Examining the Impact of Aging and Interventions towards Burden of Diabetes Mellitus in Lao Population: A Model-Based Study

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Abstract

Background: Diabetes Mellitus (DM) is a major public health concern, but with minimal data on how this affects the Lao population. We aimed at predicting the impact of the burden of DM, and determine the effectiveness of DM screening techniques to reduce related mortality in Lao PDR.

Methods: A compartmentally deterministic model was created to reflect the demography in 2005 and 2015, and DM prevalence in 2015 of the Vientiane capital population. The parameters were retrieved from calibration and literature reviews. The model predicted demographic structure and DM in 2035. The effectiveness of DM screening tests, either Fasting Plasma Glucose (FPG) or glycated hemoglobin (HbA1c), was examined in term of mortality reduction.

Results: By 2035, the Vientiane population is expected to have annual grow of 0.89% with higher proportion of more elderly people; those aged 45 years old and older are expected to account for 39.3% in 2035. Overall prevalence of DM was expected to rise from 9.65% in 2015 to 13.4% in 2035 as a result of the aging population. The model predicts that the prevalence of DM would double (28.42%) in those aged >60 years old by 2035. The mortality rate is expected to increase more than double from 890 in 2015 to 1,808 deaths per 100,000 people in 2035, with the highest rate in those with undiagnosed diabetes and those older than 60 years. Screening by FPG test at an initial age of 35 years old is estimated to reduce mortality by 17.93%, and 16.80% for initial age screening at 45 years. Screening by HbA1c test would slightly increase the mortality reduction by approximately 1.20% at both initial screening ages.

Conclusion: This mathematical modeling projected the steadily increase of prevalence and death related to DM over 30 years of simulation. Early screening by glycemia would reduce the mortality.

Keywords: Diabetes, Demographic change, Screening test, Mathematical modeling, and Lao PDR.

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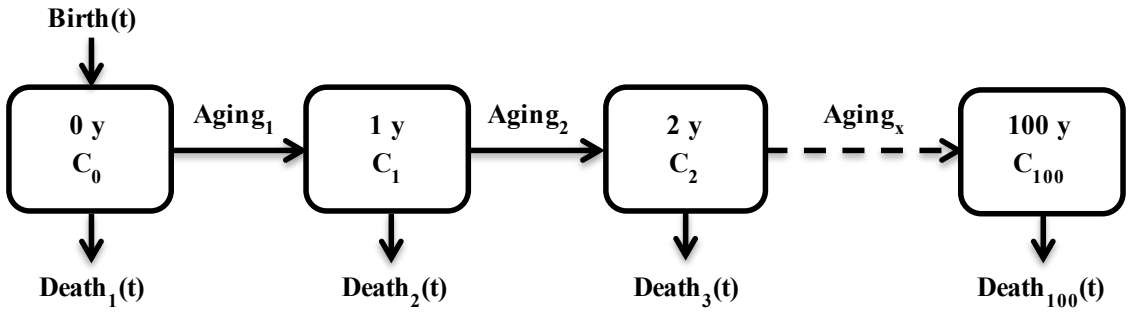
Introduction

Globally, diabetes mellitus (DM) is one of the most common non-communicable diseases (NCDs) with high mortality. DM prevalence is rapidly increasing worldwide, but predominantly in developing countries [(1,2)], particularly type 2 diabetes mellitus (T2DM) which is responsible for 90-95% of all diabetes [(3)]. The International Diabetes Federation (IDF) has estimated that 415 million people worldwide had diabetes, which is 8.8% of adult population in 2015. About 75% live in Low- and Middle Income Countries (LMIC), and this will rise to 642 million people, which is 10.4% of the adult population if the trends continue by 2040 [(4)]. In Lao People Democratic Republic (PDR), World Health Organization (WHO) reported a diabetes prevalence of 5.6% in the general population and approximately 2% of the Lao population died from diabetes each year [(5,6)]. Therefore, diabetes is one of the most health concerns of the twenty-first century and requires immediate attention.

The prevalence of this disease is increasing with age and lifestyle [(10,11)]. People with diabetes are unaware of this serious illness because of absence of signs and symptoms, which commonly occur in late stage of disease. The majority of cases were found in people older than 45 years, but some of them were currently found in children and adolescents [(12,13)]. Poor glycemic control is associated with age and the late diagnosis in which glycemic control is a huge challenge, and patients

are more likely to develop micro-vascular complications [15–17]. However, studies have shown that early screening would reduce complications and mortality thanks to better glycemic control [14]. Screening by HbA1c was currently recommended. Due to high cost and facility, the test is available only in urban settings. Therefore, providing treatment at early stage and younger age would be more effective in reducing comorbidity and mortality related to diabetes, resulting in improvement of quality of life [18,19][20].

a



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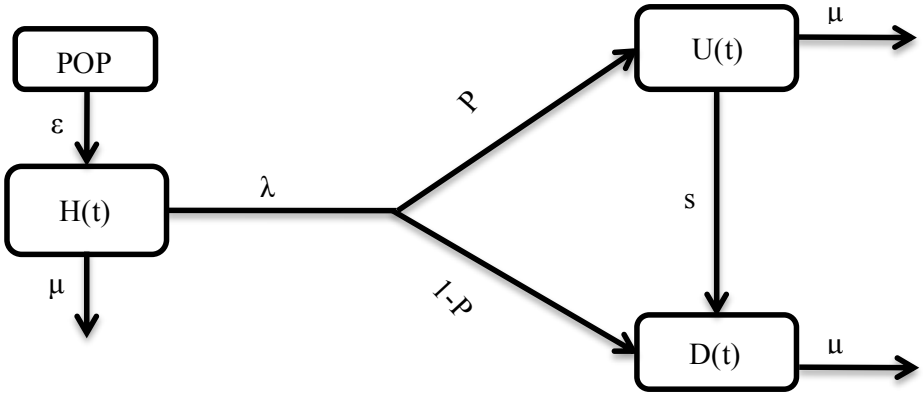

Figure 1.a: The model structure of demographic change. Demographic change model include 100 compartments as denoted C_0 to C_{100} which mean start from 0 to 100 years old. Each compartment included the size of population from natural mortality rate at time (t), denoted death (t). Only the first compartment included natural birth rate at time, denoted Birth (t).

Figure 1.b: The model structure of diabetes with parameters. H(t) healthy or non-diabetes; U(t) undiagnosed diabetes; D(t) diagnosed diabetes; ε represents birth rate; μ represents mortality rate of all causes; λ represents probability of being a diabetic; P represents proportion of undiagnosed diabetes and s represents screening parameter.

To address this problem, a large number of diabetes modelling studies to guide policy decisions was conducted particularly in high-income countries (HIC) [21,22]. The research finding showed that the predicted diabetes prevalence is estimated to increase in relation to higher risk factors and aging, which are a significant driver of the diabetes burden [23–25]. Nevertheless, very few studies have been conducted in LMIC in particular the country like Laos in which more than 70% of population live in rural settings with scarce of health facility, and population remains young compared to HIC and other LMICs.

Health policy makers lack of evidence to support this burden, and lack of evidence to deal with this problem. The effectiveness of diabetes screening to reduce mortality in diabetic patients depends upon the performance of test, uptake and disease burden in that setting. Accounting these elements, model-based study is the best tool to provide scientific evidences in long-term expectation which found high number of diabetic patients as a result of aging population. Therefore, our study aims at predicting the impact of demographic change in the burden of diabetes, and determining the effectiveness of screening tests to reduce the mortality related to diabetes using a mathematical modeling approach in Vientiane capital, Lao PDR.

Methods

Model Structure

The compartmentally deterministic model was created to reflect the Vientiane population and age and gender-specific diabetes. Compartments included 1) susceptible population or non-diabetes, 2) undiagnosed DM and 3) diagnosed DM. The susceptible population/non-diabetes (*H(t)*) was derived from the adjusted birth and death rate with exponentially decline since 1996. Demographic structure was classified from 0 to 100 years old by gender (Male and female) with the probability of aging as denoted C_0 to C_{100} ***(Figure 1.a)***.

For diabetes model, undiagnosed diabetes (*U(t)*) and diagnosed diabetes (*D(t)*) were modeled ***(Figure 1.b)***. People move from non-diabetes state to undiagnosed or diagnosed diabetes states with the transition probabilities and proportion of being undiagnosed and diagnosed. Once entering to DM states, people could not return to susceptible state because diabetes is a lifelong chronic condition. People had probability to die due to diagnosed and undiagnosed DM and by general causes. Each transition probability in the model differs by age and sex. For diabetes screening, people would move from undiagnosed to diagnosed DM compartment with the transition probability and screening coverage ***(Figure 1.b)***.

Parameters

The crude and adjusted age-specific birth and mortality rate was based on United Nation estimate for Lao PDR [26]. Age and gender-specific number of Vientiane population was based on 2005 and 2015 census obtained from the Lao Statistics Bureau. The DM prevalence was retrieved from a previous survey conducted in Vientiane population in 2015 [27]. Mortality rate of diabetes was based on a cohort study in Thailand [28]. The efficacy of screening test was based on recent systematic review and meta-analyses [29]. The probability and rate change from one to another state were retrieved from literature reviews **(Table 1)**.

Model calibration

The differential equations were numerically solved in R programing language software with Ordinary Differential Equations (ODEs), deSolve packages. Firstly, we used demographic structure model that was previously done for estimating the cost-effectiveness of Human Papillomavirus vaccination and cervical cancer screening in women in Vientiane capital [30,31]. Briefly, the model was calibrated to the population of Vientiane Capital in term of age and sex structure in 2005 and 2015 by varying related parameters using maximum likelihood. This included crude and adjusted birth and mortality rate. Secondly, the model was calibrated to age-specific prevalence of diabetes among people aged 35 years old and older in 2015 by varying incidence rate and proportion of diagnosed DM.

Table 1: Parameters of demographic change and diabetes models

Parameters	Value	Sources
Birth rate of Vientiane Capital	0.01	
Mortality rate of Vientiane Capital		United Nation estimate for Lao PDR (26)
Women	(0.001 - 0.412)	
Men	(0.001 - 0.47)	
Prevalence of diabetes		A previous survey in Vientiane Capital 2015 (27)
Women	(12% - 28.2%)	
Men	(13% - 25.8%)	
Annual mortality rate of diabetes		A cohort study in Thailand (28)
Diagnosed	(0.01 - 0.516)	
Undiagnosed	(0.01 - 1.185)	
Birth rate of Vientiane Capital		
Birth new	0.003373	
Birth old	0.001298	
Mortality rate of Vientiane Capital		
Death new	5.34304	
Death old	0.500019	
Incident rate of diabetes		Calibrated
Women		
0-50	0.60283834	
51-60	0.50232405	
61+	0.00694339	
Men		
0-50	1.96494862	
51-60	0.21219856	
61+	0.02909017	
Screening techniques		
FPG:		
Sensitivity	60%	A prospective study in India (29)
Coverage	40%	Assumption
HbA1C:		
Sensitivity	80%	A prospective study in India (29)
Coverage	40%	Assumption

Scenarios

The model consists of two main scenarios, baseline and screening, which would be implemented in

2019. The former one represents the current situation of DM in Vientiane capital where there is no screening program, and DM cases have probability to be diagnosed. The later one represents the screening program, which is either FPG and HbA1c with the effectiveness of 60% and 80%, respectively [29] and the coverage of 40%. Among this, two sub-scenarios were simulated based on initiation age of screening, either at the age of 35 to 65 years or 45 to 65 years. The age groups were selected based on the recommendation of Communicable Diseases Center (CDC) [32].

Analyses

The model was run over 30 years following model calibration in 2015. For baseline scenario, the model projected the demographic structure of Vientiane capital population by age and sex, and its impact on incidence, prevalence of diagnosed diabetes, mortality, and case fatality rate of diabetes in 2025 and 2035. For the intervention scenarios, model predicted the impact of screening techniques on mortality related to DM. Model outputs were demonstrated in curve and pyramid. These outcomes of interest were calculated by the following formula:

Incidence Proportion

$$= \frac{\text{Number of new cases of diabetes during a specific period of time}}{\text{Total number of people at risk of developing diabetes during the same period of time}} x\ 1{,}000$$

Prevalence

$$= \frac{\text{Total number of diabetes cases at one point in time}}{\text{Total number of population at the same point in time}} \text{ x } 100$$

Mortality Rate

$$= \frac{\text{Number of death of diabetes at one point in times}}{\text{Total number of population at the same point in time}} \text{ x } 100{,}000$$

Case FatalityRate

$$= \frac{\text{Number of death of diabetes at one point in times}}{\text{Total number of diabetes at the same point in time}} \text{ x } 100{,}000$$

Sensitivity analyses

Uni-way sensitivity analyses were performed to examine the impact of changing parameters on the studied outcome. We examined whether changing screening coverage or annual mortality rate in undiagnosed diabetes would change the proportion of mortality reduction.

Finding

Model calibration

Output of model calibration to demographic structure and DM in Vientiane Capital in 2005 and 2015 showed that model was fitted well to the data particularly in 2015, but less in those under 15 years old in 2005 and in those aged of 15 to 30 years old in 2015. For diabetes model, age-specific prevalence of DM derived from model and data in 2015 is very similar.

Demographic Changes

The model accounted 97 males per 100 females. Vientiane populations were estimated to grow at a rate of 0.77% annually between 2005 and 2015, and expected to annually increase by 0.89% from 2025 to 2035.

Demographic structure has been showed on age pyramid **(Figure 2)**. Age pyramid showed that the largest age group would over time have moved up in relation to larger number of elderly people. In 2005, the highest number was age group of 10-19 years old, but moved up to 20-29, to 30-39 and 40-49 in 2015, 2025 and 2035, respectively in both males and females, indicating population brooms in working age group. This corresponds to the larger number of Vientiane population, increasing from 782,250 people in 2015 to 931,603 in 2035. Among these, those aged 45 years old and older account for 21.8% and 39.3% in 2015 and 2035, respectively. However, the proportion of children would slightly drop from 20.5% in 2015 to 19.7% in 2025, and to 18.8% by 2035.

Diabetes Prediction

Prevalence of Diabetes

The number of people with diabetes was expected to increase approximately double between 2005 and 2035. The model predicted that prevalence of diabetes would be steadily increasing over time, from 9.65% in 2015 to 11.57% in 2025 and to 13.37% in 2035, but higher in male than in female (10.34% versus 8.98%, 12.01 versus 11.14% and 13.48% versus 13.25%, respectively). Moreover, the prevalence of diabetes would be increasing with aging and the highest proportion would be found in people aged more than 60 years old with slight change over 20 years of simulation (28.11% in 2015 and 28.42% in 2035).

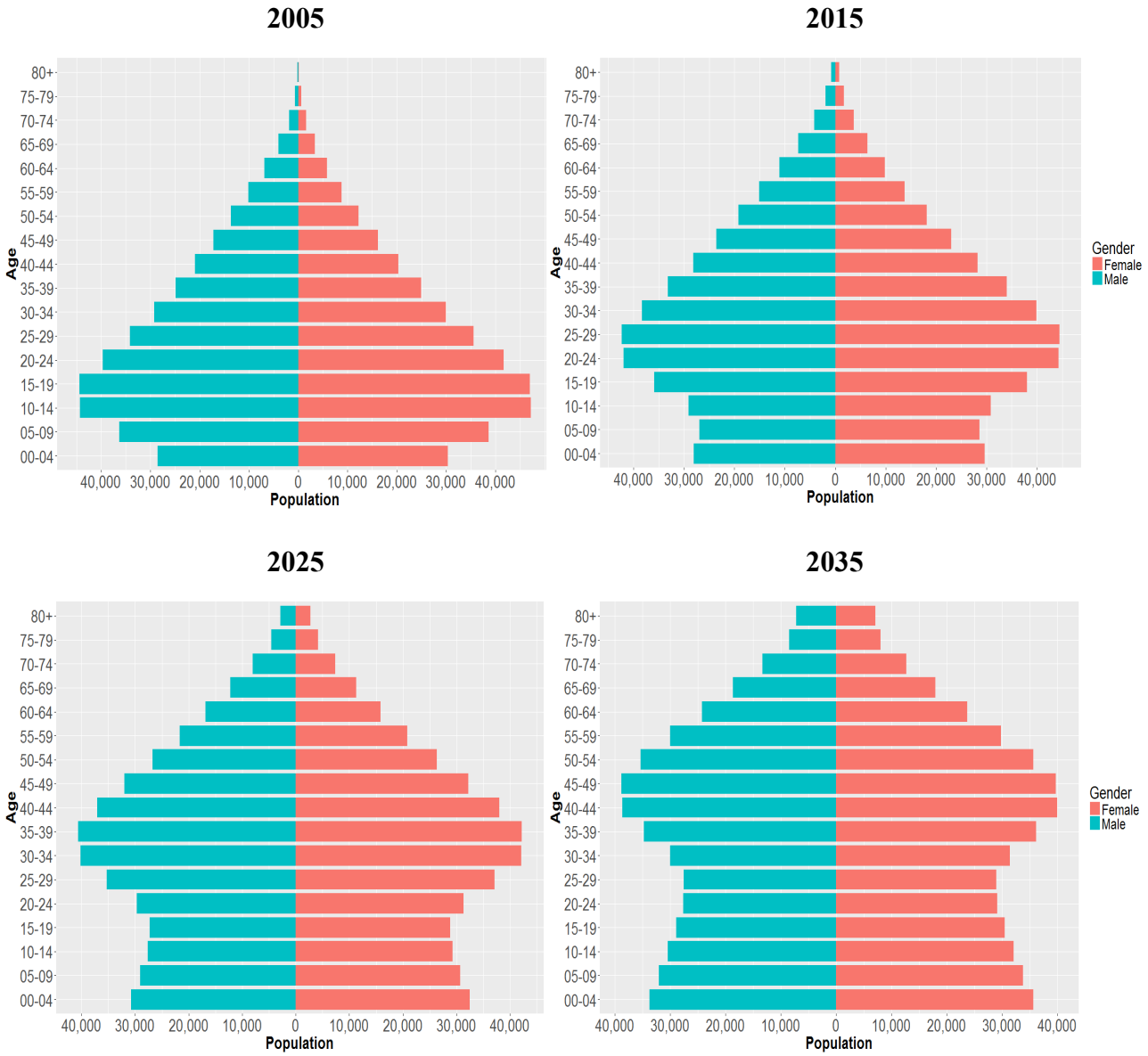

Figure 2: Population pyramid graph of Vientiane Capital by sex, 2005 – 2035. The blue color is males and the red color is females. This pyramid showed the largest age group would over time have moved up in relation to larger number of elderly people.

Mortality rate related to diabetes

The model predicted that the number of death due to DM would increase more than double from 890 in 2015 to 1,808 deaths per 100,000 people in 2035 with the highest in undiagnosed diabetes, accounting for 59.3% and 60.9% in 2015 and 2035, respectively. Males would be more likely to die than females. Moreover, the mortality rate was increasing with aging and it peaked in those aged older than 60 years, from 6,504 in 2015 to 7,545 per 100,000 people in 2035 **(Table 2)**.

Diabetes screenings

The model prediction showed that the mortality rate would decline with screening. We found that implementing screening of FPG and HbA1c test in 2019 initiating at the age of 35 years old would slightly gain the benefit compared to at the age of 45 years old. By 2035, the model predicted that the mortality rate due to DM would reduce by 17.93%, and 16.80% if screening by FPG test in those aged 35 to 65 years old and 45-64 years old, respectively compared to baseline scenarios. The mortality rate reduction would be slightly higher if screening by HbA1c for the same age group (19.08% and 18.00% for the initiation age of 35-65 and 45-65 years old, respectively).

Sensitivity Analysis

Compared to base case scenario, the model predicted approximately three-times lower proportion of mortality rate reduction in both FPG and HbA1c if the death rate was 0.941 times lower than base case (5.83% and 6.24% for FPG and HbA1c, respectively). In contrast, the proportion of mortality rate reduction would be two-fold higher than base case scenario if the death rate was 1.12 times of base case (34.36% and 36.85% for FPG

and HbA1c, respectively). However, the difference of mortality reduction between FPG and HbA1c tests remains similar to base case scenario, about 1-2% difference **(Table 3)**.

Increasing screening coverage to 70% would reduce larger number of death due to DM, but would not change the difference of mortality rate reduction between two screening techniques by 2035 (18.86% and 19.52% for FPG and HbA1c, respectively) **(Table 3)**.

Table 2: Mortality rate of overall undiagnosed and diagnosed diabetes, 2015 – 2035

Year	Age	Diabetes (per 100,000 people)			Undiagnosed diabetes (per 100,000 people)			Diagnosed diabetes (per 100,000 people)		
		Male	**Female**	**Total**	**Male**	**Female**	**Total**	**Male**	**Female**	**Total**
2015	<35	155	101	127	84	52	67	71	49	60
	35-49	837	808	823	483	443	463	354	365	359
	50-60	2,849	3,204	3,020	1,729	1,851	1,788	1,120	1,353	1,233
	61+	6,274	6,763	6,504	3,999	4,122	4,057	2,275	2,641	2,447
	Total	**920**	**861**	**890**	**557**	**499**	**528**	**362**	**362**	**362**
2025	<35	158	104	130	86	53	69	67	50	61
	35-49	858	840	849	495	461	478	363	379	371
	50-60	2,868	3,228	3,046	1,741	1,865	1,802	1,127	1,363	1,243
	61+	6,767	7,302	6,942	4,338	4,478	4,405	2,429	2,824	2,619
	Total	**1,312**	**1,290**	**1,293**	**806**	**758**	**782**	**502**	**532**	**519**
2035	<35	136	89	112	74	46	59	63	44	53
	35-49	932	939	936	539	516	527	393	423	408
	50-60	2,899	3,266	3,083	1,760	1,887	1,824	1,139	1,379	1,259
	61+	7,250	7,850	7,545	4,672	4,842	4,756	2,578	3,008	2,790
	Total	**1,784**	**1,831**	**1,808**	**1,112**	**1,091**	**1,101**	**673**	**741**	**707**

Discussion

Vientiane population was projected to steadily grow over the next 30 years particularly elderly people with larger population in people aged more than 60 years old compared to previous years. The increase in the size of elderly people was along with the increase in DM prevalence in Vientiane population. This trend is correspondent to the report from WHO in regards to the increase of chronic disease in particular diabetes as a result of larger population at high-risk of DM [33,34]. China and India also reported the similar trend [35,36].

Our study found that the prevalence of diabetes increased with age and highest in older adults aged more than 60 years old with higher in males than female. The different proportion of diabetes by sex has been documented in several review articles, some females higher than males [25,36,37] and some were opposite [23,38–40], but this trend have never been examined in detail [41]. However, these findings suggest that the increasing prevalence of diabetes is a serious concern, especially among older adults with both genders in Lao PDR.

Our finding estimated that the overall prevalence of diabetes was 9.65% in 2015, and would increase to 13.37% by 2035. This trend is similar to the estimation in Thailand [42]. However, WHO estimated prevalence of diabetes (5.6%) for Lao PDR lower than our study [5,6]. This is because our projection was performed for Vientiane capital, which is mostly urban and semi-urban setting with probably higher prevalence than other setting in the country. International Diabetes Federation (IDF) [43] and the previous study in Southeast Asia [44] also estimated higher prevalence in urban than rural setting. Actually, urbanization is associated with unhealthy diet and physical inactivity, which lead to diabetes [35]. Further model for other settings in Lao PDR will probably affirm this assumption. However, aging is the main contributor for high prevalence of DM, which results in higher death [45,46], as also found in our study.

In regards to effectiveness of screening in mortality reduction, the model found that using the HbA1c test was more effective than FPG test because HbA1c has higher potential to detect diabetic patients. This study is the first study to predict mortality rate and compare the effectiveness of diabetes screening in term of mortality rate reduction. However, international experts of diabetes recommended that HbA1c was useful as an early screening test for diabetes and as a predictor of diabetes because HbA1c can detect abnormal status in plasma glucose earlier than FPG [47–49]. The previous economic evaluation studies

demonstrated that HbA1c was cost-saving compared to no screening, also more cost-effective than FPG [50,51]. However, this needs to be examined in Lao context where the cost and disease burden are different. Further economic evaluation of diabetic control strategies in Lao PDR will be useful for health policy maker.

Table 3: Uni-way sensitivity analyses on impact of annual mortality rate (95% Confident Interval) and of screening coverage in proportion of mortality rate reduction by screening techniques in people aged 45-65 years old by 2035

Death rate	Initiation year of screening in 2019			Prediction in 2035		
	Mortality rate per 100,000 people (%)‡			Mortality rate per 100,000 people (%)‡		
	Male	Female	Both	Male	Female	Both
No screening:						
Lower bound†	886	852	868	1,450	1,501	1,476
Normal#	1,064	1,016	1,040	1,784	1,831	1,808
Upper bound§	1,606	1,520	1,563	2,856	2,892	2,874
FPG¶:						
Lower bound†	882 (0.45)	848 (0.47)	864 (0.46)	1364 (5.93)	1415 (5.73)	1390 (5.83)
Normal#	1050 (1.32)	1003 (1.30)	1026 (1.34)	1480 (17.04)	1528 (16.54)	1504 (16.79)
Upper bound§	1564 (2.62)	1479 (2.70)	1521 (2.69)	1865 (34.70)	1907 (34.06)	1886 (34.38)
HbA1c¶:						
Lower bound†	881 (0.56)	846 (0.70)	863 (0.58)	1358 (6.34)	1409 (6.13)	1384 (6.23)
Normal#	1046 (1.72)	999 (1.71)	1022 (1.74)	1458 (18.28)	1507 (17.70)	1483 (17.99)
Upper bound§	1551 (3.42)	1466 (3.55)	1508 (3.52)	1792 (37.25)	1837 (36.48)	1815 (36.85)
Screening test with coverage of 70%:						
FPG¶¶	1041 (2.16)	994 (2.17)	1017 (2.21)	1442 (19.17)	1492 (18.51)	1467 (18.86)
HbA1c¶¶	1034 (2.82)	987 (2.85)	1010 (2.88)	1429 (19.90)	1480 (19.17)	1455 (19.52)

Notes:
‡ Percentage of mortality rate reduction was compared to no screening scenario in related death rate
† Lower bound is death rate 0.941 times lower than base case scenario
# Normal bound is death rate of base case scenario
§ Upper bound is death rate 1.12 times higher than base case scenario
¶ Screening techniques is introduced at people aged 45 to 65 years old only with coverage of 40% except where noted.
¶¶ The percentage of mortality rate reduction was compared to no screening with death rate of base case scenario

This model also examined the difference between initial age of screening either at the age of 35 or 45 years old in mortality rate reduction. Screening at earlier age has slight gain, reflecting the unnecessary tests. Moreover, initiation at early age would result in large number of negativity due to the fact that diabetes is a chronic condition and known as adult-onset. Therefore the risk of being diabetes increases as getting older, especially after age of 45 years old because people probably tend to exercise less, lose muscle mass and gain weight [52]. Anyhow, the American Diabetes Association (ADA), IDF, and National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) suggested that diabetes screening should start at the age of 45 years old and old. However, early screening might be considered for those with high risk of diabetes [32,53,54], but needs further scientific evidence particularly the magnitude of high-risk population in local context. Nevertheless, our finding demonstrated the great impact of diabetes screening compared to routine diagnosis which commonly found mostly in late age at which people have difficulty to change their behavior compared to younger age, resulting in poor diabetic control with high mortality [55].

Limitations

This modeling approach has some limitations. First, the model lacks of accounting for other factors of DM such as lifestyle modification, which would modify the risk in negative or positive direction depending on prevention program and modernization. This would result in over or underestimate of DM prevalence. Second, using the diabetes mortality rate from Thailand might underestimate the mortality rate of Vientiane population because of better healthcare management in Thailand. However, we examine the lower and upper bound of annual mortality rate, and found that the difference of HbA1c and FPG remain similar. Thus, our finding remains less

biased in term of effectiveness of screenings. Finally, our study could not represent the diabetes in the entire country due to diversity of population in term of lifestyle behavior and age structure. In other setting rather than Vientiane capital, diabetes might be lower or higher than our estimate.

Conclusion

This analytical mathematical modeling projected the steady increase of prevalence and death related to diabetes over next 30 years. Implementing the screening program at aged more than 45 years old will reduce the mortality rate with preference of HbA1c, but need to investigate further whether this would be cost-effective.

Ethical consideration

Not required as secondary analysis of publicly available data.

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References

1. Ogurtsova K, da Rocha Fernandes JD, Huang Y, Linnenkamp U, Guariguata L, Cho NH, et al. IDF Diabetes Atlas: Global estimates for the prevalence of diabetes for 2015 and 2040. Diabetes Res Clin Pract [Internet]. 2017;128:40–50. Available from: http://dx.doi.org/10.1016/j.diabres.2017.03.024
2. Yuan H, Li X, Wan G, Sun L, Zhu X, Che F, et al. Type 2 diabetes epidemic in East Asia: a 35–year systematic trend analysis. Oncotarget. 2018;9(6):6718–27.
3. Tripathi K, Maheshwari A, Mohan B, Verma N, Bajaj S, Dwivedi A, et al. Classification and Diagnosis of Diabetes. Fundam Diabetes. 2016;39(January):61–73.
4. International Diabetes Federation. IDF Diabetes Atlas 7th. International Diabetes Federation. 2015. 144 p.
5. World diabetes foundation. Increasing public sector capacity for diabetes management in Laos [Internet]. 2017 [cited 2018 Jul 18]. Available from: https://www.worlddiabetesfoundation.org/projects/laos-wdf16-1419
6. Organization WH. Lao People ' s Democratic Republic Lao People ' s Democratic Republic. Diabetes Ctry profiles 2016. 2016;1–6.
7. Sen S, Chakraborty R, De B, Sen S, Chakraborty R, De B. Diabetes Mellitus: General Consideration. Diabetes Mellitus in 21st Century. 2016. 13–22 p.
8. Sharma R, Dave V, Sharma S, Jain P, Yadav S. Experimental Models on Diabetes: A Comprehensive Review. Int J Adv Pharm Sci [Internet]. 2013;4:1–8. Available from: http://www.arjournals.org/index.php/ijaps/index
9. Papatheodorou K, Papanas N, Banach M, Papazoglou D, Edmonds M. Complications of Diabetes 2016. J Diabetes Res. 2016;2016:1–3.
10. Wu Y, Ding Y, Tanaka Y, Zhang W. Risk factors contributing to type 2 diabetes and recent advances in the treatment and prevention. Int J Med Sci [Internet]. 2014;11(11):1185–200. Available from: http://www.ncbi.nlm.nih.gov/pubmed/25249787%0Ahttp://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=PMC4166864
11. Breeze PR, Thomas C, Squires H, Brennan A, Greaves C, Diggle PJ, et al. The impact of Type 2 diabetes prevention programmes based on risk-identification and lifestyle intervention intensity strategies: a cost-effectiveness analysis. Diabet Med. 2017;34(5):632–40.
12. Ramachandran A. Know the signs and symptoms of diabetes. Vol. 140, The Indian journal of medical research. 2014. p. 579–81.
13. Baynest HW. Classification, Pathophysiology, Diagnosis and Management of Diabetes Mellitus. J Diabetes Metab. 2015;06(05).
14. Richardson SA, Desai P, Serjeant GR. Type 2 Diabetes Mellitus: A Review of Current Trends. Br Med J. 2012;1(6022):1371–3.
15. Otiniano ME, Al Snih S, Goodwin JS, Ray L, Alghatrif M, Markides KS. Factors associated with poor glycemic control in older Mexican American diabetics aged 75 years and older. J Diabetes Complications. 2012;26(3):181–6.
16. Sazlina S-G, Mastura I, Cheong AT, Mohamad AB, Jamaiyah H, Lee PY, et al. Predictors of poor glycaemic control in older patients with type 2 diabetes mellitus. Singapore Med J. 2015;56(4):181–3.
17. Olsson L, Grill V, Midthjell K, Ahlbom A,

Anderssonc T, Carlsson S. Mortality in adult-onset autoimmune diabetes is associated with poor glycemic control: Results from the HUNT study. Diabetes Care. 2013;36(12):3971–8.

18. Gonzalez-Zacarias AA, Mavarez-Martinez A, Arias-Morales CE, Stoicea N, Rogers B. Impact of Demographic, Socioeconomic, and Psychological Factors on Glycemic Self-Management in Adults with Type 2 Diabetes Mellitus. Front Public Heal [Internet]. 2016;4(September):1–8. Available from: http://journal.frontiersin.org/Article/10.3389/fpubh.2016.00195/abstract

19. Feig DS, Berger H, Donovan L, Godbout A, Kader T, Keely E, et al. Retinophaty. Diabetes Canada Clinical Practice Guidelines Expert Committee. Can J Diabetes. 2018;42:255–82.

20. The CDC Diabetes Cost-Effectiveness Study Group. The Cost-effectiveness of Screening for Type 2 Diabetes. JAMA J Am Med Assoc. 2018;280(20):1757–63.

21. Quwaidhi A Al. Epidemiological modelling of type 2 diabetes in Saudi Arabia: predicted trends and public health implications. Newcastle Univ [Internet]. 2013; Available from: https://theses.ncl.ac.uk/dspace/handle/10443/2168

22. Department of Economic and Social Affairs of United Nation. World Population Prospects The 2017 Revision. New York; 2017.

23. Al Ali R, Mzayek F, Rastam S, M Fouad F, O'Flaherty M, Capewell S, et al. Forecasting future prevalence of type 2 diabetes mellitus in Syria. BMC Public Health. 2013;13(1).

24. Saidi O, O'Flaherty M, Mansour N Ben, Aissi W, Lassoued O, Capewell S, et al. Forecasting Tunisian type 2 diabetes prevalence to 2027: Validation of a simple model Biostatistics and methods. BMC Public Health. 2015;15(1):1–8.

25. Phan TP, Alkema L, Tai ES, Tan KHX, Yang Q, Lim W-Y, et al. Forecasting the burden of type 2 diabetes in Singapore using a demographic epidemiological model of Singapore. BMJ Open Diabetes Res Care. 2014;2(1):e000012.

26. Lao Statistics Bureau. The 4th Population and Housing Census (PHC) 2015. Lao Stat Bur [Internet]. 2016;280pp. Available from: http://www.lsb.gov.la/PDF/PHC-ENG-FNAL-WEB.pdf

27. Htun NSN, Odermatt P, Paboriboune P, Sayasone S, Vongsakid M, Phimolsarn-Nusith V, et al. Association between helminth infections and diabetes mellitus in adults from the Lao People's Democratic Republic: A cross-sectional study. Infect Dis Poverty. 2018;7(1):1–11.

28. Pratipanawatr T, Rawdaree P, Chetthakul T, Bunnag P, Ngarmukos C, Benjasuratwong Y, et al. Thailand diabetic registry cohort: Predicting death in Thai diabetic patients and causes of death. Vol. 93, Journal of the Medical Association of Thailand. 2010.

29. Mokta J, Kumar S, Ganju N, Mokta K, Panda P, Gupta S. High incidence of abnormal glucose metabolism in acute coronary syndrome patients at a moderate altitude: A sub-Himalayan study. Vol. 21, Indian Journal of Endocrinology and Metabolism. 2016. p. 142.

30. Chanthavilay P, Reinharz D, Mayxay M, Phongsavan K, Marsden DE, Moore L, et al. The economic evaluation of human papillomavirus vaccination strategies against cervical cancer in women in Lao PDR: A mathematical modelling approach. BMC Health Serv Res [Internet]. 2016;16(1):1–10. Available from: http://dx.doi.org/10.1186/s12913-016-1662-5

31. P. C, D. R, M. M, K. P, D.E. M, L. M. Economic evaluation of screening strategies combined with hpv vaccination of preadolescent girls for the prevention of cervical cancer in Vientiane, Lao PDR [Internet]. Vol. 11, PLoS ONE. 2016. p. no pagination. Available from: http://journals.plos.org/plosone/article/asset?id=10.1371/journal.pone.0162915.PDF%5Cnhttp://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emed18&NEWS=N&AN=612821028

32. Krisha McCoy. Guidelines for Diabetes Screening - Diabetes Center - Everyday Health [Internet]. EVERYDAY HEALTH. 2009 [cited 2018 Jul 24]. Available from: https://www.everydayhealth.com/diabetes/diabetes-screening-guidelines.aspx

33. Corriere M, Rooparinesingh N, Kalyani RR. Epidemiology of diabetes and diabetes complications in the elderly: An emerging public health burden. Curr Diab Rep. 2013;13(6):805–13.

34. Kalyani RR, Golden SH, Cefalu WT. Diabetes and Aging: Unique

Considerations and Goals of Care. Diabetes Care. 2017;40(4):440–3.

35. Smith JP, Majmundar M. Aging in Asia: Strengthening the Infrastructure for Science and Policy [Internet]. Smith JP, Majmundar M, editors. Aging in Asia: Findings from New and Emerging Data Initiatives. Woshington, D.C; 2012. 17–35 p. Available from: http://www.nap.edu.

36. Ramachandran A. Trends in prevalence of diabetes in Asian countries. World J Diabetes [Internet]. 2012;3(6):110. Available from: http://www.wjgnet.com/1948-9358/full/v3/i6/110.htm

37. RAZAK ZA. National Health and Morbidity Survey 2015 [Internet]. Malaysia; 2015. Available from: http://www.mpoc.org.my/upload/Pn Zalma National Health and Morbidity Survey NCD Risk Factors.pdf

38. Aekplakorn W, Chariyalertsak S, Kessomboon P, Assanangkornchai S, Taneepanichskul S, Putwatana P. Prevalence of Diabetes and Relationship with Socioeconomic Status in the Thai Population: National Health Examination. 2004;2018.

39. Gyawali B, Sharma R, Neupane D, Mishra SR, van Teijlingen E, Kallestrup P. Prevalence of type 2 diabetes in Nepal: A systematic review and meta-analysis from 2000 to 2014. Glob Health Action. 2015;8:4–13.

40. Mukai N, Doi Y, Ninomiya T, Hirakawa Y, Nagata M, Yoshida D, et al. Trends in the prevalence of type 2 diabetes and prediabetes in community-dwelling Japanese subjects: The Hisayama Study. J Diabetes Investig. 2014;5(2):162–9.

41. Hilawe EH, Yatsuya H, Kawaguchi L, Aoyama A. Differences by sex in the prevalence of diabetes mellitus, impaired fasting glycaemia and impaired glucose tolerance in sub-Saharan Africa: a systematic review and meta-analysis. Bull World Health Organ. 2013;91(9):671-682D.

42. Mahikul W, White LJ, Poovorawan K, Soonthornworasiri N, Sukontamarn P, Chanthavilay P, et al. A Population Dynamic Model to Assess the Diabetes Screening and Reporting Programs and Project the Burden of Undiagnosed Diabetes in Thailand. 2019;(Dm):1–10.

43. International Diabetes Federation. IDF Diabetes Atlas 8th edition. IDF Diabetes Atlas, 8th edition. 2017. 1–150 p.

44. Cheema A, Adeloye D, Sidhu S, Sridhar D, Chan KY. Urbanization and prevalence of type 2 diabetes in Southern Asia: A systematic analysis. J Glob Health. 2014;4(1).

45. Asnani S, Israni D, Williamson JD. Diabetes in Older Adults. Clin Diabetes. 2006;35(10):522–34.

46. Chentli F, Azzoug S, Mahgoun S. Diabetes mellitus in elderly. Vol. 19, Indian Journal of Endocrinology and Metabolism. India; 2015. p. 744–52.

47. Kam-On Chung J, Xue H, Wing-Hang Pang E, Chuen-Chu Tam D. Accuracy of fasting plasma glucose and hemoglobin A1c testing for the early detection of diabetes: A pilot study. Front Lab Med [Internet]. 2017;1(2):76–81. Available from: http://dx.doi.org/10.1016/j.flm.2017.06.002

48. Choi SH, Kim TH, Lim S, Park KS, Jang HC, Cho NH. Hemoglobin A1c as a diagnostic tool for diabetes screening and new-onset diabetes prediction: A 6-year community-based prospective study. Diabetes Care. 2011;34(4):944–9.

49. Buse JB, Kaufman FR, Linder B, Hirst K, El Ghormli L, Willi S. Diabetes screening with hemoglobin A1c versus fasting plasma glucose in a multiethnic middle-school cohort. Diabetes Care. 2013;36(2):429–35.

50. Gillett M, Brennan A, Watson P, Khunti K, Davies M, Mostafa S, et al. The cost-effectiveness of testing strategies for type 2 diabetes: A modelling study. Health Technol Assess (Rockv). 2015;19(33):1–80.

51. Ho-Pham LT, Nguyen UDT, Tran TX, Nguyen T V. Discordance in the diagnosis of diabetes: Comparison between HbA1c and fasting plasma glucose. PLoS One. 2017;12(8):1–11.

52. Pippitt K, Li M, Gurgle HE. Diabetes mellitus: Screening and diagnosis. Am Fam Physician. 2016;93(2):103–9.

53. Guthrie DW. The prevention or delay of type 2 diabetes mellitus. Kans Nurse [Internet]. 2004;79(5):1–2. Available from: http://www.ncbi.nlm.nih.gov/pubmed/15216606

54. National Institute of Diabetes and Digestive and Kidney Diseases. Diabetes Tests & Diagnosis | NIDDK [Internet]. 2016

[cited 2018 Jul 23]. Available from: https://www.niddk.nih.gov/health-information/diabetes/overview/tests-diagnosis

55. Milanovic Z, Pantelic S, Trajkovic N, Sporis G, Kostic R, James N. Age-related decrease in physical activity and functional fitness among elderly men and women. Clin Interv Aging [Internet]. 2013;8:549–56. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23723694%0Ahttp://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=PMC3665513.