PROLEPSIS **Working Paper Series**
www.prolepsis.org

A blueprint for a *new* commercial driving epidemiology: An emerging paradigm grounded in integrative exposome and network epistemologies

By

Yorghos Apostolopoulos[1]
Sevil Sönmez[2,*]
Matthew S. Thiese[3]
Mubo Olufemi[3]
Lazaros K. Gallos[4]

1. *PROLEPSIS: Partners in Prevention, Inc., Orlando, Florida*
2. *University of Central Florida College of Business, Orlando, Florida*
3. *University of Utah School of Medicine, Salt Lake City, Utah*
4. *DIMACS, Center for Discrete Mathematics & Theoretical Computer Science, Rutgers University, Piscataway, New Jersey*

* Corresponding author (sevil@ucf.edu)

PROLEPSIS: Partners in Prevention, Inc.
Orlando, Florida, USA
February 2024

ABSTRACT
Excess health and safety risks of commercial drivers are largely determined by, embedded in, and/or operate as complex, dynamic, and randomly-determined systems with interacting parts. Yet, prevailing epidemiology is entrenched in narrow, reductionist, deterministic, and static exposure-response frameworks along with ensuing inadequate data and limiting methods, thereby perpetuating an incomplete understanding of commercial drivers' health and safety risks. This programmatic paper is grounded in our ongoing research that conceptualizes health and safety challenges of working people as multilayered *wholes* of interacting work and nonwork factors, exemplified by complex-systems epistemologies. Building upon and expanding these evolving assumptions, herein we: (a) discuss how insights from integrative exposome/network-science-based frameworks can enhance our understanding of commercial drivers' chronic disease and injury burden; (b) introduce the *working life exposome of commercial driving (WLE-CD)*—an array of multifactorial and interdependent work, work-related, and nonwork exposures and associated biological responses that concurrently and/or sequentially impact commercial drivers' health and safety during and beyond their work tenure; (c) conceptualize commercial drivers' health and safety risks as multilayered *networks* centered on the *WLE-CD* and *network relational patterns* and *topological properties* (that is, arrangement, connections, and relationships among network components) that largely govern risk dynamics; and (d) elucidate how integrative *exposome/network-science*-based innovations can contribute to a more comprehensive understanding of commercial drivers' chronic disease and injury risk dynamics. Development, validation, and proliferation of this emerging discourse can move commercial driving epidemiology to the frontier of science with implications for policy, action, other working populations, and population health at large.

1. INTRODUCTION

Regional and long-haul drivers of large trucks (commercial drivers, hereafter) experience a disproportionate chronic disease and injury burden.[1,2] This burden is markedly characterized by a multitude of complex, multilayered, interacting, and evolving factors and nested systems.[3] Yet, prevailing epidemiological research remains grounded in traditional exposure-response epistemologies and methodologies.[4] The enduring convergence of these factors confines the comprehensive examination of commercial drivers' chronic disease and injury burden, thus maintaining a suboptimal understanding of its underlying etiology.

To overcome these far-reaching stalemates at the nexus of occupational, chronic disease, and injury epidemiology, epistemologies and methodologies conducive to studying the totality and complexity of working people's lifelong health and safety challenges, by examining them as *wholes* with interacting parts,[5] are rather overdue. Hence, in this paper, we: (a) discuss how epistemologies grounded in integrative exposome and network sciences can enhance understanding of commercial drivers' chronic disease and injury burden by introducing the *working life exposome of commercial driving*; (b) conceptualize commercial drivers' health and safety risks as *networks of networks* and initiate the unpacking of this structure; and (c) elucidate how integrative exposome/network-science-based epistemologies and methodologies can contribute to a better understanding of commercial drivers' chronic disease and injury dynamics. The recurring use of relatively new technical and transportation-specific acronyms, concepts, and terms—for both broader audiences but especially for commercial driver health and safety research readers, *Table 1* is provided as an abbreviated lexicon.

Table 1: Glossary *(adapted to population health and commercial drivers)*	
CANoNs	Complex adaptive networks of networks.
Complex networks	Graphs with non-trivial topological properties (e.g., high clustering coefficient) that do not occur in simple networks (e.g., random graphs) but in networks representing real systems (e.g., social networks).
CVD	Cardiovascular diseases.
DOT	U.S. Department of Transportation.
Edges (network)	Connections between network nodes indicating relationships (e.g., physical interactions) among connected nodes.
EPHOR	Exposome Project for Health and Occupational Research.
Exposome	Cumulative influences and associated biological responses throughout lifespan.
Exposome science	Study of all lifetime influences on health and safety grounded in diverse scientific and technological innovations.
Ex-WAS	Exposome-wide association studies.
FHWA	U.S. Federal Highway Administration.
FMCSA	U.S. Federal Motor Carrier Safety Administration.
Genome	Complete set of genes.
Graph theory	Branch of mathematics studying graphs and their properties; graphs are mathematical structures made up of nodes connected by edges—used to model pairwise relations between objects.
HOS	U.S. Department of Transportation Hours-of-Service rules for professional drivers.
Lifecourse theory	Study of interacting biological, behavioral, psychological, social and environmental factors shaping health across people's lives.
Networks	Group of entities (nodes) connected by lines (edges)—oftentimes represented by graphs.
Network science	Study of complex social, health, and other networks, drawing on graph theory (mathematics), statistical mechanics (physics), data mining/information visualization (computer science), inferential modeling (statistics), and social structure (sociology).
Network topology	Arrangement and connections of network entities.
Nodes (network)	Basic unit of a graph; depending on application, a node can represent diverse factors capable of creating, receiving, processing, sending or redistributing data over a network.
OSHA	U.S. Occupational Safety and Health Administration.
Phenome	Set of all observable traits or characteristics of organisms.
Syndemics	Aggregation of two or more concurrent or sequential interlinked disease and/or injury clusters exacerbated by underlying sociostructural and/or professional conditions.
WLE	Working life exposome.
WLE-CD	Working life exposome of commercial driving.
WLE-CD-WAS	Working life exposome of commercial driving-wide association studies.

2. COMMERCIAL DRIVING EPIDEMIOLOGY: REVIEWING THE EVIDENCE

About 3.5 million commercial drivers[6] work and live away from home for extended periods, spending most of their time in truck cabins, un/loading terminals, warehouses, truckstops, roadways, and rest areas.[7] Their broad work environment and, to an extent, their lives and overall wellbeing are largely defined by government transportation and labor policies (e.g., hours-of-service rules, medical certification)[8,9] and corporate policies, regulations and operations (e.g., by-the-mile pay systems).[10,11] In these milieux, commercial drivers experience excess strains with far-reaching, oftentimes intractable, health and safety repercussions. Thus, unsurprisingly commercial drivers are considered among the unhealthiest occupational cohorts.[12]

Largely due to the impact of large truck collisions and related traffic interruptions, injuries and/or deaths, government and corporate priorities along with research have heavily focused on roadway safety.[13,14] Epidemiological investigations have largely attributed these safety incidents to drivercentric, proximal determinants (e.g., distracted driving, traffic violations),[15,16] largely overlooking underlying organizational or structural determinants.[17] Few exceptions include studies delving into, for example, the role of compensation methods in safety outcomes.[18] Yet, despite consistent alarming statistics, the health of commercial drivers and contributing underlying etiology have taken the back seat in epidemiological research.[19]

In a labor-intensive and time-constrained work environment, commercial drivers experience a plethora of interrelated strains, including excess levels of: (a) psychological issues such as stress, loneliness, and related pressures[19,20] amidst long and irregular workshifts (up to 15 consecutive hours a day and 70 hours in a 7-day span, when adhering to hours-of-service [HOS] rules[21]) and associated fatigue and sleep deprivation;[22,23] (b) adverse physical, environmental, chemical, and noise exposures;[24-27] (c) and behavioral concerns such as sedentariness, limited physical activity, and ergonomic problems;[28,29] and (d) work-life balance and home/family pressures.[30,31] Additionally, while on the road, commercial drivers are faced with limited affordable and healthful food choices as well as access to quality and affordable healthcare services.[32,33]

In these health and safety risk-laden milieux, commercial drivers experience chronic, typically interrelated, excess comorbidities. Key among them are excess anxiety and/or depression, obesity, chronic and acute stress, cardiometabolic diseases, cancer, sleep problems and disorders, musculoskeletal risks, injuries, and fatalities.[34-37] These disease and injury outcomes are deemed quite disproportionate, especially when compared to both other occupational cohorts and the general population.[38,39] These characteristics and burden corroborate the presence of syndemics[40]—that is, aggregation of two or more concurrent or sequentially interlinked disease and injury clusters exacerbated by underlying sociostructural and professional conditions.

Unsurprisingly, originating mainly from trucking companies and the federal government, mainly roadway safety-centered prevention efforts are heavily drivercentric.[41,42] They typically focus on modifying driving behavior by addressing safety training, compliance with safety regulations, safety-related technology (e.g., electronic logging devices), and incentives for safety performance.[43,44] Yet, more recently, there has been an emphasis on improving vehicle and road environment safety as well.[45] Along these lines, relatively few trucking fleets are also implementing health and wellness programs aimed at improving safety either directly (e.g., screening for and treating sleep disorders) or indirectly (e.g., managing obesity).[46,47] These efforts have been largely shaped by federal actions, such as Department of Transportation (DOT) medical examination requirements or mandated electronic logging devices, among others.[48] While these actions have been positive for small numbers of individual drivers, they have produced overall inconsequential population-level results, thereby leading to the continuation and, in some cases, even exacerbation of drivers' disease and injury burden disparities.[49]

3. IMPASSES OF EPIDEMIOLOGICAL RESEARCH

Prevailing commercial driving epidemiology has been marked by a stark underestimation of the scale, diversity, interdependability, spatiotemporality, and complexity of a plethora of multifactorial work and relevant nonwork factors impacting drivers' overall health, safety, and wellbeing over their working lifespan and beyond. This enduring underestimation has literally shaped the epidemiological research process along lines of theory, methodology, and analysis.

Theoretical foundations are overall grounded in narrowly defined exposures unfolding primarily in a few components of commercial drivers' workplace (e.g., truck cabins), and mainly atheoretical, linear, drivercentric, reductionist, deterministic, and static conceptualizations.[50,51] Linear causal thinking and single-level causal explanations, in particular, are deliberately used by prevailing conceptualizations.[52] As for the former, profusion of reciprocal and continual connections and movements among factors and systems over time are largely absent, while regarding the latter, there is an overreliance on intrapersonal factors at the expense of crucial institutional, structural, organizational, and other meso-/macro-level factors.[53,54] Such narrow conceptualizations have typically led to the collection of inadequate data that often omit crucial macro/meso social, economic, political, and other domains.

These narrow, mainly atheoretical, conceptualizations have clearly impaired *methodological frameworks*: (a) research designs are mainly cross-sectional, drivercentric, and small scale;[55] (b) while there exist studies using (overall average quality and adequacy) longitudinal data,[56] commercial driving epidemiology is defined by the absence of quality prospective studies;[57] and (c) data collection methods are almost solely based on epidemiological surveys, thus limiting types of data that mainly include common or high-risk workplace exposures (e.g., irregular driving shifts), and common and/or hard health and/or safety outcomes (e.g., obstructive sleep apnea).[58] Of course, logistical challenges (e.g., driver mobility and turnover) and corporate barriers (e.g., frequent unwillingness of fleets and/or drivers to facilitate comprehensive/primary data collection) must be duly noted.[59,60] These factors have collectively adversely affected quality and adequacy of collected data.

Largely grounded in *a priori* hypotheses, *analytical frameworks* mainly delve into potential associations between predetermined single, common workplace driver-centered exposures—treating others as confounders or effect modifiers—and single (or classes of related), common driver health and safety outcomes at a time (e.g., relationship between fatigue, sleep disorders, and close calls for crashes).[61,62] When, rarely, mixtures of different exposures (e.g., organizational characteristics of work, dietary patterns, syndemic outcomes) are examined, neither their compositional complexity is fully disentangled, nor methodological innovations reflecting multiple exposures and components are employed. Moreover, this overall analytical inadequacy does not take full advantage of existing (inadequate) data.

The confluence of the foregoing epistemological assumptions and field realities has hampered the implementation of rigorous, especially longitudinal, large-scale research. Subsequently, we still have limited knowledge of: (a) the extent and complexity of multilayered exposures and their influences on driver health and safety; (b) how interactions among structural (e.g., corporate operations) with meso/micro-level (e.g., driver sleep and dietary patterns) exposures influence diverse health and safety outcomes; (c) the spatiotemporal variability of exposures and their influences on driver health and safety; (d) what and how biological pathways and mechanisms connect synergistic exposures and outcomes; (e) how an aging workforce can handle increasing professional pressures and effects on driver health and safety; and (f) how a complete account of drivers' work and relevant nonwork exposures and their interactions affect their health and safety over time.

4. COMMERCIAL DRIVERS' RISKS AS INCLUSIVE *WHOLES*

The foregoing analysis points toward the need for more realistic conceptualizations of commercial drivers' health and safety risks and their consequences. To that end, the following sections delve into how more comprehensive approaches can enhance commercial driving epidemiology.

4.1 Moving from drivercentric to holistic frameworks

Grounded in complex systems frameworks, the 1990s brought about an epistemological transition in population health sciences by highlighting the significance of the overlooked *whole* in explaining health and safety challenges.[63] Accumulated evidence suggests that these challenges can be more fully understood when examining them as *wholes* with interacting parts—that is, with the comprehensive inclusion of all possibly contributing domains.[64] Overall grounded in *exposome*[65] and *network*[66] *sciences*, these epistemologies highlight the health implications of lifetime nongenetic influences (with the genome explaining a small proportion of the phenome[67]) and that connections (*edges*) among factors (*nodes*) define the function of *wholes* (*networks/systems,* represented as graphs[68]), respectively. Synergies of the two provide a logical avenue for the examination of intractable health and safety challenges of working (and nonworking) people.

Yet, occupational and commercial driving epidemiology alike have barely incorporated these combined innovations (the few, limited exceptions do not go far enough[69-71]). Two research groups are presently grappling with these ideas in the context of work, health, and safety. First, empirical efforts of European Union scientists have advanced the groundbreaking *Exposome Project for Health and Occupational Research*,[72] and are currently collecting lifetime, diverse occupational and nonoccupational data to delineate working people's health. Second, going a few steps further, evolving programmatic and empirical efforts of scientists from the U.S. are exploring how integrative *exposome* and *network* science-based frameworks can unravel lifetime health and safety risks of working people. Along these lines, this group has provided a more thorough account of the *working life exposome*, while stressing its potential contribution in understanding the "indispensable *whole* of work and population health and safety."[73] These trailblazer frameworks are guiding the overdue transition from *narrow, static,* and *isolated workplace drivercentric exposures* to *holistic (work and relevant nonwork), lifetime, interacting exposures* that would only enhance occupational and commercial driving epidemiology.

4.2 Introducing the *working life exposome of commercial driving*

Expanding our ongoing work,[73] in the context of relevant research from chronic disease, injury and occupational epidemiology, exposome, and commercial driver health and safety (scanning PubMed 2000-2023), including seminal publications of the National Academies,[74-78] we introduce the emerging *working life exposome of commercial driving (WLE-CD).* We define the *WLE-CD as the totality of an array of heterogeneous, multifactorial/layered and interdependent work, work-related, and in/directly relevant nonwork exposures and associated biological responses and endogenous processes that concurrently and/or sequentially impact commercial drivers' wellbeing from conception onwards, throughout and beyond their working lifetime*. This working definition assumes that the commercial driving occupation lasts for several years, and while comprehensive data on average driver tenure are absent, the review of various reliable sources indicates that the majority of drivers drive professionally more than 10-15 years.[79-82]

Below we provide a comprehensive description of multilayered *WLE-CD* components: the first four components depict the external, while the fifth depicts the internal exposome (as per exposomic conventions). This description highlights how interdependencies between social structure and individual agency shape health and safety over the lifecourse.

Commercial driving exposures unfold in the workplace and have immediate or delayed effects on drivers' wellbeing beyond their work tenure. They fall under:[83-86] *(a) design, content, and conditions of commercial* driving including workload characteristics (e.g., hours/schedules/ irregularity, cargo types/routes, work assignment dispatching); organizational work environment and associated driver psychological demands (e.g., low job control, inadequate rewards, relationships with other drivers, dispatchers); workplace exposures, including roadway conditions, roadway users, vehicle condition, physical, ergonomic, and chemical strains for drivers, conditions in and around workplaces, and driver remuneration; *(b) driver health-/safety-related behaviors on the road* including fatigue, breaks/rest/sleep, fatigue management; healthful food consumption; physical activity; and substance use; and *(c) driver work-life balance away from home* including road/home time distribution, loneliness, stress, family/friends/significant others/partners, other pressures, and mental health/wellbeing.

Commercial driving-defining exposures originate outside the immediate workplace as mainly transportation and labor policies and regulations, but define *commercial driving exposures*, while affecting drivers' lives and have a sustained bearing on driver wellbeing during and well beyond work tenue. They mainly include:[87-90] *(a) government transportation policies* such as Motor Carrier Act, FMCSA's HOS regulations and their enforcement, and FHWA's highway funding policies; *(b) government labor policies* such as motor-carrier exemption under the Fair Labor Standards Act and minimum wage enforcement; *(c) corporate policies, regulations, and operations* including driver hiring practices, training procedures, scheduling and dispatching, use of in-truck technologies, health and wellness programs, job security, compensation methods, and benefits/rights; *(d) labor market characteristics* such as occupational segregation, labor market conditions, driver shortage/turnover, aging workforce, and supply chain problems; and *(e) labor unions* (e.g., union access to workplace, unionization protections, collective bargaining).

Commercial drivers' broad nonwork exposures involve institutional, political, socioeconomic, demographic, educational, labor, food, health, housing, land use, transport, and environmental forces, regulations, policies, practices, as well as their implementation, that shape the wellbeing of working and nonworking people alike. Representative government-based examples include:[91-93] *(a) social and health policies* (e.g., universal, quality and affordable healthcare access, subsidized housing for low-income people, retirement/pension programs); *(b) labor policies* (e.g., unemployment benefits and insurance, OSHA regulations, protections and enforcement, workers' compensation programs); *(c) environmental policies* addressing water and air quality and pollution, among other related matters; *(d) agricultural/food policies* (e.g., food production, processing, distribution of safe, affordable, and healthy food); and *(e) economic/financial, educational, and health resources.*

Commercial drivers' work-dependent, nonwork exposures originate outside broad work milieux and interact with and are affected by foregoing exposures, which synergistically shape drivers' overall wellbeing throughout their lives. They mainly include commercial drivers':[94-98] *(a) personal and family social and economic resources* (e.g., family income, educational opportunities, social capital, home ownership); *(b) personal and family neighborhood/housing conditions/realities*; *(c) personal/family health history* including family traumas (death, divorce, sickness); *(d) health-related behaviors outside work* (e.g., diet, substance misuse, sedentariness); *(e) work-life balance pressures at home* (e.g., inflexible workhours, lack of paid sick and vacation leave, unemployment, excess home responsibilities); and *(e) sociodemographic attributes and factors*.

Finally, ***commercial drivers' biological and other responses to all exposures*** occur gradually as the cumulative embodiment of the foregoing domains. As endogenous processes and mechanisms, they include various physiological disruptions, such as responses to chronic/acute psychological distress, chronic and acute stress, hormonal and metabolic challenges and imbalances, various forms of inflammation, chronobiological changes, oxidative challenges, epigenetics, and syndemic states, with far-reaching ramifications for the health, safety, and wellbeing of commercial drivers.[99-102]

4.3 Examining commercial drivers' risks as multilayered networks

The description of the *WLE-CD* reveals that the mechanisms and pathways of commercial drivers' chronic disease and injury challenges are markedly determined by, embedded in, and/or operate as *complex adaptive networks of networks (CANoNs).* This representation is important especially because exposures induce phenotype changes not as single but as a collection of interrelating agents acting in unison.[103] Hence, commercial drivers' health and safety challenges are attributable to diverse, multisource/level factors (*nodes* in a network representation) that are interdependent and self-organized, generate feedbacks and emergent patterns, follow simple rules (e.g., based on theoretical propositions), and evolve over time. These *meganodes* include multifactorial *WLE-CD* components and *commercial drivers' genome* and *chronic disease and injury outcomes,* with each node including several nested factors, layers, other networks, and larger systems. These *meganodes* interact among themselves in various ways, while similar processes and connections exist within *nodes* themselves—especially within the *WLE-CD*. The arrangement and connections (*edges*) of *nodes*, their spatial patterns, and especially their emergent topological properties (or *network topology*[104]) are of foremost importance in unravelling relational patterns and causal structures of drivers' health and safety risks. *Figure 1* represents a heuristic portrayal of commercial drivers' health and safety risks as *CANoNs.*

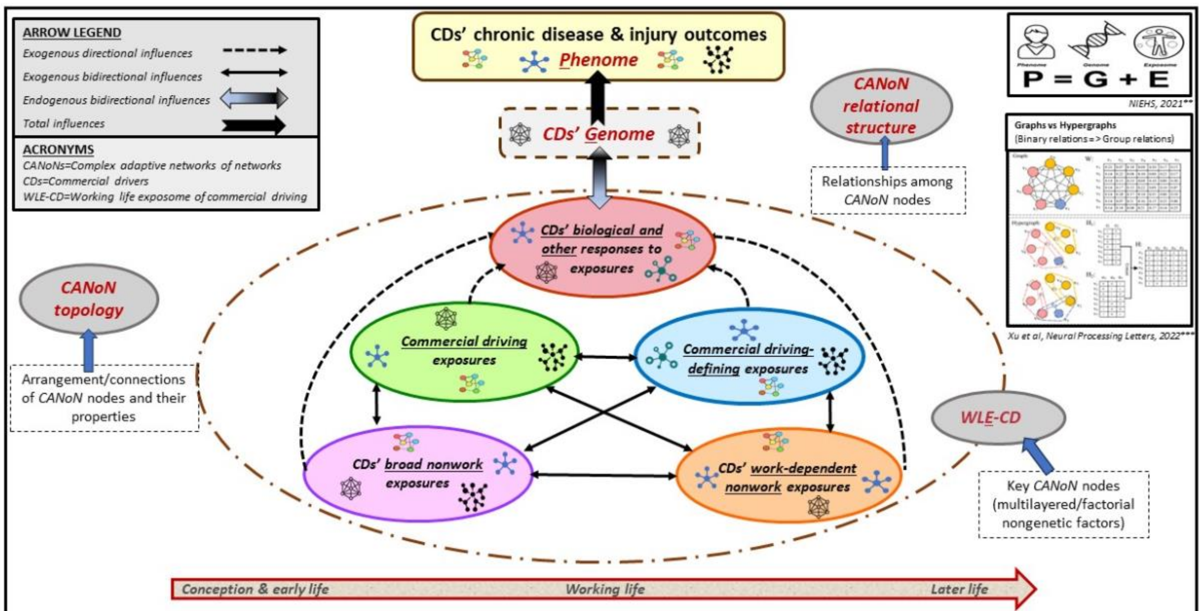

Figure 1: Simplified depiction of commercial drivers' health and safety risks as *CANoNs* (hypergraphs) centered on *WLE-CD* and *CANoN attributes.**
*Adapted from https://pubmed.ncbi.nlm.nih.gov/37952240/; **https://factor.niehs.nih.gov/2021/1/science-highlights/data-science; ***https://link.springer.com/article/10.1007/s11063-021-10684-7.

While delineating the architecture of ordinary networks—exemplified by pairwise *node* interactions represented by *edges*—has generated valuable insights in understanding and preventing risks,[105] it also comes with inherent constraints.[106] Like other complex networks (e.g., neural or metabolic systems[107]), the multifactorial/layered nodes of this *CANoN* (that is, the complex network of commercial drivers' health and safety risks) are anticipated to interact in larger groups and such interactions cannot be decomposed as linear combinations of dyadic couplings.[108] The existence of many-node, higher-order interactions are more fully represented by *hypergraphs* and *hyperedges*—with *hypergraphs* allowing us to model group instead of only binary relations.[109,110] Early *hypergraph*-based investigations indicate that higher-order interactions may bear significant influences on networks, oftentimes leading to dynamic processes and even abrupt transitions between states.[111]

Like in ordinary graphs, *hypergraphs* carry topological properties[112] that can influence the dynamics of networks. Most commonly used topological properties include: (a) *degree of a node*—number of edges connecting to a node that can influence other network properties because degree distribution provides a high level description of the network topology, e.g. a scale-free network (where most nodes are connected to a low number of neighbors and there is a small number of high-degree nodes *(hubs)* providing high connectivity to the network); (b) *shortest paths*—shortest distance between any two nodes used to model flow of information and/or transmission; (c) *transitivity (*or *modularity)*—presence of tightly interconnected nodes that are more internally connected than they are with the rest of the network *(clusters/modules/ communities)*; and (d) different types of *centralities*—denoting how important a node or an edge is for a given network property, such as the network's connectivity, proximity to other nodes, information/transmission flow, and others. Overall, these topological properties can have an influential bearing on other processes.[113] Both *network relational patterns and topology* are crucial in understanding complex health situations[114] because, together can define quantitative patterns and measures of nodes and edges, thus, network localization and organization are reflected in topological parameters.

It is because of these features that we cannot effectively examine *CANoNs* by an *a priori* determination of a set of nodes and/or properties that are studied separately (e.g., associations between irregular workhours and drivers' obesity) and then recombining these (and other) partial associations in an attempt to understand the *indispensable whole*. It is necessary, therefore, to examine and model them as *wholes* (represented by *CANoNs*), with an emphasis on understanding interactions among various network entities, pathways, mechanisms, structures, and emergent influences over time. *Table 2* depicts the lifecourse dimension of *WLE-CD*.

Table 2: The *WLE-CD*[1] influences commercial driver wellbeing throughout the lifecourse.[2]

Lifecourse (years)		0 10	20 30 40 50 60 70	80 90+
		Early life[3]	*Working life*	*Later life*
W	CD exposures		→	- - - - - - →
L	CD-defining exposures		→	- - - - - - →
E	CDs'[4] broad nonwork exposures	- - - - →	→	→
- C	CDs' work-dependent, nonwork exposures	- - - - →	→	→
D	CDs' biological/other responses to exposures	→	→	→

[1] **WLE-CD**=Working life exposome of commercial driving; [2] It assumes that occupation lasts for several years (see text); [3] **Early life** includes periconceptional and perinatal periods; [4] **CDs**=commercial drivers. **Solid** lines denote direct/actual influences and consequences; **Dotted** lines denote potential/residual/indirect influences and consequences.

5. PARADIGM SHIFT IN COMMERCIAL DRIVING EPIDEMIOLOGY

Foregoing analysis accentuates the epistemological necessity for new directions in commercial driving epidemiology grounded in the strengths of *exposome* and *network sciences.* This emerging paradigm shift corresponds to actual health and safety challenges and emphasizes how integration of *WLE-CD* and *CANoN* theories and epistemologies can more efficiently explain commercial drivers' chronic disease and injury risks.

5.1 Integrative *exposome/network* frameworks enabling the study of *wholes*

The integrative *WLE-CD/CANoN* conceptualization and associated innovations can catalyze significant enhancements in epidemiological research by extenuating the complexities of the *indispensable whole* of commercial drivers' chronic disease and injury risks. Below we outline potential contributions of emerging *WLE-CD*/*CANoN*-grounded frameworks, using “commercial drivers’ cardiometabolic syndemics” that are among the foremost concerns[115]—as a case study.

Theoretical enhancements. *WLE-CD*/*CANoN*-based frameworks enable understanding of commercial drivers’ cardiometabolic syndemics as complex and dynamic, comprehensive *wholes* with interacting parts. Specifically, they can: (1) provide the theoretical basis to portray an array of multifactorial and interdependent work and nonwork exposures that synergistically shape drivers’ wellbeing; (2) recognize the totality, complexity, and concurrency of multiple, multilayered, multiscale, heterogeneous exposures; (3) highlight how interdependencies of exposures can influence drivers’ health over their lifecourse; (4) extenuate the importance of structural transportation, labor, and other social factors and their interactions with biological mechanisms, thereby providing insights into informative biological pathways linking exposures to wellbeing; and (5) emphasize spatiotemporal dimensions of exposures, and especially how ramifications of working life exposures extend beyond drivers’ tenure. These and related assumptions can also work as key propositions toward the development of a theory that frames commercial drivers’ wellbeing. Last, these conceptual improvements will also define types of research questions asked, data collected, and hypotheses tested.

Methodological enhancements. *WLE-CD*/*CANoN*-based frameworks can allow the: (1) systematic implementation of invaluable longitudinal designs underpinned by the ubiquitous complexity of drivers’ syndemics over their lifecourse; (2) examination of diverse driver cohorts, with an emphasis in more vulnerable groups (e.g., older drivers); (3) implementation of comprehensive designs that combine bottom-up and top-down approaches; (4) employment of data collection methods, beyond surveys, grounded in exposure biomarker technologies, geographical mapping and remote sensing technologies, smartphone applications and personal exposure sensors, and high-throughput molecular ‘omics,’ among others; (5) collection of comprehensive (primary/secondary) data that cover common and less common multifactorial exposures, biological and related mechanisms, pathways, and markers, as well as diverse higher-/lower-prevalence outcomes; and (6) utilization of extant datasets[116-118] (based on large-scale data pooling from population, industry- or occupational cohorts) and various big data sources, including exploitation of both comprehensive and fragmented datasets, as well as collection of proxy measures to account for crucial pre-working life exposures. The systematic collection of comprehensive commercial driver health and safety data remains a necessity for novel epidemiological research.

Analytical enhancements. Especially due to extensive knowledge gaps, *WLE-CD*/*CANoN*-based frameworks can facilitate both discovery- and hypothesis-driven analytical approaches: (1) inductive (untargeted) research—grounded in *exposome-wide association studies/ExWAS*[119] and *network analysis,*[120] among other innovations—can contribute to discovering causal signatures and fingerprints of exposures, thereby potentially uncovering new combinations of mechanisms generating and/or perpetuating syndemics, and (2) deductive research—grounded in correlation-/regression-based analytical methods—can contribute to testing the plausibility of various evidence-supported hypotheses in delineating these syndemics. Along these lines, because traditional statistical approaches are not designed to delineate compound effects of *WLE-CD*/*CANoN*-based multifactorial/layered components, the employment of combinations of novel analytical methods—taking advantage of primarily stochastic analytical breakthroughs grounded in the use of mathematical, statistical, and/or computational innovations (e.g., machine learning, network analysis, simulation)[121,122]—can advance understanding of drivers’ syndemics over their lifecourse. Also, methods employed in other health-focused exposome and network projects as well as science-originating network projects can be replicated and/or can catalyze the development of new methods appropriate for evolving commercial driver research needs. These frameworks can facilitate the identification of those exposures that trigger biological perturbations and changes leading to cardiometabolic syndemics, with an emphasis on sources, early markers, routes, combinations, and critical phases prior to, during, and beyond drivers' working lifetime.

Beyond a "crude look at the whole." When in 1990 renowned physicist Murray Gell-Mann emphasized the importance of *"a crude look at the whole,"* he intended, among others, to underscore the imperative necessity of examining complex situations as *wholes* and then allowing possible simplifications to emerge from this approach. Over three decades later, however, integrative *WLE-CD*/*CANoN*-based epistemologies and methodologies grounded in multifaceted ongoing scientific and technological breakthroughs allow us a more complete examination of the *indispensable whole* of health and safety challenges of working people.[123] Differently put, novel integrative *WLE-CD*/*CANoN*-based epistemologies and methodologies are promising a more comprehensive, useful look at the *indispensable whole* of commercial drivers' health and safety challenges.

5.2 Leveraging network analysis within integrative frameworks

This section presents a small-scale proof-of-concept grounded in network analysis to demonstrate only indicative portions of how the analytical strengths of the emerging paradigm can enhance our understanding of commercial drivers' health and safety challenges. Given that exposures induce phenotype changes as combinations of interacting factors acting together[124] and that network relational and topological features provide invaluable insights on interrelations among exposures and outcomes,[125] network analysis is uniquely suited to describing, exploring, and understanding drivers' health and safety risks. It is our goal to substantiate how these holistic approaches can contribute to a better delineation of drivers' health and safety risks.

Uncovering network relational patterns. Understanding how relationships between *CANoN* nodes may influence the behavior of the whole system (that is, commercial drivers' health and safety risk vulnerability) is crucial. The main idea is that *WLE-CD* exposures and drivers' health and safety outcomes are interdependent, and we may miss crucial interplays unless we evaluate them as *CANoNs*. We can examine patterns of relationships between variables (e.g., relationships among *CANoN* nodes, contribution of groups of *CANoN* nodes to single/multiple outcomes), and how different *WLE-CD* exposures and outcomes may be related to each other, by either correlational or causal relationship, which will lead to large-scale networks. Network analysis allows the exploration of a larger space of *WLE-CD* exposures and outcomes, where single connections will now be substituted by subsets of factors that are densely connected in the network representation, thereby providing deeper insights into complex risk etiology.

Figure 2 demonstrates a simplified *network of commercial drivers' roadway safety*, based on a small (N=459), imperfect subsample of commercial drivers originating from our own work[126]—with roadway safety being a foremost concern for professional drivers.[127] While we anticipate the emergence of higher-order interactions and group relations among *CANoN* nodes (thus being open to highly novel network analyses), because of data limitations, we follow a more traditional network analysis path examining only binary relations between nodes—which nevertheless can reveal the strengths of the emerging paradigm.

A few explanatory variables (circles) represent factors related to drivers' work (orange color), CVD health (teal), sleep health (blue-grey) and lifestyle (purple). These variables are connected among themselves and to roadway safety outcomes (hexagons). Our main hypothesis is that drivers' roadway safety outcomes are impacted by the entire system, as expressed by the combination and interdependence of factors leading to this network representation. For clarity, we include only four roadway safety outcome variables (lemon) corresponding to "no accidents," "more than two accidents," "no near-misses," and "more than five near-misses." For each outcome, we compare the driver subsample related to this outcome ("outcome sample") with the subsample of all other drivers ("reference sample"). This comparison takes place for each explanatory variable separately and we determine whether the two variable distributions in these two subgroups can be considered statistically different from each other. If distributions are different, then we connect the variable to the outcome with a green line, when the variable value in the outcome sample is larger than in the reference sample, or with a red line, when the variable value is smaller in the outcome sample than in the reference sample. The distance between distributions is determined via a *standard Kolmogorov-Smirnov test*,[128] except for binary (yes/no) distributions which are tested using a χ^2 *test*.[129] Connections between explanatory variables are determined by linear correlations between pairs, using the whole driver sample. We use the *Pearson coefficient*[130] to quantify the connection strength between all explanatory variable pairs and impose a threshold, above which we assign a link connecting the given pair.

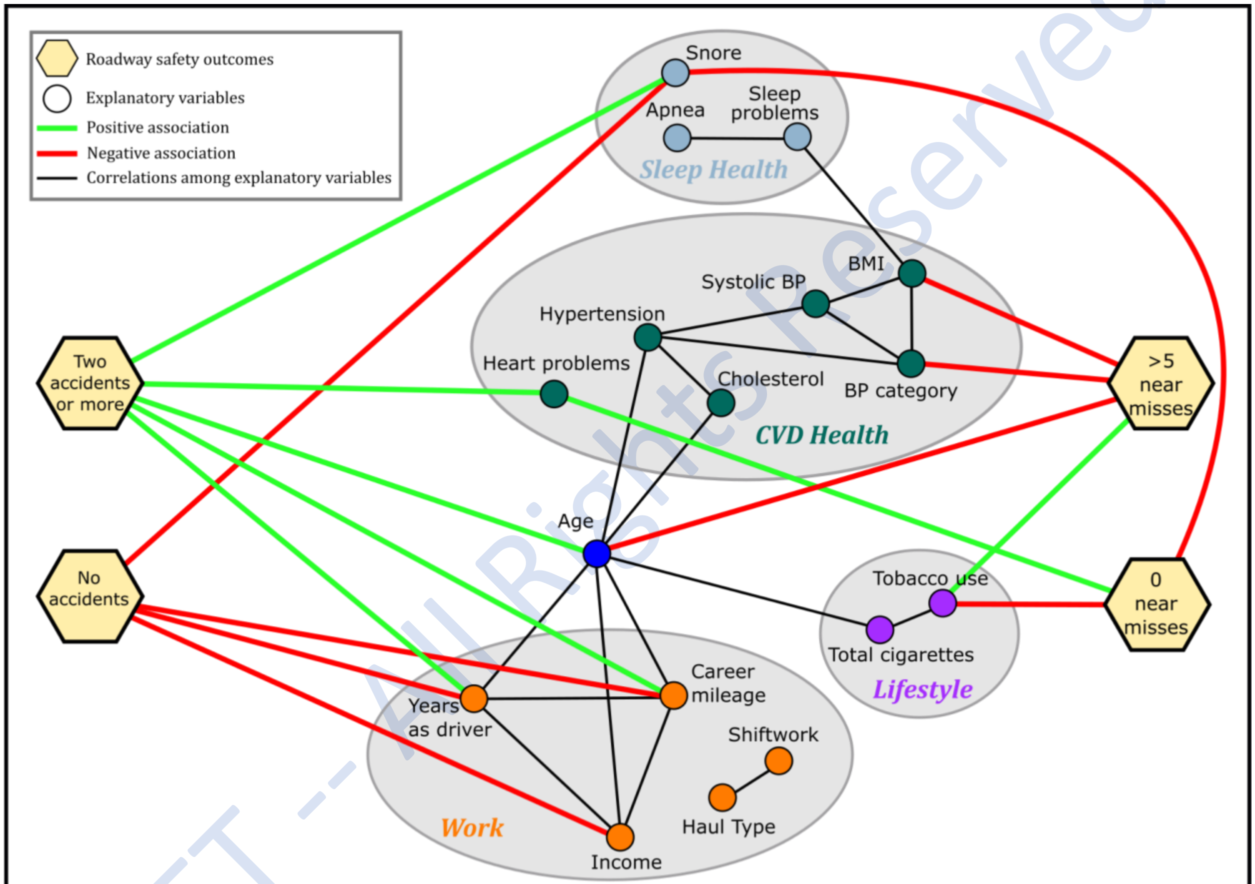

Figure 2: Network representation of commercial drivers' roadway safety.

This representation shows that even with this small, imperfect sample of commercial drivers and a few explanatory variables, we get meaningful information out of this network. For example, the "more than 5 near-misses" outcome is directly linked to BMI, blood pressure, and age. This representation also shows that these network nodes do not act independently but, together with other nodes from the "CVD health" cluster, form an intricate web of interdependencies, which need to be considered when planning possible interventions. We expect that a network of larger scale will uncover factors or groups of factors that have the highest impact on commercial drivers' roadway safety outcomes, directly or indirectly.

Identifying network topological properties. Topological interdependencies (e.g., centrality, clustering) among *WLE-CD* factors may influence commercial drivers' health and safety outcomes.[131] For example, it would be useful to know which *WLE-CD* factors are more important or central than others in this *CANoN* and whether they are isolated or form strong clusters. *Centrality measures*, for example, can reveal groups of *WLE-CD* factors, whose *CANoN* location may affect many outcomes or connect otherwise disjointed *CANoN* areas. The identification of topological properties is not possible without a holistic network consideration.

Returning to our proof-of-concept example, "commercial drivers' roadway safety network" is a useful tool to examine complex interactions between multiple exposures because we can use network analysis to evaluate how different factors influence each other as isolated nodes or as a group, determine the importance of different explanatory variables in the global structure, estimate how different interventions may change the form of the network, etc. *Centrality measures*, for example, can reveal what categories of variables are dominant in the network in terms of, for example, influencing or being influenced by most of the other exposures. In *Figure 2*, the "age" node (cobalt) has the highest *degree centrality* among explanatory variables—it is related to the largest number of exposures and outcomes and is the node that ties together different groups of factors. Even though this is an anticipated result, it demonstrates how the network structure can provide an improved picture of interactions among multiple factors forming a global exposure system.

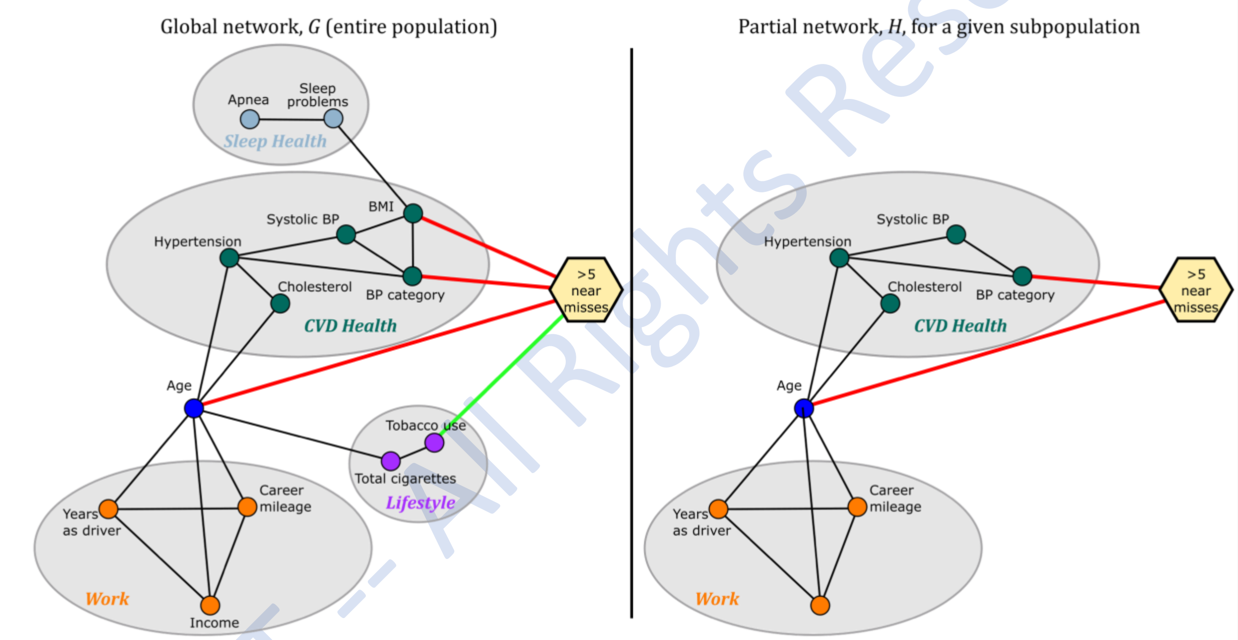

Figure 3: Networks built from the entire population (left) or a specific subpopulation (right); used to calculate closeness risk score.

This network can be used to calculate roadway safety risk scores within subpopulations—say, based on commercial driver age, given that driver aging and turnover are serious, interconnected factors with far-reaching ramifications. For a given roadway safety outcome, we can consider all connections with explanatory factors related to this outcome, implicitly or explicitly. Let us use, for example, the "more than 5 near-misses" outcome; the subnetwork built for the entire commercial driver population, *G*, is used as a reference network. For the commercial driver subpopulation, we can build a similar network, *H,* by including only exposures associated with this subpopulation. Therefore, *H* is a subset of *G* since many exposures will be missing. The *closeness centrality* (how close a node is to all other nodes in the network), *C(o)*, for a given roadway safety outcome (e.g., o="more than 5 near-misses"), is a measure of the distance from this outcome/node to all related exposures. We calculate $C^G(o)$ for the global network and $C^H(o)$ for the subpopulation. The network topology score is the ratio $C^H(o)/C^G(o)$, which is necessarily between 0 (no risk) and 1 (highest risk) and refers to the specific roadway safety outcome. We can then repeat the calculation for all outcomes and can average the results to have a global network topology score quantifying the global roadway safety for the given subpopulation. Similarly, we can use a number of centralities (e.g., degree, betweenness) to calculate risk scores placing emphasis on different network topological features. These topological scores can inform us on a variety of useful characteristics, such as, for example, existence of uniform vs localized risk across various roadway safety outcomes or extent of influence between clusters of explanatory factors, among others.

5.3 Emerging paradigm: Turning challenges into opportunities

While in an infancy phase, this emerging paradigm in commercial driving epidemiology faces challenges, not atypical of observational, exposomic, and/or network research.[132-134] Yet, comprehensive research designs and utilization of appropriate scientific and technological innovations, along with commensurate funding, can contribute to largely tackling many of these challenges and even turning them into opportunities to enhance commercial driving epidemiology.

Specifically, key challenges can be grouped as relating to the: (a) collection of large, complex datasets from diverse sources, but necessary for rigorous data analyses;[135] (b) measurement of multiple, multidimensional, heterogeneous, and oftentimes hard to access mixtures of exposures over extended periods of time;[136] (c) analyses of complex heterogeneous data along disparate spatiotemporal frames, including intricacies associated with *exposome-wide association studies* and *network analysis*, which are building blocks of an emerging paradigm;[137] and (d) assessment of causality because of confounding, reverse causation, and other uncertainties.[138]

While various "remedial" actions can largely offset these challenges, we believe that they can also be turned into opportunities for advancing commercial driving epidemiology. First, on the *data collection front*, mutually beneficial partnerships among unions, trucking fleets and terminals, truckstop companies, government agencies, insurance firms, nonprofit organizations, and research teams can collaborate in the pursuit of quality prospective data.[139] Second, on the *measurement front*, a combination of proxy exposures, different methods of data collection and tools, along with novel technologies (e.g., sensors, GIS, high throughput 'omics') can help identify exposure biomarkers and even allow integration of varied exposures to single measures.[140] Third, on the *analytical front*, because of dealing with high dimensionality, studying the combined effects of exposures and their interactions, and integrating causal pathways and high-throughput omics layers, other novel analytical methods such as mediation analysis, g-computation methods, and causal random forest can make significant contributions to this end.[141] Finally, on the *causality front*, among others, "triangulation" approaches (using diverse computational and statistical advances to address research questions) and involvement of novel "omic" technologies, combined with broad data sharing and cross-study collaborations offer opportunities to strengthen causal inference.[142] Especially when examining combinations of co-occurring exposures and outcomes, Hill's specificity criterion of causality is replete with reservations,[143] and may need to be revisited if evidence for combinations of *WLE-CD* exposures associated health and safety outcomes are realized.

This emerging paradigm can constitute the foundation for a process of actual enhancement of commercial driving epidemiology. Furthermore, foregoing steps can ultimately lead to sustainably improving commercial drivers' health and safety with far-reaching implications for broader population health, roadway safety, as well as beneficial consequences for the trucking industry, supply chains, and community economic development.

6. TOWARD A *NEW* COMMERCIAL DRIVING EPIDEMIOLOGY

Prevention efforts grounded in traditional approaches have been overall inconsequential at the population level, with commercial drivers remaining among the most underserved and unhealthiest populations in the nation. Because prevailing epistemological approaches can only go so far, emerging integrative epistemological frameworks garnered insights from the exposome and network sciences have the potential to move the science of commercial driving epidemiology forward faster, more substantively and efficiently. Continuous development, validation, and proliferation of this evolving discourse can ultimately lead to the emergence of a *new* commercial driving epidemiology that adheres to scientific and technological progress and generates more accurate and thus useful results. This *new* commercial driving epidemiology can also enrich government and corporate policies and related actions that can collectively improve the long-term health and safety of underserved commercial drivers. It can also have applications in the examination of health and safety of other working populations as well as to population health at large. Finally, this novel emerging discourse can also shed new light on the overlooked role of independent work and relevant nonwork factors in the study of population health.

7. REFERENCES

In progress.