CHAPTER 8
General discussion
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The general aim of this thesis was twofold: 1) to investigate the association between the food environment, diet quality and type 2 diabetes (T2D), and 2) to investigate the association between the physical activity (PA) environment, PA and T2D. Within these aims, we defined three main research questions. This chapter summarises the main findings and provides further interpretation of these results, discusses the methodological considerations and provides recommendations for future research, theory and practice.

8.1 Main findings

8.1.1 Which built environmental characteristics potentially associated with lifestyle are consistently linked to type 2 diabetes in the scientific literature?

In chapter 2 we conducted a systematic literature review and meta-analysis to investigate which built environmental characteristics were associated with T2D. There were three main findings:

1) Urban residence, as opposed to rural residence, was consistently associated with higher T2D risk or prevalence, especially in upper middle- and lower middle-income countries.

2) Measures of the food environment were not consistently associated with T2D. Studies were heterogeneous in the use of methods, definitions and design.

3) Walkability and green space, environmental characteristics related to PA, were consistently associated with T2D risk, such that residents of higher walkable neighbourhoods and with more access to green space had lower T2D risk.

8.1.2 How can composite and objective measures of the built environment, combined with individual characteristics, enrich our understanding of the built physical activity environment in the association with type 2 diabetes?

In chapter 5 and 6 we explored various measurement aspects related to physically inactive (‘passive’) transport choices. In chapter 5 we aimed to investigate the association of both individual and built environmental characteristics with car use in a cross-European setting. Car trips typically surpass residential neighbourhood
boundaries, and may be influenced by individual circumstances (e.g. age or household composition) as well as factors in the residential built environment. The findings from chapter 5 indicated that individual factors (higher age, male sex, being employed, and a ≥3 person household composition) and built environmental characteristics (lower residential density and lower land-use mix) equally explained variance in car use in participants across five European countries. This indicates that both individual and residential characteristics may be important determinants of car use across European urban settings.

In chapter 6 we developed and validated a novel drivability index, and investigated its association with car use, in short as well as longer trips. The index was further applied to both residential and workplace neighbourhoods. First, this study showed that an index based on factor analysis of environmental characteristics selected based on theory regarding the relation between built environment and transport behaviour, was able to predict whether local residents used passive or active modes of transport. The resulting drivability index featured three factors: urban sprawl, pedestrian facilities, and parking facilities (Figure 1). Second, the study indicated that higher neighbourhood drivability was most strongly associated with car use in short trips, indicating that car-facilitating environments are associated with passive transport choices, also when the distance can be easily crossed by active transport. Third, a high residential neighbourhood drivability combined with high drivability of the workplace environment was more strongly associated with car use than a high drivability around home or work alone.

In chapter 7 we investigated whether neighbourhood walkability was associated with glycaemic control in a population with T2D in The Netherlands. Both self-reported and objectively measured neighbourhood walkability were not associated with changes in glycaemic markers over a year of follow-up, although effect sizes were more meaningful for larger buffers than for smaller ones.
8.1.3 What are mediating pathways between built environments, physical activity and diet, and type 2 diabetes outcomes?

In chapter 4 and 7 we investigated if and to what extent diet quality and PA mediated the hypothesized pathway between built environment and T2D risk or outcomes.

In chapter 4, we investigated whether better diet quality (higher adherence to DHD15-index) mediated the association between spatial accessibility to food retailers and T2D incidence. Overall, this study did not provide evidence for the main association between spatial accessibility of food retailers and T2D incidence. The mediation analyses did not provide compelling evidence for meaningful mediation. Adults who lived further away from fast-food outlets and closer to supermarkets were somewhat more likely to have better diet quality. In turn, higher adherence to DHD15-index appeared to be somewhat associated (but not statistically significant) with lower T2D incidence, which was in line with our finding in chapter 3.

In chapter 7, we investigated the association between neighbourhood walkability and glycaemic markers, and whether these associations were mediated by levels of PA. We found no meaningful association between neighbourhood walkability and change in glycaemic markers. PA was not a mediator, as there was an inverse significant association between higher neighbourhood walkability and lower PA. Moreover, a higher PA was not associated with change in glycaemic markers in this population.

Figure 1: the left represents a low drivable area, with scarce parking space and good alternatives to driving, the right a high drivable area, with high sprawl, high parking availability and little alternatives.
8.2 Interpretation of findings and methodological considerations

In this section I aim to interpret these main findings in two sections according to the main aims of this thesis 1) food related environment and 2) built PA environment. Within those two sections, the following methodological considerations will be discussed to interpret the findings: 1) exposure assessment, 2) match between exposure and outcome, 3) operationalisation and composite measures, 4) study design and 5) pathway analysis.

8.2.1 Food environment

In this thesis, we observed mixed associations between measures of the food environment, diet quality and T2D, which is also observed in reviews that were conducted and published parallel to this thesis (1, 2). The five aspects identified may each play a role to explain these inconsistencies.

8.2.1.1 Exposure assessment

Exposure assessment was very heterogeneous, in the many studies done to date. A main distinction can be made in objectively measured (GIS-based) assessment, such as the straight-line distance to the closest food retailer, and subjective measures, such as questionnaire items on availability of food retailers. In chapter 2 we observed that findings with subjective measures could not be reproduced with objective measures, in food environment and T2D studies (1, 3). There may be some explanations for this inconsistency: self-reported measures in food environment research are hypothesized to reflect individuals’ resources and preferences. For instance, an individual may have a garden and grow vegetables, may have economic considerations to not visit the closest supermarket, or may buy groceries at the weekly market (3). Whereas the objective assessment of the food environment often assumes that when a food retailer is ‘available’, it is also used, which may of course not be the case for many reasons unrelated to geographic locations. There is currently a lack of evidence on which stores people use and for what reason, and what mode of transport participants use to access a store and for which reason they visit that store. Quantifying such subjective measures on ‘accessibility’, can help to capture a general habitual pattern of use of...
the food environment by participants and understand how people interact with their food environment. For instance, one study showed the importance of combining travel data with store access in a North-American setting, and indicated that if transportation networks were not taken into account when classifying accessibility to food retailers this may lead to misclassification. Namely, a neighbourhood was not classified as a food desert if stores could be reached by car, while the stores were inaccessible by public transit making the area a food desert for those residents without a car (4). Moreover, it should be recognised that people are exposed to more than just the residential environment, but also to commuting, work, and recreational environments (5). Not taking into account those non-residential exposures will underestimate true associations (6). Measures of such non-residential environment exposure could also be inquired by means of objective assessment, such as GPS, or subjective measures such as a trip diary. This shows the importance of combining subjective and objective measures. In chapter 4 we investigated objective measures of the food environment, in the residential area in a collection of cohorts. In line with other studies there were some inconsistencies between the cohorts, which could be due to certain characteristics of the study populations (such as age or educational attainment) that related to how these residents interact with their food environment.

8.2.1.2 Match exposure-outcome

It also seems to be important to better match (measurement of) outcome and exposures. Many studies, such as those reported in chapter 2 and chapter 4 of this thesis, use dietary indices, or intakes derived from FFQ data. Dietary patterns, such as the DHD15-index as shown in chapter 3, are associated with T2D risk, but the associations with food environment were weak, as we observed in chapter 4. An explanation could be that the food intake associated with visiting certain food outlets (e.g. fast-food) are not captured well by a dietary index. For instance, in our study the DHD15-index contains food groups that are likely to be increased by fast-food consumption, such as red and processed meat and sodium, but these are indirect measures of fast-food intake, providing a ‘diluted’ outcome measure. Moreover, FFQ’s are usually not validated for intake of fast-food. This potentially creates noise in the data, which would likely be less if assessment of food groups were tailored to the food outlets of interest, e.g. ‘how often do you consume food from McDonalds, KFC
or Domino’s?’. One study indicated that both objective and subjective measures of access to fast-food outlets were strongly associated with fast-food consumption in the neighbourhood, and less strongly associated with dietary indices (such as AHEI) (7). In observational food environment, diet and T2D studies, there is however usually a strong trade-off between data quality on the exposure, mediator or outcome. This trade-off is also visible in chapter 4, where we used high quality exposure measures, but did not have high quality T2D measures (i.e. oral glucose tolerance tests) in all cohorts, and were dependent on the FFQ’s that was administered by the studies.

8.2.1.3 Operationalisation and composite measures

Besides assessment of exposure to the food environment, also operationalisation of the food environment was very heterogeneous across studies and no consensus is yet established on how to capture complexity of and exposure to the food environment. Many studies used simple measures such as distance or density, and usually not both, limiting comparability. Therefore, in our study we used the same exposure definition (distance) for four cohorts in chapter 4 and observed low heterogeneity across the cohorts. This indicates that standardizing methods can lead to higher comparability between studies, and is therefore of importance, but this did not lead to stronger associations than earlier studies. Moreover, we investigated the same association with the density measure, to increase comparability and indicate whether conclusions would differ. Indeed, the directionality of associations was sometimes different, but overall conclusions did not change. Recent studies also indicated that distance and density measures may be individually important concepts, and that future studies should report multiple measures to improve comparability between studies (8, 9).

The more or less simple measures used to date seem to always give a too simplistic reflection of reality, because it does not capture the complexity of the food environment. In chapter 4 we adjusted for the broader food environment to take into account the clustering of food outlets, however this did not always seem to be sufficient as we observed high correlations between proximity and density of different types of food retailers. Researchers attempted to use composite measures of the food environment to capture complexity. While such indices perform well in transport-related studies, such as walkability, the food environment seems to be
difficult to capture in such an index. Many of the indices that were used involved classification of healthy and unhealthy outlets, as observed in chapter 2. This could lead to misclassification of food retailers, because within-store food availability may be diverse, making classification challenging (10). For example, we do not know what someone purchased in supermarkets, which can range from ingredients for home cooking to unhealthy snacks. Recent studies that used a less ambiguous classification in their index by taking the number of fast-food outlets (where in-store availability is more likely to be completely unhealthy) to the total of food retailers in an area, indicating the unhealthfulness of the food environment, and found associations with higher BMI and T2D incidence (11, 12). This approach seems more promising, and may also explain why in walkability indices this problem does not occur, because it is better understood which transport-related characteristics enhance PA.

8.2.1.4 Study design
Study designs may play an important role in heterogeneity between studies. In chapter 4 we used a prospective design, and found very subtle associations. However, studies on the food environment and T2D mainly used cross-sectional designs (1, 2). The Framingham heart study published a comparison of prospective and cross-sectional analyses on food environment and glycaemic markers (13). That study showed significant differences between the analytic approaches: there was no significant association between food environment and fasting plasma glucose in the cross-sectional analyses, while there was a significant association between higher density of fast-food and full-service restaurant with smaller increase in fasting plasma glucose. Although the Framingham study gives a counterintuitive result from the prospective analyses, it shows that study design may influence study outcomes and conclusions.

An explanation for such counterintuitive results may be that studies, including ours, have not taken into account changes in the food environment. A recent study indicated that the Dutch food environment changed substantially over the last 14 years, where especially food delivery increased (14) and changes in food environment have also been observed in other settings (15, 16). This may explain why findings with fast-food were so small in our study, or contradictory in other studies, because fast-food is more
likely to be delivered and in that case the proximity or density within a certain buffer area is of smaller importance. Longitudinal designs to investigate such changes in food environments and their association with diet quality and disease incidence are important (16). A nationwide study investigating such food environment, with registry based individual-level outcomes such as measurements of glycaemic markers, would be of importance.

8.2.1.5 Pathways analyses
In an attempt to understand putative pathways between exposure to the food environment and T2D incidence and to understand heterogeneity in study results, we explored the mediating role of diet quality in chapter 4. From these formal mediation analyses we learned that associations between supermarket, fast-food outlet proximity and diet quality were present in the hypothesized direction, but were very subtle. Overall, associations were too small to observe a statistically significant association with T2D in chapter 4, potentially because T2D is quite a distal endpoint of the food environment. Moreover, because we performed mediation analyses to disentangle the putative pathway we found contradictory paths between fast-food and T2D, which might explain a null finding (the paths may have cancelled each other out). This shows the importance of performing mediation analyses, also when the main association is non-significant, as argued in the mediation literature (17). Because our study and others showed (3) that associations on the putative path are small and subtle, it is important to have valid measurement instrument, and large variation in exposures.

8.2.2 Physical activity environment
In contrast to the food environment, we observed consistent associations between the PA environment and T2D, which is also observed in reviews that were published in parallel to this thesis (1, 2). Again, the five identified aspects will be used to put these findings in context.

8.2.2.1 Exposure assessment
In chapter 2 we observed a large increase of utilisation of objective GIS measures in comparison to earlier reviews on PA environment (18). Objective and subjective measures are generally poorly correlated, as we observed in chapter 7. Such
discrepancies between subjective and objective measures of environments may be due to reporting bias, which means that for instance participants who like to walk are more likely to perceive their environment as walkable. However, in the IPEN studies, across 19 countries, objective and subjective walkability showed similar associations with higher PA and lower BMI (19). Also, a recent meta-analysis on prospective studies about walkability and cardiometabolic outcomes indicated that pooled effects attenuated when the analysis was restricted to only objective measures, but still the hypothesized positive associations were observed (20). Objective walkability was consistently associated with more walking, various cardio-metabolic outcomes, including lower T2D incidence, in healthy populations and various settings (1, 20-22). The discrepancy between objective and subjective environment measures do not seem to change conclusions regarding walkability, PA and T2D in healthy populations. However, caution with interpretation is needed when studies use self-reported walkability as well as self-reported PA, as this creates a risk of same-source bias. Same-source bias may lead to artificial associations, due to correlated measurement errors or because the outcome affects the environmental perception (23). The use of such self-reported exposure and outcome was especially observed in walkability and PA studies among people with T2D (24-26). Objectively measured walkability was hardly studied in this group (27). Therefore, in chapter 7 we investigated both objectively measured and perceived walkability, where we found that both indices were poorly correlated with each other, and the association with PA was somewhat more likely to be positive when using subjective walkability, although not significant. However, the overall conclusions of our study did not change.

8.2.2.2 Match exposure-outcome
Parallel to the food environment studies, an adequate match between exposure and outcomes and context was important in PA environment studies as well. For instance, an earlier study in a population with T2D indicated that walkability was associated with increased PA within neighbourhoods, as determined by GPS and accelerometer combined devices (27). On the other hand, studies in younger populations have indicated that walkability of the activity space (i.e. including visited destinations) was most strongly associated with transport-related PA (28). The population under study, and the type of behaviour thus seems to be relevant, and in chapter 7 we encountered
the importance of these choices. We anticipated that the elderly population with T2D was likely to be active in the residential neighbourhood, and we therefore chose a relatively small buffer. However, we observed higher walkability to be associated with lower PA, which may have been due to people travelling outside their neighbourhood more (being more mobile) than we expected. In our Dutch setting, this could be explained by people being more mobile by bike to reach family or certain grocery stores, which we could not capture. Moreover, our outcome measure, accelerometer-based total PA, was quite broad while information on PA domains (leisure-, transport-, work-related PA) may give insight in the association between walkability and PA in this population. The IPEN studies showed that, in healthy populations, objective walkability was most strongly associated with PA for transport (self-report), after that MVPA (accelerometer) and PA for leisure (self-report) (19), although differences were not very large. In this population it could be conceivable that people who lived in less walkable areas are more likely to have a garden which provides them with opportunity for other leisure-time PA such as gardening, or that these residents are more likely to cross larger distances by active transport because they live further from facilities. Unfortunately, objective accelerometer data does not provide such PA domain information. Trip-level data of these participants (mode, frequency, distance and purpose) would have provided a more detailed activity pattern. We did have access to such trip-level information from the transport survey used in chapter 6. This allowed us to investigate whether the neighbourhood drivability was a stronger determinant of car use in short trips than in long trips, leading to the valuable insight that the neighbourhood built environment was most important for car use in short trips. Also we were able to apply the drivability index to the place of work, and observed that a combination of residential and work related trips were a strong determinant in trips overall. The above indicates that a match between exposure and outcome is important, and that the context is important to inform such choices.

8.2.2.3 Operationalisation & composite measures
The association between neighbourhood characteristics and car use is complex, as car driving is not a behaviour that is restricted to the residential environment, or at least much less so than walking. While there was attention in the scientific literature for the negative effects of car driving on cardio-metabolic health (29, 30), car use was
not often investigated in the association between built environment and T2D. The built environmental exposure is a complex combination of interrelated characteristics, and therefore composite indices have proven useful in walkability studies. Unlike the indices in the food environment, in walkability indices the directionality of associations between elements of the built environment that increase walking is generally clearer, i.e. close by destinations enhance walking to those destinations, especially when infrastructure supports walking. In chapter 6 we developed a composite measure for car-facilitating environments: a drivability index. The index was developed with factor analyses including single elements of the built environment that were hypothesized to enhance or inhibit car use. The factor analyses creates clusters of those variables that occur together in the setting under study. Some elements of the index were associated with car use individually in multiple settings, for instance residential density and land-use mix were consistently associated with car use in cross-European setting (chapter 5), North American (chapter 6) and in the literature (31). But a composite measure was overall more strongly associated with car use, as was also demonstrated in walkability, where single environmental measures were said to be likely to underestimate effects, whereas a composite measure provided a better reflection of the actual exposure and interplay of exposures to enhance PA (19). A next step would be to investigate associations with the drivability index and walkability index combined, and how this associates with health outcomes. Because urban development in North-America have been car-oriented in the past 50 years (i.e. creating sprawling suburbs), it is valuable to investigate whether the indices are not mutually exclusive and whether they can strengthen our understanding of associations between built environment, transport and health.

It is important to realise that the index that we developed was context-specific, as the factor analyses seeks for clusters of variables that correlate in the setting under study. Therefore, such an index is not directly generalisable to different settings, and should be investigated in multiple settings. Also for walkability the generalisability has been criticised, for instance most studies were performed in high income countries (19, 32). A generalisable index provides insights in key concepts that influence active transport in multiple settings (19), but to inform local policy a tailored index may be more beneficial. Our drivability index performs well in a North American setting, but
since urban form and development is inherently different in a European setting, such an index should be investigated in European settings as well (33).

A limitation of using indices, however, is the large amount of data needed to construct them. It has been suggested that at least three components of the walkability index should be assessed to create a multi-component index, in order to warrant comparability between countries (19). In chapter 5 we used data from the SPOTLIGHT study, which used a virtual audit tool using Google Street View to obtain harmonised environmental data from several countries (34). This is a good way to perform a primary data collection, but very time-consuming. On the other hand, secondary GIS data sources may not always be available, especially when large amounts of data are needed in an international setting. There are developments in machine learning, which may offer opportunities for future research. For instance a recent study explored automating such virtual audits, by developing algorithms to recognise features of the built environment from the street view images, such as street trees, pedestrian crossings, buildings (35), or land uses (36). Such initiatives from the field of artificial intelligence may create opportunities to use novel data sources.

8.2.2.4 Study design

Even though the drivability index performed well in predicting car use among residents, the conclusions that can be drawn from chapters 5 and 6 were based on cross-sectional studies and may have suffered from inverse causation. In this setting this is referred to as residential self-selection bias (37). Due to residential self-selection the associations may have turned out positive, because car users could be more likely to choose a residential location where they can park their car. In other words, attitudes toward active or passive transport may influence choice of residence. There has been a lot of attention and concern about residential self-selection as a limitation in transport environment and PA studies (37, 38), but the importance has also been challenged (39). Especially European studies indicate that individual travel preferences are part of a decision for residential location, but that the final choice for residential location is a much broader concept and therefore individual travel preferences cannot always be met (39). For instance, especially in low income household who do not have the luxury to select based on their travel preferences. Residential location and preferred
transport mode have been shown to be poorly correlated \( (39) \). Also, it seemed that especially in car use built environment was a stronger determinant of mode choice, than personal preferences, where even those who preferred to use their car, were less likely to do so in a non-facilitating environment, in a European setting \( (40) \). In chapter 5 we saw that personal characteristics were associated with car use, but we could not investigate whether travel preferences made a difference. Therefore, the results of cross-sectional studies may not be as prone to self-selection bias as many may fear, but this should be further investigated with validated self-selection questionnaires, to enhance causal inference.

In chapter 7, we also encountered potential residential self-selection bias, which may have contributed to the counterintuitive findings for higher walkability and lower levels of PA. Even though we were able to adjust for a, non-validated, self-selection variable based on PA environment preferences, there may have been other factors that influenced the choice of residence. In this case it is likely that participants with worse health status, or older age lived in more walkable areas, because this is where elderly/care residencies are located. However, it is likely that low PA levels were caused by their health status or age, rather than walkability, which could have distorted the associations, and reflect selection bias based on health status. Such factors, as health, should also be included in a validated self-selection questionnaire.

For these reasons, longitudinal studies are usually the preferred observational design, and may suffer less from self-selection bias. However, longitudinal designs also provide additional challenges, such as long follow-up durations to develop health outcomes, and the transport built environment to be static with slow changes leading to only small changes in environment and therefore associations are difficult to determine \( (41) \). On the other hand, the argument of a static environment supports the reliability of results from prospective studies with only one measurement of exposure at baseline. Because of the stability of environment such baseline exposure measures are likely to reflect exposure on a longer term, and as long as the follow-up duration for development disease is long enough, this can provide valuable insights. To overcome such long periods of data collection, but still be able to assess the effect of changes in the built environment, studies have explored associations between built environment
change and health outcomes or PA among people who moved residence, and thus experienced environmental changes overnight as a consequence of residential relocation (42-44). However, also in this approach self-selection bias is a risk in the choice for the new neighbourhood (41, 42). Hence, multiple observational designs have been used, and the tendency for an association between PA environment and T2D seems to be positive. This generates trust in the association between walkability and T2D, but self-selection is still not ruled out completely even though the impact on associations may be small.

There is thus a need for studies to address causality in this association. This can be done by study design, where one would, ideally, randomise people over different built environments and investigate the effect of random allocations of a PA environment on the development of T2D. Such an approach would be free of confounding and residential self-selection bias. However, this is practically challenging and unfeasible in research questions on built environment. Natural experiments may offer a solution, as an intervention is performed by a third party, not the researcher nor the participant. Natural experiments to date found positive associations between transport related PA environment and active transport. However, such studies mostly used ‘process outcomes’, which means assessment of the use of new facilities (e.g. a cycling lane), which is not an adequate measure to assess causality. Therefore, more studies that investigate the introduction of new infrastructures or policy need to focus on individual’s behaviour change (41, 45).

Besides experiments in real-life, statistical methods may offer opportunities to address causality. So called causal inference methods mimic randomised trials in observational data. Such methods search for participants in the data with the same characteristics, and assigns an ‘exposure’ to the ‘unexposed’, and vice-versa, keeping all other factors the constant. This way each participant is assigned a counter-factual: what if this same participant had lived in a different neighbourhood? Although such methods rely heavily on the assumptions that all possible factors are measured, which is never the case in observational studies, these methods could be useful to explore causal pathways, and gain insight in the mechanisms (46). For example, one study used instrumental variable approach to investigate neighbourhood walkability and BMI,
by using the number of schools, churches and younger people in the neighbourhood as an instrument (i.e. related to the choice of living in a walkable neighbourhood, but not to BMI), and this study indicated a causal association (47).

8.2.2.5 Pathway analyses
Studies on PA environment and T2D to date, usually failed to investigate putative pathways through PA (20), while this is also an important step toward confirming putative pathways and investigating causality. The prospective studies that consider mediation, investigated mediation only by observing attenuation of the association after addition of PA as a covariate (20). One longitudinal study investigated self-reported PA as a mediator between walkability and 10-year change in HbA1c, and found that PA was a significant mediator (48). Our analyses in chapter 7, also indicated the importance of performing mediation analyses by gaining insight in the putative pathway, also if these are not in the hypothesized direction. This analysis provided useful insights and hypotheses for future research, such as including PA domains. This field is now in a stage that studies need to consider such putative pathways, also including sedentary behaviour, and take a more comprehensive approach to unravel the putative pathways.

8.3 Recommendations and implications for theory and practice
For studies focusing on the food environment in relation to diet and T2D, definitions and operationalisation of exposure should be revised. The heterogeneous use of definitions, changes in the food environment, and participant mobility contribute to heterogeneity in study results. A new definition of the food environment and accessibility should consider to include factors such as home delivery of fast-food and groceries, modes of transport used to access food retailers, and trip-level exposures (vending machines, food advertisements, kiosks at the station, counter sales in non-food related stores). This will require subjective data, to indicate which stores or markets were visited, for what individual motivation, and by which transport mode, and these data should be combined with objective data on store locations, sales on online stores, and GPS to validate travel patterns. Such insights could be
gained through panel studies among smaller groups, but by collecting much more detailed exposures, to investigate determinants of use of the food environment. Such input could lead to a more informative operationalisation of exposure to the food environment that can be used in large nationwide studies to associate with health outcomes.

In transport environment and health, environmental indices seem to be promising tools to inform policy. A data challenge in PA environment will be to obtain the great abundance of data that will go into environmental indices. A next step is to tailor indices more to national or local contexts and population subgroups to inform policy. For instance, in The Netherlands variation in walkability may be small, since most neighbourhoods are relatively walkable or bikable. Therefore, future studies should investigate what could be gained in a setting like The Netherlands to reduce car use and increase active transport. A first step could be to investigate what a drivability index for The Netherlands would look like, and how this relates to travel patterns from travel survey data. It is conceivable that the use of combination of such composite measures for walkability, cyclability and drivability is especially important in The Netherlands. For example, the development in the Netherlands of the so-called Vinex neighbourhoods around 1996, created neighbourhoods to house many people, close to urban areas. While the philosophy of such neighbourhoods was to enhance accessibility and proximity to facilities, in practice the neighbourhoods were sprawled, and besides adequate walking, cycling and public transport infrastructure, possessed an excellent car infrastructure and was characterised by high car use (49). Such an environment can be used to investigate a combination of walkability and drivability measures, to indicate what the tipping point is for people to choose active over passive transport.

Studies on both the food environment and PA environment will benefit from more longitudinal designs. For the food environment changes in built environment should be associated with changes in T2D, and for the PA environment there is ground to gain by investigating causality. The food environment seems to be more prone to change, whereas the PA environment, especially with regard to transport infrastructure and density variables, is likely more stable. Therefore, PA environment studies will
more likely to move faster forward to address questions on causality, and the use of experimental or policy evaluation studies. A first step to grasp causality and self-selection could be the use of statistical causal inference methods in observational data. Besides obtaining insight in selection through statistical methods, the development of a valid self-selection measurement tools is crucial, as this plays a role in almost all research designs utilised to date. Tools should be developed to capture residential selection criteria based on e.g. income, health, personal preferences, as this is now mostly done by either of those.

Moreover, investigating the association between built environment and health outcomes may need a more systems-like approach where combinations of determinants for T2D are considered. In this thesis we observed the benefits of using mediation analyses, to gain insight into putative pathways. However, such analyses may also be too reductionist; i.e., they may not consider the many other relevant factors, besides the exposures under study, and there should be awareness of how these factors act together. This could start with investigating the combined effect of walkability and drivability, to see how and whether they complement each other. But also the food environment should be taken into account, as there may be associations between the two enhancing or reducing the effect of certain measures. For instance, if one lives in a walkable area and has many destinations to walk to, but these destinations are predominantly fast-food outlets or pubs, the positive health effects of walking may cancel out. There are no studies supporting such hypotheses yet, although this may be very useful. Such studies may lead to policy implications, such as the reduction of the number of fast-food outlets in highly walkable areas, and allow more healthy options.

A systems-based view to structure transport and health was proposed by Widener and Hatzopoulou (50). This system could be categorised into five domains: 1) direct impact of transport on the physical environment (e.g. air pollution, noise, climate change), 2) direct impact of transport on access to healthy spaces and facilities (e.g. access to healthy food stores by public transit), 3) indirect and direct impact on morbidity and mortality by transport (e.g. traffic accidents, traffic calming devices), 4) indirect impact of transport infrastructure on health behaviours (e.g. PA through active transport),
and 5) indirect impact of disease spread through transport networks (e.g. virus contamination in the metro) (50). Being aware of this system can help understand where buttons can be turned in research and practice, and what the impact may be on health. It is attractive for policy implementers, if one action can have multiple positive consequences, for instance by making land use more mixed, and thereby car use reduced, will impact the individual’s health through reduction of air pollution, increase of PA, reduction of stress due to traffic congestion, and enhance accessibility to healthy grocery stores or health services. Moreover, changes to reduce car use impact sustainability and lower carbon emissions. On the other hand, it also shows that some aspects should be changed together, for instance if infrastructure is changed to facilitate safety (in driving, cycling and walking), separated lanes may be constructed to reduce traffic accidents, but such parallel lanes will not protect cyclists from inhaling car exhaust. In such cases, the environment becomes more walk/bike friendly, but there is also a well-supported car infrastructure, and therefore increased walking and biking may lead to higher exposure to air pollution. In this sense, you should be aware of factors that enhance driving, as well as walking, to make informed decisions.

Taking into account several aspects of such a system can enhance advice to policy makers. A recent initiative of the WHO created a tool to monetise health impacts of walking and cycling. The tool translates a decreased mortality as a consequence of increased walking or cycling, due to increased PA, and decreased air pollution or injuries, to a monetary value (51). Also, it can assess the impact on carbon emissions, to assess not only monetised but also environmental impact. This is an excellent way of translating science to the policy makers, as the tool is targeted at urban planner, traffic engineers, health economists. The tool also allows for a cost-benefit analyses, where policy makers can input the price of an investment to the value of the reduced mortality. Of course, for such a tool to work efficiently policy makers would need to make adequate estimations of what the impact would be of certain environmental changes on the number of walkers and bikers that would increase. There is plenty of such evidence, with an example in The Netherlands, where nation-wide travel survey data was utilised to assess the association of built and natural environment characteristics and cycling duration (52). International evidence is abundant, and even though such evidence is also often cross-sectional, there are consistent findings overall
and even with more distal outcomes, such as demonstrated in this thesis and other studies (1, 2, 19, 20). This may be enough to use this knowledge to translate to policy and advice municipalities.

Even though researchers see issues with causality and evidence to inform policy, it seems that municipalities are ready to move forward. For instance, in The Netherlands, there are initiatives in urban planning policies, mainly to reduce the domination of cars in urban areas and use the space that is now occupied by cars to create room for walking, cycling and public open space. For instance, the municipality of Utrecht is now working on a new mobility plan up towards 2040, where aims are to increase smart mobility (such as ride-mode-share), renew parking policy (to reduce cars in the city), and create mobility for everyone (53). Some examples of possible interventions are to reduce car speed limits in the city, expand cycling networks, prioritise pedestrians in urban areas, and move car parking to outside the city. Such initiatives of urban planners and municipalities should be taken advantage of by health researchers, and changes in the health behaviours and health outcomes of residents should be investigated and evaluated at an individual level, to further promote and sustain such built environment changes nationwide. Also, what can be seen in The Netherlands is that the large urban areas are front runners in innovation of their mobility plans. However, associations between built environment and mobility choices seem to differ by municipality size where associations seem to be stronger in urban areas, but may even be different depending on municipality size (52). Therefore, policy evaluation and translation to other contexts and municipalities in The Netherlands is crucial for the broadening of a sustainable and healthy mobility innovation to a nationwide level.

In conclusion, in this thesis we observed that the built environment could be a determinant of T2D incidence, especially PA-related built environment. Even though there is little to no proof of causality of this association yet, interesting opportunities in statistical methods and policy evaluation can move this field forward. The association between food environment and T2D was found to be less consistent, and future research should rethink and redefine exposure to the food environment.
References