

Research Article



# Determining If Walkability and Bikeability Indices Reflect Pedestrian and Cyclist Safety

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#### **Abstract**

Walkability and bikeability indices are used to succinctly quantify how conducive an environment is to walking and cycling, often including factors related to comfort and perceived safety. The potential assumption that "walkable" and "bikeable" mean safe for walking and cycling (i.e., the association with objective safety or crash risk) has not yet been examined. This study investigates the association between two widely used measures (walk score and bike score) and pedestrian and cyclist crashes in Vancouver, Canada, to determine whether more walkable and bikeable areas of the city are also safer for walking and biking, after controlling for exposure. Multivariate Bayesian crash models with random and spatial effects are developed for pedestrian—motor-vehicle and cyclist—motor-vehicle crashes in 134 traffic analysis zones using 5 years of crash data with walking, cycling, and motor-vehicle traffic volume controls for exposure. Results indicate that areas of the city with higher walkability and bikeability can be potentially associated with greater pedestrian and cyclist crash risk, respectively, even after controlling for exposure. While the clear answer is that neighborhood walkability and bikeability does not indicate safety for pedestrians and cyclists, questions remain as to whether they should, and if so, how they could be modified to better incorporate objective risk.

Walking and cycling, as modes of urban transportation with potential health and environmental benefits, are promoted in cities around the world through initiatives that include the provision and improvement of pedestrian and cycling infrastructure. With increased attention on active transportation, a robust literature has developed examining associations between walking and cycling activity and the built environment. The interdependence and correlation of various attributes of the built environment that influence travel choices have resulted in the creation of indices which succinctly quantify how conducive an environment is to walking and cycling activity. These walkability and bikeability indices are used in research, transportation practice, and even real estate services.

Figure 1 illustrates the conceptual framework for this study. Diverse environmental factors influence walking and cycling activity in various ways. To focus on the scope of the study, In Figure 1, safety is separated from all other considerations such as travel time, effort, and weather. Safety as perceived by pedestrians and cyclists can diverge from objective safety, although the two are related and both negatively influenced by factors such as motor-vehicle traffic. Ultimately, it is the perceived

safety (sometimes referred to as comfort) that influences walking and cycling choices, rather than the objective crash risk (which is not precisely known to travelers). Previously developed walkability and bikeability indices incorporate various environmental factors and have been designed and validated by association with walking and cycling activity (the dashed line in the figure). Some indices include safety-relevant environmental factors, such as the presence of bike lanes, but through the lens of comfort or perceived safety (the pathway to activity outcomes). What has not yet been examined is the association between walkability and bikeability indices and objective safety or crash risk. There is likely to be an implicit assumption (at least by the traveling public) that walkable and bikeable means safe for walking and biking, but that might not be true.

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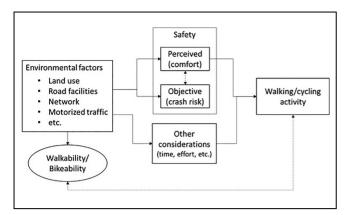


Figure 1. Study framework.

This study investigates the association between Walk Score® and Bike Score® and pedestrian and cyclist crashes, respectively, in the City of Vancouver, Canada. Walk and Bike scores are selected as two of the mostused and easily-accessed walkability and bikeability indicators. The objective is to determine whether more walkable and bikeable areas of the city are also safer for walking and biking, after controlling for exposure. Motorist–pedestrian and motorist–cyclist Bayesian crash models are developed for Vancouver's 134 traffic analysis zones (TAZ) using 5 years of crash data. The crash models include walk and bike scores and traffic exposure measures: vehicle kilometers traveled (VKT), bike kilometers traveled (BKT), and walking trips.

# Literature Review

## Walkability Indices

An early quantitative measure of walkability was the Pedestrian Environment Factor (PEF) (1). This was a composite score of four three-point parameters: ease of street crossings, sidewalk continuity, local street characteristics, and topography. Points were decided on by the reviewers and involved considerations such as block length. PEF significantly correlated with auto ownership, mode choice, and destination choice at the zone level. While reviewers were trained, and reviewer scores were relatively consistent, PEF was a subjective index of walkability.

Later measures of walkability aimed for less subjective criteria. Frank et al. developed a Walkability Index (WI) to explain objective measures of physical activity. The WI was calculated as a weighted sum of z-scores of net residential density, street connectivity (intersection density), and land-use mix within a buffer (2). The WI was found to explain variation in time spent in moderate daily physical activity, beyond socio-demographic effects. Kuzmyak et al. developed the Walk Opportunities Index

(WOI) to capture the effect of land-use factors on VMT by household (3). The WOI was calculated based on intersections and walk opportunities within a quartermile of a household, and had moderate positive correlation with several measures of household VMT.

The Pedestrian Environment Index (PEI) was developed to be an "easily computable measure of pedestrian friendliness of neighborhoods" and was based on four indices: land-use diversity (entropy), population density, commercial density, and intersection density (4). These indices were based on the sub-zonal level and are relative to other zones; therefore, the PEI could only be used to compare locations within a study area rather than comparing different study areas or zones in different cities. Park et al. developed a composite WI at the street segment level by testing 42 variables describing categories such as curb-to-curb roadways, pedestrian crossings, buffer zones, sidewalks, sidewalk facilities, street scale and enclosure, and nearby buildings and properties. These were each tested for their statistical significance relating to traveler perceptions of walkability using 13 measures related to safety from traffic, safety from crime, comfort, convenience, and visual interest. The index used 22 variables which were statistically significant, with weighting for each variable based on correlation with the travel perception scores (5).

Walk Score was developed to provide a numerical score from 0 to 100 for a single address, based on the built environment within a 1.5 mi buffer. It considered the importance of amenities in nine categories, based on previous studies, as well as block length and intersection density (6-8). Several studies have investigated the correlation between Walk Score and other walkability measures and surveys and found varying degrees of positive correlation (6, 9, 10).

Manaugh and El-Geneidy compared four walkability indices at the census tract level in Montreal: Walk Score, WOI, WI, and Pedshed Connectivity, and investigated their association with home-based non-work walking trips. They found that all indices had a significant positive correlation with walking trips. Walk Score explained "as much, if not more, of the variation in walking trips to shopping than other walkability indices," but different indices better explained different types of walking trips (11).

#### Bikeability Indices

An early study on bikeability introduced the Bicycle Compatibility Index (BCI), which included nine factors associated with road links (12). The model integrated factors for bike lane availability, bike lane width, curb width, traffic volume, traffic speed, parking, adjacent development, and right turning vehicles. The BCI was

intended to translate to a level of service (LOS), with different models based on cyclist experience level. Emery et al. investigated the effects of several road and location factors on bikeability and included speed, bike lane presence, curve frequency, severe grade, annual average daily traffic (AADT), sidewalk presence, number of lanes, outside lane width, and sight distance in a more subjective measure of quality (13).

Models of Bicycle Level of Service (BLOS) were developed in 2008 (14), which were later used in the Highway Capacity Manual (HCM) 2010, along with pedestrian level of service (PLOS). The BLOS and PLOS apply at the segment, intersection, and facility levels. BLOS is based on ten factors representing path width, vehicle volumes, vehicle speeds, and pavement condition. Lowry et al. conducted a review of various cycling LOS measures and developed a method to calculate the bikeability of a zone based on an aggregation of facility LOS, connectivity, and land use (15).

More recently, Bike Score was developed to measure bikeability at a location based on a weighted combination of a bike lane score, hill score, destinations and connectivity score, and a bike work mode share (8). These sub-scores include bicycle facilities, topographical grade, intersection density, block length, and amenities within a buffer. An evaluation of Bike Score (modified to exclude the mode share component) was found to be positively associated with work trip bike mode share in 24 North American cities (16).

# Multivariate-Spatial Crash Models for Pedestrian and Cyclist Safety

Recently, to mitigate problems resulting from unobserved heterogeneity in crash models, new methods have been developed to include spatial correlation and relationships among crash types (17, 18). Narayanamoorthy et al. proposed a spatial multivariate count model to jointly analyze pedestrian and cyclist crashes by severity. The model was applied to predict injuries at the census tract level in New York City, and results demonstrated the importance of accounting for correlations between modes and spatial dependence. More recent studies also demonstrated the importance of accounting for spatial and multivariate effects in crash models (18–20).

Lee et al. estimated multivariate and univariate crash models for motorists, pedestrians, and cyclists at the scale of TAZ (21). The models were developed using proxy traffic exposure variables along with socio-economic and road facility variables. The multivariate-spatial model again outperformed the univariate spatial models and the spatial error component significantly improved the model performance.

Huang et al. proposed a multivariate-spatial model to simultaneously analyze the occurrence of motor-vehicle, bicycle, and pedestrian crashes at urban intersections. The multivariate-spatial model outperformed the univariate spatial model and the multivariate model, confirming the highly correlated heterogeneous residuals in modeling crash risk among modes. The estimated variance for spatial correlations of all three crash modes in the multivariate and univariate models were statistically significant, however, the correlations for spatial residuals between different crash modes at adjacent sites were not statistically significant (22).

Osama and Sayed investigated the effect of mode and spatial correlations on the safety of active commuters. They developed full Bayesian univariate and multivariate models for pedestrian and cyclist crashes. The multivariate approach allowed for including different covariates for each modeled crash type. Exposure, land use, built environment, socioeconomics, and network indicator variables were used. The mode and spatial correlations were found to significantly affect the crash models' performance (23).

# Pedestrian and Cyclist Safety Correlates

Previous studies showed that cyclist/pedestrian crashes were non-linearly and positively associated with the traffic exposure variables, that is, BKT, VKT, and W respectively. The exponents of the exposure measures were less than one supporting the "safety in numbers" hypothesis (24–27). The exponents of W and BKT were higher than that of VKT showing the higher effect of the nonmotorized exposure on active transportation safety. The results also showed that the increase in cyclist/pedestrian crashes was associated with the increase in socioeconomic attributes such as employment and household densities, and built environment attributes such as transit stop and traffic signal densities. In the case of land use, a positive association was found between cyclist/pedestrian crash frequency and commercial area density, while both residential and recreational area densities had negative associations with crashes involving active commuters. For road network facilities, higher cyclist/pedestrian crash frequency was found to be associated with a greater proportion of arterial and collector roads, while a decline in those crashes was found to be associated with the increase in the proportion of local roads. Cyclist crashes were negatively associated with proportion of the off-street bike links, and pedestrian crashes were negatively associated with the pedestrian actuated traffic signals. Bike and sidewalk network connectivity indicators (except pedestrian network coverage) were all found to be positively associated with cyclist/pedestrian crashes on the contrary of the continuity (except pedestrian network linearity), infrastructure, and topography indicators of the active transportation network, which were found to be negatively associated.

100

Variable	Mean	Standard deviation	Minimum	Maximum
Crashes				
Cyclist-motor-vehicle crashes over 5 years	12.71	13.48	0	78
Pedestrian-motor-vehicle crashes over 5 years	15.45	11.45	0	54
Exposure				
Vehicle kilometers traveled (VKT)	4290	3315	189	22289
Bike kilometers traveled (BKT)	1048	2102	0	21463
Walk trips	3972	2677	247	13907
Indices				
Bike score	88	9	48	99

17

79

Table I. Summary of Data Variables (N = 134 TAZ)

Note: TAZ = traffic analysis zones.

## Methods

Walk score

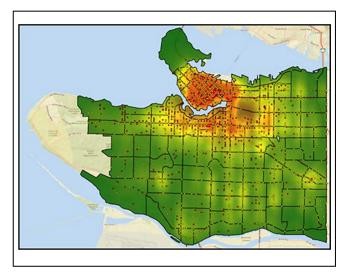
# Data

Zone-level crash models are developed in this study using data from 134 TAZs in the City of Vancouver. Walk Score and Bike Score values for each TAZ are included in the models, as well as VKT, BKT, and walk trips as traffic exposure variables. Table 1 summarizes the variables used in the crash models.

Crash data for a 5-year period (2009–2013) were obtained from the Insurance Corporation of British Columbia (ICBC), the provincial automobile insurance provider. Pedestrian-motorist and cyclist-motorist crashes at three severity levels (fatality, injury, and property damage only) were included in the analysis (locations shown in Figure 2). A 5-year period was selected to collect an adequate sample size; total crashes (rather than individual severity levels) were used as the dependent variables for the same reason. Crashes located on TAZ boundaries were distributed to the adjacent TAZ according to the relative proportion of BKT or walk trips in those zones.

VKT and walk trips in each zone were taken from the EMME2 regional travel model, developed by the regional transportation planning agency (TransLink) based on 2011 household travel survey data and cordon count (28). BKT by zone was drawn from the Vancouver Cycling Data Model, which provides estimates of annual average daily bike volumes (AADB) on links in the network based on bike counts from 2005 through 2011 (29).

Walk scores and bike scores were retrieved from www.walkscore.com. Preliminarily, for each TAZ, bike and walk scores at arbitrary sample locations (around 30 locations) within the zone were manually extracted and investigated. A walk/bike zone score was then computed as the average of three values: the minimum score within the TAZ, the maximum score within the TAZ, and the mean of five evenly dispersed points in the TAZ. Figure 3 shows the calculated TAZ scores and the raw walk score and bike score maps for the City of Vancouver, which



**Figure 2.** A heat map of pedestrian (yellow points) and cyclist (red points) crash locations.

shows similar spatial patterns. There is high spatial autocorrelation in the scores because they are calculated using buffers, in addition to the spatial patterns of the actual built environment.

# Crash Modeling

State-of-the-practice univariate generalized linear model (GLM) crash models were preliminarily developed to investigate pedestrian and cyclist crashes separately. Both crash modes were then combined in a multivariate full Bayes (FB) crash model. Both approaches are described in the following sections.

Univariate Generalized Linear Models. GLMs with nonnormal (negative binomial) error distribution are widely used in crash modeling because conventional linear regression models require error assumptions that cannot adequately describe the random, discrete, non-negative,

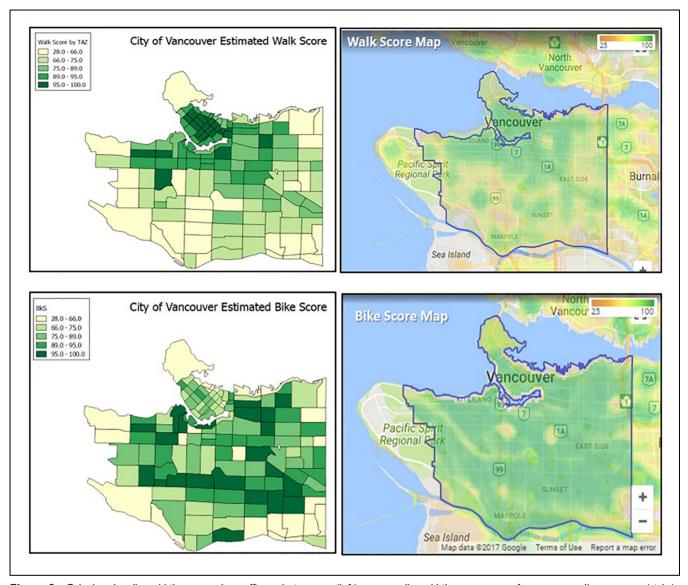


Figure 3. Calculated walk and bike scores by traffic analysis zones (left)—raw walk and bike score maps from www.walkscore.com (right).

where

and sporadic nature of crash occurrence (30). This study employs a common crash model form that includes traffic exposure measures  $V_{1i}$  and  $V_{2i}$ , and other non-exposure explanatory variables,  $x_{ni}$ :

$$Y_i = a_0 V_{1i}^{a_1} V_{2i}^{a_2} \exp \sum (b_n x_{ni})$$

where  $Y_i$  is the predicted collision frequency in zone i and  $a_0$ ,  $a_1$ ,  $a_2$ , and  $b_n$  are estimated model parameters. Pedestrian-motor-vehicle crashes are modeled using walk trips and VKT as exposure measures, and the walk score as the single non-exposure explanatory variable. Cyclist-motor-vehicle crashes are modeled using BKT and VKT as exposure measures, with bike score as the single non-exposure explanatory variable.

Multivariate Full Bayes Model. FB analysis has been shown to have several advantages over other techniques of crash modeling (31). Poisson-lognormal multivariate models incorporating random effects are used in this research based on previous work showing that this approach is suitable for active transportation safety analysis (21, 22, 25). The model is specified according to the following, as developed and discussed by Osama and Sayed.

$$Y_i^k \sim \text{Poisson}(\lambda_i^k)$$

$$\ln \lambda_i^k = a_0^k + a_1^k \ln V_{1i} + a_2^k \ln V_{2i}^k + \sum_i b_n^k x_{ni}^k + u_i^k + s_i^k$$

 $Y_i^k$  is the number of crashes of type k (pedestrian or cyclist) in zone i,

 $a_0^k$ ,  $a_1^k$ ,  $a_2^k$ , and  $b_n^k$  are estimated model parameters,

 $V_{1i}$  and  $V_{2i}^k$  are traffic exposure variables (VKT and either walk trips for pedestrians or BKT for cyclists),

and  $x_{ni}^k$  is a set of other non-exposure explanatory variables (which can vary by crash type).

Overdispersion caused by unobserved or unmeasured heterogeneity by zone is accounted for using  $u_i^k$ , an unstructured random error term that follows a multivariate normal distribution. Spatially structured error is accounted for using multivariate Gaussian conditional autoregressive (CAR) techniques, applied in the spatial error term  $s_i^k$ .

The definition of the multivariate normal and multi-

variate CAR error structures is similar to past work (20). For the multivariate k-dimensional (2 in this model) normal error, the diagonal elements of the variance–covariance matrix  $\sum$  represent the variances, and the off-diagonal elements represent the covariances. For model estimation, the following prior is used:  $\sum_{i=1}^{n} \sim \text{Wishart}(I, K)$ , where I is the  $K \times K$  identity matrix,

$$u_i^k \sim \text{Normal}(0, \sum), \sum = \begin{pmatrix} \sigma 11 & \sigma 12 \\ \sigma 21 & \sigma 22 \end{pmatrix}.$$

For the multivariate CAR model,

$$(S_{1i}, S_{2i})|(S_{-1i}, S_{-2i}) \sim \text{Normal}$$
  
 $(\bar{s}_{ki}, \frac{\omega}{m_i}), \omega = \begin{pmatrix} \sigma \text{ s} 11 & \sigma \text{ s} 12\\ \sigma \text{ s} 21 & \sigma \text{ s} 22 \end{pmatrix}$ 

where

 $(S_{-1i}, S_{-2i})$  denotes the zones of the  $k \times m$  matrix  $s_i^k$ , excluding zone i,

 $m_i$  is the number of zones adjacent to zone i, and

 $\omega$  is the variance–covariance matrix for spatial correlation.

The diagonal elements of the covariance matrix  $\omega$  represent spatial variance; the off-diagonal elements represent the spatial covariance of different severity levels. For

model estimation, the prior is assumed as  $\omega^{-1} \sim \text{Wishart}(I, K)$ , where *I* is the  $K \times K$  identity matrix.

Markov Chain Monte Carlo (MCMC) is applied using the WinBUGS tool to sample the posterior distribution as well as to estimate the model parameters. The MCMC method samples from the joint posterior distribution repeatedly to generate sequences (chains) of random points, the distribution of which converge to the target posterior distributions. A burn-in run is used to monitor convergence and is then excluded; parameter estimation, performance evaluation, and inference are based on subsequent iterations.

Two chains are used to run each model in WinBugs, and 10,000 MCMC iterations are discarded as burn-in samples. Afterward, 30,000 iterations are performed for each chain. The summary statistics of each chain are then estimated from WinBUGS and the convergences of the developed models checked to ensure that the posterior distribution has been found to begin parameter sampling. Convergence is checked by tracking parallel chains with diverse starting values to ensure full coverage of the sample space, by the ratios of the Monte Carlo errors relative to the respective standard deviations of the estimates, by visual inspection of the MCMC trace plots of model parameters, and by the Brooks–Gelman–Rubin statistic (17).

# Results

Tables 2 and 3 give the estimation results for the GLM and FB crash models. The results are similar for both modeling techniques, with all variables having positive parameters (positive associations with crashes) for both modes. The exposure variables all significantly increase crash risk, as expected, with at least 95% confidence. The exposure exponents are less than one, which affirms the "safety in numbers" effect (i.e., positive but decreasing marginal effect of volume on crash risk). The FB multivariate model also shows a significant and positive

Table 2. Empirical Bayes Generalized Linear Model Crash Model Estimation Results

	Parameter	Estimate	Standard error	Pr > ChiSq
Pedestrian-motor-vehicle crashes	Intercept	-7.15	0.74	<0.0001
	Walk trips	0.52	0.09	< 0.0001
	Vehicle kilometers travelled (VKT)	0.51	0.06	< 0.0001
	Walk Score	0.017	0.004	< 0.0001
	(Dispersion)	0.157	0.029	na
Cyclist-motor-vehicle crashes	Intercept	-4.86	0.95	< 0.0001
,	Bike kilometers travelled (BKT)	0.57	0.06	< 0.0001
	Vehicle kilometers travelled (VKT)	0.23	0.08	0.0052
	Bike Score	0.020	0.008	0.0094
	(Dispersion)	0.393	0.061	na

Table 3.	Full Bayes	Multivariate	Crash Model	Estimation	Results
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	Parameter	Mean	Standard Deviation	95% Credible interva
Pedestrian-motor-vehicle crashes	Intercept	-6.98	0.86	(-8.69, -5.32)
	Walk trips	0.57	0.10	(0.37, 0.77)
	Vehicle kilometers travelled (VKT)	0.46	0.08	(0.31, 0.60)
	Walk Score	0.015	0.005	(0.006, 0.025)
Cyclist-motor-vehicle crashes	Intercept	-5.15	1.35	(-7.80, -2.48)
	Bike kilometers travelled (BKT)	0.38	0.08	(0.22, 0.52)
	Vehicle kilometers travelled (VKT)	0.44	0.11	(0.22, 0.66)
	Bike Score	0.016	0.009	(-0.003, 0.034)
	Mode correlation because of spatial effects	0.500	0.224	(0.003, 0.828)

correlation among crash modes for the spatial effects, as expected.

Of particular importance is that walk score and bike score are positively associated with pedestrian crashes and cyclist crashes respectively, even when controlling for walking, cycling, and motor-vehicle traffic volumes. The walk score and bike score parameters are in the range of 0.015–0.020 in both models, slightly lower in the FB model controlling for spatial, random, and multivariate effects. The walk score parameters are significant at 5% in both models, while the bike score parameters are only significant at 5% in the GLM model (and significant at 10% in the FB model).

#### **Discussion**

The estimated walk and bike score effects indicate that areas of the city with higher walkability and bikeability (as indicated by walk and bike scores) are associated with greater pedestrian and cyclist crash risk, respectively, which is illustrated in both heatmaps of cyclist and pedestrian crashes in contrast to the walk and bike score heatmaps. This is potentially surprising, depending on what walkability and bikeability are expected to represent. These indices are generally developed and validated based on walking and biking activity, as described in the literature review. Active travel behavior is influenced by safety concerns, and environmental factors that increase perceived safety and comfort (facilities separated from motor-vehicle traffic, for example) will also generally increase the objective safety of walkable/bikeable neighborhoods as well (32). Another important finding of that study was that the number of crashes was nonlinearly related to the average bike and vehicle daily traffic, which confirms the safety in numbers phenomenon (24-27).

On the other hand, there are environmental factors that are conducive to walking and cycling but may reduce safety. Destinations and commercial businesses are major components of walkability and bikeability, and these

factors could increase crashes as a result of end-of-trip events such as motor-vehicles turning and parking or more distracting environments (25, 26, 33). Network connectivity is another factor, used to calculate walkability and bikeability, that makes walking and cycling more attractive by reducing travel times and distances, but can have adverse effects on safety as a result of higher intersction density and a larger number of conflict points (34–36). Therefore, controlling for exposure, these components of walkability and bikeability may offset the safety-related factors such as separation from motor-vehicle traffic.

Despite the clarity of the results and the use of stateof-the-art crash modeling methods, there are some limitations relevant to the main finding that higher walkability and bikeability is associated with lower pedestrian and cyclist safety, which require more investigation through further studies. A single set of walkability and bikeability indices was examined; additional indices should be examined in future work, although walkability indices tend to be highly correlated, and so the results are expected to hold (11). The method of TAZ aggregation of walk and bike scores was another limitation, although it probably had little influence because of the strong spatial autocorrelation of the scores. Future work should test other methods of aggregation. Another consideration is that the exposure controls (VKT, BKT, and walk trips) are imperfect measures of actual exposure to crash risk. Thus, some of the walk and bike score effects could be the result of correlation with unmeasured exposure variability. Also, total crashes (rather than individual severity levels) were used as the dependent variables to collect an adequate sample size. Further studies with larger sample size, where multivariate models accounting for different severity levels can be used. Moreover, temporal autocorrelation can be significant, especially for cyclist safety; this could be addressed with more comprehensive data. There could also be other factors that correspond to neighborhood walkability/bikeability as well as pedestrian and cyclist safety, such as age and gender of the local population (37, 38).

The objective of this study was to assess whether neighborhood walkability and bikeability also indicate safety for pedestrians and cyclists. The clear answer is: they do not. The next logical question is: should they? Walkability and bikeability indices aim to combine many factors to identify environments conducive to walking and cycling, of which safety is just one component—there must also be nearby destinations and other elements (39). Safety cannot be the only consideration, because it is not the only concern of potential walkers and cyclists. Still, it is somewhat counterintuitive to call neighborhoods that are less safe for walking and biking more walkable or bikeable.

A next step is to examine the degree to which walkability and bikeability are associated with safety by practitioners and the public. Perhaps there is not an expected association, and current walkability and bikeability indices suffice. If walkable and bikeable is understood to imply safer, then the indices should be improved, or the implication avoided. Objective safety could be introduced into walkability and bikeability indices using long-term average pedestrian and cyclist crash measures within a specified radius. This approach would be objective, but suffer from the common issues of using collision data in analysis of active transportation safety, including the omission of near-misses and unreported crashes.

In relation to practice, the findings must be viewed from the perspective of association. The results should not be interpreted as implying that making a neighborhood less walkable or bikeable will make it safer—nor that walkable and bikeable neighborhoods should be avoided for walking and cycling. Improving the safety-related components of walkability and bikeability (i.e., protected facilities) will increase both walkability/bikeability and safety.

#### **Author Contributions Statement**

The authors confirm contribution to the paper as follows: study conception and design: Tarek Sayed and Ahmed Osama; data collection: Ahmed Osama and Maria Albitar; analysis and interpretation of results: Ahmed Osama, Maria Albitar, Tarek Sayed, and Alexander Bigazzi; draft manuscript preparation: Ahmed Osama, Maria Albitar, Tarek Sayed, and Alexander Bigazzi. All authors reviewed the results and approved the final version of the manuscript.

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