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XXXI CICLO

ARE STANDARDIZED CARIES RISK ASSESSMENT MODELS EFFECTIVE IN ASSESSING CARIES RISK?

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CONTENTS

PREFACE

This thesis was written on the basis of my three years PhD studies at the Department of Biomedical Sciences, University of Sassari, Italy. The work was carried out under the supervision of Professor Guglielmo Campus and Professor Laura Strohmenger and the collaboration of Professor Maria Grazia Cagetti.

The thesis is written as a general overview based in the following articles which will be referred to in the text by their Roman numerals. All articles are reprinted with the permission from the copyright holders and appended to the end of the thesis:

I. Are standardized caries risk assessment models effective in assessing actual caries status and future caries increment? A systematic review. BMC Oral Health (2018)18:123

II. Role of sugar and other sweeteners in the maintenance of the dental health. Dental Cadmos 2018;86(4):272-282

III. Comparison among three caries risk assessment. To submit.

IV. Evaluation of a new simplified caries risk assessment model in children. To submit.

ABSTRACT

The general aim of this thesis was to evaluate the effectiveness of the methods used to identify people with an increased risk of developing carious lesions. The specific objectives were:

- identify the models used in caries risk assessment and evaluate the diagnostic accuracy of the different methods used to identify people with an increased risk of developing carious lesions (**study I**)
- identify the types of sugars and sweeteners and identify the cariogenic power of each (**study II**)
- compare standardized caries risk assessment models to evaluate their agreement (**study III**)
- propose a new method of assessing the risk of caries in pediatric subjects and compare the results with those obtained using standardized methods (**study IV**)

Study I: comprised a systematic review of caries risk assessment methods. Following methods were included for final analysis: previous caries experience, tests using microbiota, buffering capacity, salivary flow rate, dental plaque, dietary habits, and sociodemographic variables. The risk of bias assessment of the papers was scored according to the customized quality assessment tool developed by the National Heart, Lung, and Blood Institute. Sensitivity and specificity were calculated, along with the corresponding 95% confidence intervals. All papers involving assessed a statistically significant association between the risk level measured by the CRA model and the actual caries status or the caries increment in a follow-up examination. At present, only the Cariogram was used in papers of good quality to assess its efficacy in predicting caries development, while, for the other standardized CRA models, the lack of papers does not make it possible to draw conclusions on their effectiveness.

Study II: a narrative review of the literature took into consideration the scientific papers on the most used sugars and sweeteners in dental health. Papers considering the effects of sweeteners on general and oral health, caries especially, were evaluated. Sugars are present in foods in two forms: those naturally contained in foods such as fruit, honey and dairy products and those added to foods during processing to alter their flavor or consistency. Sweeteners can be classified into carbohydrates, sugar alcohols and high intensity sweeteners. While mono and disaccharides are fermented by cariogenic bacteria with production of acids that increase caries risk, sugar alcohols inhibit the metabolic activity of cariogenic microorganisms. No effect on caries is reported for high intensity sweeteners. The duration of exposure and the persistence of sugary foods in the oral cavity cause prolonged periods of acid production and consequent demineralization. The life of different foods in the oral cavity can vary considerably.

Study III: a pilot study that compare the caries risk level using three different multifactorial caries risk models. For this study, three different methods of caries risk assessment were examined: Cariogram®, CaMBRA and PreViser. The experience of caries (DMFT index) and the amount of plaque (plaque index of Silness and Loe) was measured. Salivary flow, salivary buffer capacity, and concentration counts of cariogenic bacteria, *Streptococcus mutans* and *Lactusbacillus spp*. Finally, for each subject, the level of risk was calculated. Considering caries level obtained using CaMBRA and PreViser, a quite high correspondence was observed (53 subjects on 68 - 78%). Comparing Cariogram model and PreViser a lower correspondence of the results was noted (37 subjects out of 68 - 54%). Finally comparing CaMBRA and Cariogram the lowest correspondence was found (30 subjects on 68 - 44%).

Study IV: a pilot study that to evaluate the concordance of results obtained using a new simplified assessment model of caries risk assessment with those obtained using the Cambra and the Cariogram models in a sample of children. In the comparison between the new simplified method and Cambra, 55 children out of 71 were classified with the same risk level, with a Cohen coefficient of 0.55, while comparing the new method with Cariogram model, 44 subjects were classified at the same level of risk, with a Cohen coefficient of 0.32. Moreover, comparing Cambra and Cariogram results, only 45 subjects out of 71 were classified coherently with a Cohen coefficient of 0.39. The proposed new model of caries risk assessment does not produce concordant results with those obtained using Cariogram and Cambra, which even between them do not seem to agree.

ABBREVIATIONS AND DEFINITIONS

Agreement	Agreement is definite as the degree to which scores or ratings are identical i.e. how close the results of the repeated measurements are, by estimating the measurement error in repeated measurements (Kottner et al., 2011). The terms includes reliability and reproducibility of methods as well
Caries increment	Number of new caries lesions between two points in time
Caries lesion development (synonym: caries lesion progression)	Development of a caries lesion from sound tooth surface to detectable lesion in enamel or dentin or from detectable to more extensive lesion
Caries risk assessment (synonym: caries prediction)	Methods/tests used to identify individuals with increased risk of developing coronal caries lesions
Diagnostic accuracy	The capacity to discriminate among the alternative states of the object under study (Swets & Pickett, 1982)
DMFS/DMFT	Decayed Missing Filled Surface/Decayed Missing Filling Teeth (permanent teeth)
dmfs/dmft	Decayed Missing Filled Surface/Decayed Missing Filling Teeth (deciduous teeth)
ICDAS	International Caries Detection and Assessment System (Ismail et al., 2007)
Prevalence	The proportion individuals exhibiting dental caries lesions (in percentage) or the amount of dental caries in an individual or a group of individuals (DMFT/DMFS) (WHO, Oral health database)
Risk	The probability that an event will occur. It encompasses a variety of measures of the

	probability of a generally unfavorable outcome (U.S. National Library of Medicine, 2017b)
Risk of dental caries	We considered coronal caries as an unfavourable outcome for the individual. Risk of dental caries was therefore defined as "The development either *(i)* from sound tooth surface to detectable lesion in enamel or dentin: *i.e.*, from health to disease or *(ii)* from detectable to more extensive lesion: *i.e.*, from disease to more severe disease

INTRODUCTION

Dental caries is a common and global disease. Although it is caused directly by bacteria on the teeth, it is generally accepted that a large number of different factors are involved in the process. The interactions of these factors determine whether the disease and the cavities will occur or not. This complex background can be the subject of long and interesting discussions among scientists.

However, caries should be explained in a simple and complete way to people and patients. This is why it is important to use a method that allows quick, simple and precise identification of the risk of each subject to develop new caries lesions which then represents the starting point for a preventive and therapeutic intervention plan.

DENTAL CARIES

Dental caries is an infectious and transmissible disease, characterized by the dissolution of hard tooth tissues by acids produced by bacterial metabolism. The term caries derives from the Latin "caries" and means decomposition, putrefaction. In English we speak instead of tooth decay. The grooves and the occlusal dimples of the molars and the premolars and the blind foramen of the molars and upper incisors are the areas where the bacterial plaque accumulates and remains more easily determining the beginning of the caries.

This type of pathology can only affect hard tissues at first, but it can extend and involve soft tissues up to the pulp. The simple cure of the carious lesion does not however reduce the future risk of developing the pathology again; what reduces the risk is the implementation of preventive measures. For this reason we understand how fundamental primary prevention is, which is concerned with avoiding the onset of the disease, as well as the secondary prevention that deals with early diagnosis.

EPIDEMIOLOGY OF CARIES

Over the past few decades, the prevalence of dental caries in industrialized countries has been greatly reduced (Sudjalim at al., 2006) especially among children and young adults; this thanks to health education promoted by community medicine, mass-media and also thanks to the application of evidence-based preventive protocols.

Nevertheless, it remains a very common disease in the population (Axelsson et al., 2004) with a significant impact on the quality of life of the people affected (Cagetti et al., 2009).

Consider that the incidence of caries in the population of industrialized countries affects, in some areas, 95% of individuals. (Bollero et al., 2010)

In order to control the development of this disease, the World Health Organization (WHO) promotes the implementation of national epidemiological studies to monitor the development of this disease over time.

EZIOPATHOGENESIS OF CARIES

The etiopathogenesis of dental caries is defined as multifactorial (Valletta, 1977): on an altered local microenvironment the combined acidogenic and proteolytic bacterial activity acts which leads to dissolution of the enamel and exposure of the underlying dentin. There are numerous theories formulated to explain the onset of caries: Miller's chemical-parasitic theory (1892), Gottlieb's proteolytic theory (1947) and proteolysis-chelation theory (1950). All the aforementioned theories recognize the bacterial activity in the plate conditioned by the general and local predisposing factors of the individual as the main cause. The bacteria most implicated in the etiopathogenesis of bacterial plaque are represented by: Streptococcus mutans, Lactobacilli, Actinomyces.

One of the most plausible theories is surely that of Miller (1892). This is based on the assumption of the demineralization of the tooth by organic acids produced by bacterial metabolism or deriving from the degradation of carbohydrates ingested with the diet. The demineralization of the inorganic component of the hard dental tissues, enamel in particular, is followed by the proteolytic dissolution of the organic component, by bacterial enzymes. Both the lithic phenomena are therefore linked to the presence, on the one hand of acidogenic and proteolytic bacterial jambs, on the other from the food residues such as fermentable sugars which constitute an ideal environment for these bacterial groups. (De Michelis et al., 1986) (Costa et al., 2001).

CARIES RISK

In general, "risk" is the probability that some harmful event will occur. Risk is often defined as the probability of an "undesired" event occurring within a given period of time. The risk of caries is the probability that an individual develops carious lesions, reaching a certain stage of the disease progressing during a given period of time, provided that the state of exposure to risk factors remains stable during the period in question. Therefore, the risk of caries refers to the likelihood that a person will develop carious lesions or not. The need to accurately predict the risk of caries is evident, as targeted preventative actions can be targeted at those who have a high risk of caries before cavities develop. Naturally, if the main etiological factors can be identified, the appropriate treatment for that particular individual can be performed with good results.

As a consequence, the assessment of individual risk is a prerequisite for the correct preparation of a treatment plan. These aims fall within the field of modern dentistry based on primary and secondary prevention; for this reason, in recent years more and more precise methods have been proposed for the assessment of caries risk.

The classification of patients based on their risk of caries has been recommended as a first step in the determination of appropriate prevention and treatment interventions. Identifying and determining risk should be a component in clinical decision making because:

- Caries risk assessment (CRA) and clinical examination provide an overview of exposure to potential risks of caries / protective factors such as plaque, frequency of sugar intake and exposure to fluoride, while encouraging management strategies developed specifically for the patient.
- CRA is useful for assessing the patient's risk of developing caries to determine treatment intensity and frequency of appointments or recall treatments.

- CRA helps to identify the main causative agents that contribute to the disease and/or determine the type of treatment and make restorative treatment decisions, including whether to intervene or not, design the cavity to be performed and select dental materials.
- CRA can improve the reliability of the planned treatment prognosis and evaluate the effectiveness of the proposed treatment and prevention plan during booster visits.

Caries risk assessment models currently imply a combination of risk indicators and protective factors that interact with a variety of social, cultural and behavioral factors. (Australian Research Centre for Population Oral Health, Caries Risk Assessment for Children: Information for Oral Health Practitioners)

RISK FACTORS

A risk factor is a specific condition that is statistically associated with an illness and therefore it is believed that it can contribute to its pathogenesis, favor its development or accelerate its course.

What factors should be considered in estimating caries risk?

According to the diagram proposed by Keyes in 1962, and still considered valid, to develop a carious process, three fundamental risk factors are needed: the presence of a cariogenic bacterial flora, a diet rich in fermentable carbohydrates and reduced host defenses.

We emphasize the presence of additional risk factors, among which we can include socio-economic and environmental conditions, which play an important role in the development of caries disease, also influencing habits such as personal oral hygiene and food hygiene. For example, patients with uncovered root surfaces (gingival recessions, elderly patients ...) are at greater risk of root caries. These patients must be motivated to effective hygiene and to the self-application of fluorides. (Zambon et al., 1955)

An increased risk of caries is also present in patients who take special drugs (Ciancio, 1997) or whose salivary flow, for different reasons, is reduced (Edgar & Higham, 1995; Konig, 1984).

The factors to be considered must therefore be divided into two groups:

- Factors immediately involved in the caries process, both as "attack" and "defense" mechanisms, at the site of lesion development. To this group, on the attack side, dental plaque, the presence of various specific microorganisms in plaque (including mutans streptococci) and diet can be included. With regard to defense, for example, salivary protection systems and fluoride exposure can be incorporated. These are key factors that determine whether a caries lesion will occur or not, on the specific surface of the tooth they are interacting with.
- Factors related to the presence of caries, without actually participating in the development of the injury. For this group, for example, various socio-economic factors and the past experience of caries can be added. These factors can be designated as indicators of caries risk, but do not actually participate in the "process" of a cavity. These factors indirectly contribute to changes in the factors of the first group. For example, a low socio-economic state can negatively affect an individual's oral hygiene and diet.

Factors, whose tooth surface is directly exposed and which contribute to the development of caries lesions, depend on "dose", "frequency" and "duration". Each factor must therefore be considered from this point of view. For example, a large amount of plaque (high dose) indicates only a high risk if often present (high frequency) and for a longer period of time (long duration).

THE DENTAL PLAQUE

The point of origin of the carious process is represented by the dental plaque which is formed by bacteria (60-70% of the total volume), salivary organic materials and extrasalivary bacterial products that together make up the biofilm, adhered to the enamel surface. Biofilm subjects the dental tissues to damage related to the presence of bacterial metabolism products. The predominant bacterial species in the initial stage of dental plaque is represented by the Streptococcus mutans. Plaque formation begins with the adhesion of streptococcal cells to the salivary proteins that form a film on the dental surface. It follows a firmer adhesion, by means of a series of extracellular polymers of glucose derivatives (glucans), with marked adhesive properties and synthesized by the bacteria starting from the sugars present in the diet.

The enzyme glucosyltransferase present on the surface of Streptococcus mutans is responsible for the initial adhesion of the bacteria to the film, both of the subsequent synthesis of glucans. In the mass of glucans produced by S. mutans, various cell debris, leukocytes and other bacteria that give plaque the definitive physiology remain trapped. Streptococci (S.sanguis above all) and lactobacilli in the plaque, it reaches locally concentrations able to lower the pH and to solubilize the hydroxylapatite crystals. The consequent formation of a breach in the enamel allows the entry of other bacteria that can thus reach the dentin, lending it (collagenase, protease) the organic component up to the dental pulp where the resulting inflammatory process leads to compression of the sensitive nerve roots and the appearance of the characteristic pain, as a product of the carbohydrate catabolism of the diet, a lot of lactic acid which, protected by dilution in the buccal fluid by the induction of plaque mucosa. (La Placa, 2015)

CARIOGENIC BACTERIA

The predominance of cariogenic species in the oral bacterial biofilm is the pre-requisite without which the pathology can not be established. (Poureslami et al., 2017; Parisotto et al., 2010).

Biofilm is a complex aggregation of bacteria organized within an extracellular matrix whose composition varies during the life of the individual contributing to modify the risk of caries (Law et al., 2007). The bacterial component of plaque can be evaluated through the use of selective media that allow a quantitative evaluation; however, this method requires adequate facilities and suitable staff. In the clinical practice of professionals (pediatricians, neonatologists, dentists, dental hygienists, parents) it is advisable to use semi-quantitative evaluation systems available on the market. These tests are performed on a sample of saliva, as the concentration of the cariogenic bacteria contained in it is directly proportional to that of the biofilm (Parisotto et al., 2010; Denny et al., 2007). Among the more than 300 species of microorganisms able of colonizing dental surfaces, only some are capable of damaging the hard tissues. This happens because the products of the metabolism of these microorganisms cause a reduction of the pH close to the dental surface, producing first a loss of mineral salts and, subsequently, the formation of a real cavitary lesion. At the interface between biofilm and dental surface, a dynamic process of demineralization and remineralization is repeated over time. The carious sign appears when an imbalance towards demineralization is determined.

PROTECTIVE FACTORS

The preventive modalities depend on the age and the risk of individual caries; the current approach is to personalize each type of treatment in relation to the subject. The persistence of risk factors in the Italian population, especially in early childhood, makes the promotion of oral health very important for the entire population, especially in the developmental age. The promotion of breastfeeding, healthy lifestyles, appropriate diet, proper daily oral hygiene and regular check-ups are essential for good oral health. Fluorine is the main protective factor for caries prevention and control. Furthermore, the practice of sealing furrows and dimples is of fundamental importance. Parents' role is crucial for the promotion and maintenance of oral health in the first 3 years of life. Parents should be supported by the pediatrician's and dentist's recommendations in a multidisciplinary approach. Regular visits are essential for the oral health of the child and dietary advice and instruction on correct oral hygiene maneuvers should be promoted as soon as possible. (Cagetti et al., 2009)

MODELS FOR ASSESSING THE RISK OF CARIES

Caries risk assessment methods include previous caries experience, salivary parameters such as buffering capacity and salivary flow rate, oral hygiene measures such as plaque amount, tests using microbiota such as amount of genotypes in saliva or from dental biofilm, most common amount of *S. mutans* and *Lactobacillus*, dietary measures such as frequency of intake and/or economic or socio-demographic variables such as educational years (Mejàre et al., 2014; Tellez et al., 2013; Twetman, 2016). Standardized models comprising different combinations of risk and protection factors have been developed since the 2000s onwards to predict the risk of caries; they can be summarized in two main categories, those that use an algorithm with a software program and those that use standardized questionnaires (self-submitted and/or through an interview).

Algorithm with a software program are: PreViser, Cariogram, National University of Singapore of Caries Risk Assessment (NusCra). Standardized questionnaire are: Caries Management By Risk Assessment (CaMBRA), caries risk assessment by American Dental Association (ADA), America Academy of Pediatric Dentistry's Caries Assessment Tool (CAT).

Algorithm-based programmes

Cariogram

It is a software, available in several languages, [Bratthall D, Hänsel Petersson G. Cariogram--a multifactorial risk assessment model for a multifactorial disease. Community Dent Oral Epidemiol. 2005 Aug;33(4):256-64.] that shows the risk of a patient to develop new caries interactively. It displays the caries risk graphically expressed as "the chance to avoid new carious lesion" in the near future. The software analyses the nine different factors related to caries and the risk is expressed by a pie-circle chart divided into five different coloured sectors. The green one shows the chance to avoid new carious lesions. Cariogram is the most used assessment method mainly in children (Hänsel Petersson, 2003; Tweetman, 2005; Campus, 2009; Cabral, 2014) and few in adults as reported in literature (Lee, 2013; Ruitz, 2007; Giacaman, 2013; Celik, 2012; Petersson, 2015; Sonbul, 2008).

PreVisertm

PreViser is an online risk assessment system that uses software to predict common oral diseases, periodontal disease, caries and oral cancer, based on mathematical algorithms that assign different weights to the various risk factors. The part focused on the caries risk assessment consists of a series of questions on behaviour, medical and oral health practices in order to insert it into one of three groups: low, medium and high risk caries and implement so, a preventive and therapeutic protocol. PreViser is mainly used in periodontal disease risk assessment and no scientific data reported its use regarding caries assessment.

Nus-CRA

It is a method for assessment of caries risk created by the National University of Singapore and is based on 11 items. It assigns 5 risk classes. Similar to Cariogram, Nus-CRA takes into account oral hygiene, past caries experience, and systemic health as clinical factors. (Gao, 2010)

Standardize questionnaire

Several United States dental associations developed a Caries risk assessment models, and all might be summarized together. The approach is based on the CaMBRA (Caries management by risk assessment) practice philosophy (Young et al., 2011; Doméjean et al., 2011).

CaMBRA

The first risk assessment evaluation was created in the University of California, San Francisco in January 2003 with two special editions of the Journal of the California Dental Association were totally dedicated to this method (Featherstone et al., 2003; Featherstone et al., 2007).

It consists in the evaluation of 22 risk/protective factors to assess the level of risk. There are different versions of the questionnaire to use in patients of different age (0-5 years, over 6 years).

From the results it is possible to classify each patient within one of the categories: low, medium, high or extreme risk. Clinicians after assessing caries risk should individually plan a scientific based-evidence of treatment. Nowadays also an APP for smartphone and tablets is available.

ADA (American Dental Association)

Two downloadable ADA's Caries Risk Assessment forms were developed by American Dental Association as practice tools to help dentists evaluate a patient's risk of developing caries. The ADA form use 19 factors associated with caries in evaluating patients over six years of age and 14 factors for children 0-5 years of age to determine a low, moderate, or high risk level (American Dental Association Caries Risk Assessment Forms).

CAT (America Academy of Pediatric Dentistry's Caries Assessment Tool)

The caries risk assessment tool (CAT) is a form for risk assessment of infants, children and adolescents supported by the American Academy of Pediatric Dentistry (AAPD) (American Academy of Pediatric Dentistry. 2007–2008). It was introduced in the 2002. CAT uses 14 factors to evaluate for low, moderate, or high risk and by the risk level determined it promotes their guidelines that provide preventive and treatment recommendations so it included forms (0-5 years, over 6 years) for dental professional as well as clinical guidelines.

This tool is based on a set of physical, environmental and general health factors determined by interviewing the parent/primary caregiver.

The AAPD also has a form that is promoted for use by physicians and non-dentists for 0-3 years of age. All the systems described above are quite similar and in this systematic review they will be treated as one.

Standardized models including different combinations of risk and protective factors (**Table1**).

Factors	Software programs			American Dental Association models		
	NUS-CRA 11 factors	Cariogram 9 factors	PreViser 11 factors	ADA 11 factors	CAMBRA 14 factors	CAT 12 factors
Socio-demographic						
Age	X		X			
Ethnicity	X					
Family socioeconomic status	X			X	X	X
Behavioural						
Infant feeding history	X				X	
Diet	X	X	X	X	X	X
Fluoride	X	X	X	X	X	X
Dental attendance			X	X	X	X
Clinical						
Oral hygiene	X	X	X	X	X	X
Past caries	X	X	X	X	X	X
White spot lesions				X	X	X
Enamel defects						X
Dental appliance			X	X	X	X
Systemic health	X	X	X	X	X	X
Medication				X	X	
Salivary and microbiological						
Saliva flow rate		X	X	X	X	X
Saliva buffering capacity		X				
Mutans streptococci	X	X	X		X	X
Lactobacilli	X	X	X		X	

NusCra National University of Singapore Caries Risk Assessment, *CAMBRA* Caries Management By Risk Assessment, *ADA* caries risk assessment by American Dental Association, *CAT* America Academy of Pediatric Dentistry's Caries Assessment Tool

Table 1. Different factors included in each standardized Caries Risk Model

CARIES PREVALENCE

DMFT and DMFS describe the amount - the prevalence - of dental caries in an individual. DMFT and DMFS are means to numerically express the caries prevalence and are obtained by calculating the number of

- Decayed (D)
- Missing (M)
- Filled (F)

teeth (T) or surfaces (S).

It is thus used to get an estimation illustrating how much the dentition until the day of examination has become affected by dental caries. It is either calculated for 28 (permanent) teeth, excluding 18, 28, 38 and 48 (the "wisdom" teeth) or for 32 teeth

(The Third edition of "Oral Health Surveys - Basic methods", Geneva 1987, recommends 32 teeth). Thus:

- How many teeth have caries lesions (incipient caries not included)?
- How many teeth have been extracted?
- How many teeth have fillings or crowns?

The sum of the three figures forms the DMFT-value. For example: DMFT of 4-3-9=16 means that 4 teeth are decayed, 3 teeth are missing and 9 teeth have fillings. It also means that 12 teeth are intact.

Note: If a tooth has both a caries lesion and a filling it is calculated as D only. A DMFT of 28 (or 32, if "wisdom" teeth included) is maximum, meaning that all teeth are affected.

A more detailed index is DMF calculated per tooth surface, DMFS. Molars and premolars are considered having 5 surfaces, front teeth 4 surfaces. Again, a surface with both caries and filling is scored as D. Maximum value for DMFS comes to 128 for 28 teeth.

For the primary dention, consisting of maximum 20 teeth, the corresponding designations are "deft" or "defs", where "e" indicates "extracted tooth".

Below presenting caries data for adults, the following designations are used:

DMFT: Mean number of decayed, missing or filled teeth			
%DMFT:	Percentage of population affected with dental caries	MT:	Mean number of missing teeth
%D:	Percentage with untreated decayed teeth	MNT:	Mean number of teeth
DT:	Mean number of decayed teeth	%Ed:	Percentage edentulous

OBJECTIVES

The objectives of this thesis were to:

- describe the models used in caries risk assessment and evaluate the diagnostic accuracy of the different methods used to identify people with an increased risk of developing carious lesions (**study I**)
- describe different types of sweeteners (with or without sugar) and their role in the dental health (**study II**)
- compare caries risk measured using standardised risk assessment method, Cariogram, CaMBRA and PreViser (**study III**)
- propose a new method of assessing the risk of caries in pediatric subjects and compare the results with those obtained using other standardized methods (**study IV**)

MATERIALS AND METHODS

Scientific literature on methods used to identify individuals with an increased risk for caries development was critically evaluated through a systematic literature review (study I). Thereby, knowledge gaps within the field were identified. The results from the systematic review influenced the planning, design, and reporting of studies II, III and IV. Study II constituted a narrative review on the most used sugars and sweeteners in dental health and their ability to sweeten, the caloric power, the maximum permitted doses and the cariogenicity of the different natural and the synthetic sweeteners was investigated. A clinical and laboratory pilot study on three methods to identify the level of caries risk and their agreement was performed (study III). Study IV is a pilot study that included a new simplified model of caries risk assessment designed and assessed with reference to the evaluation agreement with other models.

Reviews

Sistematic review

The systematic review (study I) was conducted and reported following the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA Statement) checklist. (Moher et al., 2010).

The review method and planning were registered at Prospero (PROSPERO 2016:CRD42016038590).

Only papers in English published from the 1st of January 2000 to the 31st of December 2017 were collected. Randomized controlled trial (RCT), cross-sectional studies, cohort studies, comparative studies, validation studies and evaluation studies, reporting CRA using standardized models in patients of any age related to caries data recorded by Decayed, Missing, Filled Tooth / Surface (DMFT/S) or the International Caries Detection and Assessment System (ICDAS) indices were included.

Three different electronic databases were searched: PubMed, Scopus® and Embase®. All the papers meeting the inclusion criteria were obtained in the full-text format.

Narrative review

The narrative review (study II) has examined selected scientific works from the PubMed database without time limits, using the key words "carbohydrates, polyols, intensive sweeteners, stevia, dental caries", used as words single and in association with each other. The papers selected are those that, according to the authors, best describe the problem of sugars and sweeteners in dental health.

Sweeteners can be classified into carbohydrates, sugar alcohols and high intensity sweeteners. While mono and disaccharides are fermented by cariogenic bacteria with production of acids that increase caries risk, sugar alcohols inhibit the metabolic activity of cariogenic microorganisms.

Clinical Trials

Pilot study (study III)

The aim of the research was to assess the risk of caries in a group of young adults through these three different methods (Cariogram®, CaMBRA and PreViser) and to compare the results obtained in order to verify if the judgment expressed by the three methods is concordant and to evaluate, if it is not, which variable means that the evaluations do not coincide.

The survey was conducted in Milan, Lombardy, Italy in March 2017. The subjects were enrolled in the Dental Clinic of the University of Milan among the students of the Degree Course in Dentistry and Dental Prosthesis in the Academic Year 2016-2017. Sixty-eight subjects were enrolled and interviewed to record hygienic-sanitary habits, oral hygiene and general hygiene, exposure to fluorine. The experience of caries (DMFT index) and the amount of plaque (plaque index of Silness and Loe) was measured.

Salivary flow, salivary buffer capacity, and concentration counts of cariogenic bacteria, *Streptococcus mutans* and *Lactusbacillus spp*. Finally, for each subject, the level of risk was calculated using the CaMBRA, PreViser and Cariogram® models. The correlation coefficient of Lin (CCA) was calculated to determine to what extent the observed data differed from the perfect concordance line. The Bradley-Blackwood (BBt) test was used for a simultaneous mean and variance test.

Sample

Sixty-eight subjects, aged between 20 and 59 years (average 23 ± 3.11 years), students at the University of Milan, were enrolled and examined. A sample size calculation was performed following the Viechtbauer et al. (2015) and resulting in a necessary number of 65 subjects (Viechtbauer et al., 2015). One hundred subjects was invited to participate. Thirty two subjects did not join the study.

Pilot study (study IV)

The aim of this study was to present a new simplified assessment method of caries risk assessment and to evaluate the concordance of results obtained using this new model with those obtained using the CaMBRA and the Cariogram models in a sample of children. A total of seventy-one pediatric patients aged 6-14 years were attending the Dental Clinic of the University of Milan, Italy from January to April 2018.

The experience of caries (DMFT index) and the amount of plaque (plaque index of Silness and Loe) was measured.

For each subject of the study a questionnaire was filled out by interviewing the parent consisting of twelve questions regarding the child's oral hygiene habits, eating habits and lifestyle such as: the toothpaste used, if a mouthwash is used, if it has been subjected to professional fluoride treatments in the last six months, if it has used xylitol-containing gums four times a day in the last six months, if it takes fluoride supplements or drugs, what kind of water drinks, how much snacks or drinks containing sugar consumes between the main meals. It is important to know even if there are pathologies, if there is have a dry mouth or reduced salivary flow, if there is an orthodontic mobile or fixed devices.

Sample

Seventy-one pediatric patients aged 6-14 years (mean age of 9.49) were randomly enrolled and examined. Power analysis, using a one-sided confidence interval, was performed to identify a sample size that gives reasonable confidence that this pilot trial is big enough to enable us to make the right decision about proceeding to a larger trial or not. The margin of error was set at 10% and a 90% confidence level with a sample size of 62 subjects. (Daniel, 1999)

Clinical and microbiological examinations

The visual and tactile examination was performed under lighting with a mirror and a sharp probe.

Each patient was examined to perform the DMFT/dmft caries index, ie the sum of decayed (missing) teeth (teeth) and filled (filled) teeth. (study III and IV)

It is an epidemiological index adopted according to the criteria recommended by the World Health Organization (WHO) as an index of health of dental arches and measures the present and past situation of caries.

It is thus used to get an estimation illustrating how much the dentition so far has become affected by dental caries. Usually, it is calculated on 28 teeth, excluding 18, 28, 38 and 48 from the index.

The older the patient is, the more unsafe is the DMFT as a picture of the patients caries situation, as several teeth could have been extracted because of reasons other than caries, for example periodontal disease.

It is considered the measure of choice widely used for its simplicity and reproducibility in the evaluation of the teeth in young subjects.

A clinical examination was then performed and the data needed to evaluate the dmft / DMFT and the plaque index of the subject were recorded.

The Plaque Index of Silness and Loe (PI) was performed, evaluating the mesial, distal, vestibular and lingual surface using a mirror and a specillo. No plaque pigmentation is required through detection substances, but must be performed via periodontal probe. (Silness, 1964, Loe 1963)

To calculate the Plaque Index a score of 0 to 3 is assigned for each dental element.

Plaque Index of Silness and Loe:

Score	**Explanation**
0 = Extremely good oral hygiene, Plaque Index, PI < 0.4	No plaque, all teeth surfaces are very clean. Very 'oral hygiene conscious' patient, uses both tooth brush and interdental cleaning.
1 = Good oral hygiene, PI = 0.4-1.0	A film of plaque adhering to the free gingival margin and adjacent area of the tooth. The plaque may be seen *in situ* only after application of disclosing solution or by using the probe on the tooth surface.
2 = Less than good oral hygiene, PI = 1.1- 2.0	Moderate accumulation of soft deposits, which can be seen with the naked eye.

3 = Poor oral hygiene, PI > 2.0	Abundance of soft matter within the gingival pocket and/or on the tooth and gingival margin. The patient is not interested in cleaning the teeth or has difficulties in cleaning. You feel like cleaning his/her teeth thoroughly, professionally and immediately!

After the execution of the dmft/DMFT and the plaque index, the salivary tests was performed. (study III)

The subjects were underwent a clinical examination to evaluate the Saliva. It plays a fundamental protective role in many ways. (Dodds et al., 2005) The variable related to the host concerns mainly saliva (Vadiakas, 2008; Taji et al., 2011). It is produced by the major and minor salivary glands according to a circadian rhythm, flowing on hard and soft tissues with a cleansing and lubricating action. It exerts a protective action, thanks to the buffer systems that act by raising the pH value, when this falls below the risk threshold for demineralization. Saliva is also provided with antimicrobial systems (lysozyme, peroxidase) and immune systems (secretory IgA) that act in the control of the cariogenic flora. The use of chewing gum stimulates salivary secretion during the first few minutes of mastication and can therefore temporarily increase the defense mechanisms against caries, provided that it is free from fermentable sugars and contains non-cariogenic sweeteners, such as xylitol (Strohmenger, et al., 2013).

The salivary characteristics involved in the etiopathogenesis of caries disease are salivary flow, buffering capacity and concentration of cariogenic bacteria.

The salivary flow determines an action of dilution on food residues, favoring their rapid removal from the oral cavity. Reduction of salivary secretion, if protracted over time, favor the development of new lesions and the expansion of existing ones. The assessment of salivary flow is simple to perform: just ask the patient to collect the saliva produced for 5 minutes in a container. The measurement should be performed at least an hour after a meal, toothbrushing or smoking preferably in the middle of the morning. It is important that the patient is relaxed and calm. The patient must not be sick or unfit and not be on any antibiotics during the past one month.

If the amount of saliva produced will be <1 ml / min, the flow is to be considered reduced. The exam must be repeated to confirm the data detected.

1. The patient should neither eat nor smoke for one hour prior to sampling.

2. The patient should be seated in an upright, relaxed position.

3. A paraffin pellet is given to the patient to chew for 30 seconds, then to spit out the accumulated saliva or swallow it.

4. The patient then continues to chew for five minutes, with the accumulated saliva collected continuously into a measuring glass. Time could be reduced if secretion rate is high, prolonged if rate is low.

5. After 5 minutes, the amount of saliva is measured and the secretion rate calculated. Example: 3.5 ml in 5 min = 0.7 ml/min

Normal saliva secretion is more than approximately 1 ml / min.

The second salivary parameter related to the risk of caries is the buffering power, which consists in the ability to rebalance the acid environment that may be created in the oral cavity. The cause is due to the acidity of some foods (citrus fruits, soft drinks, fruit juices) and acids produced by acidogenic bacteria. This evaluation can be easily carried out with appropriate test strips which, after about 5 minutes, placed in contact with the saliva, have a colorimetric change that will be evaluated by comparing it with a specific table supplied with the test. Low buffer power exposes fabrics to a higher risk of erosion.

Finally, the last salivary parameter evaluable with relative simplicity and whose result is of great importance for the risk assessment is the salivary concentration of cariogenic bacteria (Caufield et al., 2005). It should be remembered that the concentration of these microorganisms in saliva is directly proportional to that in bacterial plaque, simple tests have been developed that allow a contemporary semi-quantitative evaluation of *Streptococcus mutans* and *Lactusbacillus spp*. (D'Amario et al., 2006).

The presence of lactobacilli in high quantities indicates a risk factor related to an excessively high sugar supply, associated with poor oral hygiene. A high presence of streptococci indicates a high risk of new carious lesions (Cagetti et al., 2009).

Collection and treatment of saliva samples were performed using a standardized kit CRT Ivoclar Vivadent, composed by CRT Buffer and CRT Bacteria (studyIII).

The CRT Buffer Test [CRT® Bacteria and Buffer Test (Vivadent Ets., Lichtenstein)] was used to determine the buffer capacity of saliva using a colorimetric test strip. The CRT Bacteria Test measured the *Streptococcus mutans* and Lactobacilli count in saliva by means of selective culture media.

Paraffin-stimulated whole saliva was collected in calibrated sterile tubes. CRT Buffer Test was stripped from the package without touching the yellow test field. The entire yellow test field was wetted with saliva using a pipette. To determine the buffer capacity of saliva, the color of the test field was compared with the color samples after exactly 5 minutes of reaction time. High, medium, and low salivary buffer capacities are indicated by blue, green, and yellow test fields, respectively.

The saliva collected for the CRT Buffer Test was also used for the CRT Bacteria Test. The agar carrier was removed from the test vial, and a NaHCO3- tablet was placed at the bottom of the vial. Using a pipette, both agar surfaces were wetted with saliva. The culture broth was placed back into the vial and closed tightly.

After incubation at 37°C for 48 hour, the density of S. mutans and Lactobacilli colonies was assessed using the corresponding evaluation pictures provided with the kit.

In the study IV the bacterial count and the salivary buffering power was not calculated because the salivary tests were not performed. The salivary flow was assessed with a visual examination by the operator and asking the patient if he had the sensation of having a dry mouth.

The diet

A fundamental factor for the development of caries is represented by eating habits (study II) (Naidoo & Myburgh, 2007; Karjalainen, 2007). All study subjects are interviewed to learn about eating habits (study III and IV).

Cariogenic bacteria need carbohydrates to live and reproduce. The metabolism of these substances, especially simple carbohydrates, produces weak acids that cause the demineralization of hard dental tissues. When foods of this type are introduced into the oral cavity, the pH of the biofilm decreases due to the acids produced by the bacterial metabolism. With the pH reduction below the limit threshold of about 5.5 (demineralization threshold for enamel), oral hard tissues release minerals to the environment. Salivary buffer systems are able to buffer acids and restore the pH of the dental surface above the risk threshold in about 30 minutes. With this process, the minerals lost during the demineralization phase will then be reintegrated through an inverse process (remineralization). If foods and / or carbohydrate-rich beverages are introduced frequently in the oral cavity, the pH drop below the risk threshold will be frequent and the sum of the times when the value is low becomes high.

If the demineralization will have time to act, the white spots, or the first stage of the carious lesion, which are reversible, can be established on the dental surfaces. If this process is not interrupted, the loss of mineral component of the hard oral tissues continues and the cavity lesion will arise from the initial lesion. Sucrose, a simple cooking sugar, is the most effectively disaccharide metabolized by cariogenic bacteria (Steyn & Temple; 2012). There are other carbohydrates that have the potential to be effectively fermented by bacteria. In addition to sucrose, in order of cariogenicity, there are glucose, maltose, fructose and lactose (Karjalainen; 2007). Foods rich in starch, without the addition of sugars, on the contrary, play a limited role in the pathogenesis of caries (Harris et al., 2012; Strohmenger et al., 2013).

The maximum amount of simple sugars to be taken, considered compatible with good oral health, should not exceed 10% of the daily energy requirement. Furthermore, it is important that the frequency of intake of these carbohydrates does not exceed four daily assumptions (Moynihan & Petersen, 2004). In order to evaluate these parameters it may be useful to draw up a patient's food diary. It is important to underline the presence of a phenomenon known as "baby bottle syndrome", a baby bottle syndrome (Vadiakas, 2008) mainly determined by the administration of fermentable carbohydrates by means of drinks inside the bottle. Among the basic recommendations to be made to the parent we find: discourage the intake of fruit juices or sweet drinks with the bottle, discourage their use especially at night, suggest the consumption of non-cariogenic snacks, limit the intake of food at the main meals (Nainar & Mohummed, 2004; Cagetti et al., 2009).

In the study performed by Elamin et al. in 2018 Children who had caries (dmft> 0) consumed foods with a high sugar content more frequently than those without caries (Elamin et al., 2018)

Caries risk assessment models

A caries risk profile was calculate for each subjects. (study III and IV)

The caries risk was assessed individually in all subjects using the Cariogram software program. For each patient, nine caries-related factors, evaluated through clinical examination, saliva samples, and questionnaire, were ranked from 0 to 2 or 0 to 3, according to the Cariogram program manual. The predictor variables were salivary secretion rate, buffer capacity, mutans streptococci and lactobacilli counts, caries experience, medical diseases, dietary frequency, oral hygiene, and fluoride use. A 10th factor, own clinical judgement, was set to 1 in all patients. The values of the 10 factors were entered into the Cariogram computer program to produce a pie chart that illus- trates the chance, on a scale from 0 to 100%, of an individual avoiding caries in the immediate future. According to '% chance of avoiding caries', the subjects were placed into one of three risk groups: 0–40% = low chance (i.e. a high risk of developing caries); 41–60% = moderate chance; and 61– 100% = fairly high to high chance (i.e. low risk).

The CaMBRA test was performed by reporting the data recorded during the interview via questionnaire and the clinical examination in the form available in the online version MyCAMBRA, downloadable on PC, smartphone and tablet.

The disease indicators included visible cavitation or radiographic radiolucencies penetrating to dentin, active white spot lesions, and a history of a restored cavity in the previous 3 years. Risk factors included noticeable plaque buildup on the teeth; frequent snacking (more than three times a day between main meals); hyposalivation to observation or measurement (<1ml / min if stimulated); exposed roots; deep pits and fissures; recreational drug use; orthodontic appliance; use of mineral water daily. If so, which one... The protective factors included fluoride toothpaste at least once a day; fluoride toothpaste at least twice a day; which toothpaste used; rinses with fluorinated mouthwash (0.05%) every day; application of fluorine varnish / gel in the last 6 months; professional application of fluorine in the last 6 months; prescription or use of chlorhexidine for at least one week every month in the last 6 months; use of gums with xylitol 4 times a day in the last 6 months. *Streptococcus Mutans* (SM) and *Lactobacillus spp* (LB) elevated were inserted if micriobiological test were performed.

Only for study III the PreViser test was performed reporting the data in the online version.

The evaluated factors were: consumption of snacks or drinks containing sugar between main meals 4 or more times a day; consumption of water containing fluorine or fluorine supplements; use of fluoride products not prescribe (example: toothpastes or mouthwashes); use of chewing gums with xilitol 4 times a day in the last 6 months; use of toothpaste containing calcium and phosphate in the last 6 months; use of drugs or alcoholic beverages; dry mouth or reduced salivary flow; need special health care; which teeth were erupted and had been exposed to saliva for at least 12 months (some or all): permanent first molar, second permanent molars, premolars and permanent molars; the dental situation: in good condition or sealed, or with fillings only in the grooves / presence of interproximal obstruction / with defects in the pits / show caries; months since the last carious lesion: 36 or more / 24-35 / 12-23

/ less than 12; number of visible natural teeth; number of natural teeth that had fillings or reconstructions of crowns; number of natural teeth that had secondary caries or had a filling that requires restoration; number of natural teeth that had primary caries; if a bacteriological examination was performed in the last 12 months which indicated a high level of S. Mutans or Lactobacilli; if chlorhexidine has been used for at least one week every month in the last 6 months; if the subject examined could benefit from an improvement in oral hygiene; if the frequency of dental care of the patient is regular as recommended; if the subject had dental extractions due to caries in the last 3 years, if the subject had applied fluoride vasnish in the last 6 months; if it carries orthodontic equipment or space maintainers; presence of diseases and systemic conditions associated with caries: absence of disease / disease, mild degree / disease, severe degree that had lasted a long time.

Only for study IV a new sinplified model of caries risk assessment was performed.

Starting from the factors of risk ratings illustrated in the 2013 Health Guidelines for the Promotion of Oral Health and Prevention of Oral Diseases in children development of the Ministry of Health for the assessment of caries risk in subjects >6 years old, a new evaluation model was performed. Each evaluated factor is assigned a score (negative or positive). The result derives from the sum of all the evaluated factors. It will allow to establish the class of risk (low-moderate-high) of caries of the subject and determine the type of recall.

The new proposed model includes the evaluation of biological factors, protective and clinical factors.

The questionnaire collected information about socio-economic background (e.g., maternal and paternal education levels, self-rated financial status) assessed through completed by the parent, where the profession of both the mother and the father was requested; the eating habits, how many snacks or drinks containing sugar the child is usual to eat during the day; the presence of disability or systemic pathology was specified because child who was not able to cleanse himself or herself the oral cavity (e.g. serious motor problems, syndromes with mental retardation), was not able to perform the correct proceedings of oral hygiene; the adequate exposure to fluorine was evaluated.

The degree of oral hygiene was assessed with the clinical examination: the absence / presence of minimal plaque deposits (plaque index <15% identify a subject with good oral hygiene) was reported; the adequate salivary flow (the basal salivary flow lower than 0.1 ml / minute or stimulated below 1 ml / minute indicates a reduction in the flow below the risk threshold for the carious pathology); the presence oforthodontic appliance; the white spots, the caries experience and the presence of incongruous restorations (steps, missing material, infiltrations) were therefore taken into consideration during the clinical examination. Only the white spots that can be related to incipient caries were considered, ie where the probe feel roughness.

The sum of the factors evaluated for each subject will give a value that will place the subject in a class of risk of developing caries in the future. Negative values, below 0, correspond to a low risk of caries. Values of 0 or 1 correspond to a moderate risk of caries. Values above or equal to 2 correspond to a high risk of caries.

Simplified assessment of caries risk age >6 years BIOLOGICAL FACTORS		
	Yes	No
Low socio-economic status	+2	0
Over 4 off meal	+3	0
Disability	+2	0
PROTECTIVE FACTORS		
	Yes	No
Adequate exposure to fluorine	-1	0
Good oral hygiene	-1	0
CLINICAL FACTORS		
	Yes	No
White spot/demineralization	+3	0
1 Caries	+3	0
2 or more caries	+4	0
Low salivary flow (option)	+3	0

Incongruous restorations	**+2**	**0**
Fixed and/or mobile orthodontic appliance	**+2**	**0**
RESULTS (SUMMER SCORING)		
Low risk: **TOT <0**	**Moderate risk:** **0≤TOT≤1**	**High risk:** **TOT≥2**

Table 1. Factors evaluated for calculating the risk of caries according to the proposed simplified model

RESULTS

Systematic review

From the search in three databases, PubMed, Scopus® and Embase®, 3326 publications were identified. A total of 1934 papers were selected after removing duplicates, and after consulting title and abstract 61 were assessed in full-text and 32 publications were included for final analysis: 16 on children, 12 on adults and 4 on both, 3 of which considered children and adults as a single sample and one as two different samples. (**Fig.1**)

Many of the excluded studies focused on the correlations between caries-related factors and the development of caries.

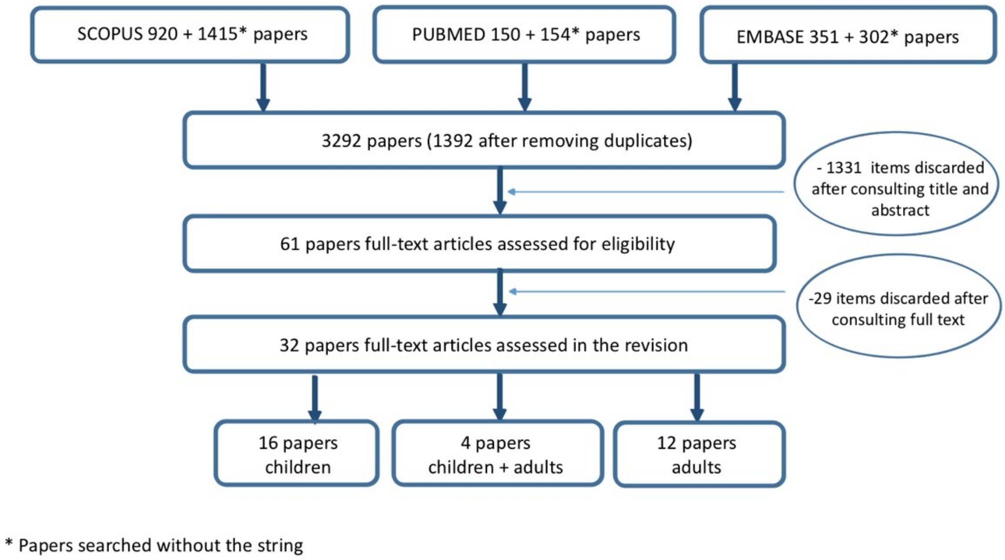

Fig. 1 Flow chart of the study

In order to record caries status (experience / prevalence / incidence), 9 papers used DMFT index or sub-components, 13 papers used DMFS index or sub-components, 9 papers used both DMFT / DMFS index or sub-components, and only 1 used the ICDAS. Four papers focused on primary teeth, 24 on permanent teeth and 4 on both dentitions.

The following methods (index tests) of identifying individuals with an increased risk of caries were investigated in the included studies: (*i*) previous caries experience, (*ii*) mutans streptococci sampled from saliva or plaque, (*iii*) lactobacilli *s*ampled from saliva, *(iv)* buffer capacity *(v)* salivary flow rate, *(vi*), dental plaque/oral hygiene, *(vii)* dietary habits, and *(viii)* sociodemographic variables.

Sample size ranged from 48 to 4468 individuals.

For each paper the following data were searched and recorded when available: *(i)* the year of publication and duration of the study; *(ii)* details of the participants including sample size at baseline, age and country of origin; *(iii)* caries data including actual caries status, caries experience and caries increment measured through DMFT/S or dmft / s or ICDAS; *(iv)* Caries risk assessment including standardized model used and categorization of the risk levels; *(v)* sensibility and specificity of the CRA model.

Caries lesions were mainly diagnosed using visual/visual-tactile examination.

The majority of papers (n = 31) estimated the caries risk using the Cariogram (Cariogram 6 / 7 / 8 factors and Cariogram 9 factor, here inafter named full Cariogram or a form based on Cariogram) as a single model or in comparison with other models. Three papers estimated the caries risk level using CaMBRA (Gao et al., 2015; Gao et al., 2013; Chaffee & Cheng, 2015), 3 papers using CAT (Gao et al., 2015; Gao et al., 2013; Zukanovich, 2013), 1 paper using NUS-CRA.

Assessment of Risk of Bias

The assessment of risk of bias of included publications in study I using the customized quality assessment tool developed by the National Heart, Lung, and Blood Institute and Research Triangle Institute International for Observational Cohort and Cross-Sectional Studies since no RCTs were obtain after studies selection [Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies Available from: https://www.nhlbi.nih.gov/health-pro/guidelines/indevelop/cardiovascular-risk-reduction/tools/cohort].

A total of 19 papers (11 on children and 8 on adult) were classified as being of good quality, 9 papers of fair quality (3 on children, 4 on adult and 2 on both) and only 4 of low quality (3 on children, 1 on adult and 1 on both). (**Table 2**)

Authors (year)	Outcome	Subjects	Indices	Caries risk model	Statistical significance	Quality assessment
Children/Adolescents						
Gao[b], (2015) [8]	CI	544	dmft	Full Cariogram, CAT, CAMBRA, NUS-CRA	+	Good
Sundel, (2015) [21]	ACS	133	dmfs/DMFS	Full Cariogram	+	Good
Cabral, (2014) [22]	ACS	150	dmft/DMFT	Form based on Cariogram 7 factors	++	Poor
Kemparaj, (2014) [37]	CI	200	DMFT/S	Full Cariogram	+	Poor
Gao[b], (2013) [36]	CI	544	dmft	Full Cariogram, CAT, CAMBRA, NUS-CRA	+	Good
Zukanovich, (2013) [41]	CI	109	DMFS/DMFT	Full Cariogram, PreViser, CAT	+	Fair
Campus, (2012) [35]	CI	957	DFS	Cariogram 7 factors	+	Good
Hebbal, (2012) [23]	ACS	100	DMFT	Full Cariogram	++	Poor
Kavvadia, (2012) [24]	ACS	814	dmft	Full Cariogram	+	Fair
Gao, (2010) [16]	CI	1576	dmft	Full Cariogram	[e]	Good
Petersson[c],(2010b) [39]	CI	392	DMFS	Full Cariogram, Cariogram 6 factors	+	Good
Petersson, (2010a) [40]	CI	392	DMFS	Full Cariogram	+	Good
Campus, (2009) [25]	ACS	957	dmfs/DMFS	Cariogram 7 factors	++	Good
Holgerson, (2009) [15]	CI	125	dmfs/DMFS	Full Cariogram	+	Fair
Twetman, (2005) [33]	CI	64	DFS	Full Cariogram	++	Good
Petersson[a,b], (2004) [34]	CI	446	DFS	Full Cariogram	++	Good
Petersson[b], (2002) [32]	CI	446	DMFT/S	Full Cariogram	+	Good
Adults						
Petersson, (2015) [44]	CI	1295	DFT/DFTS	Full Cariogram	++	Good
Carta, (2015) [31]	ACS	480	ICDAS	Full Cariogram	++	Good
Chaffee, (2015) [45]	CI	4468	DFS	CAMBRA	+	Good
Chang (2014) [30]	CI	110	DMFT/S	Cariogram 7 factors	+	Good
Chang and Kim, (2014) [42]	ACS	102	DMFT	Full Cariogram	+	Good
Lee, (2013) [29]	ACS	80	DMFT	Full Cariogram, Cariogram 7/8 factors	+	Fair
Petersson, (2013) [7]	ACS	1295	DFT/S	Cariogram 8 factors	++	Good
Celik, (2012) [43]	CI	100	DMFT/S	Full Cariogram	+	Fair
Peker, (2012) [27]	ACS	90	DMFT/S	Full Cariogram	+	Fair
Sonbul, (2008) [28]	ACS	175	DMFS	Full Cariogram	+	Good
Ruiz Miravet, (2007) [26]	ACS	48	DMFT/S	Full Cariogram	++	Poor
Petersson[a,d], (2004) [34]	CI	208	DFS	Full Cariogram	++	Fair
Petersson[d], (2003) [1]	CI	208	DMFS /DFS/DFRS	Full Cariogram	++	Good
Both Children/Adults						
Giacaman, (2013) [20]	ACS	180	DMFT	Cariogram 7 factors	–	Poor
Almosa, (2012) [18]	ACS	89	DMFS	Full Cariogram	++	Fair
Al Mulla, (2009) [19]	ACS	100	DFS	Full Cariogram	++	Fair

ACS actual caries status, *CI* Caries Increment. Subjects: number of subjects at baseline
Statistical significance: - = $p > 0.05$ + = $p < 0.05$; ++ = $p \leq 0.01$
[a]Petersson, (2004) reported in both children and adults and describes data in two different samples
[b]Gao, (2013) and (2015), and Petersson, (2002) and (2004) respectively reported data for the same sample of children
[c]Petersson, (2010a) and (2010b) reported data for the same sample of children
[d]Petersson, (2003) and (2004) reported data for the same sample of elderly people
[e]Data not obtainable from the paper

Table 2 Papers included. Association between standardized CRA and actual caries status and/or caries prediction

Association between caries prevalence and caries risk level in children/adolescents

Two papers (Al Mulla et al., 2009; Almosa et al., 2012) evaluated the association between caries prevalence (DMFS) and three Cariogram categories (low, medium and high) in orthodontic patients. In the first study (Al Mulla et al., 2009), full Cariogram was tested in two groups based on their pre-bonding caries index (≥5 or

≤2). At de-bonding (18 months after), the low caries group displayed a statistically significant difference for the DFS ($p<0.01$) and Cariogram level ($p<0.01$) compared to the high caries group. Almosa and co-workers (2012) investigated on 89 orthodontic patients the associations between the environment of treatment, governmental and private and various caries-related factors. At the de-bonding, Full Cariogram level was lower in the group showing significantly higher DMFS ($p<0.05$).

A total of 180 Chilean subjects (age range 10-56 years) were enrolled and divided using Cariogram including 7 factors in five different caries categories, from very low to very high. None was classified as very low risk, thus, only the four upper quintiles were considered for the analysis. Neither DMFT nor the number of caries lesions was significantly different among the Cariogram's risk categories ($p > 0.05$). (Giacaman et al., 2013)

The caries risk profiles in children aged 5-10 years with cleft lip and/or palate (n=133) and non-cleft controls (n=297) was calculated using Full Cariogram to classify the child into three categories, low, moderate or high (Sundel et al., 2015). In both groups, children in the high caries risk category had a higher caries experience, but a statistically significant difference was only found in non-cleft children (p data not available).

Caries prevalence was evaluated in one hundred and fifty Brazilian children aged 5-7 years from low-income families (Cabral et al., 2014), using the ICDAS II and data converted into dmft / DMFT scores. Cariogram including 7 factors was used to classify each child belonging to three categories: low, moderate or high. A significant linear regression between mean dmft and Cariogram categories was found ($p<0.01$).

A statistically significant association between caries experience and four (low, moderate, high and very high) Cariogram categories was found ($p<0.01$) in 100 Indian children (Hebbal et al., 2012).

A statistically significant reduction ($p<0.01$) in mean DMFT values was found from the highest to the lowest risk group. Full Cariogram was calculated to split 814 pre-school Grecian children in three risk categories, low, medium and high (Kavvadia et al., 2012). Caries was recorded using dmft index. Multivariate regression analysis of Cariogram variables showed that both caries experience and presence of white spot lesions were statistically significant associated to Cariogram categories ($p<0.01$).

Finally, using Cariogram including 7 factors, 957 Italian children aged 7-9 years were divided in five caries risk categories from very low to very high and examined to evaluate dmfs / DMFS (Campus et al. 2009). A significant linear trend between the five Cariogram categories and dmfs/DMFS scores was observed ($p<0.01$).

Association between caries prevalence and caries risk level in adults

In Saudi Arabia (Sonbul et al., 2008), the caries profile of 175 adults with several dental restorations using the Full Cariogram was evaluated. The mean caries prevalence of the high-risk group differed significantly from that recorded in the low-risk group ($p<0.05$). Several studies focused on young adults and all of the them reported an association between Cariogram categories and caries prevalence/experience/severity (Ruiz Miravet et al., 2007; Peker et al., 2012; Petersson et al., 2013).

A caries profile obtained from the simplified Cariogram models was compared to Full Cariogram model and correlated to caries data; all the models were statistically related to caries experience (Lee et al., 2012).

The chance to avoid caries evaluated with Full Cariogram was statistically significant associated ($p<0.01$) to caries experience in a group of Korean adults with Intellectual disabilities (Chang et al., 2014).

The correlation among socio-behavioural factors, caries status (recording using ICDAS) and caries risk, calculated through Full Cariogram, in an adult population (n=480 subjects) was evaluated (Carta et al., 2015). Caries at ICDAS levels 5-6 and the presence of more than 5 missing teeth were statistically associated with Cariogram scores (OR = 2.36, 95%CI = 1.83–3.03 and OR = 1.43, 95%CI = 1.13–1.82, respectively).

Association between caries increment and caries risk level in children and adult

Altogether 17 longitudinal studies investigated the capability of CRA models to predict new caries lesions. (**Table 3**)

Authors (year)	Age	Study time (years)	Subjects	Caries increments	Range Mean (Standard Deviation)				
				Cariogram	**0–20**	**21–40**	**41–60**	**61–80**	**81–100**
Gao (2013) [36]	C	1	485	dmft	2.67 (2.96)	2.02 (1.71)	1.56 (1.63)	0.77 (1.21)	0.34 (0.88)
Kemparaj (2014) [37]	C	2	200	DMFT	0.54 (1.2)	0.43 (1.32)	0.39 (1.04)	0.34 (0.80)	0.06 (0.09)
				DMFS	0.79 (1.73)	0.73 (1.55)	0.48 (1.72)	0.39 (1.20)	0.09 (1.12)
Celik (2012) [43]	A	2	100	DMFT	1.23 (0.86)	0.65 (0.81)	0.39 (1.02)	0.08 (0.28)	0 (0)
				DMFS	1.23 (0.86)	0.9 (0.97)	0.48 (1.6)	0.08 (0.28)	0 (0)
Petersson (2002) [32]	C	2	392	DMFT	1.67 (1.44)	1.46 (2.20)	1.07 (1.36)	0.42 (0.90)	0.23 (0.61)
				DMFS	2.58 (1.83)	2.62 (4.11)	1.47 (1.81)	0.53 (1.24)	0.27 (0.70)
Petersson (2015) [44]	A	3	982	DFT	1.00 (1.40)	0.84 (0.95)	0.82 (1.18)	0.53 (1.07)	0.24 (0.58)
Petersson (2010a) [40]	C	2	392	DMFS	3.00 (a)	2.70 (a)	1.50 (a)	0.50 (a)	0.20 (a)
				DFS	1.99 (3.00)	1.7 (1.76)	1.59 (2.55)	0.85 (1.91)	0.29 (0.89)
Petersson (2004)[b] [34]	C	2	392	DFS	1.30 (a)	1.30 (a)	0.70 (a)	0.30 (a)	0.10 (a)
	A	5	148	DFS	1.90 (a)	1.00 (a)	1.20 (a)	0.40 (a)	0 (a)
Campus (2012) [35]	C	2	861	DS	1.20 (a)	1.20 (a)	0.10 (a)	0.20 (a)	0.10 (a)
				Cariogram	**0–20**	**21–40**	**41–60**	**61–100**	
Chang and Kim (2014) [42]	C	1.3	64	DMFT	2.97 (5.2)	1.28 (1.5)	1.36 (2.2)	0.44 (0.7)	
				DMFS	5.81 (11.97)	1.28 (1.5)	3.27 (6.8)	0.44 (0.7)	
Petersson (2003) [1]	A	5		DMFS	16.21 (15.97)	7.36 (9.34)	7.96 (9.52)	5.23 (6.97)	
				Cariogram	**0–25**	**26–50**	**51–75**	**76–100**	
Twetman (2005) [33]	C	3	64	DFS	8 (10.8)	3.4 (2.6)	2.6 (3.7)	0 (0)	
				Cariogram	**0–20**		**21–80**	**81–100**	
Zukanovic (2013) [41]	C	3	70	DMFT	1.80 (1.79)		2.40 (2.36)	1.77 (1.88)	
				DMFS	5.00 (7.07)		4.71 (4.34)	2.54 (2.44)	
				Cariogram	**0–40**			**41–100**	
Holgerson (2009) [15]	C	5	125	dmfs/DMFS	2.40 (3.2)			0.10 (0.4)	
				Cambra	**High**		**Moderate**	**Low**	
Gao (2013) [36]	C	1	485	dmft	1.24 (1.58)		0.27 (0.68)	0.20 (0.76)	
Chaffee (2015) [45]	A	1.5	4468	DFT	1.74 (a)		1.16 (a)	1.01 (a)	
				CAT	**High**		**Moderate**	**Low**	
Gao (2013) [36]	C	1	485	dmft	0.79 (1.31)		0.08 (0.28)	0 (0)	
Zukanovic (2013) [41]	C	3	70	DMFT	2.19 (2.33)		2.60 (1.82)	2.38 (1.92)	
				DMFS	4.54 (4.41)		3.80 (5.81)	3.13 (2.53)	
				NUS-CRA	**Very High**	**High**	**Moderate**	**Low**	**Very Low**
Gao (2013) [36]	C	1	485	dmft	2.18 (1.87)	2.10 (1.63)	1.26 (1.38)	0.85 (1.11)	0.17 (0.69)
				PreViser	**High**		**Moderate**	**Low**	
Zukanovic (2013) [41]	C	3	70	DMFT	2.35 (2.27)		1.92 (2.18)	2.18 (2.32)	
				DMFS	5.04 (4.75)		3.08 (2.87)	2.82 (3.19)	

A Adults, *C* Children
(a) indicates that Standard Deviation data were not described in the paper. The decimal places reported are those reported in each paper
Petersson, (2004)[b] reports the increment for year of observation. Holgerson, (2009) and Petersson, (2010b) were excluded from the table since as no mean data for caries were present. Gao (2015) was excluded from the table as the data are the same as those reported for Gao, (2013)

Table 3. Association between caries increment and caries risk model categories in longitudinal papers

Twelve studies were performed on children (Petersson et al., 2002; 2004; Tweetman et al., 2005; Holgerson et al., 2009; Petersson et al., 2010a; 2010b; Gao et al., 2010; Campus et al., 2012; Gao et al., 2013; Zukanovich et al., 2013; Kemparai et al., 2014; Gao et al., 2015), of which nine studies used Cariogram and three compared different CRA models including Cariogram (Gao et al., 2013; Zukanovich et al., 2013; Gao et al., 2015).

Six studies were conducted on adults: five of them used Cariogram (Petersson et al., 2003, 2004; Celik et al., 2012; Chang et al., 2014; Petersson et al., 2015) and one the CaMBRA model (Chaffee et al., 2015).

In a 2-year prospective study on 438 schoolchildren (10–11 years), Full Cariogram (five risk groups) was tested (Petersson et al., 2002). At follow-up 392 children were examined for caries status. Subjects in the highest-risk group developed, as a mean, about 10 times more caries lesions (DMFS) and 7 times more decayed teeth (DMFT) than the lowest-risk group.

The same research group re-compared (Petersson et al., 2004), data from the previous study to a group of adults/elderly. Adults / elderly had higher mean caries increment at surface level per year for most caries risk group compared to children.

In 64 Type 1 diabetes mellitus children (8–16 years), Full Cariogram was calculated, dividing the sample in four groups respect the chance to avoiding caries (Twetman et al., 2005). Caries increment (ΔDMFS) was about 8 times higher in the highest-risk group at the 3-year check-up.

Caries risk using Full Cariogram was assessed in 125 two-year-old children participating in a 2-year caries-preventive trial with xylitol tablets (Holgerson et al., 2009). Children were divided in two groups respect the chance to avoiding caries. After five years from baseline the caries status of 103 subjects was re-evaluated (DMFT, dmft): children classified at high risk developed about four times more caries lesions. This study was not included in table 3 since it was not possible to extrapolate mean values of caries increment.

The caries increment (ΔDMFS) was evaluated in 392 schoolchildren, 10-11 years of age, using Full Cariogram after 2 years (Pertesson et al., 2010a). A statistically relationship with caries development was assessed ($p < 0.05$): five times more caries lesions were found among those children assessed with the highest risk compared to those with lowest risk. The same research tested on the same sample two different Cariogram models with and without saliva tests (9 and 6 factors). Both models displayed a statistically relationship with caries development ($p < 0.05$) at the two-year follow-up (Petersson et al., 2010b).

A prospective study (not included in table 3, as it was not possible to extrapolate the caries increment data) was conducted among 1782 children (3-6 years) with the aim to construct and/or test different risk assessment models, including Full Cariogram (Gao et al., 2010). Twelve months later, on 1576 participants the sensitivity / specificity was assessed and Cariogram showed a quite low sensitivity / specificity (71%/66%), showing that the model is not accurate in predicting early childhood caries.

On 957 schoolchildren aged 7-9 years, caries risk was assessed using the Cariogram including 8 factors and dividing the sample in five groups of risk. Two years later the caries increment (ΔDS) in 861 individuals was assessed (Campus et al., 2012).

Children classified at high risk developed about double caries lesions respect children classified as low risk. The efficiency of Full Cariogram, Previser and CAT in caries prediction over a 3-year period was evaluated on 109 children aged 12-yeas (Zukanovic et al, 2013). The subjects were divided in three risk groups using each model; Cariogram identified the majority of subjects as medium risk (70%), while the other two models gave a more unfavourable risk profiles. In only 12% of the patients the three models assessed the risk in the same way. After 3 years, caries increment (ΔDMFT / S) was evaluated: only the Cariogram model successfully predicted new caries lesions.

On 544 children aged 3 years, caries risk was evaluated using Cariogram and NUS-CRA, dividing children in five risk groups, and using CAT and CaMBRA dividing subjects in three groups (Gao et al., 2013). After one year, the caries status of 485 children was evaluated (Δdmft). Using CAT and CaMBRA, the majority of children were considered at high risk, while, using Cariogram and NUS-CRA, nearly 2/3 children were defined as very low or low risk. Overall, caries lesion increased from lower to higher risk groups under all models, but Cariogram and NUS-CRA showed the best performances: children classified at high risk using Cariogram developed about eight times more caries lesions respect those classified as low risk; while using NUS-CRA this difference reached about thirteen times, showing this model has good sensitivity and specificity in identifying pre-school children susceptible to caries.

Caries risk was evaluated on 200 children aged 12-years using Full Cariogram and dividing them in five groups of risk (Kemparaj et al., 2014). Two years later, the caries status was assessed (ΔDMFT / S) and children classified at very high risk at baseline, developed about thirty times more caries lesions respect children classified as very low risk.

Finally, the same sample of 3-years patients from a previous study (Gao et al., 2013) was re-evaluated 18 months from baseline (n=462) using the same risk assessment models (Gao et al., 2015). Overall, a gradient in caries increment from lower to higher risk groups under all programmes was found.

In a group of 208 elderlies (60-80 years) caries risk was evaluated using Full Cariogram (Petersson et al., 2002). Subjects were assigned to four risk groups. After 5 years, on 148 subjects, the caries status (crowns and roots) was evaluated using ΔDMFS: subjects with the highest risk profile showed about three times more caries lesion compared to the lowest risk group. The same sample was compared to a group of children, as describe above (Petersson et al., 2004).

On 100 subjects aged 20-21 years, caries risk was assessed using Full Cariogram and subjects were scored in five risk groups (Celik et al., 2012). After 2 years the whole sample was examined for caries (ΔDMFT/ S): subjects classified at very high risk at baseline developed about double caries lesions respect those classified as very low risk.

The Cariogram (7 factors) was used to split 110 patients, treated under general anesthesia because of their insufficient co-operation, in four risk groups (Chang and Kim, 2014). After a follow-up period (16.3 ± 9.5 months), caries status was re-evaluated in 64 patients (ΔDMFT): subjects with the highest risk profile showed about thirteen times more caries lesion compared to the lowest risk group.

CaMBRA model was used to split 18004 young adults (18 years) in four risk groups (Chaffee et al., 2015). After 18 months, the caries incidence (ΔDFT) was evaluated on 4468 subjects: caries increment was more than three times greater in subjects with high risk compared to classified as low risk.

Finally, Full Cariogram was assessed on 1,295 19-year-old patients, splitting them in five risk groups (Petersson et al., 2015). After 3 years, on 982 patients caries increment was calculated (ΔDFT/S): subjects with the highest risk profile showed about seven times more caries lesion compared to those with the lowest risk group.

Sensitivity and specificity

A perfect risk marker has a sensitivity of 100% and a specificity of 100%, implying no errors in risk assessment. Unfortunately, no such a perfect caries risk assessment method exists. In general, the validity of caries risk assessment methods remains uncertain (Mejàre et al., 2015; Tellez et al., 2013a).

The available data for the Cariogram model are displayed in **Table 4**. Sensibility values ranged from low (41.0) (Petersson et al., 2002) to fairly low (52.0) (Campus et al., 2012) while specificity values were quite high, ranging from 71.0 (Twetman et al., 2005) to 88.0 (Holgerson et al., 2009). Moreover, wide Confidences Intervals are reported for both parameters, indicating that the reliability of the model differs in the different caries risk levels.

Authors (year)	Number of factors	Sample n	Age at baseline (years)	Sensibility % ($_{95\%}$Confidence Interval)	Specificity % ($_{95\%}$Confidence Interval)
Children					
Gao (2013) [36]	Full	485	3	66.4[a]	78.5[a]
Campus (2012) [35]	7	861	7–9	52.0 (18.6–94.6)	79.5 (99.2–54.7)
Gao (2010) [16]	Full	1782	3–6	70.5[a]	65.8[a]
Holgerson[b] (2009) [15]	Full	66[b]	2	46.0 (31.0–62.0)	88.0 (71.0–104.0)
Twetman (2005) [33]	Full	64	8–16	75.0[a]	71.0[a]
Petersson (2002) [32]	Full	392	10–11	41.0 (9.0–73.0)	79.8 (99.6–60.0)
Adults					
Petersson (2015) [44]	Full	1295	19	47.0 (11.9–89.2)	72.5 (33.5–94.8)

[a]Range not available
[b]Control group only

Table 4 Sensitivity and specificity of the Cariogram model in children and adults

Pilot study III

The results obtained following the execution of the three methods taken in exams on each individual subject are been entered into a table. In the first column the results provided by the CaMBRA test were inserted, in the second column the results provided by the PreViser test and in the third column the results provided by the Cariogram test. Each row of the table therefore corresponds to a subject under investigation associated with the respective risk class in which it was placed by the three models. (**Table 2**)

It is immediately possible to notice the discrepancy of the results obtained, which corresponds to the low concordance of the results provided by the three models in question.

Of the 68 subjects analyzed in the CaMBRA method, 22 subjects were included in the low risk group, 3 subjects were included in the moderate risk group and 43 subjects were included in the high risk group. With the PreViser method of the 68 subjects 31 were inserted in the low risk group, 6 subjects were included in the moderate risk group and 31 subjects were inserted in the high risk category of caries. While with Cariogram method 35 subjects were inserted in the low risk group, 21 subjects were inserted in the moderate risk group and 12 subjects were inserted in the high risk group.

So, by dividing the subjects by caries risk group for a low risk with CaMBRA method we have 22 subjects, whit PreViser we have 31 subjects and with Cariogram we obtain 35. For the moderate risk group with the CaMBRA the subjects turn out to be 3, 6 with the PreViser method and 21 with the Cariogram method. For the high risk group we have 43 subjects evaluated with the CaMBRA, 31 with the PreViser and 12 with the Cariogram. (**Fig. 2**)

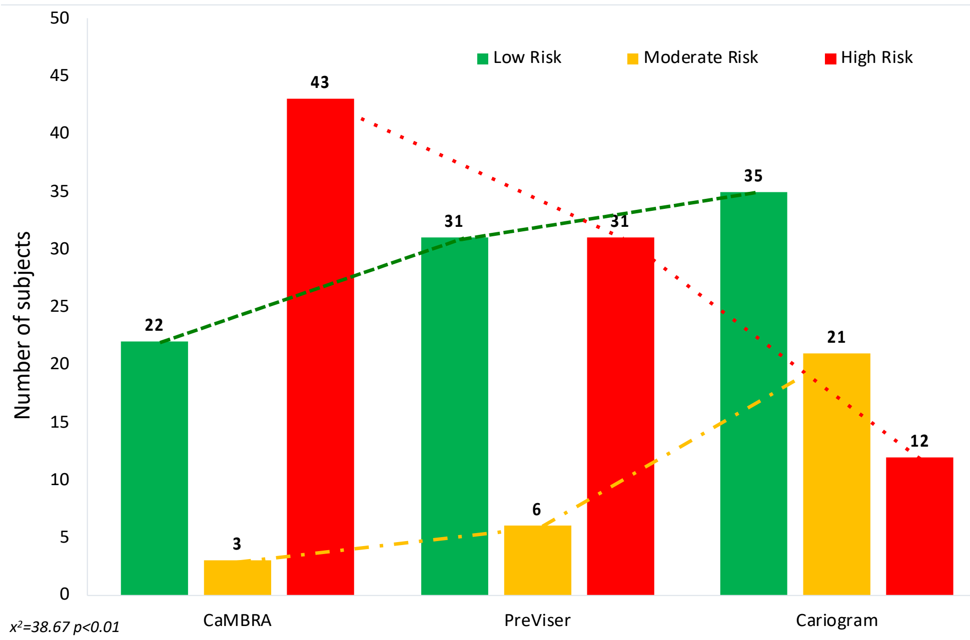

Fig. 2 The number of subjects in each risk category using the three models is shown. Using the CaMBRA model the highest number of high risk subjects was found (43 subjects on 68), while the Cariogram model showed the lowest level (12 subjects on 68) and the PreViser was in the middle. On the other hand, Cariogram identified the highest number of low risk patients (35 subjects on 68).

A total of 29 subjects out of 68 show a concordance between the three models used with 10 subjects at high risk of caries, 1 subject at moderate risk and 18 subjects at low risk of developing new caries in the future.

Considering caries level obtained using CaMBRA and PreViser, a quite high correspondence was observed with 53 subjects out of 68. Comparing Cariogram model and PreViser a lower correspondence of the results was noted with 37 subjects out of 68. Finally comparing CaMBRA and Cariogram the lowest correspondence was found with 30 subjects out of 68. Following Cohen's Kappa statistic, a value of 0.23 with an agreement of 22.73% was found among the three models. CCA was 0.65 (95%CI 0.52 – 0.78) with a BBt=8.97 (p<0.01) between CaMBRA and PreViser, CCA=0.37 (95%CI 0.21 – 0.53) with a BBt=21.22 (p<0.01) between CaMBRA and Cariogram and finally CCA=0.43 (95%CI 0.26 – 0.60) with a BBt=13.11 (p<0.01) between PreViser and Cariogram. (**Fig.3**)

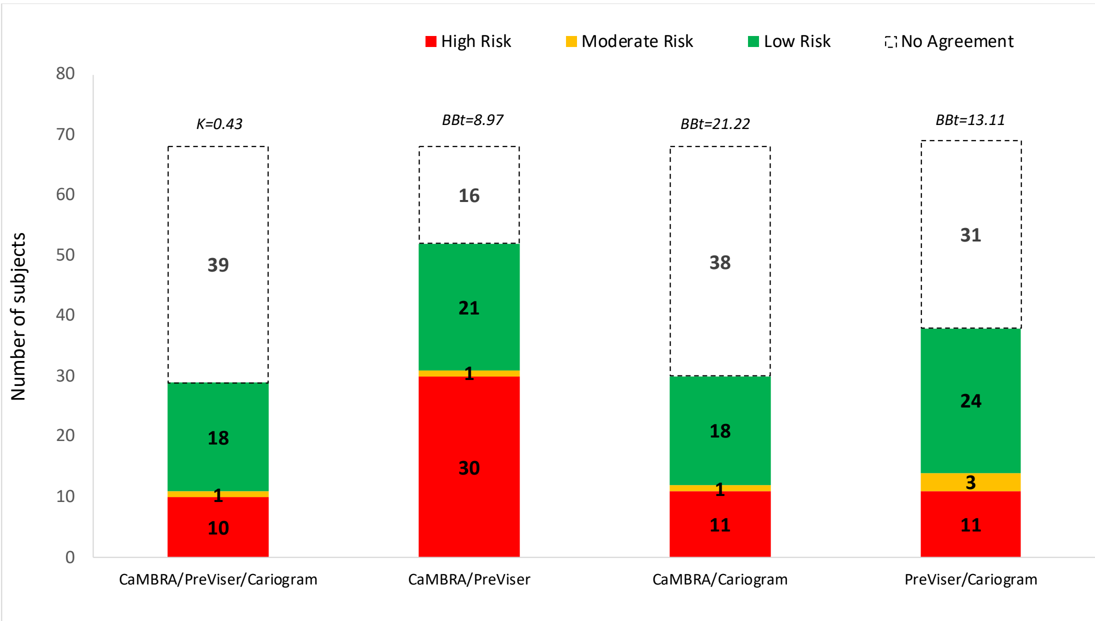

Fig. 3 Data show a range of agreement from low to good between the risk level calculated using the three models. Following Cohen's Kappa statistic, a value of 0.23 with an agreement of 22.73% was found among the three models. CCA was 0.65 (95%CI 0.52 – 0.78) with a BBt=8.97 (p<0.01) between CaMBRA and PreViser, CCA=0.37 (95%CI 0.21 – 0.53) with a BBt=21.22 (p<0.01) between CaMBRA and Cariogram and finally CCA=0.43 (95%CI 0.26 – 0.60) with a BBt=13.11 (p<0.01) between PreViser and Cariogram.

The "visible cavitation" or "filling in the last three years" factor was removed from the CaMBRA method and a new comparison was made with PreViser: a 91% agreement was observed in this case. (**Fig. 4)**

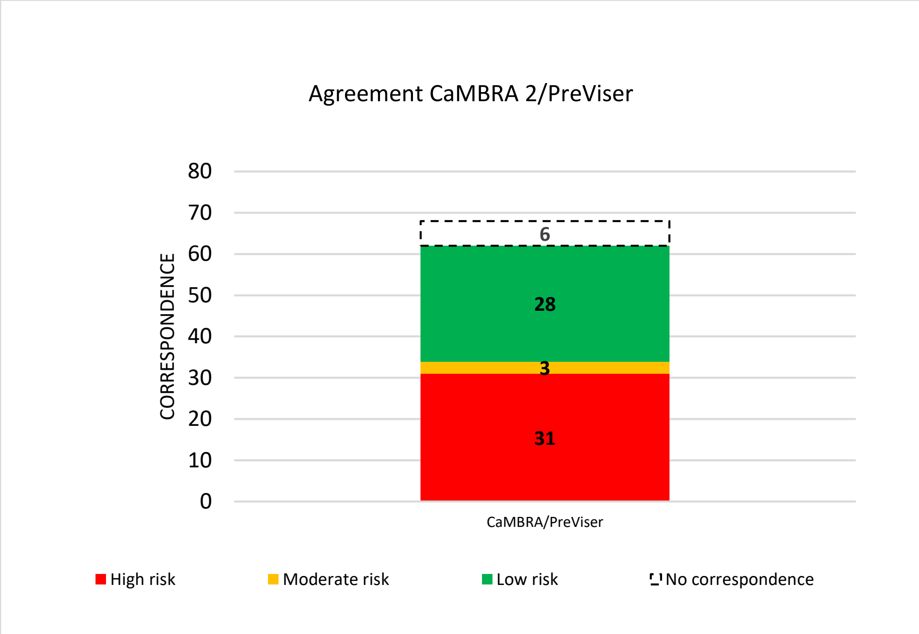

Fig. 4. Risk assessments carried out with CaMBRA without taking into account the factor "a carcinogenic element" or "an obstructed element for caries in the last three years", compared to the evaluations provided by the PreViser method.

Pilot study IV

The results were divided into three risk classes: high, moderate and low. According to this method at a high risk it corresponds 0-40% of Cariogram®, at a moderate risk corresponds 41-60% of Cariogram® and at a low risk it corresponds 61-100% of Cariogram®.

The extreme risk identified for the CaMBRA method was merged with the high risk, even if no evaluated subjects showed an extreme risk of caries.

The degree of risk assessed by the three methods for each subject is not always corresponding.

Of the 71 subjects evaluated with the new simplified model 53 subjects were at high risk, 7 at moderate risk and 11 at low risk of caries. With the CaMBRA method of the 71 subjects, 43 were at high risk of caries, 2 at moderate risk and the remaining 26 at low risk of caries. Finally, with the Cariogram method, 37 subjects out of 71 were at high risk of caries, 17 at moderate risk and 17 others at low risk. **Fig. 5**

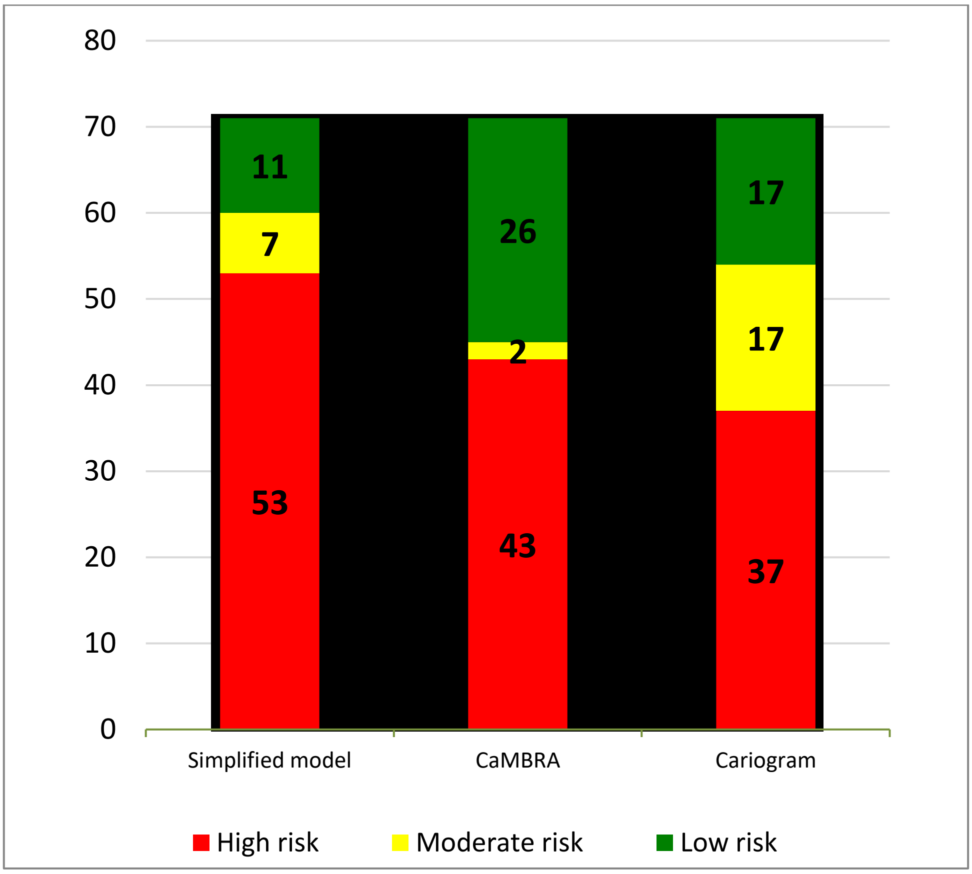

Fig. 5. The number of subjects in each risk category using the three models is shown.
The new simplified method tends to overestimate the level of the risk of developing caries in the near future, with 53 subjects on 71 classified at high risk of caries, while using the CaMBRA method 43 subjects were evaluated at high risk, and finally using the Cariogram method only 37 subjects over 71 were judged at high risk.

It was then evaluated whether there was an agreement between the results obtained from the three different evaluation models.

In the comparison between the new simplified method and CaMBRA, 55 children out of 71 (77,4%) were classified with the same risk level, with a Cohen coefficient of 0.55, with 43 subjects at high caries risk, 1 at moderate risk and 1 at low risk of caries.

While comparing the new method with Cariogram model, 44 subjects (61,9%) were classified at the same level of risk, with a Cohen coefficient of 0.32 with 35 subjects at high caries risk, 1 subject at moderate risk and 8 subjects at low risk of caries.

Moreover, comparing CaMBRA and Cariogram results, only 45 subjects out of 71 (63,3%) were classified coherently with a Cohen coefficient of 0.39 with 30 subjects at high risk of caries, no one at moderate risk and 15 subjects at low risk of caries. **Fig. 6**

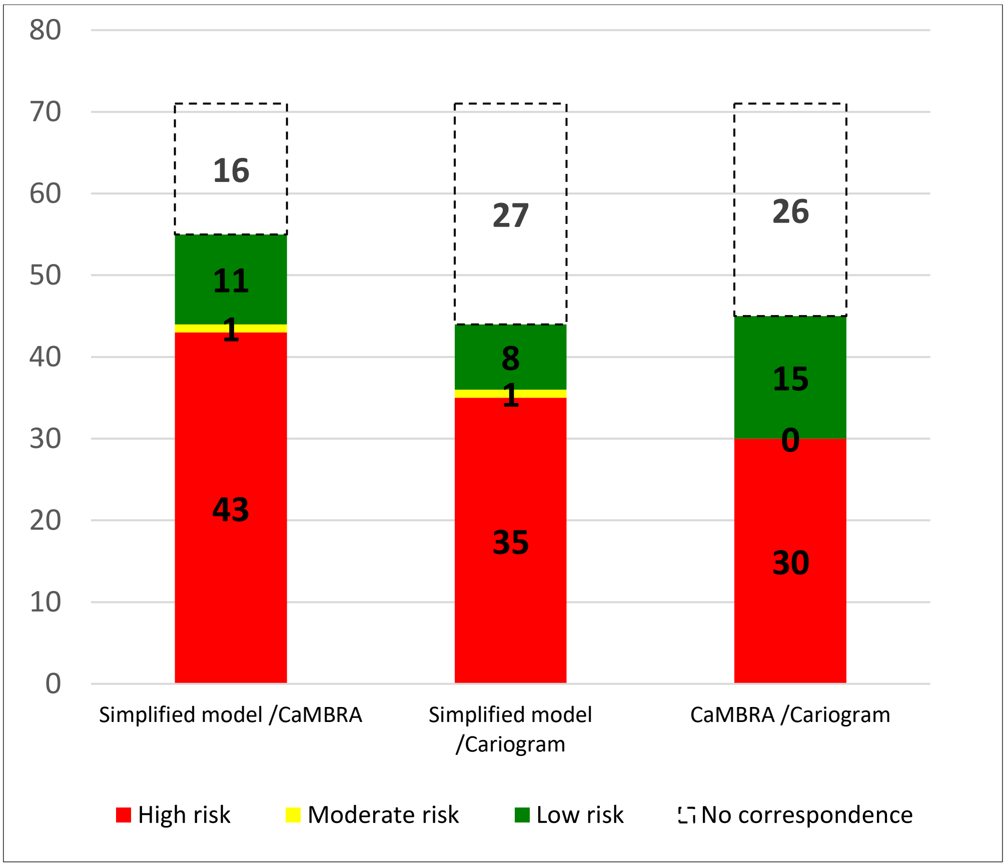

Fig. 6. Agreement between the results provided by the three models. The new simplified method and CaMBRA show the greatest agreement with 55 subjects out of 71 classified coherently.

DISCUSSION

Systematic review

The ability of different caries risk assessment models to fit with the actual caries status, analysing cross-sectional studies, and the capability of the methods to predict new caries lesions in the near future, analysing longitudinal studies, were the aims of this systematic review. The CRA models discussed in this review are the namely reasoning-based (CAT, CaMBRA and ADA model) and algorithm-driven programmes (Cariogram, PreViser and NUS-CRA).

The findings described, allow to draw same considerations. Most study support a superior validity of algorithms-driven programmes, as evidenced by the higher sensitivity and specificity and they mostly take into account the Cariogram model as risk assessment model.

All the studies carried out on children, assessed a statistically significant association between the risk evaluated using a CRA model and the actual caries status or the caries increment evaluated in a follow-up examination. Ten studies over 16 were classified as good quality, and all of them used Cariogram as single model or in addition to the other model. The capacity of Cariogram to evaluate the caries risk might be flawed since four studies were carried out on the same Scandinavian population.

About studies carried out on adult populations, a positive association between CRA model and caries data was recorded. Eight studies over 13 were classified as good quality and all of them except one used Cariogram model. Regarding the three studies carried out both on children and adults considered as a single sample, two found a positive association between risk level and caries status and one failed the association, this paper was evaluated of poor quality.

Different Cariogram models, from 9 factors (Full Cariogram) to 6, were tested. Excluded factors were salivary parameters (mutans streptococci, lactobacilli and buffer capacity). Reduced Cariogram versions were all statistically significant associated with caries data, both in cross-sectional and longitudinal studies.

Only two studies, one of good quality and one fair, compared different risk models: Full Cariogram, PreViser and CAT were compared in the first and Full Cariogram, CAT, CaMBRA and NUS-CRA in the second one. Results showed that different CRA models assessed the risk discordantly. Different findings were reported and since the few data available, it is not possible to assess clear conclusions about the most effective method in predicting caries lesions.

Nowadays, only Cariogram model was used in a quite good number of studies including samples of different age groups and with different characteristics: orthodontic patients, patient with disabilities or systemic disease, while for the other CRA models the lack of studies does not allow to reach conclusions on their effectiveness in caries prediction.

Pilot study III

It can be immediately noted that the CaMBRA method tends to overestimate the individual risk of developing caries in the near future, with 43 subjects on 68 places at high caries risk, unlike the PreViser method in which the number of high risk subjects, 31, corresponds to the number of subjects at low risk and unlike the Cariogram method which shows much more positive results, only 12 subjects out of 68 are placed in the high risk group.

In comparison, there is a low correspondence between the results provided by the three models. Only in 29 subject out of 68, so for 42% there is a correspondence of the results in all three models; instead, the correspondence between the CaMBRA and PreViser method is high with 78%, 53 cases out of 68; the correspondence of the results is lower if we compare the CaMBRA method with the Cariogram method with 44%, 30 subjects; the correspondence between Cariogram and PreViser method is slightly higher with a correspondence rate of 54%, then 37 cases out of 68.

CaMBRA method tends to overestimate the individual risk of developing caries in the near future, probably because the presence of the risk factor "tooth filling due to caries in the last 3 years" or "visible cavity affecting the dentin" immediately puts the patient in the class high risk, regardless of the protective factors of the subject, unlike the other methods for which these factors affect the least, they place the subject in a moderate/low risk group for the PreViser and Cariogram methods, both models therefore take more account of the protective factors; however, this occurs only if the elements involved do not exceed the number of 1, decayd tooth or filling tooth for caries in the last 3 years, if the elements involved were 2 or more, the CaMBRA and PreViser tend to provide concordant results for 91% while the Cariogram method continues to underestimate the risk; only in the case where the patient's DMFT exceeds the value taken as a normal population index (DMFT = 4), the Cariogram method provides results that coincide with the other 2 methods.

Pilot study IV

Dental caries affects individuals differently, which makes it essential to identify high-risk patients so that preventive strategies can be undertaken. The concept of caries-risk assessment is simple and straightforward. The idea is to identify patients who are most likely to develop caries. (Van Loveren & Helderman, 2003; Daryani et al., 2014)

Although there are many risk factors for dental caries, the post eruptive local effect of dietary sugar is one of the main factors in development of caries (Holund et al.,1985).

As can be seen from the results, the new simplified method of assessing caries risk tends to overstimate the risk compared to the others two methods with 53 subjects out of 71 judged at high risk of developing caries in the future and 43 out of 71 for the CaMBRA method and 37 out of 71 for the Cariogram method.

The new simplified method and the CaMBRA show the highest agreement with 55 subjects on 71 coherently jugdged, while between the new method and the Cariogram the agreement is lower with 44 subjects on 71, but it is similar to the agreement found between the CaMBRA and the Cariogram with 45 subjects out of 71 coherently jugdged.

According to Kappa coefficient of Cohen the agreement between the CaMBRA and the new simplified model is moderate, with a value of 0,55, while the agreement between the Cariogram and the simplified model or the Cariogram and the CaMBRA model is fair (0,32 and 0,39, respectively).

CONCLUSION

Systematic review

The evidence on the validity for existing CRA models in assessing and predicting caries lesion is limited. Only Cariogram model was tested enough to assess that the method is effective in the identification of the level of the risk associated to the actual caries status and/or the prediction of new lesion in the near future. Full Cariogram (9 factors) and reduced versions (8-6 factors) seem to produce similar results. Although other CRA models (CAT, CaMBRA, NUS-CRA, PreViser) seem effective in correctly judging the risk of new caries lesions, to date the scientific evidence is very poor.

Narrative review

Simple carbohydrates are an important source of nutriment for the body; however, their excessive consumption increases the risk of systemic and oral diseases.

As suggested by numerous national and international guidelines that deal with nutrition and health, the use of free sugars must be limited both in terms of quantity and frequency of intake. Natural or synthetic sugar substitutes can help to reduce the incidence of caries in both adults and children. However, their use is subjected to restrictions.

Pilot study III

The study showed that the CaMBRA, the PreViser and the Cariogram do not produce concordant results, probably due to the different risk/protective factors considered and the different "weights" given to different factors. The highest agreement was obtained regarding low risk subjects.

The findings of this pilot study underline how the calculation of the risk level even using standardized models is a very difficult goal not yet fully achieved. Further studies are needed to assess which methods are effective in the identification of subjects running a higher risk of caries in order to plan preventive strategies before caries lesions occured.

Effective and reliable methods for caries risk assessment are needed, based on the best evidence for caries prediction and disease management.

Pilot study IV

The new simplified caries risk assessment model, the Cariogram and the CaMBRA do not produce completely consistent results, probably due to the multifactorial aetiology of the disease and the different risk/protection factors considered by each model.

The Cariogram and the CaMBRA do not completely agree: the Cariogram tends to underestimate the risk of caries, while the CaMBRA to overestimate the risk.

The highest agreement was achieved between the new caries risk assessment method and the CaMBRA method.

In conclusion, the new simplified method of caries risk assessment seems to be as effective as other standardized methods and since it is simply to use and "time saving", it might be included in the pediatric scheduled check ups.

The results presented in this paper underline how the calculation of the risk level, even using standardized models such as the Cariogram and the CaMBRA, is a difficult objective, not yet fully achieved.

REFERENCES

1. Al Mulla AH, Kharsa SA, Kjellberg H, Birkhed D. Caries risk profiles in orthodontic patients at follow-up using Cariogram. Angle Orthod. 2009;79:323–30.

2. Almosa NA, Al-Mulla AH, Birkhed D. Caries risk profile using the Cariogram in governmental and private orthodontic patients at de-bonding. Angle Orthod. 2012;82:267–74.

3. American Academy of Pediatric Dentistry. Policy on use of a caries-risk assessment tool (CAT) for infants, children and adolescents. Reference Manual 2007–2008. Pediatr Dent 2007;29:29–33.

4. American Dental Association Caries Risk Assessment Forms. (http://www.ada.org/sections/professionalResources/pdfs/topics_caries_instructions.pdf)

5. Australian Research Centre for Population Oral Health, Caries Risk Assessment for Children: Information for Oral Health Practitioners https://www.adelaide.edu.au/arcpoh/downloads/publications/reports/annual-reports/annual-report-2015.pdf

6. Axelsson, Söder, Nordenram, & al, Effect of combined caries-preventive methods: a systematic review of controlled clinical trials. Acta Odontol Scand. 2004 Jun;62(3):163-9.

7. Bollero, P., F.R., G., Federici, A., Gherlone, E., Nardi, G., & Nardone, M. (2010, nov). Linee guida nazionali per la promozione della salute orale e la prevenzione delle patologie orali in età adulta. Ministero della salute.

8. Bratthall D, Hänsel Petersson G. Cariogram--a multifactorial risk assessment model for a multifactorial disease. Community Dent Oral Epidemiol. 2005 Aug;33(4):256-64.

9. Cabral RN, Hilgert LA, Faber J, et al. Caries risk assessment in schoolchildren–a form based on Cariogram software. J Appl Oral Sci. 2014;22:397–402.

10. Cagetti, M., Mastroberardino, S., Brambilla, E., Campus, G., & Strohmenger, L. (2009, marzo). la prevenzione della carie oggi: dalla valutazione del rischio all'applicazione di protocollli preventivi mirati. Il dentista moderno, 3, 40-56.

11. Campus G, Cagetti MG, Sacco G, Benedetti G, Strohmenger L, Lingström P. Caries risk profiles in Sardinian schoolchildren using Cariogram. Acta Odontol Scand. 2009;67:146–52.

12. Campus G, Cagetti MG, Sale S, Carta G, Lingström P. Cariogram validity in schoolchildren: a two-year follow-up study. Caries Res. 2012;46:16–22.

13. Carta G, Cagetti MG, Cocco F, Sale S, Lingström P, Campus G. Caries-risk profiles in Italian adults using computer caries assessment system and ICDAS. Braz Oral Res. 2015;29:S1806–83242015000100306.

14. Caufield, P., Li, Y., & Dasanayake, X. (2005). Dental caries: an infectious and transmissible disease. Compend Contin Educ Dent, 25, 10-6.

15. Celik EU, Gokay N, Ates M. Efficiency of caries risk assessment in young adults using Cariogram. Eur J Dent. 2012;6:270–9.

16. Chaffee BW, Cheng J, Featherstone JD. Baseline caries risk assessment as a predictor of caries incidence. J Dent. 2015;43:518–24.

17. Chang J, Kim HY. Does caries risk assessment predict the incidence of caries for special needs patients requiring general anesthesia? Acta Odontol Scand. 2014;72:721–8.

18. Chang J, Lee JH, Son HH, Kim HY. Caries risk profile of Korean dental patients with severe intellectual disabilities. Spec Care Dentist. 2014;34:201–7.

19. Ciancio, S. Medications as a risk factor for caries and periodontal disease. NYS Dent J,1977, 59, 962-971.

20. Costa, F., Formisano, G., Goracci, G., & Caiazza, S. (2001). L'esame delle superfici dentinali sclerotiche al microscopio elettronico a scansione. Istituto Superiore di Sanità.

21. D'Amario, M., Barone, A., Marzo, G., & Giannoni, M. (2006). Caries-risk assessment: the role of salivary tests. Min Stomatol, 55, 449-463.

22. Daniel WW (1999). Biostatistics: A Foundation for Analysis in the Health Sciences. 7th edition. New York: John Wiley & Sons.

23. Daryani H et al., Cariogram Model in Assessment of Dental Caries among Mentally Challenged and Visually Impaired Individuals of Udaipur, India. J Clin Diagn Res. 2014 Jan;8(1):206-10.

24. De Michelis, B., Modica, R., & Re, G. (1986) Trattato di clinica odontostomatologica (Vol. I). Torino: Ed. Minerva Medica.

25. Denny, P., Denny, P., Takashima, J., Galligan, J., & Navazesh, M. (2007). A novel caries risk test. Ann N Y Acad Sci, 1098, 204-15.

26. Dodds, M., Johnson, D., & Yeh, C. (2005). Health benefits of saliva: a review. J Dent , p. 233-33.

27. Doméjean S, White JM, Featherstone JD. Validation of the CDA CAMBRA caries risk assessment--a six-year retrospective study. J Calif Dent Assoc. 2011 Oct;39(10):709-15.

28. Edgar, W., & Higham, S. (1995). Role of saliva in caries models. Adv in Dent Res, 9, 235-245.

29. Elamin A, Garemo M, Gardner A. Dental caries and their association with socioeconomic characteristics, oral hygiene practices and eating habits among

preschool children in Abu Dhabi, United Arab Emirates - the NOPLAS project. BMC Oral Health. 2018 Jun 8;18(1):104.

30. Featherstone JD, Adair SM, Anderson MH, Berkowitz RJ, Bird WF, Crall JJ, *et al*. (2003). Caries management by risk assessment: consensus statement. *J CA Dent Assoc* 31:257-269.

31. Featherstone, J., Domejean-Orliaguet, S., Jenson, L., Wolf, M., & Young, D. (s.d.). Caries Risk Assessment in Practice for Age 6 Through Adult. Journal of the California Dental Association, 35(10), p. 703-12.

32. Gao X, Di Wu I, Lo EC, Chu CH, Hsu CY, Wong MC. Validity of caries risk assessment programmes in preschool children. J Dent. 2013;41:787–95.

33. Gao XL, Hsu CY, Xu Y, Hwarng HB, Loh T, Koh D. Building caries risk assessment models for children. J Dent Res. 2010;89:637–43.

34. Gao XL, Lo ECM, Chu CH, Hsu SC. Caries risk assessment programmes for Hong Kong children. Hong Kong Med J. 2015;21:S42–S6.

35. Giacaman RA, Miranda Reyes P, Bravo Leon V. Caries risk assessment in Chilean adolescents and adults and its association with caries experience. Braz Oral Res. 2013;27:7–13.

36. Harris, R., Gamboa, A., Dailey, Y., & Ashcroft, A. (2012, Mar). One-to-one dietary interventions undertaken in a dental setting to change dietary behavior. Cochrane Database Syst Rev., 14, 3:CD006540. Pub2.

37. Hebbal M, Ankola A, Metgud S. Caries risk profile of 12 year old school children in an Indian city using Cariogram. Med Oral Patol Oral Cir Bucal. 2012;17:e1054–61.

38. Holgerson PL, Twetman S, Stecksen-Blicks C. Validation of an age-modified caries risk assessment program (Cariogram) in preschool children. Acta Odontol Scand. 2009;67:106–12.

39. Holund U, Theilade E, Poulsen S. Validity of a dietary interviewing method for use in caries prevention. Community Dent Oral Epidemiol. 1985; 13: 219-21.

40. Ismail AI, Sohn W, Tellez M, Amaya A, Sen A, Hasson H, Pitts NB. The Inter- national Caries Detection and Assessment System (ICDAS): an integrated system for measuring dental caries. Community Dent Oral Epidemiol. 2007;35(3):170-8.

41. Karjalainen, S. (2007). Eating patterns, diet and dental caries. Dent Update., 34(5), 295-8.

42. Kavvadia K, Agouropoulos A, Gizani S, Papagiannouli L, Twetman S. Caries risk profiles in 2- to 6-year-old Greek children using the Cariogram. Eur J Dent. 2012;6:415–21.

43. Kemparaj U, Chavan S, Shetty NL. Caries risk assessment among school children in davangere city using cariogram. Int J Prev Med. 2014;5:664–71.

44. Konig, K. (1984). Remineralization. Firmenpublikation Elida Cosmetic Ag, ISBN Schweiz 3 9055 2901.

45. Kottner J, Audige L, Brorson S, Donner A, Gajewski BJ, Hróbjartsson A, Roberts C, Shoukri M, Streiner DL. Guidelines for Reporting Reliability and Agreement Studies (GRRAS) were proposed. Int J Nurs Stud. 2011a;48(6):661-71. doi: 10.1016/j.ijnurstu.2011.01.016.

46. Kottner J, Streiner DL. The difference between reliability and agreement. J Clin Epidemiol. 2011b;64(6):701-2; author reply 702. doi: 10.1016/j. jclinepi.2010.12.001.

47. La Placa, M. (2015). Principi di Microbiologia Medica. Napoli: EdiSes.

48. Law, V., Seow, W., & Townsend, G. (2007). Factors influencing oral colonization of mutans streptococci in young children. Aust Dent, 52(2), 93-100.

49. Lee JH, Son HH, Kim HY, Chang J.Caries risk profiles of Korean dental patients using simplified Cariogram models.Acta Odontol Scand.2013;71:899–905.

50. Loe h, silness j. periodontal disease in pregnancy. i. prevalence and severity. acta odontol scand. 1963 Dec;21:533-51.

51. Mejàre et al., Caries risk assessment. A systematic review.: Acta Odontol Scand. 2014 Feb;72(2):81-91.

52. Mejàre, I. (2011). Indica ions or issure sealan s and heir role in children and adolescen s. Dent Update., 38(10), 699-703.

53. Moher D, Liberati A, Tetzlaff J, Altman DG; PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Int J Surg. 2010;8(5):336-41.

54. Moynihan, P., & Petersen, P. (2004). Diet, nutrition and the prevention of dental diseases. Public Health Nutr, 7, 201-226.

55. Naidoo, S., & Myburgh, N. (2007). Nutrition, oral health and the young child. Matern Child Nutr, 3(4), 312-21.

56. Nainar, S., & Mohummed, S. (2004). Diet counselling during the infant oral health visit. Pediatr Dent, 26, 459-462.

57. Parisotto, T., Steiner-Oliveira, C., Silva, C., Rodrigues, L., & Nobre-dos-Santos, M. (2010). Early childhood caries and mutans streptococci: a systematic review. Oral Health Prev Dent, 8(1), 59-70.

58. Peker I, Mangal T, Erten H, Gulcin A, Emre A, Gulcin A. Evaluation of caries risk in a young adult population using a computer-based risk assessment model (Cariogram). J Dent Sci. 2012;7:99–104.

59. Petersson GH, Ericson E, Isberg PE, et al. Caries risk assessment in young adults: a 3-year validation of clinical guidelines used in public dental service. Acta Odontol Scand. 2013;71:1645–50.

60. Petersson GH, Fure S, Bratthall D. Evaluation of a computer-based caries risk assessment program in an elderly group of individuals. Acta Odontol Scand. 2003;61:164–71.

61. Petersson GH, Fure S, Twetman S, Bratthall D. Comparing caries risk factors and risk profiles between children and elderly. Swed Dent J. 2004;28:119–28.

62. Petersson GH, Isberg PE, Twetman S. Caries risk assessment in school children using a reduced Cariogram model without saliva tests. BMC Oral Health. 2010;10:5.

63. Petersson GH, Isberg PE, Twetman S. Caries risk profiles in schoolchildren over 2 years assessed by Cariogram. Int J Paediatr Dent. 2010;20:341–6.

64. Petersson GH, Twetman S, Bratthall D. Evaluation of a computer program for caries risk assessment in schoolchildren. Caries Res. 2002;36:327–40.

65. Poureslami, H., & Van Amerongen, W. (2009). Early Childhood Caries (ECC): an infectious transmissible oral disease. Indian J Pediatr., 76(2), 191-4. (2017). PreViser OHIS User Documentation.

66. Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies Available from: (https://www.nhlbi.nih.gov/health-pro/guidelines/indevelop/cardiovascular-risk-reduction/tools/cohort)

67. Ruiz Miravet A, Montiel Company JM, Almerich Silla JM. Evaluation of caries risk in a young adult population. Med Oral Patol Oral Cir Bucal. 2007;12:E412–8.

68. Silness j, loe h. periodontal disease in pregnancy. ii. correlation between oral hygiene and periodontal condtion. acta odontol scand. 1964 feb;22:121-35.

69. Sonbul H, Al-Otaibi M, Birkhed D. Risk profile of adults with several dental restorations using the Cariogram model. Acta Odontol Scand. 2008;66:351–7.

70. Steyn, N., & Temple, N. (2012). Evidence to support a food-based dietary guideline on sugar consumption in South Africa. BMC Public Health, 12, 502.

71. Strohmenger, L., Cagetti, M., Campus, G., Comaita, F., Corsello, G., De Giglio, G., . . . Polimeni, A. (2013). Linee guida nazionali per la promozione della salute orale e la prevenzione delle patologie orali in età evolutiva. Ministero della salute.

72. Sudjalim, Woods, & Manton, Prevention of white spot lesions in orthodontic practice: a contemporary review. Aust Dent J. 2006 Dec;51(4):284-9; quiz 347.

73. Sundell AL, Ullbro C, Marcusson A, Twetman S. Comparing caries risk profiles between 5- and 10- year-old children with cleft lip and/or palate and non-cleft controls. BMC Oral Health. 2015;15:85.

74. Swets JA, Pickett RM. Evaluation of diagnostic systems: methods from signal detection theory. New York, USA: Academic Press; 1982.

75. Taji, S., Savage, N., Holcombe, T., Khan, F., & Seow, W. (2011). Congenital aplasia of the major salivary glands: literature review and case report. Pediatr Dent., 33(2), 113-8.

76. Tellez et al., Evidence on existing caries risk assessment systems: are they predictive of future caries?; Community Dent Oral Epidemiol. 2013 Feb;41(1):67-78. doi: 10.1111/cdoe.12003.

77. Twetman S, Petersson GH, Bratthall D. Caries risk assessment as a predictor of metabolic control in young type 1 diabetics. Diabet Med. 2005;22:312–5.

78. Twetman, Caries risk assessment in children: how accurate are we? Eur Arch Paediatr Dent. 2016 Feb;17(1):27-32.

79. U.S. National Library of Medicine, National Center for Biotechnology Information. Bethesda: (cited April 30th, 2017b). Available from: gov.proxy.mah.se/mesh/?term=relative+risk.

80. Vadiakas, G. (2008). Case definition, aetiology and risk assessment of early childhood caries (ECC): a revisited review. Eur Arch Paediatr Dent, 9(3), 114-25.

81. Valletta, G. (1977) Clinica odontostomatologica. Editrice medica salernitana.

82. Van Loveren C, Helderman WH. Identi cation of caries risk patients. An overview of predictive models. Ned Tijdschr Tandheelkd.2003;110: 435-8.

83. Viechtbauer W, Smits L, Kotz D, Budé L, Spigt M, Serroyen J, Crutzen R. A simple formula for the calculation of sample size in pilot studies, J Clin Epidemiol. 2015 Nov;68(11):1375-9.

84. WHO, World Health Organization, report. Oral health: action plan for promotion and integrated disease prevention. Executive board 120th session, provisional agenda item 4.6. EB120/10, 2007 (cited April 30, 2017). Available from: http://apps.who.int/iris/handle/10665/21909.

85. WHO, World Health Organization. Health Surveys. Basic Methods. 4th edn. Geneva: World Health Organization. 1997.

86. WHO, World Health Organization. Oral health information systems. Oral health surveillance. 2017 (cited April 30, 2017) Available at: http://www. who.int/oral_health/action/information/surveillance/en/.

87. Young D, Ricks CS, Changing the face and practice of dentistry: a 10-year plan. J Calif Dent Assoc. 2011 Oct;39(10):746-51.

88. Young, D., Featherstone, J., Roth, J., Anderson, M., Autio-Gold, J., Christensen, G., . . . Wolff, M. (2007). Caries management by risk assessment: implementation guidelines. J Calif Dent Assoc., 35(11), p. 799-805.

89. Zambon, J., & Kasprzak, S. (1955). The microbiology and histopathology of human root caries. Am J of Dent, 8, 323-328.

90. Zukanovic A. Caries risk assessment models in caries prediction. Acta Med Acad. 2013;42:198–208.

PAPER I

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RESEARCH ARTICLE Open Access

Are standardized caries risk assessment models effective in assessing actual caries status and future caries increment? A systematic review

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Abstract

Background: Assessing caries risk is an essential element in the planning of preventive and therapeutic strategies. Different caries risk assessment (CRA) models have been proposed for the identification of individuals running a risk of future caries. This systematic review was designed to evaluate whether standardized caries risk assessment (CRA) models are able to evaluate the risk according to the actual caries status and/or the future caries increment.

Methods: Randomized clinical trials, cross-sectional studies, cohort studies, comparative studies, validation studies and evaluation studies, reporting caries risk assessment using standardized models (Cariogram, CAMBRA, PreViser, NUS-CRA and CAT) in patients of any age related to caries data recorded by DMFT/S or ICDAS indices, were included. PubMed, Scopus and Embase were searched from 2000 to 2016. A search string was developed. All the papers meeting the inclusion criteria were subjected to a quality assessment.

Results: One thousand three-undred ninety-two papers were identified and 32 were included. In all but one, the Cariogram was used both as sole model or in conjunction with other models. All the papers on children ($n = 16$) and adults ($n = 12$) found a statistically significant association between the risk levels and the actual caries status and/or the future caries increment. Nineteen papers, all using the Cariogram except one, were classified as being of good quality. Three of four papers comprising children and adults found a positive association. For seven of the included papers, Cariogram sensibility and specificity were calculated; sensibility ranged from low (41.0) to fairly low (75.0), while specificity was higher, ranging from 65.8 to 88.0. Wide 95% confidence intervals for both parameters were found, indicating that the reliability of the model differed in different caries risk levels.

Conclusions: The scientific evidence relating to standardized CRA models is still limited; even if Cariogram was tested in children and adults in few studies of good quality, no sufficient evidence is available to affirm the method is effective in caries assessment and prediction. New options of diagnosis, prognosis and therapy are now available to dentists but the validity of standardized CRA models still remains limited.

Keywords: Dental caries, Dental caries susceptibility, Dental health surveys, Risk assessment, Review

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Background

Different caries risk assessment (CRA) models have been proposed for the identification of individuals running a risk of future caries [1–7].

Caries is a multifactorial disease resulting from a series of events occurring in a chain that lasts for years where clinical, microbiological, behavioral and social factors are involved in the process. In view of its multifactorial nature, a multivariate approach is necessary [8]. The scientific basis for caries risk assessment, prevention and treatment on an individual patient basis requires incessant development, specification and continuing validation [9]. Scientific evidence proving CRA methods' validity is limited [3]. Past caries experience is regarded as the single most powerful caries predictor in all age groups [4–7, 10]. Different measures of past caries experience are often included in analytical models of multi-risk studies. Nevertheless, there are consequences of including past caries experience measures for both prediction and multi-risk models since this parameter will hide the effects of weaker indicators of high risk individuals or of other caries risk-factors [11].

Caries risk assessment still has great potential to enhance patient care as it is the corner stone of a minimal invasive care plan, allowing the determination of the appropriate non-invasive as well as invasive interventions and recall strategies [12], but still today, a great need to standardize study design, outcome measures and reporting of data in studies on CRA is required [13].

Standardized models including different combinations of risk and protective factors (Table 1) have been developed from the 2000s onwards to predict caries; they can be summarized in two main categories, those using an algorithm with a software program and those using standardized questionnaires (self-submitted and/or through an interview). Moreover, CRA methods could be used as an effective health-education tool to change the attitudes and behaviors of patients/parents/caregivers towards good oral hygiene and dietary habits maintenance [14].

Nowadays, no systematic reviews are available on the performances of standardized models. Recent reviews have attempted to assess the validity of different caries risk assessment models/factors [3, 10, 13]. Two reviews combined single clinical parameters and standardized

Table 1 Different factors included in each standardized Caries Risk Model

Factors	Software programs			American Dental Association models		
	NUS-CRA 11 factors	Cariogram 9 factors	PreViser 11 factors	ADA 11 factors	CAMBRA 14 factors	CAT 12 factors
Socio-demographic						
Age	X		X			
Ethnicity	X					
Family socioeconomic status	X			X	X	X
Behavioural						
Infant feeding history	X				X	
Diet	X	X	X	X	X	X
Fluoride	X	X	X	X	X	X
Dental attendance			X	X	X	X
Clinical						
Oral hygiene	X	X	X	X	X	X
Past caries	X	X	X	X	X	X
White spot lesions				X	X	X
Enamel defects						X
Dental appliance			X	X	X	X
Systemic health	X	X	X	X	X	X
Medication				X	X	
Salivary and microbiological						
Saliva flow rate		X	X	X	X	X
Saliva buffering capacity		X				
Mutans streptococci	X	X	X		X	X
Lactobacilli	X	X	X		X	

NusCra National University of Singapore Caries Risk Assessment, *CAMBRA* Caries Management By Risk Assessment, *ADA* caries risk assessment by American Dental Association, *CAT* America Academy of Pediatric Dentistry's Caries Assessment Tool caries risk assessment models [3, 13]. The only externally validated model was the Cariogram [13]; the accuracy of the standardized model was found to be limited in pre-school children, based on two papers [15, 16]. The search literature contained a time frame from 1966 to 2006 with a refresh in 2011, so the most recent papers were not included in the review. Otherwise, Tellez et al. [3] aimed to appraise the evidence in caries prediction of two standardized CRA models, Cariogram, and Caries Management by Risk Assessment (CAMBRA), and two guidelines of the American Dental Association (ADA) and the American Academy of Pediatric Dentistry (AAPD), taking into account six longitudinal studies. In this review, the literature search was also stopped in 2011. Senneby et al. [13] evaluated the association between previous caries experience, microbiological tests, buffering capacity, salivary flow rate, oral hygiene, dietary habits, socio-demographic variables and the future caries lesion development. The evidence was considered of low quality and was lacking in regards to the studied methods. The literature search was stopped in January 2015.

Starting from these premises, this review aimed to evaluate the current literature on standardized CRA models, verifying whether the risk level measured using different tools is associated with the actual caries status and/or the future caries increment.

Methods

This systematic review was conducted and reported following the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA Statement) checklist.

Protocol and registration

The review method and planning were registered at Prospero (PROSPERO 2016:CRD42016038590).

Eligibility criteria

Randomized controlled trial (RCT), cross-sectional studies, cohort studies, comparative studies, validation studies and evaluation studies, reporting CRA using standardized models in patients of any age related to caries data recorded by Decayed, Missing, Filled Tooth/Surface (DMFT/S) or the International Caries Detection and Assessment System (ICDAS) indices were included. Only papers in English published from the 1st of January 2000 to the 31st of December 2017 were collected. This time frame was chosen since no standardized CRA tools were studied before the year 2000 as emerged from a first evaluation made by two authors (GC and MGC).

Information sources and search strategy

Three different electronic databases were searched: PubMed, Scopus® and Embase®. Two search strategies were used; the first included a combination of MeSH terms and key words: caries risk assessment, caries risk assessment models, caries risk assessment tools, caries risk epidemiology, caries risk profile, Cariogram, CAMBRA, PreViser, NUS-CRA, ADA caries risk assessment, CAT caries risk assessment, AAPD caries risk assessment and dental caries susceptibility. The second strategy included the search string "((dentistry) OR (dental caries) OR (caries)) AND ((caries risk assessment) OR (Cariogram) OR (CAMBRA) OR (AAPD) OR (CAT) OR (ADA) OR (nuscra) OR (NUS-CRA) OR (PreViser)) AND ((cross-sectional studies) OR (cohort analysis risk) OR (cohort studies) OR (clinical trial) OR (clinical study) OR (controlled clinical trial) OR (observational study))".

Study selection

Repeated papers were deleted after comparing the results from the two different search strategies using the three databases. Two authors (GB and MGC) independently examined all the abstracts of the papers (see Additional file 1 for the whole list). All the papers meeting the inclusion criteria were obtained in the full-text format. The two authors independently assessed the papers to establish whether each paper should or should not be included in the systematic review (see Additional file 2 for the list of the papers excluded at this stage).

Data collection

Data collection was carried out using an ad hoc designed data extraction form without masking journal title or authors. Data were extracted by two authors (MGC, GC) independently. For each paper the following data were searched and recorded when available: a) the year of publication and duration of the study; b) details of the participants including sample size at baseline, age and country of origin; c) caries data including actual caries status, caries experience and caries increment measured through DMFT/S or dmft/s or ICDAS; d) Caries risk assessment including standardized model used and categorization of the risk levels; e) sensibility and specificity of the CRA model.

Row data were requested to authors of longitudinal studies to perform data synthesis and analysis.

Assessment of risk of bias and risk of bias across studies

The risk of bias assessment was conducted by two authors (GC and MGC). The methodological quality of the included studies was scored according to the customized quality assessment tool developed by the National Heart, Lung, and Blood Institute and Research Triangle Institute International for Observational Cohort and Cross-Sectional Studies since, as reported in the result section no RCTs were obtain after studies' selection [17] (see Additional file 3 for quality assessment of included studies). Disagreements between authors were resolved by discussion. Where this was not possible, other authors were consulted (PL).

Synthesis of the results

To facilitate a comparison of the results from different studies, the caries values were organized in two-by-two tables. Based on these tables, sensitivity and specificity were calculated, along with the corresponding 95% confidence intervals.

Results

This review provides a concise description of the findings of the included papers, structured around the association between the standardized CRA models, performed on children and/or adults, and the actual or the predicted caries status.

The search identified 3326 papers; after removing duplicates, 1934 papers were selected and, after reviewing titles, abstracts and texts, 32 papers were finally included: 16 on children, 12 on adults and 4 on both, 3 of which considered children and adults as a single sample and one as two different samples (Fig. 1). In order to record caries status (experience/prevalence/incidence), 9 papers used DMFT index or sub-components, 13 papers used DMFS index or sub-components and only 1 used the ICDAS. Four papers focused on primary teeth, 24 on permanent teeth and 4 on both dentitions. The majority of papers ($n = 31$) estimated the caries risk using the Cariogram as a single model or in comparison with other models. No RCTs were included in the systematic review. All the considered longitudinal papers were comparative studies or validation studies or retrospective cohort studies or, finally, evaluation studies. All the included papers along with the quality assessment grade are reported in Table 2. Nineteen papers were classified as being of good quality, 9 papers of fair quality and only 4 of low quality.

Association between caries risk level and actual caries status in children

Two papers [18, 19] evaluated the association between caries prevalence (DMFS) and Cariogram 9 factors (hereinafter named Full Cariogram) in orthodontic patients. The low caries group at baseline displayed a statistically significant difference regarding caries increment and Cariogram level. Neither DMFT nor the number of caries lesions differed significantly in the Cariogram's risk categories (7 factors) in a sample of Chilean subjects [20]. Children with a cleft lip and/or palate and non-cleft controls classified in the Cariogram high-risk category had a higher caries experience [21]. A significant linear regression between mean dmft and caries risk categories assessed according to a form based on the Cariogram was found in children from low-income families ($p < 0.01$) [22]. A statistically significant association between caries experience and Cariogram categories was found ($p < 0.01$) in Indian children [23]. Caries experience and the presence of white spot lesions were statistically significantly associated with Cariogram categories in Greek pre-school

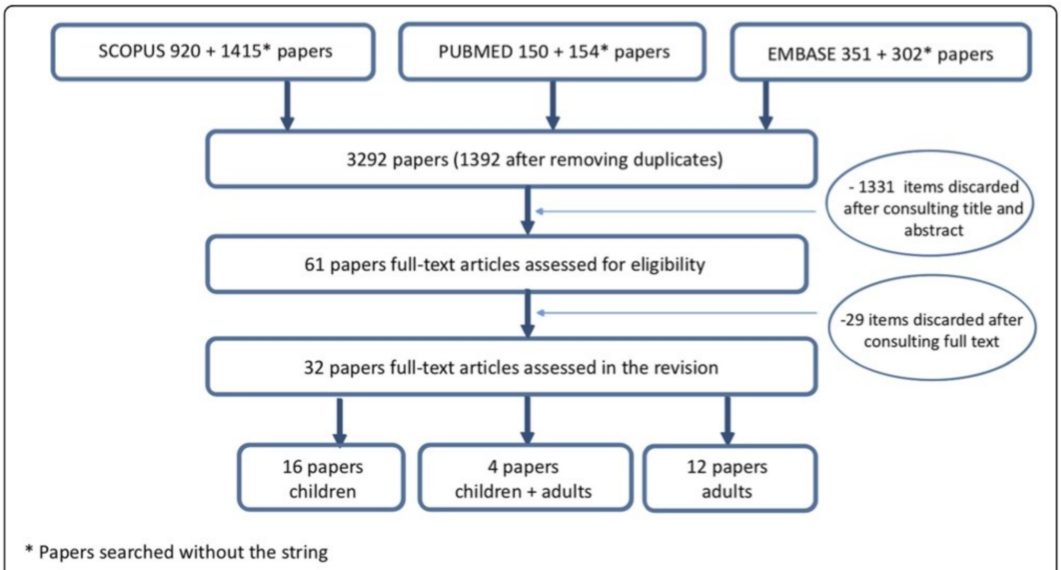

Fig. 1 Flow chart of the study

Table 2 Papers included. Association between standardized CRA and actual caries status and/or caries prediction

Authors (year)	Outcome	Subjects	Indices	Caries risk model	Statistical significance	Quality assessment
Children/Adolescents						
Gao[b], (2015) [8]	CI	544	dmft	Full Cariogram, CAT, CAMBRA, NUS-CRA	+	Good
Sundel, (2015) [21]	ACS	133	dmfs/DMFS	Full Cariogram	+	Good
Cabral, (2014) [22]	ACS	150	dmft/DMFT	Form based on Cariogram 7 factors	++	Poor
Kemparaj, (2014) [37]	CI	200	DMFT/S	Full Cariogram	+	Poor
Gao[b], (2013) [36]	CI	544	dmft	Full Cariogram, CAT, CAMBRA, NUS-CRA	+	Good
Zukanovich, (2013) [41]	CI	109	DMFS/DMFT	Full Cariogram, PreViser, CAT	+	Fair
Campus, (2012) [35]	CI	957	DFS	Cariogram 7 factors	+	Good
Hebbal, (2012) [23]	ACS	100	DMFT	Full Cariogram	++	Poor
Kavvadia, (2012) [24]	ACS	814	dmft	Full Cariogram	+	Fair
Gao, (2010) [16]	CI	1576	dmft	Full Cariogram	[e]	Good
Petersson[c],(2010b) [39]	CI	392	DMFS	Full Cariogram, Cariogram 6 factors	+	Good
Petersson, (2010a) [40]	CI	392	DMFS	Full Cariogram	+	Good
Campus, (2009) [25]	ACS	957	dmfs/DMFS	Cariogram 7 factors	++	Good
Holgerson, (2009) [15]	CI	125	dmfs/DMFS	Full Cariogram	+	Fair
Twetman, (2005) [33]	CI	64	DFS	Full Cariogram	++	Good
Petersson[a,b], (2004) [34]	CI	446	DFS	Full Cariogram	++	Good
Petersson[b], (2002) [32]	CI	446	DMFT/S	Full Cariogram	+	Good
Adults						
Petersson, (2015) [44]	CI	1295	DFT/DFTS	Full Cariogram	++	Good
Carta, (2015) [31]	ACS	480	ICDAS	Full Cariogram	++	Good
Chaffee, (2015) [45]	CI	4468	DFS	CAMBRA	+	Good
Chang (2014) [30]	CI	110	DMFT/S	Cariogram 7 factors	+	Good
Chang and Kim, (2014) [42]	ACS	102	DMFT	Full Cariogram	+	Good
Lee, (2013) [29]	ACS	80	DMFT	Full Cariogram, Cariogram 7/8 factors	+	Fair
Petersson, (2013) [7]	ACS	1295	DFT/S	Cariogram 8 factors	++	Good
Celik, (2012) [43]	CI	100	DMFT/S	Full Cariogram	+	Fair
Peker, (2012) [27]	ACS	90	DMFT/S	Full Cariogram	+	Fair
Sonbul, (2008) [28]	ACS	175	DMFS	Full Cariogram	+	Good
Ruiz Miravet, (2007) [26]	ACS	48	DMFT/S	Full Cariogram	++	Poor
Petersson[a,d], (2004) [34]	CI	208	DFS	Full Cariogram	++	Fair
Petersson[d], (2003) [1]	CI	208	DMFS /DFS/DFRS	Full Cariogram	++	Good
Both Children/Adults						
Giacaman, (2013) [20]	ACS	180	DMFT	Cariogram 7 factors	–	Poor
Almosa, (2012) [18]	ACS	89	DMFS	Full Cariogram	++	Fair
Al Mulla, (2009) [19]	ACS	100	DFS	Full Cariogram	++	Fair

ACS actual caries status, *CI* Caries Increment. Subjects: number of subjects at baseline
Statistical significance: - = $p > 0.05$ + = $p < 0.05$; ++ = $p \leq 0.01$
[a]Petersson, (2004) reported in both children and adults and describes data in two different samples
[b]Gao, (2013) and (2015), and Petersson, (2002) and (2004) respectively reported data for the same sample of children
[c]Petersson, (2010a) and (2010b) reported data for the same sample of children
[d]Petersson, (2003) and (2004) reported data for the same sample of elderly people
[e]Data not obtainable from the paper

children ($p < 0.01$) [24]. A significant linear trend between the five Cariogram categories and dmfs/DMFS scores was observed ($p < 0.01$) in Italian children [25].

Association between caries risk level and actual caries status in adults

Several papers focused on young adults and all of them reported an association between Cariogram categories and caries prevalence/experience/severity [7, 26, 27]. In Saudi Arabia [28], the mean caries prevalence in the high-risk group differed significantly from that recorded in the low-risk group ($p < 0.05$). A caries profile obtained from the Cariogram, including 7 and 8 factors, was compared to the Full Cariogram and correlated to caries experience: all models measured statistically significant associated risk levels to the caries experience [29]. The chance of avoiding caries was statistically significantly associated ($p < 0.01$) to the caries experience in a group of Korean adults [30]. Caries at ICDAS levels 5–6 and the presence of more than five missing teeth were statistically significant associated to the Cariogram scores (OR = 2.36, 95%CI = 1.83–3.03 and OR = 1.43, 95%CI = 1.13–1.82 respectively) in Italian adults [31].

Association between caries risk level and caries increment in children and adults

A total of 17 longitudinal papers investigated the validity of standardized CRA models to predict new caries lesions (Table 3). Twelve papers regarding children were included [15, 16, 32–41], nine of which used the Cariogram model and three compared different CRA models, including the Cariogram [36, 38, 41]. Six papers regarding adults were included, five of which used the Cariogram [1, 34, 42–44] and one the CAMBRA model [45].

In a two-year prospective study [32] subjects in the highest risk group developed a mean of about 10 times more caries lesions (DMFS) than the lowest risk group. The same authors compared [34] data from the previous study with those recorded in a group of adults/elderly people, showing a higher mean of caries increment per year for high-risk groups. The caries increment in children affected by Type 1 diabetes mellitus (ΔDMFS) was about eight times higher in the Cariogram highest risk category [33]. After five years from baseline, children classified at high risk (Full Cariogram) developed about four times more caries lesions [15] (study not included in Table 3). Five times more caries lesions were found in schoolchildren assessed by the Full Cariogram as running the highest risk compared with those with the lowest risk [40]. On the same sample, two different Cariogram models with and without saliva factors were tested. Both models revealed a statistically significant relationship with caries development ($p < 0.05$) at the two-year follow-up [39]. A prospective study (not included in Table 3) was conducted on preschool children with different risk assessment models, including the Full Cariogram [16]. One year after baseline the model showed a sensitivity/specificity lower values than the biopsychosocial models proposed by the authors. In Italian schoolchildren, the caries risk was assessed (7-factor Cariogram) and 2 years later the children classified as high risk developed caries lesions about as twice as much as those developed by children classified as low risk [35]. Full Cariogram, Previser and the Caries-risk Assessment Tool (CAT) were compared in children [41]. At the follow-up examination (3 years), only the Cariogram model successfully predicted new caries lesions. Full Cariogram, NUS-CRA, CAT and CAMBRA were assessed on preschool children [36]. After 1 year, using CAT and CAMBRA, the majority of children were considered to be at high risk, while, using the Full Cariogram and the National University of Singapore Caries Risk Assessment (NUS-CRA), almost 2/3 of the children were defined as very low or low risk. The CRA was evaluated in a sample of 12-year-old children using the Full Cariogram and dividing them into five groups of risk [37]. Two years later, children classified as very high risk at baseline developed about thirty times more caries lesions compared to children classified as very low risk. The same sample of three-year-old children from a previous study [36] was re-evaluated 18 months from baseline ($n = 462$) using the same risk assessment model; a gradient in caries increment from lower to higher risk groups was found using all programs [38].

Full Cariogram was evaluated in elderly people and, after 5 years, subjects with the highest risk profile had about three times more caries lesions compared to the lowest risk group [1]. Full Cariogram was assessed in two samples of young adults [43, 44]; after 2 years, subjects classified at very high risk at baseline developed caries lesions about as twice as much as those classified at very low risk; at the 3 year follow-up of the second sample [44], subjects with the highest risk profile had about seven times more caries lesions compared to those in the lowest risk group. The CAMBRA model was used to split a sample of young adults into four risk groups [45]; caries increment was more than three times higher in subjects classified as high risk than those classified at low risk.

Few of the included papers report data allowing the authors to calculate sensibility and specificity of the CRA models [15, 16, 32, 33, 35, 36, 44]. In Table 4 the available data for the Cariogram model are displayed. Sensibility values ranged from low (41.0) [32] to fairly low (52.0) [35], while specificity values were quite high, ranging from 71.0 [33] to 88.0 [15]. Moreover, wide Confidences Intervals are reported for both parameters, indicating that the reliability of the model differs in the different caries risk levels.

Table 3 Association between caries increment and caries risk model categories in longitudinal papers

Authors (year)	Age	Study time (years)	Subjects	Caries increments	Range Mean (Standard Deviation)				
				Cariogram	**0–20**	**21–40**	**41–60**	**61–80**	**81–100**
Gao (2013) [36]	C	1	485	dmft	2.67 (2.96)	2.02 (1.71)	1.56 (1.63)	0.77 (1.21)	0.34 (0.88)
Kemparaj (2014) [37]	C	2	200	DMFT	0.54 (1.2)	0.43 (1.32)	0.39 (1.04)	0.34 (0.80)	0.06 (0.09)
				DMFS	0.79 (1.73)	0.73 (1.55)	0.48 (1.72)	0.39 (1.20)	0.09 (1.12)
Celik (2012) [43]	A	2	100	DMFT	1.23 (0.86)	0.65 (0.81)	0.39 (1.02)	0.08 (0.28)	0 (0)
				DMFS	1.23 (0.86)	0.9 (0.97)	0.48 (1.6)	0.08 (0.28)	0 (0)
Petersson (2002) [32]	C	2	392	DMFT	1.67 (1.44)	1.46 (2.20)	1.07 (1.36)	0.42 (0.90)	0.23 (0.61)
				DMFS	2.58 (1.83)	2.62 (4.11)	1.47 (1.81)	0.53 (1.24)	0.27 (0.70)
Petersson (2015) [44]	A	3	982	DFT	1.00 (1.40)	0.84 (0.95)	0.82 (1.18)	0.53 (1.07)	0.24 (0.58)
Petersson (2010a) [40]	C	2	392	DMFS	3.00 (a)	2.70 (a)	1.50 (a)	0.50 (a)	0.20 (a)
				DFS	1.99 (3.00)	1.7 (1.76)	1.59 (2.55)	0.85 (1.91)	0.29 (0.89)
Petersson (2004)[b] [34]	C	2	392	DFS	1.30 (a)	1.30 (a)	0.70 (a)	0.30 (a)	0.10 (a)
	A	5	148	DFS	1.90 (a)	1.00 (a)	1.20 (a)	0.40 (a)	0 (a)
Campus (2012) [35]	C	2	861	DS	1.20 (a)	1.20 (a)	0.10 (a)	0.20 (a)	0.10 (a)
				Cariogram	**0–20**	**21–40**	**41–60**	**61–100**	
Chang and Kim (2014) [42]	C	1.3	64	DMFT	2.97 (5.2)	1.28 (1.5)	1.36 (2.2)	0.44 (0.7)	
				DMFS	5.81 (11.97)	1.28 (1.5)	3.27 (6.8)	0.44 (0.7)	
Petersson (2003) [1]	A	5		DMFS	16.21 (15.97)	7.36 (9.34)	7.96 (9.52)	5.23 (6.97)	
				Cariogram	**0–25**	**26–50**	**51–75**	**76–100**	
Twetman (2005) [33]	C	3	64	DFS	8 (10.8)	3.4 (2.6)	2.6 (3.7)	0 (0)	
				Cariogram	**0–20**		**21–80**	**81–100**	
Zukanovic (2013) [41]	C	3	70	DMFT	1.80 (1.79)		2.40 (2.36)	1.77 (1.88)	
				DMFS	5.00 (7.07)		4.71 (4.34)	2.54 (2.44)	
				Cariogram	**0–40**			**41–100**	
Holgerson (2009) [15]	C	5	125	dmfs/DMFS	2.40 (3.2)			0.10 (0.4)	
				Cambra	**High**		**Moderate**	**Low**	
Gao (2013) [36]	C	1	485	dmft	1.24 (1.58)		0.27 (0.68)	0.20 (0.76)	
Chaffee (2015) [45]	A	1.5	4468	DFT	1.74 (a)		1.16 (a)	1.01 (a)	
				CAT	**High**		**Moderate**	**Low**	
Gao (2013) [36]	C	1	485	dmft	0.79 (1.31)		0.08 (0.28)	0 (0)	
Zukanovic (2013) [41]	C	3	70	DMFT	2.19 (2.33)		2.60 (1.82)	2.38 (1.92)	
				DMFS	4.54 (4.41)		3.80 (5.81)	3.13 (2.53)	
				NUS-CRA	**Very High**	**High**	**Moderate**	**Low**	**Very Low**
Gao (2013) [36]	C	1	485	dmft	2.18 (1.87)	2.10 (1.63)	1.26 (1.38)	0.85 (1.11)	0.17 (0.69)
				PreViser	**High**		**Moderate**	**Low**	
Zukanovic (2013) [41]	C	3	70	DMFT	2.35 (2.27)		1.92 (2.18)	2.18 (2.32)	
				DMFS	5.04 (4.75)		3.08 (2.87)	2.82 (3.19)	

A Adults, *C* Children
(a) indicates that Standard Deviation data were not described in the paper. The decimal places reported are those reported in each paper
Petersson, (2004)[b] reports the increment for year of observation. Holgerson, (2009) and Petersson, (2010b) were excluded from the table since as no mean data for caries were present. Gao (2015) was excluded from the table as the data are the same as those reported for Gao, (2013)

In brief, the results of the present review show: all the included papers on children showed a statistically significant association between the risk levels and the actual caries status and/or the future increment. More than half of these papers, including the Cariogram model, were classified as being of good quality. The same positive association between the risk levels and the actual caries status and/or the future increment was reported in the included papers on adults. More than half of the papers were classified as being of good quality and all

Table 4 Sensitivity and specificity of the Cariogram model in children and adults

Authors (year)	Number of factors	Sample n	Age at baseline (years)	Sensibility % (95% Confidence Interval)	Specificity % (95% Confidence Interval)
Children					
Gao (2013) [36]	Full	485	3	66.4[a]	78.5[a]
Campus (2012) [35]	7	861	7–9	52.0 (18.6–94.6)	79.5 (99.2–54.7)
Gao (2010) [16]	Full	1782	3–6	70.5[a]	65.8[a]
Holgerson[b] (2009) [15]	Full	66[b]	2	46.0 (31.0–62.0)	88.0 (71.0–104.0)
Twetman (2005) [33]	Full	64	8–16	75.0[a]	71.0[a]
Petersson (2002) [32]	Full	392	10–11	41.0 (9.0–73.0)	79.8 (99.6–60.0)
Adults					
Petersson (2015) [44]	Full	1295	19	47.0 (11.9–89.2)	72.5 (33.5–94.8)

[a]Range not available
[b]Control group only

except one used the Cariogram. Three of four papers comprising children and adults found a positive association between the risk levels and the actual caries status and/or the future increment.

Discussion

Determining the validity of different caries risk assessment models to fit the actual caries status, analyzing cross-sectional papers, and to predict new caries lesions in the near future, analyzing longitudinal papers, was the aim of this systematic review. The CRA models that were examined were the reasoning-based (CAT, CAMBRA and ADA model) and algorithm-driven (Cariogram, NUS-CRA and PreViser).

The findings described enable to draw some conclusions.

All papers involving children [15, 16, 21–25, 32–41] assessed a statistically significant association between the risk level measured by the CRA model and the actual caries status or the caries increment in a follow-up examination. Eleven papers [16, 21, 25, 32–36, 38–40] of seventeen were classified as being of good quality, and all of them used the Cariogram as sole model or in conjunction with other models. Sensibility and specificity of the Cariogram model were evaluated in six papers [15, 16, 32, 33, 35, 36] and data showed that the model is not accurate in predicting caries lesion development. Furthermore, the validity of the Cariogram to evaluate the caries risk might be flawed: four papers [32, 34, 39, 40] involved the same population.

Papers carried out on adult populations [1, 7, 26–31, 34, 42–45] showed a positive association between the CRA model and caries data. Eight papers [1, 7, 28, 30, 31, 42, 44, 45] of thirteen were classified as being of good quality and all except one [45] used the Cariogram model. Sensibility and specificity of the Cariogram model were reported in one paper [44]; data confirm the low accuracy of the model. Within the three papers [18–20] involving both children and adults regarded as a single sample, two found a positive association between risk level and caries status and one [20] failed to find such an association. This last paper was evaluated as being of poor quality.

Different Cariogram models using from nine to seven factors were used. The excluded factors were salivary parameters, namely mutans streptococci, lactobacilli, salivary secretion rate and buffer capacity. Reduced Cariogram versions were statistically significant associated to caries data, in both cross-sectional and longitudinal papers [7, 21, 29, 30, 35], except for one paper [20].

Only three papers, two of good quality (reporting data on the same sample) [36, 38] and one fair, compared different risk models [41]: the Full Cariogram, CAT, CAMBRA and NUS-CRA were compared in two and the Full Cariogram, PreViser and CAT in the third one. The results showed that different CRA models assessed the risk differently, but, due to the small amount of available data, it is not possible to draw clear conclusions about the most effective method for predicting caries lesions.

The main limitation of this review is that the included papers do not form a homogeneous group and original databases are not available making it impossible to perform a meta-analysis. Different study populations (adults or children), different versions of the same standardized CRA model (Cariogram from seven to nine parameters), different indices used to measure carious lesions (dmfs/t, DMFS/T, DFS/T, DS, ICDAS) make the comparison of papers questionable and hamper the synthesis of results. This limitation cannot be overcome until papers with a standardized study design, outcome measurements and reporting of data will be carried out.

At present, only the Cariogram was used in papers of good quality to assess its efficacy in predicting caries development, while, for the other standardized CRA models, the lack of papers does not make it possible to draw conclusions on their effectiveness.

Conclusions

The evidence relating to the quality of existing CRA models in assessing and predicting caries lesions is limited; even if Cariogram was used in few studies of good quality carried out in children and adults, no sufficient evidence is available to affirm that the method is effective in caries assessment and prediction. The Full Cariogram and reduced versions, eight or seven factors, appear to produce similar results. Although other CRA models, such as CAT, CAMBRA, NUS-CRA and PreViser, might be effective in clinical settings, the scientific evidence to date is limited.

Additional files

Additional file 1: List of papers excluded in the first selection (XLSX 54 kb)
Additional file 2: List of papers excluded in the second selection (XLSX 11 kb)
Additional file 3: Quality assessment (XLSX 13 kb)

Abbreviations

AAPD: American academy of pediatric dentistry; ADA: American dental association; CAMBRA: Caries management by risk assessment; CAT: Caries risk-assessment tool; CRA: Caries risk assessment; DMFT/S: Decayed missed filled tooth/surface; ICDAS: International caries detection and assessment system; NUS-CRA: National university of singapore- caries risk assessment; PRISMA: Preferred reporting items for systematic reviews and meta-analyses; RCT: Randomized clinical trial

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Availability of data and materials

All data generated or analysed during this study are included in this published article (and its additional files).

Authors' contributions

MGC: selected the papers, performed the papers validity assessment and drafting the manuscript; GB: performed the search and selected the papers; FC: realized tables and figure and contributed to write the manuscript; PL: performed the final revision of the paper; LS: designed the paper; GC: was consulted in case of discussion between the examiners of the validity assessment and contributed to write the paper. All authors read and approved the final version of the manuscript.

Ethics approval and consent to participate

Not applicable as this paper is a systematic review.

Consent for publication

Not applicable.

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References

1. Petersson GH, Fure S, Bratthall D. Evaluation of a computer-based caries risk assessment program in an elderly group of individuals. Acta Odontol Scand. 2003;61:164–71.
2. Trottini M, Bossu M, Corridore D, Ierardo G, Luzzi V, Saccucci M, Polimeni A. Assessing risk factors for dental caries: a statistical modeling approach. Caries Res. 2015;49:226–35.
3. Tellez M, Gomez J, Pretty I, Ellwood R, Ismail AI. Evidence on existing caries risk assessment systems: are they predictive of future caries? Community Dent Oral Epidemiol. 2013;41:67–78.
4. Senneby A, Mejare I, Sahlin NE, Svensäter G, Rohlin M. Diagnostic accuracy of different caries risk assessment methods. A systematic review. J Dent. 2015;43:1385–93.
5. Zhang Q, van Palenstein Helderman WH. Caries experience variables as indicators in caries risk assessment in 6-7-year-old Chinese children. J Dent. 2006;34:676–81.
6. Du Q, Yu M, Li Y, Du H, Gao W, Mei H, et al. Permanent caries experience is associated with primary caries experience: a 7-year longitudinal study in China. Community Dent Oral Epidemiol. 2016;45:43–8.
7. Petersson GH, Ericson E, Isberg PE, et al. Caries risk assessment in young adults: a 3-year validation of clinical guidelines used in public dental service. Acta Odontol Scand. 2013;71:1645–50.
8. Arrica M, Carta G, Cocco F, et al. Does a social/behavioural gradient in dental health exist among adults? A cross-sectional study. J Int Med Res. 2017;45:451–61.
9. American Dental Association. Caries diagnosis and risk assessment. A review of preventive strategies and management. J Am Dent Assoc. 1995;126:1s–24s.
10. Mejare I, Axelsson S, Dahlen G, Espelid I, Norlund A, Tranæus S, et al. Caries risk assessment. A systematic review. Acta Odontol Scand. 2014;72:81–91.
11. Aleksejūnienė J, Holst D, Brukienė V. Dental caries risk studies revisited: causal approaches needed for future inquiries. Int J Environ Res Public Health. 2009;6:2992–3009.
12. Doméjean S, Banerjee A, Featherstone JDB. Caries risk/susceptibility assessment: its value in minimum intervention oral healthcare. Br Dent J. 2017;223:191–7.
13. Senneby A, Mejàre I, Sahlin NE, Svensäter G, Rohlin M. Diagnostic accuracy of different caries risk assessment methods. A systematic review. J Dent. 2015;43:1385–93.
14. Bratthall D, Petersson GH. Cariogram–a multifactorial risk assessment model for a multifactorial disease. Community Dent Oral Epidemiol. 2005;33:256–64.
15. Holgerson PL, Twetman S, Stecksen-Blicks C. Validation of an age-modified caries risk assessment program (Cariogram) in preschool children. Acta Odontol Scand. 2009;67:106–12.
16. Gao XL, Hsu CY, Xu Y, Hwarng HB, Loh T, Koh D. Building caries risk assessment models for children. J Dent Res. 2010;89:637–43.
17. Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies Available from: https://www.nhlbi.nih.gov/health-pro/guidelines/in-develop/cardiovascular-risk-reduction/tools/cohort
18. Almosa NA, Al-Mulla AH, Birkhed D. Caries risk profile using the Cariogram in governmental and private orthodontic patients at de-bonding. Angle Orthod. 2012;82:267–74.
19. Al Mulla AH, Kharsa SA, Kjellberg H, Birkhed D. Caries risk profiles in orthodontic patients at follow-up using Cariogram. Angle Orthod. 2009;79:323–30.
20. Giacaman RA, Miranda Reyes P, Bravo Leon V. Caries risk assessment in Chilean adolescents and adults and its association with caries experience. Braz Oral Res. 2013;27:7–13.
21. Sundell AL, Ullbro C, Marcusson A, Twetman S. Comparing caries risk profiles between 5- and 10- year-old children with cleft lip and/or palate and non-cleft controls. BMC Oral Health. 2015;15:85.

22. Cabral RN, Hilgert LA, Faber J, et al. Caries risk assessment in schoolchildren–a form based on Cariogram software. J Appl Oral Sci. 2014;22:397–402.
23. Hebbal M, Ankola A, Metgud S. Caries risk profile of 12 year old school children in an Indian city using Cariogram. Med Oral Patol Oral Cir Bucal. 2012;17:e1054–61.
24. Kavvadia K, Agouropoulos A, Gizani S, Papagiannouli L, Twetman S. Caries risk profiles in 2- to 6-year-old Greek children using the Cariogram. Eur J Dent. 2012;6:415–21.
25. Campus G, Cagetti MG, Sacco G, Benedetti G, Strohmenger L, Lingström P. Caries risk profiles in Sardinian schoolchildren using Cariogram. Acta Odontol Scand. 2009;67:146–52.
26. Ruiz Miravet A, Montiel Company JM, Almerich Silla JM. Evaluation of caries risk in a young adult population. Med Oral Patol Oral Cir Bucal. 2007;12:E412–8.
27. Peker I, Mangal T, Erten H, Gulcin A, Emre A, Gulcin A. Evaluation of caries risk in a young adult population using a computer-based risk assessment model (Cariogram). J Dent Sci. 2012;7:99–104.
28. Sonbul H, Al-Otaibi M, Birkhed D. Risk profile of adults with several dental restorations using the Cariogram model. Acta Odontol Scand. 2008;66:351–7.
29. Lee JH, Son HH, Kim HY, Chang J. Caries risk profiles of Korean dental patients using simplified Cariogram models. Acta Odontol Scand. 2013;71:899–905.
30. Chang J, Lee JH, Son HH, Kim HY. Caries risk profile of Korean dental patients with severe intellectual disabilities. Spec Care Dentist. 2014;34:201–7.
31. Carta G, Cagetti MG, Cocco F, Sale S, Lingström P, Campus G. Caries-risk profiles in Italian adults using computer caries assessment system and ICDAS. Braz Oral Res. 2015;29:S1806–83242015000100306.
32. Petersson GH, Twetman S, Bratthall D. Evaluation of a computer program for caries risk assessment in schoolchildren. Caries Res. 2002;36:327–40.
33. Twetman S, Petersson GH, Bratthall D. Caries risk assessment as a predictor of metabolic control in young type 1 diabetics. Diabet Med. 2005;22:312–5.
34. Petersson GH, Fure S, Twetman S, Bratthall D. Comparing caries risk factors and risk profiles between children and elderly. Swed Dent J. 2004;28:119–28.
35. Campus G, Cagetti MG, Sale S, Carta G, Lingström P. Cariogram validity in schoolchildren: a two-year follow-up study. Caries Res. 2012;46:16–22.
36. Gao X, Di Wu I, Lo EC, Chu CH, Hsu CY, Wong MC. Validity of caries risk assessment programmes in preschool children. J Dent. 2013;41:787–95.
37. Kemparaj U, Chavan S, Shetty NL. Caries risk assessment among school children in davangere city using cariogram. Int J Prev Med. 2014;5:664–71.
38. Gao XL, Lo ECM, Chu CH, Hsu SC. Caries risk assessment programmes for Hong Kong children. Hong Kong Med J. 2015;21:S42–S6.
39. Petersson GH, Isberg PE, Twetman S. Caries risk assessment in school children using a reduced Cariogram model without saliva tests. BMC Oral Health. 2010;10:5.
40. Petersson GH, Isberg PE, Twetman S. Caries risk profiles in schoolchildren over 2 years assessed by Cariogram. Int J Paediatr Dent. 2010;20:341–6.
41. Zukanovic A. Caries risk assessment models in caries prediction. Acta Med Acad. 2013;42:198–208.
42. Chang J, Kim HY. Does caries risk assessment predict the incidence of caries for special needs patients requiring general anesthesia? Acta Odontol Scand. 2014;72:721–8.
43. Celik EU, Gokay N, Ates M. Efficiency of caries risk assessment in young adults using Cariogram. Eur J Dent. 2012;6:270–9.
44. Petersson GH, Twetman S. Caries risk assessment in young adults: a 3 year validation of the Cariogram model. BMC oral health. 2015;15:17.
45. Chaffee BW, Cheng J, Featherstone JD. Baseline caries risk assessment as a predictor of caries incidence. J Dent. 2015;43:518–24.

PAPER II

ORIGINAL PAPER

Ruolo di zuccheri e altri edulcoranti nel mantenimento della salute dentale

Role of sugars and other sweeteners in the maintenance of the dental health

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RIASSUNTO

OBIETTIVI
Il presente lavoro vuole fare un *excursus* sui principali edulcoranti e valutarne gli effetti sui tessuti dentali.

MATERIALI E METODI
Sono state analizzate pubblicazioni inerenti gli effetti dei principali edulcoranti sulla salute generale e orale, in particolare sulla carie.

RISULTATI
Gli edulcoranti possono essere classificati in carboidrati, polioli e ad alta intensità. Mono e disaccaridi sono fermentati dai batteri cariogeni con produzione di acidi deboli e il conseguente aumento del rischio di carie, mentre alcuni polioli inibiscono l'attività metabolica dei batteri cariogeni. Gli edulcoranti ad alta intensità non sono in genere cariogeni.

CONCLUSIONI
I carboidrati rappresentano una fonte importante di nutrimento, ma il loro utilizzo deve essere limitato. I sostituti dello zucchero possono contribuire a ridurre l'incidenza di carie.

PAROLE CHIAVE
- Carboidrati fermentabili
- Polioli
- Dolcificanti intensivi
- Stevia
- Carie dentale

ABSTRACT

OBJECTIVES
This review aims to perform an excursus *on the most used sweeteners to evaluate their effects on the dental tissues.*

MATERIALS AND METHODS
Papers considering the effects of sweeteners on general and oral health, caries especially, were evaluated.

RESULTS
Sweeteners can be classified into carbohydrates, sugar alcohols and high intensity sweeteners. While mono and disaccharides are fermented by cariogenic bacteria with production of acids increasing caries risk, sugar alcohols inhibit the metabolic activity of cariogenic microorganisms. No effect on caries risk is reported for intensity sweeteners.

CONCLUSIONS
Although carbohydrates are an important source of nutrition, their use must be limited both in terms of quantity and frequency of intake. Sugar substitutes may contribute to reduce caries incidence.

KEY WORDS
- *Sugar*
- *Polyols*
- *Sugar substitutes*
- *Stevia*
- *Dental caries*

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DENTAL CADMOS

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1. INTRODUZIONE

Stile di vita e dieta, a causa del loro ruolo sulla salute, stanno attirando sempre più l'attenzione dei professionisti della nutrizione e dei sanitari di tutte le branche della medicina come del consumatore.

La dieta ha un compito primario nel mantenimento della salute dell'organismo, ma non di meno gioca un ruolo importante sull'integrità della cavità orale agendo sia a livello sistemico sulla formazione e sul benessere di denti, parodonto, mucosa orale e osso alveolare, sia attraverso un effetto "topico" sull'integrità dei tessuti duri, sul pH e sulla composizione della saliva e della placca batterica[1]. Cambiamenti nell'assunzione, nell'assorbimento, nel metabolismo o nell'escrezione di nutrienti possono influenzare l'omeostasi dei denti, dei tessuti molli e dell'osso, così come la risposta alla guarigione dei tessuti lesi[2].

La dieta può influenzare l'omeostasi dei tessuti duri dentali in diversi modi. Fornendo zuccheri e altri carboidrati fermentabili che vengono metabolizzati in acidi dai batteri cariogeni della placca, produce un abbassamento del pH con perdita di sali minerali dallo smalto e dalla dentina. L'assunzione frequente di zuccheri, inoltre, crea un ambiente favorevole alla moltiplicazione di batteri acidogenici e acidurici. Al contrario, una dieta povera di zuccheri aggiunti e carboidrati fermentabili e ricca di sali minerali favorisce la remineralizzazione[3]. L'assunzione di alimenti e bevande con basso valore di pH può, se frequente, produrre erosione dentale per azione diretta degli acidi portati a contatto con i denti[4].

La piramide alimentare e le linee guida per una sana alimentazione promosse dal Ministero della salute[5] insieme alle linee guida europee[6] promuovono una dieta ricca di carboidrati ottenibili da grani interi, frutta e verdura. Tuttavia, anche questi alimenti sono fonte di carboidrati fermentabili.

La carie è una patologia causata dalla dissoluzione dei tessuti minerali del dente per opera dell'acido prodotto dal metabolismo batterico dei carboidrati alimentari. Le due specie batteriche principalmente coinvolte sono gli streptococchi orali, in particolare *Streptococcus mutans*, e i lattobacilli. Negli anni Sessanta la patogenesi della carie è stata raffigurata con tre cerchi parzialmente sovrapposti (diagramma di Key) che rappresentavano i tre fattori indispensabili per il suo sviluppo: il dente, la dieta e i batteri. Da allora, molti altri fattori sono stati riconosciuti essere coinvolti nell'eziopatogenesi della malattia, con il risultato di un modello più complesso che include per esempio la saliva, il sistema immunitario, il tempo, lo stato socioeconomico, il livello di istruzione, lo stile di vita, le abitudini di igiene orale, l'uso di fluoruri. Tuttavia il contenuto di carboidrati fermentabili nella dieta resta il fattore causale senza il quale la patologia non può svilupparsi[7]. Alla mancanza di disponibilità di zucchero verificatasi durante i periodi bellici, è corrisposta una riduzione della prevalenza di carie, che è rapidamente rientrata quando la restrizione è terminata[8].

L'Autorità Europea per la Sicurezza Alimentare (EFSA) ha definito i valori di riferimento per l'assunzione dei nutrienti che è necessario assumere per godere di buona salute a seconda dell'età e del sesso[9]. Per quanto concerne gli zuccheri, l'Autorità Europea sostiene che il consumo frequente di cibi a elevato tenore zuccherino aumenti il rischio di carie dentaria e contribuisca a incrementare il peso corporeo. Il gruppo di esperti ha tuttavia riscontrato che non vi sono prove sufficienti per definire un limite massimo di assunzione degli zuccheri poiché gli effetti avversi sulla salute sono collegati alle modalità di consumo degli alimenti e al tipo e alla frequenza di assunzione piuttosto che all'apporto totale di zuccheri. L'EFSA fornirà indicazioni sul consumo quotidiano di zuccheri aggiunti agli alimenti entro l'inizio del 2020.

Recentemente l'Organizzazione Mondiale della Sanità (OMS) ha raccomandato di limitare il consumo di zuccheri liberi (cioè tutti i mono e disaccaridi aggiunti agli alimenti dall'industria o dal consumatore, più gli zuccheri presenti naturalmente in miele, sciroppi e succhi di frutta) a meno del 10% delle calorie totali assunte giornalmente con l'obiettivo di non superare il 5%, perché forti evidenze indicano che così facendo si riducono sovrappeso, obesità e carie[10]. Un recente lavoro ha associato un elevato consumo di bevande analcoliche contenenti alte percentuali di zuccheri aggiunti con le malattie cardiometaboliche tra cui l'ictus e la demenza[11]. Gruppi di persone sottoposte per ragioni terapeutiche a consumo elevato di zuccheri hanno anche livelli di carie superiori alla media della popolazione generale, come dimostra il caso di bambini con malattie croniche che richiedono una prolungata assunzione di medicinali contenenti zucchero[12]. L'esposizione ad alti livelli di zuccheri è stata oggetto di diversi studi che hanno riscontrato nei lavoratori del settore dolciario una prevalenza di carie del 71% più elevata rispetto a quella riscontrata negli addetti di altri settori[13]. Viceversa, popolazioni che seguono tradizionalmente diete a basso contenuto di zucchero – come gli inuit del Nord America, i bantu dell'Africa, i tristaniani dell'isola di Tristan da Cunha nell'Oceano Atlantico meridionale – hanno presentato una ridotta prevalenza di carie fino a quando non sono stati esposti allo zucchero, evento a cui ha fatto seguito un incremento della patologia[14].

2. MATERIALI E METODI

La presente revisione della letteratura di tipo narrativo ha preso in esame lavori scientifici selezionati dalla banca dati PubMed senza limiti temporali, utilizzando le parole chiave "carboidrati, polioli, dolcificanti intensivi, stevia, carie dentale", usate singolarmente e in associazione fra loro. I lavori scelti sono quelli che, secondo gli autori, meglio descrivono la problematica oggetto della presente trattazione. Inoltre, documenti tratti da siti web di accreditati enti nazionali e internazionali – come Ministero della salute, Organizzazione Mondiale della Sanità e Commissione Europea – sono stati valutati e, se ritenuti rilevanti al fine del lavoro di revisione, descritti per fornire al lettore una visione della normativa vigente in aggiunta all'aspetto più propriamente scientifico.

Alimenti dolci e salute orale

Tutti noi selezioniamo i cibi guidati principalmente dalle emozioni di piacere o di rifiuto che ci trasmettono attraverso l'olfatto, la vista e soprattutto il gusto.

Le ricerche indicano che il dolce è il gusto che per primo si conosce da neonati e che più piace almeno nelle prime fasi della vita; il latte materno è, infatti, ricco di zucchero (lattosio). Questo spiega perché i cibi dolci siano prodotti assai graditi da gran parte della popolazione[15].

Il lavoro di Vipeholm, uno dei più famosi studi che ha indagato la formazione della carie, dimostra una forte correlazione tra gravità della malattia e frequenza di ingestione di zucchero. Svoltosi in un istituto di salute mentale in Svezia tra il 1945 e il 1953, ha riscontrato uno sviluppo di carie assai rapido nei soggetti a cui erano somministrate elevate quantità di dolciumi. La durata dell'esposizione e la permanenza dei cibi zuccherati nel cavo orale determinano prolungati periodi di produzione di acido e conseguente demineralizzazione[16].

Zuccheri liquidi come quelli contenuti nelle bevande e nei preparati per latte in polvere, passano attraverso la cavità orale rapidamente con un tempo limitato di contatto con le superfici dentali. Tuttavia, se le bevande zuccherate sono assunte ripetutamente o lentamente sorseggiate, il rischio di carie aumenta[17]. Caramelle dure, mentine e lecca-lecca rappresentano fonti di zuccheri che vengono gradualmente rilasciati durante il loro consumo e persistono a lungo nel cavo orale e, pertanto, se la loro assunzione è frequente rappresentano un fattore di rischio significativo[18].

Il tempo di permanenza dei differenti alimenti nel cavo orale può variare notevolmente: una caramella o una gelatina pur essendo appiccicose sono eliminate dalla cavità orale più velocemente di quanto non avvenga per alimenti ritentivi come biscotti e patatine[19].

È infatti importante ricordare che:

- la capacità di eliminazione degli zuccheri dal cavo orale è soggettiva e dipende soprattutto dal flusso e dalla fluidità salivare[20];
- l'adesività del cibo non è importante quanto la quantità di carboidrati che permangono nella placca e nella saliva; infatti, un'elevata ritenzione iniziale può essere seguita da una rapida *clearance* orale[21];
- il pane bianco e l'uva passa sono mantenuti più a lungo del latte al cioccolato e di alcuni dolci e possono produrre una concentrazione maggiore di zuccheri soprattutto se vengono consumati tra i pasti[22].

3. RISULTATI

Tipologie di zuccheri

Gli zuccheri sono presenti negli alimenti in due forme: quelli naturalmente contenuti nei cibi come in frutta, miele e prodotti lattiero-caseari e quelli addizionati agli alimenti durante la lavorazione per alterarne il sapore o la consistenza.

I carboidrati **(tab. I)**, una fonte essenziale di energia per il corpo, sono generalmente classificati in semplici e complessi. Tra gli zuccheri semplici troviamo i monosaccaridi, composti organici formati da carbonio, idrogeno e ossigeno che non possono essere scissi per idrolisi. Glucosio, fruttosio e galattosio sono i più importanti monosaccaridi presenti nella dieta. Tra gli zuccheri semplici formati da più di una molecola si annoverano i disaccaridi, composti da due molecole uguali o diverse fra loro, come il saccarosio (comune zucchero da tavola), il lattosio e il maltosio. Quest'ultimo, per esempio, è formato dalla condensazione di due molecole di glucosio, mentre il lattosio è dovuto alla condensazione di glucosio e galattosio. Il saccarosio è lo zucchero più comunemente utilizzato ed è formato da glucosio e fruttosio. La maggior parte dei mono e disaccaridi viene principalmente utilizzata a scopo dolcificante, tuttavia alcuni disaccaridi sono usati con scopi differenti come il lattulosio, composto da galattosio e fruttosio, indigeribile dall'uomo, usato come preparazione lassativa, o il trealosio composto da due molecole di glucosio e diffuso in lieviti, funghi e insetti e usato come crio-conservatore. Abbiamo poi gli oligosaccaridi, formati da più di due ma meno di dieci molecole, come le maltodestrine. Infine, troviamo i polisaccaridi, caratterizzati da un gran numero di unità ripetitive legate insieme a formare molecole grandi e complesse come l'amido e il glicogeno.

Tab. I Classificazione dei carboidrati

Carboidrati	**Semplici**	Monosaccaridi	Glucosio
			Fruttosio
			Galattosio
		Disaccaridi	Saccarosio
			Lattosio
			Maltosio
		Oligosaccaridi	Maltodestrine
	Complessi (polisaccaridi)	Amidi	Amilosio
			Amilopectina
		Fibre	Fibre non idrosolubili
			Fibre idrosolubili
		Glicogeno	

Quando si parla di "carboidrati fermentabili" ci si riferisce a zuccheri o amidi di cottura che costituiscono il substrato per il metabolismo microbico orale. In **fig. 1** è schematizzato il processo metabolico che porta alla formazione di acidi con conseguente demineralizzazione dei tessuti dentali. Il più comune zucchero fermentabile è il saccarosio. L'idrolisi del saccarosio porta alla formazione dello "zucchero invertito" composto presente naturalmente nei succhi di alcuni frutti come l'uva[23]. Altri mono- e disaccaridi quali lattosio e maltosio, presenti in molti prodotti alimentari, possono essere fermentati dai microrganismi orali dando luogo alla produzione di acidi deboli in grado di demineralizzare i tessuti duri dentali. Il sacca-

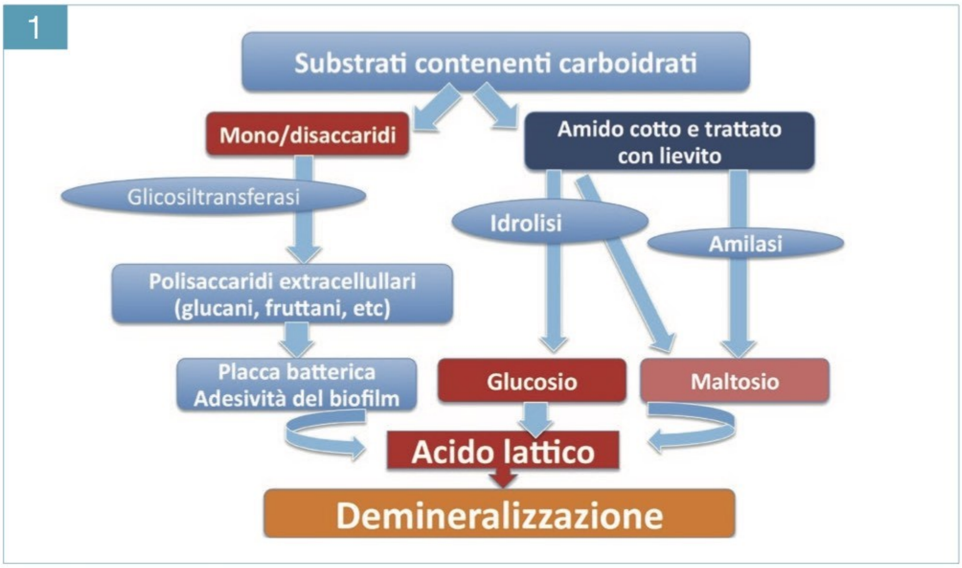

Fig. 1 Schematizzazione del processo metabolico che porta alla demineralizzazione dei tessuti dentali

rosio è lo zucchero con il maggior potere cariogeno[24]. In **fig. 2** sono riportati i principali carboidrati fermentabili in ordine di cariogenicità decrescente.

Saccarosio

Largamente presente in natura nella frutta e nel miele (in percentuale più bassa rispetto al fruttosio), è in genere ottenuto dalla barbabietola da zucchero in Europa e dalla canna da zucchero nel resto del mondo. La produzione di zucchero da altre fonti – quali per esempio l'acero, la palma da dattero e la palma da cocco – riveste invece un ruolo minoritario.
Il saccarosio così estratto viene utilizzato nell'ambito dell'industria alimentare, specialmente dolciaria e pasticciera, prendendo il nome comune di zucchero da cucina, raffinato bianco oppure integrale "grezzo". Come detto in precedenza, il suo potere cariogeno è assai elevato.

Fruttosio

Il fruttosio o fruttoso è un monosaccaride presente nella maggior parte dei frutti zuccherini e dei loro succhi, usato come dolcificante e nell'industria alimentare. Il fruttosio fu utilizzato nel celeberrimo "Turku Study", in cui un regime dietetico che prevedeva l'utilizzo o di fruttosio o di saccarosio o di xilitolo (poliolio) venne amministrato a tre diversi gruppi di soggetti adulti nella cittadina di Turku in Finlandia. Dopo 2 anni l'incremento di carie nel gruppo che aveva fatto uso del solo fruttosio rispetto al saccarosio era dimezzato, con un DMFT (numero medio di denti permanenti cariato, mancanti per carie od otturati) di 3,8 nel gruppo fruttosio contro 7,2 in quello saccarosio[25].

Lattosio

È lo zucchero contenuto nel latte vaccino (4,8 g/100 ml) come in quello umano (7 g/100 ml). Nonostante il suo potenziale cariogeno, il latte ha un'azione protettiva nei confronti dei denti grazie all'alto contenuto di calcio (125 mg/100 ml) e proteine. L'Organizzazione Mondiale della Sanità e l'UNICEF si fanno da sempre promotrici di campagne a favore dell'allattamento al seno, sottolineando l'importanza che l'alimentazione riveste specie nei primi mesi e anni di vita e sul suo ruolo determinante per il mantenimento di condizioni di salute ottimali[26].

Un'associazione tra carie nei denti decidui (*early childhood caries*) e allattamento al seno, quando questo sia consumato *ad libitum* e in frequenti assunzioni giornaliere e notturne, è stata ipotizzata in letteratura, ma a sostegno di questa correlazione non sono stati a oggi raggiunti risultati univoci[27]. Come nel caso della frutta, il latte non è considerato una minaccia per la salute orale, anche se la sua assunzione, così come per gli altri alimenti, deve essere seguita da corrette manovre di igiene orale. Viceversa la somministrazione con il biberon di succhi di frutta, latte o altre bevande addizionate di zucchero aumenta considerevolmente il rischio di carie nella prima infanzia[28].

Amido

L'amido è un polimero complesso del glucosio di origine vegetale. Può essere raffinato o assunto nel suo stato naturale, consumato crudo, come in frutta e verdura, o cotto, come nei prodotti da forno. Si trova nei frutti, nei semi e nei tuberi delle piante.
I batteri del cavo orale non sono in grado di metabolizzarlo come tale, tuttavia la cottura e le amilasi salivari favoriscono il rilascio di glucosio, maltosio e maltotriosio, a loro volta metabolizzati dai batteri orali per produrre acidi. Cibi contenenti amidi cotti, come il pane bianco, hanno mostrato di riuscire a ridurre il pH della placca al di sotto del valore soglia di 5,5, necessario affinché la demineralizzazione dello smalto si avvii. L'amido comunque è meno acidogeno del saccarosio o dei cibi contenenti amido e saccarosio, avendo un potere cariogeno di circa la metà rispetto al saccarosio[27].

Tagatosio

Il tagatosio è un dolcificante a basso contenuto di carboidrati che fornisce

Fig. 2 Cariogenicità dei principali carboidrati fermentabili in ordine decrescente

1,5 calorie al grammo. È uno zucchero da un punto di vista strutturale molto simile al fruttosio, presente in natura in piccolissime quantità, quindi la sua estrazione risulta non economica. È una polvere bianca cristallina ottenuta a partire dal lattosio. È stato approvato negli Stati Uniti nel maggio 2003 con la notifica della Food and Drug Administration (FDA) come ingrediente sicuro (GRAS-*Generally Recognised as Safe*). Il tagatosio si comporta come il fruttosio nel corpo, ma solo il 15-20% viene assorbito nell'intestino tenue. A causa di questo assorbimento incompleto, ha un effetto minimo sui livelli ematici di glucosio e insulina. Il tagatosio indigerito procede verso il grande intestino, dove agisce come prebiotico, promuovendo la produzione di probiotici, indispensabili per il mantenimento di un sano sistema digestivo. È fermentato nel colon e può quindi causare meteorismo e diarrea in individui sensibili.

Il tagatosio è uno zucchero non-cariogeno: è infatti lentamente fermentato dai microrganismi orali, producendo quantità di acidi non sufficienti a ridurre il pH della placca dentale al di sotto dei valori soglia per la demineralizzazione dei tessuti duri[29].

Il potere dolcificante e calorico, le dosi massime consentite e la cariogenicità dei diversi carboidrati sono riportati in **tab. II**.

I consigli da dare ai pazienti per ridurre il rischio di carie attraverso l'assunzione "intelligente" dei carboidrati sono riportati in **tab. III**.

Alternative allo zucchero

L'uso di dolcificanti alternativi allo zucchero è entrato prepotentemente e diffusamente sul mercato, dapprima per far fronte alle esigenze sanitarie di pazienti che richiedevano un regime dietetico a ridotto apporto di glucidi come i diabetici, ma successivamente hanno trovato larga diffusione grazie all'uso da parte di tutti coloro che desiderano ridurre il proprio peso o controllarlo per via del basso potere calorico che questi dolcificanti possono vantare.

Le sostanze dolcificanti disponibili sul mercato possono addizionarsi a cibi o bevande o essere inseriti in prodotti confezionati definiti sugar-free o dietetici e possono essere divisi in dolcificanti naturali e artificiali o di sintesi. L'argomento, tuttavia, presenta anche a livello terminologico un certo grado di confusione. Per esempio, alcuni produttori chiamano dolcificanti "naturali" anche quelli trattati o raffinati, come avviene per i preparati di stevia, oppure alcuni dolcificanti artificiali poiché derivati da sostanze che si trova-

Tab. II Potere dolcificante, dose giornaliera e cariogenicità dei diversi edulcoranti

	Edulcorante	Kcal/g	Potere dolcificante (%) in relazione al saccarosio	Dose massima giornaliera	Cariogenicità
Carboidrati	Saccarosio	4,0	1	Non stabilita	Si
	Glucosio	3,74	0,74	Non stabilita	Si
	Fruttosio	3,75	1,50	Non stabilita	Si
	Lattosio	4,0	0,60	Non stabilita	Si
	Tagatosio	1,5	0,92	15 g/die 0,25 g/kg	No
Polioli[1]	Sorbitolo ++	2,6	0,70	(1)	No
	Xilitolo ++	2,4	0,90	(1)	No
	Maltitolo ++	2,1	0,75	(1)	No
	Isomalto +++	2,0	0,50	(1)	No
	Lattitolo +	2,0	0,40	(1)	No
	Mannitolo +++	1,6	0,50	(1)	No
	Eritritolo	0,2	0,65	(1)	No
Edulcoranti intensivi	Stevia	0	300	2 mg/kg	No
	Saccarina	0	250-500	5 mg/kg	No
	Aspartame	4,0	180-250	40 mg/kg	No
	Acelsulfame K	0	160-250	9 mg/kg	No
	Ciclamati	0	30-80	11 mg/kg	No

[1]Per i polioli non è stata stabilita dalla legge una dose giornaliera massima. È stato fissato un valore di riferimento: 20 g per un adulto, 10 g per un bambino

Tab. III Consigli sul consumo dei carboidrati fermentabili in relazione alla salute orale

Ridurre il consumo totale di zuccheri a meno del 10% delle calorie complessivamente introdotte con la dieta
Ridurre la frequenza a non più di 3/4 assunzioni giornaliere
Limitare l'assunzione di cibi dolci ai pasti principali cui fa seguito l'igiene orale
Evitare l'assunzione di zuccheri fra i pasti per limitare il tempo di permanenza degli stessi nel cavo orale
Evitare di sorseggiare bevande zuccherate, specie se acide. Dopo la loro assunzione sciacquare la bocca con acqua
Ricordare che anche alimenti salutari e utili al benessere dell'organismo come latte, frutta ecc. contenendo zuccheri sono potenzialmente cariogeni se assunti frequentemente e in assenza di regolari manovre di igiene orale

no in natura come il sucralosio che deriva dallo zucchero.

Un'ulteriore classificazione dei dolcificanti tiene conto del loro potere edulcorante: vi sono infatti dolcificanti che hanno un potere edulcorante simile a quello dello zucchero come i polioli e altri chiamati dolcificanti intensivi che possiedono decine o centinaia di volte il potere dolcificante del saccarosio **(tab. II)**.

La Commissione Europea, dipartimento Health and food safety, ha istituito il *Register of nutrition and health claims*. Il registro riporta che l'assunzione di cibi o bevande contenenti polioli ed edulcoranti intensivi (articolo 13/1) e zuccheri non-fermentabili (articolo 13/5) in sostituzione di quelli fermentabili, riduce la demineralizzazione dello smalto contribuendo alla salute dentale. Inoltre, si attesta che i chewing gum sugar-free o contenenti xilitolo (articolo 14/1[a]) sono capaci di ridurre la formazione della placca contribuendo al mantenimento della salute di denti e gengive[30].

Polioli

Chiamati anche "alcoli dello zucchero" da cui il nome polialcoli, i polioli possono essere classificati come derivati da monosaccaridi (sorbitolo, eritritolo, xilitolo, mannitolo), da disaccaridi (maltitolo, isomalto, lattitolo) e da polisaccaridi (idrolizzati di amido idrogenato). Possiedono un buon potere dolcificante simile a quello dello zucchero. I polioli sono per lo più dolcificanti a ridotto apporto calorico e possono essere utilizzati nella stessa quantità dello zucchero da tavola. Sono spesso impiegati in combinazione con altri dolcificanti per migliorarne il livello di dolcezza e il gusto. Vengono utilizzati per dolcificare cibi come biscotti, caramelle, gomma da masticare, prodotti da forno, gelati oppure dentifrici, collutori e prodotti farmaceutici.

I polioli, inoltre, forniscono un effetto di freschezza (effetto "cool"), contribuiscono a mantenere l'umidità del prodotto in cui sono inseriti, ad aumentarne il volume, a non far perdere la dolcezza e a conservarne le caratteristiche organolettiche. Sono naturalmente presenti in molti frutti e vegetali ma per usi commerciali sono spesso prodotti a partire da carboidrati, quali amido, saccarosio e glucosio. L'FDA considera i polioli come sicuri per l'uso alimentare (GRAS) e sono infatti approvati come additivi alimentari.

I polioli sono assorbiti solo parzialmente dal piccolo intestino con un effetto minore sulla glicemia rispetto ai carboidrati. Quelli che non sono assorbiti continuano il loro tragitto nel grande intestino dove sono fermentati dai batteri. Quantità eccessive di polioli (superiori a 7-14 g al giorno) possono avere effetti lassativi. L'Academy of nutrition and dietetics informa che un consumo di più di 50 grammi al giorno di sorbitolo o di 20 grammi di mannitolo può causare diarrea.

I polioli non hanno azione cariogena perché i batteri del cavo orale non sono in grado di metabolizzarli e di trasformarli in acidi. L'FDA autorizza l'uso di questo *claim* sulle etichette di prodotti contenenti polioli[31].

Lo *xilitolo* viene anche chiamato lo zucchero del legno perché può essere estratto dalla corteccia di alcuni alberi come le betulle, ma lo si ritrova anche nelle fragole, nei lamponi, nelle prugne e nel grano. In Europa è usato come additivo alimentare e identificato dalla sigla E967; viene addizionato in particolare nei chewing gum e nelle caramelle allo scopo di inibire i batteri cariogeni.

Il primo studio che ha valutato il potere cariogeno dello xilitolo è stato condotto a Turku in Finlandia alla fine degli anni Sessanta: 125 soggetti adulti hanno sostituito il saccarosio nella loro dieta con lo xilitolo per un periodo di due anni durante il quale non hanno sviluppato carie, a differenza dei soggetti che avevano fatto uso di fruttosio o saccarosio.

Anche se il meccanismo d'azione dello xilitolo non è ancora del tutto noto, oltre a una sua azione antibatterica una delle ragioni della sua efficacia anti-carie è che *S. mutans* non è in grado di utilizzarlo come substrato energetico, con il risultato di una minor produzione di acidi. La sua assunzione per lunghi periodi di tempo (alcuni mesi) attraverso chewing gum o caramelle sembrerebbe determinare un processo grazie al quale batteri "meno virulenti" si sostituirebbero a quelli più cariogeni[32].

La somministrazione di xilitolo alle mamme con figli piccoli è una metodica preventiva efficace per limitare il passaggio di batteri cariogeni dalla mamma al bambino, riducendo così il rischio di carie nella dentatura decidua[33].

Un recente studio italiano[34], condotto dalle Università di Milano e Sassari sui bambini delle scuole primarie, ha valutato l'effetto della somministrazione quotidiana di xilitolo per 6 mesi attraverso un chewing gum, somministrato dagli insegnanti durante l'orario scolastico. Due anni dopo il termine della somministrazione e in assenza di altre manovre preventive, a eccezione del regolare uso di un dentifricio fluorato, i bambini che avevano fatto uso di xilitolo hanno sviluppato un numero di nuove lesioni cariose inferiore di circa 10 volte rispetto a coloro che avevano fatto uso di un chewing gum sugar-free non contente xilitolo.

Concludendo, lo xilitolo è un efficace strumento preventivo che può affiancare a pieno titolo quelli tradizionali e sempre validi rappresentati da un'alimentazione povera di zuccheri fermentabili, da un dentifricio al fluoro e da regolari controlli periodici.

Il più diffuso poliolo è il *sorbitolo*. Meno costoso dello xilitolo, non fa abbassare il pH della placca al di sotto della soglia di demineralizzazione dello smalto se assunto a basse dosi; tuttavia, è considerato un dolcificante con basso potere cariogeno ad alte dosi (più di due chewing gum al giorno) in quanto i batteri cariogeni possono "imparare" a metabolizzarlo[35]. In uno studio condotto su oltre un migliaio di soggetti l'uso di una gomma da masticare sia allo xilitolo sia al sorbitolo si è dimostrato più efficace nel ridurre l'incidenza di carie rispetto all'uso di una gomma edulcorata con il saccarosio[36].

L'*eritritolo* è un polialcol presente nella frutta e nei cibi fermentati, utilizzato come dolcificante, anche grazie alle sue caratteristiche ipocaloriche (zero calorie) e al buon sapore privo di retrogusti. È usato in combinazione a dolcificanti intensivi per aumentarne la dolcezza, incrementare la corposità e mascherare i retrogusti sgradevoli. Una recente revisione della letteratura ha preso in esame i benefici che l'eritritolo produce sulla salute orale[37], verificando che questo poliolo è in grado di ridurre la placca dentale e l'aderenza degli streptococchi orali alle superfici dentali. È stato inoltre dimostrato che inibisce la crescita e il metabolismo di batteri cariogeni come *S. mutans*, riduce l'espressione di geni batterici coinvolti nel metabolismo del saccarosio, riduce l'incidenza di carie ed è un utile ausilio attraverso l'air-polishing nel trattamento parodontale.

IL **REGISTRO** ISTITUITO DALLA COMMISSIONE EUROPEA RIPORTA CHE L'ASSUNZIONE DI CIBI O BEVANDE CONTENENTI **POLIOLI** ED **EDULCORANTI** INTENSMI E **ZUCCHERI** NON-FERMENTABILI **RIDUCE** LA DEMINERALIZZAZIONE DELLO SMALTO

Edulcoranti intensivi

Stevia rebaudiana

La Stevia rebaudiana Bertoni, dal nome del botanico italo-svizzero che nel 1889 per primo l'ha classificata, è una pianta erbaceo-arbustiva perenne originaria del Sud America, dalle cui foglie è possibile ottenere un dolcificante con un potere edulcorante assai elevato. Utilizzata da culture indigene del Sud America per secoli, fu introdotta in Europa dai conquistadores spagnoli nel XVI secolo. È stata reintrodotta all'inizio del XX secolo dal botanico italiano-svizzero Moisés S. Bertoni che nel 1905 l'ha classificata e descritta. Stevioside e rebaudioside A sono i due glicosidi più rappresentati nelle sue foglie. Lo stevioside è circa 200-300 volte più dolce del saccarosio.

La stevia è approvata come integratore alimentare in diversi paesi come il Brasile, il Giappone, gli Stati Uniti e recentemente anche nell'Unione Europea[38]. Stevioside e rebaudioside A non influenzano i valori del pH della placca, non essendo in grado di promuovere il metabolismo batterico e pertanto sono considerati edulcoranti non cariogeni[39].

Saccarina

È l'edulcorante di sintesi più noto e impiegato da più lungo tempo. Fu scoperto nel 1879 da Ira Remsen e Constantin Fahlberg della Johns Hopkins University. Per decenni è stato l'unico sostituto del saccarosio per soggetti affetti da diabete. Presenta un retrogusto amaro considerato poco gradevole; viene pertanto associata al ciclamato in proporzione

1:10 per correggere i rispettivi difetti nel retrogusto. È resistente al calore[40].
Il suo uso è in declino anche in relazione a un ipotetico rischio di indurre mutazioni geniche e all'insorgenza di tumori alla vescica in animali da laboratorio. Nessun effetto è noto sulla salute orale.

Aspartame

Scoperto casualmente nel 1965, è costituito dagli amminoacidi fenilalanina e acido aspartico. Possiede un potere calorico simile al saccarosio, ma le quantità utilizzate sono talmente esigue che il suo apporto calorico è praticamente irrilevante. I prodotti che lo contengono devono riportare in etichetta "contiene una fonte di fenilalanina", poiché soggetti affetti da chetonuria, difetto genetico dovuto a deficienza o assenza dell'enzima fenilalanina idrossilasi che catalizza la conversione della fenilalanina in tirosina, non possono assumerlo.
L'ipotizzata insorgenza di allergie, intolleranze alimentari e patologie tumorali non è mai stata dimostrata alle dosi consigliate. Nessun effetto è noto sulla salute orale.

Acelsulfame K

È un sale di potassio scoperto casualmente nel 1967. A differenza dell'aspartame è resistente al calore, il che lo rende particolarmente adatto per prodotti di pasticceria. Non è metabolizzato dall'organismo e viene escreto immodificato nelle urine.
È stato criticato per il possibile effetto cancerogeno, ma le sue conseguenze nocive sono state smentite sia dalla Food and Drug Administration sia dallo Scientific Committee on Food dell'Unione Europea. Nessun effetto è noto sulla salute orale.

Ciclamati

Sono dolcificanti intensivi di sintesi che derivano dai sali di sodio e di calcio dell'acido ciclamico (acido cicloesilsulfamico). Hanno un potere edulcorante di 30 volte superiore al saccarosio. Vengono usati in associazione con la saccarina per coprirne il retrogusto amaro. Il loro uso è stato inizialmente limitato negli USA e in Gran Bretagna in seguito a ricerche che hanno riscontrato effetti cancerogeni e disturbi dell'assorbimento in animali da laboratorio. Nel 1984 il Comitato per la valutazione del cancro della FDA ha esaminato le prove scientifiche e ha concluso che il ciclamato non è un cancerogeno. Nessun effetto è noto sulla salute orale.
Il potere dolcificante e calorico, le dosi massime consentite e la cariogenicità dei diversi edulcoranti naturali e di sintesi sono riportati in **tab. II**.
I consigli da fornire ai pazienti per ridurre il rischio di carie attraverso l'assunzione di edulcoranti alternativi ai carboidrati sono riportati in **tab. IV**.

Tab. IV Consigli sul consumo di edulcoranti in relazione alla salute orale
I polioli, soprattutto xilitolo ed eritritolo, se assunti nelle dosi consigliate e per prolungati periodi di tempo possono ridurre efficacemente il rischio di carie con nulli effetti collaterali
La stevia può sostituire il comune zucchero da tavola e può essere usata nelle preparazioni casalinghe di alimenti dolciari, riducendo così l'assunzione di carboidrati fermentabili
L'uso dei dolcificanti intesivi di sintesi può essere un valido sostituto dello zucchero per dolcificare bevande come tè e caffè

4. CONCLUSIONI

I carboidrati semplici rappresentano una fonte importante di nutrimento per l'organismo; tuttavia, un loro eccessivo consumo aumenta il rischio di contrarre patologie sistemiche e del cavo orale.
Da quanto sopra riportato e suggerito da numerosi organi nazionali e internazionali che si occupano di nutrizione e di salvaguardia della salute, l'utilizzo di zuccheri liberi deve essere limitato sia in termini di quantità sia di frequenza di assunzione. I sostituti dello zucchero, naturali o di sintesi, possono contribuire a ridurre l'incidenza di carie, sia negli adulti che nei bambini. Il loro uso è tuttavia soggetto ad alcune restrizioni. ■

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BIBLIOGRAFIA

1. **König KG.** Diet and oral health. Int Dent J 2000;50:162-74.
2. **Touger-Decker R, Van Loveren C.** Sugars and dental caries. Am J Clin Nutr 2003;78:881S-92S.
3. **Pitts NB, Zero DT, Marsh PD, Ekstrand K, Weintraub JA, Ramos-Gomez F, Tagami J et al.** Dental caries. Nat Rev Dis Primers 2017;3:17030.
4. **Kanzow P, Wegehaupt FJ, Attin T, Wiegand A.** Etiology and pathogenesis of dental erosion. Quintessence Int 2016;47:275-8.
5. **Ministero delle politiche agricole e sociali, Istituto nazionale di ricerca per gli alimenti e la nutrizione.** Linee guida per una sana alimentazione italiana 2003: http://www.salute.gov.it/imgs/C_17_pubblicazioni_652_allegato.pdf.
6. **Ruxton CHS, Garceau FJS, Cottrell RC.** Guidelines for sugar consumption in Europe: is a quantitative approach justified? Eur J Clin Nutr 1999;53:503-13.
7. **Moynihan P.** Sugars and dental caries: evidence for setting a recommended threshold for intake. Adv Nutr 2016;7:149-56.
8. **Marthaler TM.** Epidemiological and clinical dental findings in relation to intake of carbohydrates. Caries Res 1967;1:222-38.
9. **Autorità Europea per la Sicurezza Alimentare (EFSA):** http://onlinelibrary.wiley.com/doi/10.2903/j.efsa.2010.1462/pdf.
10. **WHO.** Guideline: sugars intake for adults and children 2015: http://apps.who.int/iris/bitstream/10665/149782/1/9789241549028_eng.pdf?ua=1.
11. **Pase MP, Himali JJ, Beiser AS, Aparicio HJ, Satizabal CL, Vasan RS et al.** Sugar and artificially sweetened beverages and the risks of incident stroke and dementia. Stroke 2017;48:1139-46.
12. **Roberts IF, Roberts GJ.** Relation between medicines sweetened with sucrose and dental disease. Br Med J 1979;2:14-6.
13. **Anaise JZ.** Prevalence of dental caries among workers in the sweets industry in Israel. Community Dent Oral Epidemiol 1978;8:142-5.
14. **Rugg-Gunn A.** Dental caries: strategies to control this preventable disease. Acta Med Acad 2013;42:117-30.
15. **Loper HB, La Sala M, Dotson C, Steinle N.** Taste perception, associated hormonal modulation, and nutrient intake. Nutr Rev 2015;73:83-91.
16. **Rugg-Gunn AJ.** Nutrition and dental health. Oxford: Oxford University Press, 1993.
17. **Skinner J, Byun R, Blinkhorn A, Johnson G.** Sugary drink consumption and dental caries in New South Wales teenagers. Aust Dent J 2015;60:169-75.
18. **Gupta P, Gupta N, Pawar AP, Birajdar SS, Natt AS, Singh HP.** Role of sugar and sugar substitutes in dental caries: a review. ISRN Dent 2013:519421.
19. **Lingstrom P, Van Houte J, Kashket S.** Food starches and dental caries. Crit Rev Oral Biol Med 2000;11:366-80.
20. **Dawes C.** Salivary flow patterns and the health of hard and soft oral tissues. J Am Dent Assoc 2008;139:18S-24S.
21. **Mundorff, SA, Featherstone JDB, Bibby BG, Curzon MEJ, Eisenberg A, Espeland MA.** Cariogenic potential of foods. Caries in the rat model. Caries Res 1990;24:344-55.
22. **Lingstrom P, Van Houte J, Kashket S.** Food starches and dental caries. Crit Rev Oral Biol Med 2000;11:366-80.
23. **DeMan JM.** Principles of food chemistry. Westport, Connecticut: AVI publishing Company, 1980:135-70.
24. **Touger-Decker R, Van Loveren C.** Sugars and dental caries. Am J Clin Nutr 2003;78:881S-92S.
25. **Scheinin A, Mäkinen KK, Ylitalo K.** Turku sugar studies. V. Final report on the effect of sucrose, fructose and xylitol diets on the caries incidence in man. Acta Odontol Scand 1976;34:179-216.
26. **OMS/UNICEF.** Strategia globale per l'alimentazione dei neonati e dei bambini 2003: https://www.unicef.it/Allegati/Strategia_globale_alimentazione_neonati_bambini.pdf.
27. **Bradshaw DJ, Lynch RJ.** Diet and the microbial aetiology of dental caries: new paradigms. Int Dent J 2013;63:64-72.
28. **Ministero del lavoro, della salute e delle politiche sociali.** Linee guida nazionali per la promozione della salute orale e la prevenzione delle patologie orali in età evolutiva. Aggiornamento 2013: https://www.salute.gov.it/imgs/C_17_pubblicazioni_2073_allegato.pdf
29. **Food and Drug Administration, HHS.** Food labeling: health claims; D-tagatose and dental caries. Final rule. Fed Regis 2003;68:39831-3.
30. **Commissione Europea, Dipartimento Health and Food safety:** http://ec.europa.eu/food/safety/labelling_nutrition/claims/register/public/?event=search.
31. **Saulo A.** Sugars and sweeteners in foods. Hawaii - Food Safety and Technology 2005;16 Jan.
32. **Mäkinen KK, Mäkinen PL, Pape HR Jr, Allen P, Bennett CA, Isokangas PJ et al.** Stabilisation of rampant caries: polyol gums and arrest of dentine caries in two long term cohort studies in young subjects. Int Dent J 1995;45:93-107.
33. **Yates C, Duane B.** Maternal xylitol and mutans streptococci transmission. Evid Based Dent 2015;16:41-2.
34. **Campus G, Cagetti MG, Sale S, Petruzzi M, Solinas G, Strohmenger L et al.** Six months of high-dose xylitol in high-risk caries subjects: a 2-year randomised, clinical trial. Clin Oral Investig 2013;17:785-9.
35. **Birkhed D, Svensäter G, Edwardsson S.** Cariological studies of individuals with long-term sorbitol consumption. Caries Res 1990;24:220-3.
36. **Mäkinen KK, Bennett CA, Hujoel PP, Isokangas PJ, Isotupa KP, Pape HR Jr et al.** Xylitol chewing gums and caries rates: a 40 month cohort study. J Dent Res 1995;74:1904-13.
37. **De Cock P, Mäkinen K, Honkala E, Saag M, Kennepohl E, Eapen A.** Erythritol is more effective than xylitol and sorbitol in managing oral health endpoints. Int J Dent 2016;2016:9868421.
38. **EFSA.** Scientific opinion of the panel on food additives and nutrient sources added to food on a request from the commission on the safety in use of steviol glycosides as a food additive. EFSA J 2010;1537:1-87.
39. **Brambilla E, Cagetti MG, Ionescu A, Campus G, Lingström P.** An *in vitro* and *in vivo* comparison of the effect of stevia rebaudiana extracts on different caries-related variables: a randomized controlled trial pilot study. Caries Res 2014;48:19-23.
40. **Giacaman RA, Campos P, Muñoz-Sandoval C, Castro RJ.** Cariogenic potential of commercial sweeteners in an experimental biofilm caries model on enamel. Arch Oral Biol 2013;58:1116-22.

Long Abstract

INTRODUCTION

Diet could affect the homeostasis of hard dental tissues through sugars and other fermentable carbohydrates intake. This substances are metabolized into acids by the action of the cariogenic plaque bacteria and cause a decrease in pH with the loss of mineral salts from the enamel and dentin. Frequent intake of sugars also creates a favorable environment for multiplication of acidic bacteria.

Caries is a disease caused by the dissolution of the tooth mineral tissues produced by the acid derived from bacterial metabolism of carbohydrates. The two bacterial species mainly involved in this phenomena are oral streptococci, in particular *Streptococcus mutans*, and lactobacilli.

The European Food Safety Authority (EFSA) has defined the reference values for nutrition supplements that need to be taken to enjoy good health for different ages and gender. As regard sugars, the European Authority affirms that frequent consumption of high sugary foods increases the risk of tooth decay and contributes to body weight increase.

MATERIALS AND METHODS

The present review of the literature took into consideration the scientific papers selected from PubMed database without any time limit, using the keywords "carbohydrates, polyols, intensive sweeteners, stevia, dental caries" used as single words and in association with each other.

RESULTS

Sugars are present in foods in two forms: those naturally contained in foods such as fruit, honey and dairy products and those added to foods during processing to alter their flavor or consistency. Sweeteners can be classified into carbohydrates, sugar alcohols and high intensity sweeteners. While mono and disaccharides are fermented by cariogenic bacteria with production of acids that increase caries risk, sugar alcohols inhibit the metabolic activity of cariogenic microorganisms. No effect on caries is reported for high intensity sweeteners.

The duration of exposure and the persistence of sugary foods in the oral cavity cause prolonged periods of acid production and consequent demineralization. The life of different foods in the oral cavity can vary considerably.

DISCUSSION AND CONCLUSIONS

Simple carbohydrates are an important source of nutrition for the body; however, their excessive consumption increases the risk of developing systemic and oral pathologies. Sugar substitutes, natural or synthesized, can help to reduce the incidence of caries in adults and children. However, their use is subjected to certain restrictions.

CLINICAL SIGNIFICANCE

Diet has a primary role in maintaining the health of the entire body, including the oral cavity. It is a common tendency to select foods following the emotions of pleasure or rejection that they pass through smell, sight and taste. Research indicates that sweet is the taste first known by infants, however, the use of free sugars must be limited both in terms of quantity and frequency of intake.

PAPER II

ENGLISH VERSION

Role of sugars and other sweeteners in the maintenance of the dental health

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ABSTRACT

OBJECTIVES

This review aims to perform an excursus on the most used sweeteners to evaluate their effects on the dental tissues.

MATERIAL AND METHODS

The present review of the literature took into consideration the scientific papers selected from PubMed database without any time limit, using the keywords "carbohydrates, polyols, intensive sweeteners, stevia, dental caries" used as single words and in association with each other.

RESULTS

Sugars are present in foods in two forms: those naturally contained in foods such as fruit, honey and dairy products and those added to foods during processing to alter their flavor or consistency. Sweeteners can be classified into carbohydrates, sugar alcohols and high intensity sweeteners. While mono and disaccharides are fermented by cariogenic bacteria with production of acids that increase caries risk, sugar alcohols inhibit the metabolic activity of cariogenic microorganisms. No effect on caries is reported for high intensity sweeteners. The duration of exposure and the persistence of sugary foods in the oral cavity cause prolonged periods of acid production and consequent demineralization. The life of different foods in the oral cavity can vary considerably.

CONCLUSIONS

Although carbohydrates are an important source of nutrition, their use must be limited both in terms of quantity and frequency of intake. Sugar substitutes may contribute to reduce caries incidence.

KEY WORDS: Sugar, Polyols, Sugar substitutes Stevia, Dental caries

1. INTRODUCTION

Lifestyle and diet, due to their role on health, are increasingly attracting the attention of nutrition professionals and health professionals from all branches of medicine to the consumer.
Diet has a primary role in maintaining the health of the organism, but nevertheless plays an important role in the integrity of the oral cavity by acting both at a systemic level on the formation and wellbeing of teeth, periodontal, mucus oral and alveolar bone, both through a "topical" effect on the integrity of hard tissues, on pH and on the composition of saliva and bacterial plaque [1]. Changes in the intake, absorption, metabolism or excretion of nutrients can influence the homeostasis of teeth, soft tissue and bone, as well as the response to healing of injured tissues [2].
Diet can affect homeostasis of hard dental tissues in different ways. By providing sugars and other fermentable carbohydrates that are metabolized into acids by cariogenic plaque bacteria, it produces a lowering of the pH with loss of mineral salts from the enamel and the tooth. The frequent intake of sugars also creates an environment conducive to the multiplication of acidogenic and acidic bacteria. On the contrary, a diet low in added sugars and fermentable carbohydrates and rich in mineral salts favors remineralization [3]. Intake of food and drinks with a low pH value can, if frequent, produce dental erosion by direct action of the acids brought into contact with the teeth [4].
The food pyramid and the guidelines for a healthy diet promoted by the Ministry of Health [5] together with the European guidelines [6] promote a diet rich in carbohydrates obtainable by whole nuts, fruit and vegetables. However, these foods are also a source of fermentable carbohydrates.
Caries is a disease caused by the dissolution of the mineral tissues of the body due to the acid produced by the bacterial metabolism of food carbohydrates. The two bacterial species mainly involved are oral streptococci, in particular *Streptococcus mutans*, and lactobacilli. In the sixties the caries pathogenesis was represented with three partially overlapping circles (Key diagram) that represented the three essential factors for its development: the tooth, the diet and the bacteria. Since then, many other factors have been recognized to be involved in the disease etiopathogenesis, with the result of a more complex model including, for example, saliva, the immune system, time, socioeconomic status, the level of education, lifestyle, oral hygiene habits, the use of fluorides. However the content of fermentable carbohydrates in the diet remains the causal factor without which the disease can not develop [7]. Due to the lack of availability of sugar during the war, there was a reduction in the prevalence of caries, which quickly returned when the restriction ended [8].
The European Food Safety Authority (EFSA) has defined the reference values for the intake of nutrients that must be taken to enjoy good health according to age and gender [9]. With regard to sugar, the European Authority claims that the frequent consumption of foods with a high sugar content increases the risk of dental caries and contributes to increase body weight. However, the group of experts found that there is no evidence sufficient to define a maximum sugar intake limit because the adverse health effects are related to the way food is consumed and to the type and frequency of intake rather than the total intake of sugars. EFSA will provide indications on the daily consumption of sugars added to foods by the beginning of

2020. Recently, the World Health Organization (WHO) has recommended limiting the consumption of free sugars (mono and disaccharides sugars added to foods from the industry or the consumer, plus the sugars naturally present in honey, syrups and fruit juices) to less than 10% of the total calories consumed daily with the aim of not exceeding 5%, because strong evidence indicates that doing so reduces overweight, obesity and caries [10]. Recent work has associated a high consumption of non-alcoholic drinks containing high percentages of sugars added with cardio-metabolic diseases including stroke and decency [11]. Groups of persons subjected to therapeutic reasons for high sugar consumption also have levels of excess of the general population, as shown by the case of children with chronic diseases that require prolonged intake of sugar-containing medicines [12]. Exposure to high levels of sugars has been the subject of several studies that have found in workers in the confectionery sector a prevalence of caries of 71% higher than that found in workers in other sectors [13]. Conversely, populations that traditionally follow low-sugar diets, such as the Inuit of North America, the Bantu of Africa, the inhabitants of the island of Tristan da Cunha in the South Atlantic Ocean have shown a reduced prevalence of caries not until they have been exposed to sugar, an event that has been followed by an increase in the disease [14].

2. MATERIALS AND METHODS

The present review of the narrative literature has examined selected scientific works from the PubMed database without time limits, using the key words "carbohydrates, polyols, intensive sweeteners, stevia, dental caries", used as words single and in association with each other. The papers selected are those that, according to the authors, best describe the problem that is the object of the present treatment. Furthermore, documents drawn from websites of accredited national and international bodies, such as the Ministry of Health, the World Health Organization and the European Commission have been evaluated and, if deemed relevant for the purpose of the audit work, described to provide the reader with a vision of current legislation in addition to the more properly scientific aspect.

Sweet foods and oral health

All of us select foods that are guided mainly by the emotions of pleasure or refusal that transmit us through vision, sight and above all taste.

Research indicates that sweet is the first to know about newborns and most like it at least in the early stages of life; in fact, breast milk is rich in sugar (lactose). This explains why sweet foods are produced very well by most of the population [15].

Vipeholm's work, one of the most famous studies investigating caries formation, demonstrates a strong correlation between the severity of the disease and the frequency of sugar ingestion. In a mental health institute in Sweden between 1945 and 1953, he found a development of caries very fast in subjects to whom large quantities of sweets were supplied. The duration of exposure and the permanence of sugary foods in the oral cavity lead to prolonged periods of acid production and subsequent demineralization [16]. Liquid sugars such as those contained in beverages and powdered milk preparations pass through the oral cavity rapidly with limited contact time with the dental surfaces. However, if sugary drinks are taken repeatedly or slowly, the risk of caries increases [17].

Hard candies, mints and lollipops are sources of sugars that are gradually released during consumption and persist for a long time in the oral cavity and, therefore, if their intake is frequent they represent a significant risk factor [18].
The residence time of the different foods in the oral cavity can vary considerably: a piece of candy or gelatine, even if they are sticky, are eliminated from the oral cavity faster than for retentive foods such as biscuits and crisps [19].
It is indeed important to remember that:
- the elimination capacity of sugars from the oral cavity is subjective and depends above all on the flow and the salivary fluidity [20];
- the adhesiveness of food is not important how much the quantity of carbohydrates that remain in the dental plaque and in the saliva; in fact, a high initial retention can be followed by a rapid oral evaluation [21]; white bread and raisins are kept longer than chocolate milk and some sweets and can produce a higher concentration of sugar, especially if they are consumed between meals [22].

3. RESULTS

Types of sugars

The sugars are present in foods in two forms: those naturally contained in foods such as fruit, honey and dairy products and those added to foods during processing to increase their taste or consistency.
Carbohydrates (**Table I**), an essential source of energy for the body, are generally classified as simple and complex. Among the simple sugars we find monosaccharides, organic compounds formed from carbon, hydrogen and oxygen that can not be broken down by hydrolysis. Glucose, fructose and galactose are the most important monosaccharides in the diet. Simple sugars made up of more than one molecule include disaccharides, made up of two identical or different molecules, such as sucrose (common table sugar), lactose and malt. The latter, for example, is formed by the condensation of two glucose molecules, while the lactose is due to the condensation of glucose and galactose. Sucrose is the most commonly used sugar and consists of glucose and fructose. Most of the mono and disaccharides are mainly used for the purpose of sweetening, however some disaccharides are used for different purposes such as lactulose, composed of galactose and fructose, indigestible by man, used as a laxative preparation, or trehalose composed of two molecules of glucose and diffused in yeasts, fungi and insects and used as a cryo-conservative. Then we have oligosaccharides, made up of more than two but less than ten molecules, such as maltodextrins. Finally, we have polysaccharides, characterized by a large number of repetitive units linked together to form large and complex molecules such as starch and glycogen.
When it comes to "fermentable carbohydrates", it refers to sugars or cooking starches that make up the substrate for oral microbial metabolism. In **fig. 1** schematized the metabolic process leading to the formation of acids with the demineralization of dental tissues. The most common fermentable sugar is sucrose. The hydrolysis of sucrose leads to the formation of the "invert sugar", which is naturally present in the juices of some fruits such as grapes [23].
Other mono- and disaccharides sugars such as lactose and maltose, present in many food products, can be fermented by the oral microorganisms giving rise to the production of weak acids capable of demineralizing hard dental tissues. Sucrose is

the sugar with the highest cariogenic power [24]. In **fig. 2** shows the main fermentable carbohydrates in order of decreasing cariogenicity.

Sucrose

Widely present in nature in fruit and honey (in lower percentage compared to fructose), it is generally obtained from sugar beet in Europe and from sugar cane in the rest of the world. The production of sugar from other sources, such as maple, date palm and coconut palm, is instead a minority.

The sucrose thus extracted is used in the food industry, especially confectionery and pastry, taking the common name of cooking sugar, refined white or "raw" wholemeal. As stated previously, its cariogenic power is very high.

Fructose

Fructose is a monosaccharide present in most of the sugary fruits and their juices, used as a sweetener and in the food industry. Fructose was used in the famous "Turku Study", in which a dietetic regimen using either fructose or sucrose or xylitol (polyol) was administered to three different groups of adult subjects in the town of Turku in Finland. After 2 years, the increase of caries in the group that had used only fructose compared to sucrose group was halved, with a DMFT (mean number of permanent teeth decayed, missing or filling) of 3.8 in the fructose group against 7.2 in the sucrose group [25].

Lactose

It is the sugar contained in cow's milk (4.8 g / 100 ml) and in the human milk (7 g / 100 ml). Despite its enhancement, milk has exploited tooth losses thanks to test calcium (125 mg / 100 ml) and proteins. The World Health Organization and UNICEF have always been promoting campaigns to promote breastfeeding, underlining the importance that nutrition plays in the first months and years of life and on its decisive role in maintaining optimal health conditions [26].

An association between decayed caries (early childhood caries) and breastfeeding, when this is consumed *ad libitum* and in frequent daily and nightly assumptions, has been hypothesized in the literature, but in support of this correlation no univocal results have been achieved today [28]. As in the case of fruit, milk is not considered a threat to oral health, even if its intake, as well as for other foods, must be followed by correct oral hygiene maneuvers. Conversely, the feeding of fruit juice, milk or other sugar-added drinks with the bottle considerably increases the risk of caries in infancy [27].

Starch

Starch is a complex glucose polymer of plant origin. It can be refined or taken in its natural state, consumed raw, as in fruit and hard, or cooked, as in baked goods. It is found in the fruits, seeds and tubers of plants.

Bacteria in the oral cavity are not able to metabolize it as such, however cooking and salivary amylase promote the release of glucose, maltose and maltotriose, in turn metabolized by oral bacteria to produce acids. Foods containing cooked starches, such as white bread, have been shown to be able to reduce the pH of the dental plaque to below the threshold value of 5.5, which is necessary for demineralization of the enamel to start. However, starch is less acidic than sucrose or foods containing starch and sucrose, having a cariogenic power of about half compared to sucrose [28].

Tagatose

Tagatose is a low carbohydrate sweetener that it provides 1.5 calories per gram. It is a sugar from a structural point of view very similar to fructose, present in nature in very small quantities, so its extraction is not economic. It is a crystalline white powder obtained from lactose. It was approved in the United States in May 2003 with the notification of the Food and Drug Administration (FDA) as a safe ingredient (GRAS-Generally Recognized as Safe). Tagatose behaves like fructose in the body, but only 15-20% is absorbed in the small intestine. Because of this incomplete absorption, it has a minimal effect on the glucose and insulin levels. The tagatose which is not digested proceeds towards the large intestine, where it acts as a prebiotic, promoting the production of probiotics, indispensable for the maintenance of a healthy digestive system. It is fermented in the colon and can therefore cause meteorism and diarrhea in sensitive individuals.

Tagatose is a non-cariogenic sugar: it is slowly fermented by the oral micro-organisms, producing quantities of acids not sufficient to reduce the pH of the dental plaque below the threshold values for the demineralization of hard tissues [29].

The sweetening and caloric power, the maximum permitted doses and the cariogenicity of the different carbohydrates are reported in **tab. II**. The advice given to patients to reduce the risk of caries through the "intelligent" intake of carbohydrates are shown in **tab. III.**

Alternatives to sugar

The use of alternative sweeteners to sugar has entered the market strongly and wisely, first to meet the health needs of patients that required a reduced dietary intake of carbohydrates such as diabetics, but later they were widely diffused thanks to the use by all those who wish to reduce their weight or control it due to the low caloric value of these sweeteners they can boast.

The sweetening substances available on the market can be added to foods or drinks or be placed in confectionary products called sugar-free or dietetic and can be divided into natural sweeteners and artificial or synthetic sweeteners. The argument, however, also presents a certain degree of confusion at the terminological level. For example, some producers call "natural" sweeteners even those treated or refined, as is the case with stevia preparations, or some artificial sweeteners because they are derived from naturally occurring substances such as sucralose derived from sugar.

A further classification of sweeteners takes into account their edible potency: there are in fact sweeteners that have a sweetening power similar to that of sugar like polyols and other intensive sweeteners that have tens or hundreds of times the sweetening power of sucrose (**Table II**).

The European Commission, Health and Food Safety Department, has set up the Register of nutrition and health claims. The Register report that the intake of foods or beverages containing intensive polyols and sweeteners (Article 13 [1]) and non-fermentable sugars (Article 13 [5]) in place of fermentable sugars reduces demineralization of enamel contributing to dental health. Furthermore, it is certified that sugar-free or xylitol-containing chewing gum (Article 14 [1] [a]) is capable of reducing plaque formation contributing to the maintenance of teeth and gum health [30].

Polyols

Also called "sugar alcohols" from which the name polyalcohols, polyols can be classified as derivatives of monosaccharides (sorbitol, erythritol, xylitol, mannitol), disaccharides (maltitol, isomalt, lactitol) and polysaccharides (hydrogenated starch hydrolysates). They have a good sweetening power similar to that of sugar. Polyols are mostly sweeteners with reduced caloric intake and can be used in the same amount as table sugar. They are often used in combination with other sweeteners to improve their level of sweetness and taste. They are used to sweeten foods such as biscuits, sweets, chewing gum, bakery products, ice cream or toothpaste, mouthwashes and pharmaceutical products.

The polyols, moreover, provide an effect of freshness ("cool" effect), contribute to maintaining the humidity of the product in which they are inserted, to increase the volume, not to lose the sweetness and to preserve its organoleptic characteristics. They are naturally present in many fruits and vegetables but for commercial uses they are often produced from carbohydrates, such as starch, sucrose and glucose. The FDA considers polyols to be safe for food use (GRAS) and are in fact approved as food additives.

The polyols are only partially absorbed by the small intestine with a lower effect on blood sugar than carbohydrates. Those that are not absorbed continue their journey in the large intestine where they are fermented by bacteria. Excessive amounts of polyols (above 7-14 g per day) may have laxative effects. The Academy of Nutrition and Dietetics informs that a consumption of more than 50 grams a day of sorbitol or 20 grams of mannitol may cause diarrhea.

Polyols have no cariogenic action because the bacteria in the oral cavity are unable to metabolize them and turn them into acids. The FDA authorizes the use of this claim on the labels of products containing polyols [31].

Xylitol is also called the wood sugar because it can be extracted from the bark of some trees like birch trees, but it is also found in strawberries, raspberries, prunes and wheat. In Europe it is used as a food additive and identified by the initials E967; it is added in particular to chewing gums and sweets to inhibit cariogenic bacteria.

The first study that assessed the cariogenic power of xylitol was carried out in Turku in Finland at the end of the Sixties: 125 adult subjects substituted sucrose in their diet with xylitol for a period of two years during who did not develop caries, unlike those who had used fructose or sucrose.

Although the mechanism of action of xylitol is not yet fully known, in addition to its antibacterial action, one of the reasons for its anti-caries efficacy is that *S. mutans* is not able to use it as an energy substrate, resulting in lower acid production. Taking it for long periods of time (a few months) through chewing gum or candy would seem to determine a process by which "less virulent" bacteria would replace the more cariogenic [32].

The administration of xylitol to mothers with young children is an effective preventive method to limit the passage of cariogenic bacteria from the mother to the baby, thus reducing the risk of caries in the deciduous dentition [33].

A recent Italian study [34] conducted by the Universities of Milan and Sassari on primary school children evaluated the effect of daily administration of xylitol for 6 months through a chewing gum, administered by teachers during the hours school. Two years after the end of the administration and in the absence of other preventive

maneuvers except for the regular use of a fluoride toothpaste, children who had used xylitol had a number of new inferior caries about 10 times compared to those who had made use of a sugar-free chewing gum not contented with xylitol.
In conclusion, xylitol is an effective preventive tool that can fully support the traditional and always valid ones represented by a diet that is poor in fermentable sugars, a fluoride toothpaste and regular periodic checks.
The most widespread polyol is *sorbitol.* Less expensive than xylitol, it does not lower the pH of the dental plaque below the demineralization threshold of the enamel if it is taken at low doses; however, it is considered a sweetener with low galloping power at high doses (more than two chewing gums a day) as cariogenic bacteria can "learn" how to metabolize it [35]. In a study conducted on more than a thousand subjects, the use of both chewing gum and xylitol was more effective in reducing the incidence of caries compared to the use of a sweetened gum with sucrose [36].
Erythritol is a polyalcohol present in fruit and fermented foods, used as a sweetener, thanks to its low-calorie characteristics (zero calories) and good taste without aftertaste. It is used in combination with intensive sweeteners to increase sweetness, increase bodyiness and mask unpleasant aftertaste. A recent review of the literature examined the benefits of erythritol on health today [37], verifying that this polyol is able to reduce dental plaque and the adherence of oral streptococci to surfaces dental. It has also been shown to inhibit the growth and metabolism of cariogenic bacteria such as *S. mutans*, reduce the expression of bacterial genes involved in the metabolism of sucrose, reduce the incidence of caries and is a useful aid through the air-polishing in periodontal treatment.

Intensive sweeteners

Stevia rebaudiana

The Stevia rebaudiana Bertoni, named after the Italian-Swiss botanist who in 1889 first classified it, is a perennial herbaceous-shrubby plant native to South America, from whose leaves it is possible to obtain a sweetener with a very high sweetening power. Used by indigenous cultures of South America for centuries, it was introduced to Europe by Spanish conquerors in the 16th century. It was reintroduced at the beginning of the 20th century by the Italian-Swiss botanist Moisés S. Bertoni who in 1905 classified it and described it. Stevioside and rebaudioside A are the two most represented glycosides in its leaves. The stevioside is about 200-300 times sweeter than sucrose.
Stevia is approved as a food supplement in several countries such as Brazil, Japan, the United States and recently also in the European Union [38]. Stevioside and rebaudioside A do not affect plaque pH values, since they are not able to promote bacterial metabolism and are therefore considered non-cariogenic sweeteners [39].

Saccharin

It is the most well-known and long-lasting synthetic sweetener. It was discovered in 1879 by Ira Remsen and Constantin Fahlberg of the Johns Hopkins University. For decades it was the only sucrose substitute for people with diabetes. It has a bitter aftertaste considered unpleasant; is therefore associated with the cyclamate in a proportion of 1:10 to correct the respective defects in the aftertaste. It is heat resistant [40].

Its use is also in decline in relation to a hypothetical risk of inducing gene mutations and the onset of vascular tumors in laboratory animals. No effect is known on oral health.

Aspartame
Discovered casually in 1965, it is made up of the amino acids phenylalanine and aspartic acid. It has a caloric power similar to sucrose, but the quantities used are so small that its caloric intake is practically irrelevant. The products containing it must be labeled "contains a source of phenylalanine", as subjects affected by ketonuria, genetic defect due to the lack or absence of the enzyme phenylalanine hydroxylase which catalyzes the conversion of phenylalanine into tyrosine, they can not take it.
The hypothesized onset of allergies, food intolerances and cancer pathologies has never been demonstrated at the recommended doses. No effect is known on oral health.

Acelsulfame K
It is a potassium salt discovered casually in 1967. Unlike aspartame it is heat resistant, which makes it particularly suitable for confectionery products. It is not metabolized by the body and is excreted unchanged in the urine.
It has been criticized for the possible carcinogenic effect, but its harmful consequences have been disproved by both the Food and Drug Administration and the Scientific Committee on Food of the European Union. No effect is known on oral health.

Cyclamates
They are intensive synthetic sweeteners deriving from sodium and calcium salts of the cyclic acid (cyclohexylsulphatic acid). They have a sweetening power 30 times higher than sucrose. They are used in association with saccharin to cover its bitter aftertaste. Their use was initially limited in the USA and in Great Britain following researches that found carcinogenic effects and absorption disturbances in laboratory animals. In 1984 the Committee for the FDA cancer assessment has examined the scientific evidence and has concluded that the cyclamate is not a carcinogen. No effect is known on oral health.
The sweetening and caloric power, the maximum permitted doses and the cariogenicity of the various natural and synthetic sweeteners are reported in **tab. II**.
The advice to be given to patients to reduce the risk of caries through the intake of alternative sweeteners to carbohydrates are reported in **tab. IV**.

4. CONCLUSIONS
Simple carbohydrates are an important source of nourishment for the body; however, their excessive consumption increases the risk of contracting systemic diseases and the oral cavity.
From the above and suggested by numerous national and international bodies that deal with nutrition and health protection, the use of free sugars must be limited both in terms of quantity and frequency of intake. Natural or synthetic sugar substitutes can help reduce the incidence of caries in both adults and children. However, their use is subject to certain restrictions.

PAPER III

SUBMITTED

Comparison among three standardized caries risk assessment methods

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Comparison among three standardized caries risk assessment methods

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Abstract:

Background: Caries risk assessment (CRA) is essential to plan preventive and therapeutic strategies and different models have been proposed for the identification of individuals running a risk of future caries.

Aim: The purpose of this study was to compare the caries risk level using three different multifactorial caries risk models Cariogram®, CaMBRA and Previser, in a sample of Italian adults.

Methods: 68 subjects, aged between 20 and 59 years (average 23 years), students at the University of Milan, were enrolled and examined. Salivary flow rate, salivary buffer capacity, and the evaluation of the concentration of *Streptococcus mutans* (SM) and *Lactusbacillus spp* in saliva were performed. Clinical examination was also realized and DMFT, Plaque Index and caries risk assessment were performed using the Cariogram®, CaMBRA and PreViser models.

Results: Data shows a low match among the three models. Only in 29 subjects out of 68 (42%) there was a perfect match among results obtained through the three models. Considering caries level obtained using CaMBRA and PreViser, a quite high correspondence was observed (53 subjects on 68 - 78%). Comparing Cariogram model and PreViser a lower correspondence of the results was noted (37 subjects out of 68 - 54%). Finally comparing CaMBRA and Cariogram the lowest correspondence was found (30 subjects on 68 - 44%).

Conclusion: The results showed that different caries risk assessment models evaluate the risk differently, probably due to the multifactorial aetiology of the disease. There is an urgent need to develop valid and reliable methods for caries risk assessment that are based on best evidence for caries prediction and disease management.

Key words: caries risk assessment, Cariogram, CaMBRA, PreViser, CRA models

Background

Dental caries is still one of the most common diseases in the general population [1-4] and in young people [5-8], with a significant impact on the quality of life of those affected [9].

The need to accurately predict the caries risk of each individual is evident, as targeted preventative actions can be addressed before carious lesions develop. Therefore, caries risk assessment (CRA) is an important step in preventing and making decisions about the treatment plan. It must be considered an integral part of the treatment plan.

Naturally, if the main etiological factors can be identified, the appropriate treatment for that particular individual can be performed with good results.

Caries risk assessment models currently imply a combination of risk indicators and protective factors that interact with a variety of social, cultural and behavioral factors [10].

There are several CRA models [11], which include different combinations of risk factors, protective factors and different interpretations of the results. [12]

Most of the studies have analyzed the role and the power of single or multiple risk factors as predictors of the future development of new caries lesions, but only a small part of the research evaluated the success of the multifactorial models proposed for the risk assessment of caries.

For this study, three different methods of caries risk assessment were examined: Cariogram®, CaMBRA and PreViser. [13-15]

The aim of the research was to assess the risk of caries in a group of young adults through these three different methods (Cariogram®, CaMBRA and PreViser) and to compare the results obtained in order to verify if the judgment expressed by the three methods is concordant and to evaluate, if it is not, which variable means that the evaluations do not coincide.

Material and Method

Study design

The study design followed the Declaration of Helsinki, and was approved by the Ethics Committee of the University of Milan. The survey was conducted in Milan, Lombardy, Italy in March 2017. The subjects were enrolled in the Dental Clinic of the University of Milan among the students of the Degree Course in Dentistry and Dental Prosthesis in the Academic Year 2016-2017. A sample size calculation was performed following the Viechtbauer et al. (2015) and resulting in a necessary number of 65 subjects. [16]. One hundred subjects (average age 23 ± 3.11 years), was invited to participate. Thirty two subjects did not join the study. Sixty-eight subjects were enrolled and interviewed to record hygienic-sanitary habits, oral hygiene and general hygiene, exposure to fluorine. The experience of caries (DMFT index) and the amount of plaque (plaque index of Silness and Loe) was measured. Salivary flow, salivary buffer capacity, and concentration counts of cariogenic bacteria, *Streptococcus mutans* and *Lactusbacillus spp*. Finally, for each subject, the level of risk was calculated using the CaMBRA, PreViser and Cariogram® models. The correlation coefficient of Lin (CCA) was calculated to determine to what extent the observed data differed from the perfect concordance line. The Bradley-Blackwood (BBt) test was used for a simultaneous mean and variance test.

Clinical tests

The collection of clinical data was performed by two calibrated examiners (GB and MGC) before starting the study. For calibration, five patients, not included in the study sample, were examined. The trial was carried out under standardized conditions: an optical artificial lighting, after air drying and using a plain mirror and a World Health Organization probe.

The state of the dentition was found using the DMFT Index, Decayed Missing and Filled Permanent Teeth to determine past and current caries experience. The third molars teeth have been excluded from the count due to the young age of the subjects.

The plaque index was detected using the Silness and Loe index (1964) which refers to 4 values: 0 corresponds to the absence of plaque, 1 corresponds to the presence of plaque recognized only after application of a highlighter agent or after having the probe is run along the gingival margin, 2 corresponds to plaque visible to the naked eye and finally 3 corresponds to abundant plaque.

pH evaluations

Stimulated salivary secretion rate and buffer capacity also were measured for each subjects and salivary cariogenic microflora was assessed.

Collection and treatment of saliva samples were performed using a standardized kit CRT Ivoclar Vivadent, composed by CRT Buffer and CRT Bacteria.

The CRT Buffer Test [CRT® Bacteria and Buffer Test (Vivadent Ets., Lichtenstein)] was used to determine the buffer capacity of saliva using a colorimetric test strip. The CRT Bacteria Test measured the *Streptococcus mutans* and Lactobacilli count in saliva by means of selective culture media.

Paraffin-stimulated whole saliva was collected in calibrated sterile tubes. CRT Buffer Test was stripped from the package without touching the yellow test field. The entire yellow test field was wetted with saliva using a pipette. To determine the buffer capacity of saliva, the color of the test field was compared with the color samples after exactly 5 minutes of reaction time. High, medium, and low salivary buffer capacities are indicated by blue, green, and yellow test fields, respectively.

The saliva collected for the CRT Buffer Test was also used for the CRT Bacteria Test. The agar carrier was removed from the test vial, and a NaHCO3- tablet was placed at the bottom of the vial. Using a pipette, both agar surfaces were wetted with saliva. The agar carrier was placed back into the vial and closed tightly.

After incubation at 37°C for 48 hour, the density of S. mutans and Lactobacilli colonies was assessed using the corresponding evaluation pictures provided with the kit.

Caries risk assessment

There are several models of caries risk assessment (CRA); they include different combinations of risk factors, protective factors and different interpretations of the results. For this study, three models using computer programs were used. All models are multifactorial. Inserting table with factors The data collected for each patient are then interpreted with the aid of software, which interactively identify and illustrate the risk of developing new caries lesions and therefore help to draw up personalized and targeted prevention programs. Here we will analyze the operation of Cariogram®, CaMBRA and PreViser.

Cariogram® is a software, available in several languages [13], which illustrates the risk of a patient avoiding new caries interactively. It displays the caries risk graphically as "the chance to avoid new caries lesions" in the near future. The software analyses nine different factors related to caries and the risk is expressed by a pie-circle chart divided into five different coloured sectors. The green one shows the chance to avoid new caries lesions. The Cariogram is the most used assessment method and it is used primarily in children [17-19], and secondarily in adults [20,21].

CaMBRA, the Caries Management By Risk Assessment (CaMBRA) [14,22] consists of the evaluation of 22 risk/protective factors to assess the level of risk. Different versions of the questionnaire were developed to use in patients of varying age (0-5 years, > 6 years), where the patient is classified in one of the following risk categories: low, medium, high or extreme. Clinicians, after assessing caries risk, should individually plan a based-evidence treatment. Nowadays an application for smartphone and tablet is also available.

PreViser is an online risk assessment system that is used to predict periodontal disease, dental caries and oral cancer, based on mathematical algorithms that assign different weights to the various risk factors. The part focused on the caries risk assessment consists of a series of questions on behaviour, medical and oral health practices in order to classify the individual caries risk into three categories: low, medium and high risk of caries. The PreViser is mainly used in periodontal disease risk assessment and poor scientific data reporting its use in caries assessment are available [15].

A comparative chart showing the factors included in each CRA model is displayed in **Table 1.**

The results were divided into three risk classes: high, moderate and low. According to this method at a high risk it corresponds: 0-40% of Cariogram®, high risk of CaMBRA, very high / high risk of PreViser. At a moderate risk corresponds: 41-60% of Cariogram®, moderate risk of CaMBRA, moderate risk of PreViser. At a low risk it corresponds: 61-100% of Cariogram®, low risk of CaMBRA, low / very low risk of PreViser.

Statistical analysis

Assuming a standard deviation of 1.0, a significance level of 5%, and a power of 90% for a detectable difference of 0.5, a sample size of 65 participants was required.

Cohen's Kappa was calculated to evaluate the percentage of agreement among the three risk assessment models.

Lin's Concordance Correlation Coefficient for Agreement (CCA) was calculated to determine how far the observed data deviate from the line of perfect concordance.

The Bradley-Blackwood test (BBt) was used for a simultaneous test of their means and variances.

Results

The data collected during the study were inserted using the Microsoft Excel 2013 program and then compared in order to have an analysis of the collected data.

The results obtained following the execution of the three methods taken in exams on each individual subject are been entered into a table. In the first column the results provided by the CaMBRA test were inserted, in the second column the results provided by the PreViser test and in the third column the results provided by the Cariogram test. Each row of the table therefore corresponds to a subject under investigation associated with the respective risk class in which it was placed by the three models. (**Table 2**)

It is immediately possible to notice the discrepancy of the results obtained, which corresponds to the low concordance of the results provided by the three models in question.

Of the 68 subjects analyzed in the CaMBRA method, 22 subjects were included in the low risk group, 3 subjects were included in the moderate risk group and 43 subjects were included in the high risk group. With the PreViser method of the 68 subjects 31 were inserted in the low risk group, 6 subjects were included in the moderate risk group and 31 subjects were inserted in the high risk category of caries. While with Cariogram method 35 subjects were inserted in the low risk group, 21 subjects were inserted in the moderate risk group and 12 subjects were inserted in the high risk group.

So, by dividing the subjects by caries risk group for a low risk with CaMBRA method we have 22 subjects, whit PreViser we have 31 subjects and with Cariogram we obtain 35. For the moderate risk group with the CaMBRA the subjects turn out to be 3, 6 with the PreViser method and 21 with the Cariogram method. For the high risk group we have 43 subjects evaluated with the CaMBRA, 31 with the PreViser and 12 with the Cariogram. (**Fig. 1**)

29 subjects out of 68 show a concordance between the three models used with 10 subjects at high risk of caries, 1 subject at moderate risk and 18 subjects at low risk of developing new caries in the future.

Considering caries level obtained using CaMBRA and PreViser, a quite high correspondence was observed with 53 subjects out of 68. Comparing Cariogram model and PreViser a lower correspondence of the results was noted with 37 subjects out of 68. Finally comparing CaMBRA and Cariogram the lowest correspondence was found with 30 subjects out of 68. Following Cohen's Kappa statistic, a value of 0.23 with an agreement of 22.73% was found among the three models. CCA was 0.65 (95%CI 0.52 – 0.78) with a BBt=8.97 ($p<0.01$) between CaMBRA and PreViser, CCA=0.37 (95%CI 0.21 – 0.53) with a BBt=21.22 ($p<0.01$) between CaMBRA and Cariogram and finally CCA=0.43 (95%CI 0.26 – 0.60) with a BBt=13.11 ($p<0.01$) between PreViser and Cariogram. (**Fig.2**)

The "visible cavitation" or "filling in the last three years" factor was removed from the CaMBRA method and a new comparison was made with PreViser: a 91% agreement was observed in this case. (**Fig. 3)**

Discussion

It can be immediately noted that the CaMBRA method tends to overestimate the individual risk of developing caries in the near future, with 43 subjects on 68 places at high caries risk, unlike the PreViser method in which the number of high risk subjects, 31, corresponds to the number of subjects at low risk and unlike the Cariogram method which shows much more positive results, only 12 subjects out of 68 are placed in the high risk group.

In comparison, there is a low correspondence between the results provided by the three models. Only in 29 cases out of 68, so for 42% there is a correspondence of the results in all three models; instead, the correspondence between the CaMBRA and PreViser method is high with 78%, 53 cases out of 68; the correspondence of the results is lower if we compare the CaMBRA method with the Cariogram method with 44%, 30 subjects; the correspondence between Cariogram and PreViser method is slightly higher with a correspondence rate of 54%, then 37 cases out of 68. CaMBRA method tends to overestimate the individual risk of developing caries in the near future, probably because the presence of the risk factor "tooth filling due to caries in the last 3 years" or "visible cavity affecting the dentin" immediately puts the patient in the class high risk, regardless of the protective factors of the subject, unlike the other methods for which these factors affect the least, they place the subject in a moderate/low risk group for the PreViser and Cariogram methods, both models therefore take more account of the protective factors; however, this occurs only if the elements involved do not exceed the number of 1, decayd tooth or filling tooth for caries in the last 3 years, if the elements involved were 2 or more, the CaMBRA and PreViser tend to provide concordant results for 91% while the Cariogram method continues to underestimate the risk; only in the case where the patient's DMFT exceeds the value taken as a normal population index (DMFT = 4), the Cariogram method provides results that coincide with the other 2 methods.

Conclusions

The study showed that CaMBRA, PreViser and Cariogram do not produce concordant results, probably due to the different risk/protective factors considered and the different "weights" given to different factors. The highest agreement was obtained regarding low risk subjects. The findings of this pilot study underline how the calculation of the risk level even using standardized models is a very difficult goal not yet fully achieved. Further studies are needed to assess which methods are effective in the identification of the level of the risk associated to the actual caries status and/or the prediction of new lesion in the near future. It is urgent to develop valid and reliable methods for caries risk assessment based on best evidence for caries prediction and disease management.

Conflicts of interest

The Authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

References

1. Marthaler T. Changes in dental caries 1953-2003. Caries Res. 2004 May-Jun;38(3):173-81.
2. Whelton H. Overview of the impact of changing global patterns of dental caries experience on caries clinical trials. J Dent Res. 2004;83 Spec No C:C29-34.
3. Hugoson A, Koch G, Göthberg C, Helkimo AN, Lundin SA, Norderyd O, Sjödin B, Sondell K. Oral health of individuals aged 3-80 years in Jönköping, Sweden during 30 years (1973-2003). I. Review of findings on dental care habits and knowledge of oral health. Swed Dent J. 2005;29(4):125-38.
4. Selwitz RH, Ismail AL, Pitts NB. Dental caries. Lancet. 2007 Jan 6;369(9555):51-9.
5. Tinanoff N, Kanellis MJ, Vargas CM. Current understanding of the epidemiology mechanisms, and prevention of dental caries in preschool children. Pediatr Dent. 2002 Nov-Dec;24(6):543-51.
6. Campus G, Lumbau A, Sanna AM, Solinas G, Lugliè P, Castiglia P. Oral health condition in an Italian preschool population. Eur J Paediatr Dent. 2004 Jun;5(2):86-91.
7. Cleaton-Jones P, Fatti P, Bonecker M. Dental caries trends in 5- to 6-year-old and 11- to 13-year-old children in three UNICEF designated regions--Sub Saharan Africa, Middle East and North Africa, Latin America and Caribbean: 1970-2004. Int Dent J. 2006 Oct;56(5):294-300.
8. Campus G, Solinas G, Cagetti MG, Senna A, Minelli L, Majori S, Montagna MT, Reali D, Castiglia P, Strohmenger L. National Pathfinder survey of 12-year-old Children's Oral Health in Italy.; Caries Res. 2007;41(6):512-7.
9. Cagetti, M., Mastroberardino, S., Brambilla, E., Campus, G., & Strohmenger, L. La prevenzione della carie oggi: dalla valutazione del rischio all'applicazione di protocollli preventivi mirati. Il dentista moderno. 2009;3:40-56.

10. Australian Research Centre for Population Oral Health, Caries Risk Assessment for Children: Information for Oral Health Practitioners.
11. Petersson GH, Fure S, Bratthall D. Evaluation of a computer-based caries risk assessment program in an elderly group of individuals. Acta Odontol Scand. 2003;61:164-71.
12. Cagetti MG, Bontà G, Cocco F, Lingstrom P, Strohmenger L, Campus G. Are standardized caries risk assessment models effective in assessing actual caries status and future caries increment? A systematic review. BMC Oral Health. 2018 Jul 16;18(1):123.
13. Bratthall D, Petersson GH. Cariogram: a multifactorial risk assessment model for a multifactorial disease. Community Dent Oral Epidemiol. 2005;33:256-64.
14. Young D, Ricks CS, Featherstone JD, Fontana M, Fournier SM, Geiermann SP et al. Changing the face and practice of dentistry: a 10-year plan. J Calif Dent Assoc. 2011;39:746-51.
15. Zukanovic A. Caries risk assessment models in caries prediction. Acta Med Acad. 2013;42:198-208.
16. Viechtbauer W, Smits L, Kotz D, Budé L, Spigt M, Serroyen J, Crutzen R. A simple formula for the calculation of sample size in pilot studies, J Clin Epidemiol. 2015 Nov;68(11):1375-9.
17. Campus, G., Solinas, G., Strohmenger, L., Cagetti, M., Senna, A., Minelli, L., . . . Castiglia, P. Collaborating Study Group. National pathfinder survey on children's oral health in Italy: pattern and severity of caries disease in 4-year-olds. Caries Res, 2009;43(2), 155-62.
18. Petersson GH, Twetman S, Bratthall D. Evaluation of a computer program for caries risk assessment in schoolchildren. Caries Res. 2002;36:327-40.
19. Twetman S, Petersson GH, Bratthall D. Caries risk assessment as a predictor of metabolic control in young Type 1 diabetics. Diabet Med. 2005;22:312-5.
20. Carta G, Cagetti MG, Cocco F, Sale S, Lingstrom P, Campus G. Caries-risk profiles in Italian adults using computer caries assessment system and ICDAS. Braz Oral Res. 2015;29(1):S1806-83242015000100306.

21. Fadel H, Al Hamdan K, Rhbeini Y, Heijl L, Birkhed D. Root caries and risk profiles using the Cariogram in different periodontal disease severity groups. Acta Odontol Scand. 2011 Mar;69(2):118-24.
22. Domejean S, White JM, Featherstone JD. Validation of the CDA CAMBRA caries risk assessment: a six-year retrospective study. J Calif Dent Assoc. 2011;39:709-15.

	CaMBRA	*PreViser*	*Cariogram*
Factors			
Socio-demographic			
• age	X	X	
• ethnicity			
• family socio-economic status	x		
Behavioural			
• diet	X	X	X
• fluoride	X	X	X
• chlorhexidine	X	X	
• xilitolo chewing gum	X	X	
Clinical			
• oral hygiene	X	X	X
• past caries	X	X	X
• caries	X	X	
• DMFT			X
• white spot	X	X	
• filling tooth for caries	X	X	X
• dental appliance	X	X	
Salivary and microbiological tests			
• saliva flow rate	X	X	X
• saliva buffering capacity			X
• *Mutans sterptococci*	X	X	X
• *Lactobacillus spp.*	X	X	X

Table 1. Caries risk levels of the sample (68 subjects) with the three methods.

CaMBRA	PREVISER	CARIOGRAM
LOW	LOW	74%
HIGH	VERY HIGH	61%
LOW	LOW	60%
HIGH	LOW	79%
HIGH	VERY HIGH	72%
HIGH	LOW	47%
MODERATE	LOW	75%
HIGH	VERY HIGH	39%
LOW	VERY LOW	90%
LOW	VERY LOW	85%
HIGH	VERY HIGH	40%
LOW	VERY LOW	90%
HIGH	VERY HIGH	61%
HIGH	LOW	71%
HIGH	LOW	41%
HIGH	VERY HIGH	58%
LOW	VERY LOW	64%
HIGH	VERY LOW	77%
HIGH	HIGH	58%
LOW	LOW	93%
HIGH	VERY HIGH	31%
LOW	LOW	92%
HIGH	MODERATE	40%
HIGH	VERY HIGH	45%
LOW	MODERATE	22%
MODERATE	MODERATE	41%
LOW	LOW	71%
HIGH	HIGH	87%
LOW	LOW	95%
HIGH	HIGH	64%
HIGH	HIGH	61%
LOW	VERY LOW	85%
HIGH	HIGH	60%
HIGH	HIGH	42%
LOW	VERY LOW	78%
HIGH	LOW	44%
HIGH	LOW	68%
HIGH	HIGH	45%
HIGH	HIGH	57%
HIGH	VERY HIGH	62%
HIGH	HIGH	49%
HIGH	VERY HIGH	64%
HIGH	VERY HIGH	8%
HIGH	VERY HIGH	37%
LOW	LOW	76%
HIGH	VERY HIGH	57%
HIGH	HIGH	22%
HIGH	LOW	60%
HIGH	HIGH	53%
HIGH	HIGH	45%
HIGH	HIGH	63%
HIGH	HIGH	81%
LOW	VERY LOW	83%
HIGH	HIGH	21%
LOW	LOW	60%
HIGH	VERY HIGH	29%
MODERATE	VERY LOW	93%
LOW	VERY LOW	92%
LOW	LOW	52%
HIGH	HIGH	32%
LOW	VERY LOW	94%
HIGH	MODERATE	56%
HIGH	MODERATE	47%
HIGH	MODERATE	87%
LOW	VERY LOW	93%
LOW	VERY LOW	96%
LOW	LOW	83%
HIGH	HIGH	40%

Table 2. Level of caries risk using the three different methods. The CaMBRA method provides an overestimation of the risk, with 43 subjects on 68 evaluated at high risk. Using the PreViser method, the number of high risk subjects corresponds to the number of low-risk subjects. Finally using the Cariogram model, only 12 subjects on 68 were judged at high risk level, while the majority (35 over 68) were considered at low risk.

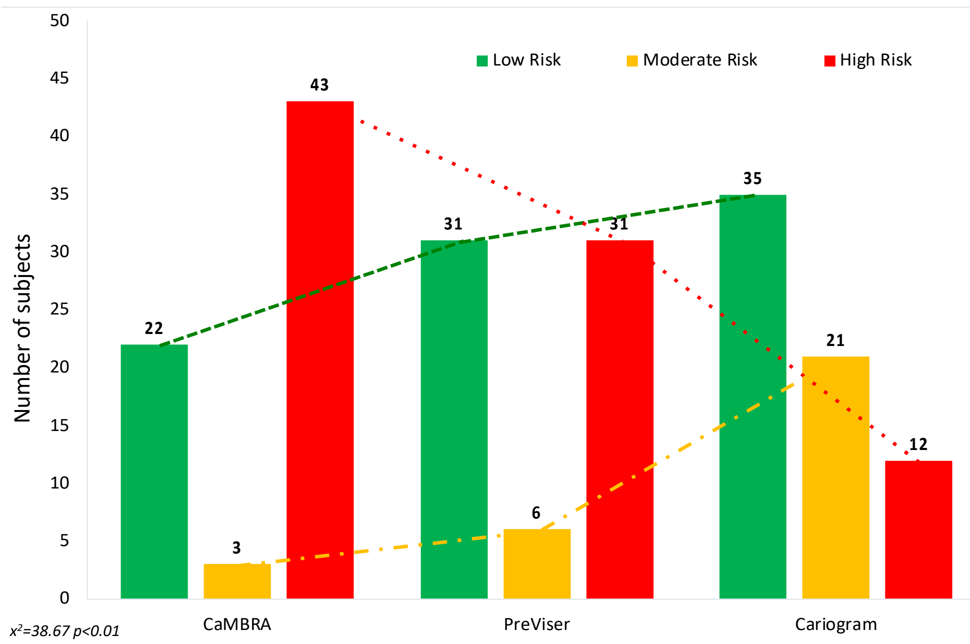

Fig. 1 The number of subjects in each risk category using the three models is shown. Using the CaMBRA model the highest number of high risk subjects was found (43 subjects on 68), while the Cariogram model showed the lowest level (12 subjects on 68) and the PreViser was in the middle. On the other hand, Cariogram identified the highest number of low risk patients (35 subjects on 68).

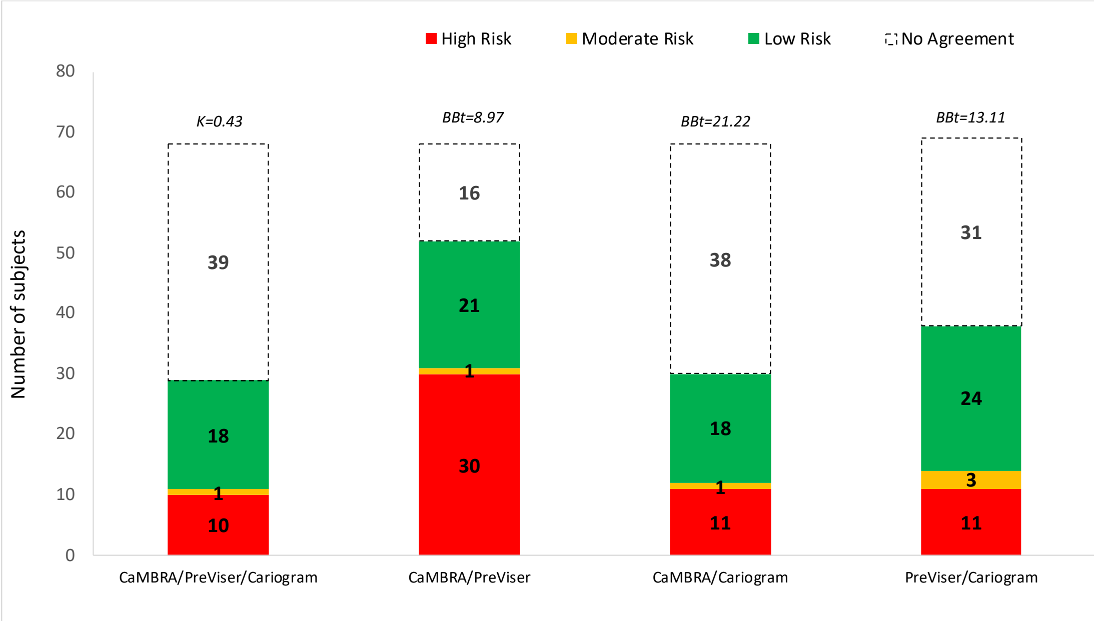

Fig. 2 Data show a range of agreement from low to good between the risk level calculated using the three models. Following Cohen's Kappa statistic, a value of 0.23 with an agreement of 22.73% was found among the three models. CCA was 0.65 (95%CI 0.52 – 0.78) with a BBt=8.97 ($p<0.01$) between CaMBRA and PreViser, CCA=0.37 (95%CI 0.21 – 0.53) with a BBt=21.22 ($p<0.01$) between CaMBRA and Cariogram and finally CCA=0.43 (95%CI 0.26 – 0.60) with a BBt=13.11 ($p<0.01$) between PreViser and Cariogram.

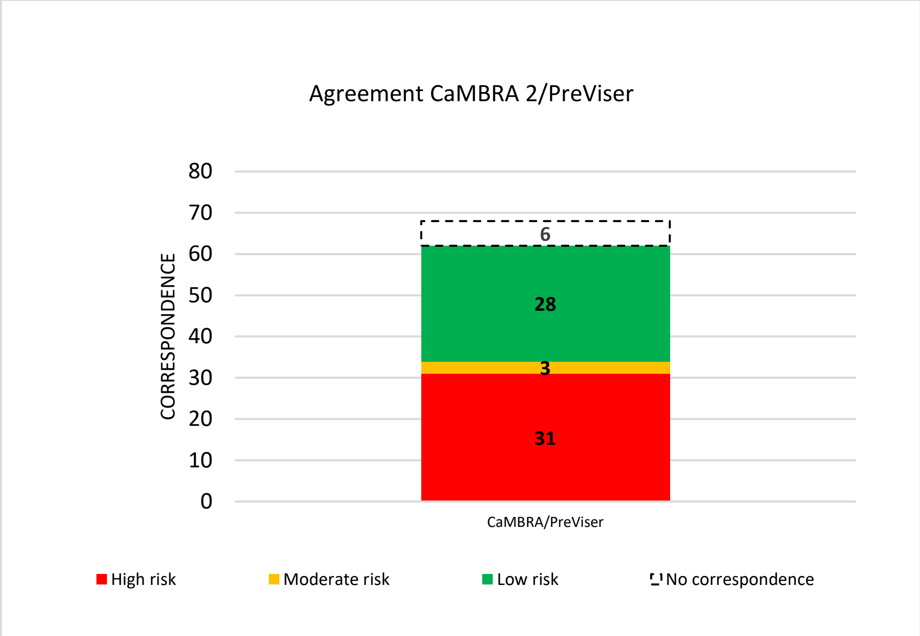

Fig. 3. Risk assessments carried out with CaMBRA without taking into account the factor "a carcinogenic element" or "an obstructed element for caries in the last three years", compared to the evaluations provided by the PreViser method.

PAPER IV

SUBMITTED

Evaluation of a new simplified caries risk assessment model in children

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Evaluation of a new simplified caries risk assessment model in children

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Abstract:

Aim: The aim of this pilot study is to present a new simplified caries risk assessment method for children based on the Italian National Guidelines for Oral Health Promotion and Prevention of Oral Desease and to compare the caries risk measured using this new method with those obtained using the CaMBRA and the Cariogram models in a sample of children.

Method: A sample size calculation for pilot study was performed and resulted in a required number of 62 subjects. 71 pediatric patients aged 6-14 years (mean age 9.5 years) attending the Dental Clinic of the University of Milan were enrolled. The caries experience (DMFT/dmft) and the plaque index (Silness and Loe index) were measured. Hygiene and dietary habits were collected through a standardized questionnaire. The caries risk level of each child was than calculated using the new method and the CaMBRA and the Cariogram models. The agreement between the simplified method and the standardized models was then calculated.

Results: In the comparison between the new simplified method and CaMBRA, 55 children out of 71 were classified with the same risk level, with a Cohen coefficient of 0.55, while comparing the new method with Cariogram model, 44 subjects were classified at the same level of risk, with a Cohen coefficient of 0.32. Moreover, comparing CaMBRA and Cariogram results, only 45 subjects out of 71 were classified coherently with a Cohen coefficient of 0.39.

Conclusion: The proposed new model of caries risk assessment does not produce concordant results with those obtained using Cariogram and CaMBRA, which even between them do not seem to agree. The findings of this pilot study underline how the calculation of the risk level, even using standardized models, is a very difficult goal not yet fully achieved. The results showed that different caries risk assessment models evaluate the risk differently, probably due to the multifactorial aetiology of the disease, and the different "weight" assigned to each factor in different models.

Key words: Caries risk assessment, Cariogram, CaMBRA, standardized caries risk assessment models, CRA models

Background

Over the past few decades, the prevalence of dental caries in industrialized countries has been greatly reduced (Sudjalim et al., 2006) especially among children and young adults; this goal was obtained thanks to health education promoted by phisicians, mass-media and also thanks to the application of evidence-based preventive protocols. Nevertheless, caries remains a very common disease in the population (Axelsson et al., 2004) with a significant impact on the quality of life of the people affected (Cagetti et al., 2009).

Caries risk assessment is the probability to predict future caries development before the clinical onset of the disease.

The etiological factors that lead to the development of caries are many. This type of assessment is therefore complex and includes physical, biological, environmental and behavioral factors. A high concentration of cariogenic bacteria, inappropriate eating habits, an inadequate salivary flow, insufficient fluoride exposure, poor oral hygiene and a low socio-economic status are recognized as determinant risk factors for the development of the disease (Young et al., 2007; Selwitz et al., 2007; de Castilho et al., 2013; Strohmenger, et al., 2013).

The result obtained using a risk assessment method classifies a patient as a subject with a low risk of caries, a moderate risk of caries or a high risk of caries.

The evaluation of the risk of caries has the purpose to identify the etiological factors involved in each subject's risk and to put in place personalized measures of prevention.

As a consequence, the assessment of individual caries risk is a prerequisite for planning the treatment plan.

The aim of this pilot study is to present a new simplified method of caries risk assessment and to evaluate the agreement of the results obtained using this new model with those obtained using the CaMBRA and the Cariogram models in a sample of children.

Material and Method

Study subjects

A total of 71 pediatric patients aged 6-14 years (mean age of 9.49) were randomly selected attending the Dental Clinic of the University of Milan, Italy.

The study protocol was reviewed and approved by the Ethical Committee of the University of Milan. An official permission to conduct the study and an informed consent from the parents'childrens was obtained before the start of the examination.

In the study were included patients in permanent, mixed and deciduous dentition who gave consent to the evaluation. All parents of the enrolled subjects have agreed to the treatment.

Power analysis, using a one-sided confidence interval, was performed to identify a sample size that gives reasonable confidence that this pilot trial is big enough to enable us to make the right decision about proceeding to a larger trial or not. The margin of error was set at 10% and a 90% confidence level with a sample size of 62 subjects. (Daniel, 1999)

Study design

The pilot study was conducted from January to April 2018.

This study included the following procedures: questionnaire, interview, clinical examination (dental status and estimation of oral hygiene), and creation of the caries risk profile using Cariogram model, CaMBRA model and a new simplified caries risk assessment model performed using a new method derived from the National

Guidelines for the Promotion of Oral Health and Prevention of Oral Diseases in Children.

The questionnaire

For each subject of the study a questionnaire was filled out by interviewing the parent consisting of twelve questions regarding the child's oral hygiene habits, eating habits and lifestyle such as: the toothpaste used, if a mouthwash is used, if it has been subjected to professional fluoride treatments in the last six months, if it has used xylitol-containing gums four times a day in the last six months, if it takes fluoride supplements or drugs, what kind of water drinks, how much snacks or drinks containing sugar consumes between the main meals. It is important to know even if there are pathologies, if there is a dry mouth or reduced salivary flow, if there is an orthodontic mobile or fixed devices.

All children were in good general health and no severe systemic diseases were reported. The information collected will then be used to calculate the risk of caries of each subject.

The clinical examination

Each patient was visited to perform the DMFT/dmft, criterion adopted by the World Health Organization (WHO) as an index of health of the dental arches; it provides information on the current presence of carious lesions (D = carioactivity) or on the past experience of caries, in deciduous, mixed or permanent dentition. (Oral Health Surveys: Basic methods. 4th ed. Geneva: WHO; 1997), (Klein et al.,1938)

The visual and tactile examination was performed under lighting with a mirror and a sharp probe.

Furthermore, the plaque index was detected for each patient. The plaque index in used for this study is the Plaque Index of Silness and Loe (PI), which is the presence in the areas adjacent to the gingival margin; it does not need the pigmentation of the plaque through detecting substances, but it must be done through a periodontal probe. To calculate the plaque index a score of 0 to 3 is assigned for each dental element. (Silness, 1964; Loe, 1963)

The bacterial count and the salivary buffering power was not calculated because the salivary tests were not performed. The salivary flow was assessed with a visual examination by the operator and asking the patient if he had the sensation of having a dry mouth.

Caries risk assessment models

A caries risk profile was calculate for each subjects using the Cariogram model, the CaMBRA model and a model that was performed using a new method derived from the National Guidelines for the Promotion of Oral Health and Prevention of Oral Diseases in Children.

The Cariogram assesses risk of future caries lesion development and presents results as ‘the chance of avoiding caries’. Seven factors have to be entered to create an individual risk profile. The Cariogram calculates the individual risk of future carious lesion development and represents the risk as a pie diagram. The sector which is left represents the chance of avoiding caries. If this sector is small, the caries risk is high, and *vice versa*. It can vary from 0 to 100%. If there is 100% chance of avoiding caries, there is no risk for caries development in the future. If there is a 0% chance of avoiding caries, caries will appear for certain. (Bratthall, 2001)

CaMBRA consists in the evaluation of 22 risk/protective factors to assess the level of risk. There are different versions of the questionnaire to use in patients of different age (0-5 years, over 6 years). From the results it is possible to classify each patient within one of the categories: low, medium, high or extreme risk. For the evaluation of the CaMBRA method the MyCaMBRA APP for smartphone and tablets was used. (Young et al., 2011)

The proposed new simplified model

Starting from the factors of risk ratings illustrated in the 2013 Health Guidelines for the Promotion of Oral Health and Prevention of Oral Diseases in children development of the Ministry of Health for the assessment of caries risk in subjects >6 years old, a new evaluation model was performed. Each evaluated factor is assigned a score (negative or positive) The result derives from the sum of all the evaluated factors. It will allow to establish the class of risk (low-moderate-high) of caries of the subject and determine the type of recall.

The new proposed model includes the evaluation of biological factors, protective and clinical factors.

The questionnaire collected information about socio-economic background (e.g., maternal and paternal education levels, self-rated financial status) assessed through completed by the parent, where the profession of both the mother and the father is requested. There is a complex relationship between personal socio-economic status (SES) and oral health. (Elamin et al.,2018). People with a low SES have poorer oral health status than do those with a higher SES and oral health worsens progressively from higher SES to lower SES. (Steele et al., 2015; Kim et al., 2014)

The questionnaire also asked about eating habits. It is asked how many snacks or drinks containing sugar the child is usual to eat during the day. In the study performed by Elamin et al. in 2018 Children who had caries (dmft> 0) consumed foods with a high sugar content more frequently than those without caries (Elamin et al., 2018)

The presence of disability or systemic pathology is specified because child who is not able to cleanse himself or herself the oral cavity (eg serious motor problems, syndromes with mental retardation), is not able to perform the correct proceedings of oral hygiene.

Fluoroprophylaxis, intended as prevention of caries through the use of fluorine, represents the milestone of caries prevention (Marinho et al., 2009, & AAPD, 2013) and is necessary for all individuals. (Twetman, 2009a; EAPD, 2009, & Walsh et al.) The adequate exposure to fluorine is then evaluated.

The effectiveness of the only mechanical cleaning of dental surfaces with brushing to prevent caries is very difficult to evaluate. However, this proceeding is also important because it represents the way in which the application of cariostatic agents such as fluorine takes place, carried into the oral cavity through the toothpaste.

Removing plaque with a toothbrush helps prevent the appearance of gingivitis, brushing with a fluoride toothpaste prevents tooth decay (Robinson et al., 2005).

The degree of oral hygiene is assessed with the clinical examination. Is reported the absence/presence of minimal plaque deposits (plaque index <15% identify a subject with good oral hygiene).

Saliva, therefore, affects many aspects of caries risk. Reduction of salivary secretion, if protracted over time, promote the development of new lesions and the enlargement of existing ones.

The basal salivary flow lower than 0.1 ml/minute or stimulated below 1 ml/minute, indicates a reduction in the flow below the risk threshold for the carious pathology (Smith & Mattos, 2008).

The most important predictors of future decay is dmft in the previous year. (Reisine et al., 1994)

The white spots, the caries experience and the presence of incongruous restorations (steps, missing material, infiltrations) are therefore taken into consideration during the clinical examination. Only the white spots that can be related to incipient caries are considered, ie where the probe feel roughness.

The presence of orthodontic devices is also detected. Fixed and/or mobile orthodontic appliance increase the surfaces to be cleaned and therefore the oral hygiene maneuvers are more difficult.

Even the mobile device, if not cleaned, can be the site of warehouse of organic residues and therefore plaque.

The sum of the factors evaluated for each subject will give a value that will place the subject in a class of risk of developing caries in the future. Negative values, below 0, correspond to a low risk of caries. Values of 0 or 1 correspond to a moderate risk of caries. Values above or equal to 2 correspond to a high risk of caries.

The future control sessions must be established according to the patient's susceptibility, then according to the class of risk to which he belongs and to the evaluation of clinical/biological and clinical data detected during the controls.(**Table1**)

Statistical Analysis

Assuming a standard deviation of 1.0, a significance level of 10%, and a power of 90% for a detectable difference of 0.5, a sample size of 62 participants was required.
Kappa values were categorized according to the scale suggested by Landis and Koch. (Landis & Koch, 1977)
According to this scale, values 0 is considered as poor agreement, 0.00–0.20 slight, 0.21–0.40 fair, 0.41–0.60 moderate, 0.61–0.80 substantial and values .0.81 as almost perfect agreement.

Results

The results were divided into three risk classes: high, moderate and low. According to this method at a high risk it corresponds 0-40% of Cariogram®, at a moderate risk corresponds 41-60% of Cariogram® and at a low risk it corresponds 61-100% of Cariogram®.

The extreme risk identified for the CaMBRA method was merged with the high risk, even if no evaluated subjects showed an extreme risk of caries.

The degree of risk assessed by the three methods for each subject is not always corresponding.

Of the 71 subjects evaluated with the new simplified model 53 subjects were at high risk, 7 at moderate risk and 11 at low risk of caries. With the CaMBRA method of the 71 subjects, 43 were at high risk of caries, 2 at moderate risk and the remaining 26 at low risk of caries. Finally, with the Cariogram method, 37 subjects out of 71 were at high risk of caries, 17 at moderate risk and 17 others at low risk. **Fig. 1**

It was then evaluated whether there was an agreement between the results obtained from the three different evaluation models.

In the comparison between the new simplified method and CaMBRA, 55 children out of 71 (77,4%) were classified with the same risk level, with a Cohen coefficient of 0.55, with 43 subjects at high caries risk, 1 at moderate risk and 1 at low risk of caries.

While comparing the new method with Cariogram model, 44 subjects (61,9%) were classified at the same level of risk, with a Cohen coefficient of 0.32 with 35 subjects at high caries risk, 1 subject at moderate risk and 8 subjects at low risk of caries.

Moreover, comparing CaMBRA and Cariogram results, only 45 subjects out of 71 (63,3%) were classified coherently with a Cohen coefficient of 0.39 with 30 subjects at high risk of caries, no one at moderate risk and 15 subjects at low risk of caries. (**Fig. 2)**

Discussion

Dental caries affects individuals differently, which makes it essential to identify high-risk patients so that preventive strategies can be undertaken. The concept of caries-risk assessment is simple and straightforward. The idea is to identify patients who are most likely to develop caries (Van Loveren & Helderman, 2003; Daryani et al., 2014).

Although there are many risk factors for dental caries, the post eruptive local effect of dietary sugar is one of the main factors in development of caries (Holund et al., 1985).

As can be seen from results the new simplified method of assessing caries risk tends to overstimate the risk compared to the others two methods with 53 subjects out of 71 with high risk of developing caries in the future and 43 out of 71 for the CaMBRA method and 37 out of 71 for the Cariogram method.

The new simplified method and CaMBRA show the maximum agreement with 55 subjects on 71 classified consistently while between the new method and the Cariogram it is lower with 44 concordants on 71, but similar to the agreement we find between the CaMBRA and the Cariogram with 45 subjects out of 71 concordants.

According to Kappa coefficient of Cohen the agreement between CaMBRA and the new simplified model is considered moderate, with a value of 0,55, while agreement between Cariogram and the simplified model or Cariogram and CaMBRA model are considered a fair agreement respectively of 0,32 and 0,39.

Conclusion

The proposed new simplified assessment of caries risk and the methods with which it has been compared do not produce completely consistent results, probably due to the multifactorial aetiology of the carious disease and the different risk/protection factors considered by the three models.

Furthermore, by comparing the results obtained by the methods used, Cariogram and CaMBRA, the obtained concordance is modest; Cariogram tends to underestimate the risk of caries, on the contrary CaMBRA overestimates the risk.

The highest concordance was achieved between the new caries risk assessment method and the CaMBRA method.

The proposed method is simpler and could be defined as "time saving", therefore it can also be used in the pediatric clinical reality that could include this evaluation in health check-ups.

In conclusion, it can be said that the simplified evaluation method of caries risk seems to be effective in the same way as the other already consolidated methods.

The results presented in this paper underline how the calculation of the risk level, even using standardized models such as Cariogram and CaMBRA, is a difficult and not yet fully achieved objective.

References

1. Sudjalim, T., Woods, M., & Manton, D. (2006). Prevention of white spot lesions in orthodontic practice: a contemporary review. Aust Dent J, 51, 284-9.
2. Axelsson, S., Söder, B., Nordenram, G., & al, e. (2004). Ef- fect of combined caries-preventive methods: a systematic review of controlled clinical trials. Acta Odontol Scand, 62, 163-9.
3. Cagetti, M., Mastroberardino, S., Brambilla, E., Campus, G., Strohmenger, L. (2009). la prevenzione della carie oggi: dalla valutazione del rischio all'applicazione di protocollli preventivi mirati. Il dentista moderno, 3, 40-56.
4. Young, D., Featherstone, J., Roth, J., Anderson, M., Autio-Gold, J., Christensen, G., Wolff, M. (2007). Caries management by risk assessment: implementation guidelines. J Calif Dent Assoc., 35(11), p. 799-805.
5. Selwitz, R., Ismail, A., & Pitts, N. (2007). Dentalcaries. Lancet, 6;369(9555), 51-9.
6. de Castilho, A., Mialhe, F., Barbosa Tde, S., & Puppin-Rontani, R. (2013). Influence of family environment on children's oral health: a systematic review. J Pediatr (Rio J), 89(2), 116-23.

7. Ministero del lavoro, della salute e delle politiche sociali. Linee guida nazionali per la promozione della salute orale e la prevenzione del- le patologie orali in età evolutiva. Aggiornamento 2013: https://www.salute.gov.it/imgs/C_17_pubblicazioni_2073_allegato.pdf
8. Daniel WW (1999). Biostatistics: A Foundation for Analysis in the Health Sciences. 7th edition. New York: John Wiley & Sons.
9. Oral Health Surveys: Basic methods. 4th ed. Geneva: WHO; 1997.
10. Klein H, Palmer CE, Knutson JW. Studies on dental caries I. Dental status and dental needs of elementary school. Pub Health Rep 1938; 53: 751-65.
11. Silness J, Loe H. Periodontal disease in pregnancy. II. Correlation between oral hygiene and periodontal condtion. Acta Odontol Scand. 1964;22:121–35.
12. Loe H, Silness J. Periodontal disease in pregnancy. I. Prevalence and severity. Acta Odontol Scand. 1963;21:533–51.
13. Bratthall D, Ramanathan Stjernswärd J et al. Assessment of caries risk in the clinic – A modern approach. In Wilson NHF, Roulet JF, Fuzzi M (eds): Advances in Operative Dentistry. pp 61-72. Chicago, Quintessence, 2001.
14. Young D, Ricks CS, Featherstone JD, Fontana M, Fournier SM, Geiermann SP et al. Changing the face and practice of dentistry: a 10-year plan. J Calif Dent Assoc. 2011;39:746-51.
15. Elamin A, Garemo M, Gardner A. Dental caries and their association with socioeconomic characteristics, oral hygiene practices and eating habits among preschool children in Abu Dhabi, United Arab Emirates - the NOPLAS project. BMC Oral Health. 2018 Jun 8;18(1):104.
16. Landis JR, Koch GG. The measurement of observer agreement for categorical data. Biometrics 1977; 33: 159–74.
17. Van Loveren C, Helderman WH. Identi cation of caries risk patients. An overview of predictive models [in Dutch]. Ned Tijdschr Tandheelkd. 2003; 110: 435-8.
18. Daryani H et al., Cariogram Model in Assessment of Dental Caries among Mentally Challenged and Visually Impaired Individuals of Udaipur, India. J Clin Diagn Res. 2014 Jan;8(1):206-10.

19. Holund U, Theilade E, Poulsen S. Validity of a dietary interviewing method for use in caries prevention. Community Dent Oral Epidemiol. 1985; 13: 219-21.
20. Schwendicke F, Dörfer CE, Schlattmann P, et al. Socioeconomic inequality and caries: a systematic review and meta-analysis. J Dent Res 2015;94:10–18.
21. Han DH, Khang YH, Choi HJ. Association of parental education with tooth loss among Korean Elders. Community Dent Oral Epidemiol 2015;43:489–99.
22. Steele J,+ Shen J, Tsakos G, et al. The Interplay between socioeconomic inequalities and clinical oral health. J Dent Res 2015;94:19–26.
23. Kim DW, Park JC, Rim TT, et al. Socioeconomic disparities of periodontitis in Koreans based on the KNHANES IV. Oral Dis 2014;20:551–9.
24. Twetman S. Caries prevention with fluoride toothpaste in children: an update. Eur Arch Paediatr Dent. 2009;10(3):162-7.
25. Robinson PG, Deacon SA, Deery C, et al. Manual versus powered toothbrushing for oral health. Cochrane Database Syst Rev 2005;CD00 2281.
26. Smith & Mattos-Graner, Secretory immunity following mutans streptococcal infection or immunization. Curr Top Microbiol Immunol. 2008;319:131-56.
27. Reisine et Al.; A biopsychosocial model to predict caries in preschool children. Pediatr Dent 1994 Nov-Dec;16(6):413-8.

Simplified assessment of caries risk age >6 years BIOLOGICAL FACTORS		
	Yes	No
Low socio-economic status	+2	0
Over 4 off meal	+3	0
Disability	+2	0
PROTECTIVE FACTORS		
	Yes	No
Adequate exposure to fluorine	-1	0
Good oral hygiene	-1	0
CLINICAL FACTORS		
	Yes	No
White spot/demineralization	+3	0
1 Caries	+3	0
2 or more caries	+4	0
Low salivary flow (option)	+3	0
Incongruous restorations	+2	0
Fixed and/or mobile orthodontic appliance	+2	0
RESULTS (SUMMER SCORING)		
Low risk: TOT <0	Moderate risk: 0≤TOT≤1	High risk: TOT≥2

Tab. 1 Factors evaluated for calculating the risk of caries according to the proposed simplified model

Simplified model	CaMBRA	Cariogram
Low risk	Low risk	Low risk
Low risk	Low risk	Low risk
Moderate risk	Low risk	Moderate risk
Low risk	Low risk	Moderate risk
High risk	High risk	High risk
High risk	Moderate risk	High risk
Low risk	Low risk	Low risk
High risk	High risk	High risk
Moderate risk	Low risk	Low risk
High risk	High risk	Moderate risk
High risk	High risk	Moderate risk
High risk	High risk	High risk
Low risk	Low risk	Low risk
High risk	High risk	High risk
High risk	High risk	High risk
High risk	Low risk	Low risk
Low risk	Low risk	Low risk
High risk	High risk	High risk
High risk	High risk	High risk
High risk	High risk	High risk
High risk	Low risk	Low risk
Low risk	Low risk	Low risk
High risk	High risk	High risk
High risk	High risk	Moderate risk
Moderate risk	Low risk	Low risk
High risk	High risk	High risk
High risk	Low risk	High risk
High risk	High risk	Moderate risk
High risk	Low risk	Low risk
Low risk	Low risk	Low risk
High risk	High risk	High risk
High risk	High risk	High risk
High risk	High risk	High risk
High risk	High risk	High risk
High risk	High risk	High risk
Moderate risk	Low risk	High risk
High risk	High risk	Moderate risk
High risk	High risk	Moderate risk
High risk	High risk	Moderate risk
Low risk	Low risk	Low risk
High risk	High risk	High risk
High risk	Low risk	Moderate risk
High risk	High risk	Low risk
High risk	High risk	Moderate risk
High risk	Low risk	Moderate risk
High risk	High risk	High risk
High risk	High risk	High risk
High risk	High risk	High risk
High risk	High risk	High risk
High risk	Low rish	High risk
High risk	High risk	Moderate risk
High risk	High risk	Moderate risk
High risk	Low risk	High risk
High risk	High risk	High risk
High risk	High risk	High risk
High risk	High risk	High risk
High risk	High risk	High risk
Low risk	Low risk	High risk
High risk	Low risk	High risk
High risk	High risk	Moderate risk
High risk	High risk	High risk
High risk	High risk	High risk
Low risk	Low risk	Moderate risk
High risk	High risk	High risk

Moderate risk	Low risk	Low risk
High risk	High risk	Moderate risk
Moderate risk	Moderate risk	Low risk
Moderate risk	Low risk	Low risk
High risk	High risk	High risk
High risk	High risk	High risk
High risk	High risk	High risk

Table 2. The level of caries risk assessed with the three methods in the 71 subjects of the study is reported. The first column contains the results obtained from the simplified evaluation model, the second the results provided by the CaMBRA test and the results of the Cariogram test in the third column.

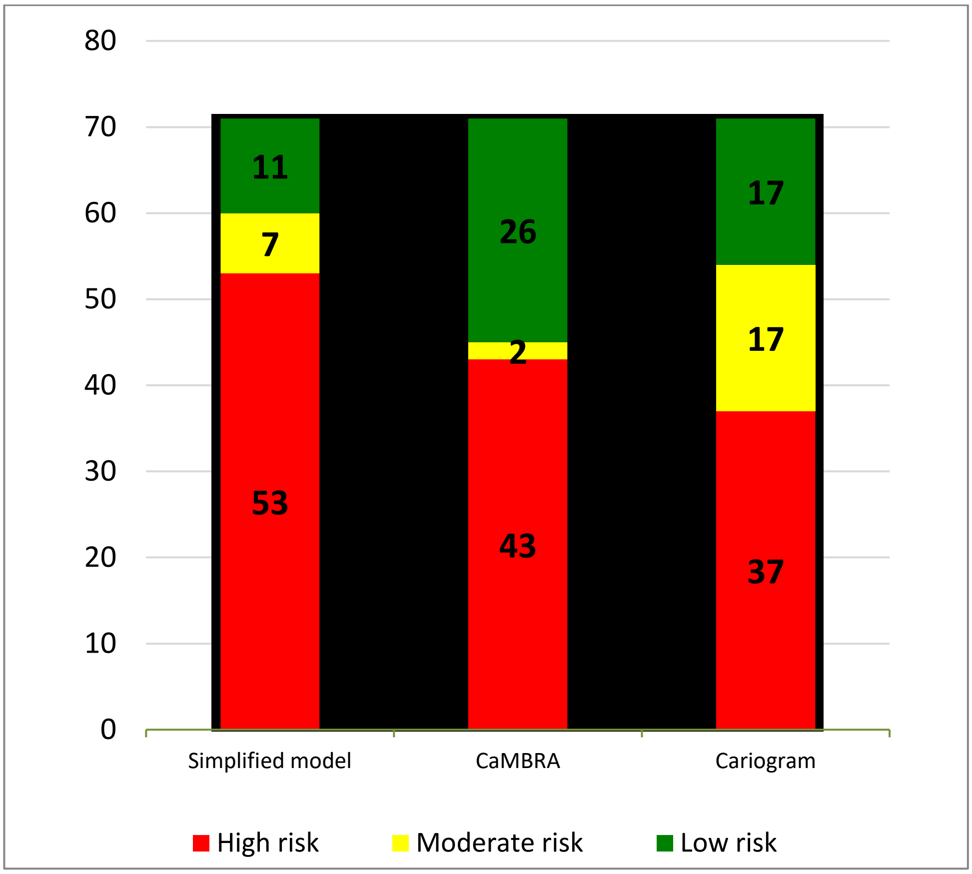

Figure 1. The number of subjects in each risk category using the three models is shown.

The new simplified method tends to overestimate the level of the risk of developing caries in the near future, with 53 subjects on 71 classified at high risk of caries, while using the CaMBRA method 43 subjects were evaluated at high risk, and finally using the Cariogram method only 37 subjects over 71 were judged at high risk.

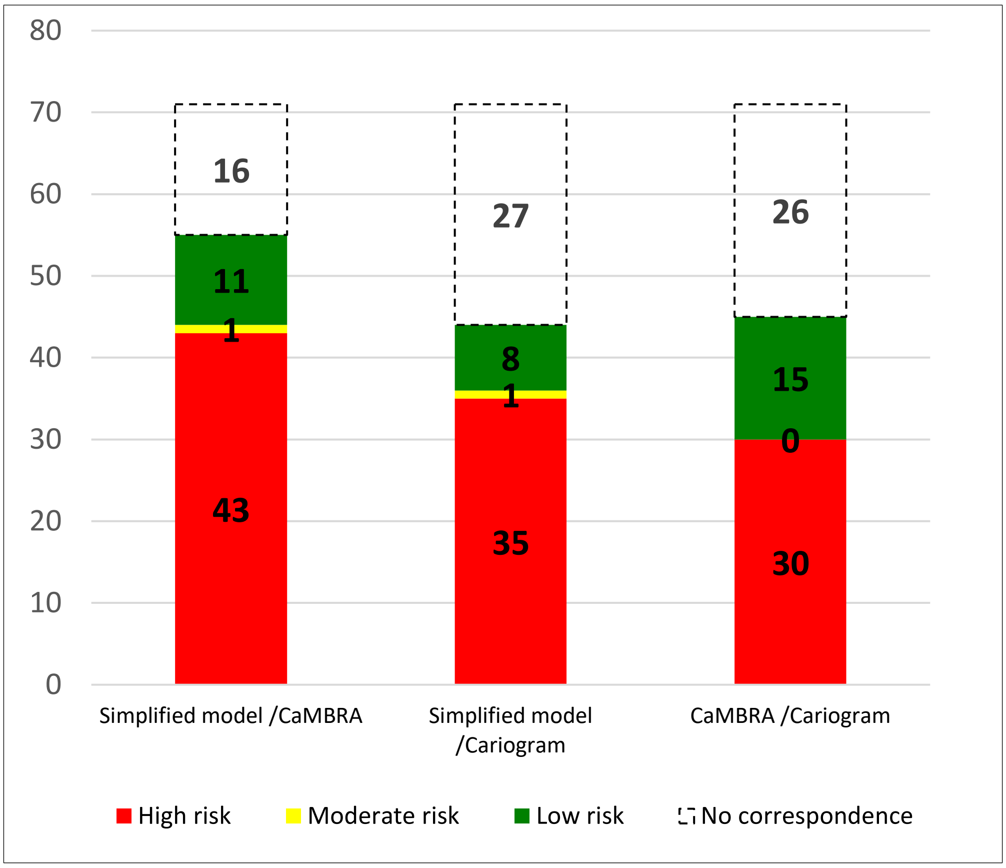

Figure 2. Agreement between the results provided by the three models. The new simplified method and CaMBRA show the greatest agreement with 55 subjects out of 71 classified coherently.