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The Manitoba Personalized Lifestyle Research (TMPLR) study protocol: a multicentre bidirectional observational cohort study with administrative health record linkage investigating the interactions between lifestyle and health in Manitoba, Canada

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ABSTRACT

Introduction Lifestyle factors, such as diet, physical activity and sleep, are associated with the development of many chronic diseases. The objective of The Manitoba Personalized Lifestyle Research study is to understand how these lifestyle factors interact with each other and with other factors, such as an individual's genetics and gut microbiome, to influence health.

Methods An observational study of adults, with extensive phenotyping by objective health and lifestyle assessments, and retrospective assessment of early life experiences, with retrospective and prospective utilisation of secondary data from administrative health records.

Study population A planned non-random convenience sample of 840 Manitobans aged 30–46 recruited from the general population, stratified by sex (equal men and women), body mass index (BMI; 60% of participants with a BMI>25 kg/m^2) and geography (25% from rural areas). These stratifications were selected based on Manitoba demographics.

Measurements Lifestyle factors assessed will include dietary pattern, physical activity, cardiovascular fitness, and sleep. Factors such as medical history, socioeconomic status, alcohol and tobacco consumption, cognition, stress, anxiety, and early life experiences will also be documented. A maternal survey will be performed. Body composition and bone density will be measured by dual energy X-ray absorptiometry. Blood pressure, pulse wave velocity, and augmentation index will be measured on two consecutive days. Chronic disease risk biomarkers will be measured in blood and urine samples. DNA will be extracted for genetic analysis. A faecal sample will be collected for microbiome analysis. Participants may provide their Manitoba personal health information number to link their study data with administrative health records.

Ethics and dissemination Ethics approval has been obtained from the University of Manitoba Health Research Ethics Board (protocol # HS18951; 05/01/2016). Data analysis, release of results and publication of manuscripts are scheduled to start in early 2019. Additional information at www.TMPLR.ca.

Trial registration number NCT03674957; Pre-results.

Strengths and limitations of this study

- The study is designed to capture extensive phenotyping of participants in the areas of diet, physical activity, sleep, genetic, gut microbiome profiles, and healthcare usage data linkage.
- The use of a mobile research unit to access rural populations makes the study unique as geographic setting can strongly influence health-related behaviours. The study uses non-random convenience sampling for feasibility reasons, which can introduce selection bias and limit generalisability.
- Some of the questionnaires used in The Manitoba Personalized Lifestyle Research (TMPLR) have not previously been validated, or not validated in the specific TMPLR study population.
- The study sample size of 840 individuals was not selected to power a specific primary hypothesis and therefore should be considered exploratory in nature.

INTRODUCTION

Manitoba is a province located in central Canada with a population of just over 1.2 million people. Most Manitobans (~60%)

live in Winnipeg, the largest city, with ~27% of the population living in rural areas.[1] Approximately half of Manitobans are living with at least one of the following chronic conditions: obesity, hypertension, type 2 diabetes (T2D), cardiovascular disease (CVD) or chronic kidney disease (CKD).[2] Additionally Manitoba has the highest incidence and prevalence of end stage renal disease in Canada, partly because of the high burden of diabetes.[2] The consequences of these chronic conditions are substantial and the financial burden, both personally and societally, is enormous. In the province of Manitoba, which has a universal healthcare system, over 40% of total provincial revenues are spent on healthcare.[3] The burden of conditions including T2D and CKD is not unique to Manitoba,[4 5] therefore the primary and secondary prevention of these chronic conditions is a major international health research priority.[6]

It is well established that diet, physical activity and sleep influence health and mortality.[7–10] Evidence-based guidelines pertaining to nutrition, physical activity, and sleep exist to educate the public on healthy lifestyle choices. However, most current lifestyle guidelines follow a one-size-fits-all format, even though they are intended for populations comprising individuals with diverse and complex health circumstances and unique factors influencing their ability to follow the guidelines. This format may be a contributing factor to the poor adherence to lifestyle guidelines. For example, although most people are aware that physical activity is important for health, only 15% of the Canadian population achieve the national recommendations.[11] Similarly, it is estimated that 50% of women and 70% of men in Canada have energy intakes that exceed their energy needs, while 50%–90% have deficiencies in calcium and vitamin D.[12]

There is now an increasing interest in the creation of lifestyle strategies or guidelines for specific subpopulations or groups of individuals with specific characteristics.[13–15] It is hoped that such tailored recommendations will be more effective, and that barriers to healthy lifestyle practices can be ameliorated through personalisation. Current one-size-fits-all recommendations and strategies may not be effective due to (1) significant inter-individual variability or (2) shared circumstances, such as geography, sleep/wake patterns or socioeconomic status, of a particular group.

We hypothesise that an individual's lifestyle will be influenced by socioeconomic status and geography, and will interact with their genotype and gut microbiota to affect health.[16 17] Accordingly, The Manitoba Personalized Lifestyle Research (TMPLR) study will involve the coordinated collection of data related to socioeconomic status, geography, nutrition, physical activity, sleep, early life experiences and health systems usage, in conjunction with the analysis of genetics, gut microbiota and risk factors for chronic conditions such as obesity, hypertension, T2D, CVD and CKD. After establishing the baseline characteristics of this study cohort, administrative health records will be used retrospectively to examine the developmental origins of health and disease,[18] and prospectively to track and investigate the development of chronic disease in the future, starting at 5 years after the initial study is complete. Consent will be obtained to contact study participants for further clinical assessments, contingent on future funding.

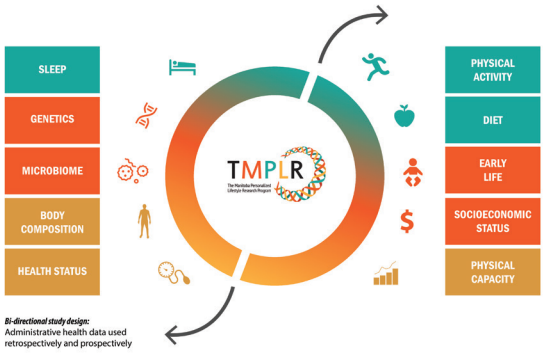

Figure 1 The Manitoba Personalized Lifestyle Research study overview.

Data from this study will provide an ideal opportunity for the exploration and potential discovery of new interactive mechanisms through which lifestyle factors affect health. We will be looking to collaborate with other existing studies[19–21] with overlapping measures to replicate such findings, or increase sample size. Findings from this research may be useful in guiding both clinical and health policy decisions, and will also facilitate the design and testing of personalised health promotion strategies. For example, if we are able to identify interactions between lifestyle factors and disease risk, such as a genetic variant that associates with short sleep to negatively impact health, a follow-up study could be designed looking to improve sleep hygiene specifically in the group with the risk variant.

METHODS

Design

This is an exploratory observational cohort study with retrospective and prospective utilisation of secondary data from administrative health records (figure 1). The Strengthening the Reporting of Observational Studies in Epidemiology guidelines were followed where applicable in the development of this protocol manuscript.[22]

Setting

Urban (Winnipeg) and rural (Morden, Winkler, Carman and Steinbach) areas with road access in southern Manitoba, Canada.

Objectives of the study

The objective of this study is to explore the complex interactions that exist between lifestyle, genetics and gut microbiota, and how these relate to risk factors for chronic conditions, especially obesity, hypertension T2D, CVD and CKD in Manitoba.

Table 1 The Manitoba Personalized Lifestyle Research study recruitment targets by strata

Age	30–46 years n=800							
Sex 50% Men 50% Women	400 Men				400 Women			
Geography 72% Urban 28% Rural	288 Urban men		112 Rural men		288 Urban women		112 Rural women	
BMI 40% Normal (BMI<25) 60% Overweight (BMI≥25)	116 Urban men BMI<25	172 Urban men BMI≥25	45 Rural menBMI<25	67 Rural menBMI≥25	116 Urban women BMI<25	172 Urban women BMI≥25	45 Rural women BMI<25	67 Rural women BMI≥25

+40 Participants with severely reduced kidney function (eGFR <30 mL/min), 20 women, 20 men, with no set stratification based on BMI or geography.
BMI, body mass index.

Inclusion and exclusion criteria

A sample of 800 Manitobans aged 30–46, stratified by sex, body mass index (BMI) and geography (table 1) are being recruited. Participants must have lived in Manitoba for a minimum of 5 years. Women who are pregnant or lactating are not eligible to participate. Additionally, because it is expected that very few of the 800 Manitobans who join TMPLR study from the general public will have reduced kidney function (eGFR<30 mL/min), 40 participants from Manitoba (20 women, 20 men, with no set stratification based on BMI or geography) who have severely reduced kidney function are being recruited from the renal health clinic at Seven Oaks General Hospital (SOGH), Winnipeg, Manitoba. Therefore, the study has a recruitment goal of 840 participants.

Recruitment

Participants are recruited through the use of printed flyers, online advertisements purchased via Google, Facebook and Twitter ad platforms and social media accounts, appearances in local TV, radio and print media, and direct contact with community groups, such as churches, sports leagues and community clubs. All patients who receive care in the SOGH renal health clinic, who are aged 30–46, have been living in Manitoba for a minimum of the last 5 years, and are able to provide informed consent are approached to enroll in the study as well.

Sample size

The sample size of TMPLR study was selected based on considerations of feasibility of recruitment, costs and logistics. However, given established values from other sources[23] and our anticipated sample size of 840 participants, we estimate that we will have an 80% power (5% significance, two-sided) to detect a minimum body fat difference of 2.5% for rare exposures (ie, experienced by 10% of participants, such as smoking) and 1.7% for more common exposures (experienced by 25% of participants, such meeting the Canadian recommended 150 min of moderate-to-vigorous physical activity). Additional estimated minimum detectable differences are presented in table 2. These lower limits should allow for the detection of clinically meaningful changes in these outcomes.

Data collection and assessments

On two consecutive days, participants come to either the urban TMPLR study site at the Richardson Centre for Functional Foods and Nutraceuticals, University of Manitoba or TMPLR's mobile research unit which travels to other areas of Winnipeg and southern Manitoba. TMPLR's mobile research unit is a custom built 12 m mobile lab which is equipped with phlebotomy area, a dual-energy X-ray absorptiometry (DXA) and a bicycle ergometer with a metabolic cart. During this visit, participants complete questionnaires, undergo various health assessments, provide urine and faecal samples, and have fasting blood samples taken (figure 2, table 3). The same protocols were followed at both sites.

Questionnaires

Questionnaires capture sociodemographic characteristics, personal and family medical history, smoking (including electronic cigarette use), current diet (three Automated Self-Administered 24 hours (ASA24) Dietary Assessment Tool recalls, Mindful Eating Questionnaire,[24] Diet History Questionnaire (DHQ)[25] and The Three-factor Eating Questionnaire[26]), alcohol consumption, physical activities, frailty using the Modified Fried Criteria,[27] stress, sleep (Pittsburgh Sleep Quality Index[28]), cognition (Montreal Cognitive Assessment Questionnaire[29]) and childhood retrospective circumstances (adapted from the US Panel Study on Income Dynamics[30]).

Anthropometric assessment

Weight is measured after participants change into lightweight scrub tops and bottoms, with shoes removed, to the nearest 0.1 kg using a digital calibrated floor scale (7562EF, Taylor Precision Products, Oak Brook, Illinois, USA). Height is measured, without shoes, to the nearest 0.1 cm using a stadiometer (Model 206, SECA North

Table 2 The Manitoba Personalized Lifestyle Research study estimated minimum detectable differences

Variable	Mean or median used	SD used	Minimum difference at 10% exposure (percentage of mean)	Minimum difference at 25% exposure (percentage of mean)	References
Body fat (%)	41.3% Women 27.8% Men	7.7% 6.6%	2.5% (6.0)	1.7% (4.0)	23
Lumbar bone mineral density (g/cm^2)	1.042 Women 1.058 Men	0.121 0.127	0.041 (3.8)	0.028 (2.6)	71
Glomerular filtration rate (mL/min per 1.73 m^2)	107.6	16.8	5.4 (5.0)	3.8 (3.5)	72
Systolic blood pressure (mm Hg)	116	12	6.5 (5.6)	4.5 (3.9)	73
Fasting glucose (mmol/L)	4.94	0.61	0.20 (4.0)	0.14 (2.8)	73
Fasting insulin (µIU/mL)	7.83	7.50	2.40 (30)	1.67 (21%)	74
LDL cholesterol (mmol/L)	2.79	0.67	0.22 (7.8)	0.15 (5.4)	73
Waist circumference (cm)	80	10	3.2 (4)	2.2 (2.75)	73

America, Chino, California, USA). BMI is calculated in kg/m^2. Waist circumference is measured in triplicate, to the nearest 0.1 cm at the umbilicus, between the last rib and the iliac crest using a fibreglass tape measure. Hip circumference is measured in triplicate at the widest portion of the buttocks and hips using a fibreglass tape measure. Body composition including fat mass, lean mass, per cent body fat, visceral adipose tissue and bone mineral density are assessed using DXA (Lunar Prodigy Advance, GE Healthcare, Mississauga, Ontario, Canada).[31] Scans are taken of the whole body, femoral neck, L1–L4 of the spine and the non-dominant forearm.

Figure 2 The Manitoba Personalized Lifestyle Research study participant schedule.

Clinical health assessment

Participants' systolic and diastolic blood pressures are measured in triplicate, on the non-dominant arm in a sitting position using a validated oscillometric blood pressure monitor (BP760CAN, Omron, Burlington, Ontario, Canada). Participants are required to rest for 5–10 min before taking the measurement. Pulse wave velocity and augmentation index are measured on the non-dominant arm in a sitting position using a Mobil-O-Graph PWA Monitor and the HMS Client Server Software (IEM GmbH, Stolberg, Germany) according to the manufacturer's protocol on two consecutive days.[32]

Collection of bio-specimens

Blood, urine and faecal samples are obtained from study participants (online supplementary protocols). Fasting blood samples are collected on two consecutive days via venipuncture by trained phlebotomists. Two blood samples on consecutive days are required to undertake the isotopic assessment of fractional cholesterol and triglyceride synthesis rates. Participants are asked to collect two urine samples at home; one sample is obtained prior to going to bed, and a second of the

Table 3 The Manitoba Personalized Lifestyle Research (TMPLR) study data, assessment tools and biological samples

Characteristic	Data	Method, instrument or source
Sociodemographic	Date of birth, sex, ethnicity, marital status	TMPLR Study Questionnaire
Medical	Personal medical history, family medical history, medication(s), pregnancy history	TMPLR Study Questionnaire, administrative health records
	Cognition	Montreal Cognitive Assessment[29]
Lifestyle	Tobacco/smoking/vaping use, alcohol use, unintentional weight loss, exhaustion, depression	TMPLR Study Questionnaire
Physical activity	Frailty	Modified Fried Criteria[27]
	Physical activity	Paffenbarger physical activity index, Actigraphy[41 42]
	Predicted VO_2 max	Modified YMCA bike test with metabolic cart
Nutrition	Dietary patterns and habits	Mindful Eating Questionnaire,[24] Three-factor Eating Questionnaire,[26] automated 24-hour dietary recall,[49] Canadian Dietary History Questionnaire[25]
Early life	Childhood health, sociodemographic status and socio-economic status; parental employment history	Childhood Retrospective Questionnaire, adapted from the US Panel Study on Income Dynamics[30]
	Maternal: pregnancy events, obstetrical history, infant feeding	TMPLR Mother's Retrospective Childhood Questionnaire, adapted from the Nurses Health Study[50]
Socioeconomic	Employment, home ownership, educational attainment, income	TMPLR Study Questionnaire
Sleep and stress	Duration of sleep	Actigraphy[46]
	Sleep quality	Pittsburgh Sleep Quality Index[28]
	Perception of stress, daily life stressors	Community-based stress and coping survey
Anthropometric	Height	Wall-mounted stadiometer
	Weight	Digital scale
	Waist circumference, hip circumference	Tape measure
	Body fat, lean mass, bone mineral density	Dual energy X-ray absorptiometry[31]
Blood pressure	Systolic and diastolic	Automated sphygmomanometer
	Pulse wave velocity, augmentation index	Mobil-O-Graph oscillometer[32]
Biomarkers	Blood clinical chemistry and biomarker assays	Fasting blood samples
	Urinary clinical chemistry and biomarker assays	Urine samples
	Microbiome 16S RNA sequencing	Faecal sample[37]

first morning void on waking up. Participants also collect a faecal sample; they are provided a collection kit and instructed to collect a single sample from three separate places on the stool using a spoon attached to the cap of the collection tube. Participants are instructed to store the collected faecal samples in their household –20°C freezer with a provided ice pack, and urine samples in the fridge, until transport back to the study centre, using provided ice pack for temperature control, where they are aliquoted and then stored at –80°C for future analysis.[33]

Clinical chemistry in blood and urine

Clinical chemistry, including lipid profile, glucose, insulin and renal and liver profiles will be measured via automated clinical chemistry analysers (Cobas C111, C311 and e411, Roche Diagnostics Laval, Quebec). Blood and urine biomarkers such as leptin, glucagon and melatonin will be measured via a ligand binding assay or ELISA. Red blood cell and plasma fatty acids will be measured by gas chromatography with flame ionisation detection (GC-FID).[34] Non-cholesterol sterols will be measured in plasma using GC-FID and mass spectrometry.[35] Vitamin C concentrations in the blood will be measured by high pressure liquid chromatography.[36]

Microbiome analyses in faecal samples

Faecal samples will be subjected to genomic DNA extraction (Zymo Research, California, USA) following the manufacturer's protocol. Experimental negative controls will be included in extraction protocols to confirm the reliability and consistency of the extracted nucleic acid. The V4 hypervariable region of 16S rRNA gene will be amplified, the sequencing library will be generated as described previously[37] and sequenced at the Gut Microbiome Laboratory, University of Manitoba. Samples will be multiplexed at the rate of 200 per run aiming for an average sequencing depth of 50 000 sequences per sample. The sequencing data will be deposited into the Sequence Read Archive of NCBI (http://www.ncbi.nlm.nih.gov/sra) and accession numbers will be provided for future access.

Deuterium oxide administration

After the blood sample collection on day 1, participants are given 0.7 g of deuterium oxide/kg of estimated body water to drink. Body water is estimated as body weight (kg)×0.60. This deuterium administration is used to enrich the body's water pool for the assessment of fractional cholesterol and triglyceride synthesis rates.[38–40]

Physical activity and capacity testing

Physical activity level in TMPLR study participants is assessed using accelerometers (Actigraph GTX3bt, Pensacola, Florida, USA) worn for 1 week.[41 42] Muscle strength is measured using a hand grip dynamometer. Cardiorespiratory fitness is assessed using a submaximal bike protocol which includes heart rate monitoring, and a metabolic cart (VMAX Encore, Carefusion, Unionville, Ontario, Canada) to measure oxygen consumption and CO_2 output. Functional walking ability is assessed using a 5 m gait speed test. Additionally, depressive symptoms, obesity history, frailty, low physical activity and cognitive impairment are assessed by validated questionnaires.[43–45]

Sleep assessment

Sleep in TMPLR study participants is measured objectively using accelerometers (Actigraph GTX3bt[46]) worn for a week and subjectively by questionnaire (Pittsburgh Sleep Quality Index[28]). While there is a strong relationship between objective and subjective sleep reports, TMPLR study is collecting both because discrepancies may provide important clinical information reflecting early dysfunction.[47 48]

Dietary assessment

Study participants complete the Canadian version of the DHQ,[25] which estimates the intake of common food items and includes portion size and dietary supplement questions. This questionnaire is on a TELEform for scanning data entry and creation of the data files. Participants also complete the Mindful Eating Questionnaire[24] to assess awareness of the physical and emotional sensations associated with eating, and The Three-Factor Eating Questionnaire[26] to assess dietary restraint, disinhibition and hunger in relation to eating. Participants also complete three dietary recall surveys using the Automated Self-Administered 24 hours Canada (ASA24, NCI, Rockville, Maryland, USA; http://asa24.ca/)[49] dietary assessment tool, a web-based tool that enables multiple, automatically coded, self-administered 24 hours recalls. Participants enrolled from March 2016 to February 2017 used the ASA24-Canada-2014 edition; those enrolled after February 2017 used the ASA24-Canada-2016 edition. Both ASA24-Canada-2014 and ASA24-Canada-2016 use the same nutrient databases.

Early life experiences

Early life exposures spanning the critical time windows of fetal development, birth, infancy and early childhood are documented in three ways: (1) through linkage with administrative health records (see Linkage to administrative health data section), (2) by self-report and (3) by maternal report. Administrative health data will provide method of birth, gestational age, birth weight, diagnosis codes for postdelivery hospitalisation and postdelivery drug prescriptions. Mothers of TMPLR study participants are asked to complete a TMPLR Mother's Questionnaire, adapted from the Nurses' Health Study,[50] capturing key pregnancy, birth and postpartum events such as method of birth; gestational age and birth weight; socioeconomic status at birth; maternal prepregnancy BMI and gestational weight gain; maternal smoking and diabetes during pregnancy; maternal prenatal care; breastfeeding initiation, exclusivity and duration; stressful life events during pregnancy and post partum; and severe illness requiring hospitalisation during infancy or early childhood. Early childhood socioeconomic status[51 52] and stressful life events[53 54] are also self-reported by TMPLR participants using the Childhood Retrospective Circumstances Questionnaire, adapted from the US Panel Study of Income Dynamics.[30]

Data quality assurance and control

Methods of data collection (questionnaires, anthropometric assessment and clinical health assessment) were standardised across the urban and mobile TMPLR study sites. Training of TMPLR study staff involved in data collection and data entry is regularly refreshed and all staff handling participant data are trained in compliance with the Manitoba Personal Health Information Act. All data will be entered in the secure digital platform. A TMPLR study data model has been created to help in visualising the different types of data the digital platform will contain. (online supplementary figure 1)

Linkage to administrative health data

At enrollment, TMPLR participants are asked to provide their personal health information number (PHIN) and grant permission to link their study data with administrative health records (including hospital discharge abstracts, physician billing claims and prescription records). These data are accessed through the Manitoba Centre for Health Policy (MCHP) Population Research Data Repository[55] and linkage is achieved using the PHIN, following the standard procedures established by the MCHP and the Manitoba Health Information Privacy Committee. The data linkage is used to capture retrospective information on early life as well as prospective information on numerous health outcomes, including diagnosis of hypertension, T2D, CVD and CKD.

Statistical analyses

Statistical analyses will be undertaken in consultation with biostatisticians from the George and Fay Yee Centre for Healthcare Innovation at the University of Manitoba. Lifestyle factors will primarily be used as explanatory variables, with chronic disease biomarkers or disease presence/absence as outcomes, in multivariable regression models. Moderating or mediating effects of genetics, gut microbiome, clinical characteristics, socioeconomic status and environmental factors will be explored. The potential confounding effects of health status and healthcare use on variable relationships will be examined using techniques such as propensity score or instrumental variable models.[56–58]

Techniques appropriate for high-dimensional data will be adopted where needed. For example, clustering of lifestyle risk factors will be examined using latent variable modelling techniques (ie, latent class analysis). Dimension reduction techniques for omics data, such as microbiome and genetic markers, will be applied.[59]

The bioinformatics and statistical analyses of microbiome data will be performed as described previously[37] and will be updated based on recommendations and technology advancements between now and the point of processing of samples. Overall microbiota community structures, alpha diversity metrics and relative abundances of operational taxonomic units will be tested for associations with lifestyle and health measures, with appropriate adjustment for multiple comparisons.

Non-response bias or inability to collect certain data may affect the validity of analyses for survey data or biological measures, necessitating the use of multiple imputation methods if the pattern of missing data is deemed to be ignorable.[60] For non-ignorable missing data, selection and pattern mixture models will be examined in sensitivity analyses.[61] Due to the use of non-random sampling there is a risk of selection bias; survey weights and weighting of responses may be used to address this bias. Standardisation or adjustment techniques may be used to address bio-specimen measurement error bias.[62]

Specialised methodological investigations will be conducted for: (1) psychometric analyses of scales, including testing for differential item functioning and measurement invariance,[63–65] (2) development of chronic disease risk prediction models,[66 67] (3) techniques to evaluate the quality of linked databases, including their accuracy, reliability and completeness[68] and (4) robust statistical methods for the analysis of outcome measures with non-normal (eg, skewed) distributions.[69 70]

Patient and public involvement

Three focus groups, one for healthcare providers and two for general public, and a public forum were held in the early design stages of this study to obtain input from Manitobans, on the study design and recruitment strategies. A study advisory board was also formed, and meets on a bi-annual basis. This advisory board includes healthcare providers, health researchers and members of the public. The board provides input regarding study recruitment, progress and conduct, and will also provide input and suggestions regarding the dissemination of study results.

Provision of clinical results to participants

Individual results of the anthropomorphic measurements, blood pressure, pulse wave velocity, augmentation index, body composition, bone density, full lipid profile, fasting blood glucose, and renal and liver profile are to be provided to participants. Participants are referred to their primary care providers for further management if their results are beyond clinical reference ranges. Participants will not be provided their genetic and microbiome information.

Ethics and dissemination

Explicit informed consent is obtained from each individual prior to participation in the study. Eligible participants are verbally informed by trained research personnel regarding the nature and purpose of the study, given time to decide whether or not to participate, and have any questions or concerns answered prior to consent and at any point throughout the study. All participants are informed that they may withdraw from the study at any time without penalty and are remunerated for the portion of the study that they have completed up to that point. The full remuneration for study participation is $100 Canadian dollars, provided as cash or as a gift card.Data analysis, release of results and publication of initial manuscripts are scheduled for 2020. Findings will be shared in peer-reviewed journals, and at regional, national and international scientific conferences. Data and findings will also be presented to healthcare policymakers within Manitoba, to develop preventive strategies that reduce chronic conditions with the intention of reducing healthcare costs. Funding applications for future clinical follow in this study population have been submitted starting in 2017.

DISCUSSION

TMPLR study has been uniquely designed to provide cross-sectional, retrospective and prospective observations that will improve our understanding of how lifestyle factors interact with each other and factors such as genetics and the gut microbiome to influence health and the risk of obesity, T2D, CVD and CKD. The coordinated collection of lifestyle-gene-environment-microbiota-health data, including objective measurements such as DXA, activity monitoring, stable isotopic tracer methodologies and direct measurement of physiological biomarkers; combined with the ability to retrospectively assess and prospectively follow health outcomes in participants using administrative health records, represents an unprecedented opportunity to collect data which can be used to improve chronic disease prevention and management.

Due to the voluntary non-random recruitment of participants, there may be an under-representation of those with lower health awareness, financial means, access or time to participate. Attempts to counteract this are implicit in the stratified recruitment design. Comparisons between TMPLR study participants and general Manitoban population demographics may allow assessment of potential selection biases. A healthy volunteer effect may impact the ability to detect weak associations between lifestyle and disease risk, but this may attenuate with longer follow-up using administrative health data.

Given a projected sample size of 840 participants may be low for some of the research questions that will be investigated, therefore harmonisation and linking of data across multiple cohorts may be required. We will be looking to other studies which have undertaken overlapping

measurements in order to increase sample sizes. The Canadian Longitudinal Study on Aging,[19] the Toronto Nutrigenomics and Health[20] and The LifeLines DEEP[21] studies among others will be approached regarding the potential of data harmonisation and cross-replication. TMPLR study will also be available to other researchers who are interested in collaboration or using the data for cross-replication.

In summary, TMPLR study will provide a unique platform of extensively phenotyped individuals that will be used to explore the interactions between lifestyle factors that associate with the development of, or protection from, obesity, hypertension, T2D, CVD and CKD. The findings from this research platform will subsequently be used to develop and test preventive and restorative lifestyle and health strategies with the aim of improving the health and reducing healthcare costs at the individual and population levels.

Study status

Data collection started in March 2016. As of the 15 August 2018, data collection is ongoing and has passed 800 participants. Data collection is expected to end in December 2018.

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Contributors DSM and RCM developed the original concept of the study for the original grant application with input from co-investigators. DSM prepared the drafts of the study protocol manuscript and compiled feedback and changes from other authors. RCM and MG assisted in the preparation of the study protocol manuscript. PF developed the branding and logo for TMPLR study, and the manuscript figures and tables. NCH prepared the data model and was involved in the public engagement. SB (project lead, indigenous health), HB (project lead, nutrition), JC, TAD (project lead, physical activity), PKE (project lead, genetics), EK (project lead, gut microbiome), LML (project lead, biostatistics), DEM (project lead, sleep), SBM, AR, NT, MBA (project lead, developmental origins of chronic disease), and PJJ (Director) are study co-investigators, and were all involved in writing the original grant application. All authors have carefully read, contributed to, and approved the final version of the study protocol manuscript.

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