

Making a complex dental care tailored to the person: Population health in focus of predictive, preventive and personalised (3P) medical approach

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Abstract

An evident underestimation of the targeted prevention of dental diseases is strongly supported by alarming epidemiologic statistics globally. For example, epidemiologists demonstrated 100% prevalence of dental caries in the Russian population followed by clinical manifestation of periodontal diseases. Inadequately provided oral health services in populations are caused by multi-factorial deficits including but not limited to low socio-economic status of affected individuals, lack of insurance in sub-populations, insufficient density of dedicated medical units. Another important aspect is the “participatory” medicine based on the active participation of population in maintaining oral health: healthcare will remain insufficient as long as the patient is not motivated and does not feel responsible for their oral health. To this end, nearly half of chronically diseased people do not comply with adequate medical services suffering from severely progressing pathologies. Noteworthy, the prominent risk factors and comorbidities linked to the severe disease course and poor outcomes in COVID-19 infected individuals, such as elderly, diabetes mellitus, hypertension and cardiovascular disease, are frequently associated with significantly altered oral microbiome profiles, systemic inflammatory processes and poor oral health. Suggested pathomechanisms consider potential preferences in the interaction between the viral particles and the host microbiota including oral cavity, the respiratory and gastrointestinal tracts. Since an aspiration of periodontopathic bacteria induces the expression of angiotensin-converting enzyme 2 – the receptor for SARS-CoV-2, and production of inflammatory cytokines in the lower respiratory tract, poor oral hygiene and periodontal disease has been proposed as leading to COVID-19 aggravation. Consequently, the issue-dedicated expert recommendations are focused on the optimal oral hygiene as being crucial for improved individual outcomes and reduced morbidity under the COVID-19 pandemic condition.

Current study demonstrated that that age, gender, socio-economic status, quality of environment and life-style, oral hygiene quality, regularity of dental services requested, level of motivation and responsibility for own health status, and corresponding behavioural patterns are the key parameters for patient stratification considering person-tailored approach in a complex dental care in the population. Consequently, innovative screening programmes and adapted treatment schemes are crucial for the complex person-tailored dental care to improve individual outcomes and healthcare provided to the population.

Introduction

Oral cavity health is pivotal for prediction and prevention of associated pathologies

Oral cavity health is in focus of advanced 3PM strategies due to its key role in predicting and preventing dental diseases which may further cascade associated systemic effects and pathologies [1-5]. Individualised approach has been demonstrated as being particularly effective in implementing 3PM strategies in dentistry [6-8].

Further, suboptimal health conditions and reversible damage are particularly attractive for the cost-effective targeted prevention in dentistry that is central for the healthcare at large [5, 6]. General chronic periodontitis (GCP) is a bacterial inflammatory disease that destroys the supporting structures of the teeth

[9, 10] affecting the majority of adults worldwide and leading to associated systemic disorders in a reciprocal manner [11, 12]. Targeted prevention of GCP is an attractive focus of PPPM strategies in dentistry considering the tremendous socio-economic impact of the disorder [13].

Periodontal disease as the prominent example requesting healthcare improvements

An evident underestimation of the targeted prevention of dental diseases is strongly supported by alarming epidemiologic statistics globally. For example, epidemiologists demonstrated 100% prevalence of dental caries in the Russian population followed by clinical manifestation of periodontal diseases [2]. In combating these trends, an important role play professional oral care and individualised medical services [14-17]. Further, to raise the awareness in the area is essential for an effective oral care in the population [18, 19].

Inadequately provided oral health services in populations are caused by multi-factorial deficits including but not limited to low socio-economic status of affected individuals (low educational level and income), lack of insurance in sub-populations, insufficient density of dedicated medical units [20, 21]. Another important aspect is the “participatory” medicine based on the active participation of population in maintaining oral health: Healthcare will remain insufficient as long as the patient is not motivated and does not feel responsible for their oral health [17, 22, 23, 24]. To this end, nearly half of chronically diseased people do not comply with adequate medical services suffering from severely progressing pathologies [25].

Age as a potential determinant for patient stratification and tailored 3PM strategies

It is evident that individual age-groups behave differently towards healthcare measures including the spectrum of medical services requested, their duration, quality and costs. Healthcare challenges in elderly should be discussed from various perspectives including medical, mental and social aspects; in particular, general “hypofunction and dysfunction” towards oral disorders has been recognised for this sub-population [26-32]. Specific psychological features of this group should be taken into consideration such as losing physical and financial independence, amongst others [33, 34]. Adapted concepts of optimal oral care have been presented specifically for Geriatrics and Gerontology demonstrating that full recovery can be reached before irreversible frailty with symptoms of decreased articulation, choking / spillage at eating, and increasingly unchewed food. Still, this is considered to be a health condition, but not a disease. Contextually, specific measures of oral hygiene and dental prevention should be appropriately adapted to the needs of this age group preventing oral dryness, reduced occlusal force, decreased tongue-lip motor function, decreased tongue pressure, decreased masticatory function, and deterioration of swallowing function which collectively lead to the oral hypo-function with advanced ageing [41-43].

The aim of this article is to investigate the age-related aspects as a variable for adapted 3PM strategies, personalized programs for prediction and prevention of diminishing oral health.

Working Hypothesis

The current study hypothesised that age, gender, socio-economic status, quality of environment and life-style, oral hygiene quality, regularity of dental services requested, level of motivation and responsibility for own health status, and corresponding behavioural patterns are the key parameters for patient stratification considering person-tailored approach in a complex dental care in the population. If so, adapted screening programmes and treatment schemes are crucial for the complex person-tailored dental care to improve individual outcomes and healthcare provided to the population.

Study Design

Patient recruitment and stratification

The study enrolled 706 dental patients (529 women and 177 men) aged between 18 and 75 years. Potential gender-related differences have not been considered by current study. The recruited patients have been stratified by the age and according to the WHO recommendations [31] have been grouped as follows: A. between 18 and 24, B. between 25 and 44, C. between 45 and 60, D. between 61 and 75 years of age.

Application of the specialised survey

The participants underwent a comprehensive survey developed at Therapeutic Dentistry and Periodontology Department, Pavlov First Saint Petersburg State Medical University specifically for the purposes of this study. The survey comprises the questions regarding

1. The current status of the individual dental health
2. the lasting exposure to specific occupational hazards such as abrasives, acids, low and high temperatures, heavy physical activity, heavy metal salts
3. The individual attitude of the patient towards cavity disease prevention and their general knowledge towards the most optimal oral care.

The specialised survey has been developed based on the expertise collected at Therapeutic Dentistry and Periodontology Department, Pavlov First Saint Petersburg State Medical University regarding the origin of the oral cavity diseases and corresponding protective measures which are in consensus with international knowledge in the area as described in the literature [1, 3, 9, 14, 15, 31, 32, 34].

Statistics:

The descriptive statistics were performed presenting corresponding data as a percentage of each feature analysed. The groups were compared by the chi-square criterion. Multiple comparisons were analysed using the Holm-Bonferroni method. Statistical estimates were carried out using IBM SPSS Statistics 20.0. Statistically significant values were considered by $P < 0.05$.

Results

Recruited respondents reflect well the demographic profile of visitors to the dental care specialists

Figure 1 demonstrates stratification of 706 patients by age and gender recruited for the study and underwent the specialised survey.

The stratified age groups differ significantly ($P < 0.001$) regarding the frequency of their visits to the dental care specialists that reflects well general statistics monitored by dental care centres in St. Petersburg, Russia. To this end, the most frequent visitors were young people aged between 18 and 24 years old (35.9% women and 45.8% men). In contrast, the rarest visitors were people aged between 61 to 75 years old (5.7% women and 2.3% men). Regularity and reasons of dental visits by patients in different age groups are outlined in Table 1. One third of the respondents within the participating groups visited a dentist twice a year. Patients aged between 61 to 75 years old visited dentists less than once a year.

Table 1

Frequency and reasons of dental visits by patients stratified by age; P_{AB} – level of significance of difference between group A and B; P_{AC} – level of significance of difference between group A and C; P_{AD} – level of significance of difference between group A and D; P_{BC} – level of significance of difference between group B and C; P_{BD} – level of significance of difference between group B and D; P_{CD} – level of significance of difference between group C and D

No	Indicator		18 to 24 years old, N = 271	25 to 44 years old, N = 226	45 to 60 years old, N = 175	61 to 75 years old, N = 34	Significance P
	Group		A	B	C	D	
1	Frequency of dental visits	Less than once a year	34(12.5%)	39(17.3%)	46(26.3%)	12(35.3%)	$P_{AB}>0,05$
							$P_{AC}<0,01$
		Less than twice a year	54(19.9%)	34(15.0%)	27(15.4%)	3(8.8%)	$P_{AD}<0,01$
							$P_{BC}>0,05$
		Once a year	84(31.0%)	76(33.6%)	53(30.3%)	7(20.6%)	$P_{BD}>0,05$
							$P_{CD}>0,05$
2	Reason for dental visits	twice a year	99(36.5%)	77(34.1%)	49(28.0%)	12(35.3%)	$P_{CD}>0,05$
		Routine oral cavity treatment	72(26.6%)	92(40.7%)	65(37.1%)	13(38.2%)	$P_{AB}>0,05$
							$P_{AC}>0,05$
							$P_{AD}>0,05$
		Acute pain	24(8.9%)	20(8.8%)	35(20.0%)	6(17.6%)	$P_{BC}<0,001$
							$P_{BD}<0,01$
		Preventive check-up	175(64.6%)	114(50.4%)	75(42.9%)	15(44.1%)	$P_{CD}<0,01$
							$P_{CD}<0,01$

Table 1 shows that the routine oral cavity treatment is more often taken by patients between 25 and 44 years old (40.7%). Therefore, in this group, the number of visits to a dentist with acute pain is lower than in other groups. Young people (between 18 and 24 years old) less often than other groups undergo this procedure; however they are most frequent visitors for preventive check-up.

The largest portion of respondents who used to seek medical treatment of acute toothache was registered for groups between 45 and 60 (20%) and between 61 and 75 (17.6%) years old, that corresponds well with the fact that only one third of them take routine oral cavity treatments.

Chronic disorders in stratified patient groups

Responders have been analysed towards their collateral chronic disorders such as cardiovascular diseases, diabetes, gastrointestinal diseases, chronic kidney disease, and liver disease, amongst others. Figure 2

summarises collected data.

Respondents in the oldest group (between 61 and 75 years old) demonstrate the highest level of chronic diseases, namely 87.5% followed by the group between 45 and 60 years old (75.8%).

Oral care preferences in stratified patient groups

Collected statistics demonstrated that 80.2% of respondents considered in all groups taken together clean their teeth twice a day. However, a significant difference ($P < 0.05$) has been observed between the oldest and youngest groups of patients, namely 29.4% versus 11.1%, respectively. More than a half of respondents replace the toothbrush every two months. However some of them replace the toothbrush only if it wears out, that is more typical for the oldest group (38.1%). The stratified patient groups differ significantly in their preferences towards oral care approach and products as demonstrated in Fig. 3.

Only a toothbrush and toothpaste are used by 10%, 14.2%, 12% and 35.3% of responders in groups A, B, C, and D, respectively, and only toothbrush is used by 15.5 %, 8.4%, 17.1%, 2.9% in corresponding groups. Floss is more frequently used by younger responders in contrast to the mouthwash preferred rather by the oldest group. Noteworthy, 0.6 % of responders in group C do not make any use of the oral hygiene measures.

Data interpretation in the context of 3P Medicine

Periodontal and systemic diseases – the functional link

Periodontal diseases (PDs) are widespread in both – developed and developing countries and affect about 20-50% of world populations. PDs are prevalent through entire age spectrum from adolescence to elderly challenging therefore global public healthcare systems [35]. Periodontal disease is characterised by the destruction of connective tissues of the periodontium and alveolar bone, which may lead not only to local symptoms, but also to systemic diseases, such as cardiovascular diseases, diabetes, liver disease, chronic obstructive pulmonary disease, and several types of cancer [36]. Proposed mechanisms include bacteraemia and concomitant systemic inflammation, elevated C-reactive protein patterns and imbalanced oxidative stress [36, 37]. Risk factors such as poor oral hygiene, irregular dental care, diabetes mellitus, smoking, aging, medication, and stress overload – individually and synergistically promote PDs development in populations [35]. Further, robust evidence demonstrates a reciprocal relationship between PDs development and systemic diseases including but not restricted to systemically altered microbiome and inflammation[37], chronic kidney disease [36, 37], neurodegenerative pathologies [38], bacterial superinfections, pneumonia and sepsis characteristic for viral epidemics such as the actual COVID-19 pandemic condition (see the dedicated subchapter provided below). PDs significantly increase risks of cardiovascular diseases and mortality rates in patients with co-incidence of diabetic history and severe PD forms compared to no or mild PD [39]. Periodontitis is highly relevant for maternal infections, preterm birth, low birth weight, and preeclampsia [35].

Although PDs are characterised by a local inflammatory process, several studies have shown that inflammatory mediators produced during this process, as well as subgingival species and bacterial

components, can disseminate from the oral cavity, leading therefore, to various extra-oral diseases including systemic inflammation and cancer [39]. To this end, carcinogenesis associated with periodontal species has been observed in both the oral cavity and in extra-oral sites known as the “oro-digestive” cancer types: oral, esophageal, gastric, colonic, and pancreatic malignancies [39].

Association between periodontal diseases, bacterial overload and poor outcomes of viral infections: Lessons for protective measures under pandemics

Experience collected in the past with influenza outbreaks

During influenza outbreaks, it has been observed that respiratory viruses were associated with bacterial superinfections as the common feature for particularly severe disease course and the primary cause of death opposed to the virus itself as evident, for example, for influenza in 1918, H1N1 influenza in 2009 [40] and others. Periodontopathic microflora has been demonstrated as being implicated in imbalanced microbiome alterations, systemic inflammation and pneumonia development, in severe cases leading to sepsis and death. Contextually, the most optimal treatments utilise the dual antiviral and antibiotic medication [41]. This rich experience actually promotes extensive research activities to explore a potential association between disease course severity and oral hygiene in COVID-19 infected individuals. Preliminary results have been reported during the year 2020.

Association between disease course severity and oral hygiene in COVID-19 infected individuals

Clear association between diagnosed periodontitis and high risk of admission to intensive care units (ICU), need for assisted ventilation and increased COVID-19 related death has been demonstrated [42]. In consensus, the study performed in UK has reported over 50% of deaths in COVID-19 infected patients exhibiting bacterial superinfections and severe disease course [41]. High levels of *Prevotella*, *Staphylococcus* and *Fusobacterium* representing periodontopathic bacteria have been demonstrated specifically for this patient cohort with poor COVID-19 outcomes. To this end, for 80% of patients treated at intensive care units, a particularly high oral bacterial load has been recorded.

Noteworthy, the prominent risk factors and comorbidities linked to the severe disease course and poor outcomes in COVID-19 infected individuals, such as elderly, diabetes mellitus, hypertension and cardiovascular disease, are frequently associated with significantly altered oral microbiome profiles, systemic inflammatory processes and poor oral health [43].

Suggested pathomechanisms consider potential preferences in the interaction between the viral particles and the host microbiota including oral cavity, the respiratory and gastrointestinal tracts [44]. Since an aspiration of periodontopathic bacteria induces the expression of angiotensin-converting enzyme 2 – the receptor for SARS-CoV-2, and production of inflammatory cytokines in the lower respiratory tract, poor oral hygiene and periodontal disease has been proposed as leading to COVID-19 aggravation [45].

Consequently, the issue-dedicated expert recommendations are focused on the optimal oral hygiene as being crucial for improved individual outcomes and reduced morbidity under the COVID-19 pandemic

condition [41; 46]. For an effective prevention, an application of oral probiotics have been proposed connecting the gut-lung axis with viral and microbial pathogenesis, inflammation, secondary infections and severe complications linked to COVID-19 [47].

Conclusions

Current study demonstrated that that age, gender, socio-economic status, quality of environment and life-style, oral hygiene quality, regularity of dental services requested, level of motivation and responsibility for own health status, and corresponding behavioural patterns are the key parameters for patient stratification considering person-tailored approach in a complex dental care in the population. Consequently, adapted screening programmes and treatment schemes are crucial for the complex person-tailored dental care to improve individual outcomes and healthcare provided to the population.

Expert Recommendations

Individualised patient profiles

Application of analytical instruments focused on phenotyping and genotyping of patients are highly recommended. For precise phenotyping relevant questionnaires have been demonstrated to be of great clinical utility and cost-efficacy. One of the prominent examples in the area is the “dry mouth syndrome” phenotype relevant for xerostomia associated complications and pathologies the predisposition to which can be detected early in life in the reversible phase of health adverse effects followed by cost-effective targeted prevention [4]. Recently published study demonstrated significant predisposition to xerostomia in young groups of population demonstrating voice perturbations under stress conditions [5]. The needs of young populations in sub-optimal health conditions are clearly in the frame-work of the 3PM concepts [48; 49].

Genotyping analytical tools to diagnose inflammatory processes in early stages are highly recommended for targeted treatments and cost-effective prevention in population [50; 51]

Application of pre- and probiotics is considered to be effective to stabilise individual microbiome and to reverse negative effects of pathogenic microflora[52] that is particularly true for disorders associated with inflammatory processes [53; 54].

Innovative screening programmes

Common origin but individual outcomes is the major challenge for differential diagnostics, disease prediction and patient stratification based on individualised patient profiling [55]. Contextually, innovative screening programmes should get well equipped by novel approaches and high-tech tools such as liquid biopsy utilising biomarker-patterns in body fluids and artificial intelligence (machine learning, disease modelling etc.) to identify and stratify disease predisposed individuals and to create an accurate person-tailored treatment regime[56; 57; 58]

To this end, bio-banking plays the key role in the era of big data, machine learning, disease prediction, targeted treatments and prevention [59].

Educational measures for professionals and stratified groups in population

Educational measures play the key role in improving the medical care literacy, broad understanding and acceptance of innovative strategies of 3P medicine by professional groups and in the population [59]. It is expected that principles of participatory medicine as an essential element of PPPM and, consequently, an active role of patients in the treatment procedure may better motivate patients for taking responsibility for their health status [22].

Collaboration with policy makers

Population health is in focus of predictive, preventive and personalised (3P) medical approach presented above. Consequently, collaboration with policy makers leading to health policy advancement, development of innovative screening programmes triggered and financially supported by the state is pivotal for a significant progress in the area of dental care benefiting healthcare system at large [60].

Figures 5, 6, 7, and 8 present treatment schemes adapted to individual profiles and needs of stratified groups A, B, C, and D.

The proposed schemes differ in the following aspects:

1. Visiting a dentist and a dental hygienist is specific for Group A;
2. Visiting a dentist, a dental hygienist, a periodontist, a psychologist for enhancing compliance is specific for Group B;
3. Visiting a dentist, a dental hygienist, a periodontist, a psychologist, a physician and appropriate specialists (cardiology, oncology etc.) is specific for Group C;
4. Visiting a dentist, a periodontist (central person), a psychologist, a physician and appropriate specialists (cardiology, oncology etc.) is specific for Group D.

In common are following considerations:

1. Group A patients have good oral and general health condition and compliance. Therefore, they mainly need to attend a dentist and a dental hygienist for treatment;
2. Good general health condition, low compliance and periodontal problems are typical for Group B patients: a periodontal consultation is necessary;
3. Group C patients have periodontal and general health problems, as well as low compliance. Therefore, they need physical examination and treatment;
4. Periodontal and general diseases are central problem for this group. Therefore, periodontal and physical examinations, as well as appropriate therapy become obligatory.

List Of Abbreviations

PPPM / 3PM - predictive preventive personalised medicine

PDs - Periodontal diseases

ICU - intensive care units

WHO – World Health Organization

GCP - General chronic periodontitis

CVD - cardiovascular disease

NCD - non-communicable disease

Declarations

Authors' contribution

VT developed concepts and design, contributed to the data collection and drafted the manuscript. LO contributed to the coordination of the project, paper concepts and design, and critically revised the paper draft. TK contributed to the project coordination, data collection and drafting the manuscript. IB provided data analysis and interpretation, contributed to the paper design and drafting. EL was responsible for data collection, contributed to the study design and statistical analysis. MP contributed to concepts, design, analysis and data interpretation. OG created the final version of the manuscript and provided expertise in 3P medicine for the data interpretation and conclusions in the international context. All the authors read and approved the final manuscript.

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Compliance with ethical standards

All procedures performed in the study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The study was approved by the ETHICAL COMMITTEE OF THE FIRST PAVLOV STATE MEDICAL UNIVERSITY OF SAINT-PETERSBURG #01-2019. All patients were informed about the purposes of the study and have signed their “consent of the patient participation”.

Competing interests: The authors declare that they have no competing interests.

Publication consent: All individuals involved were informed about the purposes of the study and have signed their consent for publishing the data. Patients were informed about the purposes of the study and

have signed their consent for publishing the data.

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Figures

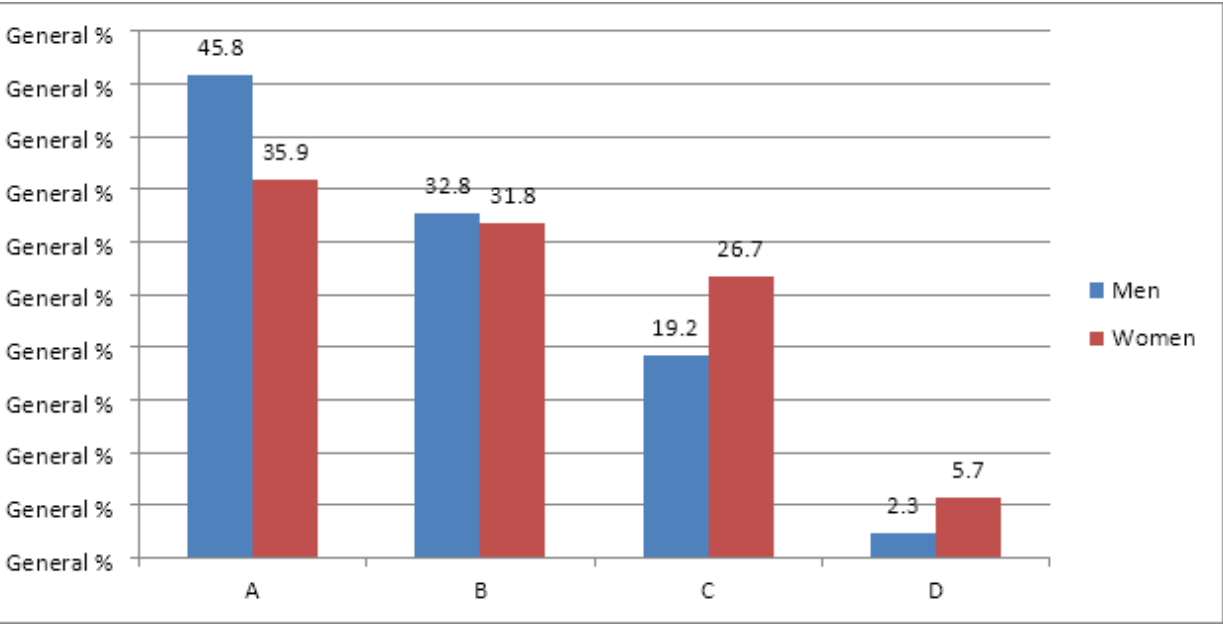


Figure 1

Respondents stratified by age and gender

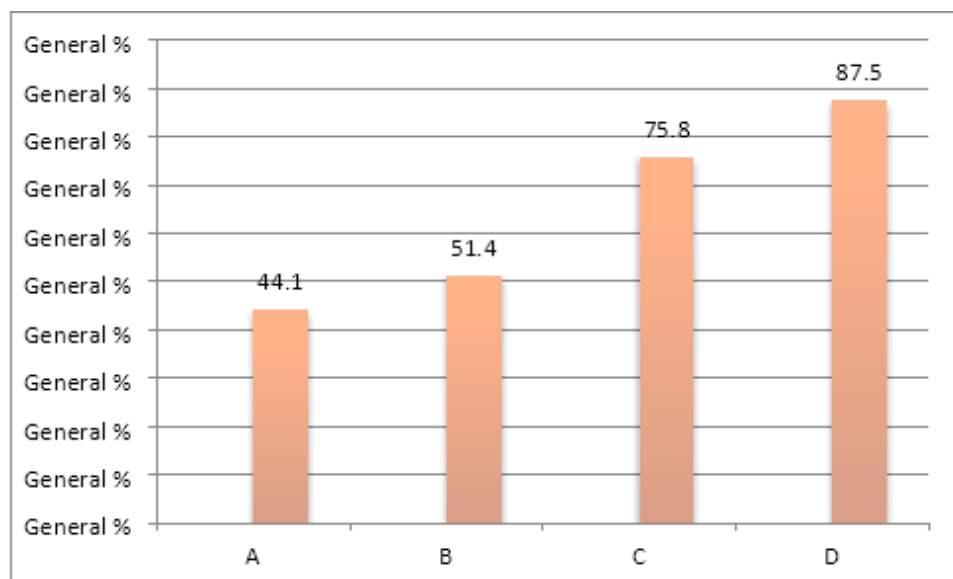


Figure 2

Frequency of chronic disorders in stratified patient groups; cardiovascular diseases, diabetes, gastrointestinal diseases, chronic kidney disease, and liver disease, amongst others have been considered; significance of difference between all groups involved is $PABCD < 0.001$

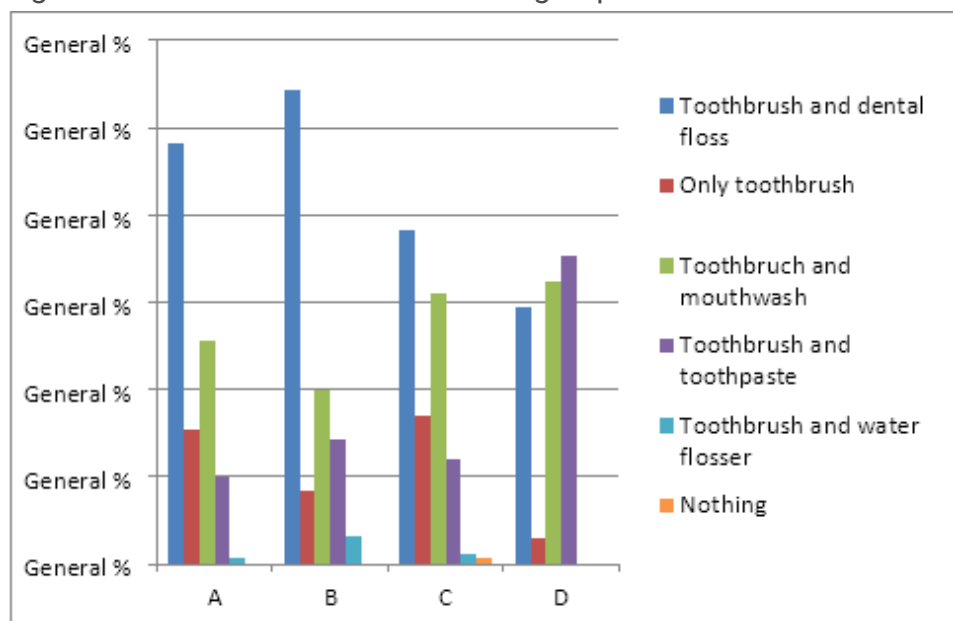


Figure 3

Oral care preferences in the stratified patient groups; significance of difference between groups A and B is $PAB < 0.05$; significance of difference between groups A and C is $PAC > 0.05$; significance of difference between groups A and D is $PAD < 0.001$; significance of difference between groups B and C is $PBC < 0.01$; significance of difference between groups B and D is $PBD < 0.01$; significance of difference between groups C and D is $PCD < 0.05$

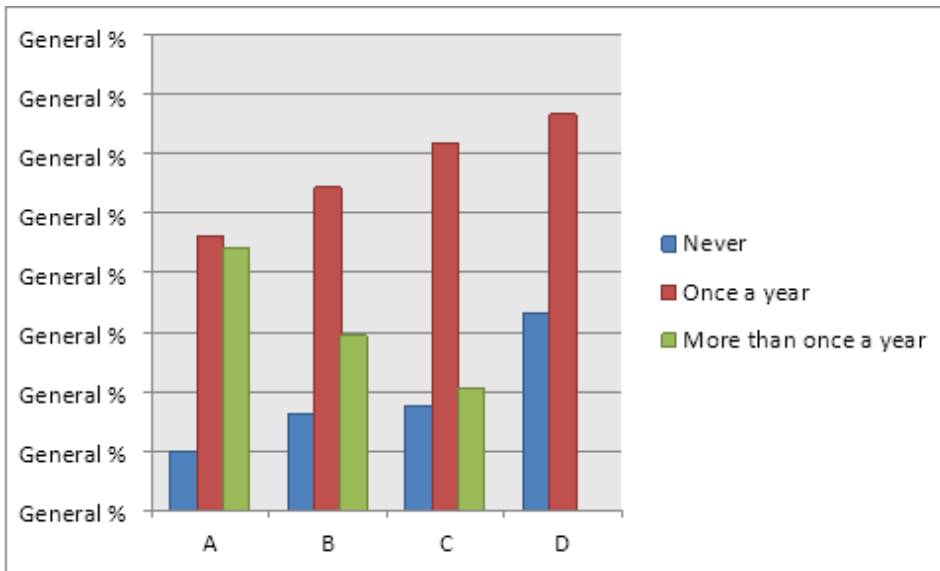


Figure 4

Regularity of professional oral care in stratified patient groups: Particular difference was observed considering the frequency of professional oral care used by youngest and oldest groups: either “never” or “once a year” were most characteristic for the oldest group compared to all other groups, whereas “more than once a year” was most characteristic for the youngest group; significance of difference between groups A and B is $P_{AB} > 0.05$; significance of difference between groups A and C is $P_{AC} > 0.05$; significance of difference between groups A and D is $P_{AD} < 0.01$; significance of difference between groups A and D is $P_{BC} > 0.05$; significance of difference between groups B and D is $P_{BD} > 0.05$; significance of difference between groups C and D is $P_{CD} > 0.05$

Predictive screening of periodontal patients group A

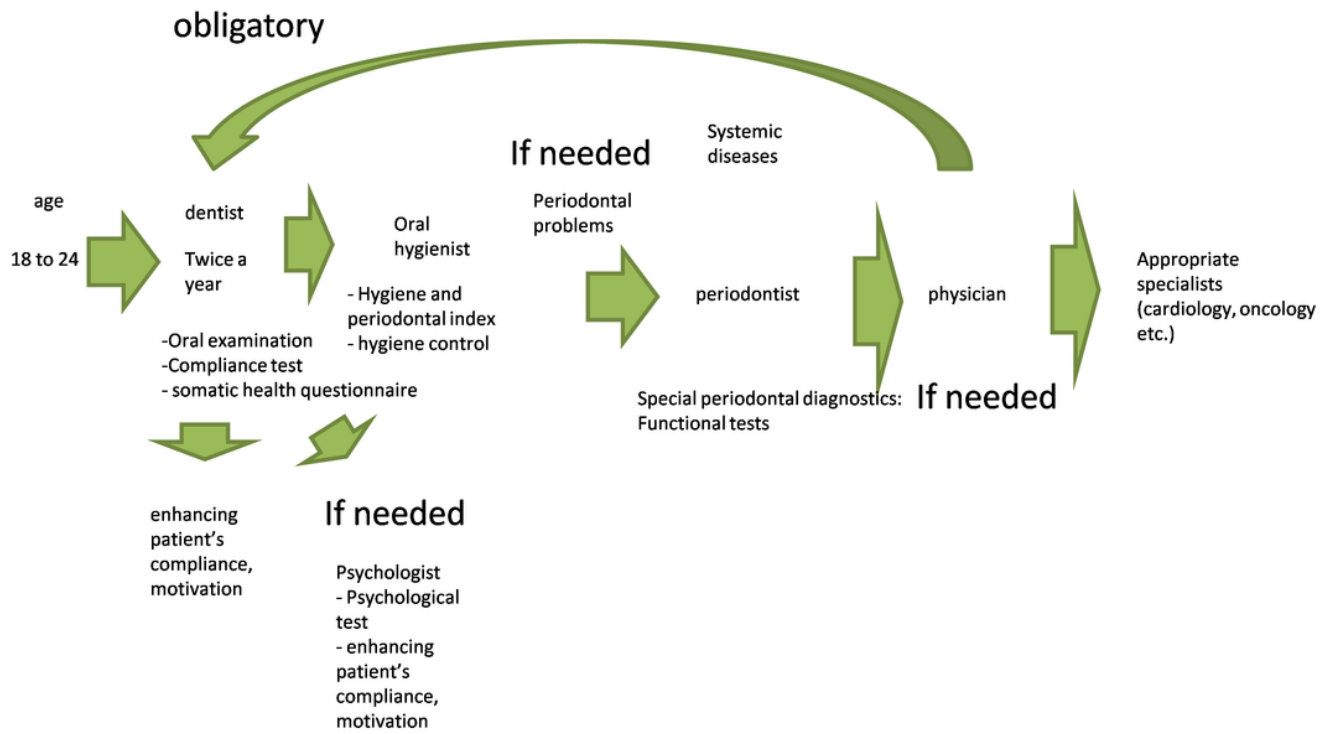


Figure 5

Predictive, preventive and personalised approach adapted to the specific needs of the stratified group A

Predictive screening of periodontal patients group B

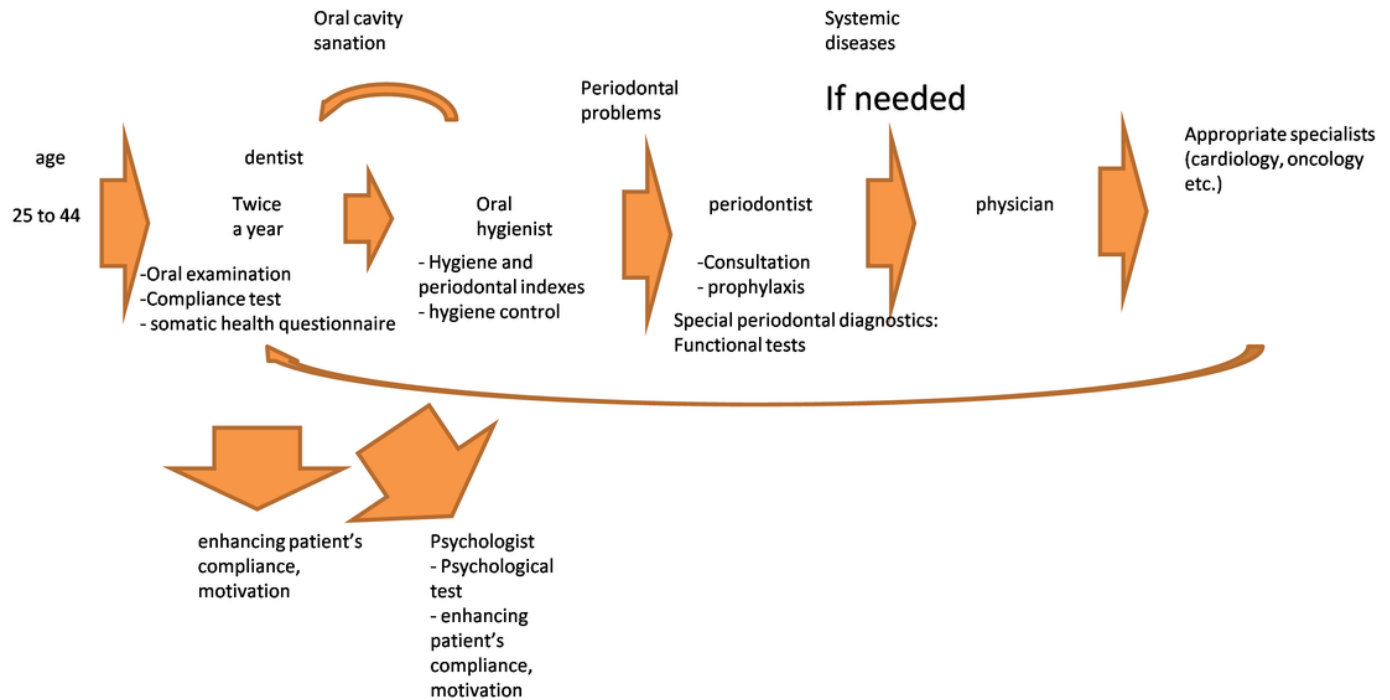


Figure 6

Predictive, preventive and personalised approach adapted to the specific needs of the stratified group B

Predictive screening of periodontal patients group C

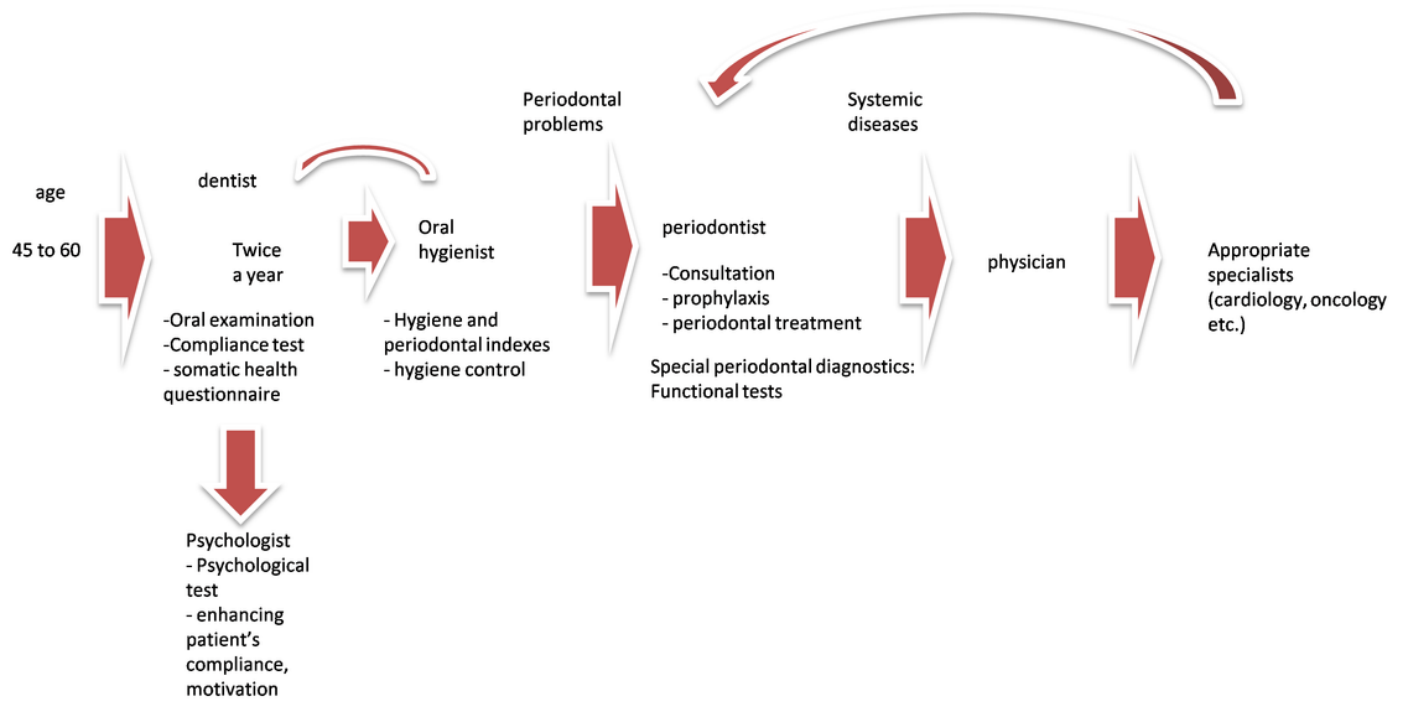


Figure 7

Predictive, preventive and personalised approach adapted to the specific needs of the stratified group C

Predictive screening of periodontal patients group D

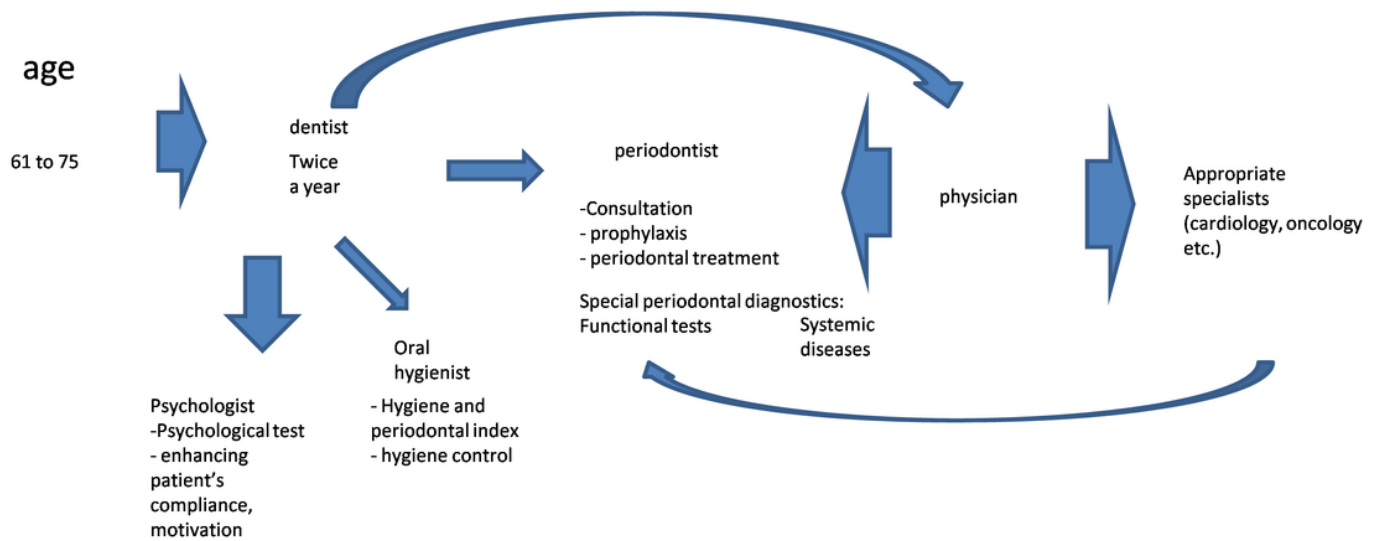


Figure 8

Predictive, preventive and personalised approach adapted to the specific needs of the stratified group D