Prevalence of new diabetes and impaired fasting glucose in Kosovo

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This dissertation was made in the five Family Medicine Centres in Kosovo; Gilan, Ferizaj, Prizren, Peja and Mitrovica

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Lists of symbols and abbreviations

ACCORD-Action to Control Cardiovascular Risk in Diabetes
ADA-American Diabetes Association
ADDITION-Anglo Danish Dutch Study of Intensive Treatment In people with screen-detected diabetes in primary care
BMI-body mass index
CDC- Diabetes Cost Effectiveness Study Group
CI-confidence interval
QALY-quality-adjusted life-year
QMF-Family Medicine Centre
DPP-The Diabetes Prevention Program Research Group
GP's –General Practitioners
HbA_{1c} -glycated hemoglobin
HR-hazard ratio
IFG-impaired fasting glucose
IGT-impaired glucose tolerance
OGTT-oral glucose tolerance test
UKPDS-United Kingdom Prospective Diabetes Study
USPSTF- U.S. Preventive Services Task Force
sBP- Systolic blood pressure
dBP- diastolic blood pressure
WHO- World Health Organization

1. Introduction

1.1. Diabetes mellitus-definition

Diabetes mellitus is a group of metabolic diseases characterized by chronic hyperglycemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action, or both. A person with diabetes has high blood glucose either because they are not producing enough insulin, or because the body does not respond properly to insulin (1).

1.2. Classification of diabetes

Classification of diabetes includes etiological types and different clinical stages of hyperglycemia as suggested by Kuzuya and Matsuda (2).
Four main etiological categories have been identified as diabetes type 1, type 2, other specific types, and gestational diabetes, as detailed in the WHO document (3).

Type 1 diabetes is characterized by the processes of beta-cell destruction that may ultimately lead to a virtually complete lack of endogenous pancreatic insulin production. Exogenous insulin is required for survival. Type 1 diabetes is typical for young people, however it may occur at any age (4). People who have antibodies to pancreatic b-cells are likely to develop either typical acute onset or slow-progressive insulin-dependent diabetes (5,6). Today antibodies to pancreatic ß-cells are considered as a marker of type 1 diabetes, although such antibodies are not detectable in all patients.

Type 2 diabetes is characterized by the disorders of insulin action and /or insulin secretion due to combination of genetic predisposition, unhealthy diet, physical inactivity, and increasing weight with a central distribution, resulting in complex pathophysiological processes. Early stages of type 2 diabetes are characterized by

insulin resistance causing excessive post-prandial hyperglycemia. This is followed by a deteriorating first-phase insulin response to increased blood glucose concentrations (7). Type 2 diabetes, comprising over 90% of adults with diabetes, typically develops after middle age.

"**Other specific types of diabetes**," is the third category of diabetes which is mainly caused by a specific and identified underlying defect, such as genetic defects that may lead to rare forms of diabetes, as for instance MODY, or diseases of the exocrine pancreas (as a result of pancreatitis, trauma, or surgery of pancreas), or drug - chemically induced diabetes.

Gestational Diabetes is a type of diabetes that constitutes any glucose perturbation that develops during pregnancy and withdraws after the delivery. Long-term follow-up studies that have been conducted over a period of more than 10 years reveal that approximately 70% of females with gestational diabetes will develop diabetes over time**.** In some cases, type 1 diabetes may be detected during pregnancy (8).

1.3. Diagnostic criteria

The current diagnostic criteria for Diabetes Mellitus are:

- Fasting plasma glucose (FPG) value is ≥ 7.0 mmol/L (126 mg/dl). Fasting is defined as no caloric intake for at least 8h, or if the
- Plasma glucose value 2 hours after 75g oral load glucose (OGTT) ≥ 11.1 mmol/L (200mg/dl), or
- In patient with classic symptoms of hyperglycemia or hyperglycemic crisis, casual plasma glucose value ≥ 11.1 mmol/L (200 mg/dl) , or
- A1c ≥ 6.5%. The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay (3,9-11).

Traditionally, diagnosis of diabetes was based on symptoms due to hyperglycaemia, but during the last decades much emphasis has been placed on the need to identify diabetes and other forms of glucose abnormalities in asymptomatic subjects. In asymptomatic subjects,
performing the test on one occasion is not enough to establish the diagnosis (i.e. basis to treat diabetes). For clinical diagnosis the ADA recommends confirmation of a diagnosis of diabetes with a repeated FPG test on a separate day, especially for patients with borderline FPG results and patients with normal FPG levels for whom suspicion of diabetes is high (12).

1.4. Burden

The number of people with type 2 diabetes is increasing rapidly (13).
Diabetes is one of the largest health emergencies of the 21st century. The World Health Organization (WHO) estimates that globally, high blood glucose is the third highest risk factor for premature mortality, after high blood pressure and tobacco use (14).
Type 2 diabetes is a more common condition. In most countries, type 2 diabetes has increased alongside rapid cultural and social changes: aging populations, increasing urbanization, reduced physical activity, increased sugar consumption and less healthy diets with low fruit and vegetable intake (15).
In 2013, over 382 million people worldwide have had diabetes; by 2035 this will rise to 592 million. In Europe, the number of people with diabetes in 2013 was 56 million with an overall estimated prevalence of 8.5%, a further increase of nearly 10 million people with diabetes is projected for the Europe by 2035 (16).
In 2015, over 415 million people worldwide, or 8.8% of adults aged 20-79, are estimated to have diabetes. About 75% live in low- and middle-income countries. If these trends continue, by 2040 over 642 million people, or one adult in ten, will have diabetes. It is estimated that one third to one half of patients with type 2 diabetes or, 193 million are unaware of their condition and therefore untreated (17).

1.5. Complications

People with diabetes are at higher risk of developing a number of disabling and life threatening health problems than people without diabetes. Consistently high blood glucose levels can lead to serious diseases causing the cardiovascular, cerebrovascular, peripheral artery disease, blindness, kidney failure, Charcot joints, lower-limb amputation and autonomic dysfunction such as sexual impairment. People with diabetes are also at increased risk of developing infections, depression, anxiety and dementia.

The growth in prevalence of type 2 diabetes in low- and middle-income countries means that without effective strategies to support better management of diabetes, it is likely that there will be large increases in the rates of these complications. Diabetes complications can be prevented or delayed by maintaining blood glucose, blood pressure and cholesterol levels as close to normal as possible. Many complications can be identified in their early stages by screening programs that allow treatment to prevent them becoming more serious (18).

1.6. Cost of treating diabetes and its complications

Treating diabetes has a cost of hundreds of billions of dollars being spend each year. World treatment costs are growing more quickly than world population. The costs associated with diabetes include increased use of health services, loss of productivity, disability and the long term support needed to overcome diabetes related complications. As a result, diabetes imposes a large economic burden on individuals and families, national health systems and countries; it therefore represents a significant obstacle to sustainable economic development. However, the larger costs of diabetes arise from disability and life loss caused by its preventable complications, including heart, kidney, eye and foot disease (19).

Estimations are that globaly more than 80% of expenditures for medical care for diabetes are made in the world's economically richest countries. Less than 20% of expenditures are made in the middle- and low-income countries where 80% of people with diabetes are living. One country, the United States of America, is home to about 8% of the world's population living with diabetes and spends more than 50% of all global expenditures for diabetes care. Europe accounts for 25% of diabetes-care spending. The remaining industrialized countries, such as Australia and Japan, account for most of the rest. In the world's poorest countries, not enough is spent to provide even the least expensive life-saving diabetes drugs (20).

The CODE 2 Study (21) was designed to measure the total healthcare costs for patients with type 2 diabetes in eight European countries using the same methodological approach. Patients from Belgium, France, Germany, Italy, the Netherlands, Spain, Sweden, and UK were included.

The total healthcare cost for patients with diabetes in the eight countries amounted to 29 billion Euro. Per capita cost varied from 1305 Euro per patient in Spain to 3576 Euro in Germany.

The results from the CODE-2 Study have shown that the main cost-driver in diabetes is not the disease itself or the treatment of diabetes, but rather the complications caused by diabetes. In the study, patients were divided into complication-free, having microvascular complications only, having macrovascular complications only, or having both macro and microvascular complications. In these three groups, the relative costs were 1.7, 2.0, and 3.5 times higher than the costs among patients without complications (22).

1.7. The natural history of type 2 diabetes, IFG and IGT

The natural history of type 2 diabetes includes an asymptomatic phase- dysglycemia or prediabetes and preclinical phase or latent diabetes.

Type 2 diabetes is usually preceded by the „prediabetes“ or non-diabetic hyperglycemia or high risk for diabetes which includes impaired fasting glucose (IFG) values of 6.1-6.9 mmol/l. 5-10% of people with prediabetes will progress to diabetes within a year. However, some proportion of these patients will convert back to normoglycemia if there is early identification and intervention (40-70% relative risk reduction) (23-24).

The pathogenesis of type 2 diabetes is not fully understood but involves gene-environment interactions, which increase susceptibility to developing three metabolic defects: insulin resistance, insulin secretory defects, and increased glucose production by the liver**.** The primary defects are believed to be insulin resistance and early pancreatic β-cell susceptibility linked to predisposing genes, which are worsened by several factors, including obesity and physical inactivity (25,26).

As the disease progresses, more global pancreatic defects result in increased hepatic glucose production. Persistent and increasing hyperglycemia further diminish the β-cells' capacity to secrete enough insulin to compensate sufficiently for the level of insulin resistance (27,28).

This state, where abnormalities in glucose metabolism are present but elevation in glucose is below the cutoff point for establishing the diagnosis of type 2 diabetes, is referred to as pre-diabetes (29). 'Pre-diabetes', is a term that has not been unanimously supported by the scientists since diabetes will not necessarily developed in those with IGT or IFG. Both IFG and IGT are asymptomatic, intermediate states of abnormal glucose regulation that precede overt type 2 diabetes.

IFG includes subjects with high fasting plasma glucose (FPG) concentration and normal response to a glucose load and impaired glucose tolerance (IGT) includes subjects with abnormal postprandial glucose excursion but normal FPG concentration (30). The IFG and IGT states are pathways that are correlated but may also appear independently. An individual falling into the IFG category on the fasting result may also have IGT on the 2-h value or, indeed, diabetes. If an individual falls into two different categories, the more severe one applies. (31).

Both IGT and IFG are insulin-resistant states, but they differ in site of insulin resistance. Subjects with IFG predominantly have hepatic insulin resistance and normal muscle insulin sensitivity (32), while individuals with IGT have normal to slightly reduced hepatic insulin sensitivity and moderate to severe muscle insulin resistance (33).

Global estimates of the burden of IFG and IGT are not available, but the number of people with IGT is likely to be even greater than the number with diabetes (34).

The prevalence of IFG also varies among ethnic groups, but its prevalence consistently is lower than IGT in all populations. IGT and IFG also differ by the age and sex distribution**.** The prevalence of both categories increases with age, but under the age of 55 years IGT is more frequent in women, while prevalence of IFG is twice as much higher in men than women (35).

In the Hoorn Study, prospective cohort study of a white population aged 50 to 75 years, investigators found that patients with IFG and normal glucose tolerance had a similar risk of developing DM to those with IGT and normal fasting glucose (33.0 vs 33.8%) but incidence of diabetes,(64.5%), was strongly related to both impaired fasting and impaired postload glucose levels at baseline, during the 6-year follow-up (36).

On average, both IFG and IGT are associated with a 20% increase in cardiovascular disease risk compared with normoglycemia (37).

It has also been clearly established that microvascular complications are associated with dysglycemia (38): around 7.9% of people with dysglycemia had signs of retinopathy in the Diabetes Prevention Program (39,40); the prevalence of neuropathy is higher among people with IFG compared with those with normoglycemia (11.9% vs. 10.5%) (41,42) and people with IGT and/or IFG have a higher prevalence of chronic kidney disease compared with those with normoglycemia (17.7% vs. 10.6%) (43). Provided these facts and data, it is ascertained that IGT and IFG, compared with normoglycemia, have also been shown to be associated with higher medical costs (44, 45).

Several cohort studies have shown a gradient of increasing mortality risk from normoglycemia to IFG, to IGT, and finally to diabetes. The relative risks for mortality among men and women, respectively, are approximately 21% and 8% higher for IFG and 51% and 60% higher for IGT than for normoglycemia (46-48).

1.8. Latent phase of diabetes

Similarly to IFG and IGT, the early stages of type 2 diabetes after biologic onset are frequently asymptomatic**;** they can live for several years without showing any symptoms, during which time high blood glucose is silently damaging the body.

They remain unaware of their condition for a long time because the symptoms are usually less marked than in type 1diabetes and may take years to be recognized. However, during this time the body is already being damaged by excess blood glucose. As a consequence, many people already have evidence of complications when they are diagnosed with type 2 diabetes

It has been estimated by IDF that globally as many as 193 million people, or close to half (46.5%) of all people with diabetes, are unaware of their disease. The earlier a person is diagnosed and management initiated, the better the chances of preventing harmful and costly complications. The complications associated with diabetes are so varied that even when symptoms do exist, diabetes may not be thought to be the cause unless accurate and appropriate testing is carried out. Those who are undiagnosed will not be taking steps to manage their blood glucose levels or lifestyle, so many of them with undiagnosed diabetes already has complications such as chronic kidney disease and heart failure, retinopathy and neuropathy (49-51).

The length of this asymptomatic period is less clear. No study has compared a screened with a comparable unscreened sample to determine the difference in the time at which diabetes is diagnosed. One group used an indirect approach to calculate this interval. After making assumptions about the rate of development of diabetic retinopathy early in diabetes, Harris and colleagues (52) estimated that the preclinical period lasted between 10 and 12 years. According to this calculation, screening a previously unscreened population would detect diabetes an average of 5 to 6 years before clinical diagnosis. Even if this estimate is correct, however, it represents a mean value. Some people will have a longer and some a shorter asymptomatic period. The true mean length of this period and the distribution of its duration are unknown. Using a nonlinear model, Thompson et al. (53) reported estimates of 7–8 years. However, these estimates

represent mean values only, and the asymptomatic period may vary widely for individuals (54).

Studies of people with newly conventionally diagnosed or screen-detected type 2 diabetes provide evidence of early diabetes-related tissue damage during the preclinical phase.

Studies of people with newly conventionally diagnosed or screen-detected type 2 diabetes provide evidence of early diabetes-related tissue damage during the preclinical phase.

In the United Kingdom Prospective Diabetes Study (UKPDS), 50% of newly diagnosed diabetes cases had evidence of diabetes-related complications (55-57). In the Hoorn screening study (58,59), the prevalences of myocardial infarction (13.3% vs. 3.4%) and ischemic heart disease (39.5% vs. 24.1%) were higher in screen-detected patients than in newly conventionally diagnosed patients, although the proportions with peripheral arterial disease were similar in both groups (10.6% vs. 10.2%).

With regard to microvascular sequelae of diabetes, the Hoorn study showed a higher prevalence of retinopathy in screen-detected patients than in newly conventionally diagnosed patients (7.6 % vs. 1.9%), while the prevalence of impaired foot sensitivity was similar in both groups (48.1% vs. 48.3%).

In the Anglo Danish Dutch Study of Intensive Treatment In people with screen-detected diabetes in primary care (ADDITION), screen-detected people had high estimated 10-year absolute risks of coronary disease events (11% in women and 21% in men) (60) and composite cardiovascular disease (38.6% in men and 24.6% in women) (61).

In US population-based surveys, compared with people without diabetes, those with undiagnosed diabetes had a significantly higher prevalence of neuropathy (11.6% vs. 10.5%) (41, 42) and chronic kidney disease (41.7% vs. 10.6%) (43).

1.9. Screening for type 2 diabetes

Strong evidence exists for the effectiveness of interventions to prevent type 2 diabetes mellitus among people with impaired glucose tolerance (IGT) (62,63). This evidence has led to recommendations to identify people with “dysglycemia” (IGT and/or IFG) and to implement diabetes prevention interventions (64). IGT/IFG and type 2 diabetes are part of a continuum; hence, the issues concerning screening for each are inseparable. It is justifiable to talk of and evaluate screening for both conditions together. Indeed, evidence from a modeling study suggests that combining screening for type 2 diabetes with screening for IGT is more likely to be cost-effective than screening for undiagnosed diabetes alone (65). The topic of screening for type 2 diabetes has been debated for some time and various reviews have been written (66-73), although they have focused on individual aspects of screening. Gaps regarding the collective issues associated with screening across the spectrum of dysglycemia and type 2 diabetes have not been fully described, nor have the implications for primary and secondary prevention.

1.9.1 Definition of screening

What is screening? The definition of the term **screening** is based on the WHO "Principles of Screening" document (74):

“Screening is the process of identifying those individuals who are at sufficiently high risk of a specific disorder to warrant further investigation or direct action.”

The definition goes on to say:

“Screening is systematically offered to a population of people who have not sought medical attention on account of symptoms of the disease for which screening is being offered and is normally initiated by medical authorities and not by a patient's request for help on account of a specific complaint. The purpose of screening is to benefit the individuals being screened.” Screening may be defined as the use of

rapidly applied tests or examinations to presumptively identify individuals with unrecognized disease in order to permit timely intervention (74).

The term diagnosis refers to confirmation of diabetes in people who have symptoms, or who have had a positive screening test. In diabetes, the screening test may be the diagnostic test, e.g. a fasting plasma glucose in someone who has symptoms or the first part of the diagnostic test if a second test, usually the OGTT is used to confirm the diagnosis in asymptomatic individuals.

Screening for type 2 diabetes **–**The main reasons for the current interest in screening for type 2 diabetes are: there is a long, latent, asymptomatic preclinical period of up to 12 years in which the condition can be detected (52,53,75,76), a substantial proportion of people with type 2 diabetes, up to 50% in most studies, remain undiagnosed for many years and a substantial proportion of newly referred cases of type 2 diabetes already have evidence of the micro-vascular complications of diabetes by the time of diagnosis (77-80). Primary care clinicians are encouraged to be more proactive in detecting and treating both diabetes and prediabetes (81).

The updated standards of medical care of the American Diabetes Association (ADA) recommend testing adults of any age who are overweight or obese and have additional diabetes risk factors. They also recommended the FPG test for screening because it is easier and faster to perform, more convenient and acceptable to patients, and less expensive than other screening tests (82).

1.9.2. Screening practices

There are several potential approaches to screening for diabetes:

- **Screening the entire population is** not recommended

- **Selective or targeted screening is** performed in a subgroup of subjects whom have already been identified as being at relatively high risk in relation to age, body weight,

ethnic origin etc. Targeting high-risk patients is recommended, as there is no evidence of a direct benefit of routine population-based screening for type 2 diabetes. (83,84).

- **Opportunistic screening** carried out at a time when people are seen, by health care professionals, for a reason other than the disorder in question. As screening should also be a systematic and continuous process opportunistic targeted screening might be a valuable screening method in primary care. This method entails screening high-risk individuals during usual care (85). The pragmatic nature of opportunistic targeted screening enables initiation of further diagnostic testing and treatment of newly diagnosed type 2 diabetes.

  These approaches are used alone or in combination.

  Screening yields are highly variable and dependent on the tests and cutoffs used. They also depend on the level of quality control and presence of adequate diagnostic resources in programs, as shown in an audit reporting the challenges to implement type 2 diabetes screening in United Kingdom primary care (86). Current evidence does not support universal screening; however, data from the United Kingdom indicate that any well-conducted targeted screening may come close to universal screening (87). Most professional organizations advocate a selective and opportunistic approach in high-risk populations (88-91).

  Selective or targeted screening and opportunistic screening are not mutually exclusive since screening may be limited to those at highest risk. In opportunistic screening, the decision to initiate the health care encounter is made by the individual, although, for reasons not related to the condition for which screening is offered. This needs to be distinguished from screening programs in which the invitation to come forward and be screened is part of the program.

  There is also **haphazard screening**, characterized by a lack of a coherent screening policy. In such cases individuals may be invited to be screened irrespective of their risk (people in a supermarket, for example) or there may be no adequate explanation of the reasons for screening or no formal system of support for those taking part, whatever the outcome of their test.

1.9.3. Screening intervals

There is no specific data that can be used to decide the optimal frequency of screening for type 2 diabetes or dysglycemia. An optimal interval between screening rounds would be one at which the prevalence of undiagnosed cases reaches the prevalence of such cases at the previous screening, and the cost-effectiveness is the same for each screening (54). The annual rate of progression from IFG and IGT to diabetes is 5%–10%, which might argue for a short screening interval for people with dysglycemia (92). The annual progression from normoglycemia to diabetes, however, is in the range of 0.6%–1.2%, depending on the population and age group studied. In a simulation quantifying the proportion of false positives with screening by OGTT, the percentage was 47.5% for annual repeat screening and 33.9% for a screening interval of 3 years (93). The US-based simulation reported that targeted screening for type 2 diabetes could be most cost-effective if repeated every 3–5 years (94).

1.9.4. Screening tests evaluation

The sensitivity of a screening test is the proportion of people with the disorder who test positive on the screening tests. A highly sensitive screening test is unlikely to miss a subject with diabetes.

The specificity of a screening test is the proportion of people who do not have the disorder who test negative on the screening tests. A highly specific test is unlikely to misclassify someone who does not have diabetes as having diabetes. Although it is desirable to have a test that is both highly sensitive and highly specific, this is usually not possible. In choosing a cut-off point a trade-off needs to be made between sensitivity and specificity, since increasing one reduces the other. The receiver operator characteristic (ROC) curve expresses this relationship.

Validity is the extent to which the test reflects the true status of the individual.

Reliability is the degree to which the results obtained by any given procedure can be replicated.

Reproducibility refers to obtaining similar or identical results on repeated measurements on the same subject. Screening tests must be shown to be valid, reliable and reproducible in the population in which screening is to take place. Uniform procedures and methods, standardized techniques, properly functioning equipment, and quality assurance are all necessary to ensure reliability and reproducibility.

Predictive value relates to the probability that a person has or does not have the disorder given the result of the test.

Positive predictive value is the probability of the disorder in a person with a positive test result and **negative predictive value** is the probability of a person not having the disorder when the test result is negative.

The predictive value of a test is determined not only by the sensitivity and the specificity of the test, but also by the prevalence of the disorder in the population being screened. Thus, a highly sensitive and specific test will have a high positive predictive value in a population with a high prevalence of the disorder. This is part of the rationale for promoting selective or targeted screening. When the prevalence is low, as may be the case when the entire population (or the entire adult population) is screened, then the positive predictive value of the same test will be considerably lower. In this case, a high specificity drives a high positive predictive value. To avoid false positives it may be necessary to increase specificity at the expense of sensitivity. Screening tests may be used in parallel (i.e. a person is deemed to be likely to have a disorder if they test positive to either test). In this case the sensitivity and the negative predictive value are generally increased and the specificity and positive predicted values decreased. On the other hand, screening tests may be used in series (i.e. a person needs to be positive to both tests in order to be deemed likely to have the disorder). In this case the specificity and positive predicted value are generally increased and the sensitivity and negative predicted value decreased. Tests in series have been advocated in type 2 diabetes when, for example, a questionnaire may precede a fasting blood sample or OGTT and be used to exclude some individuals deemed to be at low risk of having the disorder.

1.9.5. Screening tests or tools

Limited information is available regarding the optimal methods for diabetes screening. Therefore, it is uncertain how we should screen for diabetes (95-97). Many screening programmes combine population-based and targeted (directed at high-risk individuals) strategies in order to increase the yield (98).

Previous studies have reported on the advantages and limitations of a number of screening tests and tools. These have included questionnaires/risk scoring tools and the following biochemical tests: urine glucose, random blood glucose, fasting plasma glucose, glycated hemoglobin (HbA_{1c}), and the 75-g oral glucose tolerance test (OGTT) (67).

Mainly, a stepped approach is chosen starting with a simple **risk score** to identify high-risk individuals. The use of a risk score is attractive because it minimizes the number of persons who will attend glucose measurement and therefore reduces costs (99).

Questionnaires/risk scores-Various instruments have been developed to identify people at high risk of having or developing type 2 diabetes or dysglycemia.

These tools are based on risk factors that would help identify the minority of the population that accounts for the majority of people with type 2 diabetes and dysglycemia (89).

The risk appraisal tools involve use of self-reported questionnaires (100-105), health service data (106-107) or collected anthropometric, lifestyle, or biochemical data (108–127).

Questionnaires, whose performance depends on the response rate, may create undue anxiety or false reassurance, but they are likely to be more acceptable, less costly, and less time-consuming to administer than blood glucose testing or anthropometric measurements for risk prediction.

Use of existing health service data can limit the proportion of those who need to undergo blood glucose measurements to 20%–25% of the entire population, but this

tool may be limited by the availability of data on key variables. In general, including at least one blood glucose measurement improves the performance of a risk tool.

If the risk tools (100-123) developed and validated on the basis of prevalence studies were used as part of a repeated screening program, performance of the tools would likely change.

The most widely validated and used risk assessment tool is the Finnish risk score (102). It uses weighted data for 8 risk characteristics to calculate an overall score that predicts 10-year absolute risk of type 2 diabetes.

In summary, the existing simple tools to identify high-risk people are pragmatic. However, compared with OGTT, none of these tools are optimal. The efficiency of the tools may vary over time within a population (changing prevalence of risk factors), between populations and geographic areas, and they typically perform well in populations in which they were developed (128-129).

Urine glucose-The sensitivity of urine glucose testing is low (16%–64%), and the positive predictive value ranges from 11% to 37% (54). Thus, glycosuria appears to be a poor screening instrument for diabetes; large proportions of individuals with diabetes would be misclassified and remain undetected.

Random blood glucose-The use of random blood glucose as a screening tool is somewhat limited by its low screening performance (67). A large study comparing random blood glucose with OGTT for screening recommended a cost-effective random blood glucose cutoff of ≥6.9 mmol/L. At this level, random blood glucose exhibited 93% specificity and 41% sensitivity. In terms of identifying dysglycemia, the specificity was still high, at 94%, but sensitivity was only 23% (130).

A recent expert panel recommended a random blood glucose cutoff of ≥7.2 mmol/L, which has a sensitivity of 63% and specificity of 87%, based on validation against OGTT (131).

Fasting plasma glucose-The fasting plasma glucose screening test for hyperglycemia may have modest sensitivity (67). A Korean study found that a fasting plasma glucose threshold of ≥7 mmol/L detected only 55.7% of people with diabetes based on diagnosis by OGTT, with 100% specificity (132). An optimal cutoff for fasting plasma glucose was >6.1 mmol/L with a sensitivity of 85.2%, but specificity was decreased to 88.5%.

A study of young African American patients with dysglycemia found fasting plasma glucose not sensitive for the diagnosis of IGT compared with OGTT (133). A fasting plasma glucose threshold of >5.6 mmol/L detected only 28.9% of IGT cases, whereas OGTT identified 87.4% of cases.

Glycated hemoglobin- Even despite that fact that there is a need for approval in a wide range, the American Diabetes Association recently adopted HbA_{1c} as a diagnostic test for diabetes at a threshold of ≥6.5% (134). This adoption was justified by the alignment of the associations between HbA_{1c} and fasting plasma glucose with diabetes complications (particularly retinopathy) and the stronger correlation of HbA_{1c} with risks of cardiovascular disease and all-cause mortality compared with fasting plasma glucose (135).

However, the new American Diabetes Association criteria using HbA_{1c} do not specifically define IFG and IGT categories but rather a “high-risk” category corresponding to an HbA_{1c} between 5.7% and 6.4%.

The performance of HbA_{1c} ≥6.5% for type 2 diabetes diagnosis is variable in studies.

In combination with either random blood glucose or fasting plasma glucose, HbA_{1c} may add value in identifying the subgroups of individuals who need to undergo an OGTT (132).

An effective international standardization of HbA_{1c} is well under way (136–138). However, the costs and lack of availability of the test in low-resource settings remain high level concern (131).

The 50-g oral glucose challenge test-An evaluation of the 50-g oral glucose challenge test as a screening tool for adults found areas under the receiver operating

characteristic curves of 0.90, 0.82, and 0.79 for detection of undiagnosed diabetes, undiagnosed diabetes or dysglycemia, and dysglycemia, respectively, by plasma glucose challenge test (139). This performance was unaffected by time of day or proximity to meal times and is superior to that of capillary glucose challenge test, plasma random blood glucose, capillary random blood glucose, and HbA_{1c}. However, this study was limited by self-selection of participants (only black and white racial groups were included), lack of measures of intraparticipant variability, and validation in separate populations.

Capillary blood testing: finger-prick point-of-care testing-The utility of capillary blood testing for diabetes screening is unclear. An Australian study found that point-of-care capillary glucose testing underestimated blood glucose values compared with fasting plasma glucose. The areas under the receiver operating characteristic curves for prediction of dysglycemia and diabetes were 0.76 and 0.71 for point-of-care and 0.87 and 0.81 for fasting plasma glucose, respectively (140). However, among Asian Indians (141), capillary random blood glucose cutpoints >6.0 mmol/L have reasonably good sensitivity (66.5%–70.5%) and specificity (65.5%–69.5%) for type 2 diabetes, IGT, and IFG screening.

Combinations of tests-Screening tests, as mentioned above, may be combined to improve performance. In relation to type 2 diabetes this can be done using a series of tests (e.g. assessing risk by questionnaire followed by blood glucose measurement if a certain risk score is reached) or simultaneously (e.g. measurement of blood glucose and HbA1c at the same time). Combining the tests is more resource intensive, especially if applied sequentially.

Tests performed in parallel using FPG and HbA1c or fructosamine have been reported to have sensitivity ranging from 40% to 83% and specificity of 83%-99%, depending on the cut off values chosen (54). Combining the modified ADA questionnaire and RCBG ³ 6.7 mmol l-1 achieved a sensitivity of 58% and specificity of 94% (142).

An illustration of the effects of serial combination testing for a screening protocol which initially assessed risk factors, performed FPG in those at risk, then measured HbA1c in those with an FPG between 5.5 and 6.9 mmol l-1, and then tested with an OGTT those who had an HbA1c ³ 5.3%. This example illustrates that series of testing results in decreasing sensitivity, increasing specificity and PPV and reduces the number of people requiring definitive testing.

Multivariate logistic regression modelling with derivation of a probability value is another approach to combining demographic, clinical and biochemical tests in screening for undiagnosed diabetes. Tabaei and Herman(143) combined age, sex, BMI, postprandial time and random capillary plasma glucose to calculate the probability of undiagnosed diabetes and therefore the need for an OGTT. The calculation can be performed on a hand held programmable calculator and had a sensitivity of 65%, specificity of 96% and PPV of 63%.

1.9.6. Effects of screening in individuals, health systems and society

Policies and practices for screening for type 2 diabetes have profound implications for individuals, health systems and the entire society.

Implications for individuals include the time and other resources necessary to undergo the screening tests and any subsequent diagnostic tests, the psychological and social effects of the results whether the screening test proves ‘positive’ or ‘negative’ and whether or not the diagnosis of type 2 diabetes is subsequently made(144–156), and the adverse effects and costs of earlier treatment of type 2 diabetes or of any preventive measures instituted as a result of the individual being found to have diabetes. These may include occupational discrimination and/or increased costs or difficulty in obtaining insurance.

The effects on the health system and the entire society are the costs and other implications, especially in primary care and support services such as clinical

biochemistry of carrying out the screening tests and the necessary confirmatory tests, the additional costs of the earlier treatment of those found to have diabetes or to be at high risk of developing diabetes or cardiovascular disease in the future and the implications of false negative and false positive results which are inevitable given that any initial test will be a screening test and not a full diagnostic test and any loss of production as a result of the earlier diagnosis of the condition (from absence from work or reduced job opportunities, for example) (85).

1.9.7. The potential benefits of early detection of type 2 diabetes

Improvement in the quality of life and its duration which might result from a reduction in the severity and frequency of the immediate effects of diabetes or the prevention or delay of its long-term complications and any saving or redistribution of health care resources which might be possible as a result of reduced levels of care required for diabetes complications (reduced hospital admissions and lengths of stay...) (157-161).

1.10. Issues in Kosovo

Kosovo as a new country in the Balkans and in a period of transition. As a post-war country, Kosovo is facing a number of social, economic, political and especially health care related problems. Health services provided to the population require professional and technical expertise and have much room for improvement.

Health services are organised into three levels: Primary, Secondary and Tertiary level, while the Ministry of Health is the highest health authority of the Republic of Kosova.

Primary health care in Kosovo is considered to be the foundation of the delivery of health services and is carried forward mainly by family doctors. Kosovo has about 600

family doctors working in family health centres and state health institutions. Whilst in post-war Kosovo an emphasis was put on development of Family Medicine, family health centres are in many instances poorly equiped.

The delay in the population Census (the last Census in 2011 was not completed) and lack of health insurance system are two of the key obstacles to implementation and further development of family medicine in Kosovo. Patients lists have not yet been fully compiled for each Family Medicine Centre. The visits are not set in advance and electronic medical records have not been implemented as yet. Medical files avaliable in some cases are incomplete and/or not maintained properly. Under such conditions, an opportunistic screening for diabetes is still difficult to achieve in Kosovo.

Based on the American Diabetes Association's (ADA), new diabetes cases can be identified by screening patients in at risk groups, the first at risk group are those aged above 45 years who should be screened every 3 years (88). Therefore, it is considered that this level of screening is possible to do in Kosovo. In this regard, it should be emphasized that a situational assessment of diabetes diagnosis in Kosovo has previously suggested that 44.8% of cases are diagnosed from clinical symptoms, 29.6% from routine visits to medical facilities and 24.6% of diabetes cases in Kosovo are diagnosed by chance. Therefore, a pragmatic approach to screening for type 2 diabetes could improve these figures and lead to earlier detection and better prognosis of type 2 diabetes (162).

2. Hypothesis

Tools utilized during the screening process are convenient to use in family practice setting and the screening methods used in this study are suitable to Kosovo conditions and health care situation.

3. Aims and purpose of the research

To determine the prevalence of new cases of diabetes, and impaired fasting glucose (IFG) in general practices of Kosovo and to examine the potential relationships of diabetes with physical risk factors in Kosovo, where risk factors are more prominent, probably because of social and economic reasons.

Our aim was to investigate the feasibility and performance of very pragmatic system for identification of patients with type 2 diabetes and with impaired fasting glycaemia (IFG) in the primary health care. This identification system defers from those performed today in Western Europe and it was adjusted to the conditions offered by a health system of Kosovo.

4. Materials and methodology

4.1. Design and settings

In the absence of the lists of patients and also in the absence of electronic medical records, we had no opportunity to identify patients with a present risk factor and then to call them for a blood glucose test. The only way was to wait for these patients to come to the clinics for any other reason.

This prospective study was planned as a descriptive and cross-sectional study in 5 family medicine centers in 5 major cities of Kosovo with 5 GP's who were randomly selected to participate in this study during one meeting of Association of Family Doctors of Kosovo. GP's were trained in protocol of study via post or e-mail.

The project started in July 2012 and continued one year.

4.2. Study sample

The population of the study consisted of persons aged 45-70 years who required health services for any reason to any of these five ordinances, previously assigned. The process of opportunistic screening has been divided in double stratification; first-evaluation and second-physical and biomedical examination, both during consultation phase.

4.3. Study protocol

During the first step-evaluation, patients aged 45-70 with known diabetes mellitus were detected and excluded from the study. The group of remaining patients aged 45-70 were first evaluated whether any of them belonged to the persons at risk for type 2 diabetes. It was considered that at risk for type 2 diabetes were patients who showed at

least one of six risk factors for type 2 diabetes, taken from the recommendations of the American Diabetes Association (ADA) (88):

1. Positive family history for diabetes (presence of diabetes in the immediate family : parents, brothers, sisters)
2. Arterial Hypertension (>130/80)
3. High body mass index (BMI) (>25)
4. High levels of lipids in blood (LDL>1.8mmol/l ; TG>1.8mmol/l ; HDL<1.3)
5. Gestational Diabetes (in pregnant women) or the birth of a child with a weight greater than 4000gr.
6. Glycemia measured in the last 3 years with the levels between 6.1- 7.0 mmol/l.

Evaluation was done from patients self reports during the consultation, for: treated hypertension and treated lipid metabolism disorders which were defined as receiving antyhypertensive and hipolipemic medication, family history of diabetes in parents and siblings, delivering a baby with birth weight >4000gr, glycemia measured in the last 3 years with the levels between 6.1- 7.0 mmol/l and data for overweight.
Patients with at least one of six risk factors for diabetes mellitus were included in the further physical and biomedical examinations.

The capillary blood samples were collected from these patients after an overnight fasting (8-12 h) using a plasma calibrated glucometer. To reduce false-negative results and to have as convincing results as possible, we repeated the test for each patient also in the next day.
A physical examinations including anthropometric measurements of height, weight, waist and hips circumference and blood pressure were taken by the regular practice assistants.
During this time the patients were lightly dressed (the shoes were removed). Weight was measured using a calibre scales at 0.1kg and height was measured in the

stadiometer with a head in Frankfort's plan. The measurements of waist and hips were performed by thin hand meter.

1. Body weight (in kg)
2. Body height (in cm)
3. Body mass index (no decimals)
4. Waist circumference (the level of umbilicus) (in cm)
5. Hips circumference (10 cm. Under the umbilicus) (in cm)

4.4. Assessment of glucose values

Diagnosis of type 2 diabetes and Impaired Fasting Glucose were settled on the basis of measured levels of fasting blood glucose screening for two consecutive days based on the diagnostic criteria of WHO **(5).** Patients with only one value in category of IFG or undiagnosed type 2 diabetes or those that didn't responded to the second testing was removed from the further statistical analysis.
Subjects with fasting plasma glucose (FPG) ≥ 7 mmol/l were classified as diabetes mellitus. An Impaired fasting glucose (IFG) was defined: FPG ≥6.1 but <7 mmol/l. Normoglycemia was considered: FPG <6.1 mmol/l.

4.5. The interpretation of fasting blood glucose screening levels

1. If the levels of fasting blood glucose screening were between 6.1 mmol/l and 6.9 mm/l than this was Impaired Fasting Glucose or prediabetes. The patient was given advice about eating habits, physical activity and also an examination was assigned for the next year.

2. If the levels of blood glucose screening were 7.0 mmol/l and above the patient was diagnosed as Diabetes Mellitus. The patient was given advice about eating habits and

physical activity, and oral anti-diabetic medications or insulin was prescribed, besides that examinations were assigned as necessary.

4.6. Definition of obesity

BMI was calculated as weight (in kilograms) divided by the square of height (in meters). Subjects with a BMI ≥25 kg/m^2 but <30 kg/m^2 were classified as overweight, and those with a BMI ≥30 kg/m^2 were classified as obese.
Waist circumference was measured with a soft tape on standing subjects midway between the lowest rib and the iliac crest and hip circumference was measured with a soft tape on standing subject 10 cm below umbilicus. Visceral obesity was defined as a waist circumference >80 cm in women and >94 cm in men.

4.7. Definition of hypertension

Systolic blood pressure (sBP) and diastolic blood pressure (dBP) were measured twice in the sitting position after a 5-min rest, and the mean was taken in all cases. Hypertension was defined as sBP ≥140 mmHg, dBP ≥90 mmHg, or the use of antihypertensive agents.

Patients were given oral and written information letters explaining the study. Informed consent was obtained from each patient prior to their antropometric measurements.

Ethics approval for this study was obtained from the Ethics Committee of the University of Zagreb, Faculty of Medicine; Approval number: 04-76/2008-971 and from Ethics Committee of the Main Family Medicine Center-Gjilan, Kosovo; Approval number: 04-1523

4.8. Statistical methods

Data collected were analyzed using the SPSS software. Frequency distributions were analyzed and presented as percentage values in case of categorical variables. Associations between variables were analysed using the χ^2 test or Fisher's exact test where appropriate. Stepwise logistic regression analysis was performed to determine the association of independent risk factors with type 2 diabetes. Age, sex and family history of diabetes, BMI, waist and hip circumference, and hypertension were included as covariates. A *P* value <0.05 was considered statistically significant.

5. Results

The research conducted in five municipalities within one year period indicated that 18809 patients underwent a medical check-up, of whom 5334 or 28.4% belonged to the age-group of 45-70 years.(Tab.1)

Tab.1. Structure of patients age group 45-70 years in the total number of patients by municipality

Municipality	Total number of patients	From them age group 45-70 yr	
		N	%
FERIZAJ	5977	1544	25.8
PRIZREN	2336	411	17.6
PEJA	3927	1380	35.1
GJILAN	3680	1193	32.4
MITROVICA	2889	806	27.9
Total	**18809**	**5334**	**28.4**

From overall number of patients of the age-group of 45-70 years (n=5334) 815 or 15.3% were patients who had previously determined diagnosis of **Diabetes Mellitus.** (Tab.2)

Tab.2. Structure of patients with Diabetes Mellitus in the total number of patients age group 45-70 years by municipality

Municipality	Patient of age group 45-70 yr	From them with diabetes mellitus	
		N	%
FERIZAJ	1544	113	7.3
PRIZREN	411	139	33.8
PEJA	1380	279	20.2
GJILAN	1193	148	12.4
MITROVICA	806	136	16.9
Total	**5334**	**815**	**15.3**

From overall number of patients of the age-group of 45-70 years (n=5334) 1346 or 25.2% were patients with one or **more risk factors** for Diabetes Mellitus. (Tab.3 and Chart.1)

Tab. 3. Structure of patients with risk factors for Diabetes Mellitus in the total number of patients age group 45-70 years by municipality

Municipality	Patient of age group 45-70 yr	From them with risk factors	
		N	%
FERIZAJ	1544	329	21.3
PRIZREN	411	234	56.9
PEJA	1380	276	20.0
GJILAN	1193	293	24.6
MITROVICA	806	214	26.6
Total	**5334**	**1346**	**25.2**

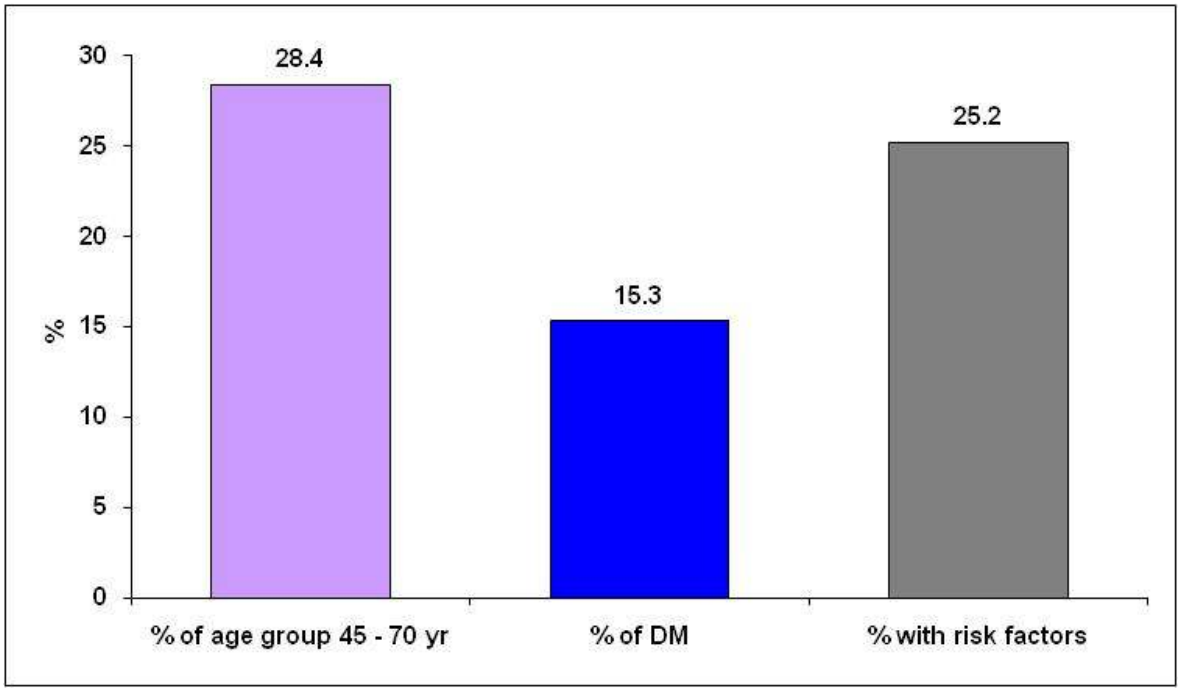

Chart 1. Structure of patients in the 5 QMF by the age group, the percentage of cases with diabetes mellitus and risk factors

Patients who have had one or more risk factors for Diabetes Mellitus were included in this research. Out of 1346 patients with one or more risk factors- 138 or 10.3% of whom have carried out **only one glycaemia test** on empty stomach and they did not come for the second test on the next day and therefore since the rules of research required to be carried out two tests on empty stomach, they were excluded from the research. The other part of patients- a number of 1208 or 89.7% were included in the research and they have carried out two glycaemia tests on empty stomach. Out of 1208 patients included in the research- 447 or 37.0% were men and 761 or 63.0% women, i.e. proportion between men and women was 1.7: 1. It happened because women have a tendency to ask more often for medical services.

As per age-groups, we have had patients more of the age-group of 65 and over. They also ask more often for medical services. (Tab.4)

Tab. 4. Patients by age group and gender

Age group		Gender				Total	
		Male		Female			
		N	%	N	%	N	%
45-49		84	18.8	141	18.5	225	18.6
50-54		80	17.9	187	24.6	267	22.1
55-59		72	16.1	136	17.9	208	17.2
60-64		70	15.7	143	18.8	213	17.6
65+		141	31.5	154	20.2	295	24.4
Total	**N**	**447**	**100.0**	**761**	**100.0**	**1208**	**100.0**
	%	**37.0**	**-**	**63.0**	**-**	**100.0**	**-**

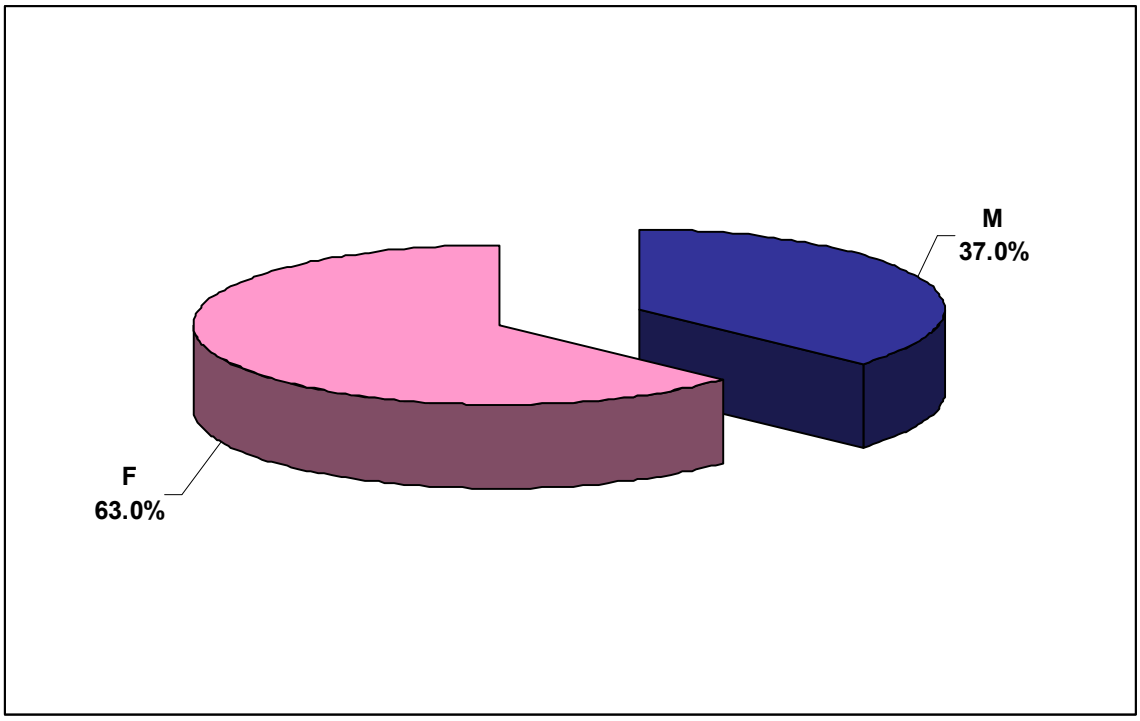

Chart 2. Structure of patients by gender

Patients were asked for six risk factors:

1. Positive family anamnesis for Diabetes, (presence of Diabetes in the first family circle: parents, brothers, sisters)
2. Treating Hypertension Arterials: TAS≥140 mmHg, TAD≥90 mmHg
3. High Body Mass Index (BMI) >25
4. Treating high level of lipids (LDL>1.8mmol/l ; TG>1.8mmol/l ; HDL<1.3)
5. Gestational Diabetes (during pregnancy) or delivery of the baby with weight over 4000gr.
6. Glycaemia measured in the last 3 years with levels ranging between 6.1mmol/- 7.0 mmol/l.

Family anamnesis for diabetes was positive in 358 cases or 29.6% of patients of similar gender structure (men 30.6% vs. women 29.0%) and without significant difference (P>0.05). (Tab.5)

Tab. 5. Patients by positive family anamnesis for Diabetes Mellitus and gender

	Gender				Total	
	Male		Female			
Family history	**N**	**%**	**N**	**%**	**N**	**%**
Yes	137	30.6	221	29.0	358	29.6
No	308	68.9	537	70.6	845	70.0
Don't know	2	0.4	3	0.4	5	0.4
Total	**447**	**100.0**	**761**	**100.0**	**1208**	**100.0**
X^2-test Yes/No	P=0.575					

At the moment of inclusion in the research, **High body weight** appeared in 937 cases or 77.6% of patients of similar gender structure who were included in this research (men 75.4% vs. women 78.8%) and without significant difference (P>0.05). (Tab.6)

Tab. 6. Patients according to the presence of large body weight and gender

	Gender				Total	
	Male		Female			
Overweight	**N**	**%**	**N**	**%**	**N**	**%**
Yes	337	75.4	600	78.8	937	77.6
No	110	24.6	160	21.0	270	22.4
Don't know	-	-	1	0.1	1	0.1
Total	**447**	**100.0**	**761**	**100.0**	**1208**	**100.0**
X^2-test Yes/No	P=0.174					

At the moment of inclusion in the research, **Hypertension arterial** appeared in 823 cases or 68.1% of patients of similar gender structure who were included in this research (men 66.4% vs. women 69.1%) and without significant difference (P>0.05). (Tab.7)

Tab. 7. Patients according to the presence of arterial hypertension and gender

Elevated blood pressure	Gender				Total	
	Male		Female			
	N	%	N	%	N	%
Yes	297	66.4	526	69.1	823	68.1
No	150	33.6	234	30.7	384	31.8
Don't know	-	-	1	0.1	1	0.1
Total	**447**	**100.0**	**761**	**100.0**	**1208**	**100.0**
X^2-test Yes/No	P=0.350					

At the moment of inclusion in the research, **high level of lipids** appeared in 465 cases or 38.5% of patients included in the research, but men were in the higher structure than women (men 42.5% vs. women 36.1%) but without significant difference (P>0.05). (Tab.8)

Tab. 8. Patients according to the presence of elevated lipids and gender

Increased lipids	Gender				Total	
	Male		Female			
	N	%	N	%	N	%
Yes	190	42.5	275	36.1	465	38.5
No	203	45.4	380	49.9	583	48.3
Don't know	54	12.1	106	13.9	160	13.2
Total	**447**	**100.0**	**761**	**100.0**	**1208**	**100.0**
X^2-test Yes/No	P=0.052					

In the last three years glycaemia on empty stomach 6.1-7.0 mmol/L appeared in 15.1% of participants in the research, 70.3% declared that they did not have it in such limit and 14.7% did not know because they did not measure it. Based on the gender, we did not get a difference of important statistical significance (P>0.05), (men 15.7 vs. women 14.7). (Tab.9)

Tab. 9. Patients who in the past three years have had blood glucose 6.1 - 7.0, by gender

In the last three years glucose was 6.1-7.0	Gender				Total	
	Male		Female			
	N	%	N	%	N	%
Yes	70	15.7	112	14.7	182	15.1
No	299	66.9	550	72.3	849	70.3
Don't know	78	17.4	99	13.0	177	14.7
Total	**447**	**100.0**	**761**	**100.0**	**1208**	**100.0**
X^2-test Yes/No	P=0.457					

Out of 761 women included in the research 120 or 15.8% declared that they have **delivered babies with large birth weight.** (Tab.10)

Tab. 10. The structure of women who had children with greater weight

Large children	Female	
	N	%
Yes	120	15.8
No	632	83.0
Don't know	9	1.2
Total	**761**	**100.0**

All of the persons included in the research **were of age 45-70**, with average age 57.5 (SD ± 7.8 years). Average age of men was 58.4 (SD ±8.1 years) whilst average age of women was 57.0 (SD ± 7.6 years). Among everage age, by gender, we have got a difference of important statistical significance (P<0.01). Average body weight of the participants in the research was 80.0 kg (SD ± 11.5 kg). Average body weight of men was 83.6 kg (SD ± 10.9 kg) whilst average body weight of women was 77.9 kg (SD ± 11.3 kg). In between average body weight, as per the gender, we have got a difference of important statistical significance (P<0.0001). Average body height of the participants in the research was 166.7 cm (SD ± 7.1 cm).). Average body height of men was 172.6 cm (SD ± 5.1 cm) whilst average body height of women was 163.2 cm (SD ± 5.6 cm). Among average body height, by gender, we have got a difference of important statistical significance (P<0.0001).

Based on the body mass index women were more obese in comparison with men, which is a difference of important statistical significance (P<0.0001). Average value of BMI in women was 29.1 (SD ±4.0), range 16-43. Average value of BMI in men was 27.8 (SD ± 3.1), range of 19 - 40.

Average value of fasting glycaemia, during the first measuring was 6.0 mmol/L (SD ± 1.9 mmol/L), range of 3.1 – 23 mmol/L without significant difference between genders, (P>0.05). Average value of fasting glycaemia during the second measuring was 5.7 mmol/L (SD ± 1.6 mmol/L), range of 3.0 – 23.9 mmol/L without significant difference, between genders (P>0.05).

Average value of **arterial systolic pressure** was 145.0 mmHg (SD ± 23.5 mmHg), range 80 – 240 mmHg without significant difference, between genders (P>0.05). Average value of arterial diastolic pressure was 89.6 mmHg (SD ± 12.1 mmHg), range of 55 – 140 mmHg without significant difference, between genders (P>0.05). (Tab.11)

Tab. 11. General characteristics of patients by gender

		Male	Female	Total	
	N	447	761	1208	**P-value**
Age	Mean ± SD	58.4 ± 8.1	57.0 ± 7.6	57.5 ± 7.8	P=0.004
	Rank	45 - 70	45 - 70	45 - 70	
Body Weight in kg.	Mean ± SD	83.6 ± 10.9	77.9 ± 11.3	80.0 ± 11.5	P<0.0001
	Rank	53 - 123	45 - 113	45 - 123	
Body height in cm.	Mean ± SD	172.6 ± 5.1	163.2 ± 5.6	166.7 ± 7.1	P<0.0001
	Rank	140 - 187	143 - 180	140 - 187	
BMI	Mean ± SD	27.8 ± 3.1	29.1 ± 4.0	28.7 ± 3.7	P<0.0001
	Rank	19 - 40	16 - 43	16 - 43	
Waist circumference in cm.	Mean ± SD	96.0 ± 11.5	94.6 ±13.7	95.2 ± 12.9	P=0.032
	Rank	63 - 132	50 - 131	50 - 132	
Hips in cm.	Mean ± SD	104.9 ± 12.1	107.2 ± 14.7	106.4 ± 13.8	P=0.0029
	Rank	67 - 143	58 - 160	58 - 160	
Fasting glucose I	Mean ± SD	6.0 ± 1.9	6.0 ± 1.9	6.0 ± 1.9	P=0.732
	Rank	3.3 - 19	3.1 - 23	3.1 - 23	
Fasting glucose II	Mean ± SD	5.8 ± 1.7	5.6 ± 1.6	5.7 ± 1.6	P=0.492
	Rank	3.2 - 15.4	3.0 - 23.9	3.0 - 23.9	
Systolic blood pressure in mmHg	Mean ± SD	144.4 ± 22.6	145.3 ± 24.0	145.0 ± 23.5	P=0.718
	Rank	85 - 230	80 - 240	80 - 240	
Diastolic blood pressure in mmHg	Mean ± SD	89.0 ± 11.9	89.9 ± 12.2	89.6 ± 12.1	P=0.473
	Rank	55 - 120	55 - 140	55 - 140	

Overall number of persons who underwent through screening (n=1208) after two tets of glycaemia was 152 or 12.6% (CI:10.8-14.6) of whom were diagnosed with Diabetes Mellitus (fasting glycaemia >7.0 mmol/l), 185 or 15.3% (CI:13.4-17.5) with Pre-diabetes (fasting glycaemia 6.1 – 6.9 mmol/l). After correction for age, crude prevalence rate of patients with diabetes in the total Kosovo population aged 45 to 70 years was 17.2%. The yield of opportunistic screening prevalence of type 2 diabetes was 1.9 %.

In 92 cases or 7.6% value of glycaemia in one measuring was pathological whilst in the other was normal and in 779 cases or 64.5% values of glycaemia were normal in two tests. In the final results, after two tests in men and women we did not get a difference of important statistical significance (P>0.05), occurrence of DM in men was 13.6% whilst in women 12.0%. Pre-diabetes occurrence in men was 14.1% whilst in women 16.0%. (Tab.12)

Tab. 12. The final result of glycemia by gender

The final result of blood glucose	Gender				Total	
	Male		Female			
	N	%	N	%	N	%
Normal	291	65.1	488	64.1	779	64.5
With one abnormal value	32	7.2	60	7.9	92	7.6
Prediabetes	63	14.1	122	16.0	185	15.3
Diabetes Mellitus	61	13.6	91	12.0	152	12.6
Total	**447**	**100.0**	**761**	**100.0**	**1208**	**100.0**
X^2-test	P=0.667					

Pre-diabetes was discovered in 168 cases or 17.3% of persons with overweight and in 17 cases or 7.1% of persons with normal weight. Diabetes mellitus was discovered in 133 cases or 13.7% of persons with overweight and in 19 cases or 7.9% of persons with normal weight. By X^2 test we have got a difference of important statistical significance (P<0.0001). Pre-diabetes occurrence and Diabetes Mellitus was much higher in the group of persons with overweight. (Tab.13)

Tab. 13. The final result of blood glucose in people with normal weight and those with overweight

The final result of blood glucose	Overweight			
	Yes		No	
	N	%	N	%
Normal	589	60.8	190	79.5
With one abnormal value	79	8.2	13	5.4
Prediabetes	168	17.3	17	7.1
Diabetes Mellitus	133	13.7	19	7.9
Total	**969**	**100.0**	**239**	**100.0**
X^2-test	P<0.0001			

Pre-diabetes was discovered in 155 cases or 18.1% of persons with visceral obesity, namely in 30 cases or 8.5% of persons without visceral obesity. Diabetes mellitus was discovered in 116 cases or 13.6% of persons with visceral obesity, namely in cases 36 or 10.2% of persons without visceral obesity. By X^2 test we have got a difference of important statistical significance (P<0.0001) Pre-diabetes occurrence and Diabetes Mellitus was much higher in the group of persons with visceral obesity. (Tab.14)

Tab. 14. The final result of blood glucose in people with visceral obesity

The final result of blood glucose	Visceral obesity			
	Yes		No	
	N	%	N	%
Normal	527	61.6	252	71.4
With one abnormal value	57	6.7	35	9.9
Prediabetes	155	18.1	30	8.5
Diabetes Mellitus	116	13.6	36	10.2
Total	**855**	**100.0**	**353**	**100.0**
X^2-test	P<0.0001			

358 persons declared that they have positive family anamnesis. Pre-diabetes was discovered in 83 cases or 23.2% of persons with positive family anamnesis and in 102 cases or 12.1% of persons with negative family anamnesis. Diabetes mellitus was discovered in 42 cases or 11.7% of persons with positive family anamnesis, namely in 109 cases or 12.9% of persons with negative family anamnesis. By X^2 test we have got a difference of important statistical significance (P<0.0001) Pre-diabetes occurrence and DM was much higher in the group of persons with positive family anamnesis. (Tab.15)

Tab. 15. The final result of blood glucose in people with a positive family history

The final result of blood glucose	Family history			
	Yes		No	
	N	%	N	%
Normal	207	57.8	568	67.2
With one abnormal value	26	7.3	66	7.8
Prediabetes	83	23.2	102	12.1
Diabetes Mellitus	42	11.7	109	12.9
Total	**358**	**100.0**	**845**	**100.0**
X^2-test	P<0.0001			

465 persons have had increased value of lipids. Pre-diabetes was discovered in 83 cases or 17.8% of persons with increased lipids, namely in 75 cases or 12.9% of persons with normal value of lipids. Diabetes mellitus was discovered in 69 cases or 14.8% of persons with increased lipids, namely in 58 cases or 9.9% of persons with normal value of lipids. By X^2 test we have got a difference of important statistical significance. (P=0.0049). Pre-diabetes occurrence and DM was much higher in the group of persons with increased lipids. (Tab.16)

Tab. 16. The final result of blood glucose in people with elevated lipids

The final result of blood glucose	An increased lipids			
	Yes		No	
	N	%	N	%
Normal	282	60.6	403	69.1
With one abnormal value	31	6.7	47	8.1
Prediabetes	83	17.8	75	12.9
Diabetes Mellitus	69	14.8	58	9.9
Total	**465**	**100.0**	**583**	**100.0**
X^2-test	P=0.0049			

There were 823 persons in the group included in screening with arterial hypertension. **Pre-diabetes was discovered in 121 cases or 14.7% of persons with arterial hypertension** and in 64 cases or 16.7% of persons had normal arteria tension. **Diabetes mellitus was discovered in 124 cases or 15.1% of persons with arterial hypertension** and in 28 cases or 7.3% of persons had normal arterial tension. By X^2 test we have got a difference of important statistical significance (P=0.0021). Pre-diabetes occurrence and DM was much higher in the group of persons with arterial hypertension. (Tab.17)

Tab. 17. The final result of blood glucose in people with arterial hypertension

The final result of blood glucose	Elevated blood pressure			
	Yes		No	
	N	%	N	%
Normal	519	63.1	259	67.4
With one abnormal value	59	7.2	33	8.6
Prediabetes	121	14.7	64	16.7
Diabetes Mellitus	124	15.1	28	7.3
Total	**823**	**100.0**	**384**	**100.0**
X^2-test	P=0.0021			

182 persons included in screening during the last three years had glycaemia 6.1 – 7.0. Pre-diabetes was discovered in 57 cases or 31.3% of persons with glycaemia 6.1 – 7.0 in the last three years and in 101 cases or 11.9% of persons who did not have glycaemia 6.1-7.0 mmol/l in the last three years. Diabetes mellitus was discovered in 28 cases or 15.4% of persons with glycaemia 6.1 – 7.0 in the last three years and in 99 cases or 11.7% of persons who did not have glycaemia 6.1-7.0 mmol/l in the last three years. DM was much higher in the group of persons who did not have glycaemia 6.1-7.0 mmol/l in the last three years. (Tab.18)

Tab. 18. The final result of blood glucose in people with glycaemia in the last three years 6.1 - 7 mmol / L

The final result of blood glucose	**In the last three years glucose was 6.1-7.0 mmol/L**			
	Yes		**No**	
	N	**%**	**N**	**%**
Normal	85	46.7	592	69.7
With one abnormal value	12	6.6	57	6.7
Prediabetes	57	31.3	101	11.9
Diabetes Mellitus	28	15.4	99	11.7
Total	**182**	**100.0**	**849**	**100.0**
X^2-test	P<0.0001			

Recurrence rate of cases with DM was higher in women who have delivered babies with large birth weight (14.2% vs. 11.7%), whereas in cases with pre-diabetes it was higher in women who did not deliver babies with large weight (12.5% vs. 16.6%) but without significant difference (P>0.05). (Tab.19)

Tab. 19. Glycemia final outcome of women who gave birth of large babies

The final result of blood glucose	Large children			
	Yes		No	
	N	%	N	%
Normal	84	70.0	398	63.0
With one abnormal value	4	3.3	55	8.7
Prediabetes	15	12.5	105	16.6
Diabetes Mellitus	17	14.2	74	11.7
Total	**120**	**100.0**	**632**	**100.0**
X^2-test	P=0.109			

All of the cases included in the research have had one or more risk factors for Diabetes Mellitus, namely 23.8% of them had one risk factor, 40.2% had two risk factors, 24.7% had three risk factors, 9.4% had four risk factors, 1.9% had five risk factors and 0.1% had six risks factors for Diabetes Mellitus with similar structure, as per the gender (Table 20a and Chart 3). Thus, 36.0% of participants in the research have had three or more risk factors (men 38.3% vs. women 34.7%) without significant difference, between genders (P>0.05).(Table 20b and Chart 4)

Tab. 20a. Patients based on the number of risk factors and gender

	Gender				Total	
	Male		Female			
Risk factors	N	%	N	%	N	%
1	110	24.6	177	23.3	287	23.8
2	166	37.1	320	42.0	486	40.2
3	124	27.7	174	22.9	298	24.7
4	40	8.9	73	9.6	113	9.4
5	7	1.6	16	2.1	23	1.9
6	-	-	1	0.1	1	0.1
Total	**447**	**100.0**	**761**	**100.0**	**1208**	**100.0**

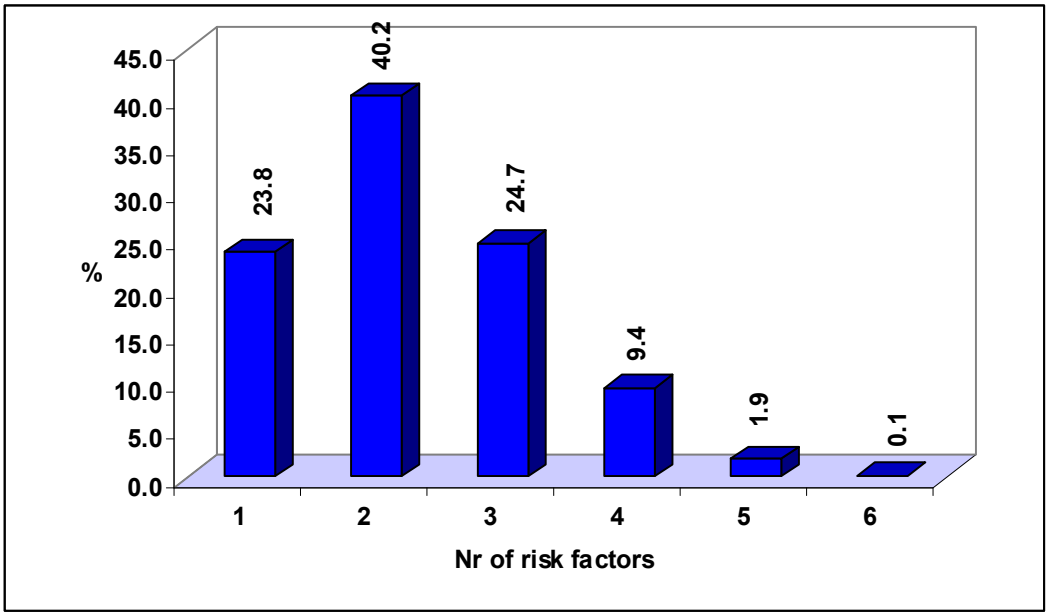

Chart 3. Structure of patients according to the number of risk factors

Tab. 20b. Patients based on the number of risk factors and gender

Risk factors	Gender				Total	
	Male		Female			
	N	%	N	%	N	%
1	110	24.6	177	23.3	287	23.8
2	166	37.1	320	42.0	486	40.2
3+	171	38.3	264	34.7	435	36.0
Total	**447**	**100.0**	**761**	**100.0**	**1208**	**100.0**
X^2-test	P=0.235					

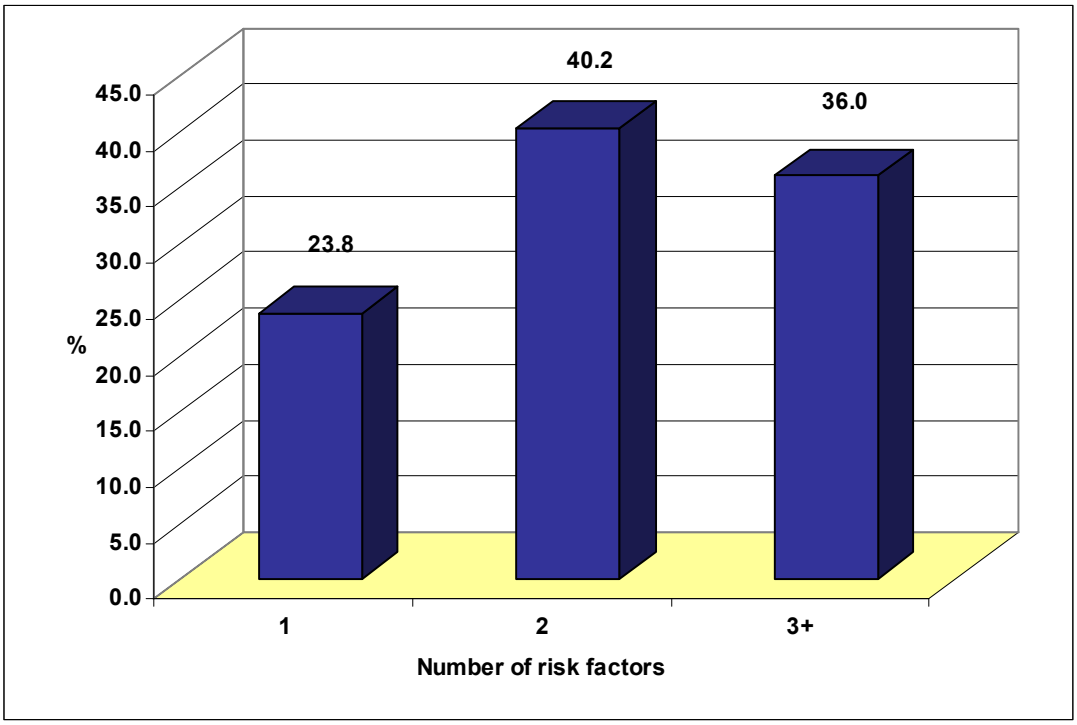

Chart 4. Structure of the patients by number of risk factors

In the cases where final result of glycaemia was normal 30.6% there were 3+ risk factors for Diabetes Mellitus, in 34.8% of cases of glycaemia with one normal measuring and the other pathological there were 3+ risk factors for Diabetes Mellitus, in 55.1% cases of Pre-diabetes there were 3+ risk factors for Diabetes Mellitus and in 41.4% of cases of Diabetes Mellitus there were 3+ risk factors for Diabetes Mellitus. (Tab.21)

Tab. 21. Glycemia final results according to the number of risk factors

The final result of blood glucose		**Nr. of risk factors**			**Total**
		1	**2**	**3+**	
Normal	N	222	319	238	779
	%	28.5	40.9	30.6	100.0
With one abnormal value	N	19	41	32	92
	%	20.7	44.6	34.8	100.0
Prediabetes	N	23	60	102	185
	%	12.4	32.4	55.1	100.0
Diabetes mellitus	N	23	66	63	152
	%	15.1	43.4	41.4	100.0
Total	**N**	**287**	**486**	**435**	**1208**
	%	**23.8**	**40.2**	**36.0**	**100.0**
X^2-test		P<0.0001			

Cases diagnosed with Pre-diabetes and Diabetes mellitus of higher structure had three or more risk factors in comparison with cases of normal values of glycaemia which is a difference of important statistical significance (P<0.0001). (Chart 5)

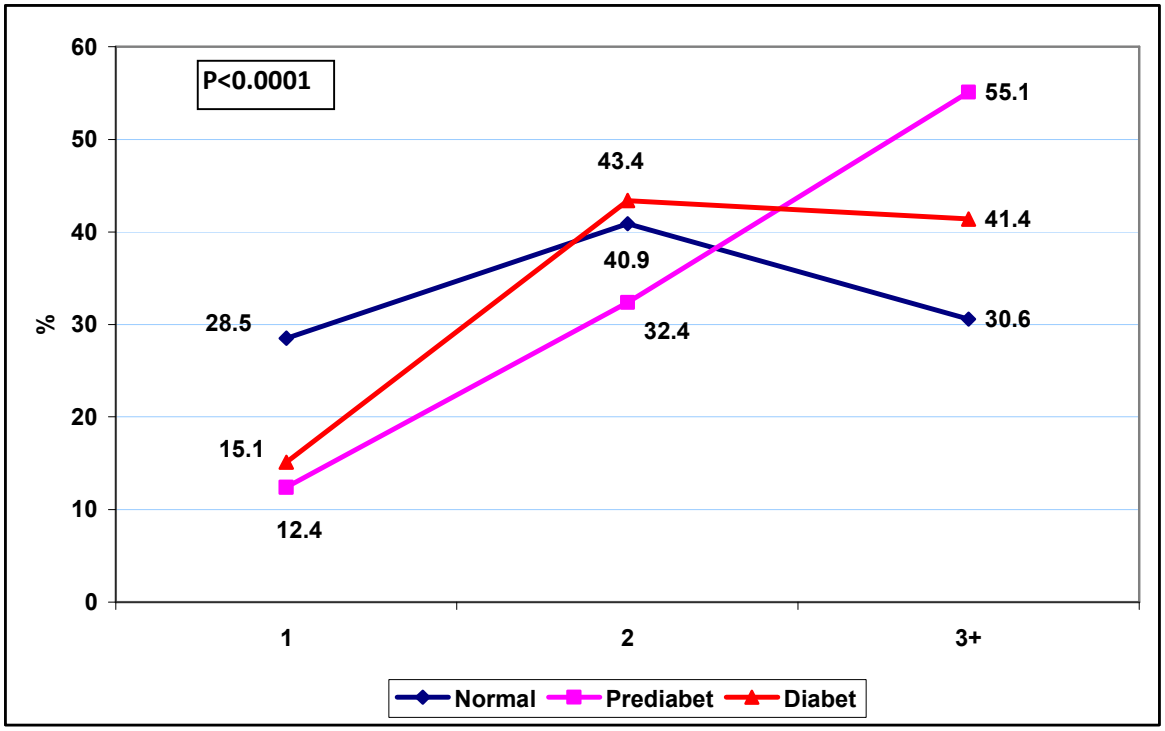

Chart 5. Structure of cases with normal hypoglycaemia, prediabetes and diabetes mellitus according to the number of risk factors

As seen (Table 22) patients with Pre-diabetes and Diabetes Mellitus of higher structure were those of age 65 and over.

Tab. 22. Glycemia final results by age group

Age group (year)	The final result of blood glucose							
	Normal		With one abnormal value		Prediabetes		Diabetes Mellitus	
	N	%	N	%	N	%	N	%
45-49	163	20.9	13	14.1	24	13.0	25	16.4
50-54	185	23.7	20	21.7	35	18.9	27	17.8
55-59	134	17.2	18	19.6	28	15.1	28	18.4
60-64	130	16.7	20	21.7	40	21.6	23	15.1
65+	167	21.4	21	22.8	58	31.4	49	32.2
Total	**779**	**100.0**	**92**	**100.0**	**185**	**100.0**	**152**	**100.0**

56.8 (SD± 7.7 years) was average age of patients whose final results of glycaemia, after two tests, was normal, whereas of those who were diagnosed with Pre-diabetes was 59.3 (SD± 7.8 years) and of those diagnosed with Diabetes Mellitus was 58.9 (SD ± 8.2 years). By Kruskal Wallis test we have got a difference of important statistical significance within average age based on final results of glycaemia (Normal vs. Pre-diabetes $P<0.001$; Normal vs. Diabetes Mellitus $P<0.05$). (Tab.23)

Tab. 23. Age parameters of patients according to the final results of glycemia

Age (Year)	The final result of blood glucose			
	Normal	**With one abnormal value**	**Prediabetes**	**Diabetes Mellitus**
N	779	92	185	152
Mean	56.8	58.1	59.3	58.9
SD	7.7	7.2	7.8	8.2
Min	45	45	45	45
Max	70	70	70	70
Kruskal Wallis test	P<0.0001			
Dunn's Multiple Comparasion test Normal vs. Prediabet P<0.001 Normal vs. Diabet Mellitus P<0.05				

Average age of participants was 57.5(SD 7.8). By Kruskal Wallis test a significant variation in the prevalence of type 2 diabetes, IFG, and normal glicemia was observed within average age: 58.9(SD 8.2), vs 59.3(SD 7.8), vs 56.8(SD 7.8); P=0.0001.

Tab.24. Multivariate stepwise logistic regression analysis for predictors of type 2 diabetes. Cumulative risks as prediction for type 2 diabetes .

Risks	OR estimates (95%CI)	P value
Single overweight	1.88 (1.39- 2.55)	<0.0001
Single family history	1.61 (1.23- 2.10)	=0.0006
Single hypertension	2.01 (1.43- 2.82)	<0.0001
Single hyperlipidemia	1.46 (1.13-1.89)	=0.0037
Hypertension + Overweight	1.90 (1.41-2.57)	<0.0001
Overweight + Family history	1.99 (1.49-2.66)	<0.0001
Hypertension + Overweight + Family history	2.10 (1.53-2.81)	<0.0001

OR:Odds Ratio.95% CI:Confidence interval

Multivariate logistic regression analysis showed that hypertension was the best predictor of undiagnosed type 2 diabetes: OR 2.01(CI; 1.43- 2.82), P<0.0001. Overweight had significant prediction for undiagnosed type 2 diabetes: OR 1.88(CI; 1.39- 2.55), P<0.0001. Family history of diabetes had also significant prediction for undiagnosed type 2 diabetes: OR 1.61(CI; 1.23- 2.10), P<0.0006. Dyslipidemia was poorer predictor of undiagnosed type 2 diabetes: OR 1.46(CI; 1.13-1.89), P<0.0037

Antihypertensive treatment was associated with a two fold increased risk of diabetes. After adjustment all significant risks the multivariate stepwise logistic regression shows, the strongest prediction for type 2 diabetes was risks in fold: hypertension, overweight and family history of diabetes. Those, patients were 2.1 more likely to have diabetes.

6. Discussion

To our knowledge this study is the first one to report screening of patients for type 2 diabetes in Kosovo.

The research conducted in five municipalities within one year period indicated that 18809 patients underwent a medical check-up, of which 5334 or 28.4% belonged to the age-group of 45-70 years.

From overall number of patients of the age-group of 45-70 years, 815 or 15.3% were patients who had previously determined diagnosis of type 2 diabetes. 1208 patients were patients with one or more risk factors for type 2 diabetes and they were screened for type 2 diabetes in this study.

The prevalence of diabetes mellitus in the population included in the study was 12.6% with 95% CI prevalence in the entire population was 10.8% to 14.6% and IFG prevalence of the population involved in the study was 15.3% with 95% CI prevalence in the entire population was 13.4% to 17.5%. After correction for age, crude prevalence rate of patients with diabetes in the total Kosovo population aged 45 to 70 years was 17.2%. The yield of opportunistic screening prevalence of T2D was 1.9 %. In 7.6% value of glycaemia in one measuring was pathological whilst in the other was normal.

Average age of participants was 57.5(SD 7.8). By Kruskal Wallis test a significant variation in the prevalence of type 2 diabetes, IFG, and normal glicemia was observed within average age: 58.9(SD 8.2), vs 59.3(SD 7.8), vs 56.8(SD 7.8); P=0.0001.

No significant variation in the prevalence of type 2 diabetes was observed between men's and women's (P>0.05), prevalence of type 2 diabetes in men was 13.6% vs 12.0% in women and the prevalence of IFG in men was 14.1% vs 16.0% in women.

Women had a lower age (57.0 ± 7.6 vs 58.4 ± 8.1 years; $P < 0.004$) and a lower body weight in kg.(77.9 ± 11.3 vs 83.6 ± 10.9 kg; $P = 0.0001$), as well as a smaller waist circumference (94.6 ± 13.7 vs 96.0 ± 11.5 cm; $P < 0.032$) than men. Abnormal waist circumference was more often found in women than men (50.4 vs 20.3%; $P < 0.001$) and the prevalence rate of overweight (body mass index >25 kg/m^2) was higher in women than men (54.0 vs 31.2%; $P = 0.0001$).

In this regard, two thirds of screened patients had at least two risk factors for type 2 diabetes. Arterial hypertension was diagnosed in majority of screened patients as opposed to one third of screened patients who also had abnormal lipid levels.

Presence of arterial hypertension, abnormal lipid profile and being overweight were olso common amongst those found to have pre-diabetes or type 2 diabetes.

It is interesting to note that patients with prediabetes had a higher number risk factors compared to patients who already had developed type 2 diabetes. Therefore, suggesting that an early screening process could potentially allow more room for clinicians to address type 2 diabetes risk factors.

Multivariate logistic regression analysis showed that hypertension was the best predictor of undiagnosed type 2 diabetes: OR 2.01(CI; 1.43- 2.82), P<0.0001. Overweight had significant prediction for undiagnosed type 2 diabetes: OR 1.88(CI; 1.39- 2.55), P<0.0001. Family history of diabetes had also significant prediction for undiagnosed type 2 diabetes: OR 1.61(CI; 1.23- 2.10), P<0.0006. Dyslipidemia was poorer predictor of undiagnosed type 2 diabetes: OR 1.46(CI; 1.13-1.89), P<0.0037

Hypertension commonly co-exists with diabetes as part of metabolic syndrome and it commonly begins in the preclinical period of diabetes. Antihypertensive treatment was associated with a two to three – fold increased risk of diabetes

It is known that obesity and overweight increases the development of type 2 diabetes and that three quarters overweight adult people are metabolically and phenotype unhealthy obesity (beta-cell dysfunction, insulin resistance, hyperglycemia) and carry risk for type 2 diabetes. Also, it is important to note that metabolically healthy obese adults show a substantially increased risk of developing type 2 diabetes compared with metabolically healthy normal-weight adults. There was a non-significant positive association with hiperlipidemia. We can contemplate that prescription of hypolipemic drugs or dietary and physical activity are important protective factors against type 2 diabetes development (182, 184, 185).

After adjustment all significant risks the multivariate stepwise logistic regression shows, the strongest prediction for type 2 diabetes was risks in fold: hypertension, overweight and family history of diabetes. Those, patients were 2.1 more likely to have diabetes.

Type 2 diabetes certainly meets many of the screening criteria (163). There is evidence that screening for diabetes has an overall benefit with no harm to patients (147). Many international organizations (164,165) have produced guidelines on screening for type 2 diabetes with information on screening tests and populations, yet none have made major recommendations regarding the strategies to approach screening and the method of invitation.

In this regard, due to undetected glucose abnormalities, at time of diagnosis there can be a significant percentage of diabetes complications already present. Evidence suggest up to 30% of patients have complications at time of diagnosis (172-175). This leads to a significant burden not only for patients but also the health care system in general. Clinicians could more adequately utilize other therapies such as antihypertensives, antihyperlipidaemics and antiplatelet therapies. The ADDITION study demonstrated that when compared to routine care, an intervention to promote target-driven, intensive management of patients with type 2 diabetes detected by screening was associated with modest but significant differences in prescribed treatment and levels of cardiovascular risk factors at five years (176).

Screening for a condition is justified only if there is a net benefit in early detection and treatment of the condition as compared to its natural clinical presentation. The ADDITION study showed declined risks for cardiovascular disease in 5 and 10- years following diagnosis, in the group of patients with diabetes detected by screening (177).

The results reported in this study suggest that a significant number of patients can be detected at prediabetes stage by utilizing a ‘pragmatic’ approach of screening.

This would potentially result in prevention of diabetes development in many of the patients screened, prevention of diabetes complications, improved quality of life and reduction of health related costs (54). Therefore, results of this study indicate that such an approach of screening should be a systematic and continuous process in countries

like Kosovo where there may be a lack of means to apply standard type 2 diabetes opportunistic screening processes to the general population. Tools utilized during the screening process are convenient to use in family practice setting and the screening methods used in this study were adopted to Kosovo conditions and health care situation. As such, it has considerable differences compared to Western European standards and those of other developed countries around the world.

Family medicine centers, where the 'pragmatic' opportunistic screening for type 2 diabetes was conducted in this project, represent a suitable primary care setting for type 2 diabetes screening to take place. However, key challenges reported especially in the developing countries should be considered. Countries in transition such as Kosovo, are often faced with overbooking and frequent visits by patients which in turn have the potential to reduce the available time for performing opportunistic screening for type 2 diabetes (178). Furthermore, deficiencies in patient documentation and database management are also obstacles to implementing opportunistic type 2 diabetes screening in transition countries. GPs need a simple process of case finding that should be performed easily, systematically and continuously, without overprevention procedures. It should be performed in country –specific context, using existing health resources, without consuming too much time and additionally burden of consultaton (167-170).

Oportunistic, stepwise approach of screening a patient, using a non-invasive risk stratification tool followed by a definite blood test seems the most cost-effective method of screening for type 2 diabetes and those at high risk (171).

The main strength of the study was the setting. High-risk patients were identified during a regular consultation, in the daily routine practice in the local family practice by their own family practitioner. Capillary blood samples were taken by the family practitioner, without any further support (e.g., from trial nurses). Although patients had to return in a fasting state for the capillary glucose measurements, they were highly willing to do so.

Several diabetes screening studies have been described in the literature. Smith et al**.** (187) undertook an opportunistic diabetes screening study performed in family practice using a questionnaire presented to patients who were waiting to see their doctor. Their

participation rate was also high (93%), and 43% of patients had at least 2 risk factors. If performed continuously or repeated regularly, such an approach might provide more complete and up-to-date information on a patient's risk status in the EMR, improving the identification of high-risk patients for screening purposes.

Greaves et al. (188) showed that identifying patients with type 2 diabetes and IFG using data stored in family practice databases was feasible but instead of using an opportunistic approach, they invited high-risk patients (those aged >50 years and with a body mass index ≥27 kg/m2) to screening clinics run by trained practice nurses. The response rate was 61%. Nevertheless, the simple screening system they describe would promote efficient use of scarce primary health care resources, especially when set up as part of a broader screening program to reduce cardiovascular disease.

In a cross sectional study in a local family practice, Lawrence et al. (98) showed that screening of invited patients whose sole risk factor for diabetes is age older than 45 years has a low yield. In this group, they found a diabetes prevalence of just 0.2%. Among individuals with 1 or more other risk factors, the figure increased to 2.8%.

In 2007, a population-based screening program for type 2 diabetes was performed in the Netherlands**.** (84) Although the increase in diabetes prevalence achieved with the program (from 6.1% to 7.0% among people aged 50 to 70 years) was good, the response to an invitation to glucose testing was 31% and the yield only 1%. The authors concluded that opportunistic screening might be more appropriate.

Other studies concerning screening for type 2 diabetes mainly used questionnaires or risk scores to identify at-risk patients, instead of data already present in the EMR**.** (103, 189, 190)

We compare the results of our study with other studies performed recently in Central Europe, despite some differences in the structure of the population and the screening method used. Detection rate of diabetes and pre-diabetes was higher than reported by previous studies. Namely, the prevalence rate of diabetes in Hungarian was 7.47% and the prevalence of IFG was 4.39% (179), in Slovakia was 7.0% and the prevalence rate of type 2 diabetes in Croatia was 6.1% (180,181). The prevalence rate of IFG in our study was much higher (4.39%) than that (11.3%) reported in Croatia (181).

In EUROASPIRE IV, a cross-sectional survey of patients aged 18–80 years with coronary artery disease in 24 European countries, 29% had undetected diabetes (182).
This study has a number of limitations. These includes limited number of patients who went through the screening, as opposed to the total number of population at risk who could benefit from such a screening.
A limiting factor was that the visits were not set in advance and electronic medical records have not been implemented as yet. Medical files avaliable, in some cases were incomplete and not maintained properly so not all risk factors were included at that time. We had to ask patients about their risk factors to confirm their status, therefore some of the information obtained from patients could have been subjected to recall bias hence suggesting a more cautious interpretation of the results.
A possible limitation was that we used the capillary glucose test rather than the oral glucose tolerance test. Although oral glucose tolerance test with fasting and 2-hour glucose values has been widely used in the clinical practice for detecting glucose intolerance in asymptomatic subjects, an epidemiological survey for screening in primary care should be based on fasting blood glucose values only, as it is easier and faster to perform, more convenient and acceptable to patients, and less expensive**.** (82, 186)
Nevertheless, given that this is the first study of this kind conducted in Kosovo, we hope that it will raise the awaraness of health policymakers, health professionals and patients in regards to screening for type 2 diabetes and identifying suitable methods that would suit conditions in Kosovo. Further, this study may also provide more insight to countries around the world going through similar transition periods and facing financial and infrastrucural challenges to implementing standard oppurtunistic type 2 diabetes screening.

7.Conclusion

1. This study is the first one to report screening of patients for type 2 diabetes in Kosovo.
2. The 'pragmatic' opportunistic screening process was suitable for implementation and could improve early detection of diabetes in developing countries like Kosovo.
815 or 15.3% were patients who had previously determined diagnosis of type 2 diabetes.
3. This opportunistic screening method for type 2 diabetes in patients of the age-group 45-70 years, resulted in detection of prevalence of previously known type 2 diabetes 15.3%
4. The main findings in this research is detection of unknown number of patients with type 2 diabetes and IFG. The prevalence of diabetes mellitus in the study was 12.6% (CI:10.8-14.6) and IFG prevalence of the population involved in the study was 15.3% (CI:13.4- 17.5).
5. After correction for age, crude prevalence rate of patients with diabetes in the total Kosovo population aged 45 to 70 years was 17.2%. The yield of opportunistic screening prevalence of type 2 diabetes was 1.9 %.
6. Detection rate of diabetes and pre-diabetes was higher than reported by previous studies.
7. Among various risks in univariate analysis hypertension was the best single predictor for unknown diabetes type 2
8. After an adjustment of all significant risks in the multivariate stepwise logistic regression, the strongest prediction for undetected diabetes type 2 was risks in fold: hypertension, overweight and family history of diabetes mellitus. Those patients were 2.1 times more likely to have diabetes.
9. Data's on the number of previously known diabetes and the data's on undiagnosed type 2 diabetes have been lacking until our research in Kosovo. We hope that this research will raise awareness of the decision-making instances so; in a near future we can undertake a survey at a much larger scale, at the national level.

8. Sazetak na hrvatskom jeziku

Uvod: Probir za secernu bolest tipa 2 u obiteljskoj medicini u zemljama u razvoju ostaje i dalje izazov. Zbog toga se istrazuje najprakticnija metoda u svakodnevnom radu.

Ciljevi: Istraziti prevalenciju neotkrivene secerne bolesti i ostecene glukoze nataste u ambulantama obiteljske medicine na Kosovu i testirati najoptimalniji model oportunistickog probira za otkrivanje ovih pacijenata

Mjesto: Pet ordinacija obiteljske medicine na Kosovu

Metode: Istrazivali smo metodu oportunistickog probira secerne bolesti u ordinaciji obiteljske medicine. Probirom su obuhvaceni svi pacijenti u dobi 45-70 godina sa najmanje jednim poznatim cimbenikom rizika koji su iz bilo kojeg razloga posjetili svog lijecnika.

Rezultati: Probirom je obuhvaceno 1208 pacijenata. Otkrivena su 152(12.6%) pacijenta sa secernom bolesti te 185(15.3%) sa predijabetesom
Statisticki znacajni rizicni faktori su ($p<0.05$); prekomjerna tjelesna tezina (77.6%), hipertenzija (68.1%) I hiperlipidemija. Vecina pacijenata (76.2%) je imala dva faktora rizika, dok je 36% imalo tri faktora rizika.

Zakljucak: Ova studija je pokazala da je metoda oportunistickog probira prikladna za implementaciju u ordinacije obiteljske medicine u zemljama u razvoju, poput Kosova. Otkriven je znacajan broj pacijenata sa secernom bolescu i predijabetesom koji su takoder imali prekomjernu tjelesnu tezinu, hipertenziju i hiperlipidemiju.

9. Abstract

Background. Screening for type 2 diabetes mellitus in primary care in developing contries remains a challenge, therefore pragmatic models of opportunistic screening should be explored.

Objective: To determine the prevalence of new cases of diabetes and impaired fasting glucose in general practices of Kosovo and investigate the feasibility and performance of a pragmatic system for identifying patients with these two conditions.

Settings: Five general practices in Kosovo.

Methods: The study utilized an opportunistic screening programme for type 2 diabetes detectection in primary care. All patients with at least one risk for undiagnosed type 2 diabetes, aged 45-70, who attended to general practices for any reason were screened. Fasting capillary blood glucose was measured on two independent days. Additionally, anthropometric measurements were also performed

Results: A total of 1208 patients were screened for type 2 diabetes. There were 152 (12.6%) undiagnosed type 2 diabetes and 185 (15.3%) prediabetes patients
Significant prediction factors ($p<0.05$) were; overweight (77.6%), hypertension (68.1%) and hyperlipidemia (38.5%). The majority of patients (76.2%) had two risk factors and 36% had three risk factors

Conclusions: The 'pragmatic' opportunistic screening process in this study was suitable for implementation in transition countries like Kosovo and resulted in detection of significant number of patients with pre-diabetes and type 2 diabetes who were also overweight, had hypertension and hyperlipidaemia

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- At the conclusion of the PhD thesis, started in 2008 University of Zagreb, Faculty of Medicine
- Completed the Postgraduate Course of the 1st category in Diabetology and Management in Diabetology, Vuk Vrhovac- University Clinic for Diabetes, Endocrinology and Metabolic Diseases, University of Zagreb, Faculty of Medicine, held in Academic year 2006/2007
- Master of Medical Sciences, School of Medicine, University of Prishtina September 2007
- Specialization of Family Medicine, School of Medicine, University of Prishtina, November 2002
- Doctor of Medicine, School of Medicine, University of Prishtina, July 1998

Work experience (starting from the most recent):

- Chef in Primary Care Diabetic Centre, Gjilan from May 2010
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- Doctor of Medicine in Main Family Medicine Centre, Gjilan from July 1999

Lists of scientific papers:

- Carkaxhiu L, Huseyin K, Berisha M, Botica MV. Problem of misuse and lack of national strategy in Kosovo. Cent Eur J Public Health 2011; 19 (2): 63-66

- Vrca Botica M, Ožvačić Adžić Z, Zelic Baričević I, Katić Milošević I, Diminić Lisica I, **Carkaxhiu L**. What When and how to measure the assesment of quality of care for chronic disease in family practice. Applying indicators of quality for diabetes mellitus. Med Jad. 2013;43:97-101.

- Zelić Baričević I, Vrca Botica M, **Carkaxhiu L.** New requirments of medical documentation in the area of chronic patients care in family medicine. Med Jad. 2014; 44:39-43.

- Vrca Botica M, **Carcaxhiu L,** Kern J, Khulien Th, I Botica, Gavran L, Zelić I, D Iliev, Haralović D. A Vrca. Missing risks in opportunistic screening for type 2 diabetes. CroDiabGP study. Med Glas (Zenica) 2017; 14(1):55-60

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Active participations at congresses:

- **Linda Carkaxhiu-Huseyin**. "Social correlates of drug misusing among Kosovar adolescents: A population-based cross-sectional study" poster, author in Wonca, Vienna 2012
- **Linda Carkaxhiu-Huseyin.** "Social correlates of alcohol consuming among Kosovar adolescents: A population-based cross-sectional study" poster, author in Wonca, Warsaw 2011
- **Linda Carkaxhiu-Huseyin.** "The Knowledge, Attitudes and Practices of Students from Secondary Schools in Gjilan regarding Smoking" poster, author in Wonca, Istambul 2008
- Vrca Botica M, **Carkaxhiu L**, Iliev D. Identifyng risk paitients for blood testing to diabetes mellitus in family practice via opportunistic screening. CroDiabGP study.Who are we and what is our future? WONCA Europe. 3th Conference of the Association of General Practice/ Family Medicine of South East Europe. U: Association of Family Physicians of FBiH. Sarajevo, Septembar 2014.