Onderzoeksprotocol

(voor aanvraag niet-WMO verklaring)

Algemene gegevens

Titel	Validation of a questionnaire for rapid, non-invasive screening of periodontitis in a medical care setting
Datum	11-06-2019
Versienummer	4.0
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Coördinerende onderzoeker	Martijn J.L. Verhulst
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Onderzoekgegevens

Rationale	Oral inflammatory processes, in particular periodontitis (gum disease), may aggravate diabetes (1), rheumatoid arthritis (2) and cardiovascular diseases (3), and may compromise their effective treatment. Notably, periodontitis treatment has been shown to reduce biomarkers of diabetes (HbA1c) (4) and cardiovascular diseases (CRP) (3). Therefore, physicians have a need to know whether their patients suffer from periodontitis. For example, according to the current doctor's guidelines (NHG), diabetes care professionals are advised to screen the oral cavity of their patients for dental and periodontal diseases (5-7). When periodontitis is present, physicians ought to refer their patients to the dentist or another dental professional. In reality, however, they lack the time, knowledge and resources to perform a robust oral inspection and to screen for

periodontitis. Also, periodontitis often remains unnoticed until it is already too late.

In a previous project from our research group, a self-reported oral health questionnaire to screen for periodontitis was internally validated (8) (for the study protocol, see Supplementary File 1). This project resulted in prediction models, which algorithms can be used to develop a screening tool for periodontitis. Before this screening tool can be implemented on a large scale, it also requires external validation. In other words, we need to assess its performance in a patient population other than the one used for the development (9). Once externally validated against a routine clinical periodontitis screening, our screening tool could support diabetes care providers to adhere to the medical guidelines and recommendations without the need of a physical inspection.

The patient will be informed about the clinical screening outcome directly after the measurement, and advised about necessary follow-up steps if needed.

References

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Doel	The main objective of this study is to externally validate a screening tool for periodontitis, based on a self-reported oral health questionnaire and demographics.
Studie design	This project concerns a multi-center cross-sectional validation study.
Studie populatie	The study population will consist of adult (≥ 18 years old), dentate (at least one tooth of their own) subjects attending a medical setting such as a general practitioner (GP) offices or a hospital.
Inclusiecriteria	≥ 18 years old
Exclusiecriteria	Edentulous Subjects in need of prophylactic antibiotics before dental screening.
Aantal proefpersonen/ sample grootte	As a rule of thumb, it is suggested in literature that external validation projects should include at least 100 events (in our case periodontitis patients) (1). With an estimated prevalence of total periodontitis of approximately 40% (2,3), this would imply a sample size of at least 250 subjects (of whom 100 patients have periodontitis). To account for

	unexpected differences in the number of events, a sample size of 300 subjects is chosen. **References** 1. Collins GS, Ogundimu EO, Altman DG. Sample size considerations for the external validation of a multivariable prognostic model: a resampling study. Stat Med. 2016;35(2):214-26. 2. Eke PI, Thornton-Evans GO, Wei L, Borgnakke WS, Dye BA, Genco RJ. Periodontitis in US Adults. The Journal of the American Dental Association. 2018;149(7):576-88.e6. 3. Wahlin Å, Papias A, Jansson H, Norderyd O. Secular trends over 40 years of periodontal health and disease in individuals aged 20–80 years in Jönköping, Sweden: Repeated cross-sectional studies. J Clin Periodontol. 2018;45(9):1016-24.
Werving proefpersonen	For external validation, a medical care setting is preferred, such as general practitioner offices and policlinics. Willing GP offices that participated in the main project (see Supplementary File 1), as well as other offices, will be asked to participate in this project, while our contacts at several departments at the Amsterdam UMC and Spaarne Gasthuis will provide the required policlinic settings. Inclusion will take place in the waiting room at these GP offices and policlinics before or during the appointment of the patient, depending on the preference of the cooperating medical care provider. At least one week before this moment of inclusion, the agenda will be screened, and information letters will be sent to eligible patients (see File E1). When the patient shows up for his/her appointment, he/she will be asked by the researcher if everything from the information letter was clear, and whether he/she is willing to participate. If yes, an informed consent (see file E2) will be signed by the patient and the researcher.
Interventie	The external validation itself will consist of conducting the self-reported oral health questionnaire, complemented by asking for age, sex, smoking, dentist visit and dentate status (File F1). This will be performed by the researcher, taking approximately 1-2 minutes. Next,

	a dentist, oral hygienist or master dental student, supervised by the GP or internist and blinded for the results of the questionnaire, will perform a validated, non-invasive periodontal screening measurement (the DPSI, taking 3 minutes to perform [1]). The timing of these measurements during the appointment of the patients will be decided in agreement with the medical care professional at the specific setting. **References** 1. Van der Velden U. The Dutch periodontal screening index validation and its application in The Netherlands. J Clin Periodontol. 2009;36(12):1018-24.
Standaardzorg / Standaardbehandeling	As mentioned in the introduction and rationale of this research protocol, medical care professionals who treat patients with for example diabetes mellitus are already expected to inspect the mouth and screen for periodontitis according to the current medical guidelines. Therefore, it *should* be part of the standard care. However, in daily practice, these guidelines are not followed-up because of lack in time, knowledge and resources amongst medical care professionals.
Studie parameters	The primary outcome parameters will be predicted periodontitis (based on the prediction model i.e. self-reported oral health questionnaire) and actual periodontal health (based on the DPSI).
Studie eindpunten	Secondary to the self-reported oral health questions, ethnicity and education level of the patient are inquired (File F1). Periodontitis is strongly associated with socio-economic status. This could influence the performance of the calculator. We aim to approximate socio-economic status by inquiring education level. Moreover, self-reported oral health is very region- and culture-dependent, which is why we want to inquire ethnicity as well. Furthermore, the following patient characteristics will be extracted from the electronic health records: weight and BMI, HbA1c level, lipid profile, kidney function, the presence of diabetic complications and medication use. This will allow us to describe the study population and to perform secondary analysis to see whether certain characteristics influence the performance of our screening tool. At the GP offices, extraction of data will be performed by the general practitioner him- or herself. In the hospital, the internist or other responsible treating practitioner will perform this. The data will be transferred to an pseudonymized data collection

	form, coded similar to the self-reported oral health questionnaire (File F2).
Statistische analyses	The performance of the screening tool will be assessed by calculating the area under the ROC curve (AURROC), and sensitivity, specificity, positive predictive value and negative predictive value in a 2x2 table with predicted periodontitis vs. actual periodontitis.
Belasting voor de proefpersoon	All measurements take place during the already planned appointment at the GP office or hospital department. The questionnaire takes approximately 1-2 minutes, while the clinical periodontal screening takes 3-5 minutes. Therefore, in total, the extra time will be 4-7 minutes for each patient. Both the questionnaire and the periodontal measurement are non-invasive.
Risico voor de proefpersoon	There are no risks for the patient when participating in this study
Voordelen deelname aan het onderzoek	It is likely that there will be no noticeable advantages for the patients. However, it is possible that the periodontal measurement reveals periodontal problems that had been unnoticed until that point. If this results in early diagnosis and treatment of periodontitis by a dentist, this will have positive effects on oral health and possible also systemic health of the patient.
Nadelen deelname aan het onderzoek	Other than the additional time that is required for this study (approximately 4-7 minutes), there are no disadvantages for participating in the study.
Vergoeding voor de proefpersoon	Patients will not receive any reimbursement.
Administratieve aspecten	Data will be collected on coded paper forms, which will be secured at ACTA in a lockable cabinet and stored for 10 years (see also the patient information letter, File E1). The data will be entered into Castor EDC and analyzed using IBM SPSS statistics.
Publicatiebeleid en amendementen	We aim to publish the results of study in a scientific medical journal. Future amendments will be submitted in case of fundamental changes to the study design, research settings, outcome measurements or patient eligibility.

Overige punten van belang voor de METc	In order to provide additional background information, we have attached the research protocol of the previous METc application, on which this version continues (Supplementary File 1).