COST-EFFECTIVENESS OF PROBIOTICS TO PREVENT DENTAL CARIES AMONG YOUNG CHILDREN IN PHAYAO PROVINCE, THAILAND

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Abstract. Probiotics have been used to prevent dental caries in children. In this study we aimed to determine the cost-effectiveness of probiotic milk tablets to prevent dental caries among children who attended 12 selected daycare centers in Phayao Province, Thailand during June 2022-May 2023 in order to determine if probiotic-fortified milk tablets are a reasonable method to prevent dental caries among children aged 2-5 years. Inclusion criteria for study subjects were being aged 2-5 years, attending one of the study daycare centers and having parental consent to participate the study. Exclusion criteria for study subjects were cow's milk allergy, serious medical conditions, such as heart disease or asthma, abnormalities related to the palate or jaw, being unable to undergo an oral health examination or having developmental delay. Study subjects were divided into a control group and a treatment group. Treatment group subjects were given 3 milk tablets daily by the caregiver and oral hygiene instructions. Each milk tablet contained the probiotic *Lactobacillus rhamnosus* SD11, but the concentration of these organisms in each milk tablet were not recorded by the manufacturer. Each subject was examined by one of two study dentists at the beginning of study initiation and then every 4 months for 12 months to evaluate for the presence of caries. The price of the milk tablets and caregiver cost were recorded. The cost-effectiveness ratio (CER) was calculated as follows: CER = (average cost of caries prevention per child by the milk tablets per year) / (the difference in carious surfaces between the control group and the milk tablet group). The minimum number of study subjects calculated to be needed for the study was 208 based on the estimated prevalence of caries in the study population. A total of 260 subjects were initially enrolled in the study: 130 in the control and 130 in the intervention group. After the 12-month study period, there were a total of 222 participants, with 112 individuals in the control group and

110 individuals in the experimental group. The mean numbers of caries per subject in the control group at 4, 8 and 12 months were 5.69, 5.60 and 7.31, respectively. The mean numbers of caries in the intervention group at 4, 8 and 12 months were 3.04, 3.12 and 3.24 respectively. The *p*-values for the differences in the mean numbers of caries between the control and intervention groups at 4, 8 and 12 months were p=0.003, p=0.016 and p=0.001, respectively. The cost-effectiveness analysis showed it cost THB 369.93 to prevent one cavity per tooth surface per year. In summary, there were significantly fewer caries among study subjects in the intervention group than the control group but the intervention was costly. We conclude, this intervention can be used effectively to prevent caries in the study population but it was expensive. Further studies are needed to determine if this intervention can be applied to other populations of similar aged children and other ages of children and how the program can be financed or the cost reduced.

Keywords: early childhood, dental caries prevention, cost-effectiveness, probiotic-enhanced milk tablets

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INTRODUCTION

Dental caries in primary teeth is an important public health problem internationally (WHO, 2019). The prevalence of dental caries among children in Thailand aged 3-5 years is high: 52.9% among children aged 3 years and 75.6% among children aged 5 years (Dental Bureau, 2018). A study from Phayao Province, Thailand reported a prevalence of dental caries among children aged 3 years was 51.2% (Wongsupa, 2023). Treatment of dental caries among children aged <5 years in the study province is usually extraction of the tooth. Restorative treatments and caries control are less commonly performed. Providing dental care for young children is difficult because it involves behavioral management and the need for parents

to take time off work, leading to irregular dental visits and inadequate care (Wongkongkathep, 2012).

Since treatment of dental caries is so challenging, it is important to have effective strategies to prevent dental caries in primary teeth. The main preventive measure is good oral hygiene (Rugg-Gunn, 2013) but also includes educating the patient, dietary management, (van Loveren, 2017), using fluoridated toothpaste or other fluoride applications (Walsh *et al*, 2019), using antibacterial agents, such as chlorhexidine varnish, and application of sealants (Innes *et al*, 2020). Another method employed to prevent dental caries in deciduous teeth is using probiotics (Sandoval *et al*, 2021). Probiotics may be incorporated into dairy products, such as powdered milk, yogurt, lozenges and milk tablets (Hasslöf and Stecksén-Blicks, 2020). Several studies (Hedayati-Hajikand *et al*, 2015; Gruner *et al*, 2016; Sakhare *et al*, 2021; Hasslöf *et al*, 2022) have reported caries prevention using probiotic products.

There is little published data about the cost-effectiveness of using probiotics to prevent dental caries, especially among children. In this study we aimed to determine the cost-effectiveness of using probiotics in the form of milk tablets to prevent dental caries in primary teeth among children aged 2-5 years in the study province in order to determine if probiotic-containing milk tablets are a reasonable method to prevent dental caries in this population.

MATERIALS AND METHODS

Study design

This study was a single-blinded, cluster-randomized control design.

Study subject inclusion and exclusion criteria

Inclusion criteria for study subjects were being aged 2-5 years and attending one of 12 daycare centers in Phayao Province, northern Thailand during June 2022-May 2023 whose parents or guardians provided consent for participation in the study. Exclusion criteria were a having a history of cow's milk allergy, cardiac condition, asthma, craniofacial anomality, inability to undergo oral health examination or a developmental disability.

Participants

The minimum number of subjects calculated to be needed for the study was calculated using the following formula:

$$n/group = \frac{(Z_{\alpha/2}+Z_{\beta})^2\ 2\sigma^2\ x IF)}{(\mu_1-\mu_2)^2}$$

where

$Z\alpha$ = Z-score at the desired level of statistical significance (α) = 0.05; $Z\alpha$ = 1.96.

$Z\beta$ = Z-score for the desired statistical power (1 - β) = 0.2; $Z\beta$ = 0.84.

σ^2 = Variance of the group of 3-year-old children in the province of Phayao = 1.00 (assumed to be the same for both intervention group and control groups).

μ_1 = Expected mean number of decayed, missing or filled tooth surfaces (dmfs) among those receiving probiotics. This was estimated by expert opinion to be = 0.84.

μ_2 = Expected mean number of dmfs among those in the control group. This was based on data collected from children aged 3 years in Phayao Province = 1.34.

IF = Inflation factor (IF) = 1.65.

n = Minimum sample size for each study group (control and intervention groups) = 104 (total of 208 for the 2 groups).

We assuming a dropout rate of 20%, giving a sample size of 260 subjects in total, 130 subjects in each group.

The intervention group subjects received 3 milk tablets daily from their caregivers containing the probiotic *Lactobacillus rhamnosus* SD11 and were given instructions on maintaining oral hygiene. The control group received only the oral hygiene instructions (Fig 1).

Clinical examination

Each subject was examined by a study dentist at the beginning of the study and then again at 4, 8 and 12 months after initiation of the study for the presence of dental carries following standard World Health Organization (WHO) criteria (WHO, 2013) using a dental mirror and probe. Each subject brushed their teeth prior to examination.

This study didn't use the ICDAS criteria for caries progression evaluation (Ekstrand *et al*, 2018). However, it is important to note that implementing a combined approach using the probing method and ICDAS criteria could yield more comprehensive data.

The inter-examiner reliability between the two study dentists

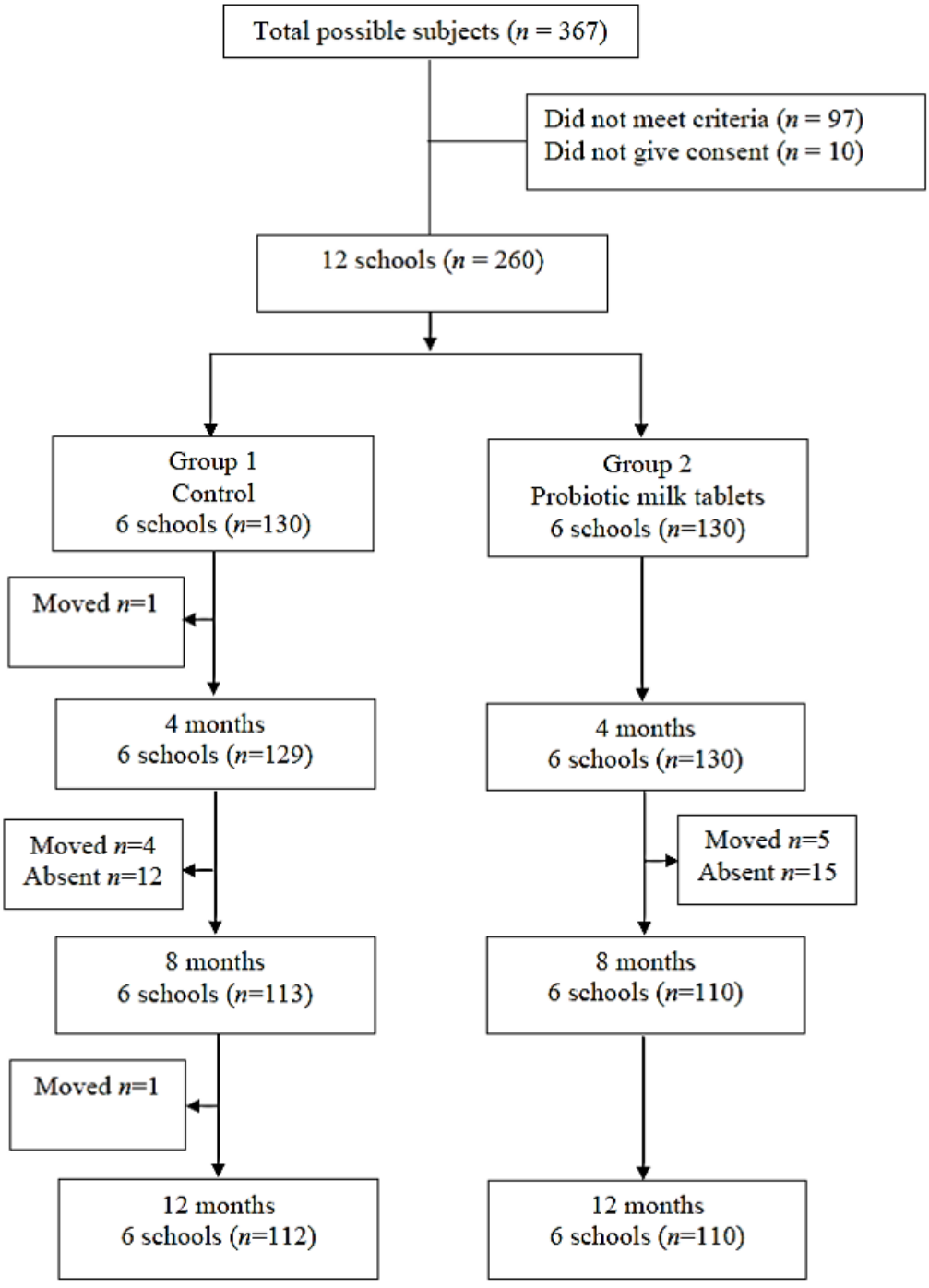

Fig 1 - Diagram of subject selection and follow up during the study period

assessed prior to the study gave a Kappa value of 0.89. The intra-examiner reliability of the two study dentists gave Kappa values of 0.91 and 0.92. The study dentists were blinded to the study group of each subject.

The cost-effectiveness of the probiotic milk tablets for caries prevention

We performed cost-analysis using the cost of the probiotic milk tablets and the cost of the caregiver time and salary to give each subject their tablets.

Statistical analysis

The subject data recorded were the subject age and gender, the number of dmfs and carious surfaces at baseline, 4 months, 8 months and 12 months. These data are presented using means and standard deviations.

Comparisons of the mean numbers of dmfs at baseline, 4 months, 8 months and 12 months were made using difference analyses and relationship comparisons were made using the Fisher's exact test and generalized mixed models.

The cost-effectiveness ratio (CER) was calculated as follows: CER = (average cost of caries prevention per child by the milk tablets per year) / (the number of caries per tooth surface in the control group – the number of caries per tooth surface in the milk tablet group).

Data analysis was conducted using the STATA program, version 18.0 (StataCorp, College Station, TX).

Definitions

For the purposes of this study, the definitions of the terms used for this paper are as follows.

Normal teeth: teeth without cavities or carious lesions.

Carious teeth: teeth with soft or softened enamel or dentin where the tooth structure can be displaced with a dental instrument.

Effectiveness: the measure of ability of a specific intervention to prevent a cavity by comparing with no intervention (control).

Cost-effectiveness: the cost per tooth surface to prevent a cavity.

Ethical clearance

Ethical clearance to conduct this study was obtained from the Research Ethics Review Committee for Studies Involving Human Research Participants, Chulalongkorn University Faculty

of Medicine. The reference number for the Institutional Review Board is IRB No.721/64 COA No.1613/2022. This study was registered with the Thai Clinical Trial Registry (Ref. no. TCTR20220329003). Written informed consent was obtained from the parents or guardians of all subjects prior to the subject being included in the study.

RESULTS

Clinical examination

The study initially included a total of 260 subjects, with 130 in the control group and 130 in the intervention group. However, by the end of the 12-month study period, the remaining sample size was 222 individuals, 114 males; 14.62%, of subjects were lost to follow up. The actual numbers of subjects included in the statistical evaluations were 112 subjects in the control group and 110 subjects in the intervention group. There were no significant differences between the control and study groups by mean ± standard deviation (SD) subject age (3.01 ± 0.57 and 3.04 ± 0.61 years) subject gender (57 males, 55 females in control group and 57 males, 53 females in study group), mean ± SD dmfs scores (6.82.52 ± 8.78 and 5.21 ± 10.31) and the mean ± SD numbers of caries surfaces at baseline (2.84 ± 4.46 and 2.42 ± 6.62), respectively (Table 1).

The mean ± SD numbers of carious surfaces at 0, 4, 8 and 12 months in the control group were 2.84 ± 4.46, 5.69 ± 8.35, 5.60 ± 8.42 and 7.31 ± 9.70 and in the intervention group were 2.42 ± 6.62, 3.04 ± 6.71, 3.12 ± 6.74 and 3.24 ± 6.80 and the p-values for differences were 0.61, 0.003, 0.016 and 0.001, respectively (Table 2). As can be seen by the above data, the intragroup numbers of carious surfaces increased over time in both study groups but the increase was more rapid in the control than the intervention group.

The mean ± SD dmfs scores at 0, 4, 8 and 12 months in the control group were 6.82 ± 8.78, 10.59 ± 11.38, 9.91 ± 11.38 and 11.77 ± 12.38 and in the intervention group were 5.21 ± 10.31, 6.01 ± 9.10, 5.75 ± 8.93 and 5.94 ± 9.10 and the *p*-values were 0.14, 0.001, 0.008 and 0.001, respectively (Table 3).

The cost-effectiveness analysis results show it cost THB 369.93 to prevent one cavity per tooth surface per year (Table 4).

DISCUSSION

In our study, there were significantly fewer caries per tooth surface among those treated with milk tablets compared with controls. The difference increased over time. Our findings are similar to the findings of a study among young children where the treatment group was given probiotic milk and controls were given regular milk and the probiotic milk group had significantly fewer caries (Rodríguez *et al*, 2016). Our findings are also similar to a study where the treatment group was given yogurt with probiotics and also given xylitol-containing chewing gum. There were significantly fewer caries in the intervention than control group (Ghasemi *et al*, 2017). Our findings are also similar to a study among children aged 3-4 years where the intervention group was given milk powder with probiotics either daily or three times a week and the controls were given regular milk powder. There were significantly fewer caries in both groups given the milk powder with probiotics than the controls (Piwat *et al*, 2020).

Table 1

Baseline characteristics of study subjects by study group (N=222)

Characteristics	Groups		*p*-value
	Control	Intervention	
Number of subjects	112	110	
Mean ± SD age in years	3.01 ± 0.57	3.04 ± 0.61	0.51
Gender			
Male, *n*	57	57	0.89
Female, *n*	55	53	
Mean ± SD dmfs score	6.82 ± 8.78	5.21 ± 10.31	0.14
Mean ± SD numbers carious surfaces	2.84 ± 4.46	2.42 ± 6.62	0.29

dmfs: decayed, missing and filled surfaces SD: standard deviation

Table 2

Mean carious surfaces at baseline, 4, 8 and 12 months by study groups (N=222)

Time of oral examination	Mean ± SD numbers carious surfaces		Difference in mean numbers of carious surfaces (Intervention - Control)	95% confidence interval	*p*-value
	Control group	Intervention group			
Baseline	2.84 ± 4.46	2.42 ± 6.62	-0.42 ± 0.82	(-2.03, 1.19)	0.61
4 months	5.69 ± 8.35	3.04 ± 6.71	-2.65 ± 0.90	(-4.41, -0.87)	0.003
8 months	5.60 ± 8.42	3.12 ± 6.74	-2.48 ± 1.03	(-4.49, -0.46)	0.016
12 months	7.31 ± 9.70	3.24 ± 6.80	-4.07 ± 1.18	(-6.38, -1.77)	0.001

SD: standard deviation

Table 3

Comparison of differences in the mean ± SD number of decayed, missing and filled surfaces (dmfs) at baseline, 4 months, 8 months, and 12 months among study subjects (N=222)

Time of examination	Mean ± SD of dmfs		Mean difference of dmfs (Intervention – Control)	95% confidence interval	*p*-value
	Control group	Intervention group			
Baseline	6.82 ± 8.78	5.21 ± 10.31	-1.61 ± 1.29	(-4.97, 0.15)	0.14
4 months	10.59 ±11.01	6.01 ± 9.10	-4.58 ± 1.39	(-7.32, -1.85)	0.001
8 months	9.91 ± 11.38	5.75 ± 8.93	-4.16 ± 1.57	(-7.22, -1.09)	0.008
12 months	11.77 ± 12.38	5.94 ± 9.10	-5.83 ± 1.77	(-9.31, -2.36)	0.001

SD: standard deviation

Table 4

Cost–effectiveness of probiotic milk tablets among study subjects

Variable	Control group	Intervention group
Labor cost for childcare providers per child per year in THB	Reference	633.33
Cost of probiotic milk tablets per child per year in THB	Reference	872.31
Direct cost per child per year in THB	Reference	1505.64
Reduction in the number of caries in the intervention group at 12 months compared to the control group.	Reference	-4.07
Cost to prevent 1 cavity per tooth surface	Reference	369.93

THB: Thai Baht

Our findings were in contrast to a study among subjects aged 12-17 years given probiotic tablets compared to controls not given probiotics (Keller *et al*, 2014). They found no significant difference in caries between the two groups. This could be due to a difference in the ages of study subjects compared to our study among young children, suggesting probiotics may be more effective in caries prevention among younger children.

Our cost analysis found it cost THB 369.93 to prevent one cavity per tooth surface. This cost is similar to the cost of treating one cavity using a composite filling (THB 363.39) or with a glass ionomer filling (THB 418.57) (Gupta *et al*, 2020; Ladewig *et al*, 2018; Ratchawong, 2022). However, this comparison does not take into account the cost to quality-of-life caused by the dental caries.

A strength of this study was its randomized controlled design, allowing for lower chance of bias. A limitation of this study was that some of the subjects could not be followed up. In our study, the milk tablets were well tolerated and easy to store and administer. However, the milk tablets do not take the place of good oral hygiene and tooth brushing.

In summary, there were significantly fewer caries among study subjects in the intervention group than the control group but the intervention was costly. We conclude, this intervention can be used effectively to prevent caries in the study population but it was expensive. Further studies are needed to determine if this intervention can be applied to other populations of similar aged children and other ages of children and how the program can be financed or the cost reduced.

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