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Cohort Profile

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Cohort Profile: TWINS study of environment, lifestyle behaviours and health

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Introduction

The role of built and social environments in supporting healthy lifestyles has received increased attention over the past decade, as research and prevention paradigms have shifted from a focus on individual-level behaviour change to macro-level influences embedded within social-ecological models of health that impact upon populations. The TWINS Cohort was set up to link biological and survey data with multiple built and social environment exposures developed from geocoded residential addresses of adult twins enrolled in the community-based Washington State Twin Registry (WSTR).

The major rationale for establishing TWINS is that co-twin control studies enable the detection of environmental effects on health while reducing the structural confounding and biases inherent in studying unrelated individuals who have not been randomly assigned to different environments,[1–3] as would happen in a randomized controlled trial. In this framework, twins are used as quasi-experimental controls for shared genetic and environmental effect confounds that cannot be held constant via random assignment.[4,5] The core logic is that observed associations between an uncontrolled risk factor (e.g. walkability) and outcome (e.g. physical activity) may be the result of a causal relationship between the two, or from uncontrolled genetic or family environment confounds. A within-pair association, in which the member of the twin pair exposed to the purported cause is more likely than the unexposed co-twin to exhibit the outcome, increases the confidence of there being a causal relationship.[5,6] Thus, twin studies are an alternative to randomized controlled trials of environmental exposure and risk when randomized trials are not possible due to practical or ethical concerns. In our research, we use the twin design to identify potentially causal associations among environmental exposures, lifestyle behaviours and a broad array of physical and mental health outcomes.[7]

Who is in the cohort?

Members of the TWINS Cohort are a subset of the larger WSTR. Construction of the WSTR is described elsewhere.[8,9] Briefly, the Department of Licensing (DOL) in Washington State assigns licence/identification numbers as an encoded version of the applicant's date of birth, last name and first and middle initial. Twins have the potential to generate the same licence number, so the DOL asks all applicants 'Are you a twin?' This method of bypassing duplicate licence numbers is unique to Washington State.[8]

Registry recruitment began in 2002.[8] By completing an initial enrolment survey, twins consent to join the Registry and to be contacted about potential studies. We made several changes to the initial survey in 2008—see Enrollment Survey at [https://wstwinregistry.org/documents/2015/09/en rollment-survey.pdf/]—including how residential addresses were recorded by providing clarifying information to the participants and using a standardized block format for entry. This allowed us to record residential address as a longitudinal data element (the same way medical records such as weight and blood pressure are stored) so that characteristics of the home neighbourhood could be temporally and spatially matched with contemporaneous survey data (and in some cases biological data). The TWINS Cohort is thus composed of all WSTR twin pairs with matched address and survey data, retrospective to all twins who completed an enrolment survey in 2008. The Cohort links longitudinal survey data with environmental exposures, to analyse changes in environments, behaviours and health. The flowchart in Figure 1 shows how twins are initially enrolled in the WSTR and then included in the TWINS Cohort (and any relevant subcohorts) after their addresses are geocoded.

As of this publication, the WSTR has 9070 complete adult twin pairs (18 140 individuals) over 18 years of age and 359 youth twin pairs (718 individuals) under 18 years of age. The TWINS Cohort has 6596 adult pairs (13 192 individuals). Over half (55%) of all twin pairs in the Cohort are monozygotic, based on survey questions about childhood similarity (which classify zygosity with an accuracy of 95–98%).[10,11] Because inclusion in the Cohort is based on enrolment in the Registry, recruitment criteria and participation are drawn from the larger WSTR. At minimum, one member of each pair has lived in

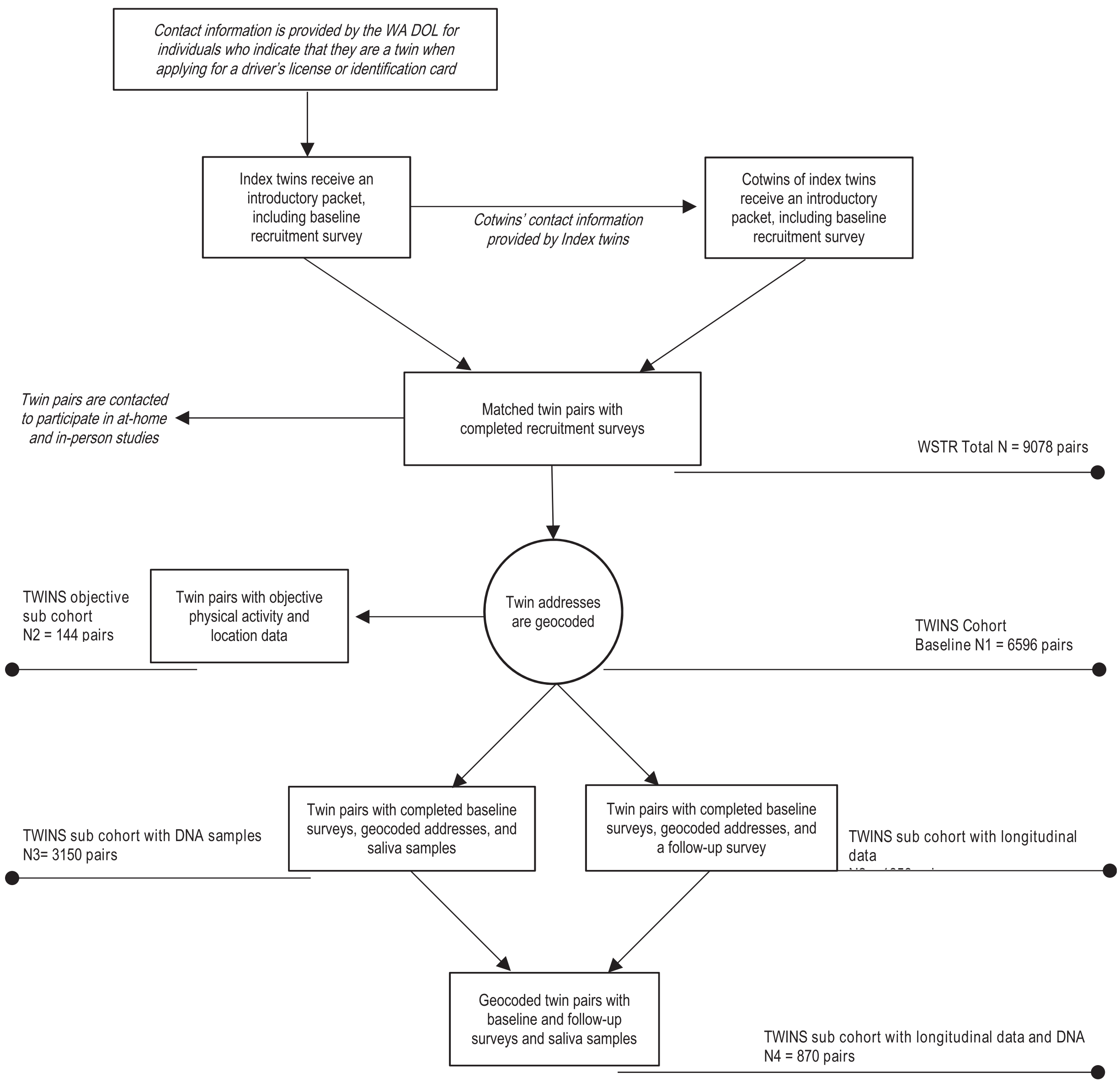

Figure 1 Flowchart of Washington State Twin Registry and TWINS cohort with subcohorts. *Twins enrolled in WSTR before 2008 are not included in the TWINS cohort. **Not all twins who completed surveys provided saliva samples.

Washington State at some point in his or her life. After eliminating twins known to have incorrect addresses, the response for index twins (the initial twin who is contacted, based on information from the DOL) ranged from 10% to 38% across 60 independent mailings to over 90 000 index twins. The response rate for co-twins (contingent on receiving an initial response from the index twin) has been higher, at 50–71%.

Select sociodemographic characteristics of the TWINS Cohort compared with the general population of Washington State are provided in Table 1. Because of its community-based construction methods, the WSTR, and by extension TWINS, are generally representative of the broader demographics of Washington State, with a few exceptions as described in the Strengths and Weaknesses section.

How often have they been followed up?

The first follow-up for the Cohort is available from twins beginning in 2010. As of this publication, 1656 complete pairs in TWINS have a baseline (Enrollment Survey) and at least one follow-up survey available—see Health and Wellbeing Questionnaire at [https://wstwinregistry.org/documents/2015/09/2628.pdf/]— including measures of environmental exposures, lifestyle behaviours and health outcomes. We conduct waves of follow-up every 2–3 years, and this is an active, ongoing process; 1313 complete pairs have two follow-up surveys, and 337 pairs have three follow-up surveys.

In addition to data collection, twins receive birthday cards and quarterly newsletters with updates about current studies and other information that may be of interest. These mailings serve as a means of communicating information to the twins and help to maintain an up-to-date address database. We use e-mail as the primary form of communication between Registry personnel and enrolled twin pairs for those who have supplied an e-mail address (approximately 70% of WSTR participants). We have an active social media presence for communication, which has greatly helped in our efforts to maintain contact and current addresses with members.

What has been measured?

The defining feature of the TWINS Cohort is its spatial data on built and social environments, which are linked to the WSTR's extensive repository of survey data. Researchers can access the enrolment and follow-up surveys on our web page, using the URLs previously noted, to get a sense of the broad array of self-reported behavioural, mental and physical

Table 1. Select sociodemographic characteristics of the TWINS cohort and Washington State

	Twins ($n = 13\ 192$)	WA State ($n = 7\ 280\ 934$)
Age at initial survey, median years (SD)	39.8 (18.2)	37.6
Sex		
Female, %	63	50
Household income, %		
US$49 999 or less	39	40
US$50 000 or more	61	60
Marital status, %		
Single	32.1	31.3
Married	49.1	47.9
Other	18.8	20.7
Hispanic, %	3.5	11.2
Race, %		
American Indian or Alaska Native	0.5	1.5
Black or African American	1.6	3.6
Native Hawaiian or Pacific Islander	0.3	0.6
Asian	2.2	7.2
White	90.5	77.3
Other	1.5	5.2
Two or more races	3.4	4.7
Completed education, %		
8th grade or less	0.2	3.9
9th-11th grade	3.2	5.5
12th grade or Equivalency	16.9	22.9
Some college or vocational school (no degree)	25.3	24.3
Associate degree	9.2	9.8
Bachelor degree or higher	45.2	33.6

Table 2. Available data by assessment area, year and sample size: Washington State Twin Registry and TWINS Cohort

Assessment area	Twin pair *n*	Ongoing recruitment	Earliest data available[a]	Most recent data available
Baseline sociodemographic survey[b]	9078	✓	2002	2018
Baseline and geocoded address[c]	6596	✓	2008	2018
Baseline survey, geocoded address and saliva sample[c]	3150		2010	2012
Follow-up survey and geocoded address[c]	1656	✓	2010	2018
Follow-up survey, geocoded address and saliva sample[c]	870		2010	2012

[a]Date refers to enrolment and hence earliest data available for follow-up.
[b]Indicates current sample size for the overall Washington State Twin Registry.
[c]Indicates current sample sizes for the TWINS Cohort and subcohorts based on availability of saliva for DNA analyses and follow-up survey data.

health measures obtained on the twins. Bio-specimens and objective physical and clinical measures are available from subsamples of the Registry (and Cohort) who have completed in-person studies. Table 2 provides a high-level overview of the measures available in the TWINS Cohort.

The environmental exposure data are made possible by the care with which we collect residential address information and keep it maintained in our database; addresses are subsequently geocoded to create spatial X and Y coordinates, then integrated with environmental data available in geographical information system (GIS) databases extending across the USA. Using these data, we developed several exposure measures associated with the built and social environments. Each twin's residential environment is described in terms of their home neighbourhood's walkability, level of urban sprawl, amount of vegetation, material and social deprivation, property values and crime rates. A brief description of built and social environment indices is provided below.

Built environment

Walkability

TWINS Cohort data include several walkability indices that differ in terms of robustness and generalizability. Accordingly they require different geospatial data, with more sophisticated measures demanding finer-grained data (e.g. parcels or tax lots). The commercially available Walk Score® index uses data derived from multiple publicly available sources to estimate walking distance to amenities in nine categories (e.g. schools, parks, restaurants) and creates a continuous score normalized on a scale of 0–100, with 100 being the most 'walkable' neighbourhood.[12] The index is a valid and reliable proxy measure of neighbourhood density and access to nearby amenities when compared with objective measures of the physical activity environment using a GIS.[13,14] The Frank *et al.*[15] walkability index calculates a walkability score using measures of land use mix, net residential density and street connectivity in a 1-km buffer around each twin's home. The output is a single value representing the walkability score for each participant.

Finally, we created a measure of neighbourhood walkability called P_{walk}[16–19] using high-resolution environmental data integrated in GIS databases for urbanized areas in Washington State. Unlike other measures of walkability, P_{walk} also includes behavioural and demographic variables in addition to geospatial variables. All these variables were modelled as predictors of twins' self-reported walking and total moderate-to-vigorous physical activity (MVPA). Using a threshold of 150 min per week,[20,21] a backward elimination approach established the best subset of independent variables to include in models predicting time in walking or MVPA within a half-mile and one-mile buffer of the residential address as a measure of the final P_{walk} index.

County Sprawl Index

Developed by Ewing *et al.*,[22] six measures related to population and urban form characteristics are combined in an index representing the degree of urban sprawl within a given county. The index was acquired from Ewing and attached to the 2000 Census County Cartographic Boundary Files using ArcGIS 9.3.1. The scores range from 55 to 352, with larger values indicating more compact counties.

Normalized Difference Vegetation Index (NDVI)

The NDVI is a measure of how 'green' an area is. It is calculated using visible and near-infrared light reflected by vegetation, obtained from satellite imagery. Healthy or dense vegetation absorbs most visible light and reflects a large portion of near infrared light. Unhealthy or sparse vegetation reflects more visible light and less near infrared light. We standardized NDVI values from –1 (usually water) to +1 (dense, healthy green vegetation), as described by others.[23–25]

Social environment

Area material and social deprivation (Singh Index)

First described by Singh in 2003,[26] factor analysis-based coefficients are derived from 17 census tract level indicators, including educational attainment, income disparity, poverty rates, home ownership rates, crowding and single-parent households. The index is calculated by standardizing the indicator values and multiplying the standardized values by the published coefficients. Standardized to Washington State, Singh index values range from −2.9 (least deprived) to +4.6 (most deprived).

Property values

Washington State property value assessment data capture measures of wealth or deprivation in the microenvironment around individual residences. Based on our previous research,[27,28] two measures related to property values are available: (i) the mean assessed property value per residential unit in the parcel where a person lives; and (ii) the mean assessed property value per residential unit in the immediate 'neighbourhood', using a radius of 833 m to represent the individual proximal neighbourhood within a 10-min walk.

Crime Index

The crime index is an aggregation of seven main offence classifications in the Uniform Crime Reporting Statistics (UCR) and used by Doyle *et al.*[29] The index is available for localities with populations above 10 000; the latest date of issue is 2009. For comparability between jurisdictions, crime rates are calculated per 100 000 population.

What has it found? key findings and publications

A complete listing of publications generated from WSTR resources, including the TWINS Cohort, is available on the WSTR website: [https://wstwinregistry.org/for-researchers/publications]. Below we highlight findings from our studies which focus on environmental influences on health.

Several recent papers detailed our expertise in characterizing the food environment,[30] integrating data from accelerometer and GPS devices using common timestamps into a *LifeLog* data structure,[31] and describing a theoretical framework in which twin research can overcome major problems in the neighbourhood-effects literature.[7] Using this framework, we tested associations between walkability (Walk Score®), activity level (neighbourhood walking and MVPA), and body mass index (BMI) in 6376 same-sex pairs using TWINS.[32] We used methods employed in behaviour genetics.[5] Specifically, regression models that do not include controls for genetic and shared environment factors, termed 'phenotypic', are compared with models that do include such controls, termed 'biometric'. We found that neighbourhood walkability was positively associated with neighbourhood walking (but not MVPA) in phenotypic analysis, and this association was unchanged when accounting for individual genetic and shared environmental pathways in biometric analysis. However, neighbourhood walkability was not associated with BMI in phenotypic or biometric analysis. As expected, both walking and MVPA were positively associated with BMI in phenotypic analysis and remained so after biometric controls were applied (i.e. after accounting for genetic and shared environmental background). These results support the hypothesis that higher neighbourhood walkability is potentially causally associated with increased neighbourhood walking and, in turn, higher neighbourhood walking levels are potentially causally associated with reduced BMI.

We extended the above findings by investigating influences of walkability and PA on variation in BMI.[33] We re-examined previous studies that found associations between PA and genetic variance in BMI (gene-environment interaction, $G \times E$) by also accounting for gene-environment correlation (*r*GE). These findings suggest that individuals with a lower genetic susceptibility to high BMI may also be more active, or that individuals with a lower genetic susceptibility to high BMI select into environments or choose environmental experiences that require more PA. Consistent with past findings,[34,35] we observed that PA (measured as both neighbourhood walking and MVPA) suppressed genetic risk for high BMI, even after accounting for *r*GE. Neighbourhood walkability decreased the genetically explained variance in BMI. However, this effect was not present when also adjusting for the effect of PA, suggesting that PA mediated the effects of walkability on BMI. This result is consistent with previous research on the main effects of walkability, which suggest that walkable neighbourhoods have stronger influences on weight reduction over 1 year compared with less walkable neighbourhoods, but only if individuals within those neighbourhoods engage in physical activity.[36]

Other recent papers from TWINS investigated access to green space and depression,[37] social deprivation and sleep,[38] fast food consumption and BMI,[39] individual- and community-level measures of socioeconomic status (SES) with genetic and environmental influences on BMI,[40] and neighbourhood deprivation and depression controlling for gene-by-environment interactions.[41] In summary, our use of genetically informed twin models is unique because it allows us to focus on macro-level influences (i.e. social and BEs) on health while controlling for as many of the individual-level influences (e.g. genetics, sociodemographics, psychological factors, family factors, social norms) as possible, leading to better estimates of causal relationships between environmental exposure and risk.

One limitation of the work discussed above was a reliance on self-report measures; a specific goal of NIH-funded projects using sub samples of TWINS was to address this and other methodological issues. Using objective accelerometer and GPS data from 102 individual twins enrolled in a study of 144 monozygotic twin pairs recruited from the TWINS Cohort (TWINS objective subcohort, see Figure 1), we estimated the association between home neighbourhood walking and walkability within different sizes and types of neighbourhood buffers.[42] The study found that objectively measured walking bouts were related to neighbourhood walkability, and that associations held when controlling for the correlated nature of the twin sample and for sex, age, BMI and income. The study findings were important from a public health standpoint because they indicated that an individual living in a 'Walker's Paradise' with a Walk Score® of 95 would perform substantially more health-enhancing walking bouts within their home neighbourhood than an individual living in a 'Car-Dependent' neighbourhood with a Walk Score® of 25.

Next, we analysed the 144 pairs from the TWINS objective subcohort to quantify physical activity conducted inside and outside empirically defined neighbourhoods. We paid careful attention to processing the extensive data from accelerometers and GPS loggers from these 144 twin pairs, all of whom completed a 2-week collection period, and subsequently placed these data into the *LifeLog* framework.[31] We computed PA levels as: (i) walking in modified 10-min bouts[42,43]; and (ii) MVPA in modified 10-min bouts (and 1-min epochs).[44–47] Home BE 'size' was represented using 833 m and 1666 m circular buffers. We computed total minutes per week of walking and MVPA within and outside the home neighbourhood; 'within' neighbourhood was conceptualized using two definitions. The 'strict' definition assumed the entire bout was contained within the buffer (see Figure 2, line a). The 'flexible' definition considered bouts to be within the neighbourhood if the bouts began or ended within, or traversed, the buffer; however, only the portion that was contained within the buffer was counted as PA within the neighbourhood (see Figure 2, lines a-e). Table 3 provides descriptive baseline data from this study. Importantly, we are currently expanding the number of twin pairs with accelerometer and GPS data and following up twins who previously collected these data approximately 3 years ago. Thus, this subcohort of TWINS has objectively measured PA bouts including spatial context to determine longitudinal, causal associations between changes in built and social environments on lifestyle behaviours and health.

What are the main strengths and weaknesses?

We are unaware of any other twin cohort that obtains spatial data for the purposes of longitudinal investigation of

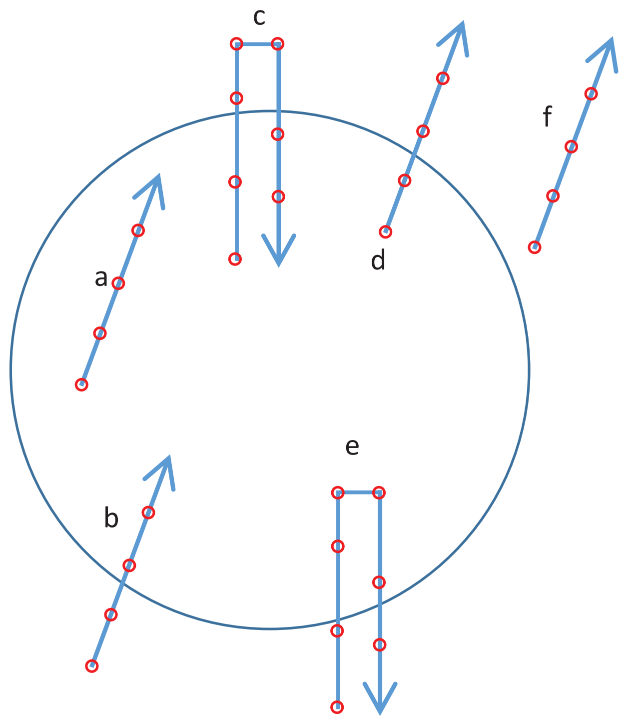

Figure 2 Spatial quantification of physical activity bouts within neighbourhoods. Line (a) indicates a bout in which all GPS points are contained within a pre-specified buffer; (b) a bout in which the GPS points end in and traverse the buffer; (c) a bout in which the GPS points start and end in and traverse the buffer; (d) a bout in which the GPS points start in and traverse, but do not end in, the buffer; (e) a bout in which the GPS points do not start or end in, but traverse, the buffer; and (f) a bout in which none of the GPS points are contained in the buffer.

environmental exposures on health behaviours and health outcomes. The main strength of the Cohort is that twins offer unique advantages for the study of potentially causal consequences of environmental factors on outcomes of interest which cannot be experimentally controlled; twin controls allow for the analysis of matched pairs that inherently adjusts for major confounding factors (e.g. age and sex) and typically unmeasured familial factors including genetic factors. Another strength is that the WSTR continues to actively recruit twins, so new twins are continually being added to the Cohort and subsequently followed up at regular intervals to track members over space (i.e. changes to place of residence and the associated built environment) and time. As such, the Cohort is a unique resource for investigators across multiple disciplines, who wish to apply twin methods to control for genetic and common familial factors in their research.

Despite its community-based construction method, the TWINS Cohort differs from the general Washington State population in terms of race/ethnicity and education (Table 1). We lack information on exposures and behaviours in childhood, although that is a new area of investigation we are pursuing. Because of the young entry age and

Table 3. Objectively measured physical activity levels in identical twins ($n = 144$ pairs) using two methods for quantifying activity bouts within neighbourhoods of differing sizes

	83-m buffer		1666-m buffer	
Strict definition	Inside	Outside	Inside	Outside
Walking (min per week)	60.3 ± 64.0	124.7 ± 139.7	75.7 ± 83.2	109.4 ± 132.0
MVPA (min per week)	35.2 ± 56.7	105.3 ± 113.4	51.1 ± 72.6	89.4 ± 102.7
Less strict definition				
Walking (min per week)	77.3 ± 85.2	107.7 ± 131.9	84.4 ± 91.4	100.6 ± 128.2
MVPA (min per week)	57.2 ± 79.7	83.3 ± 96.5	63.3 ± 84.9	77.2 ± 93.2

Neighbourhood size represented using 833 and 1666 m circular buffers. Within neighbourhood walking and MVPA bouts defined as: (i) strict, assumes the entire bout contained within the buffer; and (ii) flexible, considers bouts that begin or end within, or traverse, the buffer.

the fact that the Registry has been in operation for only a little more than a decade, the mean age of twin pairs is relatively young, so there are few of the 'hard' health events that typically occur later in life (e.g. heart disease) for use as outcomes. Finally, because of the nature of information we obtained from the DOL, we lack precise data on twin pairs who choose not to respond to the WSTR's survey mailings. We know that non-respondents are more likely to be younger males than enrolled twins (based on analysis of index twins), but we do not know what impact these differences, or other unmeasured differences, may have on our outcomes and exposures of interest.

Can I get hold of the data? where can I find out more?

Any investigator seeking to use data or samples from the TWINS Cohort in their research is invited to contact Glen Duncan, the Director of the WSTR and corresponding author for this Cohort Profile. Information describing the application process is available at the WSTR website: [https://wstwinregistry.org/]. The Registry operates as a cost-centre that is funded through extramural grants to WSTR investigators, and on a cost-recharge basis for non-WSTR investigators wishing to use twin data in their research. Access fees vary according to the data requested and opportunities for collaboration. Fees for graduate student research are typically waived, except for the use of finite resources such as biological specimens.

Profile in a nutshell

- The TWINStudy of Environment, Lifestyle Behaviours, and Health (TWINS) is a longitudinal cohort of adult monozygotic and dizygotic twins which allows for the analysis of matched pairs. Our research focuses on TWINS as a unique resource to identify potentially causal associations between environmental exposures, lifestyle behaviours and a broad array of physical and mental health outcomes in free-living individuals, which cannot be studied using randomized controlled trials.
- The initial wave of data collection began in 2008 and the sample is currently $n = 6596$ pairs. Follow-up assessments occur every 2–3 years in each pair. Sample sizes for follow-up assessments include $n = 1656$ with 1, $n = 1313$ with 2 and $n = 337$ pairs with 3 time points.
- TWINS focuses on environmental influences, including measures of the built and social environment, on lifestyle behaviours and associated health outcomes such as body mass index and cardio-metabolic disease. There is also a wide range of health topics addressed in the surveys such as mental health, pain, sleep and psychological states, as well as biospecimens and objective measures for subcohorts.
- The Registry operates as a cost-centre that is funded through extramural grants to WSTR investigators, and on a cost-recharge basis for non-WSTR investigators wishing to use twin data in their research. Access fees vary according to the data requested and opportunities for collaboration. For more information, visit: [https://wstwinregistry.org/].

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