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Updated Literature Review Of the Effects of Medical Conditions on Driving

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Executive Summary

Drivers must use a range of visual, perceptual/cognitive, and physical/psychomotor abilities to safely operate a motor vehicle. Among the factors that can compromise drivers' functional capabilities are chronic medical conditions. For the current effort, we used a previous NHTSA study to create an updated synthesis of research findings describing the effect of selected medical conditions on driving performance and safety. We started with a preliminary search for literature that related changes in performance or safety outcome measures for drivers to their medical conditions and/or their associated functional impairments using search criteria that included but were not limited to the broad categories of conditions prioritized in the earlier NHTSA study.

These broad search results served as a basis for a driving safety professionals panel where researchers elicited information and opinions from participants about the effects of medical conditions on driving and scientific literature. Information gathered from the panel and the results of the preliminary search about the likelihood of finding sufficient evidence in the literature to support a systematic review informed the selection and prioritization of medical conditions to include in the current review. The final list of medical conditions included in the review was: attention deficit hyperactive disorder (ADHD); autism spectrum disorder (ASD); cardiovascular disease (CVD); diabetes; mild cognitive impairment (MCI); obstructive sleep apnea (OSA); peripheral neuropathy; stroke; syncope; and traumatic brain injury (TBI)/concussion.

The final literature search included research from peer-reviewed journals, and technical and government reports published between 2012 and 2020. The selected medical conditions were searched in the following six databases: Transportation Research International Documentation (TRID), PsycINFO, PubMed, SafetyLit, Web of Science, and Google Scholar. Published systematic reviews and meta-analyses were also sources for the literature search. In addition, the impairing effects of medications used to treat a given condition were included in this review if an article identified based on the inclusion/exclusion criteria for the specific medical condition presented such evidence. However, the potential driver-impairing effects of prescription drugs were not an explicit target of the literature search.

The literature review indicated that while some of the conditions may have a negative effect on driving performance and safety (e.g., ADHD and TBI), others typically have little effect (e.g., CVD and stroke) or have less conclusive findings (e.g., ASD, diabetes, MCI, and OSA). Additionally, for each of the medical conditions reviewed, the severity of the condition and effects of treatment can impact driving performance and safety measures. An improved understanding of the potential effects of medical conditions on driving may inform and stimulate interactions between patients (drivers) and their physicians or other healthcare providers. The current review also gives those performing assessments at licensing agencies a current background on the crash risk associated with various medical conditions, and a focus for traffic safety researchers.

1. Background and Methods

Background

Among the factors that can compromise a drivers' functional capabilities are chronic medical conditions. The possible impact on public safety is clear when considering that the prevalence of medical conditions with the potential to affect driving increases with advancing age (National Center for Health Statistics, 2010; Alzheimer's Association, 2011; Roger et al., 2011), and the population of people 65 and older in the United States has grown by over a third since 2010 (U.S. Census Bureau (2020). Older people also continue to rely on privately-owned motor vehicles to maintain independence in their communities (Transportation for America, 2011), but only half of healthcare professionals are comfortable with their knowledge of medical-related driving impairments (Meuser et al., 2010).

This report provides an updated synthesis of the scientific literature on the effects of chronic medical conditions on driving, and the results may be used in several ways. First, a synthesis of what is known about the effects of medical conditions on driving could stimulate and inform interactions between patients (drivers) and their physicians or other healthcare providers. Second, when a licensing authority determines that a person's driving history or behavior requires a medical review, those performing assessments that may lead to a license restriction or suspension will have available the most current information describing the association between medical conditions (and the drugs used to treat them) and crash risk. Finally, traffic safety researchers can focus their time and resources more productively on gaps in the state-of-the-knowledge.

An earlier NHTSA review of the effects of medical conditions on driving considered expert and stakeholder opinion when selecting medical conditions for review (Lococoet al., 2018). This earlier work culminated in a systematic review of literature published between 2000–2011 and helped guide the present effort, i.e., focusing attention on observed driver performance (either on-road or in driving simulators) as a function of a medical condition, plus crash and citation data for drivers with known medical conditions, while allowing studies with self-reported data only in isolated circumstances (see Methods). These guidelines, augmented with a scheme to rigorously evaluate the quality of included studies, informed this updated synthesis of research findings describing the effect of medical conditions on driving performance and safety.

Methods

Medical Condition Selection

The research team conducted a preliminary literature search that related changes in performance or safety outcome measures for drivers to medical conditions and associated functional impairments. The preliminary search criteria included but were not limited to the broad categories of conditions prioritized in an earlier, related NHTSA study (Staplin et al., 2017); the full parameters of this preliminary search can be found in <u>Appendix A</u>.

These broad search results served as a basis for a driving safety professionals panel that elicited information and opinions to inform the selection and prioritization of medical conditions to include in the systematic literature review. This panel consisted of 11 professionals in the fields of driver rehabilitation, medicine, medical fitness to drive, geriatrics, and polypharmacy (see <u>Appendix B</u> for list of attendees). These professionals were asked to draw on their own

experiences to describe and explain the effects of the candidate medical conditions identified in the preliminary search on a person's ability to perform safely behind the wheel, as well as the extent to which such knowledge is represented in existing literature and accessed and applied by clinicians, pharmacists, and licensing officials.

The research team and the NHTSA COR used information obtained from the driving safety professionals panel and findings from the preliminary search about the likelihood of finding sufficient evidence in the literature to support a systematic review to select the medical conditions included in the review. The final list of medical conditions:

- ADHD
- ASD
- CVD
- Diabetes
- MCI
- OSA
- Peripheral neuropathy
- Stroke
- Syncope
- TBI/concussion

Literature Search Parameters

Search terms. The final literature search sought studies describing the effects of the selected medical conditions on driving performance or crash risk. The search included peer-reviewed journals, and technical and government reports published from 2012 to 2020. The medical conditions were searched in the following six databases: TRID, PsycINFO, PubMed, SafetyLit, Web of Science, Google Scholar. Published systematic reviews and meta-analyses were also sources. For each medical condition, terms from the Medical Subject Headings (MeSH) thesaurus were used to increase the efficiency of each target search. The following terms were included in the database searches.

- driv*
- crash
- accident
- fatal
- injur*
- diagnosis
- treatment
- perform
- brak*
- steer
- vision
- cognition (except for MCI)
- proprioception

- sensorimotor
- react
- response

Inclusion/exclusion criteria. An article was included if it met all the following criteria:

- Was an English-language publication;
- Had a publication date of 2012 or later;
- Included an outcome measure(s) with a direct relationship to driving performance and/or safety *or* reports an indirect indicator with clear safety relevance (e.g., disease-related impairment of a functional ability established in the scientific literature as a significant predictor of crash risk; changes in a behavior such as seat belt use that are influenced by symptoms associated with a particular medical condition);
- Had undergone peer review or review from an agency without the identification or appearance of a conflict of interest. We considered for inclusion reports from the following organizations: U.S. Department of Transportation, State Departments of Motor Vehicles/Departments of Transportation, Transportation Research Board, American Occupational Therapy Association, and additional organizations on a case-by-case basis. We excluded reports if there was the identification or appearance of a conflict of interest.

An article was <u>excluded</u> if it met <u>any</u> of the following criteria.

- Published exclusively in a foreign language
- Published prior to 2012
- Reported results exclusively for special populations including the following examples:
 Operators impaired by drugs or alcohol
- Published by an organization with an identified or potential conflict of interest

Allowances for self-reported data. Over the course of the multi-step screening process described below, articles that relied *solely* on self-reported driving history, behavior, and safety or performance outcomes were excluded. However, studies that included self-reported measures *in addition* to objective outcome measures were retained for in-depth review. Regarding the criteria for diagnosing a medical condition, studies that included self-reported data for conditions where validated self-screening instruments are clinically recognized markers for the condition (e.g., ADHD and ASD) qualified for inclusion in the review.

Assessments of inclusion and study quality. The articles identified in this search underwent a three-step process to assess study quality. Step 1 included only the titles and abstracts from the search results, which were analyzed and assessed via a rubric to ensure they met the inclusion and exclusion criteria listed above. This step considered items such as publication date and language, indication of peer or agency review, results distinctly related to the medical condition of interest, and the report of direct or indirect measures of driving safety or performance. Studies whose title and abstract did not meet the inclusion and exclusion criteria applied in Step 1 did not move forward in the review.

For studies retained after Step 1, an assessment of study quality was applied to the full article in Step 2. Here, 15 questions pertaining to study quality were applied to all studies, with seven additional questions pertaining to experimental studies only—the latter category including interventions or treatments to control the effects of a medical condition. The research team

consulted the *Newcastle-Ottawa Scale* and the *RTI Item Bank* when selecting the Step 2 questions. Finally, Step 3 was an optional assessment that was applied only if the body of literature was large enough to merit the application of extra discriminators like sample characteristics, type of outcome measures, etc. Appendix C presents the full Steps 1–3 Assessment Rubrics. The Step 1 assessment was reapplied in Steps 2 and 3 of the full article review to ensure the quality of the articles as they moved through the review process. An article, at any step of the process, that did not meet the inclusion and exclusion criteria as stated in Step 1 was excluded from the review. After the Step 3 assessment, we conducted a reevaluation of item 4 (distinct results for people with a medical condition) and item 5 (direct measure(s) of driving safety and/or performance) of the Step 1 documentation, where articles in which the medical condition was not clinically diagnosed and articles without clearly stated objective driving or safety measures were excluded.

Selected Medical Conditions

The remainder of this report contains the systematic literature review for each selected medical condition in separate chapters. Each chapter includes a brief overview of the medical condition and the number and type of studies included in the review. A Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) diagram, describing the number of articles found during each step in the search process, is provided at the beginning of each medical condition is within each chapter.

References for Chapter 1

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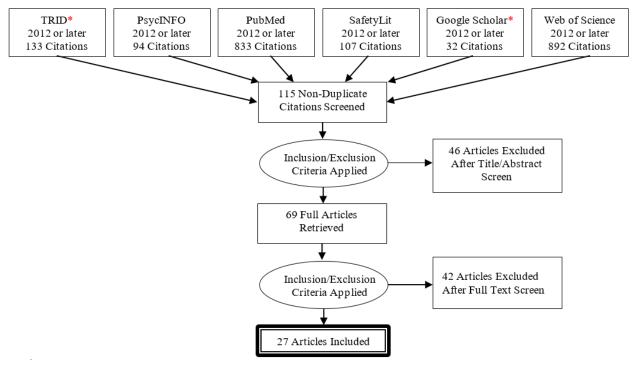
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2. Attention Deficit Hyperactivity Disorder

ADHD is a neurodevelopmental disorder that most often results in impulsiveness, attention difficulty, and hyperactivity. This disorder is one of the most common childhood chronic conditions but has been documented to persist well into adulthood for at least one-third of children diagnosed with ADHD; over this time, symptoms of ADHD can change or fade (Centers for Disease Control and Prevention, 2020b).

Definitive causes of ADHD are currently unknown, but research shows a strong connection with genetics (Faraone et al., 2021). Some other possible risk factors include low birth weight, premature delivery, or environmental factors such as exposure to lead during pregnancy. It is estimated that over six million children have had an ADHD diagnosis, according to a 2016 parent survey (Centers for Disease Control and Prevention, 2020a).

For this review, we conducted a multi-step screening of articles extracted through six database searches (see Methods for details of this process). Initially, 115 studies were returned. Of these, 46 articles were excluded after the initial abstract screening, with the most common reason for exclusion being that the article reported a literature review, not an empirical investigation. Forty-two articles were excluded after the in-depth full-text review, most commonly due to a lack of results distinctly associated with driving performance or safety. After applying all study inclusion and exclusion criteria (see Methods), 27 articles were advanced for the systematic review. Details of the inclusion and exclusion process are presented in Figure 1.



*Indicates sources that will also produce agency-reviewed publications (e.g., Government technical reports). Figure 1. Results of the multi-step process of searching and screening reports/articles for ADHD

The study methods of these 27 articles varied. Twelve studies centered on performance measures using driving simulators. Six articles used naturalistic observation or on-road assessments for participants with ADHD. Five articles relied on hospitalization or hospital-based data. Four more

articles examined data in the form of police records or recorded crash data. ADHD status was confirmed via clinical evaluation or validated screening measures in all included studies—no studies were included that relied on a self-reported diagnosis only. Additionally, any studies that reported crash or violation statistics used data from confirmed sources, either via police report or hospital records, and studies featuring learner or other unlicensed drivers were excluded.

The current research on ADHD and driving safety overwhelmingly shows that people with ADHD have a significantly higher crash rate than those without the condition, as evidenced by studies examining population data (Aduen et al., 2018; Chang et al., 2014; Chang et al., 2017; Curry et al., 2017; Sadeghi et al., 2020) which show drivers with ADHD have a crash risk approximately 1.4 times higher than controls (Aduen et al., 2018; Chang et al., 2014; Chang et al., 2017; Curry et al., 2017; Curry et al., 2019). Drivers with ADHD are also more likely to engage in risky driving behaviors like speeding and alcohol use as evidenced by structured interviews and reported violations, suggesting that risky driving behaviors could underlie the elevated crash risk among this cohort (Curry et al., 2019; Farouki et al., 2014; Koisaari et al., 2015; Wolff et al., 2019). There was also a trend for drivers with ADHD to be licensed significantly less often and later than drivers without ADHD (Curry et al., 2017; Curry et al., 2019; Koisaari et al., 2015), though Curry et al. (2019) did not find any significant differences in crash rates by age at licensure for drivers with ADHD. Curry et al. (2019) also looked specifically at the effect of ADHD on crash risk among novice drivers and found that drivers with ADHD had a 62% increased risk of crashing in the first month of licensure compared to controls, highlighting a risk elevated beyond that of an already high-risk group.

It is possible that symptom severity may be an important factor in assessing crash risk for drivers with ADHD. Research that examined data from a large naturalistic driving study found a 5–6% increase in crash and near-crash risk per increase in symptom severity (based on each point increase in the Barkley Adult ADHD Quick Screen [BAQS] score) (Aduen et al., 2018). Similarly, higher levels of ADHD symptoms (based on scores from various validated ADHD screening measures) have been shown to correlate with poorer performance on simulated driving assessments (McDonald et al., 2018, Groom et al., 2015).

The current research also shows that drivers with ADHD demonstrate significantly poorer driving performance than those without the condition. Studies using driving simulators have found that people with ADHD display deficits in lane deviation (Michaelis et al., 2012; Bioulac et al, 2015; Bioulac et al., 2020; Shaw et al., 2019) and speed variance and speeding (Groom et al., 2015; Narad et al., 2013; Shaw 2019) when compared to controls. Specifically, Groom et al. (2015) found that the ADHD group drove faster approaching hazardous events than the control group and that significantly more participants with ADHD drove past the events too fast and caused a crash or near miss, whereas more participants in the control group stopped, slowed down, and changed lanes in response to an event. Oliver et al. (2012) also found that drivers with ADHD had significantly more collisions during simulated driving than controls.

There are several other factors that could underlie the higher crash risk experienced by people with ADHD, such as emotional reactions while driving (Groom et al., 2015; Oliver et al., 2012; Wolff et al., 2019). For example, Oliver et al. (2012) revealed that a subgroup of ADHD drivers who scored higher on a measure of ADHD symptoms and had experienced multiple collisions also had significantly more tactical errors and collisions than the other ADHD participants; this subgroup also reported significantly higher levels of frustration than both their ADHD peers and controls during all driving conditions (baseline drive and conditions intended to induce

frustration). Groom et al. (2015) also found that during a simulated drive, drivers with ADHD made significantly more verbal comments than controls, particularly expressing anger and swearing at other road users; here, anger and swearing correlated significantly with hyperactivity/impulsivity scores on a validated ADHD measure (the Conners Adult ADHD Rating Scale [CAARS]). Likewise, Wolff et al. (2019) examined crash characteristics of trauma center patients and found no significant difference in the location and type of crash between people with ADHD and controls but found that drivers with ADHD reported significantly higher levels of stress prior to the crash.

In addition to experiencing more negative emotions while driving, research shows that drivers with ADHD may be less alert than drivers without ADHD (Bioulac et al., 2015; Bioulac et al., 2020). A 2015 study by Bioulac et al. found that just 15% of the ADHD group was considered 'alert' for daytime wakefulness (34–40 mean minutes of wakefulness across three 40-minute maintenance of wakefulness tests). Analysis by level of wakefulness revealed that the sleepy ADHD group (0– to 19 minutes average wakefulness) had higher lane deviance than the more-wakeful ADHD groups and the control group. Overall, the ADHD group demonstrated significantly slower reaction times than controls and scored significantly higher on the self-reported measures of sleepiness (Epworth sleepiness scale). A later study by Bioulac et al. (2020) found significantly higher steering variability and number of inappropriate lane crossings among participants with ADHD when compared to controls. These differences may be mediated by sleep latency, as the ADHD participants demonstrated poorer performance on these measures as wakefulness decreased.

Research has also examined the effect of distraction, particularly cell phone use, on the driving performance and safety of people with ADHD (Farouki et al., 2014; Narad et al., 2013; Kingery et al., 2014, Stavrinos et al.; 2015, Groom et al., 2015; Michaelis et al., 2012). Research examining driver eye gaze during regular drives and/or while using cell phones did not reveal any significant group differences in gaze measures (Groom et al., 2015; Kingery et al., 2014; Michaelis et al., 2012). However, Kingery et al. (2014) found that visual inattention (number of glances away from the roadway lasting greater than two seconds) mediated the ADHD group's deficits in lane position during hands-free phone conversation and texting conditions, and Stavrinos et al. (2015) found that, when texting, drivers with ADHD drove significantly faster through a scenario than controls. Generally, research on the effect of distraction on drivers with ADHD has found significant effects of cell phone use across all drivers without regard to group, suggesting that the negative effect of cell phone use is independent of ADHD status. This pattern holds true for roadside distractions. Shaw et al. (2019) found that both ADHD and control drivers evidenced more lane position and speed variability in the presence of a roadside distraction, but there was no significant effect of group (ADHD versus control group). In contrast, when examining the impact of retrospectively self-reported internal and external distraction among patients hospitalized from injurious crashes, Farouki et al. (2014) found a significant interaction between ADHD and exposure to external distractions prior to a crash.

The research described thus far included only non-medicated ADHD participants, except for Farouki et al. (2014) and Oliver et al. (2012), where just one and two participants, respectively, were taking ADHD medication at the time of the study protocol. However, the poorer driving performance observed among people with ADHD may be alleviated by ADHD-specific medication. A meta-analysis (Pievsky & McGrath, 2018) and systematic review (Gobbo & Louza, 2014) concluded that the use of medications, particularly stimulants, can improve driving

performance among people with ADHD. Several recent simulator and on-road studies also support this finding. Two simulator studies reviewed examined the effect of medication, both within-individual and compared to a control or placebo group, and each found significant improvements in driving performance when people with ADHD used stimulant medication (Barragan & Lee, 2018; Biederman et al., 2012). Specifically, Biederman et al. (2012) found that after six weeks of treatment, medicated drivers with ADHD demonstrated significantly better speed control and less excessive speeding and reacted, on average, 9.1% faster to surprise events than those in the placebo group. These medicated drivers were also 67% less likely to have a simulated collision than those in the placebo group. Barragan and Lee (2018) went a step further by isolating just those drivers involved in a collision during their simulated drive and found that, among this group, non-medicated ADHD drivers had significantly more crashes and showed significantly poorer driving performance than when medicated and when compared to controls. In particular, the non-medicated ADHD drivers had significantly higher velocity and brake force and significantly reduced steering movement prior to a simulated crash, compared to when medicated and to controls.

The finding that treatment with medication can improve simulated driving performance in people with ADHD is echoed in studies assessing on-road driving. The research team identified four studies that measured the effectiveness of ADHD medication on real-world driving, and each found that treatment with a stimulant or non-stimulant medication significantly improved driving performance in people with ADHD (Cox et al., 2012; Randell et al., 2020; Sobanski et al., 2012; Verster & Roth, 2014). On-road evaluations showed significant reductions in driving errors following treatment with medication (both stimulant and non-stimulant); these reductions were observed in both the overall number of errors as well as in individual measures like gap selection, speed control, weaving, and lapses in attention resulting in prolonged lane departure (Randell et al., 2020; Sobaski et al., 2012; Verster & Roth, 2014). Notably, Randell et al. (2020) also found that there was no significant difference in the number of errors between medicated ADHD drivers and controls. However, these studies also showed that the unmedicated ADHD drivers performed significantly worse than the medicated ADHD drivers and controls in areas of attention, risk-related self-control, and hazard detection (Randell et al., 2020; Sobanski et al., 2012).

Another interesting finding from the Randell et al. (2020) study was that both medicated and unmedicated ADHD drivers had significantly more errors associated with inattention and impatience during the low demand driving scenarios (highway and rural) versus high demand (urban). Moreover, unmedicated ADHD drivers had a 25 times higher error rate in the low demand environment than in the higher demand environment; this increase is compared to just a two-fold increase in this measure for controls (Randell et al., 2020). This study was conducted in the driver's own vehicle, and the researchers noted that while transmission type was not a controlled variable, both unmedicated and medicated ADHD drivers using a manual transmission showed significantly better driving performance related to transmission type among controls. These combined findings led Randell et al. (2020) to suggest that task demand may play an important role in ADHD driver performance, with high demand conditions increasing ADHD drivers' allocation of attentional resources to the driving task.

Questions remain, however, about how medication-related improvements in performance among drivers with ADHD translate to safety. Some studies that examined population data found that

the use of medication significantly decreased crash risk by 30 to 60%, based on both populationand individual-level statistics (Chang et al., 2014; Chang et al., 2017). However, not all studies reviewed came to this conclusion: several found no significant difference in crash risk between treated and untreated drivers with ADHD (Aduen et al., 2018; Curry et al., 2017; Winterstein et al., 2020). It is possible that these mixed findings are due to an artifact of the methodology used to define medication treatment for population-based studies, as these studies relied on selfreported medication use and prescription data to determine treatment status. This method does not allow for verification of medication use or adherence to a medication regimen.

Cox et al. (2012) examined this question more robustly. They fitted the vehicles of 17 high-risk young adults with ADHD with an in-car video monitoring system while for three months drivers participated in both of two treatment conditions, with and without medication. The sequence in which the two treatment conditions were administered for a given driver was randomly assigned. Here, the researchers strictly measured medication adherence and found a 56% adherence rate. There were significantly more collisions when drivers were unmedicated, with no collisions observed while drivers were medicated and eight collisions during the non-medicated condition; in seven of those eight collisions, the non-medicated ADHD driver was determined to have contributed to the crash. Blind coders also identified that the non-medicated drivers were significantly more likely to engage in risky driving behaviors such as sudden decelerations, driving in bad weather, and interacting with a passenger. Merkel et al. (2016) further examined these data by including minor incidents as well as a control group for comparison. They found that the overall ADHD group was significantly more likely than controls to be involved in a minor incident and was also significantly (specifically, four times) more likely to be driving through an intersection during these minor events. Medication use was not evaluated for minor incidents, and it is important to note that the inclusion criteria for this naturalistic driving study, from which Cox et al. (2012) and Merkel et al. (2016) derived their data, required that the ADHD participants have a history of more than one crash and/or violation in the prior two years; thus, the results from these analyses may not be generalizable to the overall population of drivers with ADHD.

The current literature search also identified a meta-analysis specific to this medical condition published within our review period (Vaa, 2014). This meta-analysis includes some individual studies that were conducted earlier but may draw in part research reported in the present review. The general findings of the meta-analysis suggest that drivers with ADHD have a significantly higher risk of being in a crash than those without (36% higher risk) even when controlling for exposure (23%) and publication bias (29%); there was also a significantly higher risk of personal injury crashes among people with ADHD. This meta-analysis also found that drivers with ADHD tend to drive more frequently without a license and have more traffic violations, speed violations, and driving license revocations than controls, and are also more likely to be culpable in the crash.

In summary, the research reviewed in this chapter brings compelling evidence that drivers with ADHD are at higher risk for adverse driving outcomes compared to drivers without this condition. It is likely that this risk increases as measurable ADHD symptoms increase. However, research also suggests that drivers with ADHD can alleviate some of the risk by taking medications designed to reduce ADHD symptoms.

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3. Autism Spectrum Disorder

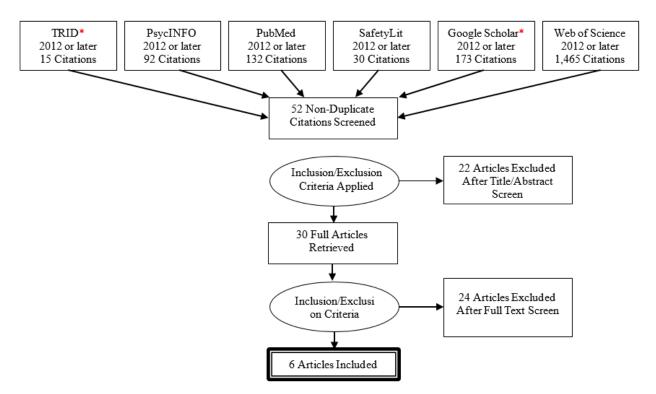
ASD is a chronic developmental disability that generally appears before the age of 3. It impacts social interaction, verbal and non-verbal communication skill, and cognitive function. The symptoms typically vary in intensity. People with ASD commonly experience numerous comorbidities (other medical conditions or diseases), including anxiety, allergies, feeding and digestive disorders, sensory integration dysfunction, sleeping disorders, and immune disorders. The most common coexisting condition in children with ASD is ADHD (Children and Adults with Attention-Deficit/Hyperactivity Disorder, n.d.). Under the definition of ASD used in this review, studies that addressed any or all the following were eligible for inclusion: autism spectrum disorder, pervasive developmental disorder, Asperger syndrome, childhood disintegrative disorder and Rett syndrome, and autistic disorder. Although studies that contained participants with both ADHD and ASD were included, studies that focused solely on ADHD were excluded from this chapter; this condition is considered in Chapter 2.

ASD is the fastest growing, but one of the most poorly understood, developmental disorders (National Autism Association, n.d.). Currently, the risk factors identified for ASD include genetic, environmental, and behavioral factors. Autism now affects 1 in 54 children; over half are classified as having an intellectual disability or borderline intellectual disability (National Autism Association, n.d.). There is higher prevalence of autism reported in males than in females; this difference was reflected in many of the samples in the studies reviewed in this research.

We conducted a multi-step screening of articles published in 2012 or later extracted through six database searches (see Methods for details of this process). The research team initially found 52 search results. Of these, 22 articles were excluded after the initial abstract screening, with the most common reason for exclusion being that the article was not found to be peer reviewed. Twenty-four articles were excluded after the full text in-depth review, most commonly due to a lack of results distinctly associated with driving safety or performance. After applying all inclusion and exclusion criteria (see Methods), six articles were advanced for the systematic review. Details of the inclusion and exclusion process are presented in Figure 2.

In four of the reviewed articles, simulators were used as the metric of driving performance. Of these, one study used on-road driving performance (along a predetermined route) as an outcome measure, and one study used both on-road and driving simulator measures. Sample sizes varied among the six articles. As noted earlier, samples tended to have more males than females, when this statistic was given.

The driving simulation studies presented a variety of hazards that potentially involve social interactions, such as pedestrians at intersections or crossing the street, and non-social hazards, such as cars in incoming traffic. One finding in these studies was a difference in reaction times between participants with ASD and a neurotypical (NT) control group. Specifically, Bishop et al. (2017) found that an NT control group reacted more quickly to social hazards versus non-social hazards, while no significant difference was found in reaction times to social versus non-social hazards for the ASD group.



*Indicates sources that will also produce agency-reviewed publications (e.g., government technical reports).

Figure 2. Results of the multi-step process of searching and screening reports/articles for ASD

Drivers with ASD also exhibited differences in gaze orientation compared to NT drivers (Reimer et al., 2013; Chee et al., 2019b). These differences were based on eye tracking data while in a driving simulator. Reimer et al. found that drivers with ASD appeared to spend less time oriented towards the lower visual field and more time gazing towards the horizon, with a mean vertical gaze in centimeters that was 44% higher than the NT control group. Chee et al. found drivers with ASD focused their gaze on the road ahead of them. Comparatively, the control group focused more on the pedestrians, traffic lights and speed limit signs while completing the simulated drive. Consequently, these researchers found the percentage of driving errors, such as stop-light infractions, to be significantly higher in the ASD group; when traffic signals changed from green to amber to red, more ASD participants drove past the light without stopping.

Reimer et al. (2013) also conducted a hands-free phone task during simulated urban driving. When compared to control participants, participants with ASD tended to shift their gaze higher and away from the forward roadway scene while completing the call. This suggests that people with ASD shift their attention to less complex portions of the visual scene during increased cognitive demand while driving. However, it was found that participants in both the control and ASD groups were involved in an equal number of collisions during simulated driving. Thus, the observed increase in driving errors among participants with ASD may not translate into a higher risk of crashes or fatalities.

Indeed, other findings point to an equivalence between ASD and NT drivers, and certain behaviors suggest ASD drivers may be less at risk for some types of collisions. Cox et al. (2020) found no difference between ASD drivers with less than two years of driving experience, NT drivers with less than two years of driving experience and 10 or more years of driving experience when tracking their glances to critical driving targets or towards the speedometer during simulated driving. Additionally, drivers with ASD were safer than NT drivers with respect to car-following distance. This finding is consistent with another study which showed that, when completing a simulated drive, drivers with ASD were observed to drive further away from the lead vehicle (Chee et al., 2019a). The authors speculated that this behavior among ASD drivers could possibly be due to differences in spatial awareness that affected their judgment in depth perception.

The results of a naturalistic on-road observational study by Chee et al. (2017) highlights additional differences that may be manifested by a convenience sample of drivers with ASD and NT drivers. Vehicle maneuvers by the ASD group such as steering at intersections were slower and more hesitant, especially when making right turns at intersections, as compared to the NT group. Also, drivers with ASD were more consistent in using their right turn indicators when exiting roundabouts compared to the control group. Accordingly, these authors caution against labeling people with ASD as "high risk" drivers.

Overall, the current research demonstrates that drivers with ASD differ from NT drivers in areas such as reaction time and vehicle maneuvering. However, the ASD drivers were found to drive more often in accordance with the road rules, such as checking for cross-traffic and using turn signals, when compared to NT drivers. The studies included in this chapter focused on those with their driver licenses; studies that used participants with learner permits or who remained under GDL restrictions were excluded, to remove the potential confound of differences in driving exposure. Additional limitations were that the evidence reported was overwhelmingly reliant on simulated driving measures, with no reports of the incidence or prevalence of involvement in actual motor vehicle crashes by drivers with ASD. Finally, as all the studies included small sample sizes, they cannot provide any firm conclusions about the risk associated with the effects of ASD on driving.

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4. Cardiovascular Disease

CVD, heart disease, is an umbrella grouping of disorders and includes coronary heart disease, cerebrovascular disease, peripheral arterial disease, rheumatic heart disease, congenital heart disease, and deep vein thrombosis. Under the definition of CVD used in this review, studies that addressed any or all the following were eligible for inclusion: the effects of blood vessel disease, such as coronary artery disease; heart rhythm problems (arrhythmias); congenital heart defects; heart valve disease; disease of the heart muscle; or heart infection. However, studies that included stroke were excluded from this chapter and detailed in Chapter 9.

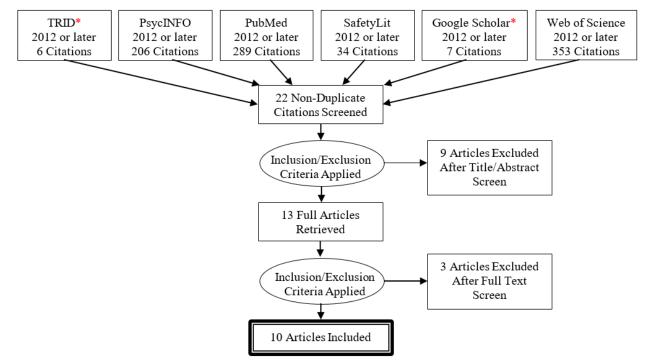
CVD commonly results from hypertension, unhealthy diet, lack of physical activity, smoking, or diabetes. Risk can be increased in the elderly and in those with family history of cardiovascular disease. Heart disease is the leading cause of death for men, women, and people of most racial and ethnic groups in the United States (CDC, 2020).

We conducted a multi-step screening of articles published in 2012 or later extracted through six databases searches (see Methods for details of this process). This followed the initial return of 22 search results. Of these, nine articles were excluded after the initial abstract screening, with the most common reason for exclusion being that the article was a literature review, not an empirical study. Three articles after the full text in-depth review, most commonly due to a lack of results distinctly associated with CVD as defined in this review. After applying all inclusion and exclusion criteria (see Methods), 10 articles were advanced for the systematic review. The multi-step inclusion and exclusion process is summarized in Figure 3.

The nature of these 10 articles varied in both study method and sample size. About half of the studies used driving simulators for performance measures but were characterized by small sample sizes. The other half of the studies retrospectively reviewed and compared data from larger samples, examining fatalities and injuries from motor vehicle collisions over multi-year periods.

Three studies that examined international fatal crash data all found similar results (Breen et al., 2018; Brodie et al., 2019; Tervo et al., 2012). Although sample sizes were relatively small (i.e., each study included fewer than 500 motor vehicle crash fatalities in total), these studies found that approximately 10% of all fatal crashes were attributed to sudden natural deaths behind the wheel. Among these deaths, a heart-related problem, predominantly ischemic heart disease, was the most common medical condition identified during the autopsy. In these studies, males over the age of 50 represented most drivers suffering a sudden natural death behind the wheel, and nearly all cases were single-vehicle crashes where the driver was the only injured party. Thus, drivers with sudden incapacitation due to cardiovascular events appear to represent a small risk to other road users. However, Norwegian researchers found that, when examined more closely, there was a discrepancy in crash type between drivers who were determined to die of natural causes behind the wheel (predominantly cardiovascular-related) and drivers who had signs of medical conditions that may have caused a sudden incapacitation before the crash (Breen et al., 2018). Here, 60% of drivers who died of crash-related injuries but who had signs of a medical condition-related incapacitation prior to the crash collided with another vehicle, compared to 11% of drivers who died from natural causes. This finding highlights a central limitation of retrospective fatal crash analyses on cardiac events while driving in fatal crashes, the role of the medical condition in contributing to the crash is often obscured by injuries determined to be the cause of death. Also, it is not always possible to determine if a driver was incapacitated by the

medical condition detected at autopsy because the behavior of the driver immediately before the crash is often unknown.



*Indicates sources that will also produce agency-reviewed publications (e.g., government technical reports).

Figure 3. Results of the multi-step process of searching and screening reports/articles for CVD

There were few crashes throughout these studies where risk of a cardiovascular event prior to the crash was identified. Brodie et al. (2019) examined medical causes of death behind the wheel and found that three of the 33 drivers with available medical histories had complained of chest pain to others or their doctor prior to the incident, and Tervo et al. (2012) identified three of 13 drivers with CVD who did not fulfill European Union health criteria and/or national regulations for their driving license. This does not speak to whether preventive measures could alleviate crash risk. Two studies explored this question. Using a Taiwanese national health database, Lai et al. (2015) investigated if patients diagnosed with atrial fibrillation (AF) had higher risk of crash-related hospitalization and, if so, whether the use of antithrombotic medication lessened this risk. The researchers found that drivers with AF had a slightly higher (1.110-fold) risk of a crash-related hospitalization than those with other comorbidities e.g., other CVDs but without this specific disorder. Those over 65 and with various medical conditions, such as coronary artery disease, chronic obstructive pulmonary disease (COPD), stroke, and liver cirrhosis were identified as positive predictive factors, particularly when combined with an increased risk of thromboembolic events according to a standard clinical screening tool. The use of oral anticoagulant (OAC) medication could significantly reduce the risk of crash-related hospitalization in patients with AF; when this medication was used regularly (over 50% of the time), the risk of crash-related hospitalization was reduced to that of controls.

Gaudet et al. (2016) found similar results when investigating the effect of a cardiac rehabilitation program on simulated driving performance between drivers having suffered recent cardiac events and demographically matched controls. These researchers found that participants in the cardiac

group showed significantly worse simulated driving performance than their healthy peers prior to intervention. Driving improvements were seen in both groups following a 12-week comprehensive exercise and education program, but the improvement was greatest among the cardiac group, to the extent that their performance was no longer statistically different from controls.

While results showing that preventative measures can help reduce the risk among people with heart conditions are promising, these studies had several limitations. In the Lai et al. (2015) study, participants in both groups were matched for comorbidities which included CVD, and no predictive analysis was done for the control group; thus, the role of CVD in crash-related hospitalization among people *without* atrial fibrillation was not examined. Also, this study did not identify if the injured people were driving the vehicle at the time of the crash or whether they were passengers or non-occupants (e.g., pedestrians). While the Gaudet et al. (2016) study did not include any CVDs among controls, the sample size was small, with just 12 cardiac and 13 healthy control participants. Another limitation of this study is that the mechanisms behind the changes in driving performance were not investigated as it did not include any measures of cardiovascular fitness or cognitive performance.

Declines in cognitive function among cardiovascular disease patients raise concern, particularly in domains like executive function and attention that have long been established as significant predictors of crash risk in older drivers (Staplin et al., 2003). Two studies were identified that sought to examine the relationship between cognitive function and reduced driving performance among people 50 and older (n = 18; n = 19) with varying CVDs, both of which relied on driving simulators rather than on-road driving performance or naturalistic driving behavior. However, the simulator measures and scoring methods used in these studies all previously showed positive correlations with on-road driving evaluation outcomes (Alosco et al., 2013; Gaudet et al., 2013). Both studies showed that people with CVD performed worse than healthy controls on simulated driving tasks, on tests of attention/executive function and on tests of motor function (Alosco et al., 2013). Gaudet et al. (2013) found that executive function was the only tested cognitive domain (alerting, orienting, and executive function) significantly associated with driving performance, but notably, executive function did not play a mediating role in the relationship between CVD and driving performance. The researchers suggest that this finding could be related to the heterogeneity of the cardiac group, which included people with various CVDs and comorbidities (i.e., diabetes and hyper-tension).

The Gaudet et al. study evaluated driving performance based on a global score, but Alosco et al. (2013) found that people with CVD (heart failure only) demonstrated significantly worse driving performance than controls on specific measures, including the number of collisions, missed stop signs, centerline crossings, and off-road excursions. The heart failure group also demonstrated reduced performance on cognitive tests, and reduced attention/executive and motor function were associated with poorer performance during the driving simulation. However, the control group did not undergo cognitive testing, so it is unknown if the same correlation was present among healthy controls.

Alosco et al. (2015) sought to extend their findings by examining the association between brain structure assessed using magnetic resonance imaging (MRI), cognitive function, and self-reported driving independence and simulated driving performance among CVD patients. Here, researchers found that decreased attention/executive function was significantly associated with a greater self-reported need for assistance with transportation among CVD patients; there was no

significant association between memory and self-reported driving independence. MRI results showed that reduced brain volume and greater white matter hyperintensities (WMH) were significantly associated with poorer simulated driving performance and/or less self-reported driving independence in CVD patients. While WMH predicted poorer simulated driving in this study, it was not significantly associated with cognitive test performance. However, this study did not examine a comparison group of healthy controls, and the sample size of simulator drivers was relatively small (n = 8). Therefore, the generalizability of these findings is limited.

Overall, the current research demonstrates that while drivers with CVD show reduced ability to perform cognitive functions relevant for driving such as attention and executive function, as well as reduced performance on a driving simulator, they do not appear to pose a great risk regarding fatal crashes because drivers suffering a CVD-related death are almost always involved in singlevehicle crashes. These findings should be interpreted with caution because the role of this medical condition in a fatal crash may be difficult to isolate. In addition, the types of driving errors made by a small sample of CVD participants (heart failure only) in the Alosco et al. (2013) study, such as collisions and center-line crossings, suggest the possibility of increased risk to both drivers and other road users. Although results were consistent across the studies reviewed, only a limited number of studies were published within the review period, and no studies were identified that examined the effects of chronic CVD on driving, outside of crashes related to acute CVD events. The studies that did evaluate driving performance used simulated driving and had small sample sizes; the fatal crash data analyses had larger overall sample sizes but each of these studies' authors suggest the results may not be indicative of the true occurrence of cardiovascular-related traffic deaths. Research into the incidence of CVDs among drivers involved in crashes at varying levels of severity and the on-road performance of drivers with chronic CVD could provide a valuable addition to the limited information available regarding the traffic risk associated with this medical condition.

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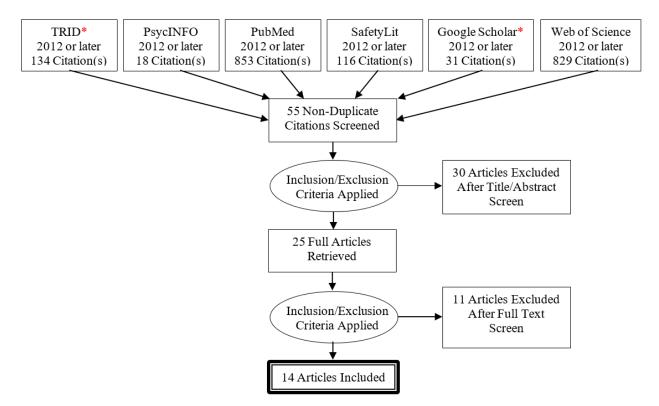
5. Diabetes

Diabetes affects levels of glucose in the blood. A stable level of glucose is referred to as euglycemia; abnormally low and high levels of glucose are referred to as hypo- and hyperglycemia, respectively. Symptoms of diabetes vary with the type of diabetes: people with type 1 diabetes (an autoimmune condition in which the pancreas does not make enough insulin) may experience symptoms that are more apparent or severe, while people with type 2 diabetes (a condition associated with resistance to insulin) may experience symptoms to a lesser degree or not at all. Symptoms can include frequent thirst, increased urination, extreme hunger, unexplained weight loss, fatigue, irritability, blurred vision, and presence of ketones in urine and frequent infections (Mayo Clinic Staff, 2020). Under the definition of diabetes used in this review, studies that address any or all the following were eligible for inclusion: gestational diabetes, type 1 diabetes, type 2 diabetes, prediabetes, and diabetic neuropathy. Studies focused specifically on CVD, a condition associated with diabetes, were excluded from this chapter, but detailed in Chapter 4. Chapter 8 also focuses on the effects of peripheral neuropathy on driving, without regard to the origin of the condition.

Type 1 diabetes often appears during childhood or adolescence, though it can develop at any age. The exact conditions that trigger type 1 diabetes are currently unknown, although risk increases with a family history of type 1 diabetes and the presence of autoantibodies. Type 2 diabetes is more common in people older than 40, although it, too, can develop at any age. Type 2 diabetes commonly results from genetic and environmental factors. Risk factors, in addition to a family history, include weight gain, physical inactivity, and increased age (Mayo Clinic Staff, 2020). Prolonged diabetes can result in neuropathy, cardiovascular disease, foot damage, hearing impairment, and Alzheimer's disease. In 2018, 10.5% of the U.S. population had diabetes (American Diabetes Association, n.d.).

We conducted a multi-step screening of articles published in 2012 or later extracted through six databases searches (see Methods for details of this process). Fifty-five search results were initially returned. Of these, 30 articles were excluded after the initial abstract screening. The most common reason for exclusion at this step was that the articles did not report new investigations; they were literature reviews. Eleven articles were excluded after the full text, indepth review. After applying all study inclusion and exclusion assessment criteria (see Methods), 14 articles were advanced for the systematic review. The most common reason for exclusion was due to a lack of results distinctly associated with driving performance or safety. Details of the multi-step inclusion and exclusion process are presented in Figure 4.

The nature of these 14 articles varied. Within these, seven studies used driving simulators, and, of these, five focused on neuropathy. Among the other seven articles, three studies measured invehicle driving performance, two examined data on crash events; one article used interviews, and one article focused on the frequency of severe hypoglycemic episodes in the context of European driving laws.



*Indicates sources that will also produce agency-reviewed publications (e.g., government technical reports).

Figure 4. Results of the multi-step process of searching and screening reports/articles for diabetes

The effect of diabetes on (simulated) driving is related to the levels of glucose in the blood. Haim et al. (2021) found that participants in a hypoglycemic state showed impaired vehicle control related to steering, accelerating, and braking variability compared to drivers without diabetes. Specifically, during hypoglycemia, drivers with type 1 diabetes maintained shorter distances between vehicles, displayed fewer glances towards hazards, and engaged the brake more often and with more force compared with diabetic drivers in a euglycemic state.

Peripheral neuropathy (discussed in more detail in a Chapter 8, as noted above) is a common comorbidity of diabetes. However, drivers with diabetes with and without peripheral neuropathy can differ from each other in driving performance. Drivers with diabetes but without peripheral neuropathy experience shorter duration of loss of control events during their drive compared to their peripheral neuropathy counterparts. In addition, drivers with diabetes but without peripheral neuropathy perform similarly to healthy controls regarding the use of the pedals, smoothly using the middle of the pedal's range of motion as opposed to more extreme pedal positions used by diabetic drivers with peripheral neuropathy (Perazzolo et al., 2020).

Drivers with diabetes report the same confidence in their driving skills as their healthy counterparts; however, Ma et al. (2020) found that there was a difference in actual and perceived simulated driving performance for male drivers ages 40 to 60 with type 2 diabetes even during non-hypoglycemic periods. Drivers with type 2 diabetes (n = 27) had significantly longer brake reaction times, deviated from the centerline for longer durations, and displayed a shorter minimum time-to-collision when compared to a healthy control group (n = 29) (Ma et al., 2020). Additionally, performance differed for drivers with diabetes and with peripheral neuropathy: researchers found a smaller distance-to-collision and longer brake reaction times for drivers with

serious diabetic peripheral neuropathy relative to drivers without diabetes or those with less severe diabetic neuropathy (Ma et al., 2019). Similarly, drivers with type 2 diabetes who presented with diabetic peripheral neuropathy had slower brake reaction times during simulated drives relative to drivers without diabetes (Meyr & Spiess, 2017), drivers with diabetes and without lower extremity neuropathy (Sansosti et al., 2017), or drivers with diabetes with lower extremity neuropathy but with no history of diabetic foot pathology (Spiess et al., 2017).

Driving impairments exhibited by drivers with type 1 diabetes are elevated during hypoglycemia, as noted above, but continue to affect vehicle control behavior fortwo to three hours after hypoglycemia resolves (Chakraborty et al., 2019). Despite this finding, many drivers with diabetes do not take additional precautions after a hypoglycemic event. A survey of 429 insulintreated drivers with diabetes in Saudi Arabia discovered that 44% (n = 189) would wait fewer than 10 minutes between the treatment of hypoglycemia and measuring their blood glucose level again, and 41% (n = 176) would wait fewer than 10 minutes between the treatment of hypoglycemia and measuring their blood glucose level again, and 41% (n = 176) would wait fewer than 10 minutes between the treatment of hypoglycemia and measuring their blood glucose level again, and 41% (n = 176) would wait fewer than 10 minutes between the treatment of hypoglycemia and measuring their blood glucose level again, and 41% (n = 176) would wait fewer than 10 minutes between the treatment of hypoglycemia and driving again (Almigbal et al., 2018). The article goes on to suggest low glucose awareness among individuals with diabetes, with 88% of participants not having in mind a specific blood glucose level that would preclude driving, 75% reporting never testing their blood glucose level during a journey, and 62% of participants never carrying a blood glucose testing kit while driving.

To better understand the extent to which fluctuations in glucose levels may be related to varying driving demands, Schmied et al. (2019) and Truninger et al. (2013) analyzed changes in glucose during on-road driving with hypoglycemic drivers. About 39 drivers, including a mix of individuals with type 1 and type 2 diabetes, completed a two-hour driving course designed to induce stress; this included driving in wet and dry conditions, a full braking exercise with water obstacles, and an exercise in which drivers had to regain control over their vehicle. Despite increases in blood pressure and heart rate, the drivers' glucose levels remained the same under high stress conditions as under control conditions in the Truninger et al. (2013) study. In contrast, Schmied et al. (2019) found fluctuations in glucose levels for a group of drivers with type 1 diabetes during a 2-hour rudimentary (low stress) drive through urban and suburban areas. These studies suggest that glucose fluctuations while driving may reflect idiopathic variables rather than environmental or task-related influences.

In a review of the distribution of multiple long-term diseases between 2005 and 2008, among drivers with recognized long-term diseases in France, drivers with type 1 and type 2 diabetes were found to be involved in 23.7% of injurious road traffic crashes. There was an increased risk (OR=1.47) of being responsible for the crash for drivers with type 1 diabetes (Orriols et al., 2014). While in an 11-year (2000–2010) study, no significant differences were found between drivers with a mix of both type 1 and type 2 diabetes, when compared to the population of people who had caused a crash or violation in Slovenia during the same 11-year study period. (Šestan et al., 2017).

Although many countries do not restrict driving for people with insulin-treated diabetes, the European Union has regulations that deem two severe hypoglycemic events within 12 months as grounds for driving license revocation. An epidemiological study used the Diabetes Control and Complications Trial (DCCT) data sets stored at the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) to calculate the potential effect of the European Union's regulation on the U.S. patients included in the DCCT 10-year (1982–1993) controlled clinical

trial (n = 1,441). Findings suggested that 30% of the DCCT cohort would have lost their driver's license at least once during the study period due to having more than one severe hypoglycemic episode within a year (Kilpatrick et al., 2013).

The evidence reviewed in this chapter, using measures of both simulated and real-world driving, largely supports the idea that shifts in glucose level impact driving performance for drivers with type 1 or type 2 diabetes. However, while the research literature in this area often groups drivers with type 1 and type 2 diabetes together, a key difference between people with type 1 and type 2 diabetes is the average age of onset, with type 1 typically developing earlier in life. The earlier onset of type 1 diabetes may allow more time for a person to understand the effects of diabetes on the body and develop compensation strategies. However, no studies in our review period examined whether the duration of drivers' diabetes influences the correlation between hyperglycemic or hypoglycemic events and driving.

The current literature search also identified a meta-analysis specific to this medical condition published within our review period (Hostiuc et al., 2016). This meta-analysis includes some individual studies that were conducted earlier but may draw in part on research reported in the present review. The general findings of the meta-analysis suggested that there is not a statistically significant increase in the risk of a collision for diabetic patients. As hyperglycemia and hypoglycemia were outside the scope of this meta-analysis, its findings reflect the overall collision risk in diabetes patients. The age, gender, insulin use, and geographic location of the drivers were not found to be statistically significant in relation to collision risk.

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6. Mild Cognitive Impairment

MCI is a condition that may develop with increased age, affecting memory or cognitive performance. Symptoms of MCI are often noticed first by friends and family. These can range from problems with memory to increasingly poor judgment. Some people with MCI may go on to develop dementia. While MCI can be an early stage on the Alzheimer's disease continuum for some, others with MCI revert to normal cognition or remain stable (Alzheimer's Association, n.d.). Under the definition of MCI used in this review, studies that address any of the following were eligible for inclusion: MCI and cognitive impairment. However, studies focused specifically on Alzheimer's disease and dementia were excluded from this review.

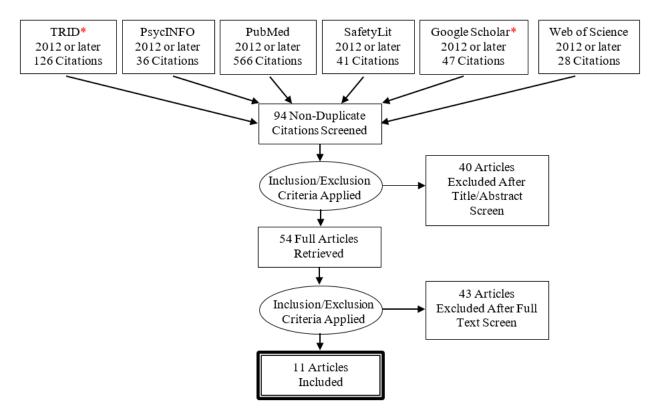
Due to the individualized nature of MCI, there is no specific test to confirm a diagnosis. Instead, diagnosis is assessed through multiple exams of basic mental abilities targeting a person's memory and processing skills, as well as neurological exams to rule out any other conditions. MCI commonly results from biological factors such as increased age or having a family history, affecting approximately 12 to 18% of people aged 60 or older and approximately 15 to 20% of people aged 65 or older (Alzheimer's Association, n.d.).

We conducted a multi-step screening of articles published in 2012 or later extracted through six databases searches (see Methods for details of this process). Ninety-four search results were initially returned. Of these, 40 articles were excluded after the initial abstract screening. The most common reasons were a lack of distinct results for the medical condition or a lack of clear implications for driving safety or performance. Forty-three articles were excluded after the full text in-depth review, again most often due to a lack of distinct results for the medical condition. After applying all study inclusion and exclusion assessment criteria (see Methods), 11 articles were advanced for the systematic review. Details of the inclusion and exclusion process are presented in Figure 5.

The nature of these 11 articles varied in method and sample size. In five articles, the outcome of interest used on-road assessments or naturalistic driving using in-vehicle instrumentation. Five articles tested participants using driving simulators or computerized tests, gathering information on reaction time or other participant responses. The last article used a validated self-report questionnaire on driving habits.

Economou et al. (2020) investigated 'accident probability' among study participants including drivers diagnosed with MCI, mild dementia, and healthy controls; accident probability was defined as the number of collisions while completing a simulated drive. Participants performed a distraction task, engaging in a conversation, while completing the drive. The drive contained two unexpected incidents involving the sudden presence of an animal on the road.

Participants navigated through four different driving simulator conditions, moderate traffic with and without distraction (conversation) and high traffic with and without distraction. Crash probability did not differ among the three groups in any of the four virtual driving conditions. Lower average speeds were displayed by the MCI group in both distraction conditions (moderate and high traffic) when compared to the control drivers. In the moderate traffic with distraction condition, drivers with MCI left larger distances between themselves and the lead car than the control drivers; in the high traffic with distraction condition, they were slower to respond to the unexpected incidents than the control drivers.



*Indicates sources that will also produce agency-reviewed publications (e.g., government technical reports).

Figure 5. Results of the multi-step process of searching and screening reports/articles for MCI

Beratis et al. (2017) also studied how distraction tasks during simulated driving affect driving performance in participants with MCI compared to healthy controls with no evidence of cognitive impairment. These researchers imposed two levels of distraction, a 'low demand' task (conversation) and a 'high demand' task (mobile phone use). They found a significant interaction for drivers with MCI, who demonstrated an increase in reaction time–calculated as the time between the first appearance of an unexpected incident and the moment the driver starts to brake–while driving and using a mobile phone (high-demand task) relative to driving with conversation (low-demand task) or driving without distraction, compared to the cognitively healthy drivers.

These researchers also examined crash risk during simulated driving, calculated as the proportion of unexpected incidents that resulted in crashes when compared to total incidents. For this measure, Beratis et al. (2017) again found an interaction effect such that drivers with MCI showed a significantly greater increase in both reaction time and crash risk under the 'high demand' (mobile phone use) simulated driving condition, compared to the group of cognitively healthy drivers. At the same time, overall, the patients with MCI demonstrated significantly lower variability in speed compared to the cognitively intact drivers; from a traffic engineering perspective, this connotes safer driving behavior.

Both Beratis et al. (2017) and Economou et al. (2021) found that, in simulators, drivers who had MCI reduced their speed under the mobile phone use level of distraction. This behavior can be looked at as an act of self-protection in which the driver slows down, anticipating a reduced ability to respond to risky situations in the driving simulation. However, Devlin et al. (2012)

found that foot hesitations, where a driver releases his/her foot from the accelerator without placing it on the brake, were made less often by participants with MCI than by healthy controls; to the extent this pattern reflects a lack of anticipation of changes in the driving task/environment for drivers with MCI, it stands in contrast to the reported speed reductions reported by Beratis et al. (2017) and Economou et al. (2021).

On-road driving evaluations conducted by Anstey et al. (2017) aggregated scores (1 to 10) from a driving instructor and an occupational therapist; a score less than four signified unsafe driving. When adjusted for age and sex, people with MCI had a lower average safety rating when completing the on-road assessment compared to a control group, 5.61 versus 6.05, respectively. This effect, while modest, was statistically significant.

However, multiple researchers have failed to find statistically significant differences in safetycritical behaviors for MCI drivers versus healthy controls (Devlin et al., 2012; Touliou et al., 2018). For example, Devlin et al. (2012) found no statistically significant difference between research participants with MCI when compared to a healthy control group regarding the number of brake applications, brake response time at critical light change intersections, number of right foot hesitations, and whether drivers stopped at both stop-sign controlled and critical light change intersections in a driving simulator. Touliou et al. (2018) reported no significant differences between MCI drivers and control drivers on computerized tests of multiple aspects of executive function that are believed to underlie safe driving in traffic, including measures of working memory, selective visual attention, response inhibition, and mental flexibility.

In a naturalistic study lasting approximately 1 month for each participant, Staplin et al. (2019) also found no differences in a range of driving performance measures between people with MCI versus a control group. Supplementing the driver performance measures, in-vehicle instrumentation also monitored driving exposure. No statistically significant differences between groups were observed for total number of trips, total miles driven, total hours driven, percentage of trips made in rain, percentage of trips made at night, percentage of trips begun during rush hour, percentage of trips on 60+ mph roadways, percentage of driving time on 60+ mph roadways, nor percentage of miles driven on 60+ mph roadways. Self-report data published by O'Connor et al. (2013), however, documented significantly higher avoidance of unfamiliar areas and high-traffic roads by MCI drivers than controls, although avoidance of other risky driving situations—left turns, night driving, and bad weather—was not significantly different between groups.

To better understand the difference between MCI drivers and their healthy counterparts, Eramudugolla et al. (2021) categorized each study participant as either a safe or unsafe driver based on the results of an open-road assessment conducted by an occupational therapist. Among study participants, 93% of the healthy controls and 83% of the people with MCI were categorized as safe drivers. An examination of specific driving behaviors found no significant differences between drivers categorized as safe with MCI and drivers categorized as safe in the healthy control group; when driving errors were noted, they were similar for both groups. However, among drivers categorized as unsafe, those with MCI demonstrated greater difficulty at intersections, roundabouts, parking, and driving on straight roads; and made more errors during self-navigation when compared to unsafe drivers in the control group.

Finally, there is a body of research involving drivers with MCI that has focused on the effects of various driving training. Teasdale et al. (2016) used a driving simulator with built-in auditory

feedback messages, to improve driving performance for people with MCI. The feedback messages were developed based on previous reports of common errors for drivers with cognitive problems, such as proper control of the vehicle and maneuvers involving executive function. During five training sessions over a 21-day period, there was a general decrease in the number of errors for nearly all performance measures, but there was no evidence of improved performance being retained after a 6-month period. In contrast, a specialized training program has been observed to sustain improved performance in drivers with MCI (Ishii et al., 2021; Shimada et al., 2018). In a randomized controlled trial, older drivers with MCI who completed a training program consisting of classroom-based vision training, driving simulator training, and tailored on-road driving lessons (20 hours total training) saw significant improvements in safe driving performance when compared to participants who only received one session of classroom-based driver education (Shimada et al., 2018). In this same group of drivers, significant effects of training were maintained 1 year after follow-up (Ishii et al., 2021).

The current literature search also identified a meta-analysis specific to this medical condition published within our review period (Hird et al., 2016). This meta-analysis includes some individual studies that were conducted earlier but may draw in part on research reported in the present review. Emphasizing the need for tools with sufficient validity to help clinicians assess driving ability among patients with MCI, these authors characterized research in this area as hampered by small sample sizes, an absence of age matching between patients and controls, and inconsistent cognitive predictors and driving outcomes across studies. Within these limitations, Hird et al. (2016) suggest that measures of executive function, attention, visuospatial function, and global cognition may be predictive of driving performance among patients diagnosed with MCI, using data pooled across multiple measurement methodologies, with the Trail Making Test Part B and the Maze Test emerging as the best single predictors. However, firm conclusions about the effect of MCI on driving risk are elusive due to a scarcity of studies pertaining to crash risk. Additionally, the idiosyncratic nature of how this condition presents among drivers, what may be a highly variable rate of progression to dementia, and co-morbidities including a decline in (other) functional abilities associated with normal aging also play a role in the quality and quantity of the studies available.

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7. Obstructive Sleep Apnea

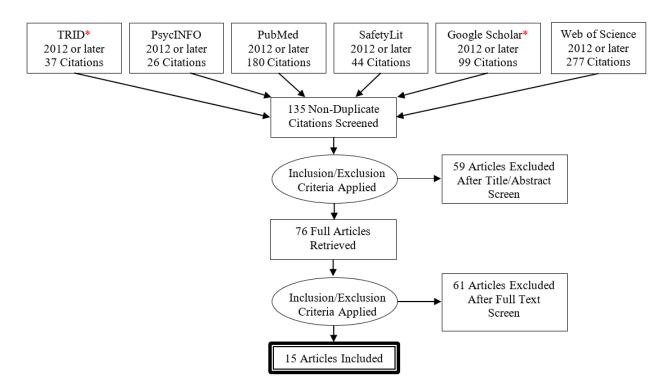
OSA is a condition affecting the airflow as one breathes during sleep. The most noticeable symptoms of obstructive sleep breathing can include snoring, excessive daytime sleepiness and morning headaches. Other signs of this condition can include momentary lapses of breath during sleep, gasping or choking upon awakening, or waking with a dry mouth or sore throat. Under the definition of OSA used in this review, studies that address any or all of the following were eligible for inclusion: OSA, sleep apnea, central sleep apnea, complex sleep apnea, and mixed sleep apnea.

OSA commonly results from the throat muscles occasionally relaxing, thus blocking the airway during sleep. Some of the main risk factors for developing obstructive sleep apnea are excess weight, a larger neck circumference, a narrow airway, a family history, nasal congestion, and medical conditions such as type 2 diabetes, high blood pressure, congestive heart failure, and Parkinson's disease. The likelihood of developing OSA is two to three times higher for males than for females; however, after menopause, women experience an increase in risk. Also, of the 22 million Americans estimated to be suffering from OSA, 80% are undiagnosed (American Sleep Apnea Association, n.d.). A continuous positive airway pressure (PAP) machine is a commonly prescribed device for people with OSA, providing a stream of air to the person overnight (Suni & Singh, 2020).

We conducted a multi-step screening of articles published in 2012 or later extracted through six databases searches (see Methods for details of this process). One hundred and thirty-five search results were initially returned. Of these, 59 articles were excluded after the initial abstract screening. The most common reason for exclusion at this level was that the article reported a literature review, not an empirical investigation. Sixty-one articles were excluded after the full text in-depth review, most commonly due to the lack of results distinctly associated with driving performance or safety. After applying all study inclusion and exclusion criteria (see Methods), 15 articles were advanced for the systematic review. The multi-step inclusion and exclusion process is summarized in Figure 6.

The study methods of these 15 articles varied. Six articles used simulated driving, while another six articles used police reports or hospitalization data to examine driving safety. The final five studies evaluated participants' on-road driving performance using in-vehicle monitoring. Most of these studies relied on polysomnography or other clinical criteria to classify drivers as having OSA; just two studies exclusively relied on validated self-report measures (Cetinoglu et al., 2014; Purtle et al., 2020).

Few studies were identified that examined whether non-commercial drivers with OSA are at increased crash risk. About two studies used police-reported crash data and found that measures of OSA were significantly associated with crash occurrence (Karimi et al., 2014; Karimi et al., 2015), particularly when PAP treatment was not used (Karimi et al., 2015). Karimi et al. (2015) found that drivers with OSA were at 2.3–2.6 times higher risk of having a police-reported crash than those without OSA; drivers with OSA also had a 1.9 times higher risk for crash-related injury compared to controls. One study was identified that looked at police-reported violations but did not find any significant risk of increased violations in the group of drivers with OSA relative to drivers without OSA (Rizzo et al., 2019).



*Indicates sources that will also produce agency-reviewed publications (e.g., government technical reports).

Figure 6. Results of the multi-step process of searching and screening reports/articles for OSA

There is a larger body of research examining behavioral safety measures in this population, but the findings are inconclusive. Generally, studies using driving simulators suggest that drivers with untreated OSA demonstrate significantly poorer lane maintenance, both compared to controls (Bajaj et al., 2015; Gieteling et al., 2012; May et al., 2016) and compared to themselves when treated with PAP (Baja et al., 2015; Filtness et al., 2012). This effect is particularly evident as the length of the simulator drive increases (Bajaj et al., 2015; Gieteling et al., 2012; May et al., 2016). However, when observed in a naturalistic setting, there appears to be conflicting evidence that people with OSA drive less safely than controls. Aksan et al. (2015) found significantly more safety errors while driving in the OSA group than in a control group, and following PAP treatment, the OSA group showed significantly *better* performance than controls. Here, performance was measured as a combined variable, looking at traffic sign and light violations, turn errors, lane maintenance, and hard accelerations together. In a later study, Aksan et al. (2018) examined only speed variability and variability in lateral and longitudinal acceleration and did not observe any significant differences that would indicate drivers with OSA were less safe than controls in a naturalistic driving environment, either pre- or post-PAP treatment. Yu et al. (2013) had similar findings, in that there were no significant group differences in naturalistic driving measures during inclement weather between drivers with OSA (primarily PAP-treated) and control drivers.

The inconclusive findings may be the result of heterogeneity in driving performance among drivers with OSA, which makes it difficult to identify which drivers in this group are at high risk. Vakulin et al. (2014) sought to isolate characteristics among drivers with OSA that make them more vulnerable to unsafe driving, measured by variability in steering/lane position, and found that only less driving exposure significantly predicted vulnerable driving status compared to

controls; specifically, the odds of qualifying as a vulnerable driver decreased as hours driving per week increased.

The reviewed studies do consistently find, however, that treatment with PAP is beneficial for improving the driving performance of drivers with OSA. When PAP treatment is used, drivers with OSA experience better attention to the driving task (Aksan et al., 2018) and show a significant reduction in safety errors (Aksan et al., 2015; Bajaj et al., 2015; Filtness et al., 2012), sometimes to the extent of having significantly better driving performance than controls (Aksan et al., 2015). The PAP-related changes in driving performance can be immediate, as Filtness et al. (2012) found that just one night without PAP use significantly worsened driving performance among compliant long-term PAP users. The PAP-related driving performance findings appear to have real-world safety implications, as well. Karimi et al. (2015) examined traffic records and PAP machine data and found that crash incidence decreased by 70% after intervention with PAP among drivers who were compliant with PAP use (at least four hours of use each night) but increased by 54% for drivers who were not compliant. This increased risk among non-compliant users may be related to significantly greater reported sleepiness. Likewise, Burks et al. (2016) found that PAP non-adherent drivers with OSA had a significantly (5 times) higher preventable crash rate than controls. However, it is important to note that these studies on PAP adherence were not randomized control trials, and the findings related to increased crash risk among drivers non-compliant with PAP are correlational.

Research on this condition is also consistent when examining the crash risk of commercial motor vehicle (CMV) drivers with OSA. OSA occurs more frequently among CMV drivers than the general population (Meuleners et al., 2015) and when untreated, CMV drivers with OSA are at 3 to five times higher risk for a crash than those using PAP and those without the diagnosis (Burks et al., 2016; Meuleners et al., 2015). Just one study was identified that examined the performance of CMV drivers with OSA using a driving simulator, but there were no significant differences in driving performance measures; however, CMV drivers with OSA demonstrated a significantly higher failure rate than controls on a computerized reaction time test (Demirdöğen Çetinoğlu et al., 2014), suggesting that reduced reaction time could be a factor in the higher crash rate among this cohort. But these results may be regarded as tentative, as this was the only study identified that measured objective driving performance among CMV drivers with OSA, and the sample size was relatively small (n = 30 OSA drivers).

The current literature search also identified three meta-analyses specific to this medical condition published within our review period (Schwartz et al., 2017; Kales & Straubel, 2014; Zhang & Chan, 2014). These meta-analyses include some individual studies that were conducted earlier but may draw in part on research reported in the present review. The general findings of these meta-analyses are consistent with the articles reviewed here, in that CMV drivers have increased prevalence of OSA and that CMV and non-commercial drivers with OSA are at increased risk of a crash, particularly when the OSA is untreated.

While the research presented here points to a higher risk of crash among both commercial and non-commercial drivers with OSA, the results should be interpreted with caution as the body of literature is relatively small. There is some evidence to suggest that this risk may be mediated by driving exposure rather than severity of the condition as studies showed that exposure was associated with driving safety among drivers with OSA (Vakulin et al., 2014), but OSA severity was not (Karimi et al., 2014). However, the heterogeneity in driving performance among drivers who have OSA makes it difficult to draw firm conclusions about the mechanisms contributing to

this potential higher risk. What is evident, based on correlational data, is that the use of PAP treatment is associated with improved driving performance and safety among drivers with untreated OSA.

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8. Peripheral Neuropathy

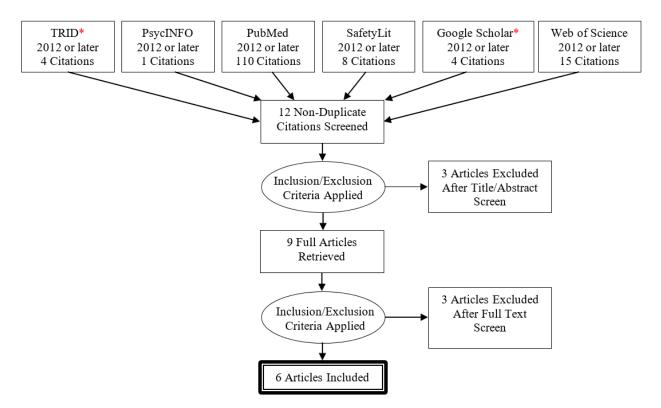
Peripheral neuropathy is a condition affecting nerves in the body, most often the hands and feet. The peripheral nervous system sends information from the brain and spinal cord (central nervous system) to the rest of the body; peripheral nerves also send sensory information to the central nervous system. Neuropathy connotes disease or dysfunction of one or more peripheral nerves. Symptoms of peripheral neuropathy are numbness (loss of sensation) and pain in the affected areas (Mayo Foundation, 2019). Under the definition of peripheral neuropathy used in this review, studies that addressed any or all the following were eligible for inclusion: peripheral nerves, lower extremity disease, peripheral nerve dysfunction, lower extremity sensorimotor neuropathy, diabetic peripheral neuropathy and neuropathy.

Peripheral neuropathy may result from traumatic injuries, infections, metabolic problems, inherited causes, and exposure to toxins. One of the leading causes of peripheral neuropathy is diabetes. However, studies focused specifically on diabetes and TBIs were excluded from this chapter but considered in Chapters 5 and 11. Neuropathy is very common. It is estimated that 25 to 30% of Americans will be affected by neuropathy. The condition affects people of all ages; however, older people are at increased risk (Cleveland Clinic, n.d.-a).

We conducted a multi-step screening of articles published in 2012 or later extracted through six databases searches (see Methods for details of this process). Twelve search results were returned. Three articles were excluded after the initial abstract screening. Another three articles were excluded after the full text in-depth review. The most common reason for exclusion at both steps was the absence of results distinctly associated with the medical condition. After applying all inclusion and exclusion criteria (see Methods), six articles were advanced for the systematic review. The multi-step inclusion and exclusion process is summarized in Figure 7.

The study methods for all six articles centered on performance measures using driving simulators. Four articles reported data in studies that elicited response times for braking. One study used the driving simulator to investigate accelerator pedal use. The remaining article analyzed acceleration and hand-eye coordination for steering.

Four studies focused on the brake response times of participants with peripheral neuropathy while interacting with driving simulators. Brake response time is defined as the interval between the triggering of an incident and the onset of the participant's braking response. When comparing brake response times, three of the four studies used the same recommended safety threshold of 0.70 seconds, with a brake reaction time less than 0.70 seconds considered normal. Twenty-five drivers with peripheral neuropathy (21 males) had a mean brake response time of 0.75 seconds (Meyr & Spiess, 2017; Spiess et al., 2017). In addition, 80% of drivers with neuropathy demonstrated at least one abnormally delayed braking response during the simulated drive. Sansosti et al. (2017) had similar findings, as a group of 20 participants with peripheral neuropathy (19 males) displayed slower brake responses than the suggested safety threshold. All 3 studies (Meyr & Spiess, 2017; Sansosti et al. 2017; Spiess et al. 2017) drew from the same sample of 25 active drivers with type 2 diabetes and lower extremity neuropathy.



*Indicates sources that will also produce agency-reviewed publications (e.g., government technical reports).

Figure 7. Results of the multi-step process of searching and screening reports and articles for peripheral neuropathy

Drivers with peripheral neuropathy had a 11.49% slower mean brake response time compared to a group of drivers with diabetes but without peripheral neuropathy (Spiess et al., 2017). When comparing drivers with peripheral neuropathy with and without foot pathology, both groups of drivers were slower than the recommended safety threshold of 0.70 seconds. However, the drivers without foot pathology demonstrated an 11.11% slower mean brake response time when compared to the drivers with foot pathology (Sansosti et al., 2017).

Ma et al. (2019) also studied the brake reaction times of patients with peripheral neuropathy who were subdivided into low- and high-severity groups. In this study, 31 male participants with type 2 diabetes and 30 healthy male participants were asked to brake as fast as possible when a simulated incident occurred during their drives. Overall, brake reaction times for participants with peripheral neuropathy at any severity were significantly longer than healthy controls. Patients with serious peripheral neuropathy had longer brake reaction times and shorter minimum distance-to-collision as compared both to healthy controls and patients with lower severity of peripheral neuropathy.

Ma et al. (2019) also examined different pedal layouts, all commonly seen in vehicles on the road, to study their effect on brake reaction time during the driving simulation for participants with peripheral neuropathy. The variations in pedal width and edge distance between the brake and accelerator pedal were reviewed. These authors found that when the lateral distance between the accelerator and break was reduced to 45 mm, participants with peripheral neuropathy and control participants drove equally safe. Interestingly, it was shown in studies by Perazzolo et al. (2020a, 2020b) that participants with peripheral neuropathy drove using the extremes of the

accelerator, either barely depressed or fully depressed. This behavior was not seen in either the group with diabetes or the healthy control group. The sample for both Perazzolo et al. (2020a, 2020b) studies consisted of 22 active drivers, 18 males and four females.

Perazzolo et al. (2020a) compared participants with peripheral neuropathy to both a healthy control group and a control group of people with diabetes to determine differences in a simulated drive. During the simulated drive, participants with peripheral neuropathy drove more slowly in both the first and second drive as compared to the healthy group or the group with diabetes. Additionally, participants with peripheral neuropathy experienced a higher quantity and longer durations of loss-of-control events during their first driving simulation as compared to all other groups (Perazzolo et al., 2020a, 2020b).

With a remote infra-red eye tracking system, Perazzolo et al. (2020b) recorded participant eye movements while they completed a simulated drive. They found that participants with peripheral neuropathy had a significantly lower correlation between eye and steering wheel movements when compared to the control group. However, only 8 of the 11 drivers with diabetes and peripheral neuropathy were able to be analyzed due to complications with the eye tracking system.

Overall, the current research suggests that drivers with a history of peripheral neuropathy show a decrease in brake reaction time relative to healthy controls or other patient groups without peripheral neuropathy. Drivers with peripheral neuropathy also spent more time using the extremes of the pedal's range while driving but drove significantly more slowly compared to the control group (Perazzolo et al., 2020a). However, these differences in driving behavior have not been correlated to an increase in crash risk. In addition, it seems that participants with peripheral neuropathy retain the ability to improve their driving performance. Ma et al. (2019) found that a closer accelerator-brake distance of 45 mm showed a protective effect for patients with serious peripheral neuropathy. Perazzolo et al. (2020a, 2020b) saw decreases in the number of loss-of-control events in participants with peripheral neuropathy after their first drive, which may indicate a benefit from practice for people with peripheral neuropathy. In the limited studies available during our selected time frame, the sample sizes were found to be small and disproportionately male.

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9. Stroke

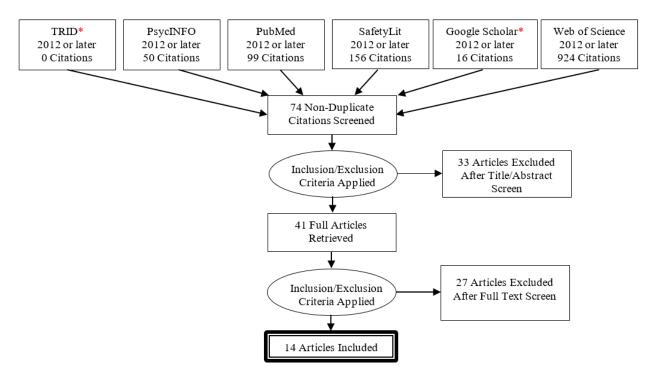
Stroke is a condition affecting the brain's tissue. Symptoms of a stroke are face drooping, arm weakness, and speech difficulty. There are five types of strokes: ischemic stroke, hemorrhagic stroke, transient ischemic attack, brain stem stroke and cryptogenic stroke; ischemic strokes are the most common (CDC, 2020). Under the definition of stroke used in this review, studies that address any or all the following were eligible for inclusion: ischemic stroke, hemorrhagic stroke, transient ischemic attack, mini-stroke, brain attack, brain stem stroke and cryptogenic stroke.

Stroke commonly results from either a blood vessel bursting in the brain or the blood supply to the brain being blocked. Risk of a stroke increases from either biological or environmental factors. Comorbidities such as high blood pressure, high cholesterol, heart disease, diabetes, and sickle cell disease can also increase risk of a stroke. Some of the environmental factors known to affect risk of stroke include smoking, drinking, and lack of exercise. Stroke kills nearly 150,000 of the 860,000 Americans who die of CVD each year—one in every 19 deaths from all causes (CDC, 2021). It should be noted that the broader category of CVD, not including stroke, is reviewed in Chapter 4.

We conducted a multi-step screening of articles published in 2012 or later extracted through six databases searches (see Methods for details of this process). Seventy-four search results were returned. Thirty-three articles were excluded after the initial abstract screening. The most common reason for exclusion was due to a lack of peer review. Twenty-eight articles were excluded after the full text in-depth review, most commonly due to a lack of results distinctly associated with driving safety or performance. After applying all study inclusion and exclusion criteria (see Methods), 14 articles were advanced for the systematic review. The multi-step inclusion and exclusion process is summarized in Figure 8.

These 14 articles had a diverse range of research methods. Eight articles assessed driving performance or safety using a driving simulator or video hazard perception task. Four articles used on-road driving assessment. The last article examined driving-related hospitalization rates.

Several recent studies were identified for this review that suggest stroke survivors may *not* be at increased risk for a crash compared to drivers with other medical conditions, and that suffering a stroke while driving is relatively rare. In one study, researchers found that drivers with history of stroke were hospitalized for crash-related injuries at a rate of 1.3 per 10,000 licensed drivers, which was much lower than most other medical conditions evaluated in the same study (i.e., diabetes, osteoarthritis, alcohol misuse and dependence, CVD including stroke, and vision disorders); in fact, drivers who were post-stroke were involved in fewer crashes resulting in injury than drivers with almost all other medical conditions, as only dementia had a lower incidence rate for drivers of all ages (1.1 per 10,000 licensed drivers) (Mitchell et al., 2020).



*Indicates sources that will also produce agency-reviewed publications (e.g., government technical reports).

Figure 8. Results of the multi-step process of searching and screening reports/articles for stroke

The risk of suffering a stroke while driving is also low. A retrospective observational study found 3.9% of 3,452 of emergency department stroke patients in Japan had suffered strokes while driving (Inamasu et al., 2020). Among these 135 patients, 16% had suffered prior strokes. The researchers suggest that people having suffered a prior stroke may be at higher risk for a stroke while driving, particularly within the first two years, as 45% had the reoccurring stroke within two years of their first strokes. However, there was no significant difference in crash frequency between drivers with a first-time stroke and those with reoccurring strokes, suggesting that crash risk is likely not elevated among drivers with a reoccurring stroke.

Time since stroke has been shown to affect driving habits and driving performance but does not appear to strongly influence driving confidence or driving status (Chua et al., 2012). Analysis of driving assessment records from 441 Australian people who had a stroke (mean age 65.4 years, 74.4% male) found only 8.8% of the patients failed the assessment completely (53.7% passed on the first attempt, and 37.4% were recommended for a downgraded license). There was no significant relationship between time post-stroke and driving status, but a younger age and shorter time between stroke onset and assessment significantly correlated with the Visual Recognition Slide Test and Road Law Test, as did age and on-road assessment outcome (Chua et al., 2012). Specifically, these findings suggest that a shorter time between stroke onset and off-road test completion, and younger age, may be related to better scores on on-road and off-road driving assessments. While a strength of this study was its relatively large sample size, there was no measure of stroke severity. As noted by the researchers, this may be important when considering the possibility that a longer time between stroke onset and driving assessment could reflect a longer hospital stay, due to more severe physical and/or cognitive impairments resulting from the stroke.

Research examining drivers who were post-stroke has increasingly taken the heterogeneity of this medical condition into account, targeting differences in driving performance among people with varying types of strokes. An on-road driving study by Devos et al (2014) found that drivers who had experienced strokes to the right hemisphere of the brain showed impairments on tactical road skills (i.e., lane changing) whereas drivers with strokes to the left hemisphere showed impairments on visuo-integrative skills like understanding, insight, and quality of traffic participation. Despite these impairments in specific tasks, there was no significant difference in road test performance between drivers with either right- and left-hemisphere stroke in this study.

In a later study Devos et al., (2015) further investigated the association between site of stroke lesion and on-road driving performance by considering location of the lesion in addition to the side (hemisphere) of the lesion. Researchers found that overall, a substantial proportion (28 of 73 or 38%) of drivers who were post-stroke exhibited poorer driving skills in each of the road test items than those who exhibited no major difficulties on the road. More specifically, the presence of lesions to the parietal lobe of the brain correlated significantly with poorer performance using the steering wheel and pedals, lane changing, and speed adaptations. Here, there were no significant correlations between right hemisphere strokes and on-road driving performance, but lesions to the temporal lobe of the left hemisphere correlated moderately with the operational road test skills, which included psychomotor aspect of driving like lateral road position and steering wheel and pedal operation.

Park (2015) also investigated differences in driving performance between people with right- and left-hemisphere strokes, during a simulated driving assessment. Like the earlier Devos et al. (2014) study, this research showed difficulties with lane maintenance for people with a right hemisphere stroke, as drivers with right hemisphere lesions were significantly more likely to cross the center line and to have a crash compared to those with left hemisphere lesions. Park also found that drivers with right hemisphere strokes had a higher overall failure rate on the simulated driving assessment than those with left hemisphere strokes.

The research presented thus far on differences in driving performance by lateralization of stroke suggests that those with right hemisphere strokes may demonstrate impairments in driving performance, specifically regarding lane positioning; the research also suggests that these impairments may also present in drivers with specific types of left hemisphere strokes (temporal lobe). However, these studies only considered such differences within groups of drivers who had experienced a stroke. When compared to people who had not experienced strokes, Hird et al. (2018) found that during simulated driving, ischemic stroke (IS) patients with right hemisphere lesions committed significantly more overall errors and drove a significantly greater distance out of the driving lane than controls. However, there was no significant difference in driving performance between controls and drivers with left hemisphere lesions. This study also examined differences in the measures between all stroke drivers and controls and found that both the IS and the subarachnoid hemorrhage (SAH) groups performed significantly worse than controls on measures of simulated driving performance and cognition. Specifically, drivers who had experienced SAH had more total driving and turning errors, lane deviations, and percentage distance outside of the driving lane than controls; drivers who had experienced IS had more total driving errors and distance out of the legal driving lane than the control group. For the drivers who had experienced SAH, significantly poorer driving performance was seen for those with MCA aneurysms and not for those with communicating artery aneurysms, when compared to controls.

Differences in driving performance between drivers who were observed post-stroke and controls may be attributable to detriments in cognitive function common among stroke survivors. In a study examining simulated driving performance and cognitive function, Motta et al. (2014) found that drivers who were post-stroke demonstrated poorer simulated driving performance than healthy controls, poorer cognitive abilities (evidenced by a mean MoCA score below the cut-off indicating impaired cognitive functioning), as well as poorer visuo-spatial judgment than controls (measured by the Benton Judgment of Line Orientation test). These drivers also had significantly reduced scores on tests of executive functioning, which correlated significantly with overall driving performance as well as the number of simulated pedestrians hit. Devos et al. (2014) also found that scores on measures of divided attention (a component of executive functioning) significantly predicted total on-road test score among drivers who were post-stroke, and Hird et al. (2018) found significant correlations between scores on several measures of executive function for drivers with a prior IS.

Research also shows that scores on indexes of independent activities of daily living correlate significantly to driving performance following a stroke. Using a driving simulator, Park & Jung (2015) investigated the effect of activities of daily living on resuming driving in 31 people who had experienced strokes. Here, researchers found significant correlations between scores on the Korean version of the Modified Barthel Index (K-MBI) of activities of daily living status and simulated driving performance, particularly total scores on both, K-MBI total scores and reaction time, speed anticipation, and steering wheel-pedal operation, and judgment. Stepwise regression revealed that higher K-MBI and speed anticipation scores predicted higher total driving performance.

In addition to cognitive impairments, stroke can also cause motor deficits that affect driving performance. Patel et al. (2021) sought to determine the impact of stroke on steering and to identify the contribution of grip strength and grip force control on steering performance following a stroke. Grip strength was significantly reduced in the stroke group as compared to controls, with an interaction between group and hand, where the grip strength of the paretic (partial paralysis) hand in the stroke group was significantly less than that of the non-dominant hand in the control group. The stroke group also demonstrated significantly increased lane deviation compared to controls. Notably, measures of grip force control (reduced maximum voluntary contraction and increased variability of force) and not grip strength significantly predicted steering force in the paretic hand, indicating impairments in steering accuracy can exist after a stroke. However, steering was evaluated using one hand only, so no conclusions could be made about the effect of stroke-related impairments in steering accuracy while using both hands.

As previously reported, Motta et al. (2014) found that impairments in executive function among drivers who were post-stroke correlated with an increased number of pedestrians hit on a simulated driving task. This may signify difficulties in hazard perception among drivers who are post-stroke. Sasaki et al. (2019) investigated the hazard perception ability of drivers with a prior stroke and age-matched controls by asking them to identify hazards during a 2-minute pre-recorded driving scenario. During this task, participants were asked to pause the video when the hazard was detected and were asked to give a verbal response identifying the hazard. Results showed that controls indicated significantly more hazards than stroke patients for all hazard types. Stroke patients also showed a significantly slower response time than controls for hazards that required predicting the behavior of others, as when a pedestrian is visible at the roadside before stepping into the roadway.

Finally, there is research demonstrating effective compensation for specific, physical strokerelated deficits. Smith et al. (2015) examined people with homonymous visual field defect (HVFD) (n=12), a common consequence of stroke that results in a varying extent and pattern of visual field loss, to determine whether they could adequately compensate to detect simulated driving hazards. Specifically, this study tested if these people could successfully use compensatory eye-movements to detect a hazard within the affected field by searching a static visual scene to detect the sudden appearance of a pedestrian. The results showed that five of the 12 people with HVFD, who would often be restricted from driving due to this defect, detected hazards at the same rate as healthy controls (n=12). This finding is partially supported by a case study by Jehkonen et al. (2012), which investigated the impact of residual visual inattention on driving ability among three patients with a right hemisphere stroke. All three patients showed residual visual inattention and mild difficulties during the driving exam, but each of the three patients passed the driving evaluation and were granted permission to drive. All patients reported that they had been successfully driving at a 2-year follow-up. In the Devos et al. (2014) study, researchers also suggested that drivers with right hemisphere strokes may adequately use compensatory strategies during driving to make up for visual field, visual neglect, visual scanning, and divided attention deficits.

This review of recent literature suggests that cognitive impairments associated with stroke are more likely to cause problems with specific elements of driving than are other (vision or motor) impairments. However, drivers who are post-stroke are also often able to apply compensatory measures to stay safely on the road. Overall, the research reviewed suggests that drivers with a prior stroke can often maintain the ability to drive safely, especially when practicing self-regulation and compensatory techniques. Additionally, personalizing assessments of driving performance regarding driving difficulties related to the type of stroke or lesion site could potentially improve both driving evaluations and rehabilitation program outcomes for stroke survivors.

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10. Syncope

Syncope is a condition in which a person faints or loses consciousness but recovers soon after the event. Syncope commonly results from a sudden drop in blood pressure that can be brought on by a wide variety of possible causes ranging from an underlying medical condition to environmental triggers (Whelan, 2017). Under the definition of syncope used in this review, studies that address any or all the following were eligible for inclusion: recurrent syncope, presyncopal spells, reflex syncope, vasovagal syncope, neurally mediated syncope, pre-syncope and vasodepressor syncope.

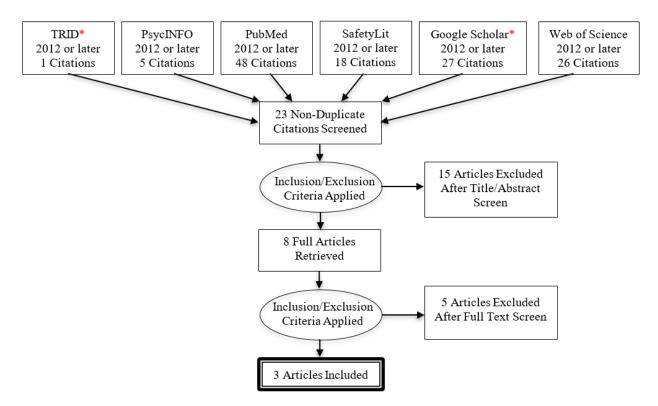
Common reasons for syncope include low blood pressure and irregular heartbeat. For some, an increased risk of syncope occurs when experiencing excessive amounts of pain, fear, stress, dehydration, or exhaustion. Syncope affects 3% of men and 3.5% of women at some point in life; it is more common with increasing age and affects up to 6% of people over age 75 (Cleveland Clinic, n.d.-b).

We conducted a multi-step screening of articles published in 2012 or later extracted through six databases searches (see Methods for details of this process). Twenty-three search results were initially returned. Fifteen articles were excluded after the initial abstract screening, and five articles were excluded after the full text in-depth review. In both steps, the most common reason to exclude an article was due to its status as a literature review. After applying all inclusion and exclusion criteria (see Methods), three articles were advanced for the systematic review. Details of the multi-step inclusion and exclusion process are presented in Figure 9.

The nature of these three articles varied in their scope and study methods. The first study was a prospective study on patients who experienced syncope while driving and patients who experienced syncope in other situations. The next study was a nationwide survey to examine the rate of motor vehicle crashes for people with syncope in Denmark. The third study was an assessment of collected data on the prevalence of syncope to estimate the risk of syncope while driving.

Folino et al. (2012) prospectively studied two groups of patients, 40 who experienced syncope while driving and 50 who experienced syncope in other circumstances but not driving; the latter served as the control group. Patients were contacted by phone every six months during the follow-up. After a mean follow-up period of $1,793\pm573$ days (range 607 to 2,785 days), no participants in either group experienced syncopal episodes while driving. Of the original group of patients who had experienced syncope while driving, eight out of the 40 (20%) had non-driving recurrences of syncope, compared to 30% of the control group. The implication for safety of these findings is that the risk of syncope reoccurring while driving is rare.

A similar conclusion may be drawn from a study assessing the likelihood of vasovagal syncope while operating a moving motor vehicle on a per-patient-year and per-faint basis (Tan et al., 2016). Of 418 patients with history of syncope (a median of 10 lifetime faints and a median of 3 faints in the previous year) who were followed for up to 1 year, only two fainted while driving. Of these 2, one patient had prodromal symptoms (a precursor to a fainting episode) while driving and was able to safely drive to the roadside before fainting.



*Indicates sources that will also produce agency-reviewed publications (e.g., government technical reports).

Figure 9. Results of the multi-step process of searching and screening reports/articles for syncope

Another perspective is offered by a nationwide study in Denmark that compared the occurrence of both fatal and non-fatal crashes for patients with syncope to the general population (Nume et al., 2016). During a (median) 2-year observation period, 4.4% (n = 1,791) of the patients with a history of syncope experienced a motor vehicle crash, with only 349 of these events occurring concurrently with a syncopal event. In the general population, 5.3% experienced crashes over a median observation period of 5.0 years. However, when these researchers conducted a multivariate analysis adjusting for age, sex and calendar year, they found a 2-fold higher risk ratio for crashes in patients with a history of a syncope compared with the general population. Further, the fully adjusted relative risk of motor vehicle crash increased with age among men with syncope but decreased with age among women with syncope when compared to the general population.

The evidence provided in these articles was too limited to permit any firm conclusions about the risk associated with the effects of syncope on driving. Overall, the strongest conclusion that can be drawn from current research is that while drivers with a history of syncope may show an increase in crash risk, their risk of having a syncopal event while driving is low. Crash risk may increase with age for men with syncope while decreasing with age for women with syncope. These findings should be interpreted with caution as only a limited number of studies were published within the review period. In addition, to the extent that studies relied on retrospective hospital data to identify patients with syncope, this could lead to the exclusion of syncopal events that did not result in hospitalization. Additional research into the involvement of syncope in crashes at varying levels of severity and the on-road performance of drivers with syncope could

provide a valuable addition to the sparse evidence now available to gauge the traffic risk associated with this medical condition.

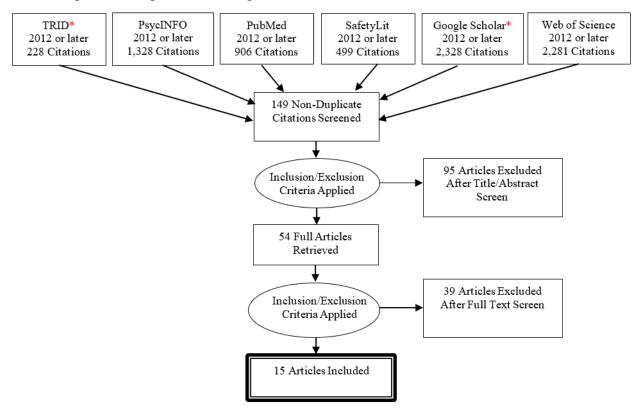
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11. Traumatic Brain Injury/Concussion

TBI is a condition affecting the brain caused by a blow or other traumatic injury to the head or body. According to the Mayo Foundation for Medical Education and Research (Mayo Clinic Staff, 2021), common reasons for experiencing a TBI include falls, vehicle-related collisions, violence, sports injuries, and combat injuries; symptoms of a TBI, both physical and psychological, can vary with severity and occurrence. Under the definition of TBI used in this review, studies that addressed any or all the following were eligible for inclusion: traumatic encephalopathy, brain trauma, severe traumatic brain injuries, TBIs and acquired brain injury, and concussion.

We conducted a multi-step screening of articles published in 2012 or later extracted through six databases searches (see Methods for details of this process). One hundred forty-nine search results were returned. Ninety-five articles were excluded after the initial abstract screening. The most common reason articles were excluded was an absence of results distinctly associated with driving safety or performance. Thirty-nine articles were excluded after the full text in-depth review, again most commonly due to a lack of results distinctly associated with driving performance or safety. After applying all study inclusion and exclusion criteria (see Methods), 15 articles were advanced for the systematic review. Details of the multi-step inclusion and exclusion process are presented in Figure 10.



*Indicates sources that will also produce agency-reviewed publications (e.g., government technical reports). Figure 10. Results of the multi-step process of searching and screening reports/articles for TBI/concussion

The study methods used in these 15 articles varied. Seven articles evaluated participants using on-road driving assessments, the use of on-road lessons, or naturalistic driving. Six articles reported on studies using driving simulators or computerized traffic video. In two studies the risk of a vehicle collision was assessed through retrospective data analysis.

Available research on the crash risk among drivers with TBI is limited, as just two studies were identified that directly investigated this outcome. Carlson et al. (2016) looked at the association between prior TBI and subsequent motor vehicle crash-related hospitalizations among a specific population (U.S. military veterans). Here, researchers examined a large U.S. Department of Veterans Affairs healthcare dataset that included 277,330 veterans of the Iraq and Afghanistan Wars, which included 28,551 veterans with a prior TBI diagnosis. Analysis showed that among the 422 patients hospitalized from a crash, over 30% had a prior TBI diagnosis, and those with a prior TBI diagnosis were four times more likely than those without to be hospitalized from a motor vehicle crash, even when controlling for comorbid physical and mental health disorders. These findings held when researchers considered only those TBI patients with an outpatient diagnosis, which signals a milder severity. While this study showed a higher rate of crash-related hospitalizations for drivers, this measure was a surrogate for crash risk among a specific population (veterans). Nevens and Boyle (2012), however, used police-reported crash data from Iowa and a registry of people in Iowa who sustained a TBI and found that drivers with a prior TBI diagnosis were at elevated crash risk. Here, drivers with a prior TBI diagnosis were more likely than drivers without a TBI diagnosis to be involved in multiple crashes, to be unbelted at the time of the crash, and to be involved in drug/alcohol-related crashes. While driving at night increased the likelihood of drivers with a prior TBI diagnosis being in a crash, driving with passengers decreased this likelihood.

While this research suggests that, broadly speaking, drivers with a TBI diagnosis may have an elevated crash risk compared to those without the diagnosis, studies evaluating on-road driving performance have not observed this difference. In fact, several studies found that most drivers with TBI pass an occupational therapist (OT) administered on-road driving assessment (Gooden et al., 2017; Ross et al., 2018; Stolwyk et al, 2019), and there is no significant difference in driving performance between the patients with TBI who pass the assessment and healthy controls (Gooden et al., 2017; Neyens et al., 2015; Stolwyk et al., 2019). The research also shows that patients with TBI who initially fail an on-road assessment may benefit from driver rehabilitation training. Ross et al. (2018) found that nearly all the patients with diagnosed TBI who initially failed the OT assessment returned to driving following rehabilitation in some capacity, with about half of these post-rehab drivers resuming with a restricted license. Just 7% of the post-rehab drivers in this study were recommended for license suspension.

It is possible that those patients with TBI deemed fit to return to driving have the self-awareness to modify their driving behavior appropriately, as research indicates that TBI patients who failed an on-road assessment overestimated their driving ability relative to TBI patients who passed the assessment and to control participants (Gooden et al., 2017). Studies that examined the independent driving habits of patients with TBI who were cleared to return to driving found that during the first 3 months back on the road, the TBI group drove significantly less frequently than controls (Gooden et al., 2019) and showed increased avoidance of driving in more challenging scenarios like driving at night (Gooden et al., 2019; Hua et al., 2018), and on freeways, long trips, in heavy traffic, and cross-traffic turns at intersections (Gooden et al., 2019). However, an important consideration in both studies (Gooden et al., 2019; Hua et al., 2018) is that data were

collected during the initial 3 months of returning to driving. The researchers in both studies caution that it is unclear if the difference in driving behaviors, while indicative of self-regulation, may be due to the recency of injury and the possibility that these drivers had not yet fully returned to everyday life activities (e.g., work) that necessitated driving in less-than-ideal conditions.

While most patients return to driving safely, a proportion of patients with TBI require driving rehabilitation, and/or modified license status such as an automatic restriction, an area restriction, and/or adaptive equipment (Ross et al., 2018). Several on-road studies have shown that those who do not initially pass an OT on-road driving assessment have TBI of higher severity (lower Glasgow Coma Scale score) (Ross et al., 2015; Ross et al., 2018); longer post-traumatic amnesia (PTA) (Ross et al., 2015; Ross et al., 2015; Ross et al., 2018); longer time between their injury and their on-road assessment (Ross et al., 2015; Ross et al., 2018; Stolwyk et al., 2019), likely due to the severity of the injury. Specifically, patients with TBI who initially fail the on-road OT assessment show significant driving difficulties relative to controls for intersection maneuvers, lane changing, merging, low speed maneuvers, driving straight, observing the on-road environment, maintaining speed control and appropriate following distance, gap selection, lane position, and basic vehicle control (Stolwyk et al., 2019).

Studies using driving simulators and computerized tasks have also identified specific driving difficulties among drivers with TBI (Masson et al., 2018; Narad et al., 2020). While a study using a driving simulator found no significant difference in driving performance between post-TBI young drivers 16 to 25 and controls for most measures, Narad et al. (2020) found that post-TBI young drivers with reduced executive functioning demonstrated greater maximum speed and speed variability during a test condition involving a cell phone conversation compared to controls and compared to a condition involving texting. Masson et al. (2018) also identified an impact of attentional load on driving skills among post-TBI drivers. The TBI group showed significantly slower reaction time compared to controls during a computerized driving task, but only during increased attentional load (i.e., presence of distracting auditory signals and/or while dual tasking). Finally, Ross et al. (2015) included a reaction time testing apparatus in their onroad driving study and found that patients with TBI who required driving rehabilitation had significantly slower reaction times than those that initially passed the OT driving assessment.

The studies presented thus far addressed TBI with severities ranging from mild to severe as rated by the Glasgow coma scale (GCS). Concussion, considered a mild form of TBI, is diagnosed using concussion symptom scales such as the Sport Concussion Assessment Tool (SCAT), which includes the GCS, or criteria from the 2013 Consensus Statement on Concussion in Sport (McCrory et al., 2013). Just four studies meeting the inclusion criteria were identified that evaluated the driving performance of people diagnosed specifically with concussion (Hoffman et al., 2018; Lempke et al., 2020; Raukar et al., 2018; Schmidt et al., 2017). All four studies used a driving simulator. Also, all were limited to small samples sizes (n = 14 concussed or fewer), with two being case study reports where researchers examined changes in simulated driving performance pre- versus post-concussion for single individuals (Hoffman et al., 2018; Raukar et al., 2018). These four simulated driving studies found that driving impairments can be seen within 48 hours of injury (Raukar et al., 2018), and these impairments can persist even after concussion symptoms (e.g., headache, neck pain, confusion, etc.) resolve (Hoffman et al., 2018; Lempke et al., 2020; Raukar et al., 2018; Schmidt et al., 2017). Specifically, impairments in simulated driving performance following concussion, whether compared to healthy controls or within-individual, were seen for reaction time (Lempke et al., 2020), speed control (Hoffman et al., 2018; Schmidt et al., 2017), and lane position, particularly during turns (Hoffman et al., 2018; Schmidt et al., 2017).

Overall, the research shows that drivers who experience TBI may be more likely to be involved in crashes (Carlson et al., 2016; Neyens & Boyle, 2012) particularly when driving during higherrisk scenarios such as at night and while under the influence of drugs and alcohol (Neyens & Boyle, 2012). Drivers with TBI also show difficulties in performing driving tasks like lane maintenance, speed control, and gap selection (Stolwyk et al., 2019), as well as impaired reaction time (Masson et al. 2018). However, there is considerable heterogeneity in the relationship between injury severity and driving performance among patients with TBI. Not all drivers with TBI experience difficulties (Gooden et al., 2017; Masson et al., 2020; Neyens et al., 2015; Ross et al., 2015; Ross et al., 2018; Stolwyk et al., 2019), and many self-restrict their exposure to more challenging driving situations (e.g., time-of-day and distance from home) (Gooden et al., 2019; Hua et al, 2018).

The current research on TBI and driving suggests that an OT driving assessment may be beneficial in determining which drivers require rehabilitation training, and in some cases a restricted license (which may include adaptive equipment) to maintain safe driving (Gooden et al., 2017; Neyens et al., 2015; Ross et al., 2018; Stolwyk et al., 2019). Regarding concussion, specifically, there currently are no formal guidelines for a test protocol for returning to driving following concussion, and not all physicians counsel concussion patients about driving (Baker et al., 2015; Harmon et al., 2019; Santana et al., 2020; Schmidt et al., 2017). The research reviewed here, while limited, suggests that concussion patients may experience persistent driving impairments even after symptom resolution.

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12. General Discussion

This review of literature published in 2012 or later describing the effect of selected medical conditions on driving performance and safety indicated that some of these conditions (e.g., ADHD, TBI) may have negative effects on driving, depending on the severity of the condition. However, treatment of these conditions can often mitigate such effects. For other medical conditions, this review found little or no evidence of negative effects on driving safety (e.g., CVD, stroke) or reported inconclusive findings due to a dearth of qualified studies (e.g., ASD, diabetes, MCI, OSA).

The information presented in this review may be useful to clinicians, licensing officials, and researchers in several ways. First, these results can help inform interactions between clinicians and their patients about the risks associated with driving with specific medical conditions and what, if any, compensatory measures the patients can take to be safer on the road. For example, clinicians treating or diagnosing people with ADHD can provide data-driven information to patients about their increased risk of being in a crash, explaining an increased propensity for engaging in risky driving behavior. At the same time, these consultations can offer suggestions for things that drivers with ADHD can do to lessen their risk, such as taking their medication before driving and choosing more engaging routes whenever possible. Clinicians can provide patients with ADHD and their families not only with a better understanding of their increased driving risk, but also, actionable solutions. This can be especially important for young ADHD patients looking to obtain their driver license, since they are at even higher risk than their already high-risk non-ADHD counterparts.

Patients with conditions for which research has not firmly established an increased risk of crashes will also benefit from consultations with their clinicians when there are known treatments that improve overall driving performance, such as PAP treatment for OSA. It is also valuable for clinicians to know which medical conditions likely are *not* placing their patients at increased risk of crashes, such as with ASD, so they can choose where to best focus their discussions with patients.

This review may also prompt clinicians to consider to how certain patients can benefit from adaptive vehicle options, such as more closely located pedals for drivers with peripheral neuropathy. Even more important is the emphasis on personalized assessment and rehabilitation: in the case of stroke survivors, understanding how specific driving difficulties are associated with the specific type of stroke or lesion site is essential for the best outcomes with these patients. Overall, the research presented here can provide clinicians and patients with specific medical conditions—and their families—with information to successfully manage their driving.

Next, the results of this literature review can be valuable to licensing officials when considering policy-related decisions and public information campaigns. Actions such as recommending relevant cognitive testing for drivers with specific medical conditions, such as CVD and MCI, can help identify those who are at greater crash risk since these conditions present with such a high degree of heterogeneity, and not all patients experience the same difficulties with driving. More broadly, licensing officials in administrative positions may find this review helpful when interacting with physicians or other health care providers in determining whether people can maintain their license or return to driving.

The medical conditions reviewed here were determined to be of high priority after consultations with driving safety professionals in the fields of driver rehabilitation, medicine, medical fitness

to drive, geriatrics, and polypharmacy. However, the searches carried out in this project revealed many gaps in the research that precluded firm conclusions about the effects of driving with a number of these conditions. Some of the most notable gaps included insufficient real-world driving studies for conditions such as ASD and CVD; lack of research on the effects of chronic CVD with varying degrees of severity; and whether the duration of diabetes diagnosis may influence a driver's ability to compensate for condition-related deficits in driving performance. There was also a limited body of research overall for some medical conditions, like syncope. Researchers may wish to target these gaps in future studies to augment the current state of knowledge on the effects of medical conditions on driving. Appendix A. Preliminary Search Criteria for Candidate Medical Conditions This search identified literature that related changes in performance or safety outcome measures for older drivers to their medical conditions (or, under certain circumstances, their medication use) and/or their associated functional impairments. The initial search parameters are indicated below.

| Search Years: 2011 to 2019 Language: English | | | | | |
|---|-----|---|-----|--|--|
| Medical Condition* OR Disease* | AND | Driv* Performance OR Operator Performance OR Crash* OR Driv* Impairment OR Safe Driving Ability | NOT | Alcohol OR Illicit OR Case Study OR Self- Report | |

*Indicates truncation to catch all forms of the term

Databases Searched:

- TRID
- AgeLine
- MedLine
- ScienceDirect
- PsycInfo
- Google Scholar
- Embase
- CINAHL (research tool for nursing and allied health professionals)
- Cochrane Library

In addition, the research team conducted searches using the same strategy but entered specific medical conditions as the first key word (using truncation to catch all forms of the condition).

• Endocrine and Metabolic Disorders

- o Diabetes
- Renal Disease
- Kidney Disease
- Cirrhosis
- Hepatic Encephalopathy
- Hypothyroidism

• Autoimmune diseases

- o Lupus
- Neurological and Physical Disorders
 - Alzheimer
 - o Arthritis (Osteoarthritis and Rheumatoid Arthritis)
 - o Dementia

- Multiple Sclerosis
- Obstructive Sleep Apnea
- Narcolepsy
- Parkinson's Disease
- Peripheral Neuropathy
- Seizure/Epilepsy
- Spinal Cord Injury
- o Stroke/Cerebral Vascular Accident/Transient Ischemic Attack
- Traumatic Brain Injury

• Respiratory Disorders. The three main COPD diseases are

- o Emphysema
- Chronic Bronchitis
- Asthmatic Bronchitis

• Visual and Other Sensory Disorders

- Age-Related Macular Degeneration
- o Cataracts
- o Glaucoma
- o Hemianopia
- o Quadrantanopia
- o Retinitis Pigmentosa
- Diabetic Retinopathy
- Vestibular Disorders (Ménière's disease, benign paroxysmal ositional vertigo [BPPV or just "Vertigo"])
- o Ocular Disorders as a Result of Hyperthyroidism/Graves Disease

• Cardiovascular Disease

- o Syncope
- o Arrhythmia
- Coronary Artery Disease
- Cancer

• Psychiatric Disease (psychotic, mood, anxiety, personality)

- o Depression
- o Anxiety
- o Schizophrenia
- Asperger Disease
- o Bipolar

• Auto-immune-related:

- Fibromyalgia
- Chronic Fatigue Syndrome:

• Hemotologic Diseases

- Hypochromic Microcytic Anemia:
- Macrocytic Anemia

Appendix B. Expert Panel Attendees

| Person | Affiliation | Specialty/Emphasis Area | | | |
|--|---|-------------------------------------|--|--|--|
| PANELISTS | | | | | |
| Peggy Barco, OTD, OTR/L, CDRS, SCDCM, FAOTA | Washington University (St. Louis) Dept. of Occupationa Therapy | Driver Rehabilitation Specialist | | | |
| Debra Carney | Iowa DOT | Driver Fitness Program Manager | | | |
| David Carr, MD | Washington University (St. Louis) School of Medicine | Dementia, Polypharmacy | | | |
| Cyndee Crompton, MS, OTR/L, CDRS | Driver Rehabilitation Services | Driver Rehabilitation Specialist | | | |
| Ashley Deemer, OD | Wilmer Eye Institute, Johns Hopkins University | Low Vision Specialist | | | |
| Barbara Hutchinson, MD, PhD | Chesapeake Cardiac Care | Cardiology, Sleep disorders | | | |
| Sean Jeffery, PharmD, BCGP, FASCP, AGSF | Integrated Care Partners/Hartford Healthcare; UConn School of Pharmacy | Polypharmacy, Geriatric pharmacy | | | |
| Richard Marottoli, MD | Yale – New Haven Hospital | Geriatrics, Internal Medicine | | | |
| Rebecca Parsio, RN | Virginia DOT | DMV Health Compliance Officer | | | |
| Gina Pervall, MD | Maryland MVA (Chief, Medical Advisory Board) | Medical Fitness to Drive | | | |
| Chad Strowmatt, LOT, CDRS | Strowmatt Rehabilitation Services | Driver Rehabilitation Specialist | | | |

Appendix C. Steps 1–3 Quality Assessment Rubrics

Step 1: Article inclusion/exclusion review

Inclusion/exclusion criteria

Please go through each article independently, evaluating the article on each criterion in the order it appears on the sheet. Once you check "No" on an inclusion criterion, stop the evaluation, and note why article was excluded in the comment section of the criterion that disqualified the study. You may also include any other notes in the comments section. If you are unsure of a particular criterion, place the article aside and bring it to the PI's attention for discussion.

| Yes | No | ? | Comments | | |
|-----------------------------------|---------|-----|---|--|--|
| | | | | | |
| | | | | | |
| | | | | | |
| | | | | | |
| | | | | | |
| Decision: Accept for full review? | | | | | |
| ı detern | ninatio | on. | | | |
| | | | Yes No ? Image: Ima | | |

Version 7.6.2020

Step 2. Study Quality Assessment

Complete all the information below for <u>every article</u> that has made it through the Step 1 inclusion/exclusion review. If you indicate NA for an item, please indicate why in the comments.

| Contents | Yes | No | NA | NR | Comments |
|--|-----|----|----|----|----------|
| NA=Not applicable NR=Not reported | | | | | |
| 1. Was the medical condition diagnosed in a consistent manner across the study sample? | | | | | |
| 2. Were co-morbidities documented and their potential impacts on outcome measures accounted for? | | | | | |
| 3. Were individual differences in disease state/ progression taken into account? | | | | | |
| 4. Was the study sample broadly representative, i.e., recruited to provide a degree of generalizability beyond a convenience sample? | | | | | |
| 5. Were control/comparison group subjects selected in a manner designed to remove or account for potential bias? | | | | | |
| 6. Is the study design prospective? | | | | | |
| 7. Are inclusion/exclusion criteria clearly stated and uniformly applied? | | | | | |
| 8. Are objective measures of safety or performance reported? | | | | | |
| 9. Are measures of effects implemented consistently across all study participants? | | | | | |
| 10. Are the statistical methods used in data analysis clearly described? | | | | | |
| 11. Were potentially confounding/effect modifying variables taken into account in the design and/or analysis? | | | | | |
| 12. For longitudinal analyses, was attrition addressed? | | | | | |
| 13. Was a power analysis reported? | | | | | |
| 14. Is the source of funding identified? | | | | | |
| 15. Is there evidence of a conflict of interest for one or more of the authors? | | | | | |

If this is not an experimental study and does not include an intervention or treatment, skip to end notes.

Step 2. Study Quality Assessment (continued)

If this article/report is an experimental study (including interventions or treatments to control the effects of a medical condition), complete the additional criteria 16-22 below.

| Experimental Studies: Additional Criteria | | | | | |
|---|----------|------|---------|--------|----------|
| Contents | Yes | No | NA | NR | Comments |
| NA=Not ap | plicable | NR = | Not rep | ported | |
| 16. Does the study have an active or social- contact control group? | | | | | |
| 17. Is sufficient detail provided describing the intervention or exposure to replicate the study? | | | | | |
| 18. Is there an attempt to match or balance the samples across groups of study participants? | | | | | |
| 19. Were the outcome assessors blinded to the intervention or exposure status of participants? | | | | | |
| 20. Were participants aware of their assigned intervention during the trial? | | | | | |
| 21. Is the length of follow-up the same for all groups? | | | | | |
| 22. Did the study control for any baseline differences in relevant variables between intervention and control groups? (If study reports no baseline differences, check 'Yes') | | | | | |
| Notes: | | | | | |

Step 3. Information Extraction [Optional]

Please complete all the information below for <u>every</u> article that has made it through the inclusion process in Step 2. If an article reports a combination of a particular criterion, write codes separated by a comma (for example, if a sample was derived from both physicians' and OT practices, enter 3,4).

| Contents | Information | Comments |
|---|-------------|----------|
| Type of article/report 1= journal article 2= agency report (specify agency in comments) 3= other (specify in comments) | | |
| 2. Study Design 1= observational 2= experimental 3= intervention 4= case study 5= other (specify in comments) | | |
| 3. Sample recruitment location 1=community (general) 2=retirement/55+ community 3=physician's practice 4=driver rehab, OT or PT practice 5=driver education/training program 6=high school, college, other education site 7=DMV/licensing agency 8=other (specify in comments) 99=Not reported 4. Analytic sample size/N | | |
| 5.Sample age (range, mean, S.D.) | | |
| 6. % Women in sample99=Not reported | | |
| 7. % Nonwhite participants in sample99=Not reported | | |
| 8. Type of outcome measure 1=direct, safety (ref Search ID) 2=direct, performance (ref Search ID) 3=self-reported driving difficulty (specify in comments) 4=indirect measure (ref Search ID) | | |

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