Study protocol for the Shanghai Integrated Diabetes Prevention and Care System - "Shanghai Integration Model (SIM)"

1. Introduction

Type 2 diabetes (T2D) has become a major health concern globally.[1-4] In China, based on a national survey in 2013, the estimated standardized prevalence of diabetes was 10.4% among adults, and there were approximately 0.82 million deaths due to diabetes and related complications in 2019.[1,4] In Shanghai, the prevalence of diabetes reached 17.6% among adults over 35 years in 2013, and nearly one-third of the aging population had diabetes.[5] However, the quality of care for patients with diabetes in communities has remained suboptimal. Among patients with diabetes in Shanghai, around 12.42% achieved adequate glycemic control (HbA_{1c}<7.0%) in 2007.[5]

In order to strengthen primary care, diabetes management of basic public health service (BPHS) packages have been generally offered through community health centers (CHCs) since 2009.[6,7] CHC health staff provide quarterly follow-up visits including assessment of risk factors and free fasting plasma glucose (FPG) tests, health education, and life-style consultations. Before 2016, there were around 630 thousand patients with diabetes receiving diabetes management services in CHCs in Shanghai. Despite an increasing number of patients receiving diabetes management services of BPHS in CHCs, only around 35.1% of patients had adequate glycemic control (HbA_{1c}<7.0%) control in 2013, whereas the control of diabetes was 50% in the United States based on the National Health and Nutrition Examination Survey 1999-2004.[8,9]

Diabetes is a complex disease requiring comprehensive medical care. According to the guideline developed by the Chinese Diabetes Society, the importance of secondary prevention remains at a

premium to promote optimal management for those with T2D.[10] Studies showed that diabetic complications could be prevented or delayed by better management of blood glucose and early detection and treatment of diabetic complications.[11-13] Thus, since 2015, the Shanghai Municipal Government has started the Shanghai Integrated Diabetes Prevention and Care System-"Shanghai Integration Model (SIM)", to strengthen the primary healthcare capability of diabetes and its complications prevention and management, and to promote care integration among tertiary, secondary hospitals and CHCs.[14,15] Prediabetes and diabetes screening for those with high risks, and diabetic complications screening for patients with diabetes in CHCs have been implemented ever since.

2 Study Objective

With funding support from the government, this quality improvement project of the SIM is designed to strengthen the primary healthcare capability of diabetes and its complications prevention and management, by promoting care integration among tertiary, secondary hospitals and CHCs with city-wide health information technology (IT) support in Shanghai. Firstly, this study is designed to investigate the current effectiveness of the quality of care for patients with diabetes in communities in Shanghai by investigating the achievement of key intermediate outcomes and associated factors. Secondly, longitudinal follow-up is designed to evaluate the long-term effectiveness of this quality improvement project by enhancing diabetes and related complications prevention and management in primary healthcare.

3. Methods and analysis

3.1 Study design and contexts

Since 2015, the Shanghai Integrated Diabetes Prevention and Care System (Figure 1) has been initiated by the government with the collaboration among Shanghai Technical Center for Diabetes Prevention and Clinical Care, Shanghai Municipal Center for Disease Control & Prevention and Shanghai Eye Disease Prevention and Treatment Center, with Shanghai Center for Clinical Laboratory and Wonders Information Co., Ltd providing laboratory tests quality control and IT support, respectively. Around 30% of the 630 thousand patients with diabetes, receiving diabetes management in CHCs in Shanghai, will undergo comprehensive assessment of metabolic control and screening for microvascular complications.

Thus, a cross-sectional observational study involving all the 240 CHCs in Shanghai is designed to evaluate the current effectiveness of the quality of care for patients with diabetes in communities in Shanghai by investigating the achievement of key intermediate outcomes and associated factors. Since then, this work is expected to be included into the Shanghai community health management framework for integrated management of chronic diseases. So, longitudinal follow-up, based on a community-based, prospective, observational study involving 240 CHCs, is designed to evaluate the long-term effectiveness of this quality improvement project by enhancing diabetes and related complications prevention and management in primary healthcare.

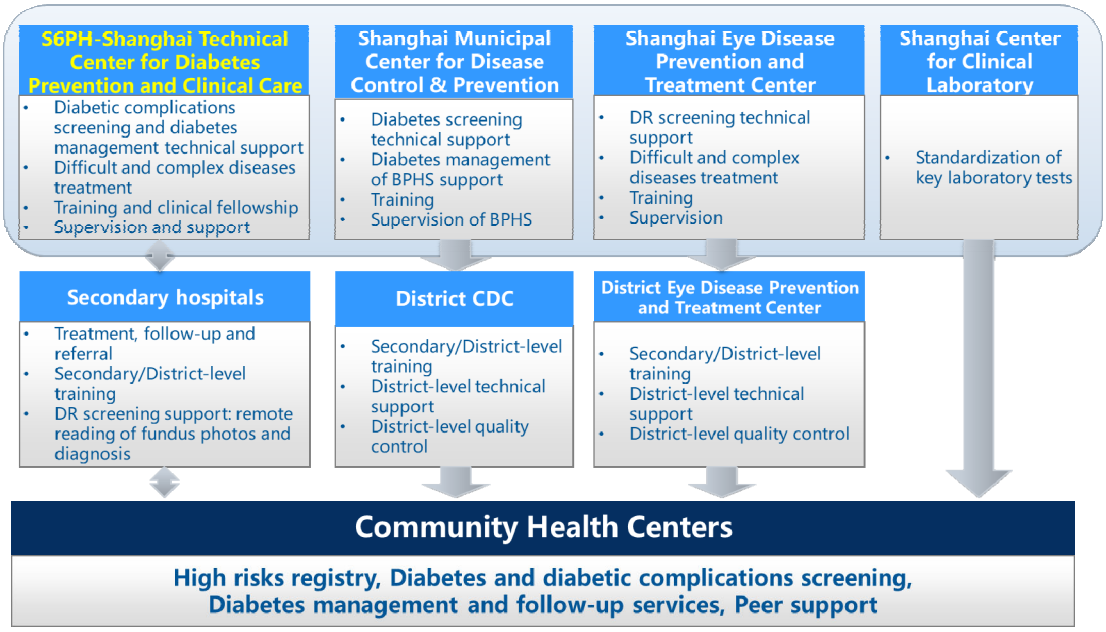

Figure 1. Framework of the Shanghai Integrated Diabetes Prevention and Care System

3.2 Study sites selection and participants

All 240 CHCs of 16 districts in Shanghai will be invited to participate in this project. For metabolic control and microvascular complications assessment, patients with diagnosed T2D and registered for receiving diabetes management in the participating CHCs will be recruited. Inclusion criteria included: age≥18 years; residing in the community for the last six months with no plan of relocating; voluntary participation with informed consent. Exclusion criteria included: with severe physical or psychological problems; unable to attend the site visit. Rejection/withdrawal criteria included: voluntary withdrawal from the study; withdrawal due to move, going abroad, and death.

3.3 Capacity building

Five structured training sessions will be held covering health staff from 240 CHCs and 16 districts, around 5 participants per CHC. The trainings will mainly focus on diabetes epidemiology and disease burden, classification and diagnosis of diabetes, diabetes risks assessment, diabetes

and diabetic complications screening, life-style intervention and treatment of diabetes and diabetic complications, etc. The trainings are standardized to ensure the assessment would be implemented in the same manner. Secondary trainings will be organized by district-level health staff with technical support from the Shanghai Technical Center for Diabetes Prevention and Clinical Care, Shanghai Municipal Center for Disease Control & Prevention and Shanghai Eye Disease Prevention and Treatment Center.

3.4 Metabolic control and microvascular complications assessment

Metabolic control and microvascular complications assessment will be implemented by CHC staff, following a standardized structured protocol. Anthropometric parameters including height, weight, and waist circumference (WC) will be obtained with the patient barefoot in light clothing. WC will be measured at the horizontal plane midway between the lower edge of the costal margin and the upper edge of the iliac crest in standing position. Physical examination and laboratory measurements includ blood pressure (BP), HbA_{1c}, FPG, lipid profile including total cholesterol (TC), LDL-c, HDL-cholesterol (HDL-c), and triglycerides (TG), renal function test, liver function test, routine blood test, routine urine test and urine albuminuria. Blood samples and random urine samples will be collected in participants after an overnight fast of at least 10 hours. Standard laboratory tests will be performed by regional medical institutions or laboratory centers, with qualification assessment done by the Shanghai Center for Clinical Laboratory. The Shanghai Center for Clinical Laboratory organizes quality control and technical skill trainings. Quality control include internal quality control, external quality assessment, and on-site inspection. Trueness verification is developed to improve the accuracy and traceability of test results. External quality assessment activities will be performed.

Albuminuria is defined as spot urinary albumin-to-creatinine ration (uACR) of 30 mg/g or higher.[10] The GFR is estimated from calibrated serum creatinine concentrations using the Chronic Kidney Disease Epidemiology Collaboration equation (CKD-EPI). Estimated GFR (eGFR)<60 ml/min/1.73 m^2 is defined as impaired eGFR.[10] Diabetes with CKD is defined as diabetes with albuminuria, impaired eGFR, or both.[10]

Diabetic retinopathy (DR) screening will be implemented by using fundus photography in each site. Fundus photography are performed by primary healthcare staff at each CHC following a standardized protocol. Retinal photographs are captured using desktop retinal cameras from Canon, ZEISS, and Topcon. Two retinal photographs (macular and optic-disc centered) will be taken for each eye according to the DR screening guidelines of the World Health Organization.[16,17] Original retinal images will be collected through a field screening information collection system (FSICS) from CHCs, and uploaded to a remote reading system (RRS), and the images of each eye will be assigned separately to two authorized ophthalmologists. They will label the images using the remote reading system and provide the graded diagnosis of diabetic retinopathy. In the case of discordant findings, a senior ophthalmologist will examine the images before he makes the final decision. Diagnosis results will be sent back to CHCs through the system. All those authorized ophthalmologists underwent trainings held by the Shanghai Eye Disease Prevention and Treatment Center to ensure standardized services. DR severity is graded into five levels (none, mild, moderate, severe, or proliferative, respectively), according to the International Clinical Diabetic Retinopathy Disease Severity Scale.[18] Mild NPDR is defined as the presence of microaneurysms only. Moderate NPDR is defined as more than just microaneurysms, but less than severe NPDR. Severe NPDR is defined as any of the following: more than 20 intraretinal hemorrhages in each of

the 4 quadrants; definite venous beading in 2+ quadrants; prominent intraretinal microvascular abnormalities (IRMA) in 1+ quadrant, and no signs of PDR. PDR is defined as one or more of the following: neovascularization, vitreous/preretinal hemorrhage. Diabetic macular edema (DME) is diagnosed if hard exudates were detected within 500 μm of the macular center according to the standard of the Early Treatment for Diabetic Retinopathy study.[19] Referable DR is defined as moderate NPDR or worse, DME, or both.[20]

All data of the metabolic control and microvascular complications assessment will be uploaded to a city-wide microvascular complications assessment system, through linking to a city-wide central health information platform, "Shanghai health information platform", identifying patients by their unique identity card number compulsory for all residents.

3.5 Management and follow-up

This work is expected to be included into the Shanghai community health management framework by the government. Patients with diabetes registered for diabetes management of BPHS will be recommended to undergo metabolic control and microvascular complications assessment annually by CHCs. It will be integrated with other related diabetes management services of BPHS, including updating health records of quarterly follow-up, assessment of risk factors, free fasting plasma glucose (FPG) tests, health education, and life-style consultations, and usual clinical care as well. Thus, further longitudinal follow-up will be implemented to evaluate the long-term effectiveness of this quality improvement project in primary healthcare in terms of diabetes care.

3.6 Study outcomes

For the cross-sectional study, investigating the effectiveness of the quality of care for patients with diabetes, the primary outcome will include the achievement of the target for HbA_1 control.

Secondary outcomes will include the achievement of the targets for blood pressure, lipids and all the three targets for metabolic control. Associated factors affecting those intermediate outcome measures will be investigated. For the evaluation of the long-term effectiveness of this quality improvement project, we will investigate the effectiveness of diabetes care, in terms of the achievement of intermediate outcome measures and trends of diabetes related complications, and also associated risk factors affecting the quality of care in Shanghai, China.

3.7 Data collection and management

Clinical medical records, regular follow-up records of BPHS and metabolic and microvascular complications assessment records will be extracted from a linked central computer system, "Shanghai health information platform", identifying patients by their unique identity card number compulsory for all residents. Information sharing mechanisms and protocols were formulated by the government, promoting data sharing between clinical and follow-up records. Data collection, storage and reporting will conform to China's privacy laws. Individual participants are encrypted and de-identified. Results and findings from this study will be reported without individual identification.

3.8 Project management and process evaluation

On-site supervision, monitoring and support of the first CHC implementing this project in each district will be carried out by a project management team to ensure the study fidelity and progress. District-level management team in each district will participate in the on-site supervision and monitoring with the project management team together, and will be responsible for the on-site monitoring of the other CHCs in their districts. Quarterly reports of this project will be sent to each district health commission to ensure the project implementation. Collaborative network

meetings will be organized to identify the implementation barriers and facilitators from the district-level and CHC-level perspective. Central monitoring of routinely collected data will be undertaken by a project management team.

3.9 Statistical analysis

Descriptive statistics will be used to present the demographics, diabetes duration, metabolic and related complications, and treatment patterns, with mean ± sd for continuous variables and percentages for categorical variables. Adequate control of the targets for HbA_{1c}, BP, LDL-c and all three outcomes will be compared between subgroups of selected variables in T2D participants. Between-group comparisons will be analyzed using χ^2 for categorical variables, and t test for continuous variables. Multivariable logistic regression modeling will be used to investigate potential risk factors independently associated with those key intermediate outcome measures. For investigating the long-term effectiveness, multivariate cox regression analysis will be used to test the effect on the achievement of intermediate outcome measures and incident complications. SPSS and SAS statistical software will be used for the analyses in this study, with a two-sided *p* value of <0.05 was considered significant.

3.10 Patient and Public Involvement

No patient will be involved in the design of this study. Participating district-level health staff will be informed of study progress through collaborative network meetings and progress reports. General results of the study will be shared with Shanghai health commission, district health commission, and CHC staff and general media in Shanghai.

3.11 Ethics and dissemination

This study was approved by the local Clinical Research Ethics Committee. Signed informed

consent is obtained from patients prior to participant recruitment. Findings from this study will be disseminated through peer reviewed journals, collaborative network meetings with Shanghai health commission, district health commission, and CHC staff, and general media.

4. Discussion

We outline the design for a large-scale, community-based, cross-sectional, observational study involving all the 240 CHCs of 16 districts in Shanghai, to evaluate the latest effectiveness of the quality of care for patients with diabetes in communities. Since this work is expected to be included into the Shanghai community health management framework by the government, a prospective observational study based on longitudinal follow-up will be implemented to further evaluate the long-term effectiveness of this quality improvement project in primary healthcare in Shanghai.

The large sample size will enable us to appraise the effectiveness overall and across each strata. Since this is the first provincial-level document/regulation of the prevention and treatment of chronic diseases integrating diabetic complications assessment into diabetes management of BPHS in primary healthcare, the findings of this study and information collected on the barriers and facilitators of the implementation will better facilitate further scale up, and provide evidence from community-based diabetic complications prevention and management strategies to other regions nationwide and globally.

We prepared for almost one year to develop the project, improve data collection systems and organize trainings. A governance system has been developed which includes management teams from the Shanghai Technical Center for Diabetes Prevention and Clinical Care, Shanghai Municipal Center for Disease Control & Prevention and Shanghai Eye Disease Prevention and

Treatment Center and district-level health staff, as well.

The use of the city-wide IT systems linking to the “Shanghai health information platform” greatly facilitate the implementation of this project in primary healthcare with standard procedures and quality. Firstly, a remote DR screening, reading and diagnosis, and management system is developed through this project, widely facilitating DR screening capabilities in primary healthcare. Secondly, Shanghai government started the development of the “Shanghai health information platform” in 2011, collecting clinical data from 422 public health organizations, including 38 tertiary hospitals, 144 secondary hospitals and specialized health institutions, and 240 CHCs since 2013. This has laid a solid foundation for data collection, storage, management and effective evaluation for this project. However, we recognize that this might influence the generalisability of this project to some regions with low resources.

We anticipate the SIM project would be implemented successfully. In order to better evaluate the effectiveness, we will record related healthcare reform policies on diabetes management and primary healthcare. Most importantly, we hope this study would contribute to the improvement of diabetes management in primary healthcare.

Reference

1. International Diabetes Federation. IDF Diabetes Atlas, 9th edn. Brussels, Belgium: 2019. Available from: http://www.diabetesatlas.org.

2. Pan X, Yang W, Li G, Liu J, The National Diabetes Prevention and Control Cooperative Group. Prevalence of Diabetes and Its Risk Factors in China, 1994. *Diabetes Care* 1997;20(11):1664-1669. DOI: 10.2337/diacare.20.11.1664

3. Yang W, Lu J, Weng J, Jia W, Ji L, Xiao J, et al. Prevalence of Diabetes among Men and Women in China. *N Engl J Med* 2010;362(12):1090-1101. DOI: 10.1056/NEJMoa0908292

4. Wang L, Gao P, Zhang M, Huang Z, Zhang D, Deng Q, et al. Prevalence and Ethnic Pattern of Diabetes and Prediabetes in China in 2013. *JAMA* 2017;317(24):2515-2523. DOI: 10.1001/jama.2017.7596

5. Ruan Y, Yan QH, Xu JY, Yang QD, Yao HH, Li R, et al. Epidemiology of Diabetes in Adults Aged 35 and Older from Shanghai, China. *Biomed Environ Sci* 2016;29(6):408-416. DOI: 10.3967/bes2016.053

6. Meng Q, Mills A, Wang L, Han Q. What can we learn from China's health system reform? *BMJ* 2019;365:l2349. DOI: 10.1136/bmj.l2349

7. Yuan B, Balabanova D, Gao J, Tang S, Guo Y. Strengthening public health services to achieve universal health coverage in China. *BMJ* 2019;365:l2358. DOI: 10.1136/bmj.l2358

8. Qin Y, Wang R, Ma X, Zhao Y, Lu J, Wu C, et al. Prevalence, Awareness, Treatment and Control of Diabetes Mellitus-A Population Based Study in Shanghai, China. *Int J Environ Res Public Health* 2016;13(5):512. DOI: 10.3390/ijerph13050512

9. McDonald M, Hertz RP, Unger AN, Lustik MB. Prevalence, awareness, and management of hypertension, dyslipidemia, and diabetes among United States adults aged 65 and older. *J Gerontol A Biol Sci Med Sci* 2009;64(2):256-63. DOI: 10.1093/gerona/gln016

10. Jia W, Weng J, Zhu D, Ji L, Lu J, Zhou Z, et al. Standards of medical care for type 2 diabetes in China 2019. *Diabetes Metab Res Rev* 2019;35(6):e3158. DOI: 10.1002/dmrr.3158

11. Fox CS, Golden SH, Anderson C, Bray GA, Burke LE, Boer LHD, et al. Update on Prevention of Cardiovascular Disease in Adults With Type 2 Diabetes Mellitus in Light of Recent

Evidence: A Scientific Statement From the American Heart Association and the American Diabetes Association. *Diabetes Care* 2015;38(9):1777-1803. DOI: 10.2337/dci15-0012

12. Nakanishi S, Hirukawa H, Shimoda M, Tatsumi F, Kohara K, Obata A, et al. Comparison of HbA1c levels and body mass index for prevention of diabetic kidney disease: A retrospective longitudinal study using outpatient clinical data in Japanese patients with type 2 diabetes mellitus. *Diabetes Res Clin Pract* 2019;155:107807. DOI: 10.1016/j.diabres.2019.107807

13. Gruss SM, Nhim K, Gregg E, Bell M, Luman E, Albright A. Public Health Approaches to Type 2 Diabetes Prevention: the US National Diabetes Prevention Program and Beyond. *Curr Diab Rep* 2019;19(9):78. DOI: 10.1007/s11892-019-1200-z.

14. Liu Y, Wu X, Cai C, Tang PY, Coufal MM, Qian Y, et al. Peer support in Shanghai's Commitment to diabetes and chronic disease self-management: program development, program expansion, and policy. *Translational behavior medicine* 2020;10(1):13-24. DOI: 10.1093/tbm/ibz194

15. Jia W, Wang H, Davies J. China—leading the way in diabetes research. *The Lancet Diabetes & Endocrinology* 2016;4 Suppl 1:S1. DOI: 10.1016/S2213-8587(16)30290-X

16. Scanlon PH, Malhotra R, Greenwood RH, Aldington SJ, Foy C, Flatman M, et al. Comparison of two reference standards in validating two field mydriatic digital photography as a method of screening for diabetic retinopathy. *British journal of ophthalmology* 2003;87(10):1258-1263. DOI: 10.1136/bjo.87.10.1258

17. Organization WH. World Health Organization. Prevention of blindness from diabetes mellitus: report of a WHO consultation in Geneva, Switzerland: 2006. Available from: https://www.who.int/diabetes/publications/prevention_diabetes2006/en/.

18. Wilkinson CP, Ferris FL, Klein RE, Lee PP, Agardh CD, Davis M, et al. Proposed international clinical diabetic retinopathy and diabetic macular edema disease severity scales. *Ophthalmology* 2003;110(9):1677-1682. DOI: 10.1016/S0161-6420(03)00475-5

19. Group ETDRSR. Treatment techniques and clinical guidelines for photocoagulation of diabetic macular edema: Early Treatment Diabetic Retinopathy Study report number 2. *Ophthalmology* 1987;94(7):761-774. DOI: 10.1016/s0161-6420(87)33527-4

20. Wong TY, Sun J, Kawasaki R, Ruamviboonsuk P, Gupta N, Lansingh VC, et al. Guidelines on Diabetic Eye Care: The International Council of Ophthalmology Recommendations for Screening, Follow-up, Referral, and Treatment Based on Resource Settings. *Ophthalmology* 2018;125(10):1608-1622. DOI: 10.1016/j.ophtha.2018.04.007