	0.48 (0.24–0.74)	0.19 (0.05–0.44)	0.01	0.99	1.58	0.12
dmfs	4.55 (2.89–7.09)	5.00 (2.79–6.66)	6.88 (4.80–8.63)	1.60	0.11	1.22	0.22
DMFS	0.06 (0.01–0.13)	0.05 (0.02–0.11)	0.02 (0.01–0.08)	0.98	0.33	0.85	0.40
Baseline measurements at age 6 years (n = 230)							
	n = 79	n = 77	n = 74				
OHI-s (0–3)	0.90 (0.76–1.05)	0.84 (0.67–1.00)	0.89 (0.75–1.05)	0.06	0.95	0.53	0.60
Sealants	0.29 (0.09–0.50)	0.46 (0.19–0.73)	0.28 (0.05–0.50)	0.11	0.91	1.05	0.30
dmfs	5.48 (3.92–7.03)	4.82 (2.98–6.67)	7.18 (4.99–9.38)	1.28	0.20	1.63	0.10
DMFS	0.05 (–0.01–0.11)	0.07 (–0.01–0.15)	0.05 (–0.03–0.14)	0.08	0.93	0.26	0.80
3-year follow-up at age 9 years (n = 179)							
	n = 54	n = 62	n = 63				
OHI-s (0–3)	0.79 (0.67–0.97)	0.99 (0.84–1.12)	1.01 (0.87–1.15)	2.15	0.03	0.21	0.84
Sealants	1.45 (1.05–1.84)	3.45 (3.10–3.82)	3.89 (3.53–4.25)	8.33	<0.001	1.95	0.05
dmfs	5.04 (3.78–7.18)	5.77 (3.93–7.06)	7.31 (5.59–8.69)	1.83	0.07	1.27	0.21
DMFS	0.21 (0.01–0.47)	0.39 (0.15–0.59)	0.48 (0.27–0.71)	1.71	0.09	0.55	0.58
3-year follow-up at age 9 years after multiple imputation of missing data (n = 230)							
	n = 79	n = 77	n = 74				
OHI-s (0–3)	0.87 (0.67–1.12)	0.98 (0.79–1.17)	0.96 (0.80–1.10)	0.70	0.49	0.20	0.84
Sealants	0.99 (0.62–1.35)	2.89 (2.48–3.27)	3.33 (2.97–3.78)	8.42	<0.001	1.52	0.13
dmfs	3.26 (2.31–4.75)	4.84 (3.70–6.28)	6.29 (4.58–7.12)	3.03	0.002	1.34	0.18
DMFS	0.15 (0.01–0.34)	0.35 (0.17–0.54)	0.45 (0.24–0.60)	2.34	0.02	0.62	0.54
Total difference scores after 3 years (n = 179)							
	n = 54	n = 62	n = 63				
OHI-s (0–3)	–0.05 (–0.27–0.13)	0.17 (–0.01–0.37)	0.14 (–0.01–0.36)	1.38	0.16	0.19	0.85
Sealants	1.26 (0.82–1.71)	2.97 (2.56–3.38)	3.70 (3.30–4.10)	8.08	<0.001	2.64	0.01
dmfs	0.49 (–1.16–0.40)	0.77 (–0.75–2.29)	0.43 (–1.08–1.93)	0.48	0.96	0.29	0.77
DMFS	0.15 (–0.05–0.40)	0.34 (0.11–0.54)	0.47 (0.26–0.68)	2.04	0.03	0.76	0.45
Total difference scores after 3 years after multiple imputation of missing data (n = 230)							
	n = 79	n = 77	n = 74				
OHI-s (0–3)	–0.03 (–0.22–0.13)	0.12 (–0.09–0.31)	0.06 (–0.09–0.28)	0.73	0.46	0.42	0.68
Sealants	0.69 (0.26–1.11)	2.43 (1.96–2.87)	3.05 (2.64–3.53)	7.42	<0.001	1.84	0.07
dmfs	–2.21 (–3.80–0.65)	0.01 (–1.48–1.51)	–0.90 (–2.83–1.04)	1.07	0.28	0.74	0.46
DMFS	0.10 (0.01–0.72)	0.28 (0.11–0.46)	0.40 (0.21–0.55)	2.56	0.01	0.77	0.44

OHI-s = Simplified oral hygiene index.

sealants was considerably lower than in the other two groups ($p < 0.001$). The total duration of the visits between the NOCTP group and the control group was not statistically significant, the difference between IPFA and NOCTP and control, however, was ($F = 106.8$; $p < 0.001$). The mean number of visits for the NOCTP group, the IPFA group and the control group was as follows: 7.8 ± 1.44, 11.2 ± 1.33 and 7.1 ± 1.02, respectively.

Discussion

This study aimed to compare the caries-preventive effect of a NOCTP strategy that is based on improving parental home care and that includes an individually assessed recall interval, with two strategies that are based in addition to routine twice-a-year dental check-ups and sealing of all erupting permanent molars on different fre-

quencies of professional topical fluoride applications (IPFA: 4 per year; control: 2 per year). The NOCTP program turned out to be an effective program for caries prevention in this regular dental practice in the Netherlands. Children in this program had better oral hygiene, a lower mean DMFS and a greater chance to be caries-free at the age of 9 compared to children in the other two programs. Furthermore, the number of sealants placed and fluoride application performed were significantly lower in the NOCTP group. The effect of the NOCTP group cannot be accredited only to the extra visits some children initially had to make. The fact that children in the IPFA group routinely had to make more visits at a lower effectiveness strongly suggests that the content of the visits is of importance and not merely the visit by itself.

When analyzing per protocol, the mean difference between the NOCTP group and the control group was significant at –0.32 (95% CI –0.39 to –0.24) DMFS. After imputation for missing data and correcting for socioeconomic status, perceived dental hygiene burden and dmfs at baseline as covariates, a mean difference of –0.25 (95% CI –0.30 to –0.20) in DMFS was found between children in the control group and the NOCTP group. The p value of this effect was 0.06, indicating that we could not demonstrate that the effect was statistically significant. However, p values close to 0.05 in small groups strongly indicate the potential of the intervention and strongly encourage repetition of the experiment or use of bigger experimental groups. Furthermore, taking into account the low caries prevalence in the study group, the results can be regarded as clinically significant. Based on the effect after imputation and correction for socioeconomic status, perceived dental hygiene burden and dmfs at baseline, approximately four children had to follow the NOCTP program to prevent one extra DMFS. Following the IPFA regime, children had a statistically non-significant reduction of 0.09 DMFS compared to the control group, which would mean a number needed to treat of about eleven children to prevent one DMFS.

A larger number of children in the NOCTP group discontinued participation compared to the other groups. This was mainly because of travel-related reasons and the discontinuation happened mostly in the first year of the trial. Apparently, the parents found that the investment that they had to make to follow the program did not outweigh the possible benefits for their child. Hopefully, the results of this and other studies can convince parents in the future that their efforts will result is better oral health for their children and that prevention is not withheld

Table 3. Differences (95% CI) between the experimental groups (NOCTP or IPFA) and the control group after 3 years

	Per protocol data (n = 179)		After imputation (n = 230)		After imputation and corrected for SES (n = 230)		After imputation and corrected for dental hygiene burden (n = 230)		After imputation and corrected for dmfs (n = 230)		After imputation and corrected for SES, dental hygiene burden and dmfs (n = 230)	
	NOCTP	IPFA	NOCTP	IPFA	NOCTP	IPFA	NOCTP	IPFA	NOCTP	IPFA	NOCTP	IPFA
OHI-s	0.17[a] (–0.03 to 0.19)	0.06 (–0.01 to 0.10)	0.10 (0.04 to 0.16)	0.07 (0.04 to 0.10)	0.05 (–0.10 to 0.14)	0.04 (0.02 to 0.07)	0.11 (0.08 to 0.12)	0.07 (0.06 to 0.08)	0.10 (0.08 to 0.12)	0.06 (0.02 to 0.08)	0.09 (0.04 to 0.14)	0.05 (0.02 to 0.10)
Sealants	2.44[b] (2.34 to 2.49)	0.73[a] (0.50 to 0.91)	2.36[b] (2.32 to 2.39)	0.62 (0.60 to 0.64)	2.35[d] (2.33 to 2.38)	0.62 (0.61 to 0.62)	2.35[d] (2.33 to –2.36)	0.63 (0.58 to –0.64)	2.38[d] (2.36 to 2.40)	0.65 (0.64 to 0.65)	2.34[d] (2.30 to 2.37)	0.61 (0.55 to 0.68)
DMFS	0.32[a] (0.24 to 0.39)	0.13 (0.09 to –0.16)	0.30[a] (0.21 to 0.38)	0.12 (0.09 to 0.13)	0.29 (0.20 to 0.37)	0.12 (0.18 to –0.04)	0.30[c] (0.27 to 0.32)	0.12 (0.11 to 0.16)	0.28 (0.20 to 0.36)	0.09 (0.07 to 0.11)	0.25 (0.20 to 0.30)	0.09 (0.07 to 0.13)

OHI-s = Simplified oral hygiene index; SES = socioeconomic status.
[a] $p < 0.05$ (t test); [b] $p < 0.001$ (t test); [c] $p < 0.05$ (ANCOVA); [d] $p < 0.001$ (ANCOVA).

Table 4. Percentages of caries-free children and mean caries scores in primary (dmfs) and permanent (DMFS) dentition (only in those who developed new caries)

	dmfs = 0		Δdmfs >0		DMFS = 0		ΔDMFS >0	
	6-year-olds	9-year-olds	n (%)	mean ± SD	6-year-olds	9-year-olds	n (%)	mean ± SD
NOCTP	39.6%	34.0%	25 (32%)	3.52±3.39	96.2%	86.8%	7 (9%)	1.57±0.79
IPFA	51.6%	40.3%	26 (34%)	5.31±4.58	96.8%	82.2%	11 (14%)	2.18±0.98
Controls	43.8%	25.0%	30 (41%)	5.17±3.82	98.4%	76.6%	15 (20%)	2.07±1.16
Total	45.3%	33.0%	81 (35%)	4.70±3.99	97.1%	81.6%	33 (14%)	2.00±1.03

Table 5. Visit-specific content of recall sessions in the NOCTP group (non-imputed data: n = 54)

Visit	Children	Reason for extra visit[a]				Intervention[b]					
		oral hygiene	diet	eruption M1	unknown	disclosing plaque and instruction	tartar removal	Fl^- application	sealing	restoration of permanent dentition	missing
First year											
1	54	30	13	22	0	30	12	5	2	1	0
2	49	27	5	35	0	31	9	3	0	2	2
3	38	16	2	25	1	21	7	4	0	0	3
4	37	14	0	7	1	5	3	2	0	0	2
5	19	→ 5th visit was 1st visit of 2nd year									
Second year											
1	54	24	9	10	1	25	14	10	3	1	1
2	35	16	1	2	1	15	9	7	5	2	6
3	20	14	1	1	2	4	5	2	3	1	0
4	18	→ 4th visit was 1st visit of 3rd year									
Third year											
1	54	17	3	0	1	7	6	2	1	3	2
2	21	6	1	0	6	6	0	2	3	1	4
3	13	1	0	0	5	1	1	0	0	0	4
4	6	→ 4th visit was 1st visit of 4th year									

[a] Double-counting possible when multiple reasons per child were recorded. [b] Multiple interventions in same visit possible.

from their children. Furthermore, the trial was executed in one single dental clinic. Performing the NOCTP program may require a certain involvement of the dental professional and as such the results may depend on his/her communication skills. Therefore successful implementation of this program in other settings may require appropriate schooling of the dental team.

Most children in the IPFA group who discontinued participation in the study did so because of inconvenience to the child; undergoing the professional fluoride application was regularly accompanied by gagging caused by the fluoride gel-filled trays. This, together with the uncertain effectiveness, limits the usefulness of this caries prevention strategy. If another fluoride application, e.g. fluoride varnish, had been used, the dropout rate because of inconvenience to the child might have been smaller. The choice of using mouth trays with fluoride gel, however, was made because of the desire not to interfere in the daily routine of the practice.

The NOCTP program in the current study was copied from the original study in Nexø, Denmark, where the program ran from the age of 8 months until the age of 18 years. In 18-year-olds, the mean number of DMFS was 1.23 ± 2.26, while in the comparison groups in other parts

of Denmark, DMFS varied between 2.73 ± 3.94 and 3.93 ± 3.77. The percentage of caries-free children was 55% in Nexø compared to 24–39% in the Denmark groups. In spite of obvious differences in the age groups between the current study and the Nexø study, a comparable effect on caries development can be seen: children following a NOCTP strategy had lower DMFS scores and more children in this group had no caries experience. This was also the case in a study where the NOCTP strategy was applied in Moscow, Russia [Ekstrand et al., 2000]. Although the opposite has also been reported [Arrow, 2000], most other studies using individually delivered caries prevention strategies have reported outcomes that are comparable to those of the current study [Pienihäkkinen and Jokela, 2002; Hausen et al., 2007; Warren et al., 2010]. Considering all of the studies mentioned above, it is clear that individualizing caries prevention results in a net positive gain in effect. It can be argued that the NOCTP approach used in the current study in the Netherlands is a feasible approach and an effective way to prevent caries in this sample of children.

A relevant issue that needs to be addressed is that of the costs involved in applying the followed strategies. The original study in Nexø reported that the mean cost of applying the NOCTP regime was approximately EUR 130/year (converted from the reported amount of 1,172 DKK/year), which was among the lowest in Denmark [Ekstrand and Christiansen, 2005]. The way healthcare (including dental health) is organized throughout countries is not identical. This implies that the associated costs of a NOCTP program will vary as well. From an earlier study we know that in the population of the current study, the mean stated parental willingness to pay to keep their children's teeth healthy until the age of 18 years was EUR 32/month [Vermaire et al., 2012], which would easily cover the Danish costs. However, money is not the only investment needed in caries prevention: the investment in the number of preventive visits, the extra time parents have to invest traveling to the clinic and accompanying their children, and the investment in brushing their children's teeth themselves may even be of greater importance. Hence, economic evaluations are necessary to compare both strategies with the control group and to identify the necessary resources used to achieve the extra gain in caries prevention.

In light of the results of this study, we can conclude that a NOCTP strategy like the one used in Nexø, Denmark can be regarded as a feasible approach in this general dental clinic in the Netherlands as well. However, after multiple imputation and statistical controlling for differences in baseline values, the clinical results of this study lost significance and the results should be interpreted with caution. Although the results in this study are promising, it has yet to be established in a larger study whether NOCTP has the ability to be effective in a regular dental practice with a mixed socioeconomic status population. In the future, it may also be useful to expand the implementation of this strategy, both in more dental clinics in more regions and in more age groups, and to take into account health economic issues in the evaluation of the strategies to assess its cost effectiveness.

Author Contributions

J.H. Vermaire: principal researcher, study design, baseline measurements, 3-year follow-up measurements, data analysis, writing of the paper. J.H.G. Poorterman: duplicate measurements at both baseline and 3-year follow-up measurements, co-writing of the paper. L. van Herwijnen: principal dentist, responsible for carrying out the research protocol and the dental care of the patients, co-writing of the paper. C. van Loveren: initiator, supervisor, data analysis, writing of the paper.

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