A comparison of treatment choices when dental caries lesions are diagnosed with two visual-tactile systems
the Nyvad and ICDAS II+LAA

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Preface

Declaration of contribution of co-authors of manuscripts contained in this thesis

Manuscript I: “Reproducibility and Diagnostic Outcomes of Two Visual-Tactile Systems for Caries Lesion Activity among General Dental Practitioners: a Cross-Over Study” represents the results of the first part of the project. The original idea, protocol development, recruitment of dentists and study subjects, training and calibration of the dental practitioners, implementation and management of the project, data analysis, preparatory work and writing of the manuscript were performed by Svetlana Tikhonova (the student). The role of the co-authors Dr Jocelyne Feine and Dr Paul Allison was advising in the results presentation, reviewing and modifying the texts and drafts of the article. The role of Dr Natallia Pustavoytava was to help in organisation and implementation of the study in Belarus.

Manuscript II: “Treatment Decisions from two Caries Diagnostic Systems: A Cross-over Trial” represents the final and main results of the study. The original idea, protocol development, recruitment of dentists and study subjects, training and calibration of the dental practitioners, implementation and management of the project, part of the data analysis, preparatory work and writing of the manuscript were performed by Svetlana Tikhonova (the student). The role of the co-authors, Dr Jocelyne Feine and Dr Paul Allison, was advising in the results presentation, reviewing and modifying the texts and drafts of the article. The role of Dr Natallia Pustavoytava was to help in organisation and implementation of the study in Belarus. The role of Dr Thiago Ardenghi was to help with multilevel regression analysis and reviewing of the article.
ABSTRACT (English)

Aim: The aim of this randomized cross-over study was to evaluate the reproducibility and differences in diagnostic and treatment outcomes by practicing dental clinicians previously inexperienced in using the Nyvad criteria and the ICDAS II criteria with Lesion Activity Assessment system (ICDAS II+LAA).

Methods: Four volunteer dentists were randomly allocated to one of two groups. Both groups of dentists examined the same voluntary sample (n=140) of caries active young adults using the Nyvad and the ICDAS II+LAA criteria in different sequences. The first group used the Nyvad criteria during period I, followed by ICDAS II+LAA during period II; the second group did the examinations in the opposite sequence. Before the period 1 and 2 examinations, dentists from both groups were trained with the Nyvad or the ICDAS II+LAA criteria, depending on the group in which they were assigned. Results: Intra-examiner agreement for the severity diagnostic threshold was high for both diagnostic instruments (weighted Kappa 0.62-0.80). For the D1 (active) diagnostic threshold, the intra-examiner unweighted Kappa values were 0.31-0.61 for the ICDAS II+LAA and 0.36-0.51 for the Nyvad. The mean number of active non-cavitated carious lesions was significantly higher for the ICDAS II+LAA (6.14, SD±5.4) than for the Nyvad criteria (3.90, SD±3.9; p<0.0001). Active cavitated/dentinal carious lesions were significantly higher for the ICDAS II+LAA (4.14, SD±4.1) than for the Nyvad criteria (2.13, SD±3.1; p<0.0001). The mean number of operative treatment decisions per surface was 1.53 (95% CI 1.43-1.65) times higher for the ICDAS II+LAA than for the Nyvad. The mean number of non-operative treatment decisions was 1.59 (95% CI 1.51-1.68) times higher for the ICDAS II+LAA than for the Nyvad. Conclusion: Both the Nyvad and the ICDAS II+LAA diagnostic systems showed high reproducibility for the lesion severity assessment. The use of the ICDAS II+LAA diagnostic system may result in more treatment, both operative and non-operative in a high caries risk population. A long-term study is needed to determine the costs and health effects with both diagnostic systems.

Trial registration: ISRCTN65592532.
RÉSUMÉ (Français)

Objectif: L'objectif de cette étude randomisée de type "crossover" était d'évaluer la reproductibilité et les différences dans la détermination des diagnostics et des traitements choisis, par des dentistes praticiens initialement inexpérimentés dans l’utilisation des critères Nyvad et des critères ICDAS II avec le système d'évaluation d'activité des lésions (ICDAS II + LAA). Méthodes: Quatre dentistes volontaires ont été répartis au hasard en deux groupes. Les deux groupes de dentistes ont examiné le même groupe volontaire de jeunes adultes (n = 140) ayant un risque élevé pour la carie dentaire, en utilisant les critères Nyvad et ICDAS II + LAA dans des séquences différentes. Le premier groupe a utilisé les critères Nyvad pendant la période I, suivie par ICDAS II + LAA pendant la période II ; le deuxième groupe a effectué les examens dans l'ordre inverse. Avant les périodes d'examens 1 et 2, les dentistes des deux groupes avaient été formés avec les critères Nyvad ou II ICDAS + LAA en fonction du groupe dans lequel ils avaient été affectés. Résultats: La concordance intra-examineur pour le seuil de sévérité des diagnostics s’est avérée élevée pour les deux instruments de diagnostic (Kappa pondéré de 0.62 à 0.80). Pour seuil de diagnostic de la D1 (active), des valeurs Kappa non pondérée intra-examineur étaient de 0.31 à 0.61 pour le ICDAS II + LAA et de 0.36 à 0.51 pour le Nyvad. Le nombre moyen de lésions carieuses actives non-cavitaires était significativement plus élevé pour le ICDAS II + LAA (6.14, SD ± 5.4) que pour le Nyvad (3.90, SD ± 3.9, p <0.0001). Des lésions actives cavitaires/de la dentine, étaient significativement plus nombreuses pour le ICDAS II + LAA (4.14, SD ± 4.1) que pour le Nyvad (2.13, SD ± 3.1, p <0.0001). Le nombre moyen de décisions de traitement opératoire par surface était 1.53 fois (IC 95% 1.43 à 1.65) plus élevé pour le ICDAS II + LAA que pour le Nyvad. Le nombre moyen de décisions de traitement non opératoire était 1.59 fois (IC 95% 1.51 à 1.68) plus élevé pour le ICDAS II + LAA que pour le Nyvad. Conclusion: Les deux systèmes de diagnostic (Nyvad et ICDAS II + LAA) ont démontré une reproductibilité élevée pour l'évaluation de la sévérité des lésions. L'utilisation du système de diagnostic ICDAS II + LAA peut entraîner
plus de décisions de traitements à la fois opératoires et non opératoires pour une population ayant un risque élevé pour la carie dentaire. Une étude à long terme est nécessaire pour déterminer les coûts et les effets sur la santé, que pourrais avoir l'utilisation des deux systèmes de diagnostic. L'enregistrement des essais: ISRCTN65592532.
1. RESEARCH BACKGROUND AND RATIONALE

1.1 Background

1.1.1 Caries disease process

Caries disease definition
Dental caries is a multifactorial chronic disease process, resulting from an imbalance in the dynamic equilibrium between the bacterial biofilm ecology and the conditions in the oral environment. This imbalance leads to loss of tooth minerals (Fejerskov, 2004; Fontana et al., 2009).

Caries process
Dental biofilm is a physiological phenomena that forms by the growth of resident oral micro-flora on any tooth surface (Fejerskov, 1997). The biofilm consists of a community of microorganisms with a collective physiology that is organised as a structure encapsulated within a matrix of extracellular polysaccharides (Kidd, 2010). The biofilm is a microbial ecosystem, resulting from a dynamic balance of microbial interactions and characterised by a degree of stability (microbial homeostasis; Marsh, 2009). The constant metabolic activity of the microorganisms causes continuous, rapid pH fluctuations inside the biofilm (Kidd and Fejerskov, 2004). The fluctuations of pH in bacterial biofilm result in a dynamic demineralization and remineralisation process. When fermentable dietary carbohydrates are consumed, the biofilm bacteria metabolise them into sugars and convert them into acids. Excess sugars are stored as intracellular polysaccharides, which are then converted into acids when sugar is limited (Takahashi and Nyvad, 2008). This lowers the pH in the biofilm fluid. When the local pH falls below a critical value (pH 5.5 for enamel), the biofilm fluid becomes under saturated with respect to the enamel minerals, and calcium and phosphate ions dissolve out of the tooth. This process is called demineralization. However, when the sugar level declines and the acid is neutralized by saliva, the biofilm fluid pH rises, supersaturated concentrations of enamel minerals are re-established and minerals that were lost are re-deposited back into the tooth.
enamel. This is called *remineralisation* (Cury and Tenuta, 2008, 2009). This dynamic de- and remineralisation phenomenon is characterised as ubiquitous and a naturally-occurring physiological process and called the *caries process* (Baelum et al., 2008a). Since microbial biofilms constantly form on tooth surfaces and are always metabolically active, the de-remineralisation process cannot be prevented (Kidd and Fejerskov, 2008). As long as this process remains in a state of physiologic equilibrium and the episodes of mineral loss are balanced by episodes of mineral gains, the mechanism is self-regulating and natural (Baelum et al., 2008a).

*Caries disease occurrence*

If the physiologic equilibrium between the tooth and biofilm is imbalanced (the rate of mineral dissolution exceeds the rate of re-deposition), the outcome of de- and remineralisation events over time will result in a net loss of mineral, leading to dissolution of hard tooth tissue (Fejerskov, 1997). If this disease process, initiated in the biofilm, is allowed to progress, the first clinical signs, *caries lesions*, will appear as a consequence (Kidd, 2011). Caries lesions represent a continuum of stages that vary in their severity from initial mineral loss, detected only ultrastructurally to clinically visible non-cavitated and, subsequently, cavitated lesions. If the disease is not controlled, carious lesions will progress and, with time, can lead to complete tooth destruction (Selwitz et al., 2007). However, this does not occur all of the time because of the dynamic nature of the caries disease process. At any stage of lesion development, if the physiological equilibrium between the tooth and the bacterial biofilm is re-established (e.g. with appropriate plaque control and fluoride exposure), cessation of the disease and an arrested lesion may be seen clinically (Kidd and Fejerskov, 2004). Thus, carious lesions may exhibit periods of lesion progression, reflecting ongoing disease, or arrest/regression, reflecting the signs of past disease (Takahashi and Nyvad, 2008). The progression and arrest/regression periods of disease are related to the activity of the bacteria in the biofilm and are associated with certain clinical signs
of carious lesions. Hence, active non-cavitated lesions are dull and rough, while inactive lesions are shiny and smooth (Takahashi and Nyvad, 2008).

The ecological plaque hypothesis
Carious disease is an endogenous infection since it is initiated by the bacteria belonging to the residential oral microflora (Marsh, 2003). Carious lesions develop in the sites where dental plaque remains for long periods of time (Selwitz et al., 2007). According to the caries ecological hypothesis (Marsh, 1994; Takahashi and Nyvad, 2008), caries disease occurs when bacterial homeostasis in dental biofilm is disturbed by changes in the environmental conditions in the oral cavity. These changes may be induced by a multitude of factors that, combined, affect the bacterial composition in tooth biofilm. For example, changes in lifestyle and behavioral factors related to frequent exposure to fermentable carbohydrates, lack of plaque control, low fluoride exposure or reduction in salivary flow rate may lead to prolonged periods of low pH levels in the biofilm that result in a microbial shift in the resident microflora to become more acidogenic and aciduric. This bacterial shift consequently affects the mineral dissolution and re-precipitation equilibrium and facilitates caries lesion development (Fejerskov, 2004).

The complex, multifactorial nature of caries disease
Although dental caries is a biofilm mediated disease, presence of biofilm is a necessary, but not in and of itself a sufficient factor, in the development of disease (Fontana et al., 2009; Tenuta and Cury, 2010). There are multiple determinants that act at the tooth-surface level and on an individual/population level that may influence caries disease progression and arrest. Tooth-surface level determinants represent strictly biological factors, such as salivary secretion rate and composition, fluoride ion concentration in the oral fluids and consumption of fermentable carbohydrates (Selwitz et al., 2007). There are also several lifestyle and behavioral determinants that influence biological factors; these are poor oral hygiene and dietary habits, as well as frequent consumption of medications that
contain sugar. Moreover, there are some structural and social determinants that can consequently shape behavioral and lifestyle factors related to caries. These include politics, economics, infrastructure, social environment, education, poverty, dental insurance coverage, access to dental care, etc. (Selwitz et al., 2007; Baelum et al., 2008b). This wide range of factors work in concert and determine whether a carious lesion will develop, progress or arrest (Kidd and Fejerskov, 2008).

1.1.2 Epidemiology of caries
Despite an overall reduction in the burden of dental caries in recent years, it remains one of the most prevalent chronic diseases worldwide, posing an important public health problem in all industrialised societies, as well as in developing countries (Featherston, 2006; Marincho et al., 2009; Pitts, 2009). Dental caries affects 60-90% of school-aged children and nearly 100% of adults and has a substantial impact on quality of life and cost (Lawrence et al., 2001; Petersen et al., 2005). According to the US National Health and Nutrition Examination Survey (2005-2008), more than one in five people (aged 5 to greater than 75 years) have untreated dental caries, and 75% have existing dental restorations which varied in prevalence by race, ethnicity and poverty level for all age groups (Dye et al., 2012). Although the burden of caries disease has decreased in Canada over the last 20 to 30 years, disparities remain, and many children and adults still develop new carious lesions (Bedos et al., 2004; Schroth et al., 2005; Leake et al., 2008). Thus, according to Canadian Health Measures Survey (2007-2009), 57% of Canadian children, 58% of adolescents and 96% of adults are affected by caries disease (CCPA report: www.policyalternatives.ca, 2011). In a recent study, income-related inequalities in oral health for Canadians were reported. Higher concentrations of decayed teeth, missing teeth and oral pain were found among economically poorer groups (Ravaghi et al., 2013). The analysis of the data collected through the Canadian Health Measures Survey (2007-2009) has shown that approximately 12 million Canadians have unmet dental treatment needs, with most requiring restorative and preventive care (Ramraj et al., 2012).
Indeed, oral diseases are among the most expensive diseases to treat in industrialised countries (Petersen et al., 2005). In Canada, $12.6 billion was spent on dental services in 2009 (CCPA report: www.policyalternatives.ca, 2011).

As with other diseases, the epidemiology of caries varies geographically. Looking at Belarus, where the work reported in this thesis was performed, there have been important social and economic changes in the country during recent years. Belarus is a country with a transitional economy. Over the past 15 years, there has been a tendency for caries disease to decline in its population (Terekhova et al., 2009, Udina et al., 2010). However, the disease still has a high prevalence and severity. Thus, only 20% of children aged 6 years are free from cavitated carious lesions (Terekhova et al., 2009). The mean DMFT values in this age group vary from 0.07(±0.002 SD) for permanent teeth to 4.35 (±0.01 SD) for primary teeth (Terekhova et al., 2009). Eighty percent of 15 year old children have caries which increases to 100% by the age of 18 and older (Tikhonova, 2003; Terekhova et al., 2009; Borisenko, 2008). Caries risk factors include: 1. Poor oral hygiene (Leous, 2001; Terekhova et al., 2009); 2. Lack of fluoride in the drinking water (less than 0.2 mg/l; Melnichenko and Terekhova, 1998); and 3. A high consumption of fermentable carbohydrates (Polianskaya et al., 2001).

Although there is a possibility for free access to dental care for most of the Belarussian population, the management approach for caries disease focuses mainly on operative treatment strategies (Sulkovskaya and Dmitrieva, 2001), which may be an additional factor in the high prevalence of caries disease.

Along with a widespread decline of caries over the past decades, the progression of caries lesions has also slowed (Pitts, 1983; Marthaler et al., 1996; Mejare et al., 1999). Thus, caries experience and presentation of the disease are becoming apparent later in a person’s life (Kidd et al., 1993). Regardless, the caries process is naturally occurring and cannot be prevented because dental biofilm is continuously formed on tooth surfaces and is always metabolically active. Thus, the risk of caries disease always exists (Kidd and Fejerskov, 2008). Its initiation and progression can occur in all ages and must be viewed as a chronic, lifetime
disease (Fejerskov, 1997; Burt et al., 2008). Therefore, caries disease control should be sustained throughout life in order to prevent disease progression (Selwitz et al., 2007).

1.1.3 Caries management

Operative approach of treatment caries disease

Historically, dental caries treatment has evolved from a time when treatment primarily involved tooth extraction to the present with interventions designed to maintain tooth structure and viability, e.g. operative treatment (Ismail et al., 2001). For many years, dentists detected only cavitated carious lesions, which we now recognise to be the terminal stage of caries disease (Pitts, 2004). In order to stop cavity progression and to restore tooth function, restorations were placed. This was considered by the dental profession to be the best possible treatment to heal the disease (Bader and Shugars, 2006). This treatment approach that focused only on operative interventions has been employed by generations of dentists and is still widely used today (Bader and Shugars, 2006; Fontana et al., 2009). However, there is scientific evidence showing that, although the restorations repair the tooth structure, they do not prevent or manage the disease (Elderton, 1990; NIH 2001; Qvist, 2008). Restorations have a finite life span, and they need to be replaced over time, which leads to additional removal of tooth structure. Thus, the tooth is destined to a re-restorative cycle future (Elderton, 2003). This cycle has been described as a ‘death spiral’ of the tooth, that includes the enlargement of the original restoration over time, risk of new ‘replacement’ restorations, an increasing risk of tooth fracture and subsequent crown placement, risk of iatrogenic damage to neighboring teeth, risk of pulpal involvement and endodontic therapy and, finally, tooth extraction (Elderton, 2003; Mjör et al., 2008; Qvist, 2008). All of this is associated with significant economic costs (Qvist, 2008). In addition, the existence of recent restorations is a risk indicator for new lesion development (NIH, 2001; Fontana et al., 2009). Operative treatment of cavitated carious lesions is necessary in most cases and cannot be
ignored; however, this treatment does not cure the disease (Pitts, 2004; Kidd, 2011). Thus, operative treatment can be regarded only as a component of a more sophisticated caries management approach that is focused on non-operative treatment to control the caries process and prevent further progression of the disease (Kidd and Fejerskov, 2008). The main role of operative treatment is to facilitate plaque control if a non-operative intervention cannot achieve this (Kidd, 2011).

Contemporary caries management approach
The contemporary caries management approach is based on risk-adjusted patient-centered strategies that aim to prevent initiation and control progression of early signs of caries disease through non-operative treatments that will preserve the tooth structure and minimise operative interventions (Ismail et al., 2013). There are several reasons to favor this strategy:

1) Understanding caries disease
The current knowledge and understanding of caries disease stresses the importance of differentiating between the caries disease process, initiated in bacterial biofilm, and the carious lesions detected visually on hard dental tissues; the latter are the consequence of the disease process (Fejerskov, 1997). Thus, caries disease management should be targeted in two directions: at the patient level, by modifying the caries risk factors that induce the initiation and progression of the disease and at the tooth surface level, managing caries lesions with a goal to arrest their progression and maximally preserve the tooth structure. (Cury and Tenuta, 2009; Pitts et al., 2011; Ismail et al., 2013). In order to control the disease process at the patient level, a caries risk assessment has been suggested as an integral component of disease management (Ismail et al., 2013). Since the set of caries risk factors and determinants is unique for each patient and always exists, caries risk assessment should be performed on an individual basis and carried out regularly throughout life (Fontana et al., 2009; Ismail et al., 2013). A caries risk assessment for an individual patient includes an evaluation of the etiologic and protective factors that might explain that patient’s carious lesion
experience, as well as establishing the probability of the formation of new lesions in the near future (Kidd, 2011; Twetman and Fontana, 2013). Caries risk assessment helps the clinician to 1) develop an adequate patient-centered prevention and management plan for caries disease and 2) determine the timing of future recall appointments (Zero et al., 2009; Twetman and Fontana, 2013).

2) The importance of non-operative treatment

Scientific evidence suggests that non-operative intervention can prevent carious lesions from occurring, as well as decrease the speed of, and potentially arrest, their progression (Carvalho et al., 1992; Nyvad, 2004; Marinho et al., 2009). The arrest or reversal of the lesions can be explained by the dynamic nature of the caries disease process: once the physiological equilibrium between tooth mineral and oral fluids is restored, the further net mineral loss and lesion progression will be stopped (Fejerskov, 2004). This can be achieved by modification or elimination of cariogenic factors (improved plaque control, reduced cariogenic diet) and by increasing protective factors (different sources of fluoride delivery, increased salivary flow) (Zandona and Zero, 2006). The effect of fluoride used in different delivery systems for caries prevention (toothpastes, varnishes, gels, solutions) has been emphasised in several systematic reviews (Marinho et al., 2002, 2003a, 2003b, 2004). Regular and effective plaque control with a fluoride-containing tooth paste is considered to be the most important method for caries control (Tenuta and Curry, 2010; Kidd, 2011). This method combines mechanical disturbance of dental biofilm with the availability of an ionic form of fluoride in saliva that, during an acid attack, inhibits demineralisation and facilitates re-precipitation of minerals into the tooth surface (Kidd, 2011; Lussi et al., 2012). In addition, fluoride accumulates for several hours in the biofilm that was not removed with tooth brushing and protects the tooth surfaces that were not reached by the tooth brush (Tenuta and Cury, 2010). There is strong evidence that using sealants is an effective approach for preventing new carious lesions, as well as arresting early lesion (Beauchamp et al., 2008). Thus, prevention and treatment of caries disease requires a more conservative approach, and non-operative treatment
is recognised as the main treatment for caries, since this approach is linked with relevant causal and determinant factors and has been shown to be associated with caries control (Kidd, 2011). The potential long-term health and economic benefits of this therapeutic/preventive approach are huge (Pitts, 2004).

3) **Staging the severity of caries lesions**

The third reason is the understanding that there are different clinical stages of carious lesions and that it is important to distinguish amongst them using a severity rating: from early non-cavitated to cavitated lesions (NIH, 2001; Pitts, 2004). Different treatment methods will be applied depending on the severity of the lesion. Thus, in order to stop or reverse progression of non-cavitated lesions, non-operative treatment can be successfully applied (Nyvad, 2004; Zero et al., 2009; Baelum, 2010; Ismail et al., 2013), while for cavitated lesions, operative treatment is usually needed (Ekstrand et al., 2007; Baelum, 2010). This is because once a cavity is formed, it is difficult to control lesion progression (Fejerskov, 1997; Kidd et al., 2003; Nyvad et al., 2008). However, if sufficient plaque control is established, even cavitated lesions can be arrested without operative interventions (Lo et al., 1998). In addition, a recent study has revealed that, depending on the severity of the lesion, its progression to cavitation can be predicted (Zandona et al., 2012).

4) **Considering the activity of caries lesions**

Through understanding the dynamic nature of the caries disease process, the importance of differentiating between active (progressing) and inactive (non-progressing) lesions is emphasized (Fejerskov, 1997; Ismail et al., 2013). The rational for this strategy is explained by different approaches for caries management: only active carious lesions need professional treatment, because without intervention, they will continue to progress (Fontana et al., 2009); on the other hand, inactive or arrested lesions need no treatment, apart from daily tooth brushing (Nyvad, 2004).
5) *Delay in caries lesions progression*

During the past few decades, the prevalence, distribution and behaviour of carious lesions have changed dramatically (NIH, 2001). Since carious lesions have been documented to progress slowly (Verdonschot et al., 1999; Mejare et al., 2004; Selwitz et al., 2007), dentists have the opportunity to catch lesions prior to their causing extensive tooth damage by applying non-operative interventions (Zandona and Zero, 2006).

Thus, the new paradigm of caries disease has led to a new era of patient-centered, non-operative caries disease management that includes control of the disease process and prevention/treatment of carious lesions from their early stages. This approach is based on identifying and clinically staging the presence, activity and severity of dental caries, as well as assessing the main causal and predisposing factors and caries risk of the individual. This is followed by treatment planning that includes modifying or eliminating risk factors, preventing future caries, arresting or reversing active non-cavitated carious lesions and, if necessary, restoring active cavitated lesions (NIH, 2001; Tranæus et al., 2005; Fontana and Zero, 2006; Ismail et al., 2013). Because of the lifelong continuing nature of caries, this process should be monitored overtime for each individual patient, with the frequency of follow up examinations determined by the individual needs of that patient, as well as his/her current caries status, caries risk and the patient’s expectations, wishes and compliance (Pitts, 2004; Fontana and Zero, 2006; Ismail et al., 2013). The main goal of this approach is to achieve and maintain a patient’s dental health by controlling or managing the caries process in order to avoid irreversible signs and symptoms of caries disease (Pitts, 2004; Baelum et al., 2008; Fontana et al., 2009).

1.1.4 *Caries diagnosis*

Caries diagnosis is the professional summation of all information about signs and symptoms of disease that can be gained from clinical examination of teeth, use of additional diagnostic tools, information about history of disease and risk factors, and biological knowledge (Pretty, 2006; Longbottom et al., 2009; Fontana et al.,
2010). The importance of diagnosis as a first step in the management of dental caries has been emphasised since the 19\textsuperscript{th} century (Ismail, 2004b; Pitts, 2004). The essential objective of making a diagnosis in dental practice is to select the best possible treatment for the patient in order to achieve excellent long-term health outcomes (Nyvad, 2004; Nyvad et al., 2008). Diagnosis of caries disease is applied at two levels: a patient level and a tooth surface level (Ismail et al., 2013). Caries diagnosis on a tooth surface level implies the collecting and analysing of information about all of the signs and symptoms of caries disease gained from lesion detection (determination of whether or not disease is present) and lesion assessment, that includes lesion severity determination (defining different stages of lesion progression) and lesion activity determination (characterization of the specific parameters of lesion activity at one point in time or monitoring lesion progression over time; Pitts, 2004; Pitts et al., 2011). The synthesis of all this information, together with the patient’s caries risk assessment, his/her preferences and best interests and monitoring of lesion behaviour over time creates a foundation for appropriate personalised caries management planning (Pitts et al., 2011). The stages of caries disease progression vary from subclinical lesions that can be detected only on a histological level to clinically obvious lesions (Pitts, 2004). In the clinic, the signs of lesion severity are visually assessed based on their surface characteristics, such as color (e.g. white/brown/black) and integrity (loss of tooth structure), and differentiated between enamel and dentinal non-cavitated and cavitated caries lesions (Ismail, 2004a; Pitts, 2004). According to their activity, carious lesions can be classified as active and inactive (arrested), based on their clinical characteristics. Active lesions are characterised by a whitish opaque appearance and a rough or soft surface, while inactive lesions are characterised by a smooth/hard shining surface (Nyvad et al., 1999). Lesion activity assessment is very important for clinical decision making (Ekstrand et al., 1998).
Uncertainty in caries diagnosis

Diagnostic tests should be accurate (able to measure or detect what it is aimed to measure, Huysmans and Longbottom, 2004) and reliable (reproducible results with the same conditions, Nyvad et al., 2008). However, precise accuracy and reproducibility are rare in caries diagnosis; irrespective of the method used, diagnostic errors occur and repeatability is not perfect (Wenzel and Hintze, 1999; Baelum et al., 2008). This may be explained by continuous changes in caries lesion progression/regression that creates a degree of imprecision in disease measurement (Fejerskov, 1997). In addition, because of the dynamic self-limited nature of the caries process, essential question exists: ‘At what threshold of net mineral loss should it be termed "caries"?’ (Huysmans and Longbottom, 2004). Some authors emphasise the absence of a real reference of ‘truth’ for caries lesions and compare caries diagnoses with geographical coastlines that have no precise value and depend upon the selected measurement scale (Baelum et al., 2008; Nyvad et al., 2008). Thus, the presence or absence of carious lesions are influenced by the diagnostic cut off point of a particular diagnostic instrument; this consequently has an impact on the dentists’ treatment decisions (Selwitz et al., 2007). It is recommended that dental practitioners recognise the presence of a certain degree of uncertainty when making caries diagnoses and, instead of looking for a precise ‘gold standard’, it is better to focus on a diagnosis that is clinically meaningful for the individual patient’s long-term health outcome (Baelum et al., 2008).

Diagnostic methods

Among the diagnostic methods available to dentists over the past decades, the most frequently used have been visual-tactile and radiographic (Bader et al., 2002). Other methods developed as additional tools to improve the visual-tactile diagnoses include laser fluorescence (DIAGNOdent, Kavo, Germany), electrical caries monitor (ECM), quantitative light-induced fluorescence (QLF), fibre-optic transillumination (FOTI) and others (Neuhaus et al., 2009).
**Visual-tactile examination**

Visual/visual-tactile examination is the main traditional caries diagnostic method that has been widely used for decades by dentists in clinical practice (Pitts N., 1993; Bader et al., 2002; Traneus et al., 2005; Zandora and Zero, 2006). Several studies have reported a low sensitivity and moderate to high specificity for traditional visual/visual-tactile clinical examinations (Lussi, 1993; Ricketts et al., 1995; Bader et al., 2001). In addition, a high variation in agreement amongst examiners using visual-tactile criteria was reported and explained by the fact that lesion diagnosis is broad-based (Bader and Shugars, 1995; Bader et al., 2002). For a long time, carious lesions were detected only at the cavitated stage, since it was believed that early non-cavitated lesions could not be reliably detected (Nyvad et al., 1999). In order to improve sensitivity, as well as reproducibility, of the visual-tactile method in detection and assessment of lesion depth from the early stages, several meticulous criteria were developed demonstrating appropriate levels of reliability when used by well-trained and calibrated examiners (Pitts and Fyffe, 1988; Ismail et al., 1992; Ekstrand et al., 1995). In addition, some of these criteria included lesion activity assessments (Fyffe et al., 2000; Nyvad et al., 1999; Ekstrand et al., 2007).

In spite of the limitations of the method, it has been stated that the visual-tactile examination is the only approach to date that would allow a differentiation between non-cavitated and cavitated carious lesions, as well as between active and inactive lesions; these are the pivotal factors on which the best caries treatment options can be determined (Nyvad et al., 2008; Baelum et al., 2012).

**Radiography and other additional diagnostic tools**

Bite-wing radiography is recommended for use as an adjunct method in order to improve detection of dentinal carious lesions on approximal and occlusal surfaces that may be overlooked by visual inspection, to provide a better estimation of lesion depth and to monitor the progression of carious lesions (Wenzel, 2004; Selwitz et al., 2007; Mendes et al., 2012). In a systematic review, radiographic examination to detect dentinal caries was reported to have a 53%-66% sensitivity.
and an 83%-95% specificity (Bader et al., 2001). Among limitations of the radiographic method are hazards of ionizing radiation, underestimations of actual lesion depth and inability of a single radiograph to estimate lesions activity (Traneus et al., 2005; Wenzel, 2004; Kidd, 2011). It has been suggested that additional diagnostic yield of bite-wing radiography would depend on the diagnostic criteria used for the clinical examination (Machiulskiene et al., 1999). For example, bite-wing radiography could provide additional information if the carious lesions are diagnosed using conventional visual tactile techniques. However, two recent studies have shown that bitewing radiography, as additional tool, provides no benefits for caries detection when meticulous visual-tactile criteria (e.g. Nyvad and ICDAS II) were used (Baleum et al., 2012; Mendes et al., 2012). Moreover, when the bite-wing method is used in populations with a low caries prevalence, a high number of false positive diagnoses can result that could consequently lead to overtreatment (Baelum, 2010; Baelum et al., 2012).

Over the last decades, several technology-based dental caries detection methods have been developed, aiming to detect carious lesions from the early stages and to be accurate and non-invasive (Traneus et al., 2005; Zandona and Zero, 2006). A laser-fluorescence device, DIAGNOdent (KaVo, Germany), was developed for caries detection on occlusal and accessible smooth surfaces. The device captures a fluorescence produced by bacterial by-products and translates this on a numerical scale (Braga et al., 2010). The method has shown to be reproducible with good sensitivity and specificity and mostly suitable to detect early and more advanced dentinal carious lesions (Lussi et al., 2004). However, some confounding factors, such as drying time and presence of plaque (Lussi et al., 2005), pigmentation (Francescut and Lussi, 2003), toothpastes and filling materials (Lussi and Reich, 2005; Lussi et al., 2006) can produce false positive results. The quantitative light-induced fluorescence (QLF) method uses a blue light source to excite the tooth, which subsequently causes dental tissues to emit fluorescence. The fluorescence is recorded by the system and analysed with software (Zandona and Zero, 2006; Neuhaus et al., 2009). The method allows detection of very early carious lesions
and quantifies their size, depth and volume. This method can be used on all tooth surfaces, except those that are approximal (Pretty, 2006). Sensitivity and specificity of the QLF method are 0.61 and 0.59, respectively, for occlusal surfaces (Pretty, 2006) and 0.76 and 0.85 for smooth surfaces (Zandona and Zero, 2006). A strong correlation between the carious lesions in enamel detected using the QLF method and directly measured mineral loss was shown (van der Veen et al., 2000). The device is recommended for detection, quantification, and monitoring of early non-cavitated carious lesions, mostly on smooth surfaces (Braga et al., 2010). Taken into account the dynamic self-limited nature of the carious process, the use of the QLF method to detect early, visually undetected carious lesions, is questioned (Kuhnisch et al., 2007). The method also has some limitations: it is sensitive to the presence of saliva, the amount of tooth surface desiccation, dental plaque, calculus and extrinsic discolorations. Furthermore, it is time-consuming (Heinrich-Weltzien et al., 2005). The fiber optic transillumination (FOTI) method is based on the principle of light scatter when a high-intensity white light source is placed on a tooth. The carious enamel and dentin appear as dark shadows on a light background (Neuhaus et al., 2009). This method is particularly useful for approximal surfaces for detection of dentinal lesions as an alternative to bite-wing radiography. This method is characterised by low sensitivity and high specificity (Braga et al., 2010). However, higher values of sensitivity were reported for dentinal lesions compared to those in the enamel (Holt and Azevedo, 1989). A comparison of bite-wing radiography and FOTI methods have shown that both have comparable specificities, but the sensitivity of FOTI was significantly lower than that of bitewing radiography (Vaarkamp et al., 2000). A charge-coupled digital intraoral camera device was developed to be combined with the FOTI (DIFOTI; Schneiderman et al., 1997). In a recent study, it was found that the diagnostic accuracy of DIFOTI to detect approximal enamel lesions is greater than that of bitewing radiography (Astvalsdóttir et al., 2012). An electronic caries monitor (ECM) device was developed to measure the difference between the conductivity of sound and demineralised surfaces.
This method was shown to have high sensitivity and low specificity values when compared with conventional methods to detect dentinal lesions on occlusal surfaces (Longbottom and Huysmans, 2004). The ECM method can be applied only on occlusal surfaces and is even sensitive to the presence of stain in the fissure (Ellwood and Cortes, 2004). This method has not been shown to be superior to conventional methods (Braga et al., 2010).

All of these described diagnostic tools have advantages and disadvantages. Some can perform only on certain surfaces or can better detect only dentinal or enamel lesions and some are sensitive to numerous confounding factors which may influence their accuracy and lead to false positive and false negative results (Zandona and Zero, 2006). Due to the fact that only a meticulous visual examination method can provide severity and activity information at one point in time, it is the method of choice for routine clinical examinations (Kuhnisch et al., 2007). All other diagnostic methods should be used as adjunct supportive tools. However, ‘the key question as to whether they improve patients’ dental health outcomes has yet to be answered’ (Zandona and Zero, 2006). Several recent studies suggest that when meticulous visual-tactile caries diagnostic criteria are used to make treatment decisions, the availability of additional diagnostic information, particularly in low caries risk populations, may lead to a considerable number of false positive diagnoses and, consequently, increase overtreatment (Pereira et al., 2009; Baelum et al., 2012).

The Nyvad and the ICDAS II+LAA criteria

Along with criterion validity (concurrent and predictive) of caries detection criteria, the importance of a content validity assessment (evaluation of how the measurement system reflects the domain of the phenomenon) was emphasised (Ismail et al., 2007). In a recent comprehensive review, content validity was evaluated for 29 visual-tactile caries detection criteria (Ismail, 2004). In this review evaluations were carried out to determine whether these diagnostic criteria 1) measure a range of severity stages of lesion progression; 2) differentiate...
between active and inactive signs of the lesions; 3) include differentiation between carious and non-carious lesions, and 4) clearly define the terms for measuring the caries process. In addition, the review took into account whether the teeth were cleaned and/or dried before an examination and the use of explorers. This review revealed that there is a lack of consistency for most of the systems designed to measure the caries disease process (Ismail, 2004).

The two promising visual/visual-tactile caries scoring systems, the Nyvad (1999) and the ICDAS II (2002), were introduced and recommended for use as the most advanced systems in research and clinical practice (Nyvad, 2008; Pitts, 2009). Both systems detect carious lesions from their early stages, as well as assess their activity, based on visual and tactile signs (Nyvad et al., 1999; Pitts, 2004; Ekstrand et al., 2007).

The Nyvad criteria

The Nyvad clinical caries diagnostic criteria reflect the dynamic nature of the caries process and are based on a concept of lesion activity assessment (Nyvad et al., 2003). The Nyvad criteria differentiate between active and inactive carious lesions based on their visual-tactile surface characteristics, along with determinations of whether they are non-cavitated, micro-cavitated or cavitated (Nyvad et al., 1999; Nyvad et al., 2008). The criteria measure lesion activity at a single time-point based on information about the presence of dental plaque, colour, luster, location and texture of the lesion. The typical active enamel lesions have a whitish/yellowish opaque appearance, look mat and feel rough on gentle probing, while active dentinal/root caries lesions feel soft or leathery on gentle probing and appear discoloured. A typical inactive lesion looks shiny and feels smooth (enamel) or hard (dental/root) on gentle probing (Nyvad et al., 1999). The explorer is recommended to be used with only a light/gentle touch (with no or very light pressure) to assess the lesion surface integrity or texture and to remove dental plaque, if needed (Nyvad et al., 1999). The use of the system necessitates clean and dry teeth as well as good light. The criteria are closely related to
contemporary evidence-based caries management approaches and facilitate treatment decisions based on lesion activity and severity (Nyvad et al., 2008). According to the results of several studies that were performed on primary and permanent teeth by well-trained and experienced examiners, the inter-examiner kappa values for the Nyvad criteria were 0.58-0.94, and the intra-examiner kappa values were 0.74-0.95 (Nyvad et al., 1999; Lima et al., 2008; Braga et al., 2009, 2010a; Sellos and Soveiro, 2011). The sensitivity of the Nyvad criteria reflecting lesion depth vary from 0.69 to 0.90 and their specificity varies from 0.74 to 0.94 (Braga et al., 2009; 2010a). Since there is no ‘gold standard’ for carious lesion activity assessment, the predictive and construct validity were assessed for the Nyvad criteria in a three-year clinical trial of the effect of daily supervised brushing with a fluoride toothpaste (Nyvad et al., 2003). The construct validity of the criteria was shown through their ability to reflect the caries–controlling effects of fluoride, while predictive validity was demonstrated by the significantly higher risk of progression of active non-cavitated lesions to cavitation than inactive non-cavitated lesions and sound surfaces (Nyvad et al., 2003). The Nyvad criteria are recommended for use in clinical research and, more relevantly, in clinical practice in order to assist dentists in caries risk assessment and in choice of treatment, as well as for monitoring individual lesions over time (Nyvad et al., 2003; Nyvad et al., 2008).

Amongst the advantages of the Nyvad system is it’s simplicity for coding the lesions, as well as the direct relationship of the caries scores with their subsequent treatment decisions. At the same time, the Nyvad system does not include detailed classifications of caries lesions severity, which could be useful for epidemiologic caries research.

The ICDAS II+LAA criteria
The International Caries Detection and Assessment System (ICDAS II) is an evidence based, standardized caries detection and assessment method, integrating the best features of existing visual/visual-tactile caries detection criteria (Pitts, 2004). The system was developed by an international group of researchers, so that
it could be used in clinical practice, clinical trials and epidemiologic research to facilitate appropriate decisions in diagnosis, prognosis and clinical management of dental caries (Pitts, 2004; 2009). The ICDAS II is intended to be modified and peer reviewed over time, making it an ‘open system’; it is available and well described on a website (Pitts, 2004; ICDAS coordinating committee: www.icdas.org, 2005). The development of the ICDAS II severity criteria were based on several visual/visual-tactile criteria that were merged into a single system, based on the best evidence (Pitts and Ekstrand, 2013). It has a detailed protocol and classifies carious lesions based on their severity and activity. Severity diagnoses are based on lesion surface characteristics associated with histological depth and have codes ranging from 0 to 6 (Ismail et al., 2007). The ICDAS II also includes a developing lesion activity assessment system (Pitts et al., 2011). To date, there are several versions of lesion activity assessment systems for the ICDAS II (Ekstrand et al., 2007; Ismail et al., 2013). One of these is the Lesion Activity Assessment system (LAA) proposed by Ekstrand and coworkers (Ekstrand et al., 2007). The LAA system is based on three main lesion parameters: visual signs (color and severity), location and roughness. Each parameter has its scores which are devised on the predictive power of the parameters. Based on the sum of the scores, the lesions are classified as ‘active’ or ‘inactive’ (Ekstrand et al., 2007). The ICDAS II system is related to the contemporary caries management approach that depends on a patient’s caries risk, a lesion’s activity and severity stage, the type of surface affected and the patient’s expectations and wishes (Ismail et al., 2013).

The inter-examiner reliability of ICDAS II severity varies from kappa values of 0.62 to 0.91, and the intra-examiner agreement varies from 0.59 to 0.88 (Ismail et al., 2007; Kuhnish et al., 2008; Jablonski-Momeni et al., 2008; Braga et al., 2009, 2010a). The sensitivity of the criteria for lesion depth varies from 0.59 to 0.92, while specificity varies from 0.65 to 0.91 (Jablonski-Momeni et al., 2008; Rodriges et al., 2008; Shoaib et al., 2009; Braga et al., 2009, 2010a).
The LAA scoring system was developed based on a predictive power of three clinical parameters: lesion visual appearance, location of the lesion in plaque stagnation area and assessment of the roughness /softness of the lesion using an impression-based diagnostic material (Clinpro Cario Diagnosis, Full Arch Lactic Acid Locator, 3M ESPE; Ekstrand et al., 2007). A construct validity of the LAA system was evaluated in a clinical study of 5 to 11 year old Colombian school children with 225 lesions/sound surfaces. The same impression material (Clinpro, 3M ESPE) was used in this clinical study as a proxy method for lesion activity assessment (Ekstrand et al., 2007). It was shown that the LAA system had an area under the curve equal to 0.84, with the highest combined sum of specificity and sensitivity at 1.67 (Ekstrand et al., 2007). When ICDAS II criteria were used with the LAA system by experienced examiners in one study, the inter-examiner kappa value was 0.89 (Braga et al., 2010a) and in two studies, the intra-examiner kappa value was 0.63 and 0.90 (Braga et al., 2009; Ekstand et al., 2007). The feasibility of the ICDAS II severity assessment criteria were tested in two studies among general dental practitioners. The results have shown that dentists were able to use the ICDAS II scoring criteria in their routine practice and that it took 5 to 14 minutes to examine adult patients (Ormond et al., 2010; Bonner et al., 2011).

Amongst the advantages of the ICDAS II system is that it is a standardised system that has been widely used and, consequently, will allow multinational comparisons of caries patterns. The detailed severity assessment scale might be useful in caries epidemiological studies. On the other hand, having a scale with six scores for lesion severity assessment, together with the additional coding system for activity, could complicate the use of the ICDAS II+LAA system in everyday dental practice.

1.2 Rationale

Modern caries management aims to control the caries process, focusing on non-operative/preventive treatment strategies (NIH, 2001; Zero et al., 2009; Pitts et al., 2011). This approach is based on a contemporary understanding of carious lesion formation and progression that requires diagnostic systems able to identify carious
lesions from their very early stages, along with their depth and activity (Verdonschot et al., 1999; Fejerskov, 2004; Fontana and Zero, 2006; Fontana et al., 2010; Kidd, 2011; Pitts et al., 2011). In addition, a good caries diagnostic system should be linked with treatment strategies (Nyvad, 2004). All of these requirements are necessary for the ultimate goal to achieve the best possible dental health outcome for the tooth and the patient (Baelum et al., 2008). It was suggested that contemporary concepts in caries management based on non-operative strategies are not yet adopted in everyday practice and that dental practitioners still focus on invasive therapeutic procedures (Tan et al., 2002; Doméjean-Orliaguet et al., 2009; Maidment et al., 2010; Da Silva et al., 2012). The evidence on over- and under-treatment of dental caries in clinical practice has been described in several studies (Bader et al., 1993; Grembowski et al., 1997; Ismail et al., 1997). A study conducted in Montreal (Canada) among 911 schoolchildren has shown that 73-86% of restorations in first permanent molars were placed by general practitioners in sound or non-cavitated tooth surfaces (Ismail et al., 1997). The reasons for over- and under-treatment may be linked to the use of diagnostic systems and restorative decision principles presently in use in most dental practices (Bader et al., 1993; Grembowski et al., 1997; Ismail et al., 1997).

Visual/visual-tactile examination is one of the principal methods currently used in dental practice to diagnose carious lesions (Bader et al., 2002). It has been stated that the visual-tactile examination is the only method, to date, that allows a differentiation between non-cavitated and cavitated lesions, as well as between active and inactive lesions; these are the pivotal factors on which the best caries treatment options can be determined (Nyvad et al., 2008; Baelum et al., 2011). Two promising visual/visual-tactile caries diagnostic systems, the Nyvad (Nyvad et al., 1999) and the ICDAS II (Ismail et al., 2007), were developed and recommended for use in research and clinical practice (Nyvad et al., 2008; Pitts, 2009). The Nyvad system differentiates carious lesions as being active or inactive, as well as non-cavitated or cavitated (Nyvad et al., 2008). The ICDAS II system
has a detailed six-category carious lesion severity scale (Ismail et al., 2007). In order to assess activity, an adjunct system (Lesion Activity Assessment system, LAA) was developed and proposed for use with the ICDAS II criteria (Ekstrand et al., 2007). Both the Nyvad and ICDAS II systems have been demonstrated to be reliable and accurate when they were used by experienced researchers and dentists in several epidemiologic surveys and clinical studies (Nyvad et al., 1999; 2003; Burt et al., 2006; Ismail et al., 2007; Jablonski-Momemi et al., 2008; Braga et al., 2009, 2010). The ICDAS II system showed significantly greater sensitivity for detecting non-cavitated enamel lesions than the Nyvad system (Braga et al., 2009). In a recent study, it was suggested that the ICDAS II system with LAA appears to estimate caries activity on occlusal surfaces in primary teeth as greater than estimates from the Nyvad system (Braga et al., 2010). With the aim to improve diagnosis and subsequent treatment decisions, the Nyvad and ICDAS II+LAA criteria can potentially be used in everyday practice by general dental practitioners who are the key individuals involved in the control and management of the caries process (Baelum, 2010). However, there is little evidence in which the use of the Nyvad and the ICDAS II+LAA systems by practicing dental clinicians previously inexperienced in their use have been considered as guiding tools for making treatment decisions. Having even one surface difference on operative decisions between two diagnostic systems can be clinically important, because any restorative treatment propels the tooth into the re-restorative cycle. Although the difference in non-operative treatment between the systems might not necessarily affect the oral health of the patients, it may increase treatment cost (Pereira et al., 2009).
1.3 Study objectives

Research question: Are dentists’ caries treatment choices in caries-active young adults different when they use the Nyvad or the ICDAS II+LAA diagnostic systems?

Hypothesis one: A mean number of operative treatments estimated by dentists with the Nyvad system will be at least one unit less in comparison with the ICDAS II+LAA system.

Hypothesis two: A mean number of non-operative treatments estimated by dentists with the Nyvad system will be at least three units less in comparison with the ICDAS II+LAA system.

Objectives:
1) To evaluate the reproducibility of general dental practitioners, previously inexperienced in the use of the Nyvad and the ICDAS II+LAA diagnostic systems, for clinical scoring of carious lesions at different diagnostic thresholds.
2) To evaluate differences in caries diagnostic outcomes when dentists use two visual-tactile systems: the Nyvad and the ICDAS II+LAA.
3) To evaluate differences in operative and non-operative caries treatment decisions when dentists use two visual-tactile systems: the Nyvad and the ICDAS II+LAA.

2. METHODS
The study was carried out at a dental unit of the Institute of Emergency Services of Belarus (Minsk, Belarus). The project was approved by the Research Ethics Committee of Belarusian State Medical University (Protocol № 06/2010) and by the Institutional Review Board of McGill University, Montreal, Canada (IRB study number: A12-E60-10A). The Institute of Emergency Services of Belarus granted permission for the study, and the volunteer dentists and examined subjects signed informed consent forms. The entire recruitment process and the study project were completed during a six-week period.
2.1 Study Design

A randomized, two-period cross-over (AB/BA), single blind design was used in order to investigate the implications of the Nyvad and the ICDAS II+LAA diagnostic systems on caries treatment decisions (Figure 1). For the four recruited dentists the purpose of the study was explained and detailed information and instructions were given regarding the study protocol. Then they participated in a lecture concerning contemporary caries management strategies with emphasis on the importance of lesion activity assessment and differentiating between cavitated and non-cavitated caries lesions when making treatment decisions. Four identical sealed allocation envelopes were generated by the investigators, and these envelopes were blindly chosen by the participating dentists. Thus, the four dentists were randomly assigned to one of two groups. Both groups of dentists examined the same subjects (n=140) using the Nyvad and the ICDAS II + LAA criteria in different sequences, with a one-week wash out period. The first group of dentists used the Nyvad criteria during Period 1, followed by the ICDAS II+LAA criteria during Period 2; the second group used the ICDAS II+LAA criteria during Period 1, followed by the Nyvad during Period 2 (Figure 1). After diagnoses, the dentists made treatment decisions for each tooth surface using the following guidelines: 1) only active lesions should be treated (Nyvad, 2004; Fontana et al., 2009), 2) active non-cavitated lesions should be treated non-operatively (Nyvad, 2004; Baelum, 2010; Ismail et al., 2013). The following options were proposed: No Active Care (NAC), Non-Operative Treatment (NOT) and Operative Treatment (OPT) (Appendix 1). The following assumptions were applicable for all examined patients, and were presented to the dentists: 1. all patients have high caries risk 2. all patients will be available for follow-up. Before each examination period, the dentists were trained for the diagnostic criteria they subsequently used when making treatment decisions and were blinded from the results of previous examinations. Trained assistants entered the data in the examination dental charts (Appendix 2, 3).
The participating patients were asked to not change their usual oral hygiene habits during the study period. At the end of the study examinations, the treatment plans were summarized by a separate person (trained dentist), and a general indication of treatment needs were given to each participant (e.g., “you have active dental caries in some of your teeth that must be treated, as well as other teeth with incipient carious activity that could be arrested”). The participants were then able to visit a dentist in the students’ policlinic to request dental care.

Figure 1. Study flow chart
2.2 Sample and participants
The study population included a voluntary sample of caries-active 18-20 year old Belarusian young adults living in Minsk. The voluntary patients (n=140) were selected according to the following inclusion criteria: 1. males and females, 2. ages 18-20 years, and 3. having ≥2 active non-cavitated and/or cavitated carious lesions. Exclusion criteria included those who had: 1. < 2 active carious lesions, 2. fixed orthodontics, 3. severe fluorosis or hypoplasia and 4. patients with complicated chronic diseases that can affect the choice of treatment.

The following 16 teeth were examined in each patient: 17, 16, 15, 12, 11, 21, 22, 25, 26, 27, 37, 36, 35, 45, 46, 47. The choice of the teeth was based on the results of previous study of caries prevalence among 101 15-16 year old Belarusian school children (unpublished study). According to that study, 80% of diagnosed active, cavitated and non-cavitated caries lesions were found on these teeth.

The voluntary dental practitioners (n=4) were recruited for the project using the following inclusion criteria: 1. no previous knowledge or experience with either the ICDAS II+LAA or the Nyvad diagnostic systems, 2. 5-10 years of clinical experience 3. graduated from the same dental school, 4. trained as operative dentists (recognised as such in Belarus) and 5. had experience of working with adult populations with similar caries prevalence and experience as the patient sample. The number of dentists (n=4) chosen to participate was based on the logistics and feasibility of the study. Each study subject was examined twice by the same four dentists. A higher number of dentists would have increased the number of examinations (e.g., 1 additional dentist=2 additional examinations, etc) potentially becoming too great a burden for the subjects, as well as increase the longevity of the project.

2.3 Recruitment and consent
The study was carried out in accordance to ethical principles of Declaration of Helsinki (2008). Before initiating the research project, the protocol was submitted to ethical review boards at McGill University and Belarusian State medical University to get ethical approval. The research co-investigator contacted chiefs
of the operative dentistry departments of four Minsk state dental policlinics to
give them information about the project and to invite dentists to participate. The
chiefs of the operative dentistry departments in each dental policlinic
disseminated the invitations. The dentists who decide to participate contacted the
project co-investigator. After it was confirmed that they met the inclusion criteria,
the first four eligible dentists were invited to participate in the study. Selected
dentists were informed about the procedure of the project and also asked to sign in
a consent form (Appendix 7). In order to select caries active 18-20 year old young
adults, students from the Institute of Emergency Services of Belarus were invited
to attend the institute’s dental office for check up examinations. The co-
investigator of the project met students and disseminated the invitation to
participate. The students who decided to participate in the project contacted the
project co-investigator to make an appointment for the examinations at the dental
office by an experienced and trained dentist. The examinations were carried by an
experienced dentist (ST), who was trained and calibrated in both caries diagnostic
systems (Nyvad and ICDAS II). During the recruitment examinations, lesion
severity was assessed using the ICDAS II criteria while lesion activity assessment
was performed with the Nyvad criteria. After the examination, the students were
informed about their oral health status, and the first 172 persons who were eligible
and agreed to participate in the study were invited to take part. The purpose of the
project was explained for each selected student and they were asked to sign a
consent form (Appendix 6). Each participant received a regular and an electrical
toothbrush, as well as fluoridated tooth paste.

2.3.1 Confidentiality
The confidentiality of the study participants, both patients and dentists, was
respected. Information that directly disclosed their identity remained only with the
principal investigator and co-investigator. All of the participants’ answers and
examination data were confidential. They were given a study number and only
this number was used for any research-related identification. All documents and
data will be kept in Canada for a period of five years. The documents will be
stored in a locked filing cabinet and the security of any information kept on a computer hard drive will be ensured by password access. When this information was used for publication or presentation, no nominative data was published or presented. At the end of the study, participants had a right to see and copy their medical information related to the project.

2.3.2 Dentist compensation
Dentists were compensated for their time in the study. Each dentist received US$500 at the end of the project.

2.4 Training and calibration of the examiners
An experienced examiner (ST), who was previously trained and calibrated for the Nyvad and the ICDAS II+LAA criteria, led two sessions of independent training and calibration for both groups of dentists. Before the Period 1 examinations, dentists from the first group were trained with the Nyvad criteria, while dentists belonging to the second group were trained with the ICDAS II+LAA. During the one-week wash out period prior to Period 2, both groups of dentists were trained again: the first group with the ICDAS II+LAA criteria and the second group with the Nyvad criteria. Each training session for the Nyvad or the ICDAS II+LAA criteria involved both theoretical and clinical components. The theoretical part included two hours of an introductory lecture about contemporary understanding of the caries process, caries diagnosis and different stages of lesion severity, as well as signs of active and inactive lesions, followed by an introduction of either the Nyvad or the ICDAS II+LAA system. Following this, a demonstration and discussion was performed using photographs for the Nyvad criteria (severity and activity signs were discussed) and the ICDAS II e-learning program’s quiz (http://www.icdas.org/) for the ICDAS II (only lesion severity signs were discussed). For the LAA system, the dentists were trained during a clinical session. The clinical part of the training contained two days of patient examinations using the Nyvad or the ICDAS II+LAA criteria. The young adults who were examined (n=32, with 16 in each training session) as part of these
training and calibration sessions for the study dentists were not involved in the main project. All cases in which there was disagreement were discussed by the dentists and the trainer.

2.5 Caries diagnostic criteria and examination

All examinations were performed using the same dental setting conditions, with a standard dental light source, dental mirrors, three-in-one air syringe, suction device and cotton rolls. Before each examination, supervised tooth brushing was carried out.

2.5.1 ICDAS II+LAA criteria

Each tooth surface was visually assessed when wet and then following air drying for 5 seconds. If in doubt or to confirm visual assessment, a ball-ended WHO probe was used to gently check for surface discontinuity and texture, as well as to remove dental plaque, if necessary. The ICDAS II criteria (Ismail et al., 2007) were used to classify each examined tooth surface according to lesion severity. The caries severity codes were organised into a 6 category ordinal scale, ranging from the first visible carious change in enamel (code 1) to extensive cavitation (code 6; see Appendix 4). Pits and fissures were assessed separately from smooth surfaces. In addition to the ICDAS II severity assessment, the activity status of carious lesions was assessed using the LAA system (Ekstrand et al., 2007). With the LAA, a combination of three clinical parameters were used: visual signs of caries (colour and severity score); lesion location in relation to plaque stagnation; and surface texture (rough/soft or smooth/hard on probing). Each clinical parameter had a corresponding score. A sum of the lesion activity scores $> 7$ indicated an active lesion, while a sum of $\leq 7$ indicated an inactive lesion (see Appendix 4). In cases in which two lesions were present on the same surface, the lesion with highest severity was recorded.

2.5.2 Nyvad criteria

Each tooth surface was firstly gently air dried, then two surface characteristics of the lesion were assessed: surface integrity, based on the presence or absence of
surface discontinuity or a cavity, and activity, based on visual and tactile characteristics of the lesion (see Appendix 5). A sharp standard dental explorer was gently used to check for loss of tooth structure, surface texture and to remove dental plaque, if necessary. Carious lesions that had a whitish/yellowish appearance with loss of lustre, a rough/soft feeling of the surface after gentle probing and located in a plaque stagnation area were categorised as active lesions. Inactive lesions were characterised by a whitish/brown/black shiny appearance, smooth/hard on gentle probing and a location some distance from the gingival margin (Nyvad et al., 1999). Mixed lesions that included characteristics of active and inactive lesions were recorded as active. In the case of the presence of two lesions on the same surface, the lesion with highest severity was recorded (active>inactive; cavitation> microcavity>intact surface). In order to have the same number of examined surfaces and to be able to make comparisons between two systems, the smooth surfaces and fissures/pits were recorded separately, analogous to ICDAS II criteria. Fillings associated with active and inactive lesions were re-coded using two digits. The first digit indicated a filling (code 7), the second digit indicated the lesion activity and integrity (codes from 1 to 6).

2.6 Outcome evaluation

*Primary outcome:* The mean number of surfaces per individual requiring operative or non-operative treatment according to the Nyvad and the ICDAS II+LAA criteria.

*Secondary outcome:* the Nyvad and ICDAS II+LAA decay components reflecting activity and depth of the lesions.

2.7 Confounding

A ‘carry-over’ effect, when knowledge of one diagnostic system can influence the diagnostic outcome of another diagnostic system can be a potential confounding factor. The best way to eliminate this confounding factor is to have a long washout period. However, the dynamic nature of the carious process does not allow for a long washout period. Even in one week, the first signs of clinical regression of a lesion’s activity can be revealed if the oral environmental
conditions are favourable (Holmen et al., 1987). Patients were asked to not change their usual oral hygiene behaviours during the study period. Because the washout period in the study is relatively short, dentists were asked to concentrate on the latest caries diagnostic system that they were trained about. In addition, they were required to use a checklist of specific diagnostic criteria during each examination period. The ‘period’ and ‘sequence’ effects of using diagnostic criteria were taken into account by Multilevel Poisson regression analyses when treatment outcomes were tested.

2.8 Sample size

The calculation of sample size was based on the results of a pilot study that was performed among 20 15-16 year old Belarusian children (Table 4). Two dentists independently performed dental examinations using Nyvad or ICDAS II+LAA criteria and made treatment decisions for each examined tooth surface. The difference of 1 surface that needs operative and 3 surfaces for non-operative treatment was considered to be clinically meaningful. The following statistical formula was applied for a sample size calculation for continuous response variables and independent samples data:

\[ 2N = 4 \cdot (Z_\alpha + Z_\beta)^2 \cdot \sigma^2 / \delta^2, \]

Where:
- \( 2N \) – number of patients needed for both groups
- \( Z_\alpha \) – Standard Normal Deviate corresponding to selected significance criteria
- \( Z_\beta \) - Standard Normal Deviate corresponding to selected statistical powers
- \( \sigma^2 \) – Sample variance
- \( \delta \) – Clinically meaningful mean difference

The sample size estimates for the hypothesis one and two represents in Table 5.
Table 4. Pilot study data (not published)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Diagnostic System</th>
<th>Mean number of surfaces that need treatment (mean ± SD)</th>
<th>Number of patients</th>
<th>Mean difference ± SD</th>
<th>95% CI of the difference</th>
<th>Sample SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Operative treatment</td>
<td>ICDAS II + LAA</td>
<td>3.4±3.4</td>
<td>20</td>
<td>1.9±1.9</td>
<td>0.99</td>
<td>2.8</td>
</tr>
<tr>
<td>Nyvad</td>
<td></td>
<td>1.5±1.9</td>
<td>20</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-operative treatment</td>
<td>ICDAS II + LAA</td>
<td>13.5±8.9</td>
<td>20</td>
<td>5.2±4.5</td>
<td>3.1</td>
<td>7.2</td>
</tr>
<tr>
<td>Nyvad</td>
<td></td>
<td>8.4±7.3</td>
<td>20</td>
<td></td>
<td></td>
<td>8.5</td>
</tr>
</tbody>
</table>

Table 5. Sample size estimates (significance level constant at 0.05; power constant at 0.8)

<table>
<thead>
<tr>
<th>Hypothesis</th>
<th>Sample SD</th>
<th>Difference sought</th>
<th>Sample required per group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypothesis one: A mean number of operative treatments estimated by dentists with the Nyvad system will be at least one unit less in comparison with the ICDAS II system.</td>
<td>2.9</td>
<td>1</td>
<td>132</td>
</tr>
<tr>
<td></td>
<td>2.9</td>
<td>2</td>
<td>34</td>
</tr>
<tr>
<td>Hypothesis two: A mean number of non-operative treatments estimated by dentists with the Nyvad system will be at least three units less in comparison with the ICDAS II system.</td>
<td>8.5</td>
<td>5</td>
<td>46</td>
</tr>
<tr>
<td></td>
<td>8.5</td>
<td>4</td>
<td>71</td>
</tr>
<tr>
<td></td>
<td>8.5</td>
<td>3</td>
<td>126</td>
</tr>
<tr>
<td></td>
<td>8.5</td>
<td>2</td>
<td>282</td>
</tr>
</tbody>
</table>

Taking into account the sample size calculations and the feasibility of the study, a sample requirement of 140 student patients was set to permit us to observe a
difference of 1 tooth surface between the diagnostic systems that, while adding a few to allow for any students not returning for the examinations a second time.

2.9 Statistical analyses

Objective 1: In order to evaluate examiners’ agreement for lesion severity, weighted quadratic Cohen’s kappa coefficients were calculated. According to lesion severity, the Nyvad codes were re-grouped in the following order: 1 and 4 (non-cavitated lesions); 2 and 5 (micro-cavities); 3 and 6 (cavities). The order of the ICDAS II scores was not changed. For the evaluation of examiner agreement for caries lesion activity, unweighted Cohen’s kappa coefficients were calculated. Agreement for lesion activity was evaluated with two diagnostic thresholds: D1 (non-cavitated and cavitated carious lesions) and D2 (cavitated carious lesions). The inter-examiner agreement was calculated based on a sample of the 140 participants who were involved in the main project. Ten out of 140 subjects were examined twice by both groups of dentists at the beginning and at the end of each examination period in order to assess intra-examiner agreement. The results (kappa values and their 95% confidence intervals) were organised according to diagnostic criteria, period of examination (Period 1 or Period 2) and inter- and intra-examiner agreement.

Objective 2: The mean DMFS (decayed, missed and filled surfaces) values, decay components and prevalence of carious lesions for both the Nyvad and the ICDAS II+LAA diagnostic systems were calculated based on the data of the pooled sample (all examiners together). Non-cavitated lesions were classified as lesions, using codes 1 and 4 (Nyvad) and 1 and 2 (ICDAS II). Cavitated /dentinal lesions were classified with codes 2, 5, 3 and 6 (Nyvad) and codes 3, 4, 5 and 6 (ICDAS II). In addition, the mean number and prevalence of active carious lesions was calculated for different tooth surfaces with both diagnostic systems. In order to compare DMFS values and D components of the ICDAS II+LAA and the Nyvad criteria, the Wilcoxon sign rank test, that takes into account the clustering effect, was used. The prevalence of caries disease was compared between the two systems using McNemar’s test. The Bland-Altman method was used in order to
graphically plot the difference scores of two diagnostic systems against the mean of each subject with presentation of the 95% limits of agreement, based on the data of four examiners. The adjusted variance of the differences for the Bland-Altman method was calculated using one-way analysis of variance, in order to take into account repeated measurements. IBM SPSS Statistics 19 was used.

**Objective 3**: For evaluating treatment outcomes, cross-tabulation for treatment decisions was performed using the pooled data sample (four examiners). The Wilcoxon sign rank test was used to determine whether there was a carryover effect. Multilevel Poisson regression analyses were used to assess differences between mean number of surfaces indicated for operative and non-operative treatments. The scheme of a random coefficient model using Stata’s “xtmposison” command was applied. The rate ratio (ratio of geometric means) and 95% confidence interval were calculated to assess the difference between diagnostic systems adjusted by sequence and period of examination and examiners’ variations (fixed effects), with random slopes for subjects and examiners. STATA 12.0 software (Stata Corporation, College Station, TX, USA) was used.

3. **RESULTS**

The results of our study are presented in two paper manuscripts that represent the different parts of the research project. Manuscript I addresses the diagnostic part of the study: dentists’ agreement and diagnostic outcomes using the Nyvad or the ICDAS II+LAA systems. Manuscript II describes the most important part of the study, which is the treatment decisions made by dental practitioners with the Nyvad or the ICDAS II+LAA systems. Among treatment outcomes, the operative treatment decisions generated by the use of the Nyvad or the ICDAS II+LAA system are considered to be the most important, since the decision to restore the tooth is the start of a re-restorative cycle that leads to progressive tooth tissue loss and, eventually, to tooth extraction (Elderton, 1990; Amerongen et al., 2008). Furthermore, tooth restorations are costly both to the individual and to society (Mjor and Gordon, 2002).
3.1  Manuscript I: “Reproducibility and Diagnostic Outcomes of Two Visual-Tactile Systems for Caries Lesion Activity among General Dental Practitioners: a Cross-Over Study”


Key words:
dental caries; diagnosis; caries activity; visual examination; randomized; reproducibility

Declaration of interests
There is no conflict of interest exists for any of the authors.

Abstract
Aim: The aim of this randomized cross-over study was to evaluate the reproducibility and differences in diagnostic outcomes by practicing dental clinicians previously inexperienced in using the Nyvad (NY) and the ICDAS II with LAA (IC+LAA) systems. Methods: Four volunteer dentists were randomly allocated to one of two groups. Both groups of dentists examined the same voluntary sample (n=140) of caries active young adults using the NY and the IC+LAA criteria in different sequences. The first group used the NY criteria during period I, followed by IC+LAA during period II; the second group did the examinations in the opposite sequence. Before the period 1 and 2 examinations, dentists from both groups were trained with the NY or the IC+LAA criteria, depending on the group in which they were assigned. Results: Inter-examiner agreement for the severity diagnostic threshold was high for both diagnostic instruments (Kappa 0.71-0.73). For the D1 (active) diagnostic threshold, the inter-examiner Kappa values were 0.48-0.51 for the IC+LAA and 0.45-0.57 for the NY. The mean number of active non-cavitated carious lesions was significantly higher for the IC+LAA (6.14(SD±5.4)) than for the NY criteria (3.90(SD±3.9),
Active cavitated/dentinal carious lesions were significantly higher for the IC+LAA (4.14, SD±4.1) than for the NY criteria (2.13, SD±3.1; p<0.0001).

Conclusion: Both the NY and the IC+LAA diagnostic systems showed high reproducibility for the severity assessment. The mean number of active carious lesions was significantly higher using the IC+LAA criteria, which may subsequently lead to more caries treatment. Trial registration: ISRCTN65592532.

**Introduction**

Caries diagnosis is the professional summation of all information about signs and symptoms of disease that can be gained from clinical examination of teeth, use of additional diagnostic tools, information about history of disease and risk factors, and biological knowledge (Pretty, 2006; Longbottom et al., 2009; Fontana et al., 2010). The essential objective in making a diagnosis in dental practice is to select the best possible treatment for the patient (Nyvad, 2004; Kidd, 2001).

Modern caries management aims to control the caries process, focusing on non-operative/preventive treatment strategies (NIH, 2001; Zero et al., 2009; Pitts, 2011). This approach is based on a contemporary understanding of carious lesion formation and progression that requires diagnostic systems that can identify carious lesions from very early stages, along with their depth and activity assessment (Verdonschot et al., 1999; Fejerskov, 2004; Fontana and Zero, 2006; Fontana et al., 2010; Kidd, 2011; Pitts, 2011).

Visual/visual-tactile examination is one of the principal methods currently used in dental practice to diagnose carious lesions (Bader et al., 2002; Pitts and Stamm, 2004). It has been stated that the visual-tactile examination is the only method to date that allows a differentiation between non-cavitated and cavitated caries lesions, as well as between active and inactive lesions; these are the pivotal factors on which the best caries treatment options can be determined (Nyvad et al., 2008; Baelum et al., 2011).

In recent years, two promising visual/visual-tactile caries diagnostic systems, the Nyvad (Nyvad et al., 1999) and the ICDAS II (Ismail et al., 2007), were developed and recommended for use in research and clinical practice (Pitts, 2009;
Nyvad et al., 2008). The Nyvad system differentiates carious lesions as being active or inactive, as well as non-cavitated or cavitated (Nyvad et al., 2008). The ICDAS II system has a detailed six-category carious lesion severity scale (Ismail et al., 2007). In order to assess activity, an adjunct system (Lesion Activity Assessment system, LAA) was developed and proposed for use with the ICDAS II criteria (Ekstrand et al., 2007). Both the Nyvad and ICDAS II systems have been demonstrated to be reliable and accurate when they were used by experienced researchers and dentists in several epidemiologic surveys and clinical studies (Nyvad et al., 1999; 2003; Burt et al., 2006; Ismail et al., 2007; Jablonski-Momemi et al., 2008; Braga et al., 2009, 2010). With the aim to improve diagnosis and subsequent treatment decisions, these measurement tools could potentially be used in everyday practice. However, there is little evidence on the reproducibility of the Nyvad and the ICDAS II+LAA systems by practicing dental clinicians previously inexperienced in their use. In addition, it is important to compare caries diagnostic outcomes using of these two systems because of their implication to the caries treatment decisions.

**Study objectives:**
1. To measure the reproducibility of general dental practitioners, previously inexperienced in the use of the Nyvad and the ICDAS II+LAA diagnostic systems, for clinical scoring of carious lesions at different diagnostic thresholds.
2. To measure differences in diagnostic decisions between the Nyvad and the ICDAS II+LAA systems by dental practitioners previously inexperienced in their use.

**Materials and Methods**
The study was carried out at a dental unit of the Institute of Emergency Services of Belarus (Minsk, Belarus). The project was approved by the Research Ethics Committee of Belarusian State Medical University (Protocol № 06/2010) and by the Institutional Review Board of McGill University, Montreal, Canada (IRB study number: A12-E60-10A). The Institute of Emergency Services of Belarus granted permission for the study, and the volunteer dentists and examined subjects
signed informed consent forms. The entire recruitment process and the study project were completed during a six-week period.

Study design
This study is the first part of a primary project that focused on a comparison of treatment choices among dental clinicians when dental caries lesions are diagnosed with two visual-tactile activity assessment systems, the Nyvad and the ICDAS II+LAA. A randomized, cross-over two-period (AB/BA) clinical trial design was used (Figure 1). Four identical sealed allocation envelopes were generated by the investigators, and these envelopes were blindly chosen by the participating dentists. Thus, four dentists were randomly assigned to one of two groups. Both groups of dentists examined the same subjects (n=140) using the Nyvad and the ICDAS II + LAA criteria in different sequences, with a one-week wash out period. The first group of dentists used the Nyvad criteria during Period 1, followed by the ICDAS II+LAA criteria during Period 2; the second group used the ICDAS II+LAA criteria during Period 1, followed by the Nyvad during Period 2. The examiners were blinded from the results of previous examinations. No participating patients were lost during Period 2.
Figure 1. Study flow chart

Four dentists

Lecture of a contemporary approach of caries management

Random allocation

Group 1 (n=2)

Training and calibration for Nyvad criteria

Period 1: Examination of 18-20 years old young adults (n=140)

Diagnostic and Treatment decisions using Nyvad criteria

Training and calibration for ICDAS II+LAA criteria

Washout period (one week)

Group 2 (n=2)

Diagnostic and Treatment decisions using ICDAS II+LAA criteria

Training and calibration for Nyvad criteria

Period 2: Examination of the same group of 18-20 years old adults (n=140)

Diagnostic and Treatment decisions using ICDAS II+LAA criteria

Diagnostic and Treatment decisions using Nyvad criteria
**Sample and participants**

The study population included a voluntary sample of caries active 18-20 year old Belarusian young adults living in Minsk (n=140). Those participants who had two or more active non-cavitated and/or cavitated carious lesions were included in the study. Participants who had fixed orthodontic devices, severe fluorosis or hypoplasia were excluded. The following 16 teeth were examined in each patient: 17, 16, 15, 12, 11, 21, 22, 25, 26, 27, 37, 36, 35, 45, 46, 47. The choice of the teeth was based on the results of previous study of caries prevalence among 101 15-16 year old Belarusian school children (unpublished study). Four dental practitioners who agreed to take part in the project were recruited. The dentists had no previous experience of using the ICDAS II+LAA or the Nyvad diagnostic systems, graduated from the same university and had 5-10 years of clinical experience as operative dentists (recognised as such in Belarus) working with adult populations.

**Training and calibration of the examiners**

An experienced examiner (ST), who was previously trained and calibrated for the Nyvad and the ICDAS II+LAA criteria, led two sessions of independent training and calibration for both groups of dentists. Before the Period 1 examinations, dentists from the first group were trained with the Nyvad criteria, while dentists belonging to the second group were trained with the ICDAS II+LAA. During the one-week wash out period prior to Period 2, both groups of dentists were trained again: the first group with the ICDAS II+LAA criteria and the second group with the Nyvad criteria.

Each training session for the Nyvad or the ICDAS II+LAA criteria involved both theoretical and clinical components. The theoretical part included two hours of an introductory lecture about contemporary understanding of the caries process, caries diagnosis and different stages of lesion severity, as well as signs of active and inactive lesions, followed by an introduction of either the Nyvad or the ICDAS II+LAA system. Following this, a demonstration and discussion was performed using photographs for the Nyvad criteria (severity and activity signs
were discussed) and the ICDAS II e-learning program’s quiz (http://www.icdas.org/) for the ICDAS II (only lesion severity signs were discussed). For the LAA system, the dentists were trained during a clinical session. The clinical part of the training contained two days of patient examinations using the Nyvad or the ICDAS II+LAA criteria. The young adults who were examined (n=32, with 16 in each training session) were not involved in the main project. All cases in which there was disagreement were discussed by the dentists and the trainer.

*Caries diagnostic criteria and examination*

All examinations were performed using the same dental setting conditions, with a standard dental light source, dental mirrors, three-in-one air syringe, suction device and cotton rolls. Before each examination, all examined participants brushed their teeth under supervision.

*ICDAS II+LAA criteria*

Each tooth surface was visually assessed when wet and then following air drying for 5 seconds. If in doubt or to confirm visual assessment, a ball-ended WHO probe was used to gently check for surface discontinuity and texture, as well as to remove dental plaque, if necessary. The ICDAS II criteria (Ismail et al., 2007) were used to classify each examined tooth surface according to lesion severity. The caries severity codes were organised into a 6 category ordinal scale, ranging from the first visible carious change in enamel (code 1) to extensive cavitation (code 6; see Table 1). Pits and fissures were assessed separately from smooth surfaces. In addition to the ICDAS II severity assessment, the activity status of carious lesions was assessed using the LAA system (Ekstrand et al., 2007). With the LAA, a combination of three clinical parameters were used: visual signs of caries (colour and severity score), lesion location in relation to plaque stagnation, and surface texture (rough/soft or smooth/hard on probing). Each clinical parameter had a corresponding score. A sum of the lesion activity scores > 7 indicated an active lesion, while a sum of ≤ 7 indicated an inactive lesion (see
Table 1). In cases in which two lesions were present on the same surface, the lesion with highest severity was recorded.

Table 1. ICDAS II severity codes (Ismail et al., 2007) and LAA system (Ekstrand et al., 2007)

<table>
<thead>
<tr>
<th>ICDAS II severity codes</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 = Sound tooth surface</td>
</tr>
<tr>
<td>1 = First visual change in enamel</td>
</tr>
<tr>
<td>2 = Distinct visual change in enamel</td>
</tr>
<tr>
<td>3 = Enamel breakdown, no dentine visible</td>
</tr>
<tr>
<td>4 = Dentinal shadow</td>
</tr>
<tr>
<td>5 = Distinct cavity with visible dentine</td>
</tr>
<tr>
<td>6 = Extensive distinct cavity with visible dentine</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Lesion Activity Assessment system (LAA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical parameter</td>
</tr>
<tr>
<td>Activity scores</td>
</tr>
<tr>
<td><strong>Visual appearance: severity score</strong></td>
</tr>
<tr>
<td>- ICDAS II score 1, 2 (brown lesions)</td>
</tr>
<tr>
<td>- ICDAS II score 1, 2 (white lesions)</td>
</tr>
<tr>
<td>- ICDAS II score 3,4,5 or 6</td>
</tr>
<tr>
<td><strong>Plaque stagnation</strong></td>
</tr>
<tr>
<td>- Plaque stagnation area</td>
</tr>
<tr>
<td>- Non-plaque stagnation area</td>
</tr>
<tr>
<td><strong>Surface texture</strong></td>
</tr>
<tr>
<td>- Rough or soft surface on gentle probing</td>
</tr>
<tr>
<td>- Smooth or hard surface on gentle probing</td>
</tr>
</tbody>
</table>
**Nyvad criteria**

Each tooth surface was firstly gently air dried, then two surface characteristics of the lesion were assessed: surface integrity, based on the presence or absence of surface discontinuity or a cavity, and activity, based on visual and tactile characteristics of the lesion (see Table 2). A sharp standard dental explorer was gently used to check for loss of tooth structure, surface texture and to remove dental plaque, if necessary. Carious lesions that had a whitish/yellowish appearance with loss of lustre, a rough/soft feeling of the surface after gentle probing and located in a plaque stagnation area were categorised as active lesions. Inactive lesions were characterised by a whitish/brown/black shiny appearance, smooth/hard on gentle probing and a location some distance from the gingival margin (Nyvad et al., 1999). Mixed lesions that included characteristics of active and inactive lesions were recorded as active. In the case of the presence of two lesions on the same surface, the lesion with highest severity was recorded (active>inactive; cavitation> microcavity> intact surface). In order to have the same number of examined surfaces for both systems, the smooth surfaces and fissures/pits were recorded separately.
Table 2. Nyvad caries diagnostic criteria (Nyvad et al., 1999)

<table>
<thead>
<tr>
<th>Score</th>
<th>Category</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Sound</td>
<td>Normal enamel translucency and texture (slight staining allowed in otherwise sound fissure).</td>
</tr>
<tr>
<td>1</td>
<td>Active caries (intact surface)</td>
<td>Surface of enamel is whitish/yellowish opaque with loss of luster; feels rough when the tip of the probe is moved gently across the surface; generally covered with plaque. No clinically detectable loss of substance.</td>
</tr>
<tr>
<td>2</td>
<td>Active caries (surface discontinuity)</td>
<td>Same criteria as score 1. Localized surface defect (microcavity), no more than 2 mm in width, may be in enamel or in dentine*.</td>
</tr>
<tr>
<td>3</td>
<td>Active caries (cavity)</td>
<td>Enamel/dentin cavity easily visible with the naked eye; surface of cavity feels soft or leathery on gentle probing. There may or may not be pulpal involvement.</td>
</tr>
<tr>
<td>4</td>
<td>Inactive caries (intact surface)</td>
<td>Surface of enamel is whitish, brownish or black. Enamel may be shiny and feels hard and smooth when the tip of the probe is moved gently across the surface. No clinically detectable loss of substance.</td>
</tr>
<tr>
<td>5</td>
<td>Inactive caries (surface discontinuity)</td>
<td>Same criteria as score 4. Localized surface defect (microcavity), no more than 2 mm in width, may be in enamel or in dentine.</td>
</tr>
<tr>
<td>6</td>
<td>Inactive caries (cavity)</td>
<td>Enamel/dentin cavity easily visible with the naked eye; surface of cavity may be shiny and feels hard on probing with gentle pressure. No pulpal involvement.</td>
</tr>
</tbody>
</table>

*Modified after training with experts
The sample size calculation was based on the primary outcome of the main project: the number of surfaces per individual requiring operative or non-operative treatment. A SD of 2.9 for operative treatment and 8.5 for non-operative treatment (SD’s generated from a pilot project data) and a clinically meaningful between system difference of 1 surface (operative treatment) and 3 surfaces (non-operative treatment) were used to calculate a sample size with 80% power and a 0.05 significance level. Thus, a sample of 140 subjects was included. In this current study, the secondary outcome of the main project (the Nyvad and ICDAS II+LAA decay components reflecting activity and depth of the lesions) was analysed. The mean DMFS values, decay components and prevalence of carious lesions for both the Nyvad and the ICDAS II+LAA diagnostic systems were calculated based on the data of the pooled sample (all examiners together). Non-cavitated lesions were classified as lesions, using codes 1 and 4 (Nyvad) and 1 and 2 (ICDAS II). Cavitated /dentinal lesions were classified with codes 2, 5, 3 and 6 (Nyvad) and codes 3, 4, 5 and 6 (ICDAS II). In addition, the mean number and prevalence of active carious lesions was calculated for different tooth surfaces with both diagnostic systems. In order to compare DMFS values and D components of the ICDAS II+LAA and the Nyvad criteria, the Wilcoxon sign rank test, that takes into account the clustering effect, was used. The prevalence of caries disease was compared between the two systems using McNemar’s test. The Bland-Altman method was used in order to graphically plot the difference scores of two diagnostic systems against the mean of each subject with presentation of the 95% limits of agreement, based on the data of four examiners. The adjusted variance of the differences for the Bland-Altman test was calculated using one-way analysis of variance, in order to take into account repeated measurements. In order to evaluate examiners’ agreement for lesion severity, weighted quadratic Cohen’s kappa coefficients were calculated. Examiners’ agreement for lesion severity (surfaces presenting with no lesion were classified as ‘sound’ while surfaces with any severity score of caries lesion were classified as ‘disease’) for
both diagnostic criteria was evaluated using weighted quadratic Cohen’s kappa coefficients. According to lesion severity, the Nyvad codes were re-grouped in the following order: 1 and 4 (non-cavitated lesions); 2 and 5 (micro-cavities); 3 and 6 (cavities). The order of the ICDAS II scores was not changed. Agreement for lesion activity assessment was evaluated using unweighted Cohen's kappa coefficients with two diagnostic thresholds: D1 – surfaces with non-cavitated or cavitated/dentinal active lesions (ICDAS II+LAA scores 1–6 active and Nyvad scores 1–3) were classified as ‘disease’ while all other surfaces were classified as ‘sound’, and D2 – surfaces with cavitated/dentinal active lesions (ICDAS II+LAA scores 3–6 active and Nyvad scores 2, 3) were classified as ‘disease’, while all other surfaces were classified as ‘sound’. The inter-examiner agreement was calculated based on a sample of the 140 participants who were involved in the main project. Ten out of 140 subjects were examined twice by both groups of dentists at the beginning and at the end of each examination period in order to assess intra-examiner agreement. The results (kappa values and their 95% confidence intervals) were organised according to diagnostic criteria, period of examination (Period 1 or Period 2) and inter- and intra-examiner agreement. IBM SPSS Statistics 19 was used.

**Results**

One hundred and forty male (n=122) and female (n=18) subjects aged 19.5, SD ± 1.2 were examined. For each subject, 112 tooth surfaces were assessed. The mean DMFS values across all measurements by all dentists were 41.9 (±12.7SD) for the ICDAS II criteria and 32.5 (±13.3SD) for the Nyvad (p<0.001). Among 62,720 examined surfaces (pooled sample), 63% of sound surfaces were detected with the ICDAS II+LAA and 71% with the Nyvad criteria.

**Calibration**

Intra- and inter-examiner Kappa values for the severity diagnostic threshold ranged from 0.62 to 0.78 for the ICDAS II and from 0.70 to 0.76 for the Nyvad criteria (see Table 3). The lowest Kappa values were observed for both diagnostic systems when both the intra- and inter-examiner agreement were measured using
the D1 activity diagnostic threshold (see Table 3). For the Period 1 examination, intra- and inter-examiner Kappa values ranged from 0.31 to 0.48 for the ICDAS II+LAA and from 0.36 to 0.45 for the Nyvad. For the Period 2 examination, the intra- and inter-examiner Kappa values were higher than in Period 1 for both diagnostic systems and varied from 0.51 to 0.61 (see Table 3). For the D2 activity diagnostic threshold, the intra- and inter-examiner Kappa values were systematically higher for the ICDAS II+LAA criteria than for the Nyvad (see Table 3).

Table 3. Intra- and inter-examiner agreement for the ICDAS II+LAA and the Nyvad criteria.

The cells in gray color relate to Period 1 examination.

<table>
<thead>
<tr>
<th>Examiners</th>
<th>Severity</th>
<th>Activity, D1</th>
<th>Activity, D2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ICDAS II</td>
<td>Nyvad</td>
<td>ICDAS II+LAA</td>
</tr>
<tr>
<td></td>
<td>Intra-examiner agreement (Kappa, 95% CI)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ex.1 vs Ex.1</td>
<td>0.77 (0.62; 0.92)</td>
<td>0.76 (0.60; 0.93)</td>
<td>0.61 (0.54; 0.69)</td>
</tr>
<tr>
<td>Ex.2 vs Ex.2</td>
<td>0.78 (0.74; 0.81)</td>
<td>0.70 (0.53; 0.88)</td>
<td>0.52 (0.45; 0.59)</td>
</tr>
<tr>
<td>Ex.3 vs Ex.3</td>
<td>0.69 (0.65; 0.73)</td>
<td>0.74 (0.63; 0.86)</td>
<td>0.46 (0.34; 0.57)</td>
</tr>
<tr>
<td>Ex.4 vs Ex.4</td>
<td>0.62 (0.47; 0.77)</td>
<td>0.75 (0.62; 0.88)</td>
<td>0.31 (0.18; 0.43)</td>
</tr>
<tr>
<td>ST vs ST (Benchmark)</td>
<td>0.87 (0.74; 0.99)</td>
<td>0.80 (0.64; 0.96)</td>
<td>0.72 (0.64; 0.79)</td>
</tr>
<tr>
<td>Intra-examiner agreement (Kappa, 95% CI)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ex.1 vs Ex.2</td>
<td>0.73 (0.68; 0.77)</td>
<td>0.71 (0.66; 0.75)</td>
<td>0.51 (0.48; 0.53)</td>
</tr>
<tr>
<td>Ex.3 vs Ex.4</td>
<td>0.71 (0.67; 0.76)</td>
<td>0.73 (0.69; 0.77)</td>
<td>0.48 (0.45; 0.51)</td>
</tr>
</tbody>
</table>
Decay component of the ICDAS II+LAA and the Nyvad criteria

Most of the carious lesions were inactive according to ICDAS II+LAA (22.71 ±6.3SD) and Nyvad (16.32 ±6.2SD) criteria (Table 4). The prevalence of active carious lesions was 99% for the ICDAS II+LAA and 94% for the Nyvad criteria (p<0.001). The mean number and prevalence of active non-cavitated carious lesions was significantly higher (p<0.001) with the ICDAS II+LAA (mean 6.14±5.4 SD; prevalence 93%) than with the Nyvad criteria (mean 3.9 ±3.9 SD; prevalence 88%). Active cavitated/dentinal lesions were significantly higher (p<0.001) with the ICDAS II+LAA (mean 4.14 ±4.1SD; prevalence 89%) than with the Nyvad criteria (mean 2.13 ±3.1 SD; prevalence 65%; Table 4).
Table 4. Caries experience among 18-21 year old young adults according to the ICDAS II+LAA and the Nyvad criteria (pooled data)

<table>
<thead>
<tr>
<th>Caries lesions</th>
<th>System</th>
<th>Mean</th>
<th>Difference</th>
<th>Prevalence (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DMFS</td>
<td>ICDAS II</td>
<td>41.87 (12.7)</td>
<td>9.41 (6.5)*</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>Nyvad</td>
<td>32.46 (13.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>D_Inactive</td>
<td>ICDAS II+LAA</td>
<td>22.71 (6.3)</td>
<td>6.4 (6.2)*</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>Nyvad</td>
<td>16.32 (6.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>D_Active</td>
<td>ICDAS II+LAA</td>
<td>10.32 (7.6)</td>
<td>4.3 (5.2)*</td>
<td>99* (0.98;0.99)</td>
</tr>
<tr>
<td></td>
<td>Nyvad</td>
<td>6.02 (5.5)</td>
<td></td>
<td>94 (0.92;0.96)</td>
</tr>
<tr>
<td>D_Active Non-cavitated</td>
<td>ICDAS II+LAA</td>
<td>6.14 (5.4)</td>
<td>2.2 (4.1)*</td>
<td>93* (0.93;0.96)</td>
</tr>
<tr>
<td></td>
<td>Nyvad</td>
<td>3.90 (3.9)</td>
<td></td>
<td>88 (0.85;0.90)</td>
</tr>
<tr>
<td>D_Active Cavitated/dentinal</td>
<td>ICDAS II+LAA</td>
<td>4.14 (4.1)</td>
<td>2.0 (2.7)*</td>
<td>89* (0.86;0.91)</td>
</tr>
<tr>
<td></td>
<td>Nyvad</td>
<td>2.13 (3.1)</td>
<td></td>
<td>65 (0.61;0.68)</td>
</tr>
</tbody>
</table>

*p<0.001, Wilcoxon sign rank test (differences in mean values), McNemar’s test (differences for prevalence)
Active carious lesions location

Most active non-cavitated carious lesions were located on proximal surfaces, according to both diagnostic systems (ICDAS II+LAA - prevalence 89%; Nyvad – prevalence 84%). These surfaces were responsible for the 1.5±3.2SD difference in mean numbers of active non-cavitated lesions between two systems (Table 5). The rest of the active non-cavitated lesions were located mostly on buccal or lingual smooth surfaces (ICDAS II+LAA - prevalence 55%; Nyvad - prevalence 34%) and were responsible for the 0.7 ±1.8SD difference between the diagnostic systems (Table 5). Most active cavitated/dentinal carious lesions were located on proximal surfaces (ICDAS II+LAA 77%; Nyvad 52%) and in pits and fissures (ICDAS II+LAA 58%; Nyvad 33%) (Table 5). These surfaces were responsible for the 1.2 (±1.9SD; proximal) and 0.6 (±1.2SD; pits/fissures) differences in mean numbers of active cavitated/dentinal lesions between the two diagnostic systems (Table 5).
Table 5. The mean number and prevalence of active carious lesions located on different tooth surfaces according to the ICDAS II+LAA and the Nyvad diagnostic systems

<table>
<thead>
<tr>
<th>Surfaces</th>
<th>System</th>
<th>Mean (± SD)</th>
<th>Difference (± SD)</th>
<th>Prevalence (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active non-cavitated carious lesions</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>fissures/pits</td>
<td>ICDAS II+LAA</td>
<td>0.29 (0.7)</td>
<td>0.07±0.9</td>
<td>20 (0.16; 0.23)</td>
</tr>
<tr>
<td></td>
<td>Nyvad</td>
<td>0.22 (0.7)</td>
<td></td>
<td>16 (0.13; 0.19)</td>
</tr>
<tr>
<td>buccal/lingual smooth</td>
<td>ICDAS II+LAA</td>
<td>1.59 (2.3)</td>
<td>0.72±1.8*</td>
<td>55* (0.51; 0.59)</td>
</tr>
<tr>
<td></td>
<td>Nyvad</td>
<td>0.86 (1.7)</td>
<td></td>
<td>34 (0.30; 0.38)</td>
</tr>
<tr>
<td>mesial/distal</td>
<td>ICDAS II+LAA</td>
<td>4.26 (3.8)</td>
<td>1.45±3.2*</td>
<td>89* (0.86; 0.91)</td>
</tr>
<tr>
<td></td>
<td>Nyvad</td>
<td>2.81 (2.7)</td>
<td></td>
<td>84 (0.81; 0.87)</td>
</tr>
<tr>
<td>Active cavitated/dentinal carious lesions</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>fissures/pits</td>
<td>ICDAS II+LAA</td>
<td>1.19 (1.5)</td>
<td>0.63±1.2*</td>
<td>58* (0.54; 0.62)</td>
</tr>
<tr>
<td></td>
<td>Nyvad</td>
<td>0.56 (0.9)</td>
<td></td>
<td>33 (0.29; 0.37)</td>
</tr>
<tr>
<td>buccal/lingual smooth</td>
<td>ICDAS II+LAA</td>
<td>0.51 (1.1)</td>
<td>0.18±0.7*</td>
<td>28* (0.24; 0.32)</td>
</tr>
<tr>
<td></td>
<td>Nyvad</td>
<td>0.32 (0.9)</td>
<td></td>
<td>18 (0.15; 0.21)</td>
</tr>
<tr>
<td>mesial/distal</td>
<td>ICDAS II+LAA</td>
<td>2.44 (2.6)</td>
<td>1.2±1.9*</td>
<td>77* (0.73; 0.80)</td>
</tr>
<tr>
<td></td>
<td>Nyvad</td>
<td>1.24 (1.9)</td>
<td></td>
<td>52 (0.48; 0.56)</td>
</tr>
</tbody>
</table>

*p<0.001, Wilcoxon sign rank test (differences in mean values), McNemar’s test (differences for prevalence)
**Bland-Altman plots**

The Bland-Altman plots (Figure 2) represent the difference scores (ICDAS II+LAA - Nyvad) between the two diagnostic criteria for active non-cavitated (a) and active cavitated/dentinal (b) carious lesions, according to each of the four examiners. There is a consistent tendency for the ICDAS II+LAA criteria to exceed the Nyvad criteria for both active non-cavitated and active cavitated/dentinal lesions. The variation in between-diagnostic methods is higher for the active non-cavitated carious lesions (mean 2.3; 95% limits of agreement 11.91; -7.41) than the active cavitated/dentinal lesions (mean 2.1; 95% limits of agreement 7.36; -3.26; Figure 2).
Figure 2. Bland-Altman plots: difference ((ICDAS II+LAA) – Nyvad) versus average number of active non-cavitated (a) and active cavitated/dentinal (b) carious lesions measured by the ICDAS II+LAA and the Nyvad criteria, with 95% limits of agreement.
Discussion
In this study, we evaluated the reproducibility of the ICDAS II+LAA and the Nyvad diagnostic criteria in scoring carious lesions at different diagnostic thresholds. In addition, we compared the diagnostic decisions made by general dental practitioners who were previously inexperienced in using these systems. The results of the study have shown that it is possible to achieve acceptable levels of agreement for the severity of carious lesions with both the ICDAS II and the Nyvad diagnostic systems, even when these criteria are used by dental practitioners who were previously inexperienced with these systems. At the same time, the results demonstrated that there was less agreement for activity assessment with the ICDAS II+LAA and Nyvad diagnostic systems. Regarding the evaluation of diagnostic outcomes, the results showed that the mean number and the prevalence of active non-cavitated and cavitated/dentinal lesions are consistently higher with the ICDAS II+LAA than with the Nyvad criteria.

It has been well-documented that there is wide-spread variation in the accuracy and reliability scores for visual/visual-tactile caries detection methods (Bader and Shugars, 2008). One factor that may be responsible for this variation is how well the signs of the carious process are defined and classified for a particular diagnostic system (Ismail, 2004; Braga et al., 2009). It has been suggested that the use of meticulous caries scoring criteria could improve the reliability of diagnoses (Braga et al., 2009; Diniz et al., 2009; Cortes et al., 2000). Although carious lesion activity assessment, based on visual and tactile signs, is an essential part of the diagnostic process, its subjective nature could increase variation among and within dentists (Nyvad et al., 1999). Therefore, training and experience acquisition by examiners is needed (Zandonà et al., 2009; Ekstrand et al., 2005; Nyvad et al., 1999).

There are several studies in which the reliability and validity of the Nyvad system is reported (Nyvad et al., 1999, 2003; Lima et al., 2008; Machiulskiene et al., 2009; Braga et al., 2009, 2010; Séllos and Soviero, 2011); most of them were performed in clinical settings. There are more published studies on the ICDAS II
system, in which reproducibility and accuracy is measured. However, most of these studies were carried out in vitro on occlusal surfaces and/or only severity of carious lesions with the ICDAS II system was assessed (Sohn et al., 2007; Kunisch et al., 2008; Rodriges et al., 2008; Shoaiib et al., 2009; Braga et al., 2009, 2010; Diniz et al., 2009, 2010; Zandona et al., 2010).

According to our study results, the level of dentists’ intra- and inter-examiner agreement was quite high for both diagnostic systems when they were used to assess the severity of carious lesions. These results are in agreement with other in vivo studies and confirm the possibility of diagnosing non-cavitated carious lesions with a high level of agreement (Nyvad et al., 1999; Shoaiib et al., 2009; Zandona et al., 2010; Braga et al., 2010). The lowest kappa values of lesion activity for both diagnostic systems were observed for the D1 activity diagnostic threshold. These results are in agreement with the Nyvad et al. reliability study (1999), in which the most dramatic change in kappa was found on the ‘active vs inactive’ diagnostic threshold. In this current study, the agreement scores for the D1 activity diagnostic threshold were low for both diagnostic systems. These scores were lower than those reported in previous investigations (Nyvad et al., 1999; Ekstrand et al., 2007; Braga et al., 2009, 2010). This could be explained by differences in training and calibration, as well as experience in lesion activity assessment of the participating examiners. Thus, in a clinical calibration study (Nyvad et al., 1999), ‘substantial’ and ‘perfect’ agreement was reported when the Nyvad criteria were used by two examiners in school-age children. Extensive one-month training sessions were performed prior to the start of that study. There are two studies conducted by Braga, et al. (2009, 2010) (one in vitro and one in vivo), in which reproducibility and accuracy of the Nyvad and the ICDAS II+LAA diagnostic systems were compared for lesion severity and activity. A high level of inter- and intra-examiner agreement was reported for the severity and activity of the lesions with both systems. In these two studies, the training of the examiners was performed in-vitro using tooth images, followed by examination of occlusal surfaces of primary extracted teeth. In order to achieve appropriate inter-examiner
agreement, the training was performed in two sessions with a two week interval between (Braga et al., 2009). It should be emphasised that cariology experts participated in all of these reported studies. We hypothesised that examiners who are less experienced in using the criteria would produce a lower reliability rating; this hypothesis is supported by the results of several studies that used examiners, previously inexperienced in the use of ICDAS II diagnostic criteria with lesion activity assessment (Zandona et al., 2009; Braga et al., 2009; Nelson et al., 2011).

In the current study, the Kappa values for the D1 activity threshold for both diagnostic systems were slightly improved from Period 1 to Period 2. This change could possibly be explained by the examiners becoming more experienced and having learned more skills, as well as their being more aware and involved in the process of carious lesion severity and activity assessment from the early stages. However, this improvement in activity assessment in most cases still did not reach an acceptable level of agreement. The intra- and inter-examiner kappa values for the D2 activity cut-off were higher for the ICDAS II+LAA criteria than the Nyvad criteria. This can be explained by the different approaches in activity assessment with the two systems. According to the ICDAS II+LAA system, any cavitated/dentinal lesion located in a plaque stagnation area is scored as an active lesion (Braga et al., 2010). The above-mentioned approach simplifies the activity assessment for cavitated lesions with the ICDAS II+LAA criteria and can, therefore, increase examiner agreement.

It has been suggested that regular calibration exercises might improve diagnostic agreement (Baelum et al., 2008). More time for preliminary training may be needed to obtain good agreement for lesion activity assessment. An additional research study, in which the agreement on carious lesion activity is evaluated at different time points after training and with greater experience using the systems may provide more evidence regarding this issue. However, it should be recognised that it is not possible to eliminate all measurement errors, and clinical diagnostic decisions are always made under some extent of uncertainty (Baelum et al., 2008).
The differences in mean number and prevalence of active non-cavitated lesions between the two diagnostic criteria can be explained by the higher sensitivity of ICDAS II criteria for detecting early stages of carious lesions than the Nyvad system (Braga et al., 2009). An additional factor that could explain the difference between the two diagnostic systems is the way in which activity of the lesions is determined. Activity assessment with the Nyvad system is based on the summation of all visual-tactile signs of lesion activity, followed by a decision on whether a lesion is active or not (Nyvad et al., 2008). The LAA system with the ICDAS II is based on three main parameters of the lesions activity, each with a specific assigned score that, when totalled, determines if a lesion is active or not (Ekstrand et al., 2007). In other words, with the Nyvad system a dentist would make a judgement on activity, where with ICDAS II + LAA activity is determined based on a calculation.

We found a higher number and prevalence of active cavitated/dentinal lesions with the ICDAS II+LAA than with the Nyvad system. This can also be explained by the different lesion activity assessments in the two systems. According to the LAA system with the ICDAS II: any lesion having ICDAS II severity scores from 3 to 6 (micro-cavities, shadows, cavities) and located in a plaque stagnation area would be scored as active (Ekstrand et al., 2007; Braga et al., 2010). Our findings are in agreement with a recent study in which it was reported that the ICDAS II system, together with LAA, scored more lesions as active than did the Nyvad system (Braga et al., 2010).

The differences in diagnostic outcomes for active lesions with the two systems were found on all surfaces except active non-cavitated lesions on occlusal surfaces. This can be explained by the low prevalence of active non-cavitated lesions in the examined population age group (18-20 years old) and the nature of carious lesion development. Most of the active lesions in the current study were located on proximal surfaces. These results are in agreement with Mejare et al. (2004), in which the relative increase in the proportion of proximal, compared with occlusal, caries was observed in subjects aged between 12 and 22 years.
To our knowledge, the present *in vivo* study is the first in which the reproducibility and diagnostic outcomes of two caries scoring systems, the Nyvad and the ICDAS II+LAA, were compared: 1) using general dental practitioners previously inexperienced in use of both criteria 2) in a population of caries active young adults and 3) in which all surfaces of the teeth were assessed. We believe that such a design is closer to a real-life situation and can provide valuable information about the use of lesion activity assessment criteria in general dental practices. In addition, the design used in this study allowed minimization of dentist variability in assessment of carious lesions with the two systems, since the same dentists examined the same patients using the ICDAS II+LAA or the Nyvad criteria with a one-week wash out period. A high-risk population in the study was chosen so that a wide variety of carious lesions with different stages and activity could be assessed. The involvement of a caries active population in this study may produce lower reliability values, since a higher number of different stages of carious lesions detected could lead to greater variation in diagnoses (Braga et al., 2009).

Amongst the limitations of our study is the high variation among dentists using both diagnostic criteria to diagnose active non-cavitated carious lesions. In addition, it is possible that a carry-over effect could occur when knowledge of one diagnostic system could influence the outcome of another diagnostic system. The best way to eliminate this confounding factor is to have a long washout period. However, the dynamic nature of the carious process did not allow for a long washout period. Even in one week, the first clinical signs of a lesion’s activity change can be revealed if the oral environmental conditions are favourable (Holmen et al., 1987). In order to minimise the carry-over effect, detailed explanations of differences in carious diagnoses between the two systems were given to the examiners during the training session prior to the Period 2 examination. In addition, the examiners were asked to focus on the latest caries diagnostic system for which they were trained; also, they were required to use a checklist of specific diagnostic criteria during each examination period. Despite
the possible confounding factors mentioned above, the Bland-Altman plots clearly show a consistent tendency for the ICDAS II+LAA to exceed the Nyvad diagnoses of active carious lesions. A similar trend was shown when the two diagnostic systems were compared using a Wilcoxon sign rank test, taking into account between-dentist variation. It may be suggested that a recall bias could have occurred during the second period of examination. However, a one-week time period between the first and the second examinations, and the additional examination of the other 130 participants during this week, should have minimised any potential recall bias.

The generalisability of the results with regard to the measured parameter (carious lesions) is likely to be good, since the biological process of caries disease is universal and a large number of active carious lesions were assessed. On the other hand, having a high risk population could limit the external validity of the study, since it is not a common condition in general population. It should be emphasised that the current study addressed only the reproducibly of each evaluation system, but not the validity, since there is no gold standard for clinical caries diagnosis (Wenzel and Hintze, 1999); thus, we can only report on whether examiners scored the lesions similarly and cannot comment on the accuracy of the results with each system.

In conclusion, the results of this study have shown that carious lesion severity can be assessed with a substantial level of agreement by general dental practitioners previously inexperienced in the use of the Nyvad and ICDAS II+LAA diagnostic systems. The ICDAS II+LAA criteria produced diagnoses of more active carious lesions than the Nyvad system. This difference suggests that more caries treatment may be carried out if the ICDAS II+LAA system is used in dental practice among high caries risk population.

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References


3.1.1 Summary of results from Manuscript I

The results of this Manuscript I addressed the first two parts of our project providing valuable information about dentists’ agreement and diagnostic outcomes made by dental practitioners using the ICDAS II+LAA and Nyvad systems. The results of the study have shown that it is possible to achieve acceptable levels of reproducibility for the severity of carious lesions using both the ICDAS II and Nyvad diagnostic systems, even when the criteria are used by dental practitioners who were previously inexperienced with these systems. At the same time, the results demonstrated that there was less agreement for lesion activity assessment with the ICDAS II+LAA and Nyvad diagnostic systems. More time for preliminary training may be needed to obtain better agreement for lesion activity assessment.

Regarding the evaluation of the diagnostic outcomes, the results showed that the mean number and prevalence of active non-cavitated and cavitated/dentinal lesions are consistently higher with the ICDAS II+LAA than with the Nyvad criteria. The Bland-Altman plots also showed a consistent tendency for the ICDAS II+LAA to exceed the Nyvad diagnoses of active carious lesions. This difference suggests that more caries treatment may be carried out, both non-operative and operative, if the ICDAS II+LAA system is used in dental practice with a caries active population.

Manuscript II follows the same diagnoses, describing the subsequent treatment decisions made by the same dentists.
3.2 Manuscript II: “Treatment Decisions from two Caries Diagnostic Systems: A Cross-over Trial”

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Key words: dental caries; diagnosis; clinical trials, randomized; early diagnosis; disease management

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Abstract

Aim: The aim of this randomized cross-over study was to evaluate differences in operative and non-operative treatment decisions when dentists diagnose carious lesions with two systems: the Nyvad (NY) and the ICDAS II with LAA system (IC+LAA).

Methods: Four volunteer dentists were randomly allocated to one of two groups, with two dentists per group. Both groups examined the same voluntary sample (n=140) of 18-20 year-old caries active young adults using NY and IC+LAA criteria in different sequences, with a one-week washout period. After diagnosis, the dentists made treatment decisions of ‘no active care’, ‘non-operative treatment’ and ‘operative treatment’. Adjusted multilevel Poisson regression analyses were carried out.

Results: The mean number of operative treatment decisions per surface was 1.53 (95% CI 1.43-1.65) times higher for the IC+LAA than for the NY. The mean number of non-operative treatment decisions was 1.59 (95% CI 1.51-1.68) times higher for the IC+LAA than for the NY.

Conclusion: The use of the ICDAS II+LAA diagnostic system may result in more treatment, both operative and non-operative in a high caries risk population. A long-term study is needed to determine the costs and health effects with both diagnostic systems. Trial registration: ISRCTN65592532.
Introduction
Numerous studies have reported that there is considerable variation among and within dentists in their diagnosis of caries and consequent treatment decisions (Bader and Shugars, 1993, 1995; Lewis et al., 1996; Pereira et al., 2009). It has been suggested that this variation is ubiquitous and will inevitably lead to over- or under treatment, thereby negatively affecting the appropriateness of dental care (Bader and Shugars, 1995; Grembowski et al., 1997; Zero et al., 2011). Among factors responsible for dentists’ variation in decision-making, their understanding of the carious process, beliefs about lesion progression and alternative treatment outcomes, skills and diligence in clinical examination, diagnostic methods and use of diagnostic criteria are all important (Bader and Sugars, 1995). To minimise variation, several authors have emphasized the need for standardized diagnostic criteria, as a first step in improving treatment decisions (Bader & Shugars, 1993; Grembowski et al., 1997).

Modern caries management approaches require diagnostic systems that can detect lesions from the early stages, as well as assessing lesion depth and activity (Fejerskov, 2004; Fontana et al., 2010); in addition, a good carious diagnostic system should be linked with treatment strategies (Nyvad, 2004). All these requirements are necessary with the ultimate goal to achieve the best possible dental health outcome for the tooth and the patient (Baelum et al., 2008).

Two visual/visual-tactile caries diagnostic systems, the Nyvad (Nyvad et al., 1999) and the ICDAS II (Ismail et al., 2007) were recently introduced and shown to be accurate and reliable when used by experienced dentists (Nyvad et al., 1999, 2003; Ismail et al., 2007; Jablonski-Momemi, 2008; Braga et al., 2009, 2010; Machiulskiene et al., 2009). In order to assess activity, an adjunct system (Lesion Activity Assessment system, LAA) was developed, validated and proposed for use with the ICDAS II criteria (Ekstrand et al., 2007). Since both diagnostic systems have the potential to be applied in clinical practice, it is important to investigate their implications on treatment decisions. To our knowledge, this is the first clinical study in which the activity of carious lesions for the ICDAS II and the Nyvad systems was assessed by general dentists with limited training in the systems, rather than assessment by experts (Braga et al., 2009, 2010; Nyvad et al., 1999).
**The aim** of this study was to evaluate differences in operative and non-operative treatment decisions when dental practitioners used the Nyvad and ICDAS II+LAA systems to diagnose carious lesions in a sample of high caries risk young adults.

**Materials and Methods**

The study was carried out at a dental unit of the Institute of Emergency Services of Belarus, Minsk. The project was approved by the Research Ethics Committee of Belarusian State Medical University (Protocol № 06/2010) and by the IRB McGill University, Montreal, Canada (Study Number: A12-E60-10A). Whole recruitment process and the study project were completed during six weeks period.

**Study Design**

A randomised, cross-over, two-period, single blind, clinical trial design was used (Figure 1). A lecture of a contemporary approach of caries management was given to the dentists. They were then randomly assigned to one of two groups, through drawing sealed allocation envelopes that were generated by the investigators. Both groups examined the same subjects in different sequences using Nyvad and ICDAS II+LAA criteria (for criteria descriptions see Tikhonova et al., 2013). The first group used the Nyvad criteria during Period 1, followed by ICDAS II+LAA criteria during period II; the second group did the examinations in the opposite sequence. A one-week wash out period was used (Figure 1). All examinations were performed using the same setting, with a standard dental light source, dental mirrors, three-in-one air syringe, suction device and cotton rolls. The ball-ended WHO probe was used for the ICDAS II+LAA and a sharp standard dental explorer for the Nyvad criteria. Before each examination, supervised tooth brushing was carried out. After diagnoses, the dentists made treatment decisions for each tooth surface using the following guidelines: 1) only active lesions should be treated, 2) active non-cavitated lesions should be treated non-operatively. The following options were proposed: No Active Care (NAC), Non-Operative Treatment (NOT) and Operative Treatment (OPT). Before each examination period, the dentists were trained for the diagnostic criteria they subsequently used when making treatment decisions and were blinded from the results of previous examinations. The inter-examiner Kappa values for
D1 diagnostic threshold (non-caviteted and cavitated lesions) varied from 0.48 to 0.51 for the ICDAS II+LAA criteria and from 0.45 to 0.57 for the Nyvad criteria (for details see Tiknonova et al., 2013).

Figure 1. Study flow chart
Sample and participants
The voluntary dental practitioners (n=4) were recruited for the project using the following inclusion criteria: 1. no previous knowledge or experience with either the ICDAS II+LAA or the Nyvad diagnostic systems, 2. 5-10 years of clinical experience 3. graduated from the same dental school, 4. trained as operative dentists and 5. had experience of working with adult populations with similar caries prevalence and experience as the patient sample. The voluntary patients (n=140) were selected according to the following inclusion criteria: 1. males and females, 2. ages 18-20 years, and 3. having ≥2 active non-cavitated and/or cavitated carious lesions. Exclusion criteria included those who had: 1. < 2 active carious lesions, 2. fixed orthodontics, and 3. severe fluorosis or hypoplasia.

Statistical analysis
The primary outcome was the number of surfaces/individual requiring operative or non-operative treatment. Sample size was based on results of a pilot study (SD 2.9, OPT; SD 8.5, NOT). A difference of 1 surface requiring operative and 3 surfaces for non-operative treatment was considered to be clinically meaningful. Thus, a sample of 140 patients was chosen to meet 80% of power, a 0.05 significance level and to account for loss.

Cross-tabulation for treatment decisions was performed using the pooled data sample (four examiners). The Wilcoxon sign rank test was used to determine whether there was a carryover effect. Multilevel Poisson regression analyses were used to assess differences between mean number of surfaces indicated for operative and non-operative treatments. The scheme of a random coefficient model using Stata’s “xtmipoisson” command was applied. The rate ratio (ratio of arithmetic means) and 95% confidence interval were calculated to assess the difference between diagnostic systems, adjusted by sequence and period of examination and examiner variation (fixed effects), with random slopes for subjects and examiners. STATA 12.0 software (Stata Corporation, College Station, TX, USA) was used.
Results
One hundred and forty male (n=122) and female (n=18) Belarusians aged 19.5 ± 1.2SD were examined twice by four recruited dentists; no participants were lost during Period 2. For each subject, 112 tooth surfaces were examined. The ICDAS II+LAA resulted in a higher number of both operative (n=1815) and non-operative (n=3769) treatment decisions than the Nyvad system (1263 operative and 2279 non-operative) (Table 1).

Table 1. Cross-tabulation of treatment decisions for the ICDAS II+LAA and the Nyvad systems (pooled data, 62720 surfaces)

<table>
<thead>
<tr>
<th>ICDAS II + LAA system</th>
<th>Nyvad system</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NAC</td>
<td>NOT</td>
<td>OPT</td>
<td>Total</td>
<td></td>
</tr>
<tr>
<td>NAC</td>
<td>55825 (89%)</td>
<td>1041 (2%)</td>
<td>270 (0.4%)</td>
<td>57136 (91%)</td>
<td></td>
</tr>
<tr>
<td>NOT</td>
<td>2601 (4%)</td>
<td>1083 (2%)</td>
<td>85 (0.1%)</td>
<td>3769 (6%)</td>
<td></td>
</tr>
<tr>
<td>OPT</td>
<td>752 (1%)</td>
<td>155 (0.2%)</td>
<td>908 (1.4%)</td>
<td>1815 (3%)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>59178 (94%)</td>
<td>2279 (4%)</td>
<td>1263 (2%)</td>
<td>62720 (100%)</td>
<td></td>
</tr>
</tbody>
</table>

The number of “no active care” decisions was highest for the Nyvad criteria. The differences in operative decisions between systems were significant in the Period 1 examinations (p<0.001), while the differences in non-operative decisions were significant only in the Period 2 examinations (p<0.001; Table 2).
Table 2. Evidence of a **carry-over effect**. Average number (± SD) of tooth surfaces with non-operative and operative treatment decisions.

<table>
<thead>
<tr>
<th></th>
<th>Nyvad system</th>
<th></th>
<th>ICDAS II+LAA system</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NOT</td>
<td>OPT</td>
<td>NOT</td>
<td>OPT</td>
</tr>
<tr>
<td>Period 1</td>
<td>Ex.1</td>
<td>3.6±3.6</td>
<td><strong>1.5±2.5</strong>*</td>
<td>Ex.3</td>
</tr>
<tr>
<td></td>
<td>Ex.2</td>
<td>5.9±5.1</td>
<td><strong>1.7±2.8</strong>*</td>
<td>Ex.4</td>
</tr>
<tr>
<td>Ex.3</td>
<td><strong>3.7±3.6</strong>**</td>
<td>2.9±3.5</td>
<td>Ex.1</td>
<td><strong>7.4±5.4</strong>**</td>
</tr>
<tr>
<td>Ex.4</td>
<td><strong>3.1±2.9</strong>**</td>
<td>2.5±3.1</td>
<td>Ex.2</td>
<td><strong>11.5±6.9</strong>**</td>
</tr>
<tr>
<td>Total</td>
<td>4.1±4.0</td>
<td>2.2±3.0</td>
<td>Total</td>
<td>6.8±5.9</td>
</tr>
</tbody>
</table>

* Differences in operative treatment decisions are clinically and statistically significant only in Period 1 (p<0.001, Wilcoxon sign rank test). ** Differences in non-operative treatment decisions are clinically and statistically significant only in Period 2 (p<0.001, Wilcoxon sign rank test).

The comparison of the ICDAS II+LAA and Nyvad operative and non-operative treatment decisions using multilevel Poisson regression modeling is demonstrated in Table 3. After adjustments, the results show that the mean number of surfaces with operative treatment decisions according to the ICDAS II+LAA criteria was 59% higher than for the Nyvad criteria (RR=1.59, 95% CI 1.51-1.68), while the mean number of surfaces with non-operative treatment decisions according to the ICDAS II+LAA criteria was 53% higher than for the Nyvad criteria (RR=1.53, 95% CI 1.43-1.65).
Table 3. Operative and non-operative treatment decisions according to diagnostic system. Adjusted Multilevel Poisson Regression model.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Operative</th>
<th>Non-operative</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RR*</td>
<td>95%CI</td>
</tr>
<tr>
<td>Fixed effect</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nyvad</td>
<td>Ref.</td>
<td></td>
</tr>
<tr>
<td>ICDASII+LAA</td>
<td>1.53</td>
<td>1.43-1.65</td>
</tr>
<tr>
<td>Random effects</td>
<td>Variance</td>
<td>SE</td>
</tr>
<tr>
<td>Examiner</td>
<td>0.004</td>
<td>0.003</td>
</tr>
<tr>
<td>Subject</td>
<td>1.66</td>
<td>0.23</td>
</tr>
</tbody>
</table>

* RR = Rate ratio (ratio of arithmetic means)

**Discussion**

The essential objective in making a diagnosis is to select the best possible treatment for the patient (Baelum et al., 2008). The Nyvad and ICDAS II+LAA caries diagnostic systems are the most advanced systems meticulously assessing the severity of carious lesions, as well as their activity which are the decisive factors in choosing the most appropriate treatment options (Nyvad et al., 2008; Pitts, 2009). In this study, we evaluated the impact of the Nyvad and ICDAS II+LAA systems on dentists’ treatment decisions in caries active young adults, since both systems have been suggested for use in clinical practice. The results of the study demonstrate that the ICDAS II+LAA system produces more operative and non-operative treatments than the Nyvad system.

To our knowledge, this is the first comparison of the treatment decisions resulting from the ICDAS II+LAA and Nyvad systems. A strong correlation between the ICDAS II lesion severity criteria and treatment decisions has been reported (Diniz et al., 2011). In another recent study, the authors concluded that the use of a visual-tactile method alone resulted in the most correct treatment decisions made by dentists (Baelum et al., 2012).
However, in both these studies only the severity of carious lesions was assessed, while lesion activity was not evaluated.

The greater number of operative treatment decisions with the ICDAS II+LAA system in this current study can be explained by the different approaches to activity assessment used by the two systems. According to the LAA system with the ICDAS II, any lesion having severity scores from 3 to 6 (micro-cavities, shadows, cavities) and located in a plaque stagnation area would be scored as active (Ekstrand et al., 2007). Our findings are in agreement with a recent study, in which it was shown that the ICDAS II+LAA, resulted in higher caries activity scores than the Nyvad (Braga et al., 2010). The difference in the number of non-operative treatment decisions between the two systems may be explained by the higher sensitivity of ICDAS II for detecting non-cavitated enamel lesions than the Nyvad (Braga et al., 2009). The additional factor may be the difference between the two diagnostic systems for the lesion activity assessment. The activity assessment by the Nyvad system is based on the summation by the examiner of all visual-tactile signs of lesion activity which are: the presence of dental plaque, lesion roughness/softness, lesion luster, lesion location and its color, and then making a decision whether a lesion is active or not (Nyvad et al., 2008). The LAA system of the ICDAS II is based on three main parameters of the lesions: visual signs (color and severity; location in a plaque stagnation area; and lesion roughness). Each parameter has its scores and a sum of the scores of all parameters higher than 7 indicates that a lesion is active (Ekstrand et al., 2007). If the lesion is non-cavitated and white (LAA score 3), and it is located in a plaque stagnation area (LAA score 3) it will be scored as active (sum of scores >7) since the third parameter (roughness) has a minimum score of 2.

Because of the absence of a diagnostic reference standard, one cannot conclude that one system is more accurate for making diagnostic and treatment decisions. However, since clinically and statistically significant differences in treatment decisions were documented between the two diagnostic systems, it suggests the possibility of over- or under-treatment (Bader and Shugars, 1995). Speculating about the potential consequences of over- and under-treatment, several factors should be taken into account: stage of the carious lesion (non-cavitated or cavitated), caries risk of the patient (high or low) and the availability of
the patient for follow up examination (Baelum et al., 2008). A number of authors have concluded that over-treatment may have a more negative impact than under-treatment (Kay and Nuttall 1994; Baelum et al., 2012), since it is well-documented that carious lesions in many populations have slow progression (Marthaler, 2004), and if lesions are not detected during one visit, there will be another opportunity to detect the lesions at a follow-up examination (Baelum et al., 2008). Non-operative over-treatment will not affect the oral health of the patients, however it may increase treatment cost. Finally, over-treatment associated with operative treatment would have the greatest negative impact (Pereira et al., 2009).

It is well recognised that operative treatment is not a cure for caries; what it does is to start the tooth down the path of a re-restorative cycle (Elderton, 2003; Kidd, 2011). This cycle has been described as a ‘death spiral’ of the tooth, which include the enlargement of the original restoration over time, risk of new ‘replacement’ restorations, an increasing risk of tooth fracture and subsequent crown placement, risk of iatrogenic damage to neighboring teeth, a risk of pulp involvement and endodontic therapy and, finally, tooth extraction (Elderton, 2003; Qvist, 2008). All of this is associated with significant economic costs to the patient (Qvist, 2008). On the other hand, the greatest risk from under-treatment is when lesions are not detected on time in patients with a high caries risk and/or when a patient does not attend a follow-up, resulting in lesion progression (Baelum et al., 2008).

A distinct strength of the study is in its randomized cross-over design that offers a powerful method of controlling for potential confounding effects, as well as offering a robust analytic approach. Several authors have emphasised the need for clinical studies that are more valid indicators of real life situations (Pereira et al., 2009; Bader and Shugars, 1995; Baelum et al., 2012). This current study was an in vivo study, in which patients and general dental practitioners were involved. Most of the studies involving evaluation of dentists’ treatment decisions were performed in vitro using bite-wing radiographs, extracted teeth and/or questionnaires (Kay and Nuttall, 1994; Lewis et al., 1996; Pereira et al., 2009; Diniz et al., 2011).
A limitation of the study could have been the low level of dentists’ agreement on the activity of carious lesions in the D1 (non-cavitated and cavitated lesions) diagnostic threshold, which may have produced additional variation in the non-operative treatment decisions. The reason for the low level of agreement may be linked with a lack of experience among the dentists in assessing lesion activity, subjectivity of the signs of carious lesion severity and activity and the short training and calibration time (Nyvad et al., 1999; Ekstrand et al., 2005; Zandona et al., 2009). A ‘carry-over’ effect, when knowledge of one diagnostic system can influence the diagnostic outcome of another system (Senn, 2002), was also revealed in this study. This effect can be associated with the period of examination and the sequence of using two diagnostic systems. Thus, the differences in non-operative treatment decisions between two diagnostic systems were statistically significant only in Period 2. This may be explained by the fact that, by Period 2, the examiners obtained more experience and skills for detection of carious lesions from the early stages. On the other hand, the differences in operative treatment decisions were statistically significant only in Period 1. These findings may be explained by the influence of ICDAS II+LAA system that dentists previously used in Period 1 on the diagnosis of cavitated/dentinal lesions and subsequent operative treatment decisions with the Nyvad system in Period 2 (examiners who used the Nyvad criteria in Period 2 produced consistently higher number of operative treatment decisions than examiners who used the same criteria in Period 1). All of these factors were taken into account statistically in the multilevel regression model. The effect of the differences in operative and non-operative treatment decisions between the two systems persisted, even after the adjustments.

The generalisability of the results with regard to the measured parameter (carious lesions) is likely to be good, since the biological process of caries disease is universal and a large number of active carious lesions assessed. On the other hand, having a high risk population could limit the external validity of the study, since it is not a common condition in general population.

In conclusion, this study suggests that the use of the ICDAS II+LAA diagnostic system may result in more treatment, both non-operative and operative in a high caries risk population. This study alone does not permit us to answer the question: “which system is
most appropriate?” Indeed, it should be recognised that both may be erroneous and given the nature of caries, imprecise assessment of lesion severity and activity is likely to be a reality for the foreseeable future. The important issue at present is, therefore, understanding the implications of using different diagnostic tools. With this in mind, there is a need to carry out long-term clinical studies to determine the impact of these diagnostic systems on both health outcomes and the cost of caries management.

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3.2.1 Summary of results from Manuscript II

In this study, we evaluated the impact of the Nyvad and ICDAS II+LAA systems on dental practitioners’ treatment decisions when the systems were used in different sequences in the same sample of caries active young adults. The differences in operative decisions between systems were significant in the period 1 examinations, while the differences in non-operative decisions were significant only in the period 2 examinations. These results demonstrate the presence of a period and sequence effect. In order to take both of these effects into account, as well as examiner variation, we used a multilevel Poisson regression analyses. After adjustments, this study showed that the ICDAS II+LAA system resulted in more operative and non-operative treatment decisions than the Nyvad system.
4. SUMMARY, CONCLUSION AND IMPLICATIONS FOR FUTURE WORK

4.1 Summary of research findings

In this study, we evaluated differences in operative and non-operative caries treatment decisions when dental practitioners used two visual-tactile diagnostic systems, the Nyvad and the ICDAS II+LAA in caries active young adults. The manuscripts from this study addressed three main parts of the project: 1. training and calibration of the examiners, 2. dentists’ diagnostic decisions and 3. dentists’ treatment decisions. The results of the training and calibration of the examiners have shown that carious lesion severity can be assessed with a substantial level of agreement by general dental practitioners previously inexperienced in the use of the Nyvad and ICDAS II+LAA diagnostic systems. These results are in agreement with other in vivo studies and confirm the possibility of diagnosing non-cavitated carious lesions with a high level of agreement (Nyvad et al., 1999; Shoaib et al., 2009; Zandona et al., 2010; Braga et al., 2010a). At the same time, the results demonstrated that there was less agreement for activity assessment with the ICDAS II+LAA and Nyvad diagnostic systems. These findings are also supported by the results of several published studies that also used examiners who were previously inexperienced in the use of ICDAS II diagnostic criteria with lesion activity assessment (Zandona et al., 2009; Nelson et al., 2011).

The results of the second part of the study that addressed the dentists’ diagnostic outcomes revealed that the ICDAS II+LAA criteria produced diagnoses of more active non-cavitated and cavitated carious lesions than the Nyvad system. These results also agree with previous studies, in which the two diagnostic systems were compared (Braga et al., 2009, 2010a).

The results of the third part of the study address our main objective and represent the treatment decisions of dental practitioners when they used the two caries diagnostic systems. The results have demonstrated that the ICDAS II+LAA system produces more operative and non-operative treatment decisions than the Nyvad system in a high caries risk population. These findings can be explained...
by the differences in lesion activity assessment between the ICDAS II+LAA and the Nyvad diagnostic systems, as well as their different diagnostic thresholds of carious lesion detection.

Because of the absence of a clinical diagnostic reference standard, one cannot conclude that one system is more accurate for making diagnostic and treatment decisions. However, since clinically and statistically significant differences in treatment decisions were documented between the two diagnostic systems, this suggests the possibility of over- or under-treatment (Bader & Shugars, 1995). Thus, it is important to understand the implications of using different diagnostic tools when planning caries management decisions.

A number of authors have concluded that over-treatment may have a more negative impact than under-treatment oral health (Kay & Nuttall 1994; Baelum et al., 2012), since it is well-documented that carious lesions in many populations have a slow progression (Marthaler, 2004), and if lesions are not detected during one visit, there will be another opportunity to detect the lesions at a follow-up examination (Baelum et al., 2008a). Non-operative over-treatment will not affect oral health, however it may increase treatment cost (Pereira et al., 2009). Finally, over-treatment associated with operative treatment would have the greatest negative impact, since it propels the tooth down the path of a re-restorative cycle (Grembowski et al. 1997; Elderton, 2003). Moreover, operative treatment is associated with significant economic costs to the patient and society, which increase over a lifetime (Qvist, 2008). On the other hand, the greatest risk from under-treatment is when lesions are not detected in time in high caries risk patients and/or when a patient does not attend a follow-up, resulting in lesion progression (Baelum et al., 2008a). This study alone does not permit us to answer the question: ‘Which system is most appropriate’? There is a need to carry out long-term clinical studies to determine the impact of the Nyvad and ICDAD II+LAA diagnostic systems on both health outcomes and the cost of caries management.
It should be emphasised that the Nyvad and the ICDAS II caries diagnostic criteria are, to date, the most advanced diagnostic systems that can play an important role in contemporary caries management (Nyvad et al., 2008; Pitts et al., 2013). The impact for the oral health of such meticulous diagnostic systems within a non-operative caries disease management approach, supported by a caries risk assessment, will be huge for both individual patients and populations (Pitts, 2004). It will help to control the carious disease process, while preserving tooth structure and minimizing operative intervention and costs for operative care (Ismail et al., 2013; Pitts, 2004). Following long term studies to establish the most appropriate system, the next important challenge will be its implementation in everyday clinical dental practice settings.

A more detailed discussion of the results of our study is presented in the discussion sections of the two articles included in this thesis.

4.2 Research Limitations

One limitation of the study could have been the low level of dentists’ agreement on the assessment of activity in the D1 (non-cavitated and cavitated lesions) diagnostic threshold, which may have produced additional variation in non-operative treatment decisions. The reason for the low level of agreement may be linked with a lack of experience amongst the dentists in assessing lesion activity, personal interpretation of the signs of carious lesion severity and activity and the short training and calibration time (Nyvad et al., 1999; Ekstrand et al., 2005; Zandona et al., 2009).

A ‘carry-over’ effect, when knowledge of one diagnostic system can influence the diagnostic outcome of another system (Senn, 2002), was also revealed in this study. The best way to eliminate this confounding factor is to have a long washout period. However, the dynamic nature of the carious process did not allow for a long washout period. In fact, the first clinical signs of a change in lesion activity can be revealed in one week if the oral environmental conditions are favourable (Holmen et al., 1987). A carry-over effect can be associated with the sequence of using two diagnostic systems and the period of examination. In order to minimise
the carry-over effect, detailed explanations of differences in carious diagnoses between the two systems were given to the examiners during the training session prior to the Period 2 examination. In addition, the examiners were asked to focus on the latest caries diagnostic system for which they were trained; also, they were required to use a checklist of specific diagnostic criteria during each examination period. In order to take into account both the period and the sequence effect, a multilevel regression model was used to analyse the data. Even with this adjustment, the effect of the differences in operative and non-operative treatment decisions between the two systems persists.

It may be suggested that a recall bias could have occurred during the second examination period. However, a one-week time period between the first and the second examinations and the additional examination of the other 130 participants during the examination week, should have minimised any potential recall bias.

Some may state that involvement of Belarusian dentists into the study may limit external validity of the results, since treatment decisions vary amongst dentists from different countries (Kay and Locker, 1996; Espelid et al., 2001). However, training the dentists using meticulous diagnostic criteria and following two specific rules when making treatment decisions (1. only active lesions should be treated 2. active non-cavitated lesions should be treated non-operatively) allowed us to minimize this limitation. On the other hand, the involvement of a high risk population in the study could limit its external validity, since this may not be a common condition in other populations.

4.3 Conclusions

1) Dentists can be trained and reliably diagnose different severity stages of carious lesions using the Nyvad or ICDAS II systems.

2) Additional training and experience is needed in order to obtain good agreement for lesion activity assessment by dentists.

3) The use of the ICDAS II+LAA diagnostic system may result in more treatment, both non-operative and operative, compared with the Nyvad system, when used in a high caries risk population. Prior to introducing en
mass (to all dentists) a new caries diagnostic system, long term studies on the oral health outcomes and costs of both systems must be carried out.

4.4 Original contribution of the work within the thesis
A distinct strength of the study is in its randomized cross-over design that offers a powerful method of controlling for potential confounding effects, as well as offering a robust analytic approach. Several authors have emphasised the need for clinical studies to assess caries diagnostic and treatment outcomes that are true indicators of real life situations (Bader and Shugars, 1995; Pereira et al., 2009; Baelum et al., 2012). To our knowledge, this is the first clinical study in which the caries activity criteria (the ICDAS II+LAA and Nyvad) were used by general dentists with limited training in the systems in order to make caries treatment decisions. We believe that such a design is closer to a real-life situation and can provide valuable information about the use of caries lesion activity assessment criteria in general dental practices. In addition, the design used in this study allowed minimization of dentist variability in assessment of carious lesions with the two systems, since the same dentists examined the same patients using the ICDAS II+LAA or the Nyvad criteria with a one-week wash out period.

4.5 Implications for future work
Our research can be used as a first step for planning a longitudinal clinical trial to determine the impact of the ICDAS II+LAA and Nyvad diagnostic systems on both health outcomes and the cost of caries management. In addition, future research is needed in order to assess the impact of training and educating dentists for contemporary caries management approaches using lesion activity assessment systems for their caries treatment decisions. Moreover, we recommend a future research study designed to determine the most appropriate training approach for lesion activity assessment by dentists.
REFERENCES


Bonner BC, Bourgeois DM, Douglas GV, Chan K, Pitts NB: The feasibility of data collection in dental practices, using codes for the international caries detection and assessment system (ICDAS), to allow european general dental practitioners to monitor dental caries at local, national, and international levels. Primary dental care : Journal of the Faculty of General Dental Practitioners (UK) 2011;18:83-90.


Declaration of Helsinki (2008), http://ethics.iit.edu


Senn SS: Cross-over Trials in Clinical Research. 2nd ed. Chichester: John Willey&Sons Ltd, 2002.


## Treatment options

| NAC (No Active Care) | - No active preventive or operative care is needed  
|                      | - Maintenance and monitoring of preventive  
|                      | caries control between routine visits  
|                      | - Patient education and individual assessment of  
|                      | caries risk: oral hygiene instruction (including  
|                      | use of fluoride tooth paste), patient-specific  
|                      | dietary assessment and motivation, appropriate  
|                      | recall intervals.  
| NOT (Non Operative Treatment): | - Home and professional fluoride application (F toothpaste with appropriate concentration, F varnish), including enhanced oral hygiene instruction for secondary prevention.  
| - Additional fluoride application | - Pit and fissure sealants application for secondary and primary prevention.  
| - Sealants |  
| OPT (Operative Treatment) | - Composite, sealant, GIC, amalgam restorations  

### Appendix 2: Examination dental chart, ICDAS II+LAA

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</table>

*N/A - dentists do not agree with the treatment imposed by the study diagnostic system*
Appendix 4

ICDAS II severity codes (Ismail et al., 2007) and Lesion Activity Assessment System (LAA, Ekstrand et al., 2007)

<table>
<thead>
<tr>
<th>ICDAS II severity codes</th>
<th>Activity scores</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 = Sound tooth surface</td>
<td></td>
</tr>
<tr>
<td>1 = First visual change in enamel</td>
<td></td>
</tr>
<tr>
<td>2 = Distinct visual change in enamel</td>
<td></td>
</tr>
<tr>
<td>3 = Enamel breakdown, no dentine visible</td>
<td></td>
</tr>
<tr>
<td>4 = Dentinal shadow</td>
<td></td>
</tr>
<tr>
<td>5 = Distinct cavity with visible dentine</td>
<td></td>
</tr>
<tr>
<td>6 = Extensive distinct cavity with visible dentine</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Lesion Activity Assessment system (LAA)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical parameter</td>
<td>Activity scores</td>
</tr>
<tr>
<td><strong>Visual appearance: severity score</strong></td>
<td></td>
</tr>
<tr>
<td>- ICDAS II score 1, 2 (brown lesions)</td>
<td>1</td>
</tr>
<tr>
<td>- ICDAS II score 1, 2 (white lesions)</td>
<td>3</td>
</tr>
<tr>
<td>- ICDAS II score 3,4,5 or 6</td>
<td>4</td>
</tr>
<tr>
<td><strong>Plaque stagnation</strong></td>
<td></td>
</tr>
<tr>
<td>- Plaque stagnation area</td>
<td>3</td>
</tr>
<tr>
<td>- Non-plaque stagnation area</td>
<td>1</td>
</tr>
<tr>
<td><strong>Surface texture</strong></td>
<td></td>
</tr>
<tr>
<td>- Rough of soft surface on gentle probing</td>
<td>4</td>
</tr>
<tr>
<td>- Smooth or hard surface on gentle probing</td>
<td>2</td>
</tr>
</tbody>
</table>
### Appendix 5

**Nyvad caries diagnostic criteria (Nyvad et al., 1999)**

<table>
<thead>
<tr>
<th>Score</th>
<th>Category</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Sound</td>
<td>Normal enamel translucency and texture (slight staining allowed in otherwise sound fissure).</td>
</tr>
<tr>
<td>1</td>
<td>Active caries (intact surface)</td>
<td>Surface of enamel is whitish/yellowish opaque with loss of luster; feels rough when the tip of the probe is moved gently across the surface; generally covered with plaque. No clinically detectable loss of substance.</td>
</tr>
<tr>
<td>2</td>
<td>Active caries (surface discontinuity)</td>
<td>Same criteria as score 1. Localized surface defect (microcavity), no more than 2 mm in width, may be in enamel or in dentine*.</td>
</tr>
<tr>
<td>3</td>
<td>Active caries (cavity)</td>
<td>Enamel/dentin cavity easily visible with the naked eye; surface of cavity feels soft or leathery on gentle probing. There may or may not be pulpal involvement.</td>
</tr>
<tr>
<td>4</td>
<td>Inactive caries (intact surface)</td>
<td>Surface of enamel is whitish, brownish or black. Enamel may be shiny and feels hard and smooth when the tip of the probe is moved gently across the surface. No clinically detectable loss of substance.</td>
</tr>
<tr>
<td>5</td>
<td>Inactive caries (surface discontinuity)</td>
<td>Same criteria as score 4. Localized surface defect (microcavity), no more than 2 mm in width, may be in enamel or in dentine.</td>
</tr>
<tr>
<td>6</td>
<td>Inactive caries (cavity)</td>
<td>Enamel/dentin cavity easily visible with the naked eye; surface of cavity may be shiny and feels hard on probing with gentle pressure. No pulpal involvement.</td>
</tr>
</tbody>
</table>

*Modified after training with experts*
Appendix 6: Consent form, patients

A comparison of treatment choices when dental caries lesions are diagnosed with two visual-tactile systems the Nyvad and the ICDAS II

Principal Investigators:
Dr. Svetlana Tikhonova, PhD student, Faculty of Dentistry, McGill University
Dr. Jocelyne Feine, Faculty of Dentistry, McGill University
Dr. Paul Allison, Faculty of Dentistry, McGill University

Co-Investigator:
Dr. Natallia Pustavoitava, Assistant Professor
Faculty of Dentistry
Belarusian State Medical University, Minsk, Belarus

Introduction
Dental caries (cavities) is a health problem for young adult population in Belarus. Caries is usually diagnosed when it is in a late stage; it is treated by drilling away decayed tooth tissue and applying filling material. However, the fillings have a limited life span; they can be broken, worn out or lost over time. They will then have to be replaced and that always means that the replacement will be larger and cost more and more over a lifetime. It is well known that tooth decay has several stages, from an early to a late stage, and both stages can be active or inactive. Active decay should be treated, while in-active decay should not. On early stage active tooth decay can be treated and stopped without any drilling. Therefore, a dentist needs to be able to tell when tooth decay is early or late and whether it is active or not.

The purpose of the study is to compare two ways of examining teeth that will help dentists to know exactly what stage of tooth decay and amount of activity there is so that they can choose the most appropriate treatment.
**Study Procedures**

- You will be asked to visit the dental clinic two times over a period of three weeks.
- Each time you will be examined by four dentists and each examination will be performed one after other.
- Before the examination you will be asked:
  - ✓ to fill a questionnaire that includes questions concerning your age, sex and education (your and your parents)
  - ✓ to perform a supervised tooth brushing
- After that, each dentist will perform a detailed visual examination of your teeth
- Dental probes will be used to gently feel the texture of the tooth surface or to remove dental plaque, if needed
- Following the examination, the dentists will make treatment decisions for each examined tooth surface
- Each examination will take about 10-15 minutes
- At the end of your second appointment, you will be provided with all the information concerning the results of your examination and treatment needs
- In addition, all questions you have about your oral health condition will be answered.
- You will be asked not to change your usual tooth brushing or flossing habits during the study period.
- Some of you (20 out of 151 patients) will be asked to come for a third additional examination that will be performed by four dentists during the study period.
**Risks or Discomfort**

Any potential discomfort that you may experience during your visits would be due to feeling fatigue from having kept your jaw open. The project dental examiners will do everything that they can to keep you comfortable during the examination by allowing you to rest and close your jaw for a few minutes if that occurs.

**Benefits**

After the second examination, you will receive detailed information concerning your teeth and oral health, as well as information on any need for treatment. If any fillings are needed, you will be advised to have an appointment with a dentist in a state or private dental clinic. If you have any cavities that can be treated without fillings, we will give you instructions about brushing your teeth better and about using fluoride to strengthen your teeth.

During the first appointment, you will receive a regular toothbrush and fluoridated tooth paste. At the second visit, you will receive an electrical toothbrush.

**Withdrawal from Study**

You may withdraw from the study at any time without penalty by calling Natallia Pustavaytava (tel. 296 33 03 90), the Research Co-Investigator.

**Subject Rights**

- You have the right to ask questions about the study at any time. If you have any questions about this project, ask the research study examiners or the co-investigator (Natallia Pustavoitava - tel. 296 33 03 90).

- If you have any concerns about you rights as a subject in this study, you may contact the Secretariat of Research Ethic in Belarusian State Medical University, at tel. 2 71 97 09.

- Your participation is voluntary. You may refuse to take part or stop taking part in the research project at any time without penalty or loss of benefits to which you are entitled. You may also refuse to answer any questions.
Confidentiality

Your confidentiality will be respected. Information that directly discloses your identity will be available to only the Principal Investigator and Co-Investigator. All of your answers and examination data will be kept confidential. You will be given a study number and only this number will be used for any research-related information. Thus, your name or any other information that can identify you as a subject in the study will not appear. All documents will be kept in Canada for a period of five years. The documents will be stored in a locked filing cabinet and security of any information kept on a computer hard drive will be done by password access. If the information will be used for publication, teaching or presentation, only the data will be published or presented and you will not be personally identified. At the end of the study you have a right to see and copy your own medical information related to the project.

Contact

You have the right to ask questions about this project at any time. If you have any questions, please, ask the Research Co-investigator:
Dr. Natallia Pustavoitava, telephone: 296 33 60 90
Belarussian State Medical University
Department of Operative Dentistry #1
28 Sukhaya Street, Minsk, Belarus
I, ______________________ (name of subject), have read all the information in this consent form. The study has been explained to me and my questions have been answered to my satisfaction. I agree to take part in this study. I will receive a copy of my signed and witnessed consent form.

By signing this consent form, I have not given up any of the legal rights, which I otherwise would have as a subject in a research study.

I authorize the collection, use and disclosure of my medical information in accordance with this form.

__________________________  _______________________
Signature of Subject          Date of Signature

__________________________
Printed name of Subject (BLOCK CAPITALS)

__________________________  _______________________
Signature of Person who obtained consent          Date of Signature

__________________________
Printed name of Person who obtained consent (BLOCK CAPITALS)
Appendix 7: Consent form, dentists

A comparison of treatment choices when dental caries lesions are diagnosed with two visual-tactile systems the Nyvad and the ICDAS II

Principal Investigators:
Dr. Svetlana Tikhonova, PhD student, Faculty of Dentistry, McGill University
Dr. Jocelyne Feine, Faculty of Dentistry, McGill University
Dr. Paul Allison, Faculty of Dentistry, McGill University

Co-Investigator:
Dr. Natallia Pustavoitava, Assistant professor
Faculty of dentistry
Belarussian State Medical University, Minsk, Belarus

Introduction
Dental caries is a health problem for young adult populations in Belarus. Caries is usually diagnosed on its cavitated stage and treated by drilling tooth tissue and applying restorative material. However, the restorations have their own life span and can be broken or lost with time. This will lead to re-restoration procedures, with subsequent tooth tissue loss. It is well known that the caries process includes several stages, from non-cavitated (early) to cavitated, and both stages can be active and inactive. Active caries should be treated, while in-active stages should not. Moreover, active non-cavitated caries can be treated and stopped using non-operative treatment. Therefore, using appropriate diagnostic criteria that can detect caries from its early stage, as well as assess its activity, is of great importance in general dentistry. Recently, two promising visual/visual-tactile caries diagnostic systems, the Nyvad (1999) and the ICDAS II (2002) were introduced. They have been demonstrated to be reliable and accurate and were used in several epidemiologic surveys and clinical studies. However, since both systems have the potential to be used in clinical practice, it is important to investigate their implications on caries treatment decisions amongst dentists.
The purpose of the study is to evaluate differences in operative and non-operative treatment decisions when dentists use two visual-tactile systems: the Nyvad and the ICDAS II.

Study Procedures
- The project will take five weeks
- During study examination periods you will examine approximately 20 patients per day, spending 10-15 minutes for each examination.
- Before the beginning of the project, you will receive an explanation and detailed information regarding the study protocol.
- After that, a lecture concerning contemporary caries management strategies will be given with emphasis on the importance of lesion activity assessment and differentiating between cavitated and non cavitated carious lesions when making treatment decisions.
- You will be randomly allocated to one of two groups; each group will have two dentists.
- Before the first period of examinations, dentists from the first group will be trained and calibrated with the Nyvad criteria, while dentists belonging to the second group will be trained and calibrated with the ICDAS II criteria.
- After that, both groups of dentists will be asked to examine 151 patients using the Nyvad criteria (first group) or the ICDAS II criteria (second group) and make treatment decisions for each surface of the patients’ teeth.
- After the examinations, both groups of dentists will be trained again: the first group with the ICDAS II criteria and the second group with the Nyvad criteria.
- Then, the second examination period will be started in which both groups of dentists will be asked to again examine 132 patients using the ICDAS II criteria (first group) or the Nyvad criteria (second group) and make treatment decisions for each surface of the patients’ teeth.

129
**Risks or Discomfort**
The potential discomfort that you may experience is that associated with repeated dental examinations. A 10-15 minutes break between each examination will allow you to take a rest.

**Benefits**
You will be trained and calibrated in two modern visual-tactile caries diagnostic systems, the Nyvad and the ICDAS II. These two systems were developed in relation to the new paradigm of caries management that are based on early detection and non-operative treatment of carious lesions. The acquired knowledge and skills will allow you to use these diagnostic systems in your clinical practice in order to make appropriate treatment decisions for each patient, taking into account the stage and activity of carious lesions.

**Withdrawal from Study**
You may withdraw from the study at any time without penalty by calling to research co-investigator Natallia Pustavoytava (tel. 296 33 03 90).

**Compensation**
You will be compensated for your role in this study. You will receive 500 USD at the end of the study.

**Subject Rights**
- You have the right to ask questions about the study at any time. If you have any questions about this project, ask the co-investigator (Natallia Pustavoitava tel. 296 33 60 90.).
- If you have any concerns about you rights as a subject in this study, you may contact the Secretariat of Research Ethic in Belarusian State Medical University, at tel. 271 97 09.
- Your participation is voluntary. You may refuse to take part or stop taking part in the research project at any time without penalty or loss of benefits to which you are entitled.
Confidentiality
Your confidentiality will be respected. Information that directly discloses your identity will remain only with Principal Investigator and Co-Investigator. You will be given a study number and only this number will be used for any research-related information. Thus, your name or any other information that can identify you as a subject in the study will not appear. All documents will be kept in Canada for period of five years. The documents will be stored in a locked filing cabinet and security of any information kept on a computer hard drive will be done by password access. If this information will be used for publication, teaching or presentation, only nominative data will be published or presented.

Contact
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telephone: 296 33 60 90
Belarussian State Medical University
Department of Operative Dentistry #1
28 Sukhaya Street, Minsk, Belarus
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By signing this consent form, I have not given up any of the legal rights, which I otherwise would have as a subject in a research study.

_________________________________________  __________________________
Signature of Subject                          Date of Signature

_________________________________________
Printed name of Subject (BLOCK CAPITALS)

_________________________________________  __________________________
Signature of Person who obtained consent      Date of Signature

_________________________________________
Printed name of Person who obtained consent (BLOCK CAPITALS)