

Evidence in Primary Prevention of Type 2 Diabetes Mellitus—What It Means for Primary Prevention of Type 2 Diabetes Mellitus Epidemic in Papua New Guinea

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Abstract

Type 2 diabetes is in epidemic proportion in Papua New Guinea. Although many people are at high-risk of developing diabetes, there is no diabetes prevention policy and services in Papua New Guinea to address this problem. A literature search was carried out to assess the available evidence in the primary prevention of type 2 diabetes mellitus among the population with prediabetes. The result shows that the primary preventative studies conducted on lifestyle modification and the use of metformin in prediabetes patients reduced overt type 2 diabetes mellitus. The application of the evidence in the prevention of the type 2 diabetes epidemic in Papua New Guinea, driven by a policy is feasible to address the diabetes epidemic.

Keywords

Primary Prevention, Prevention Trials, Type 2 Diabetes Mellitus, Prediabetes

1. Introduction

Diabetes is a blood sugar disorder that is characterized by either the lack of or resistance in the function of insulin resulting in persistent high blood sugar which, if left untreated, will inevitably lead to stroke, blindness, coronary artery disease, nerve problems, blood vessel diseases and kidney failure [1]. It also lowers the body's immunity and renders it susceptible to all kinds of infections and diseases.

Diabetes is a global epidemic causing devastating ill effects on the lives of millions of people worldwide. There were 171 million people with diabetes in 2000

and it is projected to rise to 360 million by 2030. Over half of these people live in developing countries [2].

Papua New Guinea (PNG), a country of 10 million people in the Pacific Region is experiencing a rise in type 2 diabetes mellitus (T2DM). It is among the top ten causes of morbidity and mortality according to a recent National Department of Health Report (NDOH) [3].

A World Health Organization (WHO) sponsored survey in 2004 showed that 14% of the working class in Port Moresby City were identified as having impaired fasting glucose (IFG) [4]. A recent survey in 2019, among both the rural and urban population showed the prevalence of prediabetes at 19% [5], suggesting that a large population with potential to develop diabetes remain undetected in their communities. Meanwhile, the diabetes admissions into the Port Moresby General Hospital medical wards have doubled over the last decade [6]. This suggests that the need for diabetes primary prevention is ever more pressing than it was before.

A search of literature on the primary prevention of type 2 diabetes mellitus using lifestyle modification (LSM) and drugs among the impaired fasting glucose and the impaired glucose tolerance (prediabetes) over the last two decades has shown significant reductions in development of overt type 2 diabetes worldwide.

This review reflects on these randomized clinical trials and proposes adoption of these strategies into the PNG healthcare system. Although the PNG healthcare system does not have a preventative policy on the rising diabetes epidemic, the adoption of LSM and metformin into the existing healthcare system are simple and cost-effective and can reduce the rising incidences of overt type 2 diabetes mellitus.

2. Content

There is no evidence on the benefits and the risks of early screening of the asymptomatic population for diabetes [7] and arguments still exist today among the experts on whether to screen for diabetes [8] [9]. However, it is generally accepted that early screening of the high-risk groups will lead to the reduction of diabetes and the prevention of the dreaded complications.

2.1. Methodology

A literature search of seven core databases (Cochrane, PubMed, CINAHL-PLUS, TRIP & SCOPUS, Embase and clinical Trials.gov) and two related databases (Google, NICE) were conducted on the 4th - 5th of November 2021. A combination of search and Medical Subject Heading (MeSH), using the “Key words” of the study documenting the use of “high risk”, “prediabetes” (IFG & IGT) and “primary prevention” of “type 2 diabetes mellitus” were used to search for studies published between January 1990 to January 2021.

A total of 24,500 papers were identified. Filtering of duplicates resulted in

10,234 papers addressed primary prevention of T2DM using both pharmacological and non-pharmacological interventions. 10,220 papers did not meet the inclusion criteria (**Table 1**) and were excluded. Fourteen papers met the criteria and were of moderate to high strength when assessed with CASP tool for randomized controlled trials [10]. Five were in the non-pharmacological category with a sample size of 5275 and seven were in the pharmacological category with sample size of 11,301 (**Figure 1**).

2.2. Pre-Diabetes—High Risk Group

Pre-diabetes is an intermediate state of glycemic disturbances between normoglycemia and diabetes. The WHO regards pre-diabetes as a state of ‘intermediate hyperglycemia’ which is in a high-risk category that can progress into overt diabetes [11]. The WHO criteria for diagnosis of diabetes and prediabetes (impaired fasting glucose and impaired glucose tolerance test) are: Fasting plasma glucose (FPG) is ≥ 7 mmol/L, 2 hr-postprandial glucose (PG) ≥ 11.1 mmol/L for diabetes and the impaired fasting glucose (IFG) $\geq 6.1 - 6.9$ mmol/L and the impaired glucose tolerance (IGT) after 75 g glucose sachet ≥ 7.8 mmol/L < 11.1 mmol/L respectively [11]. The IFG and the IGT are collectively regarded as the pre-diabetes state. This state has been studied by all the preventive trials from which the current pool of evidence is derived.

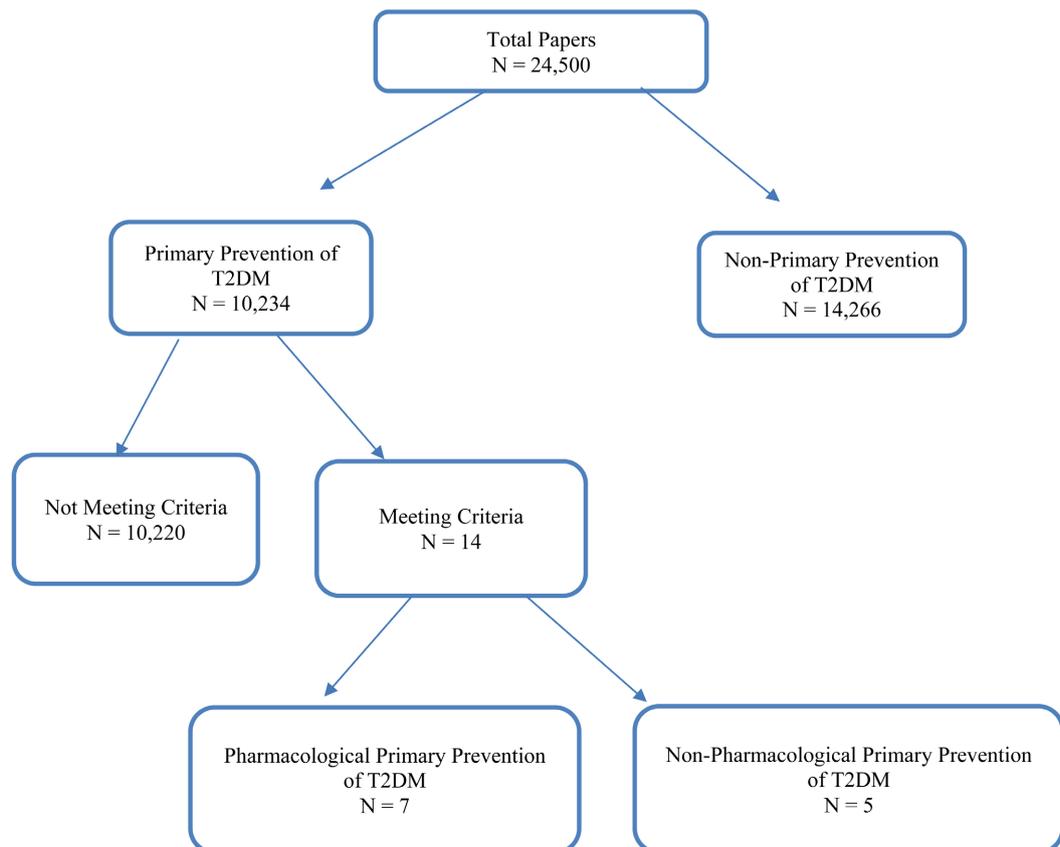


Figure 1. Results of literature search on the primary prevention of type 2 diabetes mellitus.

Table 1. Inclusion/exclusion criteria.

Inclusion Criteria
<ul style="list-style-type: none"> • Only Randomized controlled trials (RCT) • RCTs including primary prevention of overt type 2 diabetes mellitus from prediabetes states • RCTs that include drug (pharmacological) in primary prevention of type 2 diabetes • RCTs that include lifestyle changes (non-pharmacological) primary of type 2 diabetes prevention • Articles in English only • Moderate to high strength according to CASP tool for RCT
Exclusion Criteria
<ul style="list-style-type: none"> • Secondary prevention of type 2 diabetes mellitus • Non inferiority trials • Non RCT • Non-human trials • Low strength according to CASP tool for RCT

2.3. Non-Pharmacological Primary Prevention (Intensive Lifestyle Modifications)

Several preventative studies done in the last two decades have shown that T2DM is a preventable disease (**Table 2**). The earliest of these trials was done by Sartor et.al, in 1980. They studied 267 people with IGT in four arms namely, diet, placebo, tolbutamide or diet plus tolbutamide. They showed that those in the diet plus tolbutamide arm had lower progression to diabetes compared to the other arms [12].

This triggered a flurry of studies that followed suit including the Malmo Feasibility Study (non-randomized) published in 1998, which showed that LSM not only reduced the onset of diabetes among the IGT but also remitted early diabetes and improved the metabolic profiles of these two groups preventing cardiovascular complications [13].

The Chinese Da Qing study published in 1997 was the largest prevention trial that studied 577 cohorts with IGT. Subjects were randomized into four groups: dieting and exercise, dieting alone, exercise alone and the control groups. The dietary arm received the luxury of customized food variations with personalized counselling and educational materials. The exercise group was asked to exercise according to individual quantified needs. The combined group was given both interventions. The diet alone arm of the study did not show any significant reduction in diabetes incidence, but the combined diet and exercise arm reduced diabetes by 31% compared with the control [14].

The Finnish Diabetes Prevention Program (FDPP) Study published in 2001 was another large randomized controlled study that followed the Da Qing study.

Table 2. Summary of lifestyle treatment RCT in the prevention of T2DM among the IFG.

Study	Publication	Intervention	Cumulative Incidence %	RRR in the intervention arm (%)
Chinese Da Qing Study	1997	Exercise 141	41.8	38
		Dieting 130	43.8	
		Exercise+ Dieting 126	46	
		Control 133	67.7	
Finnish DPPP	2001	Exercise+ Dieting 265	10	58
		Control 257	22.95	
American DPPP	2002	Exercise+ Dieting 1079	14.7	58
		Metformin 1073	21.7	
		Control 1082	28.9	
Indian DPPP	2006	Exercise+ Dieting 133	39.3	29
		Metformin 133	40.5	
		Lifestyle + Metformin 129	39.5	
		Control 136	55	
Japanese Prevention Trial	2004	Exercise+ Dieting 103	3	67
		Control 110	9.3	

It randomized 522 individuals with IGT into two arms, the intensive LSM plus dieting arm and the control arm with standard care. The cohorts in the interventional arm received individualized counselling, circuit training program and regular follow up with dieting. This trial showed that intervention reduced diabetes by 58% compared with the control group [15].

The findings of diabetes prevention with intensive lifestyle modifications were further supported by a bigger trial called the American Diabetes Prevention Program (ADPP) published in 2002. This study recruited 3234 subjects with prediabetes and divided them into 3 arms (lifestyle intervention + placebo, lifestyle intervention + metformin and Lifestyle intervention alone).

In the intensive lifestyle arm, the cohorts were subjected to dieting, exercise (150 minutes/week with approximate weight loss of 7% - 10%) and behavioral modifications on a one-one basis with monthly reinforcement classes for individuals. It showed a reduction of diabetes by 58% in the intensive LSM arm with the effect more pronounced in the lean elderly cohorts [16].

The Indian Diabetes Prevention Program (IDPP) was another study that attempted to show that the application of the intensive LSM and pharmacotherapy in reducing diabetes were consistent across geography and ethnicities with different physical attributes. It studied 531 young lean Indians with IGT and followed for 30 months. The result showed that LSM reduced diabetes by 28.5% and metformin by 26.4% but there was no cumulative benefit [17].

Collectively, these studies showed that intensive LSM interventions can reduce and prevent the high-risk individuals from developing overt T2DM. In addition, they show that lifestyle intervention is effective across all multiracial and ethnic populations that spans different geographies.

2.4. Pharmacological Interventions in Primary Prevention

Several pharmacological agents have also been studied in the prevention trials of T2DM (**Table 3**). Sartor *et al.* mentioned earlier, have shown that tolbutamide, a sulphonylureas class of oral hypoglycemic agent can be used with lifestyle intervention to reduce diabetes. They showed that none of the patients on tolbutamide arm progressed to overt diabetes compared with 29% in the control group.

The more robust ADPP showed that metformin, a biguanide oral hypoglycemic agent reduced overt T2DM in cohorts with IGT by 31%. The effect was more pronounced in younger cohorts with obesity [16]. This was supported by the IDPP study which reported a reduction of 26% in the metformin treated arm compared to the placebo [17].

Acarbose, a glucosidase inhibitor of the small intestine was also shown in the STOP NIDDM Trial (n = 506) to reduce T2DM among the 221 cohorts with IGT by 32% compared to 285 cohorts who received placebo. A relative reduction of 10% compared to the controls [18].

The FDPP and the ADPP have shown that reduction of obesity as a risk factor for diabetes was associated with reduced incidence of T2DM among the high-risk group [15] [16]. This was followed up by the XENDOS study which recruited normal glucose tolerance (NGT) and IGT (N = 3305) obese individuals and randomized to lifestyle plus orlistat a weight reducing agent or placebo. There was a 37% reduction in diabetes progression after 5 years, predominantly in the IGT group [19].

Table 3. A Summary of RCT of pharmacotherapy in the prevention of T2DM among the IFG.

Study	Publication	Intervention	Cumulative Incidences (%)	RRR (%)
US DPP	2002	Metformin 1073	21.7	31
		Control 1082	28.9	
Indian DPP	2006	Metformin 133	40.5	26
		Control 136	55	
STOP NIDDM	2002	Acarbose 714	32	25
		Control 715	42	
ACT-NOW	2009	Pioglitazone 213	3.1	81
		Control 228	8.2	
US DPP@	2005	Troglitazone 585	30	45
		Control 582	35	
TRIPOD**	1998	Troglitazone 133	20	55
		Control 133	45	
DREAM	2006	Rosiglitazone 2635	11.6	60
		Control 2634	26	

**33% Attrition rate.

Another class of drug called the glitazones was also studied in several prevention trials. They all have shown a significant reduction in T2DM among the high-risk groups in these trials, however, all the drugs were limited by significant side effects and intolerability [20] [21] [22].

Like the intensive LSM strategy, pharmacotherapy has therefore, been shown conclusively to reduce the T2DM incidences among the high-risk groups. However, none of these studied drugs except for metformin has been recommended for diabetes prevention by the American Diabetes Association (ADA) since 2006 [23].

2.5. Papua New Guinea Health Care System

PNG's health care system is tri level-tiered system made up of primary, secondary and the tertiary levels of care. Over the last three decades, the primary system has been neglected and as a result, 70% of the healthcare facilities throughout the country are non-functional. That has caused people to use the secondary and the tertiary healthcare systems leading to resources shortages, lack of service innovation and general decline in the minimum standard of healthcare.

With the rise of T2DM in PNG, the country finds itself unable to cope with the new disease burden.

Reinvigoration of the primary healthcare system is needed to address the primary healthcare needs as well as the rising diabetes epidemic. Restructuring and re-organization of the urban clinics to bring services close to the masses in the urban and the periurban areas seems appropriate to address the bulk of the high-risk patients.

Training of manpower in medical and nursing specialties to address new challenges in health, advocated by the health authorities could help alleviate challenges in education and diabetes supervision. Non-health sector participation is also crucial to address the diabetes epidemic. The recent government policy of 'Public-Private Partnership' paves way for the engagement of the private sector, including local gyms and exercise programs that could have an impact on the LSM strategy.

3. Implications for Local Practice in Papua New Guinea

Both the LSM and the pharmacotherapy have been shown to reduce development of overt T2DM among those with prediabetes worldwide. These strategies can be adopted into the PNG healthcare system. And to start with, the prediabetes cohort, must be identified by targeted screening. This is cost effective, convenient and can be easily assimilated into the primary prevention programs of all healthcare facilities. Those patients confirmed having prediabetes can be subjected to either intensive supervised LSM and or metformin prophylaxis to reduce the development of overt T2DM.

The integration of intensive LSM strategy into the PNG healthcare system appears challenging from many fronts and these include the despairing primary

healthcare system, lack of specialist staff and service innovation. However, with the current rejuvenation of the primary healthcare system by the health authorities, the integration of the LSM in the primary health care is feasible. The general nurses, physiotherapists, and gymnasium instructors can be trained to implement the lifestyle interventions under supervision. Diabetes trained nurses can also be deployed into the urban and the periurban clinics where most high-risk population reside to provide care, support, and mitigate patient's inconveniences of travel.

Metformin has been more effective and safer, particularly among the young and the obese patients as shown in the IDPP and the ADPP trials. Among the many drugs trialed in the primary prevention of type 2 diabetes, metformin has been recommended for use in those at high risk (obese with IGT) by the American Diabetes Association (ADA).

These demographic profiles of the high-risk in the development of diabetes are remarkably similar to the population at high risk of T2DM in PNG. In addition, metformin is cheap and is readily available at all levels of the healthcare system in PNG. Further, metformin is more tolerable than any other drugs and its metabolic profile and the pleiotropic effects in glycemic control are well known. Therefore, metformin can be easily used at all levels of healthcare in those with prediabetes to prevent the development of overt T2DM.

Other drugs have not been recommended for prevention of T2DM and should not be used in PNG because of their side effects and their intolerability. Further, their costs and the non-availability in the health system preclude their use.

There is no government policy on addressing the rising non-communicable diseases including the diabetes epidemic among the Papua New Guineans. It is in the author's opinion that the Ministry of Health should produce a policy on how to address the rising non-communicable disease and more specifically diabetes. This will guide the country's response through capacity building, integration of diabetes care into the different tiers of healthcare system and advocate for private sector involvement.

Capacity building will include the rejuvenation of the primary health care system and the urban clinics including establishing diabetes regional centers with improved facilities for testing and monitoring. These can be complemented by training of diabetes staff. The policy must advocate for more development of more leisure centers, walkways, and parks in the urban centers to improve urban community's exercise and mobility levels.

Further, the policy can advocate for the diabetic care pathway to be incorporated into the tiered structures of the healthcare system starting from the district health services to the provincial and regional levels, address information, record keeping and research. This has been shown in both the developing and the developed world to improve patient outcomes in the chronic care model [24].

The non-communicable disease policy could spell out collaboration with the Public Private Partnership Policy in addressing the rising diabetes epidemic.

These can be done by engaging the private gymnasiums and exercises programs to address the exercise aspects of prevention. Further, the employers can be encouraged to directly involve in their staff's health care and wellbeing. In fact, a study by the Global Research Identifier Database (GRiD), the industry body for group risk found that 89% of employers say that supporting the health and well-being of their staff has a positive impact on their business [25]. This serves as a reminder that businesses do benefit from taking care of their employee's health and well-being and therefore it is important to involve the private sector to participate in the prevention program by ensuring regular medical checks of their employees and providing incentives for those who improve their weights and metabolic profiles.

The WHO has identified food taxes as a strategy to address obesity and lifestyle diseases [26]. An Australian modelling showed that if there is a 20% rise in soft drinks and flavored mineral water, the sugar sweetened beverages consumption would drop by 12.6% [27]. Many countries world-wide are considering the Sugar Sweetened Beverages Tax (SSB Tax) to help curb obesity and other lifestyle diseases including diabetes [28]. PNG could potentially consider this SSB Tax in the non-communicable disease policy on foods with sugar, and others that are deemed as risk to the health of its population.

The non-communicable disease policy is therefore expected to provide a pathway to address and help reduce the incidences of T2DM epidemic in PNG.

4. Conclusions

PNG is currently experiencing T2DM in epidemic proportion with a significant high-risk population remaining undiagnosed in the communities and that is expected to fuel the epidemic in the country.

Intensive LSM and metformin prophylaxis among the prediabetes population in PNG driven by a diabetes policy could help reduce the rising epidemic and its related costs.

Conflicts of Interest

The author declares no conflicts of interest in the publication of this paper.

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