Method for Assessing the Environmental Impact of Chronic Disease Treatments:

A Life Cycle Environmental Emissions Analysis of Type 2 Diabetes Treatment Pathways in the United States and Sri Lanka

By

Danielle Wilkins

A Thesis submitted in partial fulfillment of the requirements for the degree of Master of Science (Environmental Science) from the University of Michigan School for Environment and Sustainability

Thesis Advisors

Assistant Professor of Practice Jose Alfaro, School for Environment and Sustainability, University of Michigan

Assistant Professor Cassandra Thiel, Department of Population Health & Department of Ophthalmology, New York University

For JT.

1 Acknowledgements

I would like to acknowledge and extend thanks to Dr. Jennifer Ann Wyckoff M.D., Sonja Hughbanks and their medical assistant colleagues at the University of Michigan's Metabolism, Endocrinology and Diabetes Clinic at Domino's Farms, to Dr. Mahen Wijesuriya and his colleagues at the National Diabetes Center in Sri Lanka, to Dr. B. Ganaikabahu and his colleagues at the Trincomalee General Hospital Diabetes Clinic, and to Dr. Naresh Gunaratnam and the entire community of the Grace Girls Home of Trincomalee, in particular Angela, Jessi, Shobana and Vinu. Without your support and generosity in sharing your knowledge and experiences in treating Type 2 diabetes this paper would not be possible.

A tremendous thanks are due to my advisors, Cassie Thiel and Jose Alfaro. I am forever grateful that you continued to respond to my e-mails during a process that went on far longer than I ever expected. I could not have completed this work without your support and encouragement.

To my parents and JT, your persistence was my persistence and it kept me going in the face of multiple jobs, growing responsibilities and life in general.

Table of Contents

Abstract

The healthcare industry is increasingly being asked to account for the negative environmental impacts generated in the course of providing medical care. This study expands on a growing body of research to present a model for the use of established process life cycle assessment (LCA) methodologies to quantify the environmental and public health impacts of chronic disease treatments. The study investigates the impacts generated by two Type 2 diabetes (T2d) treatment protocols in the United States and Sri Lanka. The functional unit of the study was the inputs required to treat one T2d patient, with no additional medical complications, for one year. Inventory data for each treatment protocol was gathered from published literature, U.S. patent filings and in-person observations of medical clinics in the United States and Sri Lanka. Inventory data emissions were calculated using the Ecoinvent 3.0, Industry 2.0 and USCLI databases.

The results of the study show that T2d as a global epidemic is measurably contributing to environmental degradation and negative public health outcomes of the wider non-diabetic community. Different treatment components contribute differently according to the specific impact being assessed. The results suggest that energy production, transportation and medication dosage strongly influence negative impacts. Improving and remotely monitoring patient health to lower medication dosages and reducing doctor visits are actions that can be taken by patients and healthcare providers. Governments and private sector actors can also champion renewable energy grids and safe active transportation infrastructure to promote the low impact exercise, decreased motor-vehicle transportation and decarbonized electricity.

1 Introduction

Ecosystem services underpin the economic and public health of human society (Costanza et al. 1997; Corvalán et al. 2005; Hester and Harrison 2010; Daily 2012). We are dependent on ecosystems yet, according the IPCC's Fifth Assessment Report, humanity's actions in the form of rapid increases in greenhouse gas emissions, immense resource extractions, and the release of concentrated effluents are contributing to the massive breakdown of these services and the protections they provide. Ecosystem collapses are a part of the broader changes to the global climate that human activity –like medical care delivery- is accelerating (Pachauri and Meyer 2015).

The 2015 Lancet Commission on Health and Climate Change reports that "the implications of climate change…threatens to undermine the last half century of gains in development and global health" (Watts et al. 2015; Haines et al. 2006).Statements such as these suggest that in addition to well documented impacts to the environment, climate change will have a substantially negative effect on global human health. At the same time, while topics such as energy production and consumer behavior often dominate public discourse on climate change solutions, the environmental impacts associated with medical care itself are frequently absent from these discussions. This is despite the fact that the healthcare industry is estimated to be the source of 4.4% of global greenhouse gas emissions (GHGs) (Karliner et al. 2019a), including 10% of the GHGs emitted by the United States (Eckelman & Sherman, 2016).

These emissions have a real human cost. One study estimates that just one year of health care in the United States results in 123,000 reduced years of life for the global population (Eckelman and Sherman 2018). That is to say that the emissions generated to save and prolong the lives of people in the United States are negatively impacting the long-term health of people in the United States and the wider global community. The growing cost of medical treatment to human health is not going unnoticed in a profession with the motto "do no harm". The American College of Physicians formally recommends the global health community adopt environmentally sustainable practices to reduce carbon emissions and the negative health impacts associated with environmental degradation (Crowley 2016). In 2019 the Australian Medical Association followed suit with a motion from its Federal Council stating, "The Federal Council recognizes climate change as a health emergency…" (Australian Medical Association 2019).

To begin to understand how the medical community can eliminate harmful emissions, it must first identify the source and causes of its emissions. Over the past several years researchers have begun this work (Cimprich et al. 2019). Many studies have centered on the role of medical buildings and very energy intensive medical procedures, such as surgery (Campion et al. 2015; Cassandra Thiel et al. 2015; CL Thiel et al. 2017; Cassandra Thiel, Woods, and Bilec 2018). While it is vital that the health care industry address the waste and emissions generated by these intensive components of medical care, the industry should also consider the impacts of medically treating common ailments such as chronic non-communicable diseases (NCDs). Unlike a surgery, that is often resource intensive and performed once per patient, or hospital stays associated with other forms of treatment for acute diseases, chronic diseases often require a self-administered, relatively low-resource treatment for an extended period of time. While chronic diseases require less resources to treat, the effects of not adequately managing these diseases can be severe. NCDs and their associated medical complications are currently the leading cause of death worldwide("WHO | Noncommunicable Diseases" 2018).

Diabetes mellitus type 2 or Type 2 Diabetes (T2d) is a chronic, non-communicable metabolic condition characterized by the body's inability to effectively use insulin, an endocrine hormone necessary to remove glucose from the blood stream (American Diabetes Association 2017). Treatment of the disease involves maintaining a stable blood glucose range defined by an A1c test result of less than 7% or 53 mmol/mol (American Diabetes Association 2019). If managed properly and blood glucose is kept within a healthy range, the negative health implications of the disease are minimal. If patients do not receive proper treatment the effects of prolonged elevated blood sugar or hyperglycemia are serious and require significant medical resources to manage. Hyperglycemia is one of the leading causes of amputations and blindness, and often results in acute conditions such as heart attack and stroke. In addition, prolonged hyperglycemia is a common co-morbidity of other deadly non-communicable diseases (NCDs) such as heart and kidney disease (Burant 2012), all of which require increased medical care.

Despite the severity of medical complications associated with diabetes, rates of T2d are increasing rapidly. In 1980 the global prevalence of diabetes was 4.7%, by 2014 global prevalence had risen to 8.5% (Roglic and World Health Organization 2016; The Emerging Risk Factors Collaboration 2010) Not only are the number of patients increasing, but the location of diabetes prevalence has shifted. Long considered a disease of the wealthy, the highest growth in rates of T2d diagnosis are now occurring in low and middle-income countries (Roglic and World Health Organization 2016). The trend is not unique to T2d. Chronic diseases, which encompasses but are not limited to cardiovascular diseases, cancer, chronic obstructive pulmonary disease and T2d, are incurring the fastest growth in low and middle-income countries Similar to T2d, if left untreated most NCDs will result in severe medical complications. To avoid the negative impacts of these diseases, countries around the world will need to offer effective medical treatments. But what are the environmental, and by extension, human health impacts of these treatments when scaled to global proportions?

This study offers a framework for how the environmental impacts of chronic disease may be modeled in a variety of contexts. Taking T2d as a model, this research uses a standard life cycle assessment (LCA) methodology to provide health care practitioners and other interested stakeholders with a preliminary baseline indication of the cumulative environmental and health impacts of treating Type 2 diabetes (T2d) at two sites – one in the United States (US) and one in Sri Lanka. Four treatment pathways associated with the management of T2d are assessed in the context of climate change, terrestrial acidification, water consumption and human health. Using data from the sites in the United States and Sri Lanka as proxies for High-Income and Low-Middle-Income countries respectively, preliminary results are estimated for the global impacts of T2d treatment.

2 Literature Review

2.1 Health and the Environment

For most of human history there has been a recognition of the relationship between human health and the natural environment. Writings dating back to the ancient Greeks along with ancient archeological findings, suggest a fatalist approach to this relationship whereby humanity is acted upon by the natural world around it. This view would begin to alter as human society and its technologies evolved to more intensely and effectively shape the natural world (Berridge and Gorsky 2011). Observations of strong correlations between place and health would lead various societies to adopt the study of what we now refer to as Public Health. In the West this area of study became clearly defined in the eighteenth century

with what has been called 'The Great Sanitary Awakening' (Berridge and Gorsky 2011) . The recognition that human-made waste created an environment that fostered disease supported the logic that human action could create an environment that fostered good health. The discovery of bacteria and their role in disease transmission in the late 19th century further worked to impart a sense of freedom from environmental fatalism (Berridge and Gorsky 2011). Armed with a greater understanding of the workings of the natural environment, society could now overcome its ill effects. In this new conceptualization the environment was now a place of other, something to be either exploited or protected, but fundamentally distinct from the civilization of human society (Berridge and Gorsky 2011). Human health was now a matter of individual choices and behaviors. Built environments, Individual hygiene practices and medications would ensure or destroy good health. Evidence of this perspective is readily available in the published health journals of the era.

A keyword search of "environmental impact" + "healthcare" through the University of Michigan's library collection of more than 2000 databases, including PubMed, Google Scholar, JSTOR, Web of Science, ProQuest, WorldCat among many others, filtered for the years 1900 through 1960 yielded more than 10,000 articles. An in-depth review of the 50 articles thought to be most relevant, as well as a random sample of no less than 200 articles from the entire body of work confirmed the assertion that the public health discourse of the period viewed natural ecosystems as in general need of alteration to benefit human health(McINTYRE 1943; Mark D. Hollis 1951; 1953; BERRY 1940; HATTIE 1929; Childe 1923; Blanchard 1928; BERRY 1960). The World Health Organization in 1952 itself defined the problems of environmental health as "The ravages of water-borne, insect-carried and excreta-transmitted disease" (Herbert Bosch 1952). Of the hundreds of articles reviewed, only a handful indicated a consideration for the importance of natural ecosystems to public health (Conklin 1949; SALISBURY 1938; "The Scientific Basis Of Ventilation And Open-Air Treatment" 1920; Lewis 1911; Frost 1916; Watrous 1947; Price 1958; 1959; "Responsibilities of Local Health Agencies for Air Pollution Control: Statement, Conference of Municipal Public Health Engineers on Air Pollution Control, October 6, 1958" 1959; Decker 1960; Mark D. Hollis 1952; Kehoe et al. 1958). It would not be until the 1960s with widespread environmental degradation highlighted by works such as Rachel Carlson's "Silent Spring" that the general public and public health officials would take meaningful account of the positive impact of dynamic natural ecosystems for human health (Baratta 2016; Johnson, Greenberg, and Greenberg 2017). This realization came at a time when as described by Adam Rome in his article ""Give Earth a Chance": The Environmental Movement and the Sixties", "newly affluent Americans were able to insist on environmental quality, the development of atomic energy, the chemical revolution in agriculture, the proliferation of synthetic materials, and the increased scale of power generation and resource extraction technology created new environmental hazards…, the insights of ecology gave countless citizens a new appreciation for the risks of transforming nature"(Rome 2003). Still, while the 1960s marked the beginning of greater modern public awareness of the impact of the environment on human health, there was no observable recognition in the academic literature of the role of human medical care on the environment.

The waste crisis of the 1980's begins the period in which academic publications specifically note the role of the healthcare industry in contributing to negative environmental impacts. Articles such as Susan Schlepp's "Regulating Disposal of Infectious Waste" details the dangers of unregulated disposal of infectious waste into the natural environment and the increased risk of human exposure these practices yield (Schlepp 1988; Bennett 1988; Doucet 1988; Holthaus 1988). These writings are limited in that they

do not speak to the harm of medical waste on the environment, rather the direct harm of direct human contact with medical waste in the environment. The conversation further evolves in the 1990s with the addition of articles such as “Green Medicine: Environmental Impact of Health Care” and the WHO’s Safe Management of Wastes from Health-Care Activities, both of which are calls to address the role of healthcare in environmental pollution (Worton 1995; Prüss et al. 1999). But it would not be until the new millennium that the realization would surface more widely in published academic discourse that as a profession dependent on industrial scale production to provide care, the medical community is itself responsible for environmental pollution.

Between 2000-2010 there is a notable increase in the amount of research dedicated to raising awareness of medical waste as an environmental pollutant(Christian G. Daughton 2003; Daughton 2002; Jameton and Pierce 2001; Brown 2009; Daughton 2009; Cotton and Cohen 2010) . The American Journal of Nursing published an article titled, “Catching the Environmental Health Wave: The ANA, Nurses Work to Improve Health Care Industry’s Impact on the Environment” (Trossman 2004) and followed this work with a full report on improving environmental health through nursing (American Nurses Association 2007). Other publications looked at the environmental impacts of general practitioner follow-up (Murchie 2007) and the actual emissions generated by healthcare-related incineration (Alvim-Ferraz and Afonso 2005). A number of studies investigated approaches to pollution prevention in healthcare (Allen 2006; Stichler 2009) and systems approaches to managing healthcare waste (Zimmer and McKinley 2008).

The last nine years (2010-2019) have seen an even greater increase in number and relevancy of publications. Moving beyond awareness raising, the discourse has begun to advocate for institutionalized measures to ensure environmental accountability in medical care (Hensher 2020; Daughton 2014; Jeswani and Azapagic 2019) and detailed studies are providing greater insights into how different medical treatments and systems are contributing to negative environmental impacts (Dunbar-Reid and Buikstra 2017). Building on its success in cataloguing resource consumption and the subsequent environmental impacts attributable to the industrial manufacturing sector, Life Cycle Assessment studies are increasingly being used to assess medical services.

2.2 Early History of LCA

Life cycle assessment methodologies trace their beginnings to the 1960s. While there is some dispute as to which study marks the beginning of the method (some articles report the private 1969 beverage container study by Coca-Coloa, while others note the 1963 study by Harold Smith quantifying energy requirement needs for chemical production), the method and its adoption are closely related to the rise of the modern environmental movement in the United States (Bjørn et al. 2018; Hunt, Sellers, and Franklin 1992). Known as Resource and Environmental Profile Analysis (REPA) in the U.S. and Ecobalances in Europe, these early methods drew heavily from the concept of material flow accounting which focused on tracking the amount of materials cycling into the economy and entering the environment at all phases of a commodity’s life cycle (Wernick, Irwin, and World Resources Institute 2005; Hunt, Sellers, and Franklin 1992). Early iterations of REPA/Ecobalance were not able to provide an impact assessment to quantify the direct damage being wrought to the environment or to human health, but they did provide an estimated scale of the material outflows to the environment (Hunt, Sellers, and Franklin 1992). The ability to conduct impact assessments would be defined later in the evolution of the LCA methodology.

The authors of the 1969 Coca-Cola beverage container study write that between 1970 and 1975 there were several additional REPAs conducted with considerable effort being put into working with major materials manufacturers, the U.S. Environmental Protection Agency, environmental groups, researchers and other stakeholders to review and advance the protocol's methodology and assumptions. As it proved complex and expensive to implement, adoption of the method remained limited (Hunt, Sellers, and Franklin 1992). A small number of studies continued to be conducted throughout the mid-70's to mid-80's. The European scientific community renewed interest in furthering what has become current LCA methods. In the mid-1980's a number of European researchers conducted similar studies looking at the impacts of milk packaging across different European countries. Despite similar focus areas, the studies yielded significantly divergent results. The findings prompted collaborations among researchers and practitioners to develop standardized research methods throughout the 1990s (Bjørn et al. 2018). In 1993 the Society of Environmental Toxicology and Chemistry (SETAC) published the first Life Cycle Assessment guidelines and this year marked the beginning of a standardization process overseen by the International Organization of Standards (ISO). Refinement of the methodology continued throughout the 1990s with significant contributions from the research by Scandinavian governments. In 2002 the United Nations Environmental Program (UNEP) partnered with SETAC to create the UNEP/SETAC Life Cycle Initiative which has continued to improve LCA methods and works increasingly to disseminate the methodology to emerging economies (Bjørn et al. 2018).

2.3 Life Cycle Assessments

Today an LCA refers to the process of analyzing a product, service or activity from the very beginning of its life. This may refer to the extraction of a raw resource for a product or the creation of a new idea for a service. From the initial beginning or 'cradle', the unit in question is then traced from inception, throughout its growth/development to detail how it is formed, to its maturity to assess how it is used, and then finally through its 'grave' to understand how it ceases to be used and how any remaining elements are disposed of or otherwise recycled (International Organization for Standardization 1997).

The concept is one of several methods used to assess environmental impact. In addition to Life Cycle Assessment, common environmental analysis tools include substance flow analysis, risk assessments, material flow analysis, carbon footprints, water footprints and environmental impact assessment (EIA). Table 1 in Appendix A, published by Jolliet et al. in their book, Environmental Life Cycle Assessment, provides a comprehensive overview of each of these methods. Of the discussed seven environmental analysis tools, only LCA, carbon footprint, water footprint and EIA are designed to study products and services/activities. Of these four, only LCA is designed to assess the function of a product or a service.

in a variety of contexts that range from policy development to industrial-scale production. It focuses on impacts as diverse as total cost to social justice and human rights. In the context of studying the environmental impacts of healthcare, it is most frequently applied as either a process LCA, economic input-output LCA or a hybrid combination of the two.

2.3.1 Standard Life Cycle Assessment

Standard life cycle assessment, also referred to as Process LCA, is a technique to model the complete environmental life cycle of a product or process. The technique begins with an inventory of everything necessary to the produce or process, including the raw materials, energy and inputs required for its manufacture, transport and use, to the transportation and inputs required for disposal or recycling. This method is frequently combined with data from an Environmental Impact Assessment (EIA),

environmental impact assessment (International Organization for Standardization 1997). For each input a corresponding environmental impact is identified, quantified and analyzed as part of the total impacts associated with the product/process life cycle. For example, if the production of a toy requires 1 kWh of energy and that 1 kWh of energy requires 10 gallons of water to produce. A Standard LCA using EIA will record that the water consumption of the toy production process is 10 gallons of water. The frequent combination of these two methods allows researchers to assess the environmental impacts of specific inputs or processes along the life cycle of a product or process.

At times the Standard LCA method is criticized for the need to define strict system boundaries and thus the difficulties it presents in modeling the global scale attributed to modern supply chains. This is an important point when considering complex supply chains vital to most healthcare systems and medical treatments. The precision of the method, particularly when it combines an EIA, is also limited by the availability of accurate data and the role of the individual researcher's assumptions in determining the outcome of the study (Jolliet et al. 2015). Nevertheless, this process of analysis is known for its effectiveness in modeling the environmental impacts of discrete products and processes. The National Health Service of the United Kingdom was an early adopter of this method. In a 2000 paper authors Erica Ison and Anne Miller describe a case-study of the use of life-cycle assessment to evaluate the selection of durable medical devices (Ison and Miller 2000). Additional studies have developed life cycle assessment methodologies to focus on various aspects of the health care sector including a system for evaluating the building components of hospitals (Rossi et al. n.d.) and single-use medical supplies (Campion et al. 2015). In 2011 Andreas Pfützner and his co-authors published a study using LCA methods to compare the environmental impacts of insulin infusion sets to the waste generated by a coffee cup or aluminum can (Pfützner et al. 2011).

2.3.1.1 *Environmentally Extended Input-Output Life Cycle Assessment*

To overcome some of the limitations of standard LCAs researchers developed the environmentally extended input-output life cycle assessment (EEIO-LCA). An EEIO- LCA has a defined goal, scope and product inventory like a standard LCA, however, the boundary may be considerably larger as the inventory data is the cost of a transaction (i.e., the price of a vehicle or the cost of an apple). These costs are analyzed using economic input-output data tables which model activity in an economic system by tracking all inputs and outputs/final consumption of the system. Using matrix algebra and a technique pioneered by the Russian economist Vassily Leontief, industry transactions (i.e., purchases of materials from one industry to another) are combined with physical accounting data that measures direct and indirect environmental emissions, to estimate the total environmental emissions of a product through a supply chain (Schaffartzik et al. 2014). The concept may be applied to data at a country-level to estimate nationwide environmental impact or by using multi-regional input-output (MIRO) datasets that allow for regional and global analysis (Kitzes 2013).

As with the standard LCA, there are some drawbacks to the EEIO-LCA method. The foremost being the lack of specificity in results. Using published economic data allows for a high-level overview of the material flows within an economy, but at the same time it also requires the use of pre-determined economic sectors that do not allow for a nuanced review of individual inputs such as a specific product, company or even industry (Carnegie Mellon University 2016). Nevertheless, researchers have successfully used the method to provide insight into the functioning of national and global healthcare systems. In 2009 Chung & Meltzer estimated the carbon footprint of the US healthcare sector (Chung and Meltzer 2009). In 2016 Eckelman & Sherman built upon this work and their own research to publish

their findings on the public health effects of the US and Canadian healthcare systems (M. Eckelman and Sherman 2016; M. J. Eckelman, Sherman, and MacNeill 2018). In 2016 a group of private sector researchers from Evidera, a health research firm and Novo Nordisk, a leading global insulin producer, published a study using EEIO-LCA principles and data from the UK's National Health Service Sustainable Development Unit, to quantify the environmental impacts of adding insulin to diabetes treatment protocols in the United Kingdom. The study specifically considered the avoided costs of diabetes related complications (i.e., dialysis and eye surgery) associated with effective insulin therapy (Marsh et al. 2016).

A more complete overview of the advantages and disadvantages of the EEIO-LCA and standard LCA is provided in Table 2 of Appendix A.

2.3.2 Hybrid Life Cycle Assessment

To leverage the unique advantages and mitigate some of the pitfalls of the Standard LCA and the EEIO-LCA, researchers are combining the two methods into a hybrid approach. In a chapter of the book 'Special Types of Life Cycle Assessment' titled 'Input-Output and Hybrid LCA', authors Shinichiro Nakamura and Keisuke Nansai describe three forms of hybrid analysis, tiered, input-output and integrated (Finkbeiner 2016).

The input-output based hybrid analysis uses the concept of a process LCA inventory but does not actually include any data from a process LCA inventory. This approach is typically characterized by using input-output tables to gather information about higher-order elements and collecting separate process LCA data for more detailed elements that are not broken out in the input-output table. The result is that researchers may conduct an LCA when either a lack of macro-level economic data or specific process data would prevent a direct standard LCA or EIO-LCA analysis.

In one of the first studies of its kind Campion et al. used input-output hybrid LCA methodology to compare the environmental impacts of a vaginal versus cesarean human birth (Campion et al. 2012).

2.4 Identified Literature Gaps

Despite impressive efforts over the past decade to investigate the environmental impacts of healthcare, research is currently lacking in the environmental cost of treating chronic disease. As stated above, efforts have been made to consider the impacts of individual diabetes treatments using both standard LCA, in the case of Pfützner et al. and their work to quantify the environmental impacts of insulin infusion sets, and EIO-LCA methods, in the case of the research team from Evidera and Novo Nordisk. In the case of the work by Pfützner et al., insulin infusion sets are not typically used by T2d patients. Insulin infusion is required by Type 1 diabetes patients, a sub-set of diabetes patients consisting of at most 10% of the general diabetic population (Roglic and World Health Organization 2016). The EIO-LCA analysis completed by the research team from Evidera and Novo Nordisk is an important first step in quantifying the environmental impacts of diabetes treatment, but it does not account for the differences in treatment options available in different resource settings. This study seeks to build upon this work by offering a method to assess chronic disease treatment options with greater detail in a variety of resource settings according to different treatment needs.

3 Materials and Methods

To quantify the environmental and human impacts of T2d treatments the process LCA method is used to estimate emissions of material production, use, and disposal based on unit quantities used within the system being modeled. This study initially attempted to apply both the economic input output LCA (EEIO-LCA) and process LCA into a hybrid framework. However, a lack of specification in global economic data relevant to pharmaceutical supply chains or medical equipment supply chains reduced the relevance of any input-output calculations beyond a scope of usefulness in an EEIO-LCA or hybrid assessment. Therefore, the methods used in this study adhere to the process LCA standards developed and maintained by the International Organization for Standardization (ISO) (International Organization for Standardization 1997). The standards are listed under the title ISO 14040:2006 and include four primary phases: goal and scope definition, life cycle inventory analysis, impact analysis and interpretation.

3.1 Goal and Scope: T2d Care Pathways

The objective of this LCA study is to develop a flexible model that can be replicated in a variety of resource settings and medical contexts to assess the life cycle environmental and human health implications of chronic disease treatment. To achieve this objective this study provides a baseline assessment of the life cycle for T2d treatments.

Hyperglycemia (elevated blood glucose levels) over the course of an extended period generates the most severe negative health outcomes of diabetic patients. In the absence of a direct cure for the disease, treatments for T2d are focused on the monitoring and treatment of hyperglycemia. The scope of this LCA study is therefore defined by the goods and services required to effectively regulate the blood glucose levels of T2d patients. This will be measured through a functional unit defined as: *The services and resources used to control blood glucose levels in a Type 2 diabetes patient, with no associated health complications, for 1 year, or 365 days.*

A primary difficulty when defining the boundaries that characterize this study's scope was the problem of defining a treatment protocol. The American Diabetes Association (ADA) and the U.S. Food and Drug Administration currently recognize 11 classes and over 30 different compounds of medications for treating T2d (FDA Office of Women's Health, n.d.; American Diabetes Association 2019). T2d treatment protocols are inherently variable to accommodate the unique physiologies, lifestyles and access to medications and supplies of patients. The treatment protocol that has optimal health outcomes for one patient may not generate the same outcomes for another patient. Additionally, the expanded nature of the global medical supply chain has improved the production capacity and availability of many forms of diabetic supplies in many countries, especially in private-sector markets. In many countries, particularly for patients without access to a well-funded and managed national health service, affordability rather than availability is the most significant barrier to effective T2d medical care. (Zgibor and Songer 2001; Beran 2015)

To ensure the modeled treatment protocols were representative of the care that would reasonably be available to a wide cross section of patients, this study focuses on treatments and supply chains used in two different healthcare contexts, the United States and Sri Lanka. These two countries were selected because each has a government-subsidized or government-provided health care option that strives to ensure citizens have basic access to T2d treatments. However, the structure of these healthcare systems and the average income of citizens differs, offering a range for emissions estimates. While there are

well-documented gaps in these systems and neither country has completely universal care, the coverage provided is assumed to summarize an average standard of care.

The boundaries of this study are defined by the treatment options covered by government-sponsored Medicare insurance plans in the United States and free or very low-cost treatments at government-run medical facilities in Sri Lanka, shown in **Error! Reference source not found.**. The timeframe for this study is 2016-2018. The Sri Lankan national medical system and U.S. Medicare insurance coverage provide patients with access to oral diabetes medications and insulin. Depending on patient needs, the ADA recommends the oral diabetes medication Metformin as the preferred pharmacologic treatment agent for T2d patients with low to moderately elevated blood glucose levels at diagnosis. The use of insulin is recommended for patients with severely elevated blood glucose levels at diagnosis (American Diabetes Association 2019).

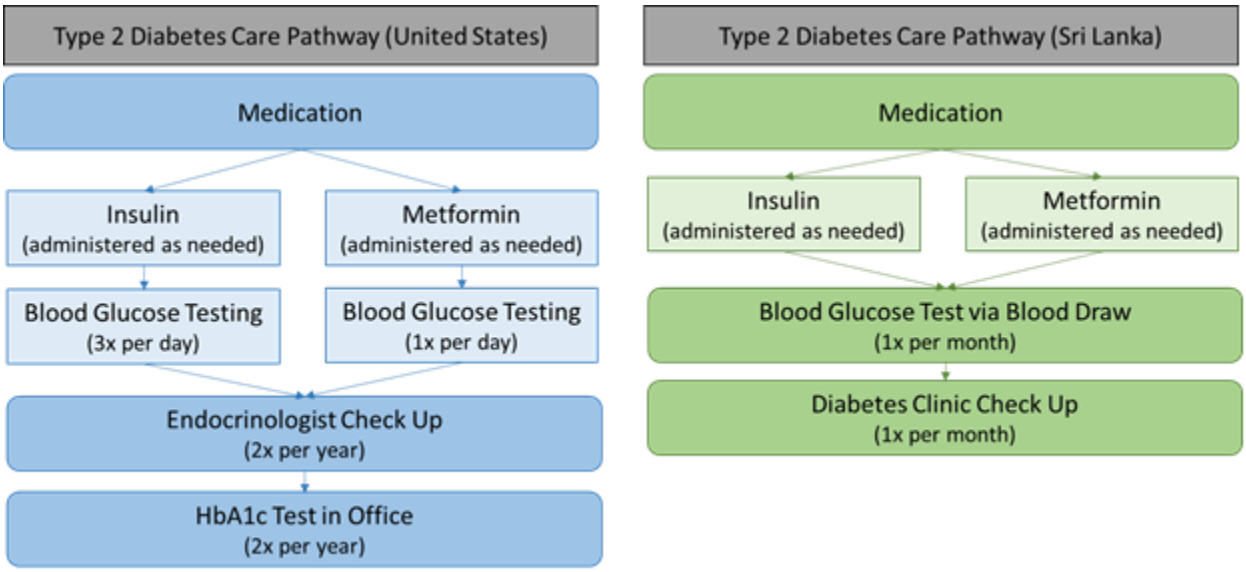


Figure 1: Modeled Care Pathways for Type 2 Diabetes in the United States and Sri Lanka

Specifically excluded from this study are system elements related to common healthy lifestyle practices, i.e., a sensible diet and exercise plans. While diet and exercise are necessary factors in successfully managing hyperglycemia, and doctors prescribe these plans to effectively manage T2d, they were excluded given their lack of specificity to T2d. Healthy diet and exercise are practices that are almost universally advisable irrespective of a diabetes diagnosis. This study seeks to investigate environmental and health impacts of medical treatments that are specific to treating T2d. Similarly, the impacts of diagnosing T2d and treating any complications that may arise from prolonged elevated blood sugar (i.e., stroke, heart attack, blindness, amputations, etc.) are not included in this study as they do not directly contribute to efforts to reduce hyperglycemia in patients.

3.2 Data Collection

This LCA study seeks to demonstrably quantify the natural resource extractions, transportation, processing, use phase, and end-of-life disposal/reuse of all primary components used to treat T2d with either insulin or metformin in Sri Lanka and the United States. The full life cycle of each individual component in each model is considered. The data used in this study should be considered relevant for treatment protocols used in 2017 and 2018. To detail each of the components used in each system, in-

person observations and interviews were conducted with physicians and patients in the United States and Sri Lanka. Specific data on each of the identified system components was collected using published academic studies, professional publications, US patent filing data along with additional in-person observations and interviews. By breaking down the modeled treatments into their composite components and assessing the environmental impacts of each component, it was possible to link impacts to process components.

Figures 2 and 3 below present the data used to model each system. The figures are broken down by system, then component and finally by individual input. Following the figures is an account of the of the data collection process and relevant assumptions. A complete data inventory with accompanying assumptions is provided in Appendix B.

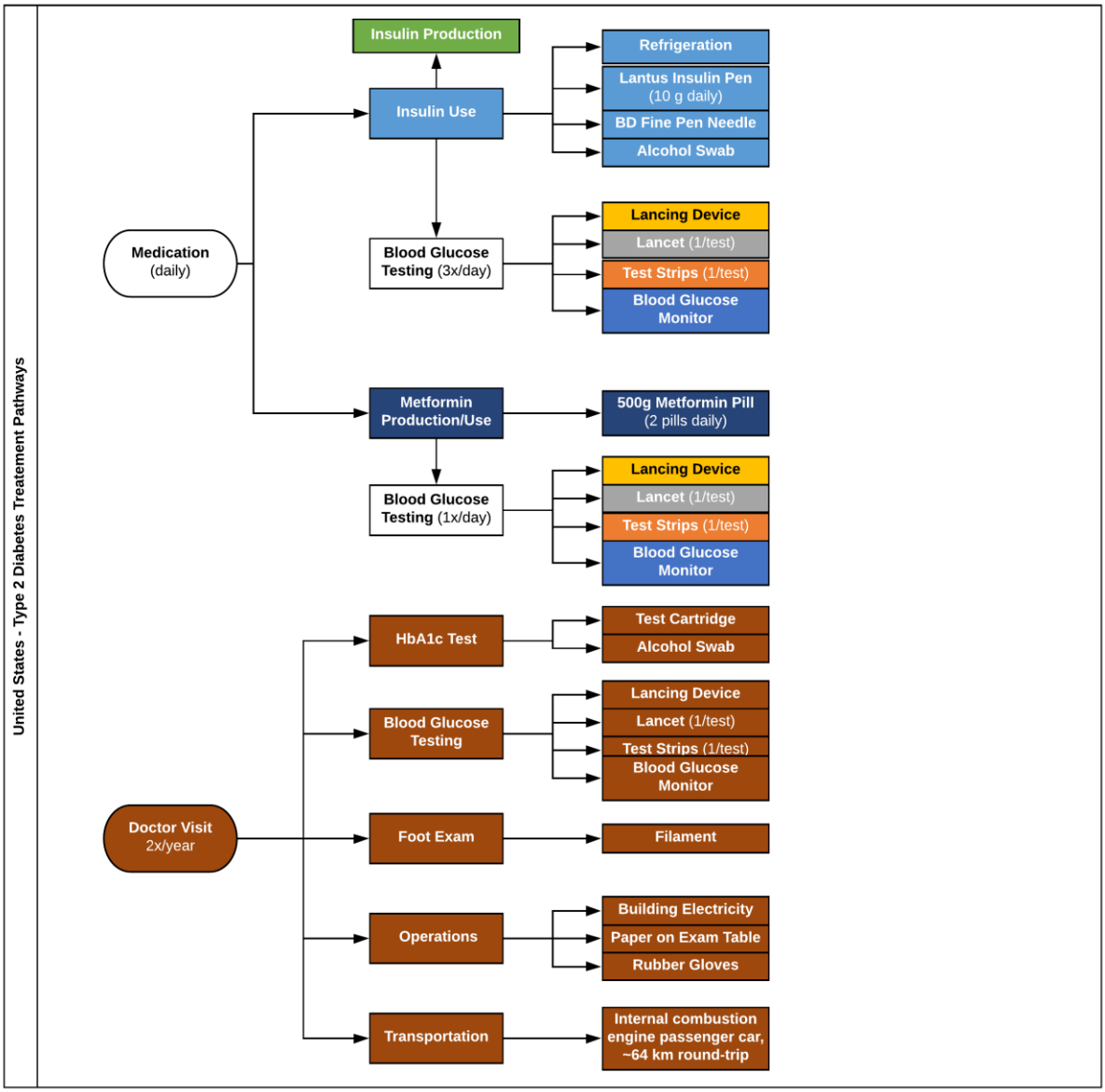


Figure 2: Component breakdown of United States T2d Treatment Pathways. Components are color-coded to correspond with results graphs.

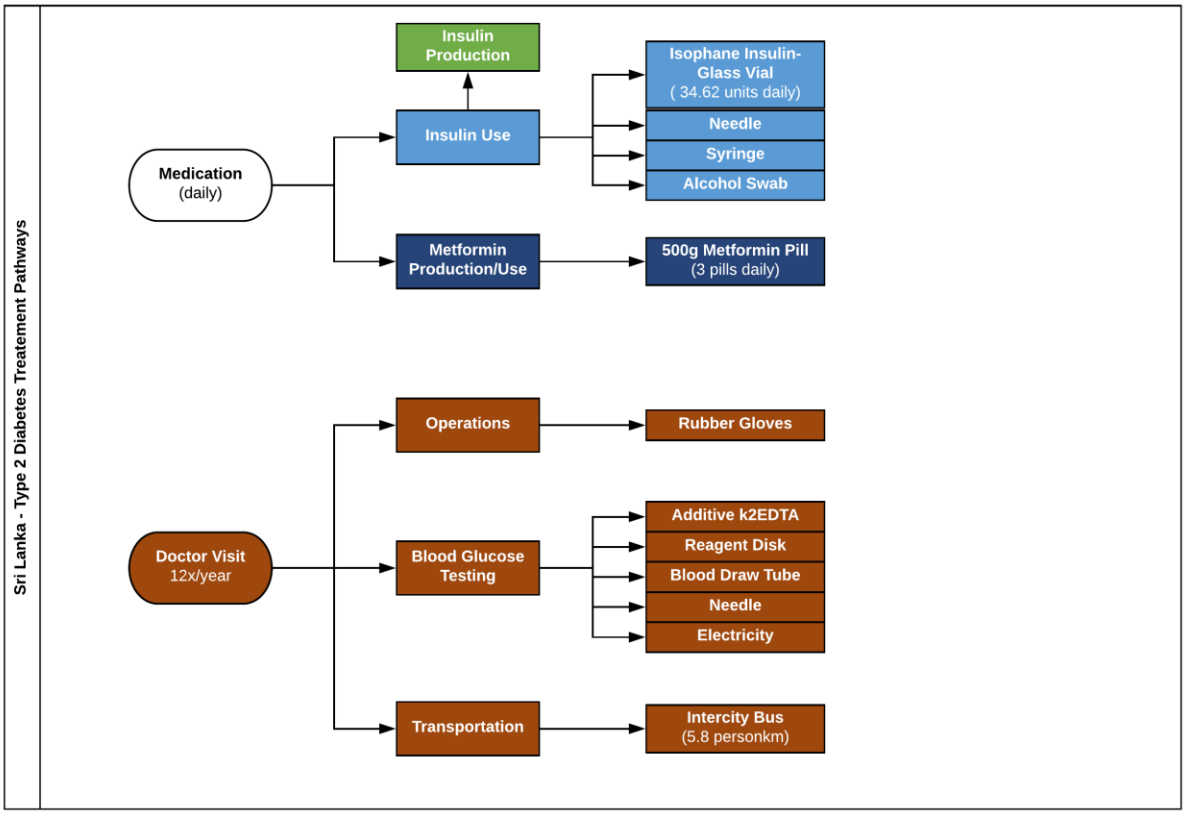


Figure 3: Component breakdown of Sri Lankan T2d treatment pathways. Components are color-coded to correspond with results graphs.

In the United States, the researcher interviewed and shadowed the nursing and physician assistant team at the University of Michigan's Metabolism, Endocrinology and Diabetes Clinic at Dominos Farm in Ann Arbor, Michigan. The results of these interactions were cross-referenced with the 2017 ADA's published Standards of Care document.(American Diabetes Association 2017) and the payment coverage provided by government Medicare and Medicaid programs (Centers for Medicare and Medicaid Services 2017b). The information from these sources is used to inform the types of medications used in the study (insulin and metformin), frequency of blood glucose testing (1x/day for patients using metformin and 3x/day for patients using insulin), and the frequency of clinic visits (2x/year for a T2d with well managed blood glucose and no health complications).

The same researcher observed the care received by patients of the Diabetes Clinic located within the Trincomalee General Hospital in Trincomalee Sri Lanka, and the Uppevelli Public Health Clinic in Uppevelli, Sri Lanka. Additional sources of information on Sri Lankan T2d care pathways were obtained through series of interviews with T2d patients and three local physicians. Collected primary data was cross-referenced with the directives outlined in the Diabetes Treatment Protocol published by the Endocrine Association of Sri Lanka. This information was used to inform the types of medication used in the models (insulin and metformin), to confirm that personal blood glucose testing is not a standard practice in managing T2d for many patients in Sri Lanka, and to provide guidance on the modeling of regular clinic visits (1x/month). Interviews with Sri Lankan T2d patients and physicians confirmed that

government-sponsored prescriptions require monthly in-person renewals which necessitates monthly clinic visits for continued free/very low-cost medications.

3.2.1 Medication Production and Use (US and Sri Lanka)

3.2.1.1 *Insulin Production Assumptions*

For the US Insulin pathway, we assumed the use of Sanofi's Lantus Insulin Glargine distributed as an injection pen. This plastic container resembles a marker and stores the insulin in a glass vial enclosed in a plastic casing. It is designed to be transportable and does not need to be refrigerated for up to 28 days after removing from refrigerated storage (Sanofi-Aventis 2019). Per the insulin container label, a single insulin pen contains 3.6378 mg of insulin which is equal to 100 insulin units. A base dosage of 10 u/day is assumed based on dosing recommendations from the manufacturer (Sanofi-Aventis 2017). Transportation was estimated from Sanofi's largest insulin production facility located in Frankfurt, Germany (Industriepark Höchst 2018). The waste scenario modeled here accounts for the disposal of the packaging used to house and transport the produced insulin. It does not account for waste generated in the insulin production process as data on waste generated from this process was not available. The disposal scenario assumes that patients dispose of their used packaging along with standard household municipal solid waste. This assumption is based on discussions with medical professionals, as well as a review of several dozen diabetes patient online community message threads discussing how to dispose of diabetes treatment materials.

For the Sri Lankan insulin pathway, procurement documents from the Sri Lankan Ministry of Health suggest the government generally provides patients with a form of Isophane Human Insulin (Somasundaram et al. 2013; Sri Lankan Ministry of Health 2018). It is assumed that as both insulin Glargine and Isophane insulin are manufactured from recombinant human DNA, that they both share a similar production process. The daily dosage is assumed to be 34.62 units of insulin, based on the dosing recommendations of the Endocrine Society of Sri Lanka (Somasundaram et al. 2013). Manual measurements indicated a mass of 24.584 g/vial. It is assumed that the insulin used in Sri Lanka is primarily being manufactured in India (IBM Micromedex 2019; BioPharm International Editors 2017; Ganguly 2017) and its transportation was modeled accordingly. The notable differences between the production of insulin used in Sri Lanka versus the US are the containers in which they are stored and the locations where they are manufactured. The insulin procured by the Sri Lankan government is primarily stored in 10 mL glass vials, which after use are assumed to be landfilled. Without published data indicating waste by-products from the insulin production process, neither the U.S. nor Sri Lankan scenarios account for waste generated during the production process.

In the absence of direct process data of the insulin glargine and/or insulin isophane production process, this study recreated the production process using the process data published by Gusarov, et al. in their paper, Systematic Approach to Production Technology Development for Therapeutic Proteins (Using Insulin-Glargine As An Example), and Hwang, et al.'s published paper, Recombinant Glargine Insulin Production Process Using Escherichia coli. To calculate the energy used in the manufacturing process of the insulin a total energy estimate was derived using the FineChem tool, designed by the Safety and Environmental Technology Group within ETH Zurich. (Wernet et al. 2008) The FineChem tool uses the molecular structure of a compound to estimate the energy needs and environmental impacts of that molecule's production. While the tool was originally designed for the petrochemical industry, it serves to provide a rough estimate of energy use in the absence of process data. All molecular data used in the

calculations were sourced from PubChem. The FineChem tool estimated the total energy use to produce insulin glargine at 758.6 MJ/kg. The breakdown of the types of energy used in this total was established using the work by Cespi, et al in their 2017 Green Chemistry publication. This study indicated an energy breakdown in pharmaceutical production of 50% natural gas, 38% electricity and 12% steam. These proportions were used in the study's calculations (Cespi et al. 2015).

3.2.1.2 *Insulin Use Assumptions*

For the US insulin use pathway, we assume that the patient will be using a long-lasting insulin that needs to be taken once daily. Administration requires one needle and one alcohol swab. The needle is necessary to inject the insulin below the skin. The alcohol pad is a standard precaution used to protect the patient from infection during the injection process. While the insulin in insulin pens modeled in this study can be stored at room temperature for approximately 28 days, the manufacturer notes that longer storage requires refrigeration to prevent degradation of the insulin (Sanofi-Aventis 2019). Prescriptions and insurance plans in the United States typically allow for 30 to 90-day supplies of a medication (Centers for Medicare and Medicaid Services 2017b). As such, this study assumes patients will have a continual need to refrigerate insulin pens year-round. The waste treatment scenario included in this model assumes that patients are disposing of their used needles as medical waste. Interviewed medical professionals all recommend disposing of used needles in a sealed medical waste container. These containers are then disposed of with standard municipal solid waste. This practice aligns with several dozen reviewed online diabetes community discussion boards where patients documented their methods for disposing of diabetes-related waste. The disposal of the alcohol swab is assumed to be the same as for standard municipal solid waste.

For the Sri Lankan insulin treatment pathway, this study assumes one injection a day with a single-use, 1 mL syringe and needle. Transportation to Sri Lanka was estimated assuming the production of the syringe and needle occurred in Aurangabad, Maharashtra, India. Waste disposal modeling is based off the assumption that households are disposing of their needles and syringes in a community landfill. Observations of T2d diabetes patients in Sri Lanka indicated that disposal of diabetes supplies along with standard municipal solid waste is a common practice, as is on-site incineration, with many families incinerating their medical waste along with household waste. For the purposes of this study it was decided to model an inert landfill option. It is worth considering that incineration disposal is also a common, but inadvisable, method.

3.2.1.3 *Metformin Production Assumptions*

For the US Metformin pathway, we assume patients use 1000 mg of metformin daily, based upon dosing recommendations provided by IBM's Micromedex database. It should be noted that both interviews and published literature have established a precedent that patients often find it difficult to take their oral medication daily (Cramer 2004). However, per ADA recommendations for avoiding diabetes-related medical complications, this study assumes adherence to a daily dosage schedule. The production process for metformin (both in US and Sri Lanka) modeled in this study is based on the process outlined in Rohokale, Jadhav et Kadam's 2010 paper on metformin process development (Rohokale, Jadhav, and Kadam 2010). It is acknowledged that there are a variety of production methods to produce pharmaceutical quality metformin and that the type of production process may influence scenario outcomes. This model assumes US metformin is produced and shipped from Humacao, Puerto Rico. The FineChem tool estimated the total energy used in production to be 145 MJ/kg. The breakdown of the

types of energy used in this total again used the work by Cespi, et al. and assumed 50% natural gas, 38% electricity and 12% steam.

Sri Lankan T2d patients are assumed to use 1500 mg of Metformin daily. This is based upon dosing recommendations provided by the Endocrine Society of Sri Lanka. The drug was assumed to be manufactured in Aurangabad, Maharashtra, India and transported by sea and land to Sri Lanka, and energy estimates were made using the FineChem tool as described above.

3.2.2 Blood Glucose Testing (US)

Personal blood glucose testing requires 1) a blood glucose meter, 2) a reusable lancing device, and 3) a single-use lancet and test strip. Use of other forms of glucose monitoring such as continuous glucose monitoring systems are excluded from this study given their relatively low adoption among T2d patients. The glucose meter modeled in this study is a Freestyle Lite meter manufactured by Abbott. The Freestyle Lite meter was modeled given the relative ubiquity among glucose meter design and functioning, and the researchers' ability to access several devices for deconstruction. Based on the information provided in the user manual, the meter has an assumed lifespan of five years or 1825 days and an expected battery life of 500 tests *(Abbott 2016)*. The study establishes two different battery scenarios based on either insulin or metformin treatment pathways. Transportation of the device to the US was modeled assuming it was manufactured in Shenzhen province in China. This study assumed that patients dispose of their glucose meter as an electronic device. The U.S. EPA reports that Americans recycle approximately 40% of selected consumer electronics *(U.S.* Environmental Protection Agency 2018*)*. As this is less than half of all produced electronics, it was assumed for this study that glucose meters would be included with standard municipal solid waste landfill disposal in the majority of households.

The lancing device is assumed to have a lifespan of two years or 730 days, and is used by only one individual (Abbott 2016). To determine the components and materials used in the construction of the device, the lancing device was manually taken apart and weighed. It was assumed the unit was produced by Own Mumford in Oxfordshire, UK (Owen Mumford Ltd. 2018). The waste scenario for the lancing device assumes that the used device is not considered biohazardous or medical waste and that it is disposed of along with standard municipal solid waste.

This study assumes one, single-use lancet and one single-use test strip is used for every blood glucose test. It is assumed the lancet is manufactured and shipped from Atlanta, Georgia (Facet Medical Technologies 2018). The waste treatment scenario included in this model assumes that patients are disposing of their used lancets as medical waste. This study assumes the test strips are Abbott Freestyle Lite test strips made for use with the Freestyle Lite glucose meter and are manufactured in Donegal, Ireland (Abbott Ireland Diabetes Care 2019). The composition of the test strips base layer is assumed to be polyester with the electrode materials comprised of silver and carbon, as described in a published white paper by the strip's manufacturer (Abbott Diabetes Care Inc. 2015). Regarding the additional enzymes and reactant materials used in the test strip, it was not feasible to conduct an analysis to determine the exact amount of each material used in the adhesive and electrodes of the test strip. Given that the combined mass of these materials is so small (>.001 g) an approximate mass was estimated by dividing the balance of the test strip mass (after subtracting the known elements) among the five additional inputs. The waste treatment scenario included in this model assumes that patients

are disposing of their glucose test strips in a sealed container disposed of with standard municipal solid waste.

3.2.3 Clinic Visits

This study models two different clinic visit scenarios to reflect differences in clinic visits between the United States and Sri Lanka. The models described below are referenced for both metformin and insulin treatment pathways.

3.2.3.1 *United States*

Studies show the average patient in the United States travels approximately 10 miles to a medical clinic (Probst et al. 2006). Using this estimate, the study accounts for a 20-mile round-trip use of a single-occupancy gasoline-powered vehicle. The US clinic visit was modeled on observations conducted at the University of Michigan Metabolism, Endocrinology & Diabetes Clinic in Ann Arbor, Michigan. Clinic staff reported that patient appointments are scheduled for 30-minute blocks and that the clinic serves an estimated 300 diabetic patients a week. The assumed size of the clinic is 43,000 ft, and the assumed average overhead energy use rate is 245 kBtu/ft^2 which includes power for the clinic's lights, HVAC system, computers and the HbA1c analysis machine (U.S. EPA Energy Star 2015). During the 30-minute appointments the medical assistants record patient vital information, including blood glucose levels and HbA1c test results. Medications are then verified before patients meet with the doctor for a physical examination. This study models diabetes-specific and single-use materials used during a standard clinic visit. These materials include: a glucose meter, glucose test strips, lancet, HbA1c testing cartridge, rubber gloves, exam-room table cover paper, and neuropathy testing filament. Additional materials such as a scale, blood pressure cuff and clinic computers were omitted from the study due to initial calculations suggesting that their long use life as well as universal attribution to each clinic patient, would result in a miniscule impact attribution.

Durable medical devices including the glucose meter and lancing device allocate their impacts across the T2d patient population of the clinic. All other modeled medical supplies are considered single use and the entire impact of the item is attributed to one patient. The waste disposal scenario is modeled based on guidelines from the Michigan Medical Waste Regulatory Act. A third-party medical waste management firm disposes of all medical waste from the clinic by first decontaminating the waste through autoclaving before the waste is landfilled (Michigan Department of Environmental Quailty: Resource Management Division and Wyant 1990). Absent published process data or direct access to primary data for commercial medical waste autoclave processes, this study models only the landfill portion of the waste scenario.

3.2.3.2 *Sri Lanka*

Individual car ownership is not as pervasive in Sri Lanka as in the US. Referencing research from the World Bank and estimates of public bus occupancy rates, this model assumes patients will travel a distance of 9.6 km roundtrip on a public bus with a total of 20 passengers (Govindaraj et al. 2014). The hospital/clinic buildings were open-air buildings with no central air systems used around the clinics. Clinic energy use was not modeled, as energy use appeared to be quite negligible. Windows provided natural sunlight negating the need for electrical light. While doctors did use computers in the Trincomalee Regional Hospital setting to automatically refill patient prescriptions, the energy use of the computer systems was emitted from this model. As each physician can see on average between 50 and 70 patients during clinic hours each day, preliminary calculations considering the energy intensity of the

computer use per patient allocated over the sum total of patients for each computer, generated a negligible impact.

The observed government-sponsored clinics did not have the resources to do on-site blood glucose testing. Interviews with doctors reinforced that most public-run diabetes clinics do not have this capability owing to the expense of blood glucose test-strips. Diabetic patients are instructed to bring the results of a previously ordered blood test to their clinic appointments. Blood tests are included in the modeled scenario by estimating the impacts associated with the single-use blood collection vial and electricity used in the testing process. Published studies on medical waste disposal in Sri Lankan healthcare facilities notes the prevalence of various incineration practices as a primary means of waste disposal. A general incineration model from the Ecoinvent 3 database was applied to simulate the disposal of contaminated waste generated by a patient visit (Wernet et al. 2016).

3.3 Life Cycle Inventory

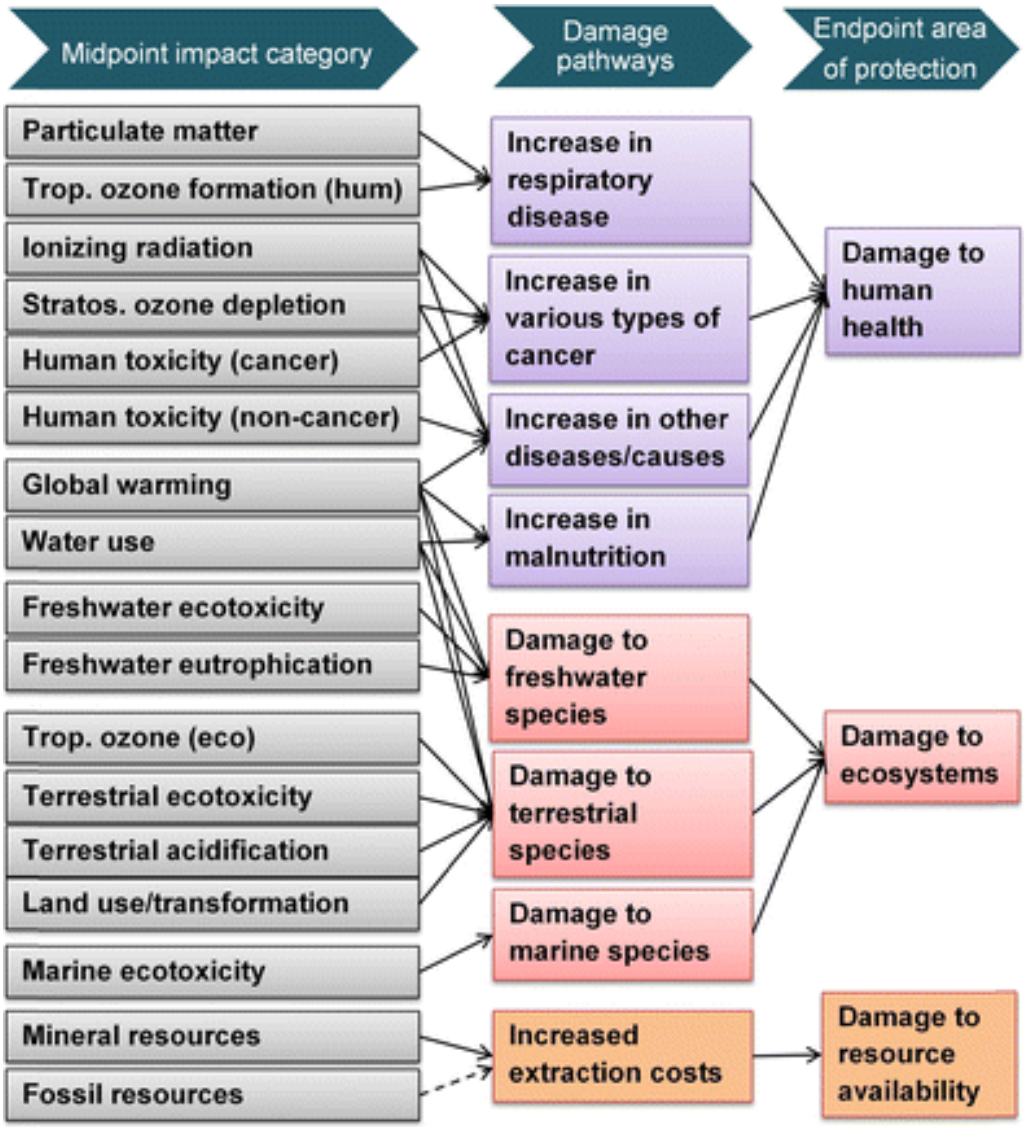
Life cycle inventory data was compiled using SimaPro version 8.5.2.0 by Pré Sustainability. The software provides a transparent method for combining Life Cycle Inventory database information with automated analytical processes to facilitate the LCA process. Gathered data was assigned to life cycle inventory (LCI) databases to model the emissions from those items' production, use, and disposal. Every attempt was made to model the exact materials that comprise the components of each system. However, appropriate material substitutions were made where a lack of data made direct modeling impossible or unfeasible. Ecoinvent 3.0 was the preferred database, as it is one of the most comprehensive global LCI databases (Wernet et al. 2016). Additional data was sourced from the Industry 2.0 and the USLCI databases. The Industry 2.0 database lists data made available from industry associations such as Plastics Europe, World Steel and ERASM (World Steel Association 2017; PlasticsEurope 2011; Schowanek et al. 2018; Pre Consultants 2019). The USLCI database is the U.S. Life Cycle Inventory database (National Renewable Energy Laboratory 2018).

3.4 Impact Assessment

The impact assessment was conducted using the ReCiPe 2016 impact characterization method (Huijbregts et al. 2017). Calculations used the database's hierarchist uncertainty valuation based on a consensus model using 100-year time frames estimates. This study expands on several assessed impact indicators as proxies to understand the range of system-wide damage to ecosystems associated with the treatment of T2d. These indicators are Climate Change (kilograms of CO2 equivalents, kg CO2-eq), Terrestrial Acidification (kilograms SO_2 equivalents, kg SO_2-eq) and Water Consumption (M_3 water-equivalent consumed). Results for additional environmental impact indicators are included in the supplemental materials.

Human health impacts are assessed through an aggregate end-point measured in Disability Adjusted Life Years (DAILYs).

The human health indicator is an endpoint-damage indicator of the ReCiPe 2016 life cycle impact assessment method. It is defined in the 2016 paper by Hujibregts et al., as a characterization factor designed to capture the combined midpoint impacts effects on human health (Huijbregts et al. 2017). Figure 1 below demonstrates the relationship between environmental stressors (midpoint impacts) and an area of protection or concern (endpoint). The ways in which environmental stressors impact human health are explained through the damage pathways highlighted in purple.



The human health impact indicator is measured using the unit of Disability Adjusted Life Years (DALY). DALYs are a traditionally public health measure that are used to quantify the years of healthy life lost. According to the World Health Organization, the difference between an entire population living a healthy lifespan and one that is disrupted due to the measured external factors is considered a measure of the health burden that the external factor is posing on the measured population.

This definition along with a summary of useful calculation methods for DALYs are available on the WHO's website: https://www.who.int/healthinfo/global_burden_disease/metrics_daly/en/

In addition to the functional unit measure of each tested scenario, aggregate impact results were considered in the context of T2d populations of the United States, Sri Lanka and globally. Recognizing the need to consider impacts in relation to the extended time-period that most T2D patients seek to manage their disease, the calculated population-level impacts were also evaluated according to the estimated average number of years an otherwise healthy individual would seek to treat their T2D.

3.4.1 Population-Level Impact Assessment

In 2016 the United States Center for Disease Control (CDC) estimated that there were 30.3 million diagnosed diabetics in the United States. 1.25 million diabetic patients are reported as being diagnosed with Type 1 diabetes patients, a population excluded from this study. Subtracting this population from the total diabetic population yielded an estimated 29,050,000 T2d patients in the United States (National Center for Chronic Disease Prevention and Health Promotion 2017). It is worth noting that the CDC estimates that more than ~81 million Americans are currently pre-diabetic and will likely receive a full diagnosis within 5 years.

The average rate of diabetes prevalence in Sri Lanka is estimated to be 7.9% of the total population (World Health Organization 2016b). Assuming a current population of 21.44 million (World Bank 2017), it is assumed there are ~1,693,000 T2d patients. National insulin bank registries suggest a negligible number of Type 1 diabetes patients that will not impact the validity of this overall T2d assessment (Wijesuriya et al. 2019).

Treatment Option	Number of T2d Population Using Treatment Option
Sri Lanka	
Insulin Use Only	67,720 (4%)
Metformin Use Only	1,472,910 (87%)
Both Insulin & Metformin	15,0677 (8.9%)
United States	
Insulin Use Only	5,170,900 (17.35%)
Metformin Use Only	14,612,150 (66.21%)
Both Insulin & Metformin	3,776,500 (16.44%)
Global- High Income Country	
Insulin Use Only	11,492,748 (17.35%)
Metformin Use Only	32,476,698 (66.21%)
Both Insulin & Metformin	8,393,580 (16.44%)
Global- Low & Middle Income Country	
Insulin Use Only	12,609,360 (4%)
Metformin Use Only	274,253,580 (87%)
Both Insulin & Metformin	28,055,826 (8.9%)

Table 1: A breakdown of the Type 2 diabetes populations of Sri Lanka, the United States, High-Income Countries and Low- and Middle-Income Countries, according to pharmacological treatment type. Listed percentages are in relation to the total Type 2 diabetes population of that particular country/economic region. United States and High-Income pharmacological treatment rates are citied from from Diabetes in America, 3rd Edition. In the initial publication the given rates assume ~88% of the T2d population is treating their T2d.(Saydah 2018) These estimates rates have been updated by the study's authors to account for 100% of the T2d population receiving treatment.

The International Diabetes Federation reported an estimated 463 million diabetic patients globally in 2019 (International Diabetes Federation 2019). This figure is inclusive of Type 1 and Type 2 diabetic populations. To estimate the global T2d population the Type 1 population was subtracted from the overall global diabetic patient estimate. Using Type 1 diabetes prevalence data compiled by Menke et al, this study assumes a highly conservative estimate of 8% of Type 1 prevalence globally(Menke et al. 2013). This generated a global T2d population estimate of 416,700,000.

To account for variances in treatment options throughout all analyzed populations, population totals were divided among the treatment scenarios according to the rates established in Table 1. The percentage estimates of patients treating their diabetes using either insulin or oral medication in the United States and Sri Lanka were derived from published literature (Gunathilake, Kottahachchi, and Siyambalapitiya 2017; Saydah 2018). Lacking published information for global usage rates of insulin or metformin, the author assumed treatment rates for the U.S. when calculating the total number of T2d patients using insulin and metformin in High-Income countries. The treatment rates established for Sri Lanka were used to estimate the number of patients using insulin and metformin in Low- and Middle-Income countries. Definitions of High, Low and Middle-Income countries were derived from the World Bank (World Bank 2019b). Based on a global population distribution data from the World Bank, it was assumed that 17% of the global diabetic population lives in a High-Income country and 83% live in a Low or Middle Income country (World Bank 2019a).

To account for the impacts associated with both insulin and metformin use, but so as not to double-count impacts associated with other treatment components (i.e., blood glucose testing and clinic visits) the following equations were used to calculate impact for patient populations using both Metformin and Insulin treatments for High-Income and Low- and Middle-Income populations respectively:

High-Income Scenario Both Treatment Use Functional Unit Result *= (50%*U.S. Blood Glucose Testing Component Impact for Impact Category X) + (50%*U.S. Clinic Visit Component Impact for Impact Category X)*

Low- & Middle-Income Scenario Both Treatment Use Functional Unit Result *= (50%*Sri Lankan Clinic Visit Component Impact for Impact Category X)*

Overall global treatment impacts were calculated according to the following equation:

Scenario A Impact Indicator Population Result *= (Scenario A Functional Unit Result for Impact Category X * Scenario A T2d population * % Single Treatment Population) + ((Scenario A Functional Unit Result for Impact Category X - Scenario A Both Treatment Use Functional Unit Result for Impact Category X) * Scenario A T2d population * % Both Treatment Population))*

3.4.2 Lifetime Impact Assessment

As a chronic disease this study assumes a T2d diagnosis is a lifetime diagnosis. Daily treatments are required from diagnosis to the end of life. Assuming, as this study does, that the patient remains free of medical complications and other significant medical conditions, it is expected that the patient's lifespan corresponds to the average national lifespan of their country of residence. Research suggests the average natural life-expectancy rage for a healthy 55-year old is at least 19 years, or 74 years of age (Leal, Gray, and Clarke 2009). In 2016 the WHO reported the average global life expectancy to be 72 years (World Health Organization 2016a). Using these age projections it is deemed reasonable that an otherwise healthy individual diagnosed with T2d at age 50 could be expected to attain a full life-span of 72 years. This assumption requires ~22 years of T2d treatments. The results analysis of this study, assumes a diagnosis age of 50 and uses 22 years as a standard multiplier when calculating lifetime impacts. Calculations use the following equation:

*Population Lifetime Impact Indicator Results = Impact Indicator Population Result * 22 years*

3.5 Sensitivity Analysis

After a preliminary assessment of the functional unit results the research team conducted a sensitivity analysis to assess the dependence of nine variables identified as significant contributors to overall impacts. The analysis used a wide range of data points to test the sensitivity of impacts according to variable values. Highly sensitive variables are discussed in the results section as important qualifiers of the study's findings.

To assess the sensitivity of the modeled scenario's impact results to fluctuations in component inputs, 11 input variables were tested using at least 10 alternative values for each input variable. The sub-sections below provided detailed information and results associated for each of the 11 tested variables. These variables included:

U.S. Treatment Pathway	**Sri Lankan Treatment Pathway**
Number of Doctor Visits	Insulin Dosage
Doctor Visit Overhead Energy Use	Insulin Production Energy
Insulin Dosage	Metformin Dosage
Insulin Production Energy	Metformin Production Energy
Metformin Dosage	
Metformin Production Energy	

Number of Doctor Visits, Distance to Doctor's Office and Doctor Office Overhead Energy were not included in the Sri Lankan context given the comparatively minor contributions of doctor visits to the overall assessed impacts.

To conduct the analysis a separate model was created for each of the minimum 10 scenarios tested for every input variable. The results were calculated for 19 different impact categories: Human Health (DALY), Global Warming Impact (kg CO_2-eq), Stratospheric Ozone Depletion (kg CFC11-eq), Ionizing Radiation (kg Co-60-eq), Ozone Formation (kg NOx-eq), Fine Particulate Matter (kg PM2.5-eq), Ozone Formation- Terrestrial Systems (kg NOx-eq), Terrestrial Acidification (kg SO2-eq), Freshwater Eutrophication (kg P-eq), Marine Eutrophication (kg N-eq), Terrestrial Ecotoxicity (kg 1,4-DCB-eq), Freshwater Ecotoxicity (kg 1,4- DCB -eq), Marine Ecotoxicity (kg 1,4-DCB-eq), Total Human Carcinogenic Toxicity (kg 1,4-DCB-eq), Human Non-Carcinogenic Toxicity (kg 1,4-DCB-eq), Land Use (m^2 crop eq), Mineral Resource Scarcity (kg CU-eq), Fossil Resource Scarcity (kg oil eq), and Water Consumption (m^3)

To best orient the sensitivity results to the findings articulated in this paper, only the impact categories Human Health, Global Warming, Terrestrial Acidification and Water Consumption are addressed henceforward.

Each of the assessed variables were assessed according to their functional unit values, that is to say the absolute impact emissions that the models attributed to the specific variable being analyzed, and according to their impacts on the overall emission impacts of the treatment scenario. Overall emission impacts are comprehensive of the impacts attribute to all of the components in the treatment scenario.

5 Results

5.1 LCA Results for One Year of T2d Treatment for One Patient

	U.S. Insulin	U.S. Metformin	Sri Lanka Insulin	Sri Lanka Metformin
Climate Change (kg CO2-eq)	34.8	30.6	20.6	6.58
Terrestrial Acidification (kg SO2-eq)	0.13	0.47	0.32	0.21
Water Consumption	3.94	0.894	0.603	0.323
Human Health (DALY Lost)	0.0001	0.000074	0.000049	0.000015

Table 2: Results of the SimaPro analysis using the ReCiPe2016 impact characterization database for the functional unit for all modeled scenarios.

Table 2 lists the environmental and human health impacts, per functional unit, for each of the four modeled scenarios. These functional unit impacts are reflective of the frequent, low resource intensity medical interventions characteristic of chronic disease treatments.

The U.S. Insulin Use scenario is overall the most impactful. It generates the highest emission rates for the impact categories of climate change, water consumption and human health. The only outlier is Terrestrial Acidification. The U.S. Metformin Use scenario and both Sri Lankan scenarios generated greater Terrestrial Acidification impacts.

The results for Terrestrial Acidification stand out due to differences in the component make-up of each treatment pathway. Referencing the treatment pathway components illustrated in Figures 2 and 3 of the Methods section, Figure 4 demonstrates how each of the treatment components contribute to the impact results. The breakdown indicates U.S. doctor visits are a leading contributor of negative Climate Change and Human Health impacts within the U.S. scenarios and overall. Within the Sri Lankan scenarios first insulin production, then the use phase of the insulin scenario, are the greatest source of negative Climate Change and Human Health impacts. Doctor visits in Sri Lanka contribute the least to negative Climate Change impacts.

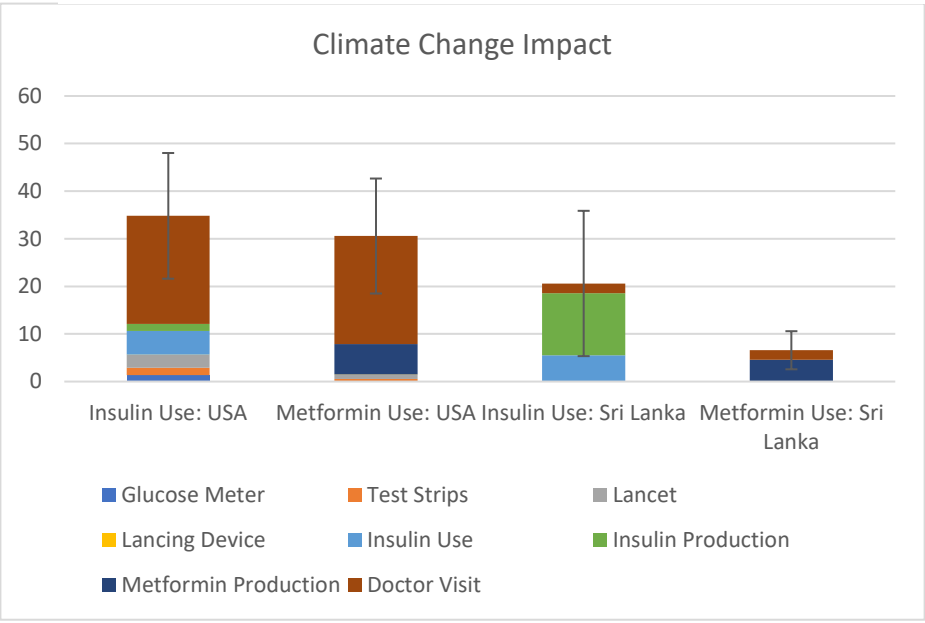
Terrestrial acidification impacts are consistent when comparing the Metformin treatment pathway in the U.S. and the Insulin and Metformin treatment pathways in Sri Lanka. That the U.S. Insulin pathway contributes very little to this impact category is believed to be a function of different methods of energy production during the pharmaceutical production process. The insulin used in the U.S. treatment pathway is produced in Germany. The energy models for Germany assume significantly lower impact characterization factors for each unit of energy produced. This is in comparison to the energy grid models used to represent energy production in India and Puerto Rico, the sites of manufacture for the other modeled pharmaceuticals.

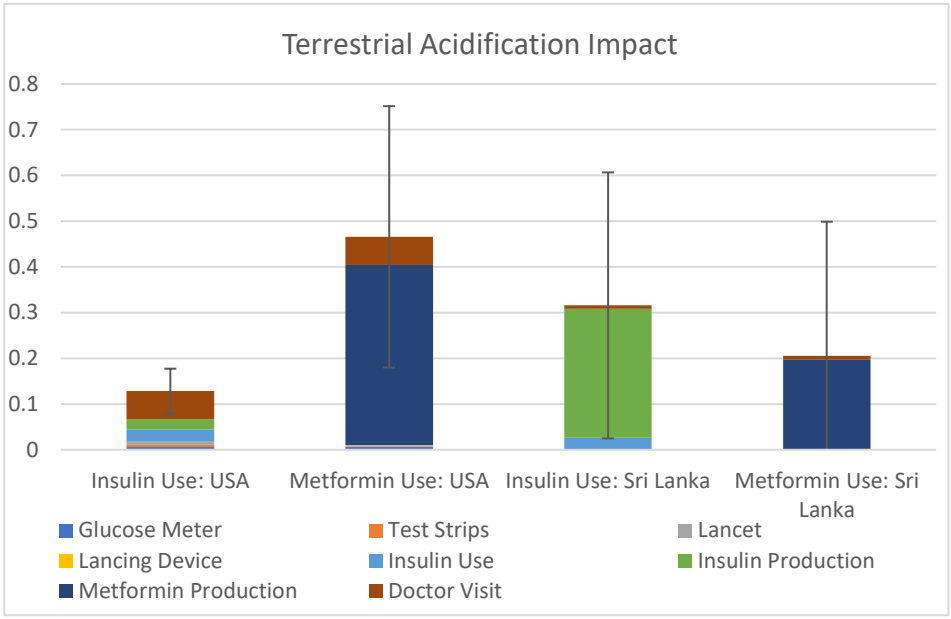
Water consumption rates are significantly higher for the U.S. Insulin pathway and are attributable to the Insulin Use component of the treatment. The unique spike in water consumption is the result of the assumed refrigeration of the insulin. Similar refrigeration rates are not included in the other scenarios due to Metformin medication not requiring temperature control, and the temperature regulation of insulin in Sri Lanka assumed to be achieved through storage in a dark, cool environment.

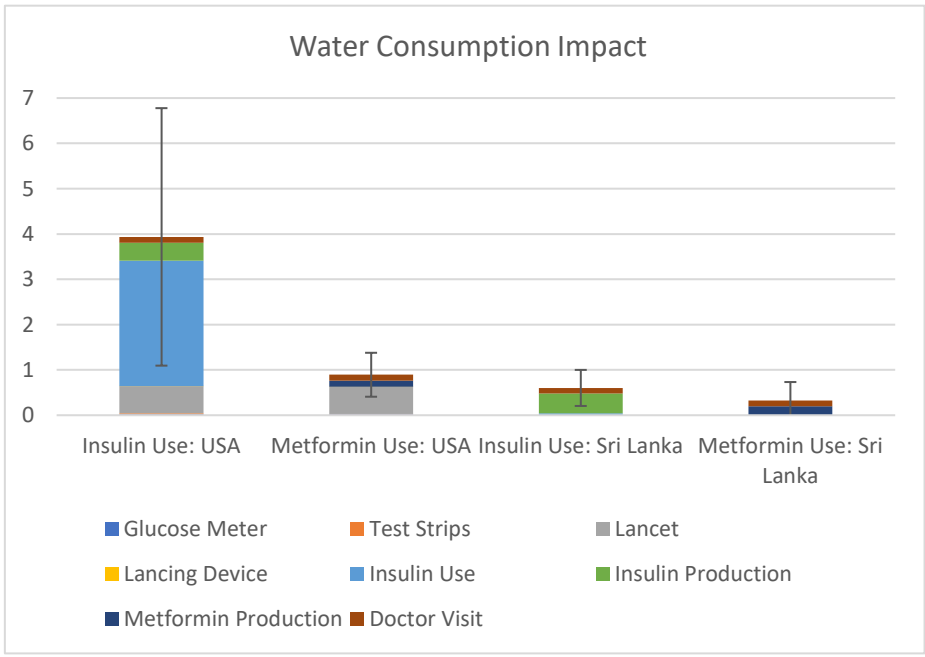
Overall the results per functional unit highlight the importance of several key components of the tested treatment pathways. Doctor visits and pharmaceutical production are shown to account for a notable amount of emissions in each of the scenarios. Nevertheless, in the context of one individual's treatment over the course of a year diabetic treatments, whether in the United States or Sri Lanka, do not significantly contribute to negative environmental impacts or negative human health impacts. Unfortunately, T2d is a global epidemic that must be treated for the duration of an individual's lifetime following diagnosis. Does this picture change when we consider these results in the context of broader populations seeking treatment over extended periods of time?

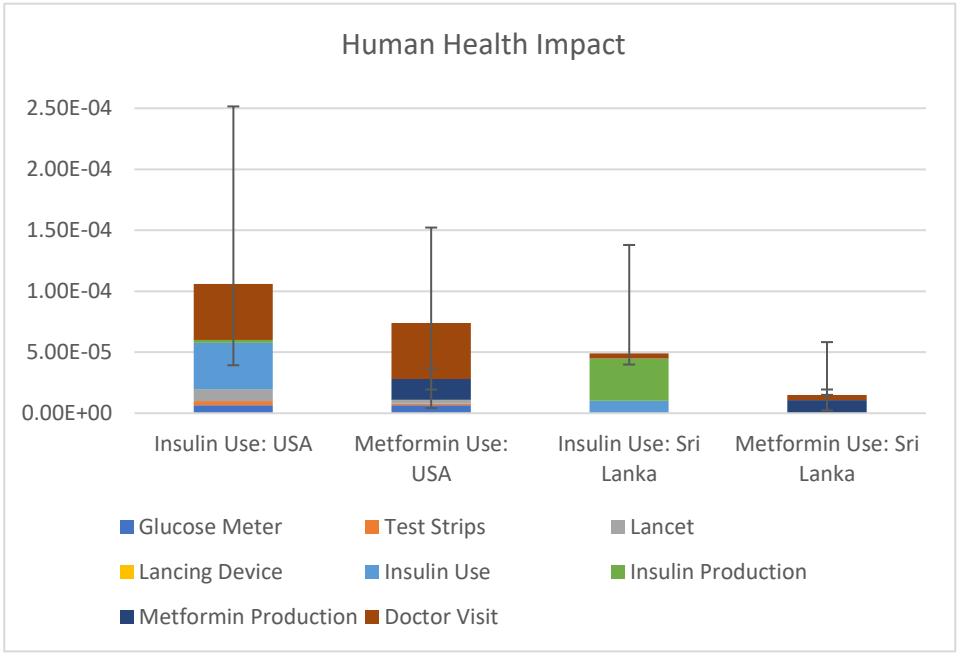
1

Figure 4: Functional unit impact results for the U.S. Insulin Use, U.S. Metformin Use, Sri Lankan Insulin Use and Sri Lankan Metformin Use scenarios, disaggregated by treatment component. .









5.2 Population and Lifetime Impact Results

	High-Income : Insulin	**High-Income : Metformin**	**Low & Middle Income : Insulin**	**Low & Middle Income : Metformin**	**Total Annual T2d Global Impact**	**Annual U.S. Healthcare Emissions** (M. J. Eckelman and Sherman 2016)	**Annual Global Healthcare Emissions** (Karliner et al. 2019b)
Climate Change (kg CO2-eq)	628,769,522	1,529,628,066	906,266,506	2,177,052,872	5,241,716,966	660,000,000,000	2,000,000,000,000
Terrestrial Acidification (kg SO2-eq)	2,452,654	25,220,265	14,251,778	68,783,450	110,708,146	3,100,000,000	n/a
Water Consumption (m3)	84,420,458	44,983,308	25,468,828	106,302,002	261,174,596	n/a	n/a
Human Health (DALY Lost)	2,032	3,720	2,165	4,992	12,909	470,554	n/a

*Table 3: **Environmental and Health Footprint from treating the Global T2d population for one year.** Annual aggregate total impacts of High-Income and Low-and Middle-Income treatment scenarios listed according to impact category. The Total Global Impact provides the combined annual impacts associated with all global population results. Annual US Healthcare Emissions and Annual Global Healthcare Emissions are included as comparative references and are cited respectively from Eckelman MJ, Sherman J., 2016, and Karliner J, Slotterback S, Boyd R, Ashby B, Steele K., 2019.*

5.3 Global Population Lifetime of T2d Treatment Impact Results

	High-Income: Insulin	**High-Income: Metformin**	**Low & Middle Income: Insulin**	**Low & Middle Income: Metformin**	**Total Lifetime T2d Global Impact**
Climate Change (kg CO2-eq)	13,832,929,481	33,651,817,457	19,937,863,127	47,895,163,180	115,317,773,245
Terrestrial Acidification (kg SO2-eq)	53,958,395	554,845,821	313,539,110	1,513,235,890	2,435,579,216
Water Consumption (m3)	1,857,250,075	989,632,784	560,314,215	2,338,644,033	5,745,841,107
Human Health (DALY Lost)	44,697	81,840	47,630	109,840	284,007

*Table 4: Environmental footprint from Treating the Current Global T2d **Population over their Estimated Lifetime**: The population lifetime impact results are calculated by multiplying the annual population impact results by 22 years. The Total Global Impact column provides the combined global impact for all global populations treating T2d.*

Overall the actual impacts of treating T2d appear slight. The 34.8 kg of CO_2-eq generated by the High-Income Insulin Use scenario, the largest CO_2 emitting scenario, is equivalent to the annual CO_2 emissions of 0.007th of an average, gasoline-powered passenger vehicle (US EPA 2015). Even as impacts are scaled across population and extended time frames the actual effects of adequate universal T2d treatments are minimal in the context of the overall global healthcare emissions (annual global T2d CO_2-eq emissions account for ~.26% of annual global healthcare CO_2-eq emissions). That is not to say these impacts are irrelevant. The global lifetime results reported in Table 4 are a conservative snapshot of the cumulative global environmental impact generated by T2d. Avoiding these total Lifetime T2d Global CO_2-eq impacts would have the same effect as nurturing 2 billion new trees for 10 years(US EPA 2015).

5.4 Sensitivity Analysis

An overview of each treatment scenario's components is available in the Methods Section of this paper.

Figure 1 shows the combined results for the sensitivity analysis findings of each of the assessed variables according to their estimated actual emissions per functional unit. The graph clearly demonstrates the outsized impacts of metformin dosages in the Sri Lankan and United States scenarios. These variables are highly elastic in the sense that while large dosages contribute notable CO_2 impacts, any decrease in dosage amount shows a clear and substantive decrease in emissions. Although never reaching the same potential for amount of CO_2 emitted, metformin production energy in the United States and Sri Lanka contribute notably to Global Warming impacts with little variability. These impacts remain mostly stable irrespective of the amount of energy being used.

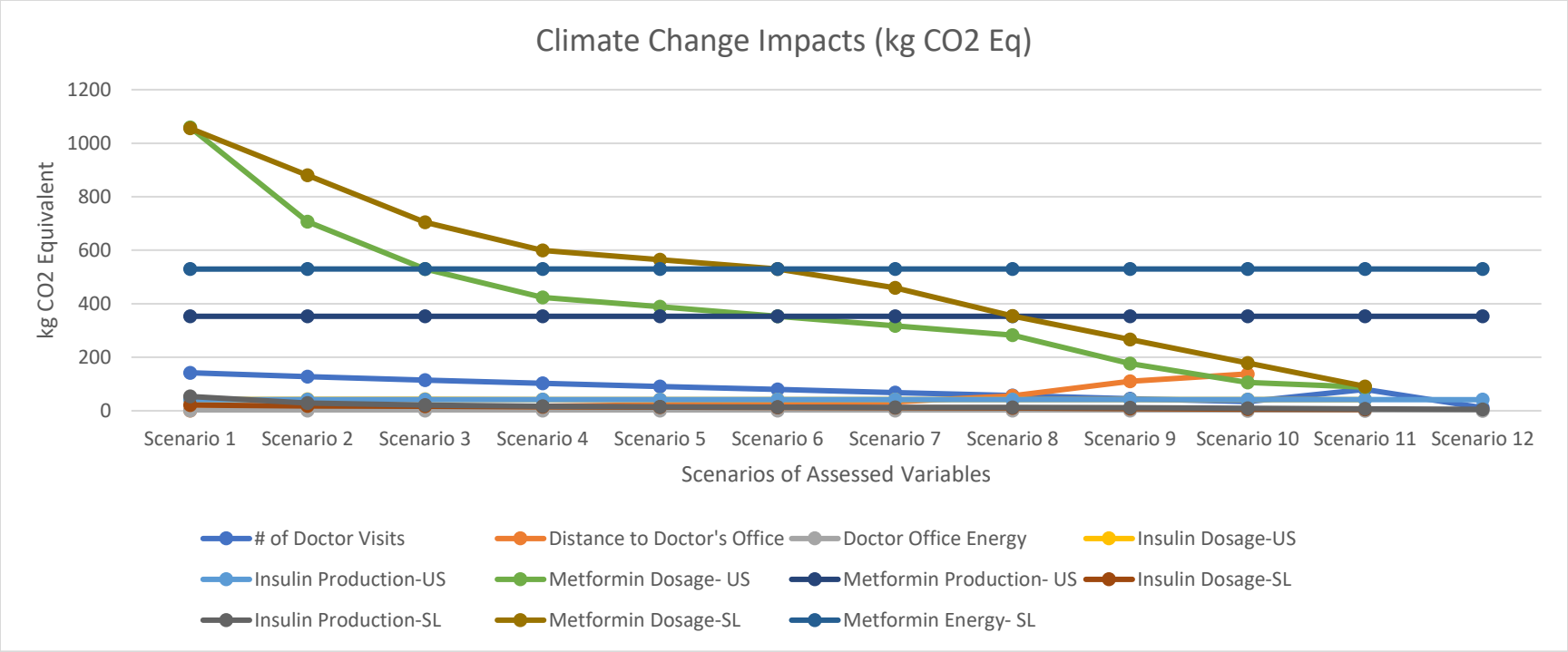


Figure 5: Climate Change Impacts (kg CO2 eq) Sensitivity Analysis per Tested Variable Per Functional Unit

Figure 2 presents the combined results of the assessed variables according to their impacts on the overall treatment scenario impact results. These findings indicate the impact of each variable on the overall total impact of the scenario. From figure 2 it is clear that metformin dosages in the United States and Sri Lanka continue to significantly impact CO_2 emissions. As with Figure 1, there is a notable decrease in CO_2 emission outputs as metformin dosages are reduced. Figure 2 differs from Figure 1 when considering other significant causes of Co_2 emissions. In the context of overall impacts, U.S. in-person doctor visits and distance traveled to the clinic in the Insulin Use and Metformin Use scenario are both notable contributors to CO_2 emissions.

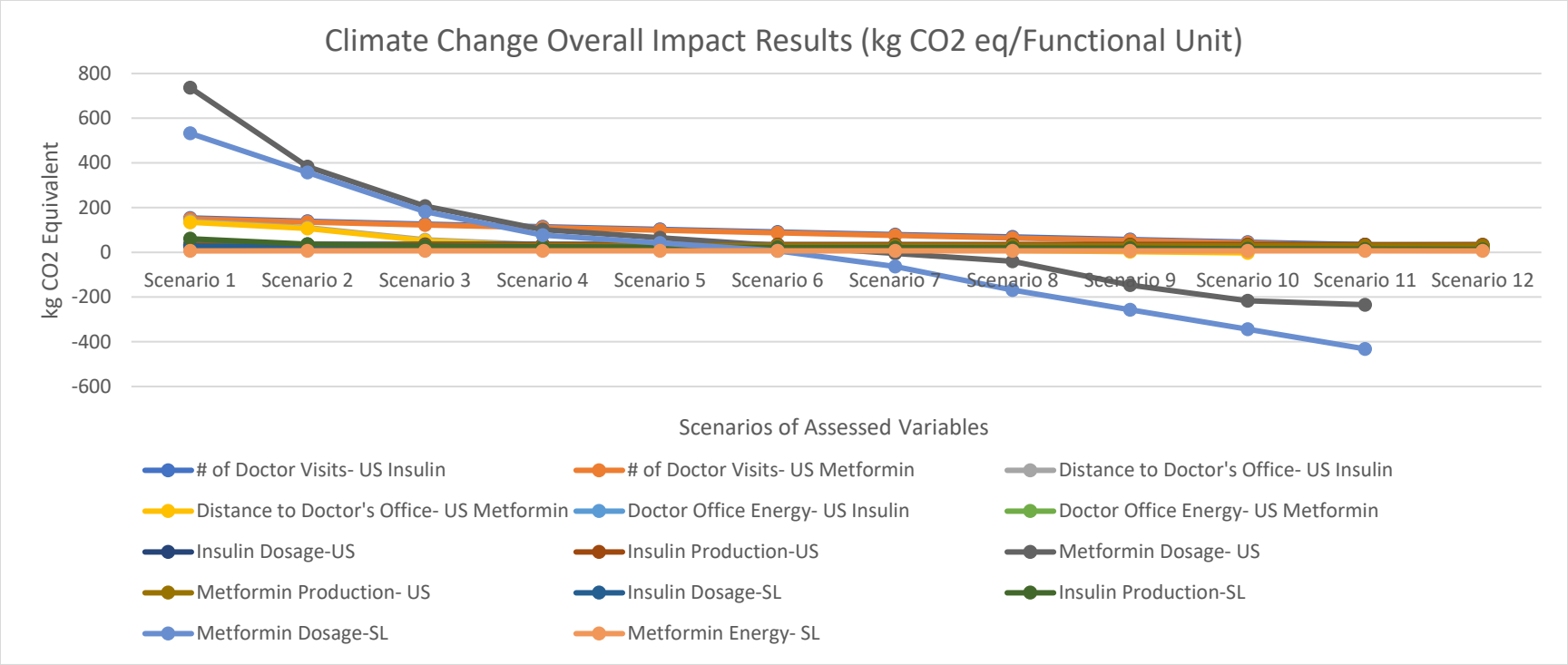


Figure 6: Climate Change Impacts Sensitivity Analysis as Variables Impact Final T2d Scenario Impact Results

Figure 3 is the combined variable findings of the sensitivity analysis results for Terrestrial Acidification. The graph clearly indicates the importance of energy in insulin production in the Sri Lankan scenario as a large overall producer of terrestrial acidification impacts. Apart from insulin production, the amount of insulin used per dosage, the number of in-person doctor visits and the distance to the doctor's office all generate the highest terrestrial acidification impacts.

The overall scenario impacts displayed in Figure 4 also highlight the importance of the energy used in insulin production in the Sri Lankan scenario as a key contributor to terrestrial acidification impacts. However, these impacts are reduced to substantially lower levels once the energy used in production is decreased below 110 MJ per functional unit. At that point, the number of in-person doctor visits in the U.S. Metformin Use scenario becomes the most impactful contributor to overall terrestrial acidification emissions, followed closely by the energy used to produce metformin in the U.S. Metformin Use scenario.

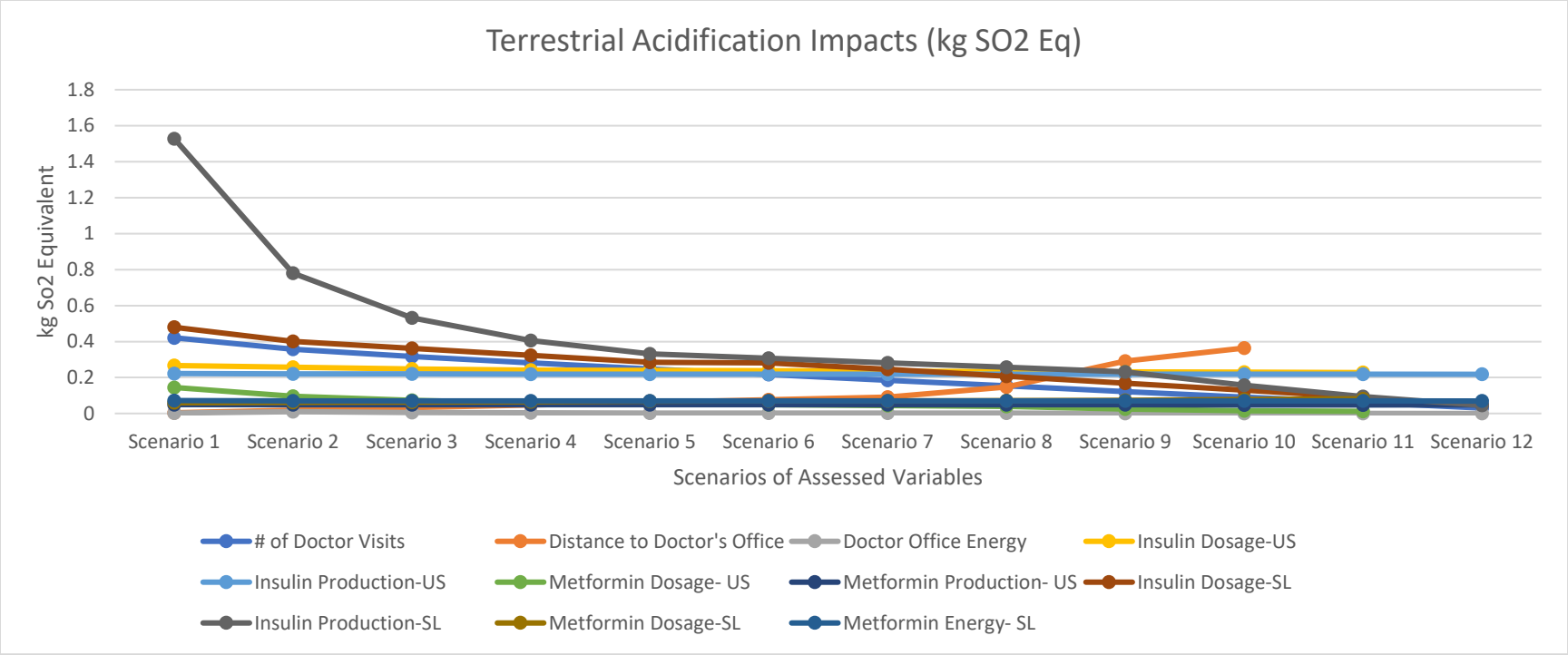


Figure 7: Sensitivity Analysis of Terrestrial Acidification Impacts Per Tested Variable

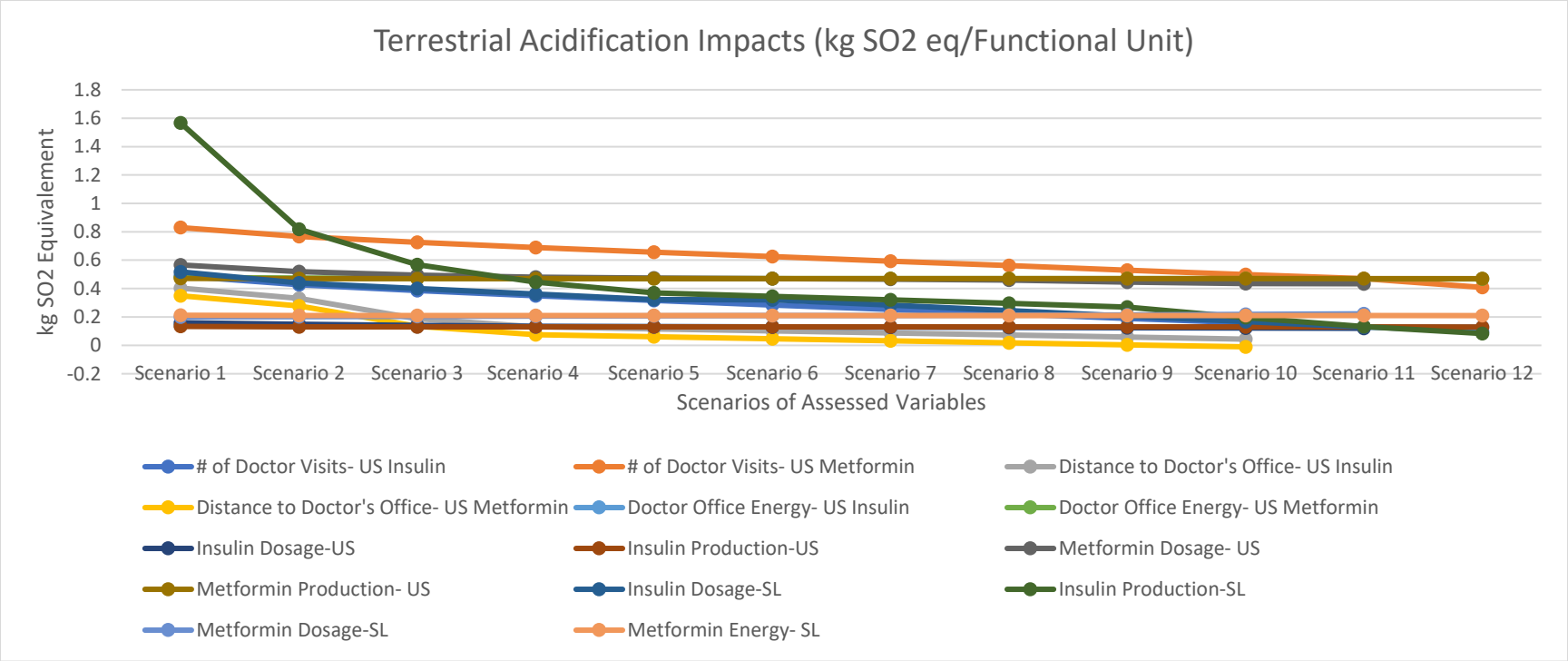


Figure 8: Sensitivity Analysis of Terrestrial Acidificatino Impacts per Final T2d Treatment Functional Unit Impact Results

Figure 5 presents the sensitivity analysis findings for the water consumption variable results. Similar to Terrestrial Acidification, the energy used in insulin production in the Sri Lankan context has the greatest potential for water consumption impacts, although this potential is diminished when energy use decreases below 110 MJ/functional unit. The number of in-person doctor visits is also a large consumer of water, although the attributable impact decreases greatly as the number of visits declines. Insulin dosage in the U.S. context remains a persistently high source of water consumption throughout the variable scenarios.

Figure 6's depiction of the results of the sensitivity analysis in the context of overall treatment impacts indicates that there is a very clear distinction between highly impactful categories and those that are less impactful. The highly impactful categories remain persistently high despite variations in variable values. The high impact categories are Number of In-Person Doctor Visits in the U.S. insulin scenario, distance to the doctor office in the U.S. insulin scenario, insulin dosage in the U.S. scenarios, insulin production in the United States. It is very clear from these findings that treatments in the United States using insulin are responsible for the highest rates of water consumption.

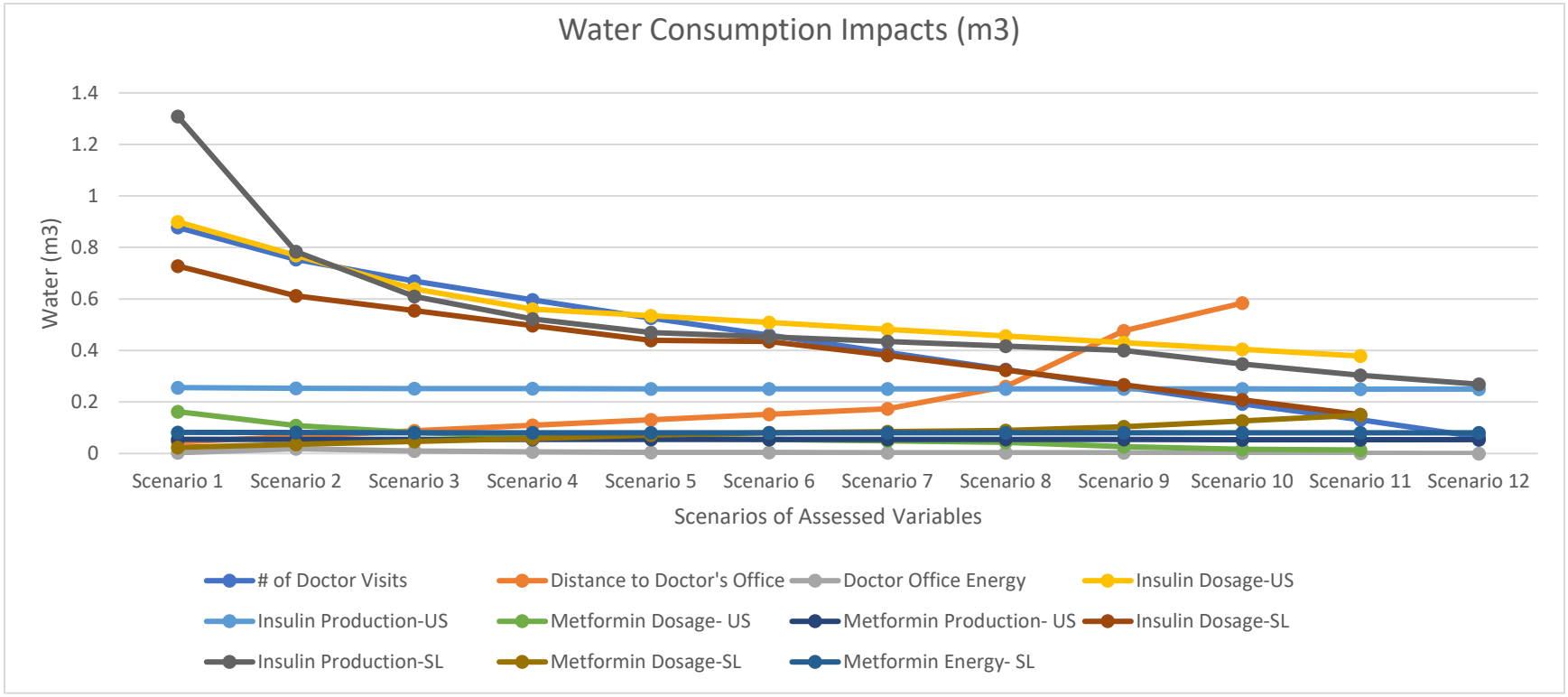


Figure 9: Sensitivity Analysis on Water Consumption per Tested Variable

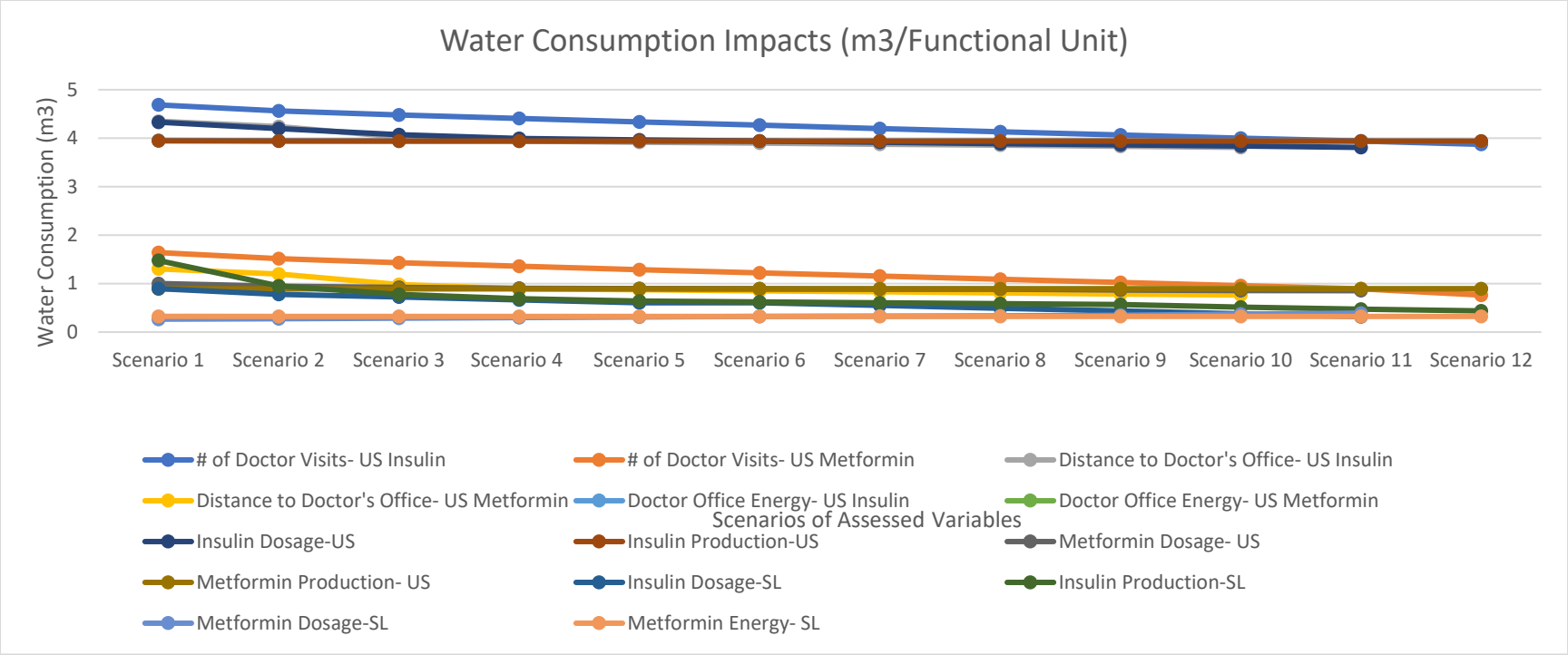


Figure 10: Sensitivity Analysis of Water Consumption Impacts per T2d Treatment Scenario Overall Functional Unit Results

Figure 7 shows the individual variable results of the Human Health sensitivity analysis. At an individual variable level, human health is most significantly impacted by the Number of Doctor Visits and the Distance to the Doctor's Office. The greatest impacts are generated from these variables, but their impacts are highly elastic. They depend greatly on the variable. The impacts are reduced to almost zero when the number of doctor visits is cut to one or two in-person visits and round-trip distances are less than 25 miles. Two variables that remain relatively unchanged with regard to human health throughout the scenarios and have a higher impact than the majority of the variables, are those of U.S. insulin production and U.S. insulin dosage. They show very little sensitivity to different scenario values.

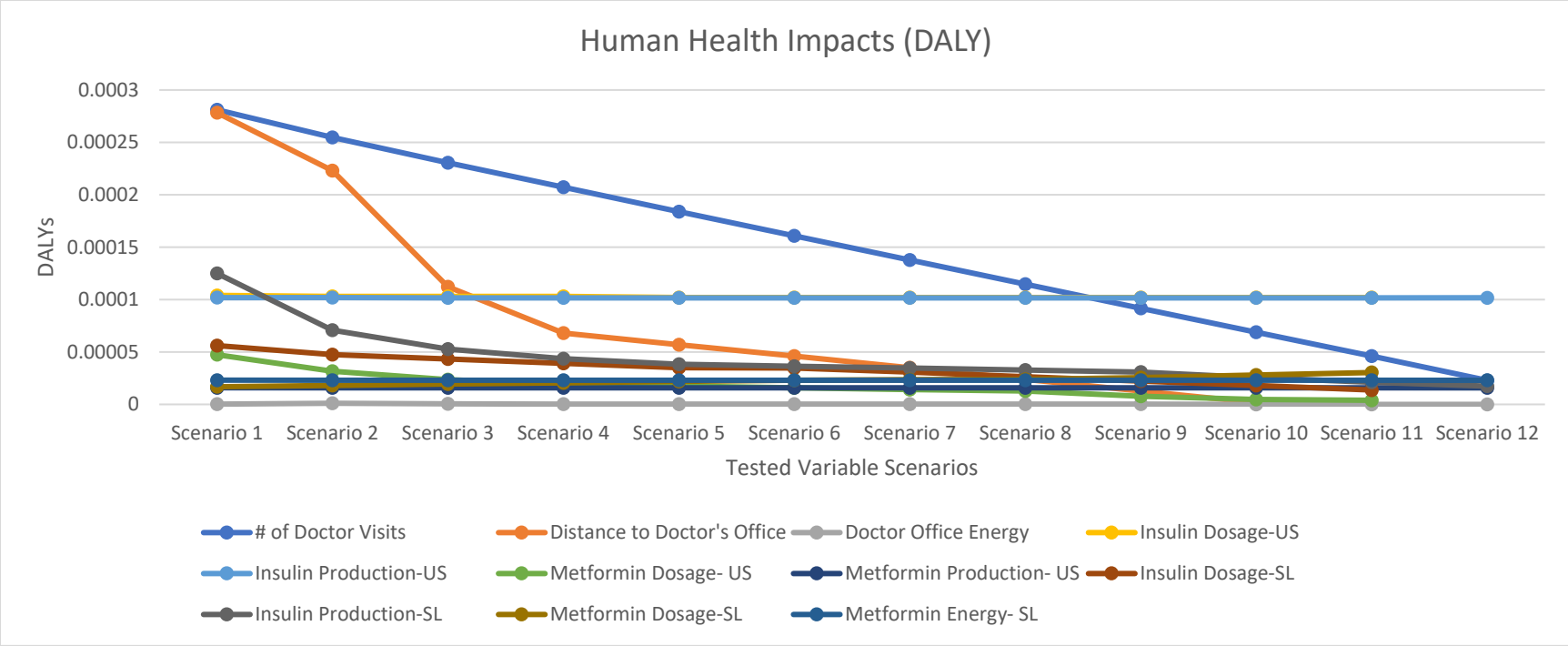


Figure 11: Sensitivity Analysis of Human Health Impacts per Tested Variable

Figure 8 demonstrates the sensitivity analysis results per variable in the context of the overall treatment scenario functional unit results. The impactful variables are yet again somewhat different. Number of doctor visits in the U.S. insulin scenario and number of in-person doctor visits in the U.S. metformin scenario are what have the most sensitivity to the different variables. Distance to the doctor's office in the U.S. Insulin Use scenario and Metformin scenarios are also large sources of impact, although these impacts are greatly muted once the round-trip distance in both scenarios is less than 15 miles. The two least sensitive variables, although not significantly impactful, are insulin and metformin production in the United States. Metformin energy production and metformin dosage amounts in the Sri Lankan model are also not very sensitive to variable value fluctuations.

Tables 1 and 2 below show the standard deviation results for the sensitivity analysis of each assessed variable. The green cells indicate a standard deviation value of less than 3. Yellow cells indicate standard deviation values between 3 and 30. Any cells with a standard deviation above 30 are marked orange, with the highest deviations noted in red.

Table 5: U.S. Scenarios Sensitivity Analysis Results

	Climate Change	Terrestrial Acidification	Water Consumption	Human Health
# of Doctor Visits	40.41720876	0.117134933	0.245016028	8.04264E-05
Distance to Doctor Office	43.75549561	0.115025378	0.172395726	8.83258E-05
Doctor Office Overhead Energy	0.305050087	0.002649043	0.004698552	2.87107E-07
Insulin Dosage	0.34675512	0.011554956	0.153234377	4.37623E-07
Insulin Production	2.835090974	0.102407685	1.369210046	3.54632E-06
Metformin Dosage	270.0292748	0.03691134	0.041394925	1.20759E-05
Metformin Production	0.010581014	0.000405159	0.000286133	2.7212E-08

Table 6: Sri Lanka Scenarios Sensitivity Analysis Results

	Climate Change	Terrestrial Acidification	Water Consumption	Human Health
Insulin Dosage	4.786863138	0.11283181	0.167410918	1.22864E-05
Insulin Production	12.49497328	0.385833321	0.270365509	2.80039E-05
Metformin Dosage	278.7108235	0.006357084	0.036236901	3.92679E-06
Metformin Production	0.015871544	0.000607738	0.000429084	4.26237E-08

6 Discussion: Reducing Negative Impacts of T2d

Informed by the results of this study, the following discussion suggests preliminary actions to be considered by healthcare providers and patients, private sector actors, and governments to reduce if not eliminate negative T2d impacts. The second half of the section comments on the lessons learned from the study's research and identifies additional methods and research to be developed in future publications.

The most obvious and definitive method of eliminating the negative impacts associated with T2d is to eliminate T2d. In the absence of a cure for the disease, T2d prevention reduces the risk of patient health complications and eliminates the need to expend resources managing the disease. Unfortunately, an individuals' personal circumstances, genetics, and environmental realities mean that T2d prevention is not always possible. Where the disease cannot be prevented, moral and ethical obligations require that any patient treatment decision prioritize optimal healthcare. The results of this study identify common T2d treatment elements that substantively contribute to negative environmental and human health impacts so that all relevant stakeholders may consider options for reducing the environmental and health impacts of these treatment elements.

While the impacts of T2d treatments may not substantially contribute to global healthcare emissions, the sources of T2d treatment emissions align with with previous studies have identified as major sources of pollution. A sensitivity analysis (detailed in the supplemental materials) indicates that metformin dosages in both the U.S. and Sri Lankan scenarios, the energy used in medication production, the number of U.S. in-person doctor visits and the distance U.S. patients travel to the doctor's office all contribute significantly to negative environmental and human health impacts. These findings are in accordance with previously published results in which medical buildings and prescription medication are consistently cited as major emission sources (M. J. Eckelman and Sherman 2016; Karliner et al. 2019b; M. J. Eckelman, Sherman, and MacNeill 2018). Transportation is specificly mentioned by as an important driver of pollution associated with the health care supply chain, the source of 71% of energy-related emissions(Karliner et al. 2019b).

6.1 Suggested Actions

Healthcare Providers and Patients

Optimal health outcomes must always be the priority when making decisions regarding patient health. It is acknowledged and encouraged that any potential trade-off or alteration to patient care should foremost explicitly contribute to the patient's overall health outcome. Taking into consideration patient health outcomes, both medical practitioners and healthcare administrators are well poised to address the impacts associated with high medication dosages and doctor visits.

For practitioners in the U.S. and Sri Lanka, prioritizing the prescription of a sensible diet and exercise plans as legitimate and effective treatment options for T2d may help to reduce patient reliance on increasingly high dosages of metformin and/or

insulin. This recommendation is supported by research that confirms the importance of even slight dietary and exercise improvements for enhancing the patient's own blood glucose regulation. (Kraus et al. 2019; Shima et al. 1996; Grimm 1999) For their part, patients must recognize the legitimacy of behavior change as an effective method in treating and managing their T2d. Continuous health metric tracking and real-time video conferencing may also present an opportunity for practitioners to engage with patients outside of a clinical setting, reducing impacts associated with clinic operations and the need to travel to a medical clinic. It should be noted that while technology costs are continually decreasing, the availability of the necessary technology and capacity to virtually monitor and consult with patients is presently limited in many settings. (Shaw et al. 2018; Drake et al. 2019; Combi, Pozzani, and Pozzi 2016; Holmner et al. 2014; Wickramasinghe et al. 2016; Mohammadzadeh and Safdari 2014; Weenk et al. 2017)

Private Sector Actors

The private sector is vital as the source of most of the inputs necessary to effectively managed T2d. With active encouragement from healthcare practitioners and administrators, producers and manufacturers have the ability to reform product designs, supply chains and production processes to drastically reduce emissions associated with T2d treatments. (Alsaffar et al. 2016; Unger and Landis 2016) This study implicates electricity production used in the service of pharmaceutical production as one of the largest contributors to negative T2d treatment impacts. Sourcing production energy from renewable sources and consciously considering the entire environmental life-cycle impacts of all products (including packaging materials), are just a few examples of the potential actions the private sector may embrace to reduce emissions. (Rafique, Bahaidarah, and Anwar 2019; Tonn et al. 2014; Obama 2017; Hede et al. 2013; Verghese and Lewis 2007; Wear 2010) The incentive for choosing less impactful product designs and production processes may be increased profitability due to increases in efficiencies or streamlined supply chains. However, market realities will likely require that any substantive changes in business practices be drive by sector-wide changes in procurement policies that prioritize the purchase of low-impact products.

Government

Government support is crucial for the development of infrastructure that will facilitate actions to reduce the impacts of T2d treatments. To address the notable impacts associated with pharmaceutical production, governments should prioritize developing public health fund procurement guidelines that reward firms who commit to low-impact production processes throughout each phase of their product's lifecycle. As stated above, the production of pharmaceuticals accounts for one of the major negative T2d treatment-related impacts. At the same time the government spending on healthcare is approximately $82 million USD of healthcare

expenditures in the United States and 40% of healthcare expenditures in Sri Lanka.[1] (World Health Organization 2014) Using similar principles and applying a low-impact life-cycle analysis as a key criterion in product procurement and regulation, governments have significant leverage to influence the products that are introduced in their domestic markets. (Ison and Miller 2000; Lingg et al. 2018)

In addition to procurement and pricing regulations, electricity generation is a key area where government action can quickly reduce impacts. Electricity production is a major source of T2d treatment emissions for both of Sri Lanka's modeled treatment pathways and for U.S. metformin production and U.S. doctor visits. Supporting the decarbonization of electrical grids through incentives and direct investments are direct-action governments can take that will immediately eliminate a major source of T2d treatment emissions for the private sector and healthcare practitioners alike. (Santoyo-Castelazo, Stamford, and Azapagic 2014; Panwar, Kaushik, and Kothari 2011; Paramati, Sinha, and Dogan 2017; Yao, Zhang, and Zhang 2019)

As identified in the results section, transportation for doctor visits in the U.S. treatment scenarios and increased dosages of medications across all the treatment scenarios, are significant sources of T2d-related emissions. Government has a role to play in reducing these emissions by creating environments that allow for easy commuting by walking, biking, or public transit. Governments should adopt zoning regulations that prioritize dense, multipurpose developments and prioritize transportation infrastructure that supports safe public transportation and active transportation (i.e., walking and bicycling). Walking and biking are healthy behaviors that can not only prevent the development of T2d, but also limit the health and environmental burdens generated by those who already have the disease. Sedentary behavior, such as long periods sitting in a motor vehicle, has been strongly linked to increased rates of obesity and insulin resistance, two known causes of patients requiring higher dosages of diabetes-related medications. (Edwardson et al. 2012; Helmerhorst et al. 2009; González, Fuentes, and Márquez 2017; Thyfault et al. 2015) A recent review of more than 50 relevant studies confirms the positive effects of physical activities, such as walking and biking, on increased insulin sensitivity. (Bird and Hawley 2017) Making active transportation a feasible alternative to sedentary motor transportation will reduce motor transport trips, which generate ~73 kg of CO_2 per U.S. doctor visit (US EPA 2015) and will also reduce the amount of diabetes medication required by patients.

6.2 Lessons Learned and Next Steps

This study is a preliminary iteration of a proposed method for quantifying the environmental and human health impacts of chronic disease. Future studies should

[1] Government spending on healthcare in the United States and Sri Lanka figures are cited from the WHO's Global Health Expenditure Database data for the Domestic General Government Health Expenditure as % Current Health Expenditure. Results were reported in current US$ millions.

improve upon this method. As a first step, the data used in this assessment is heavily sourced from secondary sources, particularly with regards to medication production information. Given the suggested importance of pharmaceutical production to impacts, future studies should seek to validate these findings by engaging directly with pharmaceutical and medical device manufacturers to access current primary production data wherever possible.

Second, while the modeled scenarios attempted to provide a range of plausible treatment scenarios for patients managing their T2d under optimal conditions, the reality for most diabetic patients is that they do not live within optimal conditions. Many patients have at least one co-morbidity, such as heart disease, and the vast majority of patients are not 100% compliant with a treatment regimen. Even for those who are compliant, the prescribed treatment may not be ideal for the individual's physiology and an ideal health outcome may not be achieved. Future studies should attempt to consider treatment pathways in the context of lived, as opposed to optimal, patient conditions.

Finally, the method discussed in this paper presents parameters for measuring impacts directly linked to the identified treatment pathways, it is clear that the presented method does not fully consolidate all the information required to make a decision regarding patient treatments. The method does not presently account for the role of quality health outcomes in its assessment of environmental and human health impacts. Moral and ethical obligations require that any patient treatment decision prioritize an optimal healthcare outcome. Furthermore, there is anecdotal evidence that suggests that a failure to prioritize optimal healthcare may result in even greater negative environmental and human health impacts. As such, future research should establish a uniform definition of the criteria that define an optimal healthcare outcome, as well as investigate how to establish alignment between studied treatment scenarios, and ideally treatment components, with patient outcomes. Such an undertaking will likely require close collaboration between medical and life-cycle researchers.

7 Conclusion

This study provides a model for using process life cycle assessment methodology to quantify the environmental and public health impacts of chronic disease treatments. Focusing on Type 2 diabetes, the study analyzed a functional unit of the climate change, terrestrial acidification, water consumption and public health impacts of treating one type 2 diabetes patient for one year. It is assumed that the patient has no additional medical complications. The functional unit was applied to four treatment scenarios modeling insulin and metformin use in the United States and Sri Lanka. The subsequent results highlight that while the impacts of one individual over one year are relatively inconsequential, the global epidemic of the disease combined with its chronic nature result in substantive environmental and public health impacts. In the case of public health impacts, the global impact of treating the Type 2 diabetes population over the life of their disease will likely

exceed the disability adjusted life years generated by the entire US healthcare system.

The most effective method of reducing emissions associated with Type 2 diabetes is a comprehensive cure for the disease that will preclude the need for treatment. As the medical community strives towards this objective, patients, healthcare providers, the private sector, and governments are positioned to take actions that will at the very least reduce the associated impacts with treating Type 2 diabetes. Healthcare providers and governments should prioritize healthy lifestyle choices and the development of infrastructure that incentivizes active mobility. The private sector and governments should focus efforts to develop and source energy from carbon-free energy sources such as wind, solar or geo-thermal. Active transport among patients should be prioritized, healthcare providers can invest in remote technologies that reduce the need for clinic visits, while the private sector should critically review supply chains and production processes to assess where more localized production is feasible.

Human health and well-being are directly related to the health and well-being of our environments. Chronic disease affects hundreds of millions of people around the world. If we are to provide each of these individuals with the care they need to effectively manage their conditions it is the responsibility of the healthcare community to consider the impacts of these treatments on the environment. This study is a step in understanding the environmental costs of our current treatment methods so that we may work towards implementing solutions that are good for a patient's health and their environment.

8 Acknowledgements

The authors would like to acknowledge and extend thanks to Dr. Jennifer Ann Wyckoff M.D., Sonja Hughbanks and their medical assistant colleagues at the University of Michigan's Metabolism, Endocrinology and Diabetes Clinic at Domino's Farms, to Dr. Mahen Wijesuriya and his colleagues at the National Diabetes Center in Sri Lanka, to Dr. B. Ganaikabahu and his colleagues at the Trincomalee General Hospital Diabetes Clinic, and to Dr. Naresh Gunaratnam and the entire community of the Grace Girls Home of Trincomalee, without whose support and generosity in sharing their knowledge and experiences in treating Type 2 diabetes this paper would not be possible.

9 Bibliography

Abaxix, Inc. 2014. "Piccolo Xpress Chemistry Analyzer Operator's Manual." https://med.abaxis.co.uk/wp-content/uploads/2017/03/1100-7108-1ENG-Rev.-B-JenII-Piccolo-Xpress-User-Operators-Manual.pdf.

Abbott. 2016. "Freestyle Lite Owner's Booklet." https://freestyleserver.com/Payloads/IFU/2017july/ART22813-003_rev-A_Web.pdf.

Abbott Diabetes Care Inc. 2015. "Evaluation of the FreeStyle Precision Neo Blood Glucose Monitoring System."

https://www.myfreestyle.com/neo/whitepaper/EVALUATION-OF-THE-FS-PRECISION-NEO-BLOOD-GLUCOSE-MONITORING-SYSTEM-HCP-CONSUMER.pdf.

Abbott Ireland Diabetes Care. 2019. “Abbott In Ireland | Diabetes Care: Donegal.” 2019. https://www.ie.abbott/about-us/abbott-in-ireland/diabetes-care-donegal.html.

Allen, Matthew R. 2006. “Effective Pollution Prevention in Healthcare Environments.” *Journal of Cleaner Production* 14 (6): 610.

Alsaffar, Ahmed J., Kamyar Raoufi, Kyoung-Yun Kim, Gül E. Okudan Kremer, and Karl R. Haapala. 2016. “Simultaneous Consideration of Unit Manufacturing Processes and Supply Chain Activities for Reduction of Product Environmental and Social Impacts.” *Journal of Manufacturing Science and Engineering* 138 (10): 101009-101009–18. https://doi.org/10.1115/1.4034481.

Alvim-Ferraz, M. C. M., and S. A. V. Afonso. 2005. “Incineration of Healthcare Wastes: Management of Atmospheric Emissions through Waste Segregation.” *Waste Management* 25 (6): 638–48. https://doi.org/10.1016/j.wasman.2004.07.017.

American Diabetes Association. 2017. “Standards of Medical Care in Diabetes—2017 Abridged for Primary Care Providers.” *Clinical Diabetes* 35 (1): 5–26. https://doi.org/10.2337/cd16-0067.

———. 2019. “9. Pharmacologic Approaches to Glycemic Treatment: Standards of Medical Care in Diabetes—2019.” *Diabetes Care* 42 (Supplement 1): S90–102. https://doi.org/10.2337/dc19-S009.

American Nurses Association. 2007. “ANA’s Principles of Environmental Health for Nursing Practice with Implementation Strategies.” Silver Spring, MD: American Nurses Association. http://ojin.nursingworld.org/MainMenuCategories/WorkplaceSafety/Healthy-Nurse/ANAsPrinciplesofEnvironmentalHealthforNursingPractice.pd.

Athapattu, Bandunee, A. Priyantha, and Masafumi Tateda. 2015. “Recommendations through a Complete Study on Healthcare Solid Waste Management Practices of Government Hospitals in Colombo, Sri Lanka.” *Journal of Scientific Research and Reports* 7 (3): 228–39. https://doi.org/10.9734/JSRR/2015/16828.

Baratta, Chris. 2016. “‘Interdisciplinarity’ Achieved: A Brief Look at Interdisciplinary Environmentalism in the 1960s.” *Interdisciplinary Literary Studies* 18 (3): 301–24. https://doi.org/10.5325/intelitestud.18.3.0301.

Bennett, N. M. 1988. “Yes, I’m Talking Rubbish.” *Australian Health Review: A Publication of the Australian Hospital Association* 11 (4): 333–38.

Beran, David. 2015. “The Impact of Health Systems on Diabetes Care in Low and Lower Middle Income Countries.” *Current Diabetes Reports* 15 (4): 20. https://doi.org/10.1007/s11892-015-0591-8.

Berridge, V., and M. Gorsky, eds. 2011. *Environment, Health and History*. 2012 edition. New York: Palgrave Macmillan.

BERRY, A. E. 1940. “Fallacies Associated with Environmental Control of Disease.” *Canadian Public Health Journal* 31 (5): 228–32.

———. 1960. “Environment and Public Health Programs.” *Canadian Journal of Public Health / Revue Canadienne de Sante’e Publique* 51 (7): 255–63.

Berton, Elena. 2013. “Sanofi Steps up Diabetes Drive as Rivals Raise the Stakes.” *Reuters*, June 7, 2013. https://www.reuters.com/article/us-sanofi-diabetes-idUSBRE9560IG20130607.

BioPharm International Editors. 2017. “Novo Nordisk Expands Insulin Manufacturing Facility in India.” December 13, 2017. http://www.biopharminternational.com/novo-nordisk-expands-insulin-manufacturing-facility-india-0.

Bird, Stephen R, and John A Hawley. 2017. “Update on the Effects of Physical Activity on Insulin Sensitivity in Humans.” *BMJ Open Sport — Exercise Medicine* 2 (1). https://doi.org/10.1136/bmjsem-2016-000143.

Bjørn, Anders, Mikołaj Owsianiak, Christine Molin, and Michael Z. Hauschild. 2018. “LCA History.” In *Life Cycle Assessment: Theory and Practice*, edited by Michael Z. Hauschild, Ralph K. Rosenbaum, and Stig Irving Olsen, 17–30. Cham: Springer International Publishing. https://doi.org/10.1007/978-3-319-56475-3_3.

Blanchard, W. O. 1928. “Malaria as a Factor in Italian Environment.” *The Scientific Monthly* 27 (2): 172–76.

Bristol-Myers Squibb. 2010. “Significant Changes. Significant Results. Our Biopharma Transformation.” Annual Report. https://s21.q4cdn.com/104148044/files/doc_financials/annual_reports/BMS_2010_AR_lowres.pdf.

Brown, Janet. 2009. “The Challenge of Environmental Sustainability in Healthcare.” *HERD: Health Environments Research & Design Journal* 3 (1): 106.

Burant, Charles. 2012. *Medical Management of Type 2 Diabetes*. American Diabetes Association.

Campion, N., Cassandra L Thiel, Justin DeBlois, Noe C Woods, Amy E Landis, and Melissa M Bilec. 2012. “Life Cycle Assessment Perspectives on Delivering an Infant in the US.” *Science of the Total Environment* 425: 191.

Campion, N, CL Thiel, NC Woods, L Swanzy, AE Landis, and MM Bilec. 2015. “Sustainable Healthcare and Environmental Life-Cycle Impacts of Disposable Supplies: A Focus on Disposable Custom Packs.” *JOURNAL OF CLEANER PRODUCTION* 94: 46.

Carnegie Mellon University. 2016. “Limitations of the EIO-LCA Method - Economic Input-Output Life Cycle Assessment - Carnegie Mellon University.” EIO-LCA: Free, Fast, Easy Life Cycle Assessment. 2016. http://www.eiolca.net/Method/Limitations.html.

Centers for Medicare and Medicaid Services. 2017a. “Medicare Coverage of Diabetes Supplies, Services, & Prevention Programs.” Department of Health and Human Services. https://www.medicare.gov/Pubs/pdf/11022-Medicare-Diabetes-Coverage.pdf.

———. 2017b. “Medicare’s Coverage of Diabetes Supplies and Services.” Medicare.gov. https://www.medicare.gov/Pubs/pdf/11022-Medicare-Diabetes-Coverage.pdf.

Cespi, Daniele, Evan S. Beach, Thomas E. Swarr, Fabrizio Passarini, I. Vassura, Peter J. Dunn, and Paul T. Anastas. 2015. “Life Cycle Inventory Improvement in the Pharmaceutical Sector: Assessment of the Sustainability Combining PMI and LCA Tools.” *Green Chemistry* 17 (6): 3390–3400. https://doi.org/10.1039/C5GC00424A.

Childe, Charles P. 1923. “British Medical Association. Ninety-First Annual Meeting, Portsmouth, 1923. President’s Address On Environment And Health.” *The British Medical Journal* 2 (3265): 135–40.

Christian G. Daughton. 2003. “Cradle-to-Cradle Stewardship of Drugs for Minimizing Their Environmental Disposition While Promoting Human Health. I. Rationale for and Avenues toward a Green Pharmacy.” *Environmental Health Perspectives* 111 (5): 757.

Chung, Jeanette W., and David O. Meltzer. 2009. “Estimate of the Carbon Footprint of the US Health Care Sector.” *JAMA* 302 (18): 1970–72. https://doi.org/10.1001/jama.2009.1610.

Cimprich, Alexander, Jair Santillán-Saldivar, Cassandra L. Thiel, Guido Sonnemann, and Steven B. Young. 2019. “Potential for Industrial Ecology to Support Healthcare Sustainability: Scoping Review of a Fragmented Literature and Conceptual Framework for Future Research.” *Journal of Industrial Ecology* 0 (0). https://doi.org/10.1111/jiec.12921.

Combi, Carlo, Gabriele Pozzani, and Giuseppe Pozzi. 2016. “Telemedicine for Developing Countries.” *Applied Clinical Informatics* 7 (4): 1025–50. https://doi.org/10.4338/ACI-2016-06-R-0089.

Conklin, Groff. 1949. “Cancer and Environment.” *Scientific American* 180 (1): 11–15.

Corvalán, C., Simon Hales, A. J. McMichael, Millennium Ecosystem Assessment (Program), and World Health Organization, eds. 2005. *Ecosystems and Human Well-Being: Health Synthesis*. Millennium Ecosystem Assessment. Geneva, Switzerland: World Health Organization.

Costanza, Robert, Ralph d’Arge, Rudolf de Groot, Stephen Farber, Monica Grasso, Bruce Hannon, Karin Limburg, et al. 1997. “The Value of the World’s Ecosystem Services and Natural Capital.” *Nature* 387 (6630): 253–60. https://doi.org/10.1038/387253a0.

Cotton, Robin T., and Aliza P. Cohen. 2010. “Eco-Conservation and Healthcare Ethics: A Call to Action.” *The Laryngoscope* 120 (1): 4–8. https://doi.org/10.1002/lary.20663.

Cramer, Joyce A. 2004. “A Systematic Review of Adherence with Medications for Diabetes.” *Diabetes Care* 27 (5): 1218–24. https://doi.org/10.2337/diacare.27.5.1218.

Crowley, Ryan A. 2016. “Climate Change and Health: A Position Paper of the American College of Physicians.” *Annals of Internal Medicine* 164 (9): 608. https://doi.org/10.7326/M15-2766.

Daily, Gretchen Cara. 2012. *Nature’s Services: Societal Dependence On Natural Ecosystems*. Island Press.

Daughton, Christian G. 2002. “Environmental Stewardship and Drugs as Pollutants.” *The Lancet* 360 (9339): 1035–36. https://doi.org/10.1016/S0140-6736(02)11176-7.

Daughton, Christian G. 2009. “Chemicals from the Practice of Healthcare: Challenges and Unknowns Posed by Residues in the Environment.” *Environmental Toxicology and Chemistry* 28 (12): 2490.

Daughton, Christian G. 2014. “Eco-Directed Sustainable Prescribing: Feasibility for Reducing Water Contamination by Drugs.” *Science of the Total Environment* 493 (September): 392–404. https://doi.org/10.1016/j.scitotenv.2014.06.013.

Decker, George C. 1960. “Insecticides in the 20th Century Environment.” *AIBS Bulletin* 10 (2): 27–31. https://doi.org/10.2307/1292826.

Doucet, L. G. 1988. “Hospital Infectious-Waste Incineration Dilemmas.” *Hospitals* 62 (13): 80.

Drake, Coleman, Yuehan Zhang, Krisda H. Chaiyachati, and Daniel Polsky. 2019. “The Limitations of Poor Broadband Internet Access for Telemedicine Use in Rural America: An Observational Study.” *Annals of Internal Medicine*, May. https://doi.org/10.7326/M19-0283.

Dunbar-Reid, Kylie, and Elizabeth Buikstra. 2017. “The Environmental Impact of Healthcare and Haemodialysis: The Jekyll and Hyde Dilemma.” Renal Society of Australasia Journal. July 1, 2017. http://link.galegroup.com/apps/doc/A509016638/AONE?sid=lms.

Eckelman, Matthew J., and Jodi Sherman. 2016. “Environmental Impacts of the U.S. Health Care System and Effects on Public Health.” *PloS One* 11 (6): e0157014.

Eckelman, Matthew J., Jodi D. Sherman, and Andrea J. MacNeill. 2018. “Life Cycle Environmental Emissions and Health Damages from the Canadian Healthcare System: An Economic-Environmental-Epidemiological Analysis.” *PLoS Medicine* 15 (7): e1002623. https://doi.org/10.1371/journal.pmed.1002623.

Eckelman, MJ, and J Sherman. 2016. “Environmental Impacts of the US Health Care System and Effects on Public Health.” *PLOS ONE* 11 (6): e0157014.

Eckelman, and Jodi D. Sherman. 2018. “Estimated Global Disease Burden From US Health Care Sector Greenhouse Gas Emissions.” *American Journal of Public Health* 108 (S2): S120–22. https://doi.org/10.2105/AJPH.2017.303846.

Edwardson, Charlotte L., Trish Gorely, Melanie J. Davies, Laura J. Gray, Kamlesh Khunti, Emma G. Wilmot, Thomas Yates, and Stuart J. H. Biddle. 2012. “Association of Sedentary Behaviour with Metabolic Syndrome: A Meta-Analysis.” *PLOS ONE* 7 (4): e34916. https://doi.org/10.1371/journal.pone.0034916.

Facet Medical Technologies. 2018. “Products | Facet Medical Technologies.” 2018. https://facetmed.com/products-services/products/.

FDA Office of Women’s Health. n.d. “Diabetes Medicines.” U.S. Food & Drug Administration. https://www.fda.gov/media/119148/download.

Fernandes, Thomson A., Deepak K. Kurhe, Anant A. Chavan, and Radha V. Jayaram. 2016. “Recovery and Reuse of Palladium from Spent Glucometer Electrochemical Test Strips.” *Hydrometallurgy*, SI: IC-LGO 2015, 165 (October): 199–205. https://doi.org/10.1016/j.hydromet.2015.09.002.

Finkbeiner, Matthias, ed. 2016. “Input-Output and Hybrid LCA.” In *Special Types of Life Cycle Assessment*. LCA Compendium – The Complete World of Life Cycle Assessment. Springer Netherlands. https://doi.org/10.1007/978-94-017-7610-3.

Fischer Scientific. 2018. “BD Vacutainer Plastic Blood Collection Tubes with K2EDTA: Tube Stopper - Test Tubes, Vials, Caps and Closures,Tubes.” Fisherscientific. 2018. https://www.fishersci.com/shop/products/bd-vacutainer-plastic-blood-collection-tubes-k-sub-2-sub-edta-tube-stopper-4/p-179488.

Frost, W. H. 1916. “The Sewage Pollution of Streams: Its Relation to the Public Health.” *Public Health Reports (1896-1970)* 31 (37): 2486–97. https://doi.org/10.2307/4574107.

Ganguly, Shramana. 2017. “Novo Nordisk India and Torrent Pharma Expand Their Insulin Manufacturing Facility - The Economic Times.” The Economic Times. December 11, 2017. https://economictimes.indiatimes.com/industry/healthcare/biotech/pharmaceuticals/novo-nordisk-india-and-torrent-pharma-expand-their-insulin-manufacturing-facility/articleshow/62022499.cms.

González, Karimé, Jorge Fuentes, and José Luis Márquez. 2017. “Physical Inactivity, Sedentary Behavior and Chronic Diseases.” *Korean Journal of Family Medicine* 38 (3): 111–15. https://doi.org/10.4082/kjfm.2017.38.3.111.

Govindaraj, Ramesh, Kumari Navaratne, Eleonora Cavagnero, and Shreelata Rao Seshadri. 2014. “Health Care in Sri Lanka : What Can the Private Health Sector Offer?” 89554. Health, Nutrition and Population (HNP) Discussion Paper Series. The World Bank. https://ideas.repec.org/p/wbk/hnpdps/89554.html.

Grimm, Jean-Jacques. 1999. “Interaction of Physical Activity and Diet: Implications for Insulin-Glucose Dynamics.” *Public Health Nutrition* 2 (3a): 363–68. https://doi.org/10.1017/S136898009900049X.

Gunathilake, G, Dulani Kottahachchi, and Sajith Siyambalapitiya. 2017. “The Drug Compliance among Patients with Diabetes in Sri Lankan Setting” 7 (February): 16-20.

Gusarov, D. A., D. V. Byrikhina, F. M. Izhaeva, A. I. Gosudarev, P. V. Mikhailov, V. D. Gusarova, T. A. Budyl’skaya, A. F. Mironov, and V. I. Shvets. 2015. “Systematic Approach to Production Technology Development for Therapeutic Proteins (Using Insulin–Glargine as an Example).” *Pharmaceutical Chemistry Journal* 48 (12): 822–29. https://doi.org/10.1007/s11094-015-1203-2.

Haines, A., R. S. Kovats, D. Campbell-Lendrum, and C. Corvalan. 2006. “Climate Change and Human Health: Impacts, Vulnerability and Public Health.” *Public Health* 120 (7): 585–96. https://doi.org/10.1016/j.puhe.2006.01.002.

HATTIE, W. H. 1929. “Teaching Medical Students the Importance of Environment.” *Canadian Public Health Journal* 20 (11): 541–44.

Hede, Shantesh, Manuel Jose Lopes Nunes, Paula Fernanda Varandas Ferreira, and Luis Alexandre Rocha. 2013. “Incorporating Sustainability in Decision-Making for Medical Device Development.” *Technology in Society* 35 (4): 276–93. https://doi.org/10.1016/j.techsoc.2013.09.003.

Helmerhorst, Hendrik J. F., Katrien Wijndaele, Søren Brage, Nicholas J. Wareham, and Ulf Ekelund. 2009. “Objectively Measured Sedentary Time May Predict Insulin Resistance Independent of Moderate- and Vigorous-Intensity Physical Activity.” *Diabetes* 58 (8): 1776–79. https://doi.org/10.2337/db08-1773.

Hensher, Martin. 2020. “Incorporating Environmental Impacts into the Economic Evaluation of Health Care Systems: Perspectives from Ecological Economics.” *Resources, Conservation and Recycling* 154 (March): 104623. https://doi.org/10.1016/j.resconrec.2019.104623.

Herbert Bosch. 1952. “WHO and Environmental Health.” *Public Health Reports (1896-1970)* 67 (4): 370–75. https://doi.org/10.2307/4588081.

Hester, R. E., and Roy M. Harrison, eds. 2010. *Ecosystem Services*. Issues in Environmental Science and Technology, v. 30. Cambridge, [UK]: RSC Pub.

Holmner, A, KL Ebi, L Lazuardi, and M Nilsson. 2014. “Carbon Footprint of Telemedicine Solutions - Unexplored Opportunity for Reducing Carbon Emissions in the Health Sector.” *PLOS ONE* 9 (9): e105040.

Holthaus, D. 1988. “States Seek Tighter Rules on Infectious Waste.” *Hospitals* 62 (17): 70.

Huijbregts, Mark A. J., Zoran J. N. Steinmann, Pieter M. F. Elshout, Gea Stam, Francesca Verones, Marisa Vieira, Michiel Zijp, Anne Hollander, and Rosalie van Zelm. 2017. “ReCiPe2016: A Harmonised Life Cycle Impact Assessment Method at Midpoint and Endpoint Level.” *The International Journal of Life Cycle Assessment* 22 (2): 138–47. https://doi.org/10.1007/s11367-016-1246-y.

Hunt, Robert G, Jere D Sellers, and William E Franklin. 1992. “Resource and Environmental Profile Analysis: A Life Cycle Environmental Assessment for Products and Procedures.” *Environmental Impact Assessment Review* 12 (3): 245–69. https://doi.org/10.1016/0195-9255(92)90020-X.

Hwang, Hae-Gwang, Kwang-Jin Kim, Se-Hoon Lee, Chang-Kyu Kim, Cheol-Ki Min, Jung-Mi Yun, Su Ui Lee, and Young-Jin Son. 2016. “Recombinant Glargine Insulin Production Process Using Escherichia Coli.” *Journal of Microbiology and Biotechnology* 26 (10): 1781–89. https://doi.org/10.4014/jmb.1602.02053.

IBM Micromedex. 2018. “Metformin: Dosing/Administration.” IBM Micromedex. 2018. Micromedex.com.

———. 2019. “RED BOOK Search Results- ‘Active Ingredient: Insulin Human Isophane (Nph).’” IBM Micromedex. August 10, 2019. https://www-micromedexsolutions-com.proxy.lib.umich.edu/micromedex2/librarian/CS/07BB6E/ND_PR/evidencexpert/ND_P/evidencexpert/DUPLICATIONSHIELDSYNC/FBBF8A/ND_PG/evidencexpert/ND_B/evidencexpert/ND_AppProduct/evidencexpert/ND_T/evidencexpert/PFActionId/redbook.ShowProductSearchResults?SearchTerm=insulin%20human%20isophane%20(nph)&searchType=redbookGenericName&searchTermId=301564&searchContent=REDBOOK&searchFilterAD=filterADActive&searchFilterRepackager=filterExcludeRepackager&searchPattern=%5Einsulin.

Industriepark Höchst. 2018. “Sanofi - Pharmaceuticals.” Industriepark Höchst. 2018. https://www.industriepark-hoechst.com/en/stp/menu/the-industriepark-hoechst/companies-on-site/sanofi.html.

International Diabetes Federation. 2019. “IDF Diabetes Atlas.” Atlas 9th Edition. International Diabetes Federation. https://www.diabetesatlas.org/en/sections/worldwide-toll-of-diabetes.html.

International Organization for Standardization. 1997. “ISO 14040, Environmental Management-Life Cycle Assessment-Principles and Framework.” http://www.iso.org/cms/render/live/en/sites/isoorg/contents/data/standard/03/74/37456.html.

Ison, Erica, and Anne Miller. 2000. “The Use of Lca to Introduce Life-Cycle Thinking into Decision-Making for the Purchase of Medical Devices in the Nhs.” *Journal of Environmental Assessment Policy and Management* 02 (04): 453–76. https://doi.org/10.1142/S1464333200000497.

Jameton, Andrew, and Jessica Pierce. 2001. “Environment and Health: 8. Sustainable Health Care and Emerging Ethical Responsibilities.” *CMAJ: Canadian Medical Association Journal* 164 (3): 365–69.

Jeswani, Harish Kumar, and Adisa Azapagic. 2019. “Environmental Impacts of Healthcare and Pharmaceutical Products: Influence of Product Design and Consumer Behaviour.” *Journal of Cleaner Production*, December, 119860. https://doi.org/10.1016/j.jclepro.2019.119860.

Jiaxing Zhiming Machinery Manufacture. 2014. “Alcohol Prep Pad Machine PPD-ZM-AHT Supplier,China Alcohol Prep Pad Machine,Automatic Alcohol Pad Making Machine Manufacturer & Supplier.” Alcohol Swab Packing Machine. 2014. http://www.alcoholpadmachine.com/Alcohol-Prep-Pad-Machine-PPD-ZM-AHT_p9.html.

Johnson, Erik W., Pierce Greenberg, and Pierce Greenberg. 2017. “The US Environmental Movement of the 1960s and 1970s : Building Frameworks of Sustainability.” Routledge Handbook of the History of Sustainability. October 18, 2017. https://doi.org/10.4324/9781315543017-10.

Jolliet, Olivier, Myriam Saade-Sbeih, Shanna Shaked, Alexandre Jolliet, and Pierre Crettaz. 2015. *Environmental Life Cycle Assessment*. 1 edition. Boca Raton: CRC Press.

Karliner, Josh, Scott Slotterback, Richard Boyd, Ben Ashby, and Kristian Steele. 2019a. “Health Care’s Climate Footprint: How the Health Sector Contributes to the Global Climate Crisis and Opportunities for Action, Healthcare Without Harm.” ARUP: 48. https://www.arup.com/-/media/arup/files/publications/h/health-cares-climate-footprint.pdf.

———. 2019b. “Health Care’s Climate Footprint: How the Health Sector Contributes To The Global Climate Crisis and Opportunities for Action.” Health Care Without Harm; ARUP. https://noharm-global.org/documents/health-care-climate-footprint-report.

Kaushik, Manu, T.V. Mahalingam, K.R. Balasubramanyam, and Nitya Varadarajan. 2008. “India’s Best Manufacturing Hubs- Business News.” *Business Today*, June 15, 2008. https://www.businesstoday.in/magazine/features/indias-best-manufacturing-hubs/story/2270.html.

Kehoe, Robert A., Mark D. Hollis, Ralph E. Fuhrman, J. E. McKee, Leslie A. Chambers, and Emil M. Mrak. 1958. “Man and Environment: Conference Report.” *Public Health Reports (1896-1970)* 73 (12): 1073–81. https://doi.org/10.2307/4590331.

Kitzes, Justin. 2013. “An Introduction to Environmentally-Extended Input-Output Analysis.” In . https://doi.org/10.3390/resources2040489.

Kraus, William E, Manjushri Bhapkar, Kim M Huffman, Carl F Pieper, Sai Krupa Das, Leanne M Redman, Dennis T Villareal, et al. 2019. “2 Years of Calorie Restriction and Cardiometabolic Risk (CALERIE): Exploratory Outcomes of a Multicentre, Phase 2, Randomised Controlled Trial.” *The Lancet Diabetes & Endocrinology*, July, S2213858719301512. https://doi.org/10.1016/S2213-8587(19)30151-2.

Leal, Jose, Alastair M. Gray, and Philip M. Clarke. 2009. “Development of Life-Expectancy Tables for People with Type 2 Diabetes.” *European Heart Journal* 30 (7): 834–39. https://doi.org/10.1093/eurheartj/ehn567.

Lewis, Percy G. 1911. “On The Influence Of Calcareous Drinking Water In Health And Disease.” *The British Medical Journal* 2 (2638): 158–60.

Lingg, Myriam, Anahi Dreser, Luis Durán-Arenas, and Kaspar Wyss. 2018. “Strategies to Improve the Medical Device Life Cycle in Mexico.” *Salud Pública de México* 60 (4, jul-ago): 462–71. https://doi.org/10.21149/9060.

Loew, Noya, Wakako Tsugawa, Daichi Nagae, Katsuhiro Kojima, and Koji Sode. 2017. “Mediator Preference of Two Different FAD-Dependent Glucose Dehydrogenases Employed in Disposable Enzyme Glucose Sensors.” *Sensors (Basel, Switzerland)* 17 (11). https://doi.org/10.3390/s17112636.

Mark D. Hollis. 1951. “Environmental Health: A Critique.” *Public Health Reports (1896-1970)* 66 (13): 400–409. https://doi.org/10.2307/4587680.

———. 1952. “Environmental Health Needs in a Dynamic Society.” *Public Health Reports (1896-1970)* 67 (9): 903–8. https://doi.org/10.2307/4588237.

———. 1953. “Environmental Health in a Rural Economy.” *Public Health Reports (1896-1970)* 68 (11): 1107–14. https://doi.org/10.2307/4588646.

Marsh, Kevin, Michael Ganz, Emil Nørtoft, Niels Lund, and Joshua Graff-Zivin. 2016. “INCORPORATING ENVIRONMENTAL OUTCOMES INTO A HEALTH ECONOMIC MODEL.” *International Journal of Technology Assessment in Health Care* 32 (6): 400–406. https://doi.org/10.1017/S0266462316000581.

McINTYRE, HUGH. 1943. “The Influence of Physical Environment on the Public Health.” *Canadian Journal of Public Health / Revue Canadienne de Sante’e Publique* 34 (1): 17–21.

Menke, Andy, Trevor J. Orchard, Giuseppina Imperatore, Kai McKeever Bullard, Elizabeth Mayer-Davis, and Catherine C. Cowie. 2013. “The Prevalence of Type 1 Diabetes in the United States:” *Epidemiology* 24 (5): 773–74. https://doi.org/10.1097/EDE.0b013e31829ef01a.

Michigan Department of Environmental Quailty: Resource Management Division, and Dan Wyant. 1990. *Medical Waste: Public Act and Rules Governing Disposal of Medical Waste*.

Mohammadzadeh, Niloofar, and Reza Safdari. 2014. “Patient Monitoring in Mobile Health: Opportunities and Challenges.” *Medical Archives* 68 (1): 57–60. https://doi.org/10.5455/medarh.2014.68.57-60.

Murchie, Peter. 2007. “Environmental Impact of GP-Led Melanoma Follow Up.” *The British Journal of General Practice* 57 (543): 837–38.

National Center for Chronic Disease Prevention and Health Promotion. 2017. “National Diabetes Statistics Report | Data & Statistics | Diabetes | CDC.” 2017. https://www.cdc.gov/diabetes/data/statistics-report/index.html.

National Institute of Health. 2018. “ALCOHOL- Isopropyl Alcohol Swab.” DailyMed. 2018. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=5e6e6d6f-4472-40f1-b0a9-96cee7ef075b.

National Renewable Energy Laboratory. 2018. “U.S. Life Cycle Inventory Database.” 2018. https://www.lcacommons.gov/nrel/search.

Obama, Barack. 2017. “The Irreversible Momentum of Clean Energy.” *Science* 355 (6321): 126–29. https://doi.org/10.1126/science.aam6284.

Owen Mumford. 2017. “Capillary Blood Sampling - Owen Mumford Corporate.” UK - Owen Mumford. 2017. https://www.owenmumford.com/en/healthcare-professionals/point-of-care-testing/.

Owen Mumford Ltd. 2018. “Owen Mumford: Diagnostics.” www.omdevicesolutions.com/diagnostics/.

Pachauri, R.K., and L.A. Meyer, eds. 2015. *Climate Change 2014: Synthesis Report. Contribution of Working Groups I, II and III to the Fifth Assessment Report of the Intergovernmental Panel on Climate Change*. Geneva, Switzerland: Cambridge University Press. https://www.ipcc.ch/report/ar5/syr/.

Panwar, N. L., S. C. Kaushik, and Surendra Kothari. 2011. “Role of Renewable Energy Sources in Environmental Protection: A Review.” *Renewable and Sustainable Energy Reviews* 15 (3): 1513–24. https://doi.org/10.1016/j.rser.2010.11.037.

Paramati, Sudharshan Reddy, Avik Sinha, and Eyup Dogan. 2017. “The Significance of Renewable Energy Use for Economic Output and Environmental Protection: Evidence from the Next 11 Developing Economies.” *Environmental Science and Pollution Research International; Heidelberg* 24 (15): 13546–60. http://dx.doi.org.proxy.lib.umich.edu/10.1007/s11356-017-8985-6.

Pfützner, Andreas, Petra B Musholt, Bjoern Malmgren-Hansen, Nils H Nilsson, and Thomas Forst. 2011. “Analysis of the Environmental Impact of Insulin Infusion Sets Based on Loss of Resources with Waste.” *Journal of Diabetes Science and Technology* 5 (4): 843–47. https://doi.org/10.1177/193229681100500403.

Pharmaceutical Technology. 2016. “The World’s Top Selling Diabetes Drugs.” Pharmaceutical Technology. March 29, 2016. https://www.pharmaceutical-technology.com/features/featurethe-worlds-top-selling-diabetes-drugs-4852441/.

PlasticsEurope. 2011. “Eco-Profiles and Environmental Declarations.” Version 2.0. https://www.plasticseurope.org/application/files/7415/1747/5136/eco-profile_methodology_version2-0_April2011.pdf.

“Ports in Gujarat.” n.d. Maps of India. Accessed January 3, 2020. https://www.mapsofindia.com/maps/gujarat/gujarat-port-map.html.

Pre Consultants. 2019. “Industry Data LCA Library.” SimaPro. 2019. https://simapro.com/databases/industry-data-lca-library/.

Price, David E. 1958. “Radiation as a Public Health Problem.” *Public Health Reports (1896-1970)* 73 (3): 197–202. https://doi.org/10.2307/4590082.

———. 1959. “Is Man Becoming Obsolete?” *Public Health Reports (1896-1970)* 74 (8): 693–99. https://doi.org/10.2307/4590550.

Probst, Janice C., Sarah B. Laditka, Jong-Yi Wang, and Andrew O. Johnson. 2006. “Mode of Travel and Actual Distance Traveled For Medical or Dental Care By Rural and Urban Residents.” South Carolina Rural Health Research Center. https://sc.edu/study/colleges_schools/public_health/research/research_centers/sc_rural_health_research_center/documents/61modeoftravelandactualdistancetraveled2006.pdf.

Prüss, A., E. Giroult, Philip Rushbrook, and World Health Organization, eds. 1999. *Safe Management of Wastes from Health-Care Activities*. Geneva: World Health Organization.

Rafique, M. Mujahid, Haitham M. S. Bahaidarah, and M. Khalil Anwar. 2019. "Enabling Private Sector Investment in Off-Grid Electrification for Cleaner Production: Optimum Designing and Achievable Rate of Unit Electricity." *Journal of Cleaner Production* 206 (January): 508–23. https://doi.org/10.1016/j.jclepro.2018.09.123.

"Responsibilities of Local Health Agencies for Air Pollution Control: Statement, Conference of Municipal Public Health Engineers on Air Pollution Control, October 6, 1958." 1959. *Public Health Reports (1896-1970)* 74 (2): 181–85.

Riggs, A. D. 1981. "Bacterial Production of Human Insulin." *Diabetes Care* 4 (1): 64–68. https://doi.org/10.2337/diacare.4.1.64.

Roglic, Gojka, and World Health Organization, eds. 2016. *Global Report on Diabetes*. Geneva, Switzerland: World Health Organization.

Rohokale, Bs, Vm Jadhav, and Vj Kadam. 2010. "Studies in Process Development of Metformin HCL Tablet Dosage Formulation." *International Journal of Pharmacy and Pharmaceutical Sciences* 2 (4): 80–81.

Rome, Adam. 2003. "'Give Earth a Chance': The Environmental Movement and the Sixties." *The Journal of American History* 90 (2): 525–54. https://doi.org/10.2307/3659443.

Rossi, Mark, Tracey Easthope, Ted Schettler, and Charlotte Brody. n.d. "The Green Screen: A Method for Evaluating Materials Used in Health Care Based on Toxicity and Environmental Performance at End-of-Use-Life." Health Care Without Harm. Accessed January 2, 2020. https://www.usgbc.org/drupal/legacy/usgbc/docs/LEED_tsac/HCWH_Alts_Assess_Method.pdf.

Safety and Environmental Technology Group. 2018. "Fine Chem." ETH Zurich. 2018. https://emeritus.setg.ethz.ch/research/downloads/software---tools/fine-chem.html.

SALISBURY, E. J. 1938. "PLANTS IN RELATION TO THE HUMAN ENVIRONMENT." *Science Progress (1933-)* 33 (130): 230–39.

Sanofi-Aventis. 2017. "Dosing Lantus (Insulin Glargine Injection)." Hcp. December 2017. https://www.lantus.com/hcp/dosing-injection/insulin-dose-and-dosing-calculator.

———. 2019. "Insulin Glargine | Lantus® (Insulin Glargine Injection) 100 Units/ML." Home. 2019. https://www.lantus.com/.

Santoyo-Castelazo, Edgar, Laurence Stamford, and Adisa Azapagic. 2014. "Environmental Implications of Decarbonising Electricity Supply in Large Economies: The Case of Mexico." *Energy Conversion and Management* 85 (September): 272–91. https://doi.org/10.1016/j.enconman.2014.05.051.

Saydah, Sharon. 2018. "Medication Use and Self-Care Practices in Persons with Diabetes." In *Diabetes in America, 3rd Edition | NIDDK*. National Institute of Diabetes and Digestive and Kidney Diseases. https://www.niddk.nih.gov/about-niddk/strategic-plans-reports/diabetes-in-america-3rd-edition.

Schaffartzik, Anke, Magdalena Sachs, Dominik Wiedenhofer, and Nina Eisenmenger. 2014. "Environmentally Extended Input-Output Analysis." Working Paper 154. Social Ecology Working Paper 154. Vienna: Institute of Social Ecology; Alpen-Adria Universitaet. http://folk.ntnu.no/daniemor/pdf/Schaffartzik_IntroToEEMRIO.pdf.

Schlepp, Susan. 1988. “Regulating Disposal of Infectious Waste.” *AORN Journal* 48 (4): 747,749-747,751. https://doi.org/10.1016/S0001-2092(07)69131-5.

Schowanek, Diederik, Tilly Borsboom-Patel, Alain Bouvy, John Colling, Juan Antonio de Ferrer, Diana Eggers, Karsten Groenke, et al. 2018. “New and Updated Life Cycle Inventories for Surfactants Used in European Detergents: Summary of the ERASM Surfactant Life Cycle and Ecofootprinting Project.” *The International Journal of Life Cycle Assessment* 23 (4): 867–86. https://doi.org/10.1007/s11367-017-1384-x.

Shaw, Sara, Joseph Wherton, Shanti Vijayaraghavan, Joanne Morris, Satya Bhattacharya, Philippa Hanson, Desirée Campbell-Richards, et al. 2018. “Advantages and Limitations of Virtual Online Consultations in a NHS Acute Trust: The VOCAL Mixed-Methods Study.” *Health Services and Delivery Research*, Health Services and Delivery Research, 6 (21). http://www.ncbi.nlm.nih.gov/books/NBK507677/.

Shima, Kenji, Keju Shi, Akira Mizuno, and Toshiaki Sano. 1996. “Exercise Training Has a Long-Lasting Effect on Prevention of Non—Insulin-Dependent Diabetes Mellitus in Otsuka-Long-Evans-Tokushima Fatty Rats.” *Metabolism* 45 (4): 475–80. https://doi.org/10.1016/S0026-0495(96)90222-X.

Somasundaram, Noel P., Chandrika N. Wijeyaratne, Shamya De Silva, Sisira Siribaddana, Upali Illangasekera, Henry Rajaratnam, Prasad Katulanda, et al. 2013. “Diabetes Mellitus: Glucose Control.” *Sri Lanka Journal of Diabetes Endocrinology and Metabolism* 3 (1): 45–57. https://doi.org/10.4038/sjdem.v3i1.5505.

Sri Lankan Ministry of Health. 2018. “Medical Supplies Division 2018 Estimate List.” Sri Lankan Ministry of Health. http://www.msd.gov.lk/images/stories/estimate_item_2018.xlsx.

Stichler, Jaynelle F. 2009. “Code Green.” *JONA: The Journal of Nursing Administration* 39 (2): 51–54. https://doi.org/10.1097/NNA.0b013e318197bb88.

The Emerging Risk Factors Collaboration. 2010. “Diabetes Mellitus, Fasting Blood Glucose Concentration, and Risk of Vascular Disease: A Collaborative Meta-Analysis of 102 Prospective Studies.” *The Lancet* 375 (9733): 2215–22. https://doi.org/10.1016/S0140-6736(10)60484-9.

The Home Depot Inc. 2018. “Whirlpool 25 Cu. Ft. French Door Refrigerator in Fingerprint Resistant Stainless Steel-WRF535SMHZ - The Home Depot.” Homedepot.Com. 2018. https://www.homedepot.com/p/Whirlpool-25-cu-ft-French-Door-Refrigerator-in-Fingerprint-Resistant-Stainless-Steel-WRF535SMHZ/302002378.

“The Scientific Basis Of Ventilation And Open-Air Treatment.” 1920. *The British Medical Journal* 2 (3117): 484–85.

Thiel, Cassandra, M Eckelman, R Guido, M Huddleston, AE Landis, J Sherman, SO Shrake, N Copley-Woods, and MM Bilec. 2015. “Environmental Impacts of Surgical Procedures: Life Cycle Assessment of Hysterectomy in the United States.” *ENVIRONMENTAL SCIENCE & TECHNOLOGY* 49 (3): 1779.

Thiel, Cassandra, Noe C. Woods, and Melissa M. Bilec. 2018. “Strategies to Reduce Greenhouse Gas Emissions from Laparoscopic Surgery.” *American Journal of Public Health; Washington* 108 (S2): S158–64. http://dx.doi.org.proxy.lib.umich.edu/10.2105/AJPH.2018.304397.

Thiel, CL, E Schehlein, T Ravilla, RD Ravindran, AL Robin, OJ Saeedi, JS Schuman, and R Venkatesh. 2017. “Cataract Surgery and Environmental Sustainability: Waste and Lifecycle Assessment of Phacoemulsification at a Private Healthcare Facility.” *JOURNAL OF CATARACT AND REFRACTIVE SURGERY* 43 (11): 1391.

Thyfault, John P, Mengmeng Du, William E Kraus, James A Levine, and Frank W Booth. 2015. “Physiology of Sedentary Behavior and Its Relationship to Health Outcomes.” *Medicine and Science in Sports and Exercise* 47 (6): 1301–5. https://doi.org/10.1249/MSS.0000000000000518.

Tonn, Bruce, Paul D. Frymier, Dorian Stiefel, and Leah Soro Skinner. 2014. “Toward an Infinitely Reusable, Recyclable, and Renewable Industrial Ecosystem.” *Journal of Cleaner Production* 66 (March): 392–406. https://doi.org/10.1016/j.jclepro.2013.11.008.

Trossman, Susan. 2004. “Catching the Environmental Health Wave: The ANA, Nurses Work to Improve Health Care Industry’s Impact on the Environment.” *The American Journal of Nursing* 104 (3): 73–74.

Unger, S, and A Landis. 2016. “Assessing the Environmental, Human Health, and Economic Impacts of Reprocessed Medical Devices in a Phoenix Hospital’s Supply Chain.” *JOURNAL OF CLEANER PRODUCTION* 112: 1995.

U.S. Department of Energy. 2018. “Estimating Appliance and Home Electronic Energy Use.” Energy.Gov. 2018. https://www.energy.gov/energysaver/save-electricity-and-fuel/appliances-and-electronics/estimating-appliance-and-home.

U.S. Environmental Protection Agency. 2018. “National Overview: Facts and Figures on Materials, Wastes and Recycling.” United States Environmental Protection Agency. https://www.epa.gov/facts-and-figures-about-materials-waste-and-recycling/national-overview-facts-and-figures-materials.

U.S. EPA Energy Star. 2015. “Energy Use in Medical Offices.” *United States Environmental Protection Agency*, January, 2.

US EPA, OAR. 2015. “Greenhouse Gas Equivalencies Calculator.” Data and Tools. US EPA. August 28, 2015. https://www.epa.gov/energy/greenhouse-gas-equivalencies-calculator.

Verghese, K., and H. Lewis. 2007. “Environmental Innovation in Industrial Packaging: A Supply Chain Approach.” *International Journal of Production Research* 45 (18–19): 4381–4401. https://doi.org/10.1080/00207540701450211.

VPET Plastico Industrial Co., Ltd. 2018. “Blood Collection Tube 5c.c, 13x75mm-3.4g - VPET Plastic Industrial Co., LTD.” VPET Plastico Industrial Co., Ltd. 2018. http://www.vpet-preform.com/style/Frame/m2/product_detail.asp?customer_id=2670&lang=2&content_set=color_3&name_id=129847&Directory_ID=73210&id=396623.

Watrous, R. M. 1947. “Health Hazards of the Pharmaceutical Industry.” *British Journal of Industrial Medicine* 4 (2): 111–25.

Watts, Nick, W. Neil Adger, Paolo Agnolucci, Jason Blackstock, Peter Byass, Wenjia Cai, Sarah Chaytor, et al. 2015. “Health and Climate Change: Policy Responses to Protect Public Health.” *The Lancet* 386 (10006): 1861–1914. https://doi.org/10.1016/S0140-6736(15)60854-6.

Wear, Jon. 2010. “Is Pharma Doing Enough to Reduce the Environmental Impact of Packaging?” *Pharmaceutical Technology Europe; Cheshire* 22 (11): 27.

Weenk, Mariska, Harry van Goor, Bas Frietman, Lucien JLPG Engelen, Cornelis JHM van Laarhoven, Jan Smit, Sebastian JH Bredie, and Tom H van de Belt. 2017. “Continuous Monitoring of Vital Signs Using Wearable Devices on the General Ward: Pilot Study.” *JMIR MHealth and UHealth* 5 (7). https://doi.org/10.2196/mhealth.7208.

Wernet, Gregor, Christian Bauer, Bernhard Steubing, Jürgen Reinhard, Emilia Moreno-Ruiz, and Bo Weidema. 2016. “The Ecoinvent Database Version 3 (Part I): Overview and Methodology.” *The International Journal of Life Cycle Assessment* 21 (9): 1218–30. https://doi.org/10.1007/s11367-016-1087-8.

Wernet, Gregor, Stefanie Hellweg, Ulrich Fischer, Stavros Papadokonstantakis, and Konrad Hungerbühler. 2008. “Molecular-Structure-Based Models of Chemical Inventories Using Neural Networks.” *Environmental Science & Technology* 42 (17): 6717–22. https://doi.org/10.1021/es7022362.

Wernet, Gregor, Stavros Papadokonstantakis, Stefanie Hellweg, and Konrad Hungerbühler. 2009. “Bridging Data Gaps in Environmental Assessments: Modeling Impacts of Fine and Basic Chemical Production.” *Green Chemistry* 11 (11): 1826–31. https://doi.org/10.1039/B905558D.

Wernick, Iddo Kalir, Frances H Irwin, and World Resources Institute. 2005. *Material Flows Accounts: A Tool for Making Environmental Policy*. Washington, DC: World Resources Institute. http://pdf.wri.org/WRI_MFA_Policy.pdf.

“WHO | Noncommunicable Diseases.” 2018. WHO. June 1, 2018. http://www.who.int/mediacentre/factsheets/fs355/en/.

Wickramasinghe, Sumudu I, Liam J Caffery, Natalie K Bradford, and Anthony C Smith. 2016. “Enablers and Barriers in Providing Telediabetes Services for Indigenous Communities: A Systematic Review.” *Journal of Telemedicine and Telecare* 22 (8): 465.

Wijesuriya, MahendraArunashanthi, JessicaLynn Sandy, ChamariLalani Warnapura, AngelaC Middlehurst, and GrahamD Ogle. 2019. “Characteristics of Insulin Registry Patients with Type 1 Diabetes in Sri Lanka.” *Journal of Diabetology* 10 (1): 37. https://doi.org/10.4103/jod.jod_26_18.

Wirecutter. 2018. “The Best Refrigerators.” Wirecutter: Reviews for the Real World. May 21, 2018. https://thewirecutter.com/reviews/the-best-refrigerator/.

Wirtz, Veronika, Ryan Knox, Chenzhe Cao, Hedieh Mehrtash, Nathaniel Posner, and Jane McClenathan. 2016. “Insulin Market Profile.” Amsterdam: Health Action International. http://haiweb.org/wp-content/uploads/2016/04/ACCISS_Insulin-Market-Profile_FINAL.pdf.

World Bank. 2017. “Sri Lanka | Data.” The World Bank| Data. 2017. https://data.worldbank.org/country/sri-lanka.

———. 2019a. “Diabetes Prevalence (% of Population Ages 20 to 79) | Data.” 2019. https://data.worldbank.org/indicator/SH.STA.DIAB.ZS.

———. 2019b. “World Bank Country and Lending Groups – World Bank Data Help Desk.” 2019. https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-world-bank-country-and-lending-groups.

World Health Organization. 2014. “Global Health Expenditure Database.” Global Health Expenditure Database. 2014. https://apps.who.int/nha/database/Select/Indicators/en.

———. 2016a. “Life Expectancy.” WHO. 2016. http://www.who.int/gho/mortality_burden_disease/life_tables/situation_trends/en/.

———. 2016b. “World Health Organization- Diabetes Country Profiles: Sri Lanka.” http://www.searo.who.int/srilanka/lka_en.pdf?ua=1.

World Steel Association. 2017. *Life Cycle Inventory Methodology Report*. https://www.worldsteel.org/en/dam/jcr:6eefabf4-f562-4868-b919-f232280fd8b9/LCI%2520methodology%2520report_2017_vfinal.pdf.

Worton, K. S. 1995. “Green Medicine. Environmental Impact of Health Care.” *Canadian Family Physician* 41 (June): 977–80.

Yao, Shujie, Shuai Zhang, and Xingmin Zhang. 2019. “Renewable Energy, Carbon Emission and Economic Growth: A Revised Environmental Kuznets Curve Perspective.” *Journal of Cleaner Production* 235 (October): 1338–52. https://doi.org/10.1016/j.jclepro.2019.07.069.

Zgibor, Janice C., and Thomas J. Songer. 2001. “External Barriers to Diabetes Care: Addressing Personal and Health Systems Issues.” *Diabetes Spectrum* 14 (1): 23–28. https://doi.org/10.2337/diaspect.14.1.23.

Zimmer, Catherine, and Deb McKinley. 2008. “New Approaches to Pollution Prevention in the Healthcare Industry.” *Journal of Cleaner Production* 16 (6): 734–42. https://doi.org/10.1016/j.jclepro.2007.02.014.

10 Appendix A:

Table 7: Description of the main characteristics of available tools of environmental analysis. Table sourced from the book Environmental Life Cycle Assessment cited as (Jolliet et al. 2015)

Main Characteristics of Environmental Analysis Tools

Tool	Object of Study	Scale and Scope	Considered Substances and Impacts	Basis for Comparison	Basic Elements
Life cycle assessment (LCA)	Product or service	Global or regional Entire life cycle	Many substances Multiple impacts on humans and ecosystems	Function of the product or service	Mass balance Multimedia model Effects assessment
Substance flow analysis (SFA)	Polluting substance	Regional or global Substance cycle	Single substance No impact	Given time and region	Mass balance Multimedia model
Risk assessment (RA)	Installation or chemical substance	Local or regional Selected stage	Relevant substances Toxicity	Maximum level of risk	Multimedia model Effects assessment
Material flow analysis (MFA)	Raw material or compound	Regional or national Material life cycle	Single or multiple material No impact	Given time and region	Mass balance Material flow tracking
Carbon footprint (CF)	Product, activity, or company	Global Entire life cycle	Greenhouse gases Climate change	Product function, activity, or company	Mass balance Global warming potential
Water footprint (WF)	Product, activity, or company	Local or regional Most important life cycle stages	Water consumed and water-related exposure Water quantity and quality-related impacts	Product function, activity, or company	Water balance Consumption Competition Adaptation
Environmental impact assessment (EIA)	New localized activity	Local scale Local activity	Highly variable	Local carrying capacity	Highly variable

Table 8: Describes the advantages and disadvantages of process-based LCA, also refered to as Standard LCA and EIO-LCA methods. The table is sourced from the book Environmental Life Cycle Assessment, cited as

	Process-Based LCA	EIO-LCA
Advantages	results are detailed, process specific	results are economy-wide, comprehensive assessments
	allows for specific product comparisons	allows for systems-level comparisons
	identifies areas for process improvements, weak point analysis	uses publicly available, reproducible results
	provides for future product development assessments	provides for future product development assessments
		provides information on every commodity in the economy
Disadvantages	setting system boundary is subjective	product assessments contain aggregate data
	tend to be time intensive and costly	process assessments difficult
	difficult to apply to new process design	must link monetary values with physical units
	use proprietary data	imports treated as products created within economic boundaries
	cannot be replicated if confidential data are used	availability of data for complete environmental effects
	uncertainty in data	difficult to apply to an open economy (with substantial non-comparable imports)
		uncertainty in data

11 Appendix B. Detailed Data Inventory

11.1 Sri Lanka Standard LCA Inventory

11.1.1 Sri Lanka: Insulin Production

11.1.1.1 *Insulin Production Inventory*

Component Description	Measurement/ Functional Unit	Data Source	SimaPro Inventory Description
Energy Input-Natural Gas	18.33 MJ	(Wernet et al. 2008) (Wernet et al. 2009) (Cespi et al. 2015), Pubchem	Combustion of natural gas, consumption mix, at plant/NL Energy
Energy Input – Electricity	13.93 MJ		Electricity, medium voltage {IN-Western grid}| market for electricity, medium voltage | APOS, U
Energy Input-Steam	4.40 MJ		Process steam from natural gas, heat plant, consumption mix, at plant, MJ EU-27 S
Tryptone	1211 g	(Hwang et al. 2016; Gusarov et al. 2015)	Unable to find a suitable equivalent in SimaPro. Therefore not included in model.
Yeast Extract	605.5 g		Protein feed, 100% crude {GLO}| fodder yeast to generic market for protein feed | APOS, U
Sodium Chloride	605.5 g		Sodium chloride, at plant/RNA
Dipotassium phosphate	605.5 g		Sodium phosphate {RER}| production | APOS, U
Water	249.6 g		Water, ultrapure {GLO}| market for | APOS, U
Urea	58.12 g		Urea, as N {RER}| production | APOS, U
Tris	1.1 g		Unable to find a suitable equivalent in SimaPro. Therefore not included in model.
EDTA	0.04 g		EDTA, ethylenediaminetetraacetic acid {RER}| EDTA production | APOS, U
Dithiothreitol (reductant)	0.19 g		Unable to find a suitable equivalent in SimaPro. Therefore not included in model.
NaOH	4.84 g		Sodium hydroxide, without water, in 50% solution state {RER}| chlor-alkali electrolysis, diaphragm cell | APOS, U
Acetic Acid	7.27 g		Acetic acid, without water, in 98% solution state {RER}| acetic acid production, product in 98% solution state | APOS, U
Trypsin	0.44 g		Enzymes {RER}| enzymes production | APOS, U

Hypersil BDS C-18 (Sorbent)	868.89 g		Activated silica {GLO}| market for | APOS, U
Citric Acid	0.23 g		Citric acid {RER}| production | APOS, U
Zinc	0.002 g		Zinc, special high grade/GLO
Glycerine	2.02 g		Glycerine {GLO}| market for | APOS, U
Metacresol	0.32 g		Unable to find a suitable equivalent in SimaPro. Therefore not included in model.
Cardboard Package	25.84 g	Manual Measurement	Folding boxboard/chipboard {GLO}| market for | APOS, U
Glass Vial 10 ml	73.67 g		Glass tube, borosilicate {GLO}| market for | APOS, U
Aluminum Top	1.75 g		Aluminum ingot, production mix, at plant/US
Rubber Stopper on Top	2.14 g		Seal, natural rubber based {DE}| production | APOS, U
Plastic Stopper	0.71 g		PET, bottle grade, at plant/RER
Paper Insert	13.0 g		Graphic paper, 100% recycled {RER}| production | APOS, U
Refrigerated Lorry from Indrad, Gujarat to Kandla Port	0.08 tkm	(Ganguly 2017; BioPharm International Editors 2017), Google Maps	Transport, freight, lorry with refrigeration machine, 3.5-7.5 ton, EURO3, R134a refrigerant, cooling {GLO}| transport, freight, lorry with refrigeration machine, 3.5-7.5 ton, EURO3, R134a refrigerant, cooling | APOS, U
Refrigerated Shipping Container from Kandla Port to Colombo Port	0.66 tkm	Ports.com	Transport, freight, sea, transoceanic ship with reefer, cooling {GLO}| market for | APOS, U
Waste-Landfill	0.32 g	Manual Measurement	Inert waste, for final disposal {RoW}| market for inert waste, for final disposal | APOS, U

11.1.1.2 *Insulin Production Assumptions*

- Functional Unit: 365 days/1 Type 2 diabetes patient with no medical complications.
- The mass and amount of insulin used in this study was derived from first the Sri Lankan government's Ministry of Health 2018 Medical Procurement list. This list provided the type and size of insulin sought by the government. For this study it is assumed that the Ministry of Health is providing patients with a form of Isophane Human Insulin (Sri Lankan Ministry of Health 2018). As this is a human insulin it is manufactured from recombinant DNA (Riggs 1981) and it is therefore assumed that the production process is largely the same as that for insulin glargine. As such the process listed below is that which is assumed to be used in the production of insulin glargine.

- The notable differences between the production of insulin used in Sri Lanka versus that which is used in the United States are containers in which they are stored and the locations where they are manufactured. The insulin procured by the Sri Lankan government is primarily stored in 10 mL glass vials (Sri Lankan Ministry of Health 2018).
- It is assumed that the insulin used in Sri Lanka is primarily being manufactured in India. Many large insulin producers have partnered with local Indian firms to expand insulin production (Wirtz et al. 2016). Novo Nordisk, the manufacturer of the low-cost Novolin R insulin has a partnership with the Indian pharmaceutical firm, Torrent Pharmaceuticals, to manufacture the medication at their Gujarat facility (BioPharm International Editors 2017; Ganguly 2017). This study assumes that the insulin used in the Sri Lankan models is being transported from Gujarat to Colombo, Sri Lanka on a combination of refrigerated lorries and shipping containers. The decision to model the transportation from the port of Kandla was based on an assessment that this port is the largest in the region for international shipping ("Ports in Gujarat" n.d.). A Google Map search yielded a distance of 295.7 km from the city of Indrad to the port of Kandla. The distance between the Kandla port and the Port of Colombo is assumed to be 1395 nautical miles as estimated by the website ports.com.
- The daily dosage is assumed to be 34.62 units of insulin. This dosage is based on the dosing recommendations of 0.4-1.0 units/kg or more for patients with Type 2 diabetes by the Endocrine Society of Sri Lanka (Somasundaram et al. 2013). This study assumes a mid-range value of 0.6 units/kg.
- Per the insulin container label, a vial of 10 mL of insulin contains 100 units/mL for a total of 1000 units of insulin.
- Manual measurements indicated a mass of 24.584 g/vial
- To calculate the energy used in the manufacturing process of the insulin a total energy estimate was derived using the FineChem tool. Designed by the Safety and Environmental Technology Group within ETH Zurich the FineChem tool uses the molecular structure of a compound to estimate the energy needs and environmental impacts of that molecule's production. While the tool was originally designed for the petrochemical industry, it serves to provide a rough estimate of energy use in the absence of process data. A full description of the workings of the tool are available on the Fine Chem website and on the tools associated published papers (Wernet et al. 2008; 2009; Safety and Environmental Technology Group 2018). All molecular data used in the calculations were sourced from PubChem. The FineChem tool estimated the total energy use to produce insulin glargine at 758.6 MJ/kg. The breakdown of the types of energy used in this total was established using the work by Cespi, et al (Cespi et al. 2015). This study indicated an energy breakdown in pharmaceutical production of 50% natural gas, 38% electricity and 12% steam. These proportions were used in the study's calculations.
- In the absence of direct process data of the insulin glargine and/or insulin isophane production process, this study recreated the production process using the process data published by Gusarov, et al. in their paper, Systematic Approach to Production Technology Development for Therapeutic Proteins (Using Insulin-Glargine As An Example), and Hwang, et al.'s published paper, Recombinant Glargine Insulin Production Process Using Escherichia coli.

- Waste disposal modeling is based off of the assumption that the packaging used to transport the insulin is disposed of in landfill. Without published data indicating waste by-products from the insulin production process, this scenario does not account for waste generated during the production process. This assumption is based on observed disposal methods used by Type 2 diabetes patients in Sri Lanka.

11.1.2 Insulin Use

11.1.2.1 *Insulin Use Inventory*

Component Description	Measurement/Functional Unit	Data Source	SimaPro Inventory Description
Syringe	992.8 g	Manual Measurement	Polypropylene granulate (PP), production mix, at plant RER; Injection molding, rigid polypropylene part, at plant/kg/RNA
Needle	1.095 g	Manual Measurement	Steel, stainless 304, flat rolled coil/kg/RNA; Wire drawing, steel {RER}| processing | APOS, U
Lorry	0.38 tkm	Google Maps	Transport, light commercial truck, gasoline powered/tkm/RNA
Sea Shipping	1.65 tkm		Transport, freight, sea, transoceanic ship {GLO}| market for | APOS, U
Waste-Landfill	993.86 g	Manual Measurement	Inert waste, for final disposal {RoW}| market for inert waste, for final disposal | APOS, U

11.1.2.2 *Insulin Use Assumptions*

- Functional Unit: 365 days/1 Type 2 diabetes patient with no medical complications.
- Assumes one injection a day
- Assumes the syringe and needle are one, single-use unit.
- 1 ml is assumed to be the standard size of a syringe used to inject insulin based on feedback from general searches for insulin injection syringes.
- Assumed production in Aurangabad, Maharashtra, India. This assumption was based on an article by India's Business Today (Kaushik et al. 2008) which lists Mumbai as a growing hub for pharmaceutical production. As such, it was assumed there would be a growing market for ancillary pharmaceutical products, such as syringes, developing in this market as well.
- Sea shipping is inclusive of a one-way trip from the port of Mumbai (Jawaharlal Nehru Port) to the Colombo Port.
- Ground transportation is inclusive of a one-way trip from Aurangabad, Maharashtra to the port of Mumbai.

- Waste disposal modeling is based off of the assumption that households are disposing of their needles and syringes in a community landfill. Observations of Type 2 diabetes patients in Sri Lanka indicated that disposal of diabetes supplies along with standard municipal solid waste is a common practice, as is on-site incineration, with many families incinerating their medical waste along with household waste. For the purposes of this study it was decided to model an inert landfill option. It is worth considering that incineration disposal is also a common method.

11.1.3 Sri Lanka: Metformin Production

11.1.3.1 *Metformin Production Inventory*

Component Description	Measurement/ Functional Unit	Data Source	SimaPro Inventory Description
Natural Gas	22.6332394 MJ-eq/mg	(Wernet et al. 2008) (Wernet et al. 2009), (Safety and Environmental Technology Group 2018), (Cespi et al. 2015)	Natural gas, low pressure {RoW}| market for | APOS, U
Electricity	17.2012619 MJ-eq/mg		Electricity, low voltage {IN-Southern grid}| market for electricity, low voltage | APOS, U
Steam	5.43197745 MJ-eq/mg		Heat, from steam, in chemical industry {RoW}| market for heat, from steam, in chemical industry | APOS, U
Dicyandiamide	407431.3 mg	(Rohokale, Jadhav, and Kadam 2010)	Dimethylacetamide {GLO}| market for | APOS, U
Dimethylamine Hydrochloride	488917.5 mg		Dimethylamine {GLO}| market for | APOS, U
Cyclohexanol	162972.5 mg		Cyclohexanol {GLO}| market for | APOS, U
Ethanol	206294.3 mg		Ethanol, without water, in 95% solution state, from fermentation {BR}| cane sugar production with ethanol by-product | APOS, U
Package	304.2 g	Manual measurement	Polyethylene, HDPE, granulate, at plant/RER; Injection molding, rigid polypropylene part, at plant/kg/RNA
Lorry	2.19298E-08 tkm	Google Maps	Transport, freight, light commercial vehicle {GLO}| market for | APOS, U
Sea Shipping	5.01633E-09 tkm		Transport, freight, sea, transoceanic ship {GLO}| market for | APOS, U

11.1.3.2 *Metformin Production Assumptions*

- Functional Unit: 365 days/1 Type 2 diabetes patient with no medical complications.

- Sri Lankan T2D patients are assumed to use 1500 mg of Metformin daily. This is based upon dosing recommendations provided by the Sri Lankan Endocrine Society's Clinical Guidelines (Somasundaram et al. 2013). This document provides a range of dosing recommendations. The higher end of the range is selected based on feedback from Sri Lankan physicians and patients who stated that they patients generally prefer higher doses of oral medication as opposed to insulin treatments or in many cases, lifestyle adjustments. This preference generally results in patients requiring very high doses of medication.
- It should be noted that both interviews and published literature have established a precedent that patients often find it difficult to take their oral medication daily (Cramer 2004). However, given that daily medication use is often a prerequisite to treating diabetes without complications, this study assumes adherence to a daily dosage schedule.
- The production process modeled in this study is based on the process outlined in Rohokale, Jadhav et Kadam's 2010 paper on metformin process development (Rohokale, Jadhav, and Kadam 2010). It is acknowledged that there are a variety of production methods to produce pharmaceutical quality metformin hydrochloride and that the type of production process may influence scenario outcomes.
- Assumed production in Aurangabad, Maharashtra, India. This assumption was based on an article by India's Business Today (Kaushik et al. 2008) which lists Mumbai as a growing hub for pharmaceutical production.
- Sea shipping is inclusive of a one-way trip from the port of Mumbai (Jawaharlal Nehru Port) to the Colombo Port.
- Ground transportation is inclusive of a one-way trip from Aurangabad, Maharashtra to the port of Mumbai.
- To calculate the energy used in the manufacturing process of the metformin a total energy estimate was derived using the FineChem tool. Designed by the Safety and Environmental Technology Group within ETH Zurich the FineChem tool uses the molecular structure of a compound to estimate the energy needs and environmental impacts of that molecule's production. While the tool was originally designed for the petrochemical industry, it serves to provide a rough estimate of energy use in the absence of process data. A full description of the workings of the tool are available on the Fine Chem website and on the tools associated published papers (Wernet et al. 2008; 2009; Safety and Environmental Technology Group 2018). All molecular data used in the calculations were sourced from PubChem. The FineChem tool estimated the total energy use to produce metformin at 145 MJ/kg. The breakdown of the types of energy used in this total was established using the work by Cespi, et al (Cespi et al. 2015). This study indicated an energy breakdown in pharmaceutical production of 50% natural gas, 38% electricity and 12% steam. These proportions were used in the study's calculations.
- Where possible, energy production values for India were selected in the SimaPro program.
- In the absence of published data on waste disposal methods during the metformin production process a waste process was not specifically modeled.

11.1.4 Sri Lanka: Doctor Visit

11.1.4.1 *Doctor Visit Inventory*

Component Description	Measurement/ Functional Unit	Data Source	SimaPro Inventory Description
Rubber Gloves (Set of 2)	120 g	Manual Measurement	Acrylonitrile butadiene styrene (ABS)/EU-27; Thermoforming, with calendering {RER}| production | APOS, U
Additive k2EDTA	.028 g	(Fischer Scientific 2018)	EDTA, ethylenediaminetetraacetic acid {GLO}| market for | APOS, U
Plastic Container for Reagent Disk	68.81 g	(Abaxix, Inc. 2014)	Polyethylene, HDPE, granulate, at plant/RER; Blow moulding {GLO}| market for | APOS, U
Needle for Blood Draw	.03 g	Manual Measurement	Steel, stainless 304, flat rolled coil/kg/RNA; Wire drawing, steel {RoW}| processing | APOS, U
Plastic Tube for Blood Draw	13.6 g	(VPET Plastico Industrial Co., Ltd. 2018)	Polyethylene terephthalate (PET) granulate, production mix, at plant, bottle grade RER; Extrusion of plastic sheets and thermoforming, inline {GLO}| market for | APOS, U
Electricity for Blood Sugar Test	0.033 kWh	Referenced from US Army Medical Material Agency	Electricity, low voltage {RoW}| market for | APOS, U
Transportation to the Clinic	5.76 person/km	(Govindaraj et al. 2014)	Transport, intercity bus, diesel powered/personkm/RNA
Waste-Incineration	30.6 g	(Athapattu, Priyantha, and Tateda 2015)	Municipal solid waste {RoW}| market for | APOS, S (Incineration)

11.1.4.2 *Doctor Visit Assumptions*

- Functional Unit: 365 days/1 Type 2 diabetes patient with no medical complications.
- Assumes 12 clinic visits a year or one every month. The frequency of visits is required based on the requirement in Sri Lanka that if a patient receives free diabetes medication from the government (a previous assumption of this study), that the patient must have that prescription renewed each month.
- The inventory list used in this model is based on personal observations of three government-sponsored diabetes clinics located in the country's Eastern Province. Two of the clinics were located in the Trincomalee Regional Hospital, while a third clinic was located in a small local health care facility outside of Trincomalee.
- Observations indicated that the amount of electricity used during the exam period was quite negligible. The hospital/clinic settings were designed to be passively cooled with no central air systems and windows provided natural sunlight in place of electricity. While doctors did use computers to re-order prescriptions for patients, it was not possible to obtain electric records to

verify the energy use of these machines. As physicians may see between 50 and 70 patients a day, the energy intensity of the computer use per patient was deemed to be small enough that it was emitted from this model.

- The observed clinics did not have resources to do on-site blood glucose testing. Interviews with doctors indicated that most public diabetes clinics do not have this capability. Diabetic patients are instructed to receive a lab blood test with blood glucose as an output of the test. The printed results are then taken by the patient to the appointment and reviewed prior to the reauthorization of any prescriptions. These tests are modeled above.
- Published studies on medical waste disposal in Sri Lankan healthcare facilities notes the prevalence of various incineration practices as a primary means of waste disposal. As the incineration of medical waste specifically is not modeled any of the associated SimaPro databases, a general incineration model was applied to simulate the disposal of contaminated waste generated in the course of a doctor visit.

11.2 United States Standard LCA Inventory

11.2.1 United States: Glucose Meter

11.2.1.1 *Glucose Meter Inventory*

Component Description	Measurement/Functional Unit	Data Source	SimaPro Inventory Description
Circuit	1.32056 g	Manual Measurement	Integrated circuit, memory type {GLO}| market for | Alloc Def, U
Screen	0.71966 g		Panel glass, for cathode ray tube display {GLO}| market for | APOS, U
Outer Case	2.35792 g		Injection molding, rigid polypropylene part, at plant/kg/RNA
Circuit (Under Buttons)	0.2314 g		Integrated circuit, logic type {GLO}| market for | APOS, U
Metal Clip	0.06952 g		Brass {CH}| market for brass | APOS, U; Casting, brass {CH}| processing | APOS, U
Small Metal Clip	0.04332 g		Brass {CH}| market for brass | APOS, U; Casting, brass {CH}| processing | APOS, U
Plastic Cover	0.03402 g		Injection molding, rigid polypropylene part, at plant/kg/RNA
Battery- Oral meds	2.22478 g	(Abbott 2016)	Battery cell, Li-ion {GLO}| market for | APOS, U
Battery- Insulin	6.67424 g		Battery cell, Li-ion {GLO}| market for | APOS, U

Packaging	7.4 g	Manual Measurement	Carton board box production, with offset printing {RoW}| carton board box production service, with offset printing | APOS, U
Paper Insert	21.2 g		Graphic paper, 100% recycled {GLO}| market for | APOS, U
Carrying Bag	5.8 g		Textile, woven cotton {GLO}| production | APOS, U
Ship Transportation	0.42919 tkm	Google Maps	Transport, freight, sea, transoceanic ship {GLO}| market for | APOS, U
Truck Transportation	0.1472562 tkm		Transport, combination truck, diesel powered/US
Waste- Landfill	6.17 g	Manual Measurement	Inert waste, for final disposal {RoW}| market for inert waste, for final disposal | APOS, U

11.2.1.2 *Glucose Meter Assumptions*

- Functional Unit: 365 days/1 Type 2 diabetes patient with no medical complications.
- The glucose meter modeled in this study is a Freestyle Lite meter manufactured by Abbott. The Freestyle Lite meter was modeled given the relative ubiquity among glucose meter design and functioning, and the author's ability to access a number of devices for deconstruction.
- Based on the information provided in the user manual it was assumed that the meter has a use life of five years or 1825 days.
- Two different battery scenarios were used. Both were based on published Medicare guidelines. Medicare guidelines are considered to be the standard of care in the United States for the purposes of this study. Medicare coverage allows for 100 test strips every 90 days for someone on oral medication (Centers for Medicare and Medicaid Services 2017a). This equates to approximately one test every day with some additional strips left over for contingencies. For patients on insulin treatments Medicare allows for 300 test strips every 90 days which equates to approximately three tests every day with some additional strips left over for contingencies (Centers for Medicare and Medicaid Services 2017a).
- An estimated battery life of 500 tests based on information provided in the user manual (Abbott 2016).
- The Freestyle Lite packaging indicates that the device is manufactured in China. However, it does not specify where in China. Without a specific location this study assumes production is located in the Shenzhen province and then shipped to Long Beach port in California. From there it is trucked to Ann Arbor, Michigan.
- This study assumed that patients dispose of their glucose meter as an electronic device. The United States Environmental Protection Agency reports that Americans recycle approximately 40% of selected consumer electronics (U.S. Environmental Protection Agency 2018). As this is less than half of all produced electronics it was assumed for this study that glucose meters

would be included with standard municipal solid waste landfill disposal in the majority of households.

11.2.2 United States: Test Strips

11.2.2.1 *Test Strip Inventory*

Component Description	Measurement/ Functional Unit (Insulin)	Measurement/ Functional Unit (Oral Meds)	Data Source	SimaPro Inventory Description
Base A	66.2475 g	22.0825 g	Manual Measurement; (Abbott Diabetes Care Inc. 2015)	Polyester resin, unsaturated {GLO}| market for | APOS, U; Injection moulding {RER}| processing | APOS, U
Base B	67.5615 g	22.5205 g		Polyester resin, unsaturated {GLO}| market for | APOS, U; Injection moulding {RER}| processing | APOS, U
Glucose Oxidase Enzyme	0.0219 g	0.0073 g	(Fernandes et al. 2016)	Enzyme, Glucoamylase, Novozyme Spirizyme/kg/RER
Co-Enzyme Flavine Adenine Dinucleotide	0.0219 g	0.0073 g		Enzyme, Alpha-amylase, Novozyme Liquozyme/kg/RER
Mediator-Ferricyanide	0.0219 g	0.0073 g	(Loew et al. 2017)	Sodium cyanide {GLO}| market for | APOS, U
Indicator-Silver	0.0219 g	0.0073 g	(Fernandes et al. 2016)	Silver {GLO}| market for | APOS, U
Indicator-Carbon	0.0219 g	0.0073 g		Carbon black {GLO}| market for | APOS, U
Plastic Tube Package	2.409 g	0.803 g	Manual Measurement	Polyethylene, high density, granulate {CH}| polyethylene, high density, granulate, recycled to generic market for high density PE granulate | APOS, U; Injection moulding {GLO}| market for | APOS, U
Cardboard Package	1.2180 g	0.406 g		Folding boxboard/chipboard {GLO}| market for | APOS, U
Transportation Ship	2.7319E-10 tkm	9.1064E-11 tkm	Google Maps	Transport, freight, sea, transoceanic ship {GLO}| market for | APOS, U

Transportation Truck	1.3662E-09 tkm	4.5541-10 tkm		Transport, combination truck, long-haul, diesel powered, East North Central/tkm/RNA
Waste-Landfill	133.92 g	44.64 g	Manual Measurement	Inert waste, for final disposal {RoW}| market for inert waste, for final disposal | Cut-off, U

11.2.2.2 *Test Strips Assumptions*

- Functional Unit: 365 days/1 Type 2 diabetes patient with no medical complications.
- The test strips used in this study are the Abbott Freestyle Lite test strips made for use with the Freestyle Lite glucose meter.
- The number of test strips modeled required two different scenarios to account for a difference in allowed allocation by Medicare based on whether or not a patient is managing their diabetes with oral medication or insulin. Medicare guidelines are considered to be the standard of care in the United States for the purposes of this study. Medicare coverage allows for 100 test strips every 90 days for someone on oral medication (Centers for Medicare and Medicaid Services 2017a). This equates to approximately one test every day with some additional strips left over for contingencies. For patients on insulin treatments Medicare allows for 300 test strips every 90 days which equates to approximately three tests every day with some additional strips left over for contingencies (Centers for Medicare and Medicaid Services 2017a).
- The composition of the test strips base layer is assumed to be polyester as described in a published white paper by the strip's manufacturer, Abbott Diabetes Care Inc (Abbott Diabetes Care Inc. 2015).
- This model assumes the electrode materials of this test strip are comprised of silver and carbon (Abbott Diabetes Care Inc. 2015).
- Regarding the additional enzymes and reactant materials used in the test strip, it was not feasible to conduct an analysis to determine the exact amount of each material used in the adhesive and electrodes of the test strip. Given that the combined mass of these materials is so small (>.001 g) an approximate mass was estimated by dividing the balance of the test strip mass (after subtracting the known elements) among the five additional inputs.
- In most cases it was not possible to find an exact equivalent for the enzyme and mediator materials used in test strip production. In these cases, an effort was made to select like materials that share similarities in production processes.
- As published on the Abbott website, the company produces its Freestyle Lite test strips at its Donegal facility in Ireland (Abbott Ireland Diabetes Care 2019).
- The waste treatment scenario included in this model assumes that patients are disposing of their glucose test strips as medical waste. Interviewed medical professionals all recommend disposing of used test strips in a sealed medical waste container. These containers are then disposed of with standard municipal solid waste. This practice aligns with several dozen

reviewed online diabetes community discussion boards where patients documented their methods for disposing of diabetes-related waste.

11.2.3 United States: Lancet

11.2.3.1 *Lancet Inventory*

Component Description	Measurement/ Functional Unit (Insulin)	Measurement/ Functional Unit (Orals)	Data Source	SimaPro Inventory Description
Needle	249.66 g	83.22 g	Manual Measurement	Steel, stainless 304, flat rolled coil/kg/RNA; Deep drawing, steel, 10000 kN press, automode {GLO}| market for | APOS, U
Plastic Casing	517.856 g	172.61 g		Packaging film, low density polyethylene {GLO}| market for | Conseq, S; Injection moulding {GLO}| market for | Conseq, U
Packaging	186.15 g	62.05 g		Folding boxboard/chipboard {GLO}| market for | APOS, U
Truck Transportation	8.2694E-06 tkm	2.7564E-06 tkm	Google Maps	Transport, combination truck, diesel powered/US
Waste-Landfill	767.4855 g	255.8285 g	Manual Measurement	Inert waste, for final disposal {RoW}| market for inert waste, for final disposal | Cut-off, U

11.2.3.2 *Lancet Assumptions*

- Functional Unit: 365 days/1 Type 2 diabetes patient with no medical complications.
- The use phase for the lancets occurs in Ann Arbor, Michigan, transportation via truck from the production facility is assumed.
- The company Facet Medical Technologies in Atlanta, Georgia is a producer of lancets. It is assumed their production facility in Georgia is where the lancets used in this study are manufactured.
- The number of lancets modeled required two different scenarios to account for a difference in allowed allocation by Medicare based on whether or not a patient is managing their diabetes with oral medication or insulin. Medicare guidelines are considered to be the standard of care in the United States for the purposes of this study. Medicare coverage allows for 100 lancets every 90 days for someone on oral medication (Centers for Medicare and Medicaid Services 2017a). This equates to approximately one lancet for one glucose test every day with some additional lancets left over for contingencies. For patients on insulin treatments Medicare allows for 300 lancets every 90 days which equates to approximately three lancets for three blood glucose tests every day with some additional lancets left over for contingencies (Centers for Medicare and Medicaid Services 2017a).
- Assumes one lancet for every blood glucose test.
- The waste treatment scenario included in this model assumes that patients are disposing of their used lancets as medical waste. Interviewed medical professionals all recommend disposing

of used lancets as one would a used needle, in a sealed medical waste container. These containers are then disposed of with standard municipal solid waste. This practice aligns with several dozen reviewed online diabetes community discussion boards where patients documented their methods for disposing of diabetes-related waste.

11.2.4 United States: Lancing Device

11.2.4.1 *Lancing Device Inventory*

Component Description	Measurement/ Functional Unit	Data Source	SimaPro Inventory Description
Wheel	0.30945 g	Manual Measurement	Polyethylene, high density, resin, at plant, CTR/kg/RNA; Injection moulding {RER}| processing | APOS, U
Outer Part- Back	1.3296 g		Injection moulding {RER}| processing | APOS, U; Polyethylene, high density, resin, at plant, CTR/kg/RNA
Outer Part- Front	1.3025 g		Polyethylene, high density, resin, at plant, CTR/kg/RNA; Injection moulding {RER}| processing | Conseq, U
Protective Cover	0.9011 g		Injection moulding {RER}| processing | Conseq, U; Polyethylene, high density, resin, at plant, CTR/kg/RNA
Thumb Part- Female	0.45015 g		Polyethylene, high density, resin, at plant, CTR/kg/RNA; Injection moulding {RER}| processing | APOS, U
Thumb Part- Male	0.50195 g		Injection moulding {RER}| processing | APOS, U; Polyethylene, high density, resin, at plant, CTR/kg/RNA
Spring Container	0.75785 g		Polyethylene, high density, resin, at plant, CTR/kg/RNA; Injection moulding {RER}| processing | APOS, U
Small Spring	0.1041 g		Steel, stainless 304, flat rolled coil/kg/RNA; Wire drawing, steel {RoW}| processing | APOS, U
Big Spring	0.0462 g		Wire drawing, steel {RoW}| processing | APOS, U; Steel, stainless 304, flat rolled coil/kg/RNA
Cardboard Package	10 g		Folding boxboard/chipboard {GLO}| market for | APOS, U
Paper Insert	3 g		Paper, freesheet, coated, average production, at mill/kg/RNA
Truck Transportation (Oxford to Tilbury Port)	9.92655E-10 tkm	Google Maps	Transport, freight, sea, transoceanic ship {GLO}| market for | APOS, U
Ship Transportation (Tilbury Port to	2.78162E-11 tkm		Transport, freight, lorry 16-32 metric ton, EURO3 {GLO}| market for | APOS, U

NY Container Port)			
Truck Transportation (NY Container Port to Ann Arbor)	1.56856E-10 tkm		Transport, combination truck, diesel powered/US
Waste-Landfill	5.7 g	Manual Measurement	Inert waste, for final disposal {RoW}| market for inert waste, for final disposal | Cut-off, U

11.2.4.2 *Lancing Device Assumptions*

- Functional Unit: 365 days/1 Type 2 diabetes patient with no medical complications.
- As per the specifications in the User Manual, this study assumes a use life of two years or 730 days. All calculations to derive the amount of material attributed to a single day are made based on this assumption (Abbott 2016).
- Per standard use conventions in the United States, it is assumed that the lancing device is used by only one individual.
- To determine the components and materials used in the construction of the device the lancing device was manually taken apart and measured.
- There are many different types of lancing devices available to consumers. A popular model is produced by Own Mumford in Oxfordshire, UK and this production facility is used to calculate distance traveled in this mode (Owen Mumford 2017).
- It is assumed the use phase takes place in Ann Arbor, Michigan and that the product will be shipped from the closes largest port, the Tilbury Port and will arrive at the closest largest port in the U.S., the NY Container Port. From the container port it is assumed the produce is taken via truck to Ann Arbor, Michigan.
- The waste scenario for the lancing device assumes that the used device is not considered biohazardous or medical waste and that it is disposed of along with standard municipal solid waste.

11.2.5 United States: Insulin Production

11.2.5.1 *Insulin Production Inventory*

Component Description	Measurement/ Functional Unit	Data Source	SimaPro Inventory Description
Energy Input- Natural Gas	52.94 MJ	(Wernet et al. 2008), (Wernet et al. 2009), (Safety and Environmental Technology Group 2018), (Cespi et al. 2015), PubChem	Combustion of natural gas, consumption mix, at plant/NL Energy
Energy Input – Electricity	40.23 MJ		Electricity, medium voltage {IN-Western grid} | market for electricity, medium voltage | APOS, U

Energy Input- Steam	12.71 MJ		Process steam from natural gas, heat plant, consumption mix, at plant, MJ EU-27 S
Tryptone	1211 g	(Gusarov et al. 2015; Hwang et al. 2016)	Unable to find a suitable equivalent in SimaPro. therefore, not included in model.
Yeast Extract	605.5 g		Protein feed, 100% crude {GLO}| fodder yeast to generic market for protein feed | APOS, U
Sodium Chloride	605.5 g		Sodium chloride, at plant/RNA
Dipotassium phosphate	605.5 g		Sodium phosphate {RER}| production | APOS, U
Water	249.6 g		Water, ultrapure {GLO}| market for | APOS, U
Urea	58.12 g		Urea, as N {RER}| production | APOS, U
Tris	1.1 g		Unable to find a suitable equivalent in SimaPro. Therefore, not included in model.
EDTA	0.04 g		EDTA, ethylenediaminetetraacetic acid {RER}| EDTA production | APOS, U
Dithiothreitol (reductant)	0.19 g		Unable to find a suitable equivalent in SimaPro. Therefore, not included in model.
NaOH	4.84 g		Sodium hydroxide, without water, in 50% solution state {RER}| chlor-alkali electrolysis, diaphragm cell | APOS, U
Acetic Acid	7.27 g		Acetic acid, without water, in 98% solution state {RER}| acetic acid production, product in 98% solution state | APOS, U
Trypsin	0.44 g		Enzymes {RER}| enzymes production | APOS, U
Hypersil BDS C-18 (Sorbent)	0.42 g		Activated silica {GLO}| market for | APOS, U
Citric Acid	0.23 g		Citric acid {RER}| production | APOS, U
Zinc	0.002 g		Zinc, special high grade/GLO
Glycerine	2.02 g		Glycerine {GLO}| market for | APOS, U

Metacresol	0.32 g	(Gusarov et al. 2015; Hwang et al. 2016)	Unable to find a suitable equivalent in SimaPro. Therefore, not included in model.
Cardboard Package	25.84 g	Manual Measurement	Folding boxboard/chipboard {GLO}| market for | APOS, U
Glass Vial 10 ml	73.67 g		Glass tube, borosilicate {GLO}| market for | APOS, U
Aluminum Top	1.75 g		Aluminum ingot, production mix, at plant/US
Rubber Stopper on Top	2.14 g		Seal, natural rubber based {DE}| production | APOS, U
Plastic Stopper	0.71 g		PET, bottle grade, at plant/RER
Paper Insert	13.0 g		Graphic paper, 100% recycled {RER}| production | APOS, U
Refrigerated truck from Frankfort to Port of Rotterdam	0.0173375 tkm	(Industriepark Höchst 2018), Google Maps	Transport, freight, lorry with refrigeration machine, 3.5-7.5 ton, EURO3, carbon dioxide, liquid refrigerant, cooling {GLO}| market for transport, freight, lorry with refrigeration machine, 3.5-7.5 ton, EURO3, carbon dioxide, liquid refri(...)_1 | APOS, U
Refrigerated Shipping Container from Rotterdam Port to New York Container Port	0.212795 tkm	Google Maps	Transport, freight, sea, transoceanic ship with reefer, cooling {GLO}| market for | APOS, U
Refrigerated truck from New York Container Port	0.036208 tkm		Transport, freight, lorry with refrigeration machine, 3.5-7.5 ton, EURO3, carbon dioxide, liquid refrigerant, cooling {GLO}| market for transport, freight, lorry with refrigeration machine, 3.5-7.5 ton, EURO3, carbon dioxide, liquid refri(...)_1 | APOS, U
Waste-Landfill	367.43 g	Manual Measurement	Inert waste, for final disposal {RoW}| market for inert waste, for final disposal | Cut-off, U

11.2.5.2 *Insulin Production Assumptions*

- Functional Unit: 365 days/1 Type 2 diabetes patient with no medical complications.

Sanofi's Lantus Insulin Glargine is modeled in this study. This particular type of insulin was selected based on its status as the best-selling insulin brand (Pharmaceutical Technology 2016). As a

long-lasting insulin this is ideal for type 2 diabetic patients who often need a supportive basil dosage to supplement residual biological insulin production.

- The notable differences between the production of insulin used in Sri Lanka versus that which is used in the United States are containers in which they are stored and the locations where they are manufactured. The insulin used in the United States is assumed to come in an injection pen. This plastic container resembles a marker and stores the insulin in a glass vial enclosed in a plastic casing. It is designed to be transportable and does not need to be refrigerated for up to 20 days after removing from refrigerated storage (Sanofi-Aventis 2019).

- Sanofi's largest insulin production facility is located in Frankfurt, Germany (Berton 2013). The model assumes production at this location and transportation via refrigerated container to the Rotterdam port, where it is then shipped to the New York Container Port. From the New York Container Port it is taken by refrigerated container to Ann Arbor, Michigan, the site of the assumed use phase. All distances are calculated using Google Maps.

- Per the insulin container label, a single insulin pen contains 3.6378 mg of insulin which is equal to 100 insulin units.

- A base dosage of 10 u/day is assumed based on dosing recommendations from the manufacturer(Sanofi-Aventis 2017).

- To calculate the energy used in the manufacturing process of the insulin a total energy estimate was derived using the FineChem tool. Designed by the Safety and Environmental Technology Group within ETH Zurich the FineChem tool uses the molecular structure of a compound to estimate the energy needs and environmental impacts of that molecule's production. While the tool was originally designed for the petrochemical industry, it serves to provide a rough estimate of energy use in the absence of process data. A full description of the workings of the tool are available on the Fine Chem website and on the tools associated published papers (Wernet et al. 2008; 2009; Safety and Environmental Technology Group 2018). All molecular data used in the calculations were sourced from PubChem. The FineChem tool estimated the total energy use to produce insulin glargine at 758.6 MJ/kg. The breakdown of the types of energy used in this total was established using the work by Cespi, et al (Cespi et al. 2015). This study indicated an energy breakdown in pharmaceutical production of 50% natural gas, 38% electricity and 12% steam. These proportions were used in the study's calculations.

- In the absence of direct process data of the insulin glargine and/or insulin isophane production process, this study recreated the production process using the process data published by Gusarov, et al. in their paper, Systematic Approach to Production Technology Development for Therapeutic Proteins (Using Insulin-Glargine As An Example), and Hwang, et al.'s published paper, Recombinant Glargine Insulin Production Process Using Escherichia coli.

- The waste scenario modeled here accounts for the disposal of the packaging used to house and transport the produced insulin. It does not account for waste generated in the insulin production process as data on waste generated from this process was not available. The disposal scenario assumes that patients dispose of their used packaging along with standard household municipal solid waste. This assumption is based on discussions with medical

professionals, as well as a review of several dozen diabetes patient online community message threads discussing how to dispose of diabetes treatment materials.

11.2.6 United States: Insulin Use

11.2.6.1 *Insulin Use Inventory*

Component Description	Measurement/ Functional Unit	Data Source	SimaPro Inventory Description
Pen Needle_ Plastic Casing	352.298 g	Manual Measurement	Injection molding, rigid polypropylene part, at plant/kg/RNA; Polypropylene, granulate {GLO}| market for | APOS, U
Pen Needle_ Plastic Neck	72.307 g		Injection molding, rigid polypropylene part, at plant/kg/RNA; Polypropylene, granulate {GLO}| market for | APOS, U
Pen Needle_Plastic Cover	33.471 g		Injection molding, rigid LLDPE part, at plant/kg/RNA; Polyethylene, linear low density, granulate {GLO}| market for | APOS, U
Pen Needle_Needle	0.584 g		Steel, stainless 304, flat rolled coil/kg/RNA; Wire drawing, steel {GLO}| market for | APOS, U
Pen Needle_Seal	15.8775 g		Polyethylene, HDPE, granulate, at plant/RER; Aluminum ingot, production mix, at plant/US; Thermoforming, with calendering {GLO}| market for | APOS, U
Pen Needle_Cardboard Package	62.05 g		Folding boxboard/chipboard {RER}| chipboard production, white lined | APOS, U
Pen Needle_ Ship Transportation	2.751 tkm	Google Maps	Transport, freight, sea, transoceanic ship {GLO}| market for | APOS, U
Pen Needle_ Truck Transportation	0.533 tkm		Transport, combination truck, long-haul, diesel powered/tkm/RNA
Alcohol Swab_Cotton	40.555 g	Manual Measurement	Textile, woven cotton {GLO}| production | APOS, U
Alcohol Swab_Isopropyl Alchohol	54.515 mL	Stated amount as reported in product information available on NIH website (National Institute of Health 2018)	Isopropanol {GLO}| market for | APOS, U
Alcohol Swab_Wrapper	81.111 g	Information published on supplier website (Jiaxing Zhiming Machinery Manufacture 2014)	Polyethylene, HDPE, granulate, at plant/RER; Aluminum ingot, production mix, at plant/US; Thermoforming, with calendering {GLO}| market for | APOS, U

Alcohol Swab _Cardboard Package	51.708 g	Manual Measurement	Folding boxboard/chipboard {RER}| chipboard production, white lined | APOS, U
Alcohol Swab_ Truck Transportation	4.323 tkm	Google Maps	Transport, combination truck, long-haul, diesel powered/tkm/RNA
Alcohol Swab _ Ship Transportation	1.323 tkm		Transport, freight, sea, transoceanic ship {GLO}| market for | APOS, U
Refrigeration	3.153 kWh	(U.S. Department of Energy, 2018), (Wirecutter, 2018), (The Home Depot Inc, 2018)	Electricity, low voltage {US}| market group for | APOS, U
Waste-Landfill	751.06 g	Manual Measurement	Inert waste, for final disposal {RoW}| market for inert waste, for final disposal | Cut-off, U

11.2.6.2 *Insulin Use Assumptions*

- Functional Unit: 365 days/1 Type 2 diabetes patient with no medical complications.
- The model of insulin use in the United States assumes that the patient will be using a long-lasting insulin that needs to be taken only once a day.
- It is assumed that one needle and one alcohol swab are necessary to inject the long-lasting insulin. The pen is necessary to inject the insulin below the skin, while the alcohol pad is a standard precaution used to protect the patient from infection during the injection process.
- While the insulin in insulin pens modeled in this study can be stored at room temperature for approximately 20 days, longer storage requires refrigeration to prevent degradation of the insulin(Sanofi-Aventis 2019). This study assumes the energy used to cool one pen year-round. This energy calculation was calculated by dividing the total energy use of the appliance by the percentage of space in the refrigerator used by the insulin pen. To determine energy use associated with refrigeration, in light of the wide variety of refrigeration appliances in the United States, a search was done to estimate the most frequently purchased refrigerator. In this case an article from Wirecutter listing the best refrigerator model for 2018 was taken as a proxy to indicate the most frequently purchased refrigerator (Wirecutter 2018). The specifications for this refrigerator (the LG LFX25974ST), were obtained from the Home Depot website (The Home Depot Inc. 2018). Based on the size of the refrigerator, energy use was estimated using a calculator provided by the U.S. Department of Energy's EnergyStar website (U.S. Department of Energy 2018).
- The waste treatment scenario included in this model assumes that patients are disposing of their used needles as medical waste. Interviewed medical professionals all recommend disposing of used needles in a sealed medical waste container. These containers are then disposed of with standard municipal solid waste. This practice aligns with several dozen reviewed online diabetes community discussion boards where patients documented their methods for disposing of diabetes-related waste. The disposal of the alcohol swab is assumed to be the same as for standard municipal solid waste.

11.2.7 United States: Metformin Production

11.2.7.1 *Metformin Production Inventory*

Component Description	Measurement/ Functional Unit	Data Source	SimaPro Inventory Description
Natural Gas	22.6332394 MJ-eq/mg	(Wernet et al. 2008), (Wernet et al. 2009), (Safety and Environmental Technology Group 2018), (Cespi, et al., 2017)	Natural gas, low pressure {RoW}| market for | APOS, U
Electricity	17.2012619 MJ-eq/mg		Electricity, medium voltage {US}| market group for | APOS, U
Steam	5.43197745 MJ-eq/mg		Heat, from steam, in chemical industry {RoW}| market for heat, from steam, in chemical industry | APOS, U
Dicyandiamide	407431.3 mg	(Rohokale, Jadhav, and Kadam 2010)	Dimethylacetamide {GLO}| market for | APOS, U
Dimethylamine Hydrochloride	488917.5 mg		Dimethylamine {GLO}| market for | APOS, U
Cyclohexanol	162972.5 mg		Cyclohexanol {GLO}| market for | APOS, U
Ethanol	206294.3 mg		Ethanol, without water, in 95% solution state, from fermentation {BR}| cane sugar production with ethanol by-product | APOS, U
Package	304.2 g	Manual Measurement	Polyethylene, HDPE, granulate, at plant/RER; Injection molding, rigid polypropylene part, at plant/kg/RNA
Truck Transportation	1.04636E-08 tkm	Google Maps	Transport, freight, light commercial vehicle {GLO}| market for | APOS, U
Sea Shipping	1.35341E-08 tkm		Transport, freight, sea, transoceanic ship {GLO}| market for | APOS, U

11.2.7.2 *Metformin Production Assumptions*

- Functional Unit: 365 days/1 Type 2 diabetes patient with no medical complications.
- US T2D patients are assumed to use 1000 mg of Metformin daily. This is based upon dosing recommendations provided by IBM's Micromedex database (IBM Micromedex 2018). A comprehensive medical database that lists recommended dosages and uses for active pharmaceutical ingredients. While initial recommended dosage is 850 mg once daily with meals, it is assumed in this study that patients living with the disease will require a higher dosage throughout the course of daily maintenance. The 1000 mg daily dosage reflects this assumption.
- It should be noted that both interviews and published literature have established a precedent that patients often find it difficult to take their oral medication daily. However, given that daily medication use is often a prerequisite to treating diabetes without complications, this study assumes adherence to a daily dosage schedule (Cramer 2004).

- The production process modeled in this study is based on the process outlined in Rohokale, Jadhav et Kadam's 2010 paper on metformin process development (Rohokale, Jadhav, and Kadam 2010). It is acknowledged that there are a variety of production methods to produce pharmaceutical quality metformin hydrochloride and that the type of production process may influence scenario outcomes.
- Assumed production in Humacao, Puerto Rico (Bristol-Myers Squibb 2010). Use phase is assumed to take place in Ann Arbor, Michigan. So therefore, it is also assumed that the medication is transported via ship from the production site in Puerto Rico to the Miami port. From the port it is assumed that the medication is transported via truck to Ann Arbor, Michigan. The model accounts for the environmental impacts of the shipping via sea and truck.
- To calculate the energy used in the manufacturing process of the metformin a total energy estimate was derived using the FineChem tool. Designed by the Safety and Environmental Technology Group within ETH Zurich the FineChem tool uses the molecular structure of a compound to estimate the energy needs and environmental impacts of that molecule's production. While the tool was originally designed for the petrochemical industry, it serves to provide a rough estimate of energy use in the absence of process data. A full description of the workings of the tool are available on the Fine Chem website and on the tools associated published papers (Wernet et al. 2008; 2009; Safety and Environmental Technology Group 2018). All molecular data used in the calculations were sourced from PubChem. The FineChem tool estimated the total energy use to produce metformin at 145 MJ/kg. The breakdown of the types of energy used in this total was established using the work by Cespi, et al (Cespi et al. 2015). This study indicated an energy breakdown in pharmaceutical production of 50% natural gas, 38% electricity and 12% steam. These proportions were used in the study's calculations.
- Where possible, energy production values for the US were selected in the SimaPro program.
- In the absence of published data on waste disposal methods during the metformin production process a waste process was not specifically modeled.

11.2.8 United States: Clinic Visit

11.2.8.1 *Clinic Visit Inventory*

Component Description	Measurement/ Functional Unit	Data Source	SimaPro Inventory Description
Transportation to Doctor's office	64.3736 personkm	(Probst, Laditka, Wang, & Johnson, 2006)	Transport, passenger car with internal combustion engine {RER}| market for | APOS, U
Lancet_Needle	0.456 g	Manual Measurement	Steel, stainless 304, flat rolled coil/kg/RNA; Deep drawing, steel, 10000 kN press, automod e {RER}| deep drawing, steel, 10000 kN press, automode | APOS, U
Lancet_ Plastic Case	0.456 g		Low density polyethylene resin, at plant/RNA; Injection molding,

			rigid polypropylene part, at plant/kg/RNA
Lancing Device_Wheel	7.93462E-05 g		Polyethylene, high density, resin, at plant, CTR/kg/RNA; Injection molding, rigid polypropylene part, at plant/kg/RNA
Lancing Device_ Outer Part-Back	0.000349 g		Polyethylene, high density, resin, at plant, CTR/kg/RNA; LLDPE scrap, from LLDPE injection molding, at plant/kg/RNA
Lancing Device_ Outer Part- Front	0.000333 g		Polyethylene, high density, resin, at plant, CTR/kg/RNA; Injection molding, rigid polypropylene part, at plant/kg/RNA
Lancing Device_ Protective Cover	0.000231 g		Injection molding, rigid polypropylene part, at plant/kg/RNA; Polyethylene, high density, resin, at plant, CTR/kg/RNA
Lancing Device_ Thumb Part-Female	0.0001154 g		Polyethylene, high density, resin, at plant, CTR/kg/RNA; Injection molding, rigid polypropylene part, at plant/kg/RNA
Lancing Device_ Thumb Part- Male	0.000128 g		Injection molding, rigid polypropylene part, at plant/kg/RNA; Polyethylene, high density, resin, at plant, CTR/kg/RNA
Lancing Device_ Spring Container	0.0001943 g		Polyethylene, high density, resin, at plant, CTR/kg/RNA; Injection molding, rigid polypropylene part, at plant/kg/RNA
Lancing Device_ Small Spring	2.66923E-05 g	Manual Measurement	Steel, stainless 304, flat rolled coil/kg/RNA; Wire drawing, steel {GLO}| market for | APOS, U
Lancing Device_ Large Spring	1.18462E-05 g		Wire drawing, steel {GLO}| market for | APOS, U; Steel, stainless 304, flat rolled coil/kg/RNA
Test Strip_ Base A	0.121 g	Manual measurement; (Abbott Diabetes Care Inc, 2015)	Polyester resin, unsaturated {GLO}| market for | APOS, U; Injection moulding {GLO}| market for | APOS, U
Test Strip_ Base B	0.123 g	Manual measurement; (Abbott Diabetes Care Inc, 2015)	Injection moulding {GLO}| market for | APOS, U; Polyester resin, unsaturated {GLO}| market for | APOS, U

Test Strip_ Glucose Oxidase Enzyme	4E-05 g	(Fernandes, Kurhe, Chavan, & Jayaram, 2016)	Enzyme, Glucoamylase, Novozyme Spirizyme/kg/RER
Test Strip_Co-Enzyme Flavine Adenine Dinucleotide	4E-05 g	(Fernandes, Kurhe, Chavan, & Jayaram, 2016)	Enzyme, Alpha-amylase, Novozyme Liquozyme/kg/RER
Test Strip_ Mediator-Ferricyanide	4E-05 g	(Loew, Tsugawa, Nagae, Kojima, & Sode, 2017)	Sodium cyanide {GLO}| market for | APOS, U
Test Strip_ Indicator-Silver	4E-05 g	(Fernandes, Kurhe, Chavan, & Jayaram, 2016)	Silver {GLO}| market for | APOS, U
Test Strip_ Indicator- Carbon	4E-05 g	(Fernandes, Kurhe, Chavan, & Jayaram, 2016)	Activated carbon, granular {GLO}| market for activated carbon, granular | APOS, U
Glucose Meter_ Circuit	4.63843E-07 g	Manual Measurement	Integrated circuit, memory type {GLO}| market for | APOS, U
Glucose Meter_ Screen	2.52778E-07 g		Panel glass, for cathode ray tube display {GLO}| market for | APOS, U
Glucose Meter_ Outer Case	8.28212E-07 g		Injection molding, rigid polypropylene part, at plant/kg/RNA; Polypropylene granulate (PP), production mix, at plant RER
Glucose Meter_ Circuit (under button)	8.12785E-08 g		Integrated circuit, memory type {GLO}| market for | APOS, U
Glucose Meter_ Metal Clip	2.44187E-08 g		Brass {RoW}| market for brass | APOS, U
Glucose Meter_ Small Metal Clip	1.5216E-08 g		Brass {RoW}| market for brass | APOS, U
Glucose Meter_ Plastic Cover	1.19494E-08 g		Injection molding, rigid polypropylene part, at plant/kg/RNA; Polypropylene granulate (PP), production mix, at plant RER
Glucose Meter_ Rubber Buttons	6.72076E-08 g		Synthetic rubber {GLO}| market for | APOS, U; Injection moulding {GLO}| market for | APOS, U
Glucose Meter_Battery	0.0121904 g	(Abbott, 2016)	Battery cell, Li-ion {RoW}| production | APOS, U

Glucose Meter_ Ground Transportation	5.17233E-08 tkm	Google Maps	Truck Transportation_Glucose Meter_USA
Glucose Meter_ Sea Shipping	1.50752E-07 tkm		Transport, freight, sea, transoceanic ship {GLO}| market for | APOS, U
Alcohol Wipe_ Cotton	0.22222 g	Manual Measurement	Textile, woven cotton {GLO}| market for | APOS, U
Alcohol Wipe_ Isopropyl Alcohol	10 g	Stated amount as reported in product information available on NIH website (National Institute of Health 2018)	Isopropyl acetate {GLO}| market for | APOS, U
Alcohol Wipe_ Wrapper	0.44444 g	Information published on supplier website (Jiaxing Zhiming Machinery Manufacture 2014)	Polyethylene, HDPE, granulate, at plant/RER; Aluminum ingot, production mix, at plant/US; Thermoforming, with calendering {GLO}| market for | APOS, U
Alcohol Wipe_ Cardboard Package	0.28333 g	Manual Measurement	Folding boxboard/chipboard {GLO}| market for | APOS, U
HBa1c_Cartridge	76.8 g		Polyethylene, HDPE, granulate, at plant/RER; Injection moulding {GLO}| market for | APOS, U
Paper on exam table	864 in		Tissue paper {GLO}| market for | APOS, U
Rubber Gloves (2 gloves)	20 g		Acrylonitrile-butadiene-styrene copolymer {RoW}| production | APOS, U; Extrusion of plastic sheets and thermoforming, inline {GLO}| market for | APOS, U
Foot Exam_ Filament	1 g	Manual Measurement (estimation)	Polyethylene terephthalate, granulate, bottle grade, recycled {RoW}| polyethylene terephthalate production, granulate, bottle grade, recycled | APOS, U; Extrusion, plastic film {GLO}| market for | APOS, U
Overhead Energy	48773.15 Btu	(United States Environmental Protection Agency, 2015)	Electricity, low voltage {US}| market group for | APOS, U
Waste-Landfill	973.41 g	Manual Measurement	Inert waste, for final disposal {RoW}| market for inert waste, for final disposal | Cut-off, U

11.2.8.2 *Clinic Assumptions*

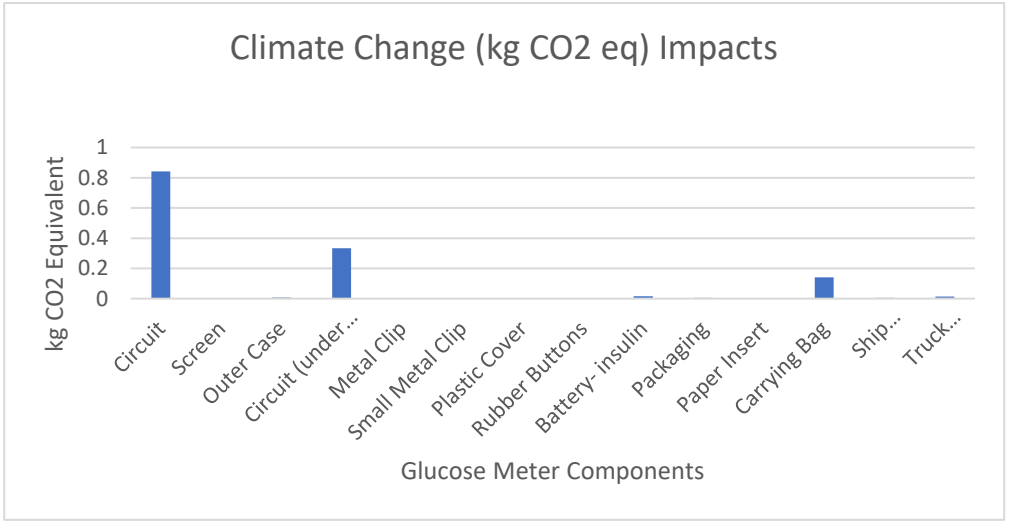
- Functional Unit: 365 days/1 Type 2 diabetes patient with no medical complications.
- There is an assumption built into this model that in accordance with guidance from the American Diabetes Association, patients with well controlled Type 2 diabetes and no complications require only two endocrinologist check-ups per year. This guidance aligns with coverage provide by Medicare and Medicaid.
- The components of an annual endocrine check-up were compiled based on observations conducted at the University of Michigan Metabolism, Endocrinology & Diabetes Clinic. The components listed in the inventory correspond to the appointment protocol followed by the clinic. The appointment protocol is as follows:
    - Once patients sign in for their appointment, they are taken to a vitals station where their weight, height, blood pressure, blood glucose levels and HBa1c are measured and recorded by a Medical Assistant.
    - Patients are then taken to an exam room where they have their medical information reviewed and verified by a Medical Assistant.
    - A physician conducts a physical exam, answering any questions.
    - Patients are then checked-out by a Medical Assistant
- In addition to diabetes related medical equipment including a glucose meter, glucose test strip, lancet, lancing device and HbA1c testing cartridge, the exam requires paper to cover the exam table, a filament used to detect neuropathy and the electricity used to power the lights, HVAC, computer and diagnostic equipment.
- EIA data for a standard medical facility was used to calculate energy usage. The computer was not included in this calculation because the allocation of the computer over thousands of patient appointments per year resulted in a contribution of insignificant impact to the final total.
- Assumes the clinic handles 15,600 patient visits a year and that equipment impacts are allocated across these 15,600 appointments. The 15,600 figure is derived from interviews with UM Clinic staff where they cite handling approximately 300 patients/week. Assumes 52 weeks in a year with 65 operational hours each week (U.S. EPA Energy Star 2015).
- The average appointment time is calculated as 30 min/patient. This is based on information provided from UM Clinic staff.
- Assumed average clinic size is 43,000 square feet (U.S. EPA Energy Star 2015). A noted average medical clinic size according to information provided by the U.S. EPA's Energy Star data.
- Assumes an average overhead energy use rate of 245 kBtu/ft^2 (U.S. EPA Energy Star 2015).
- Studies show average distance patients in the U.S. travel to a medical clinic is 10 miles. This study thus assumes a 20-mile round trip for each clinic visit (Probst et al. 2006).

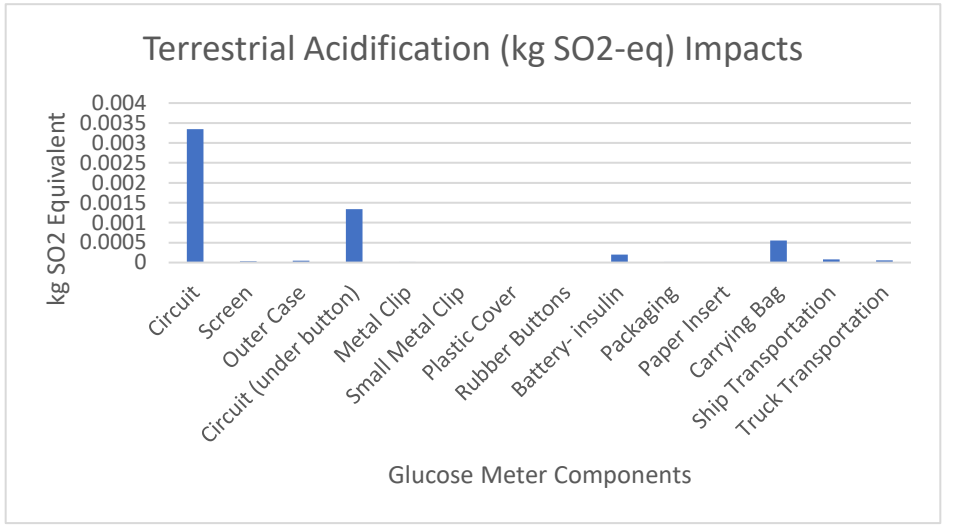
- Waste disposal scenario is modeled based on conversations with Medical Assistants that a third party medical waste management firm disposes of all medical-related waste from the clinic. A review of common medical waste disposal practices in the United States indicates a strong probability that the waste from the clinic is autoclaved before being sent to landfill. Absent data or an established method of modeling medical-waste autoclave procedures, this study models only the landfill portion of the waste scenario.

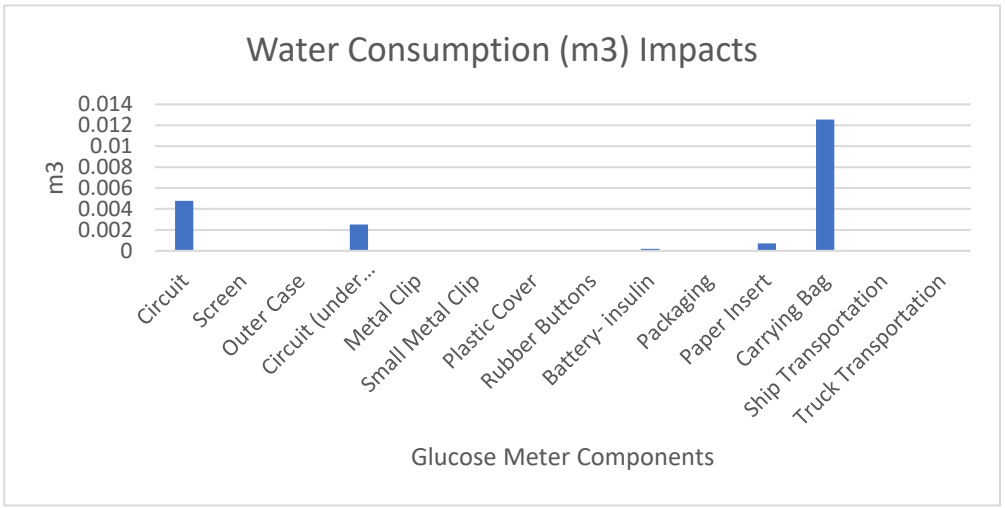
12 Appendix C: Impact Breakdown Per Treatment Component

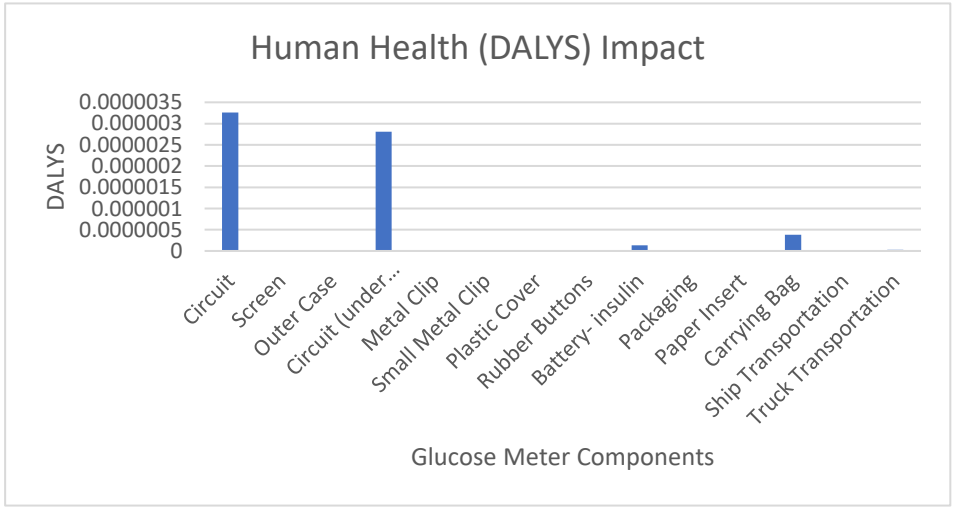
The following section provides greater insight into how each of the elements of a treatment component contribute to the overall impact total.

12.1 Glucose Meter

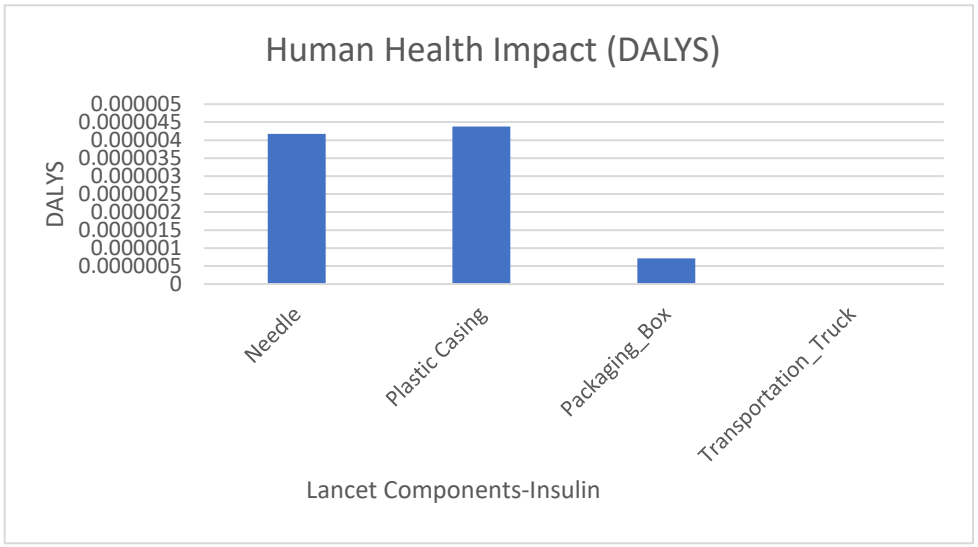


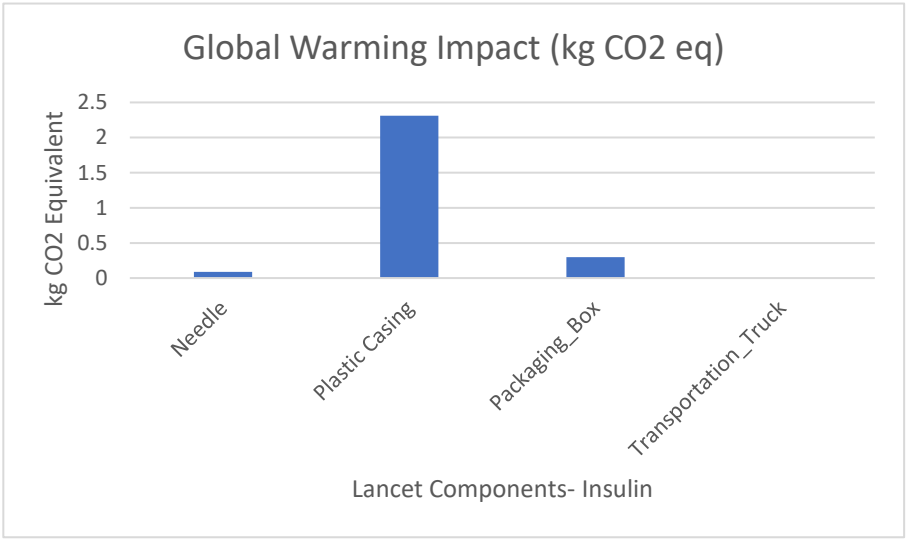


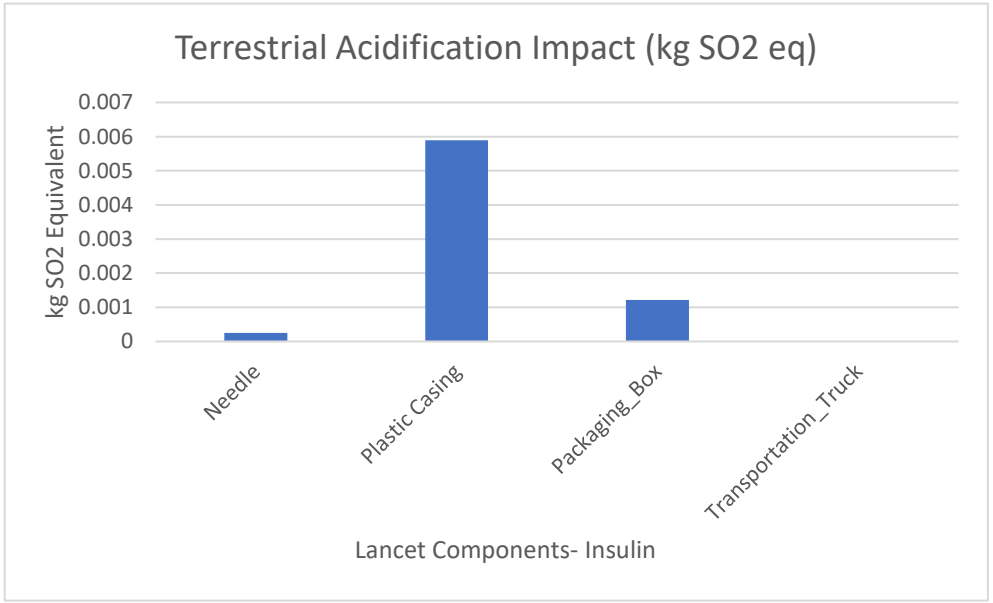


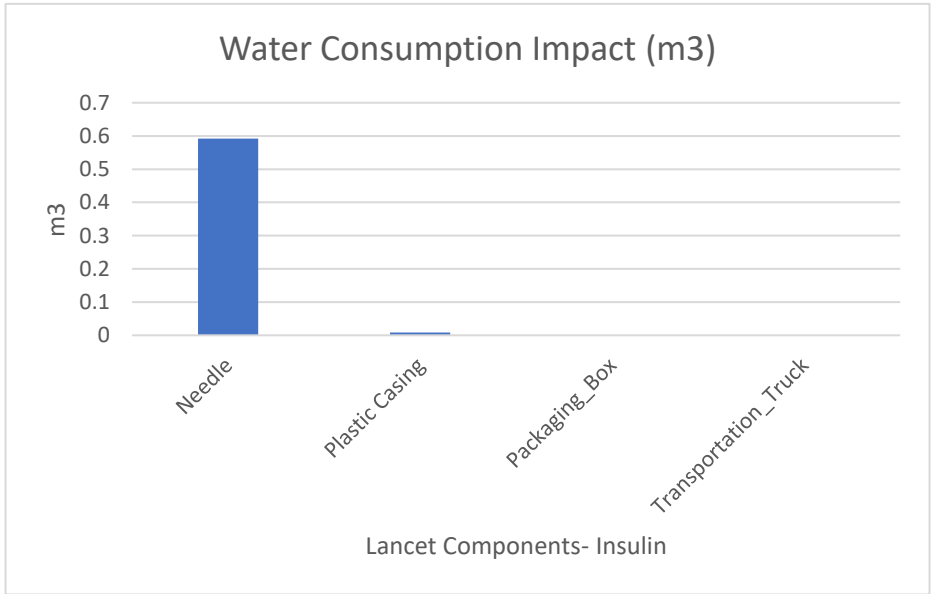


12.2 Lancet – Insulin

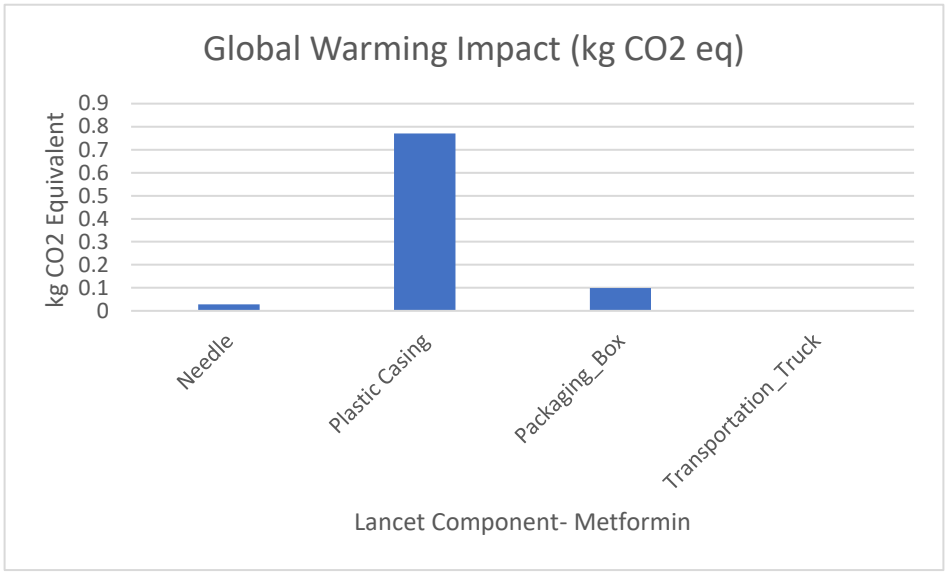


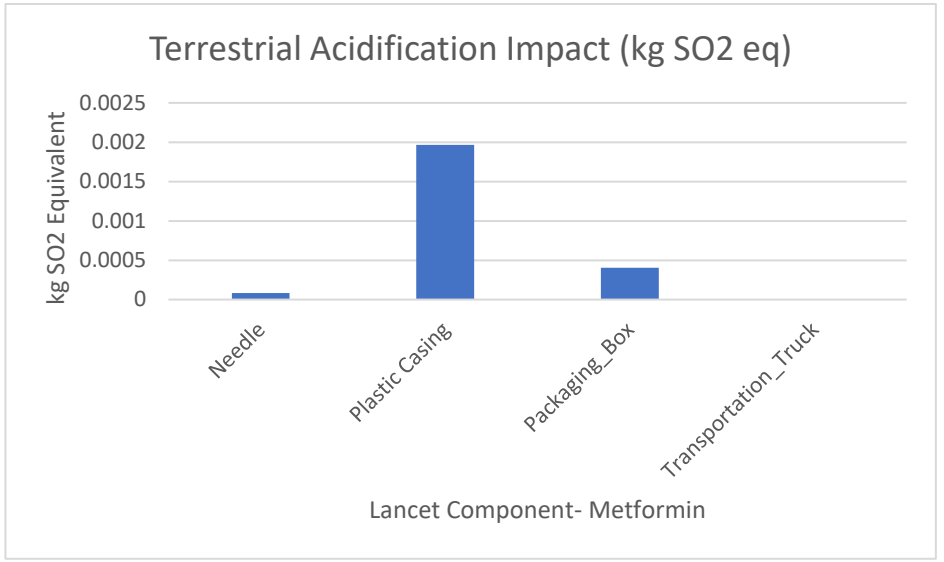


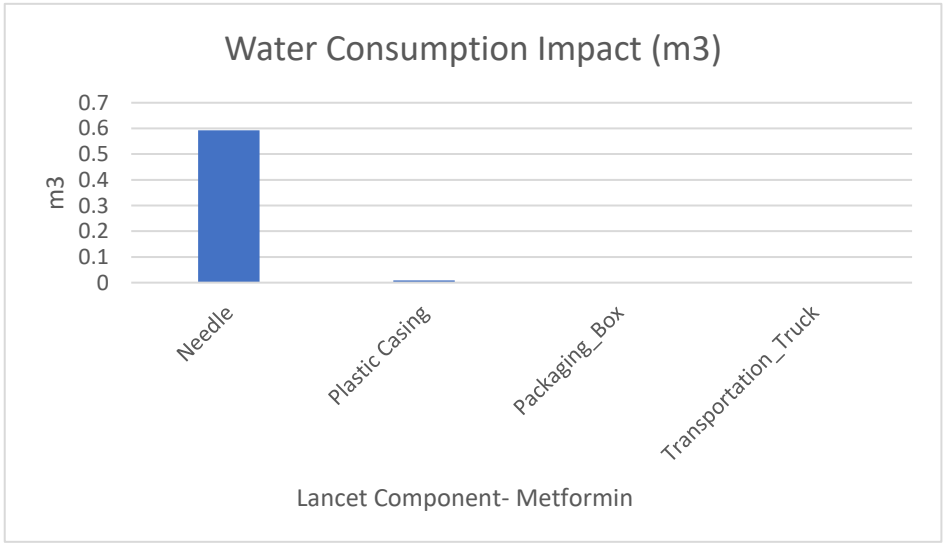


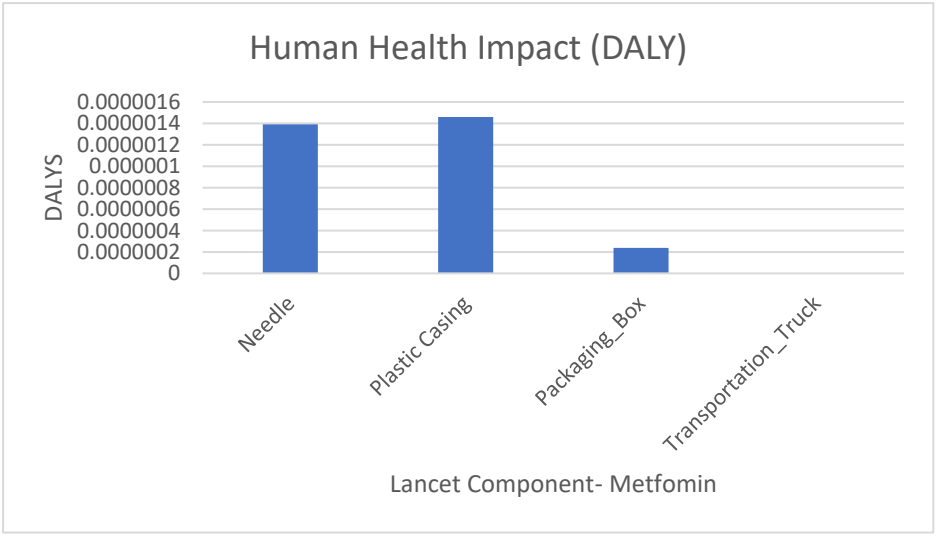


12.3 Lancet - Metformin

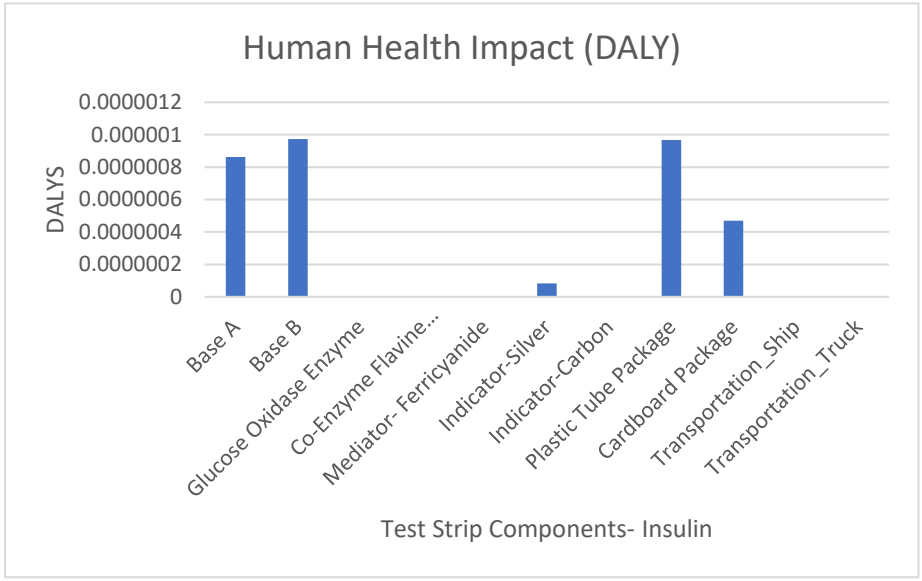


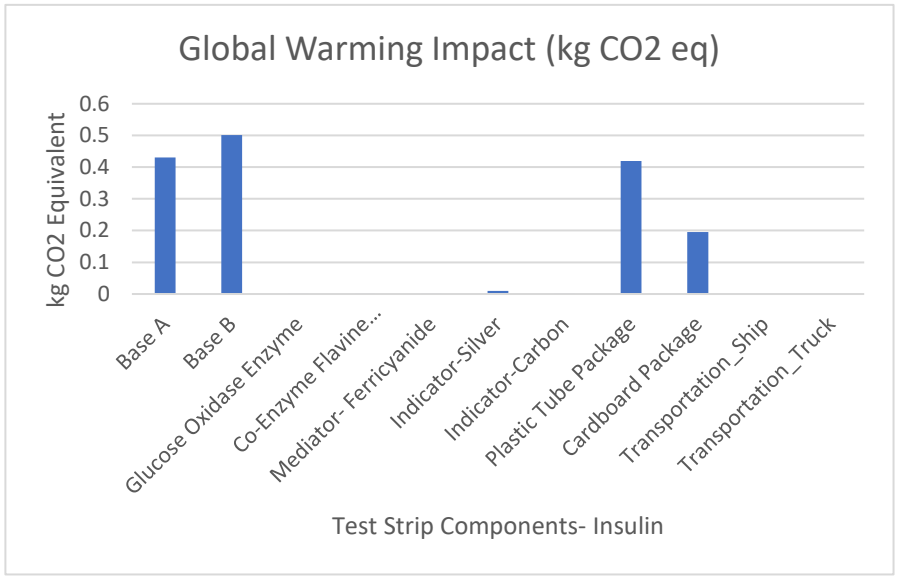


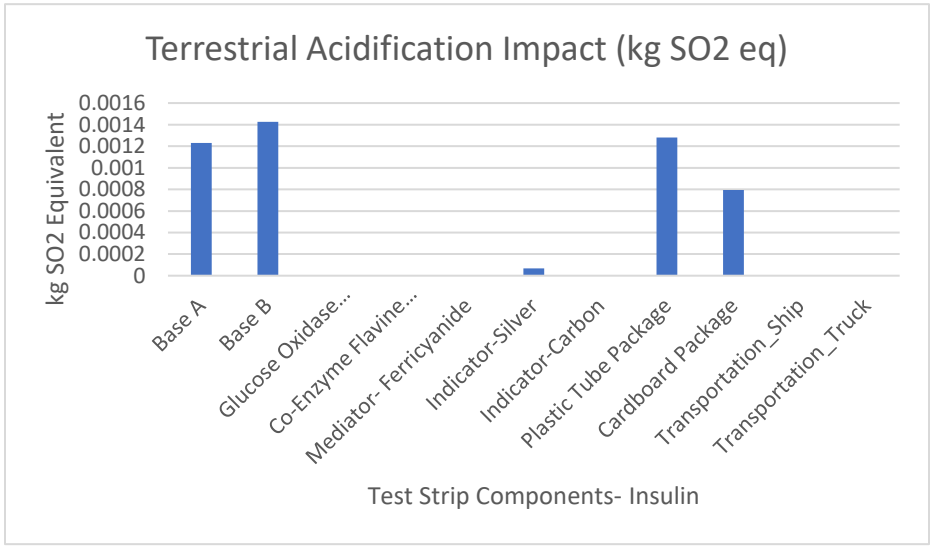


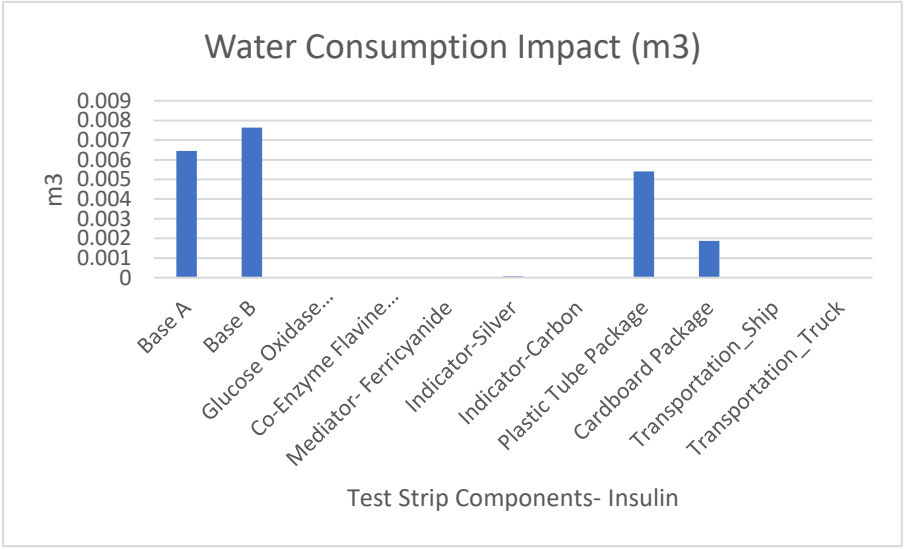


12.4 Test Strips – Insulin

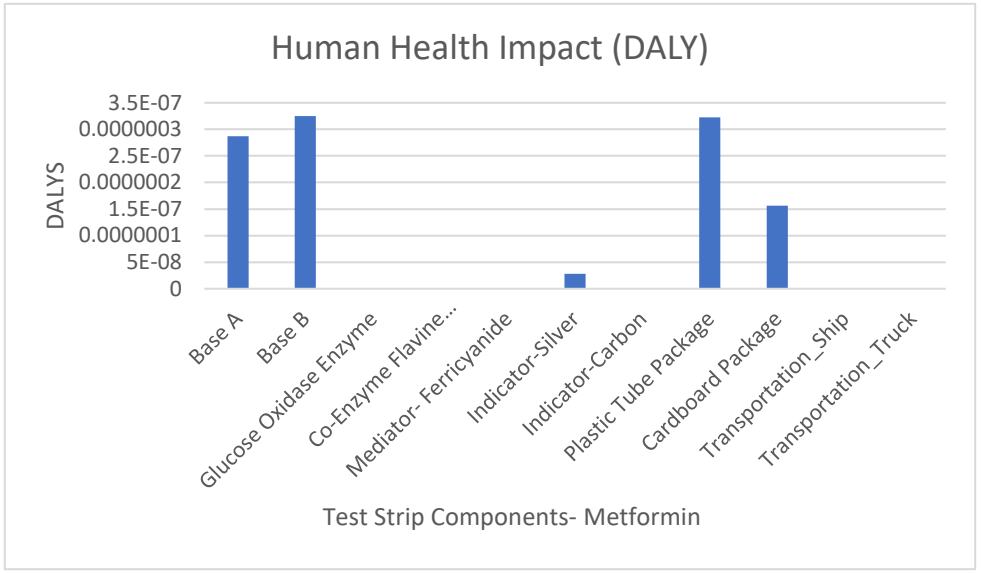


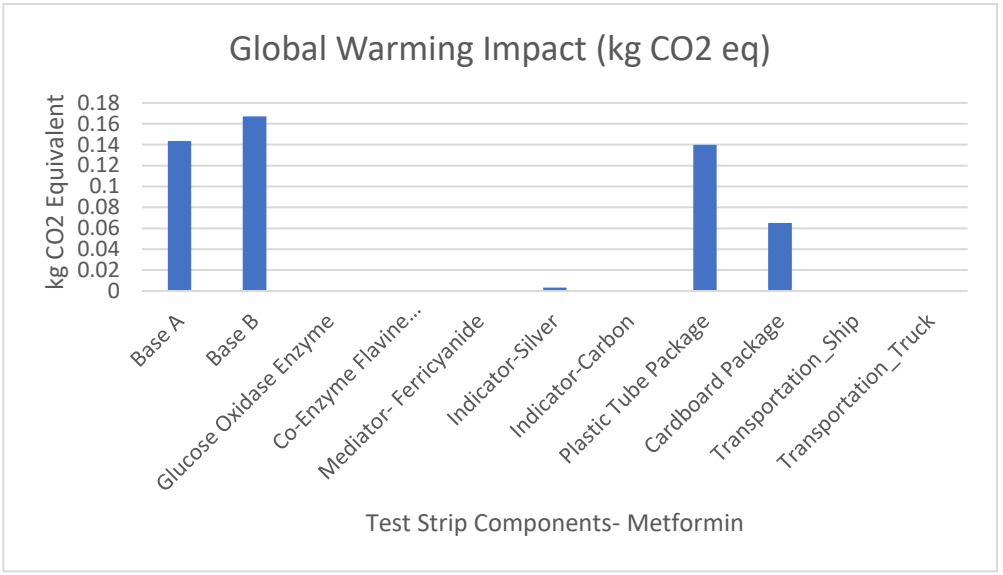


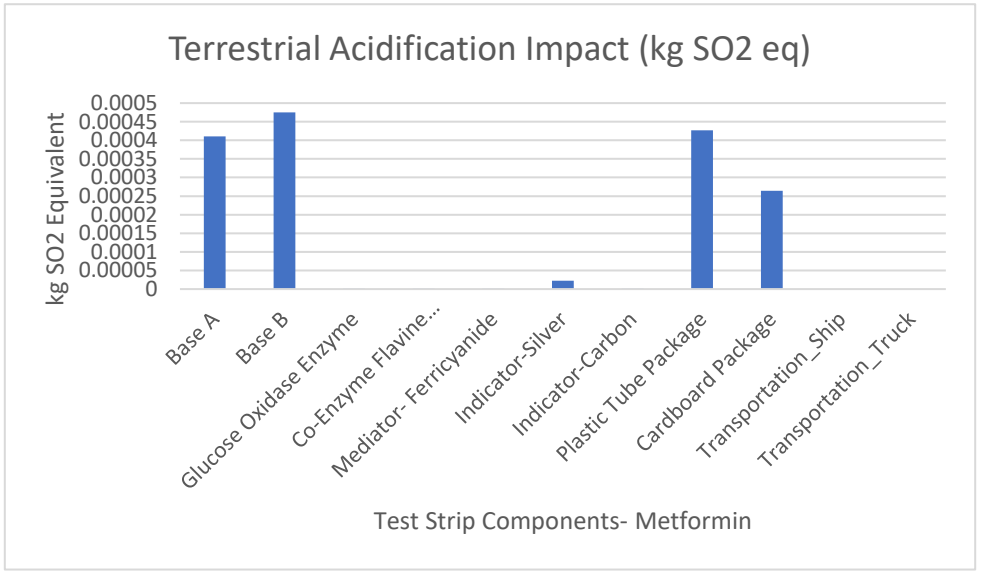


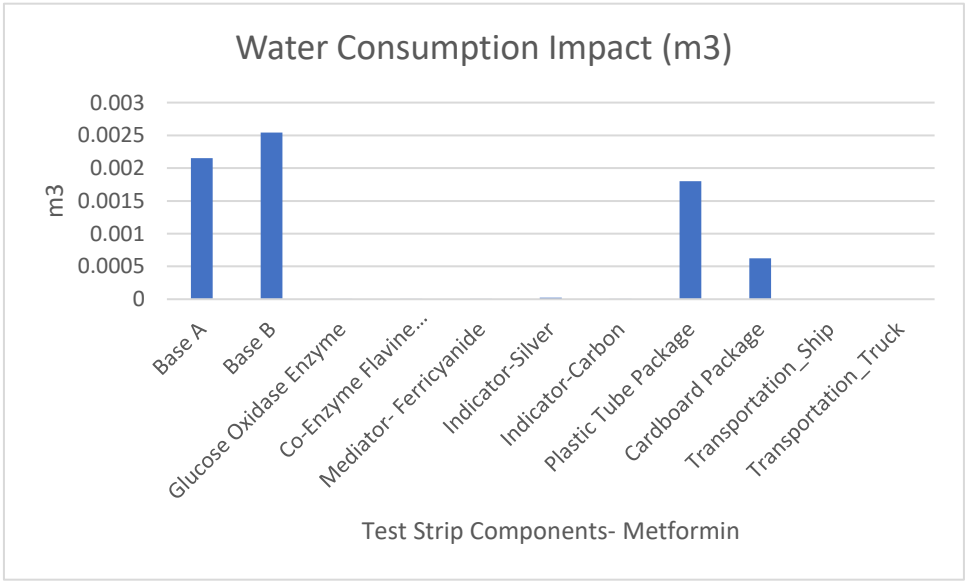


12.5 Test Strips - Metformin

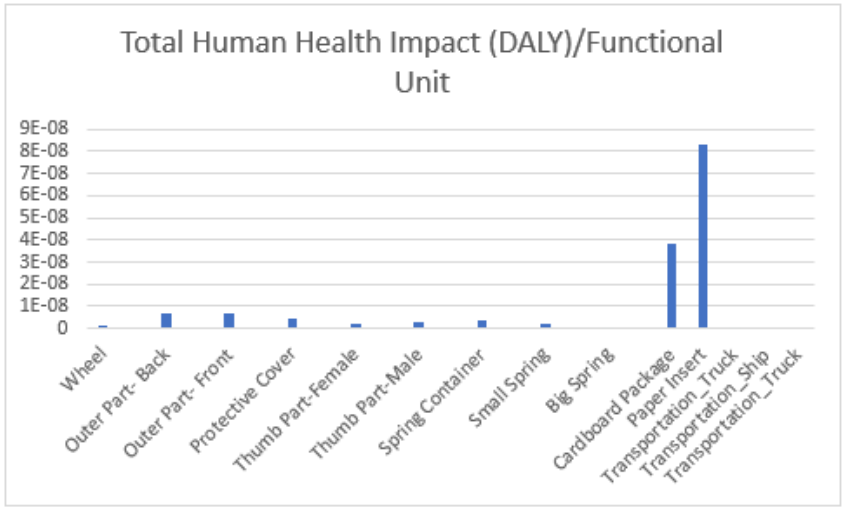


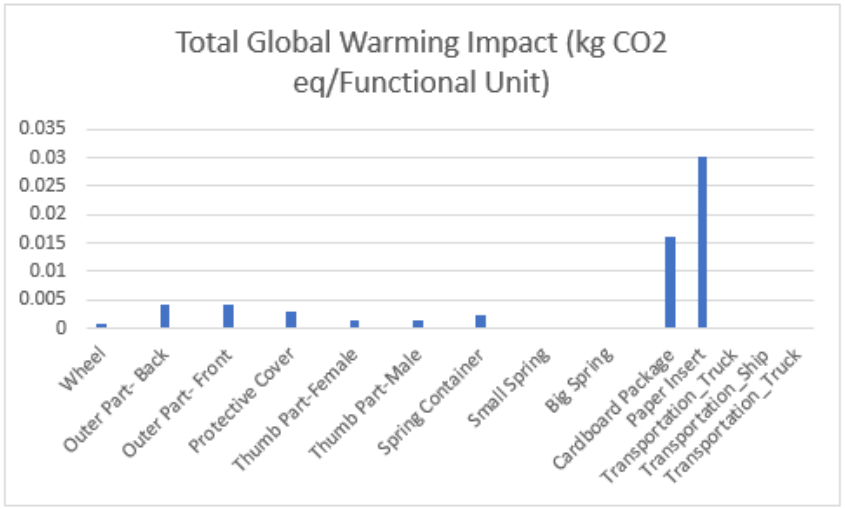


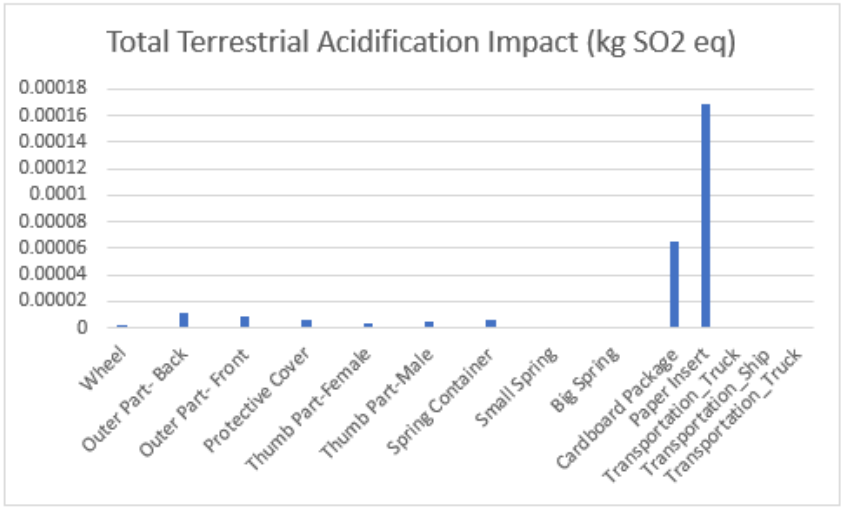


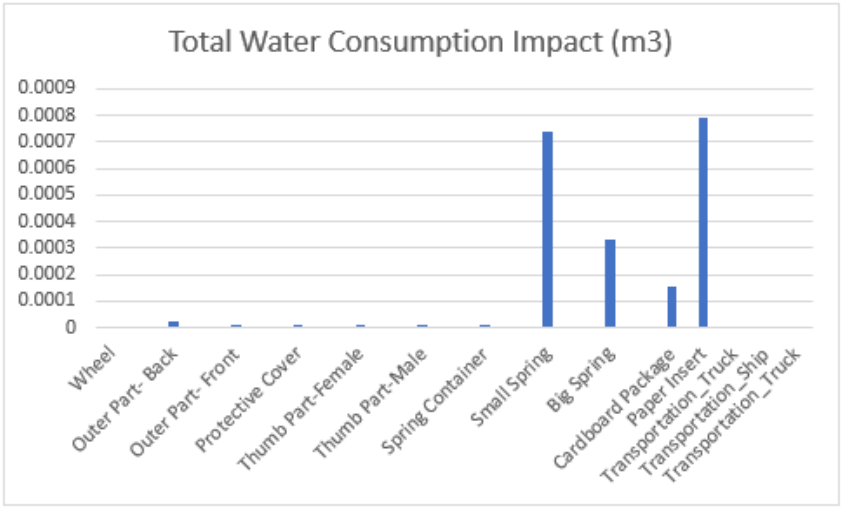


12.6 Lancing Device

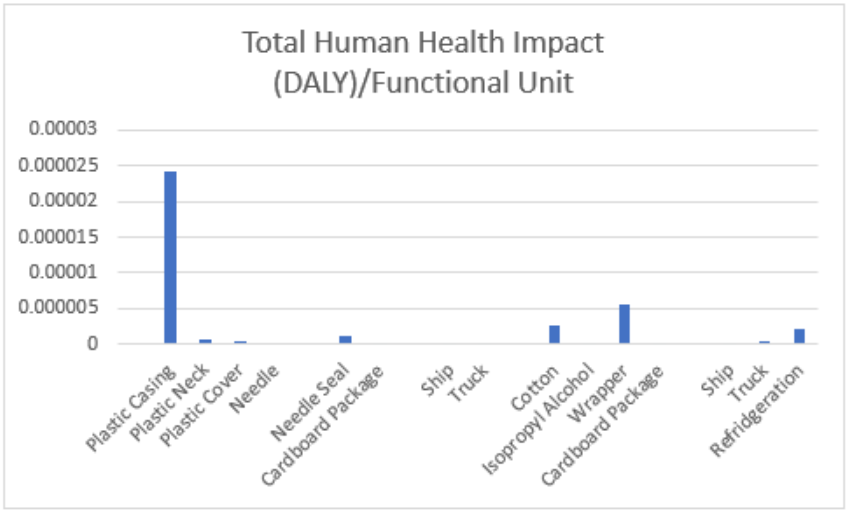


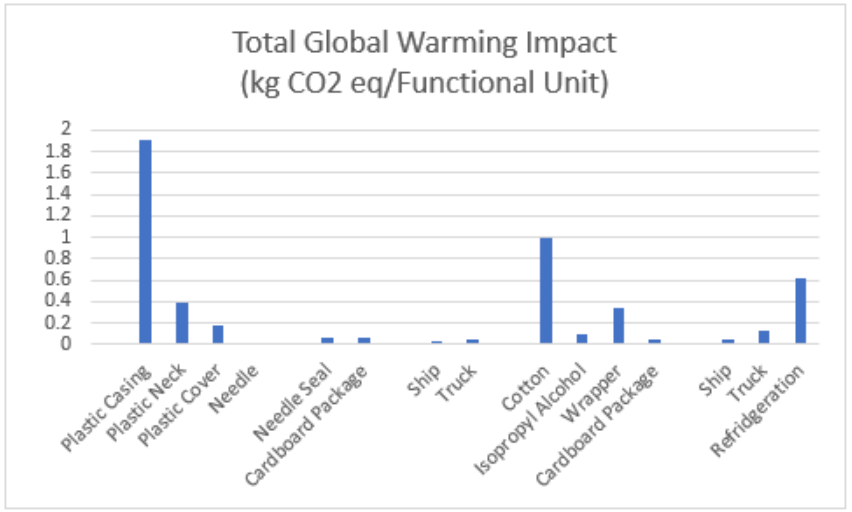


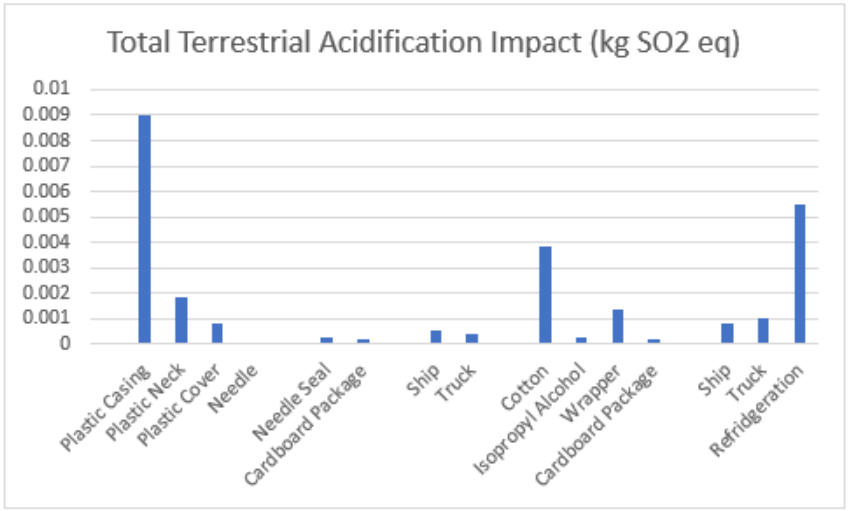


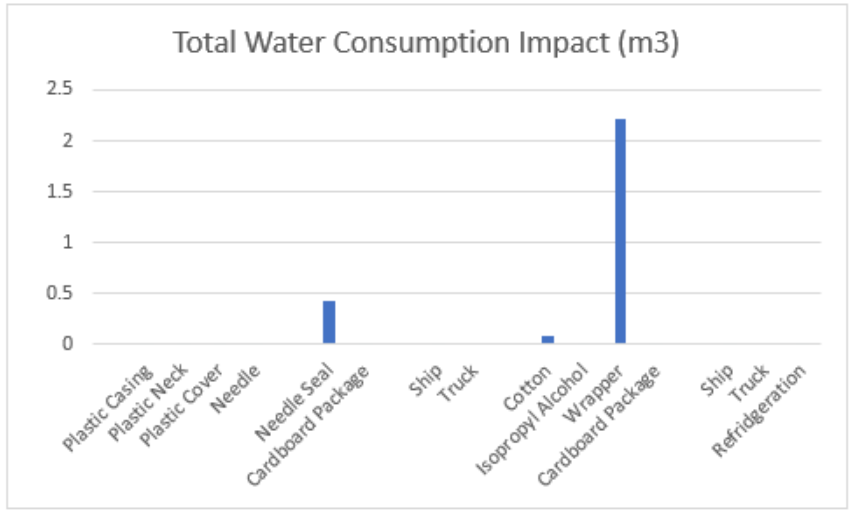


12.7 Insulin Use: United States

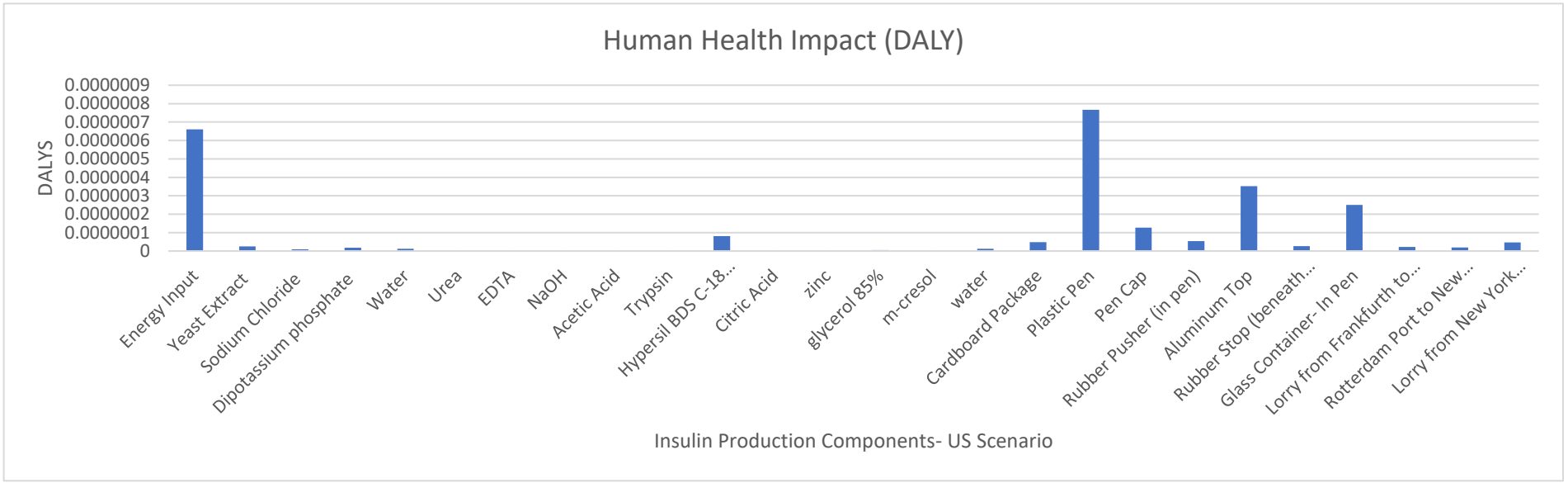


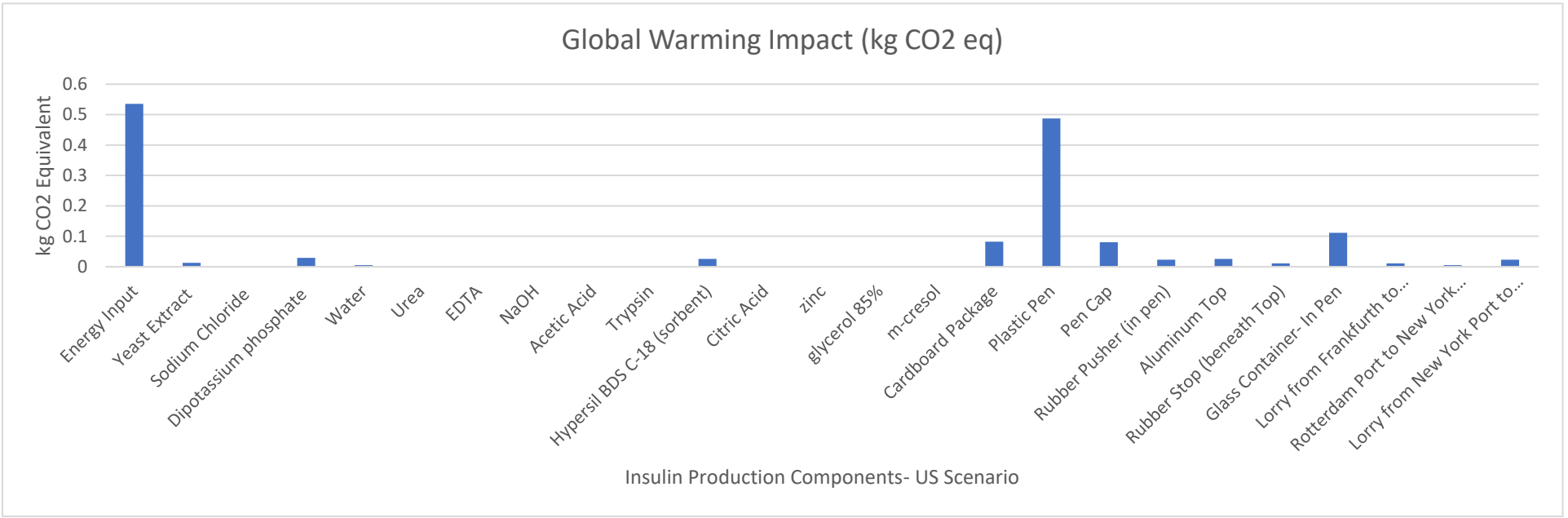


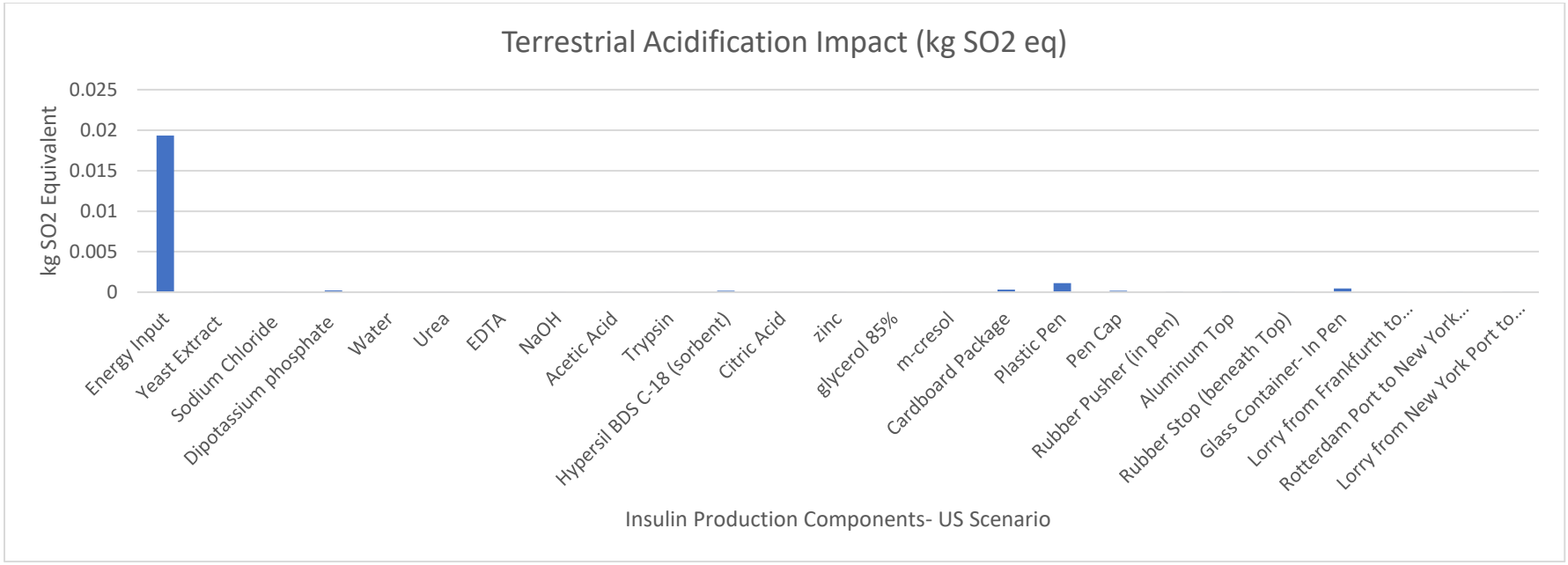




12.8 Insulin Production: United States





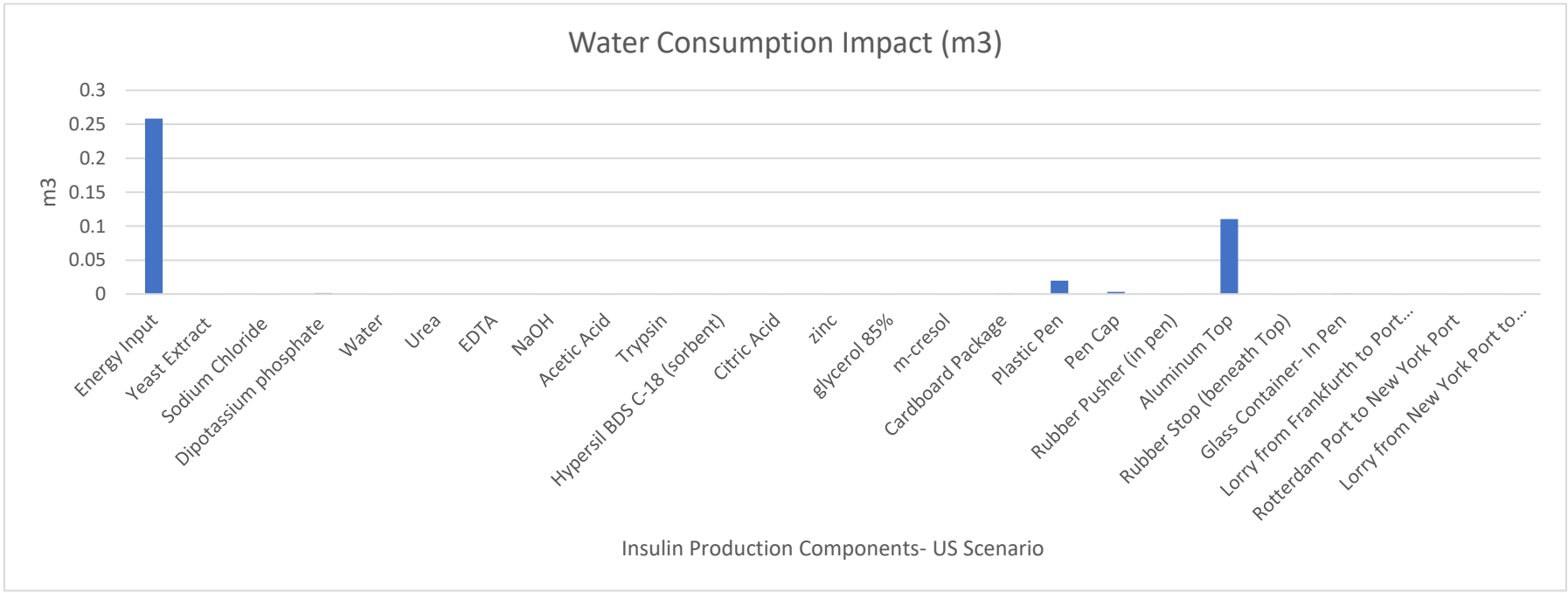

Terrestrial Acidification Impact (kg SO2 eq)
kg SO2 Equivalent
0.025
0.02
0.015
0.01
0.005
0
Energy Input
Yeast Extract
Sodium Chloride
Dipotassium phosphate
Water
Urea
EDTA
NaOH
Acetic Acid
Trypsin
Hypersil BDS C-18 (sorbent)
Citric Acid
zinc
glycerol 85%
m-cresol
Cardboard Package
Plastic Pen
Pen Cap
Rubber Pusher (in pen)
Aluminum Top
Rubber Stop (beneath Top)
Glass Container- In Pen
Lorry from Frankfurth to...
Rotterdam Port to New York...
Lorry from New York Port to...
Insulin Production Components- US Scenario

1

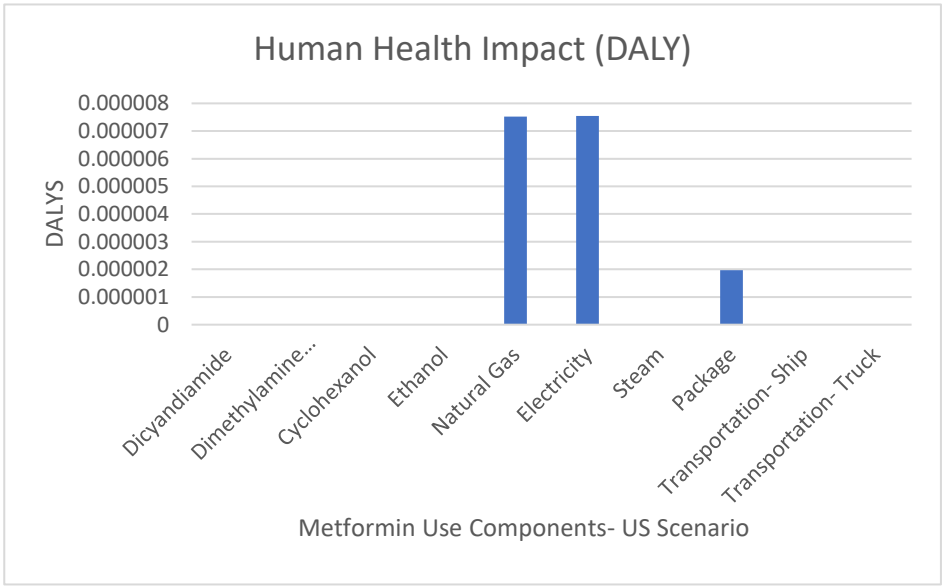
2

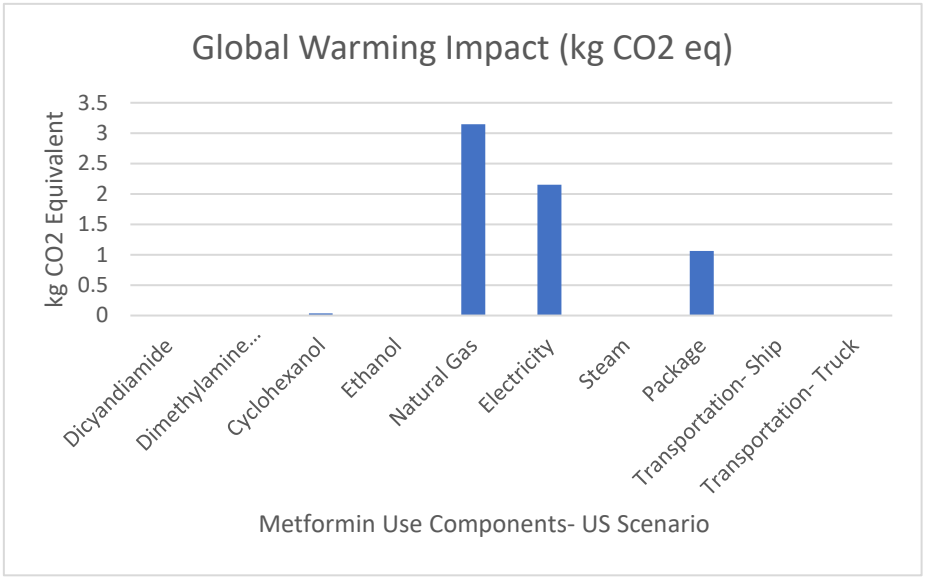
3

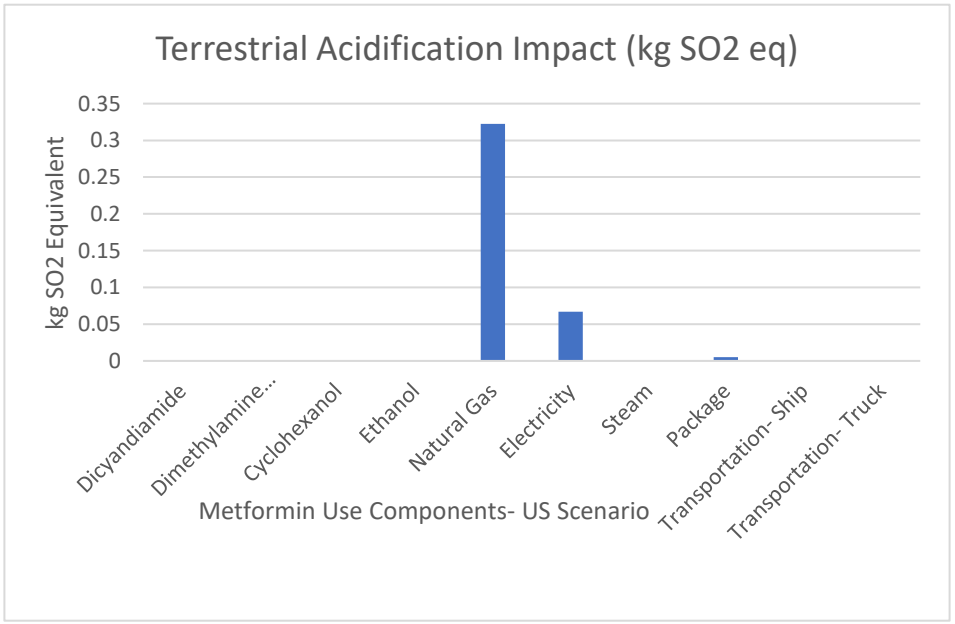
4

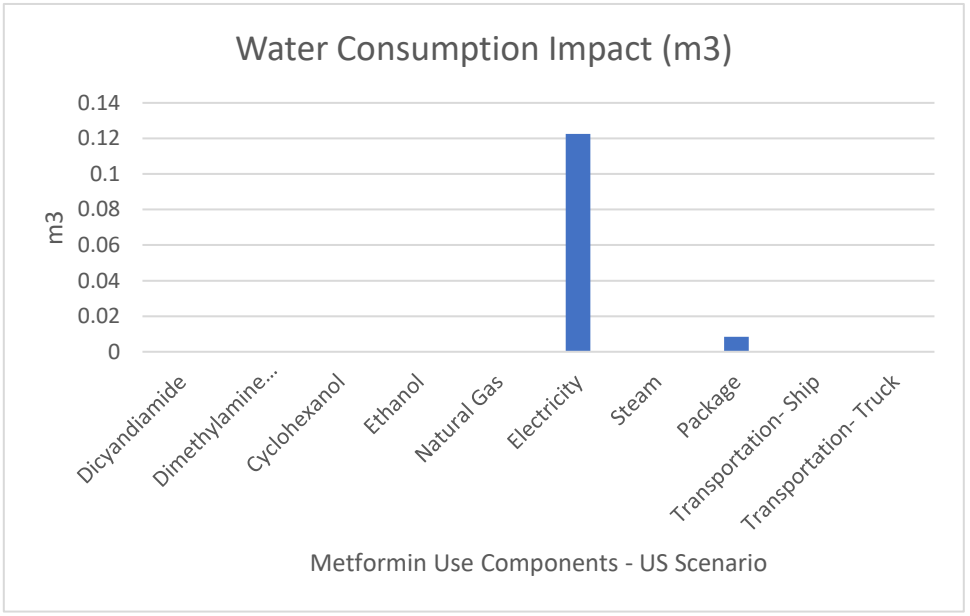

Water Consumption Impact (m3)
m3
0.3
0.25
0.2
0.15
0.1
0.05
0
Energy Input
Yeast Extract
Sodium Chloride
Dipotassium phosphate
Water
Urea
EDTA
NaOH
Acetic Acid
Trypsin
Hypersil BDS C-18 (sorbent)
Citric Acid
zinc
glycerol 85%
m-cresol
Cardboard Package
Plastic Pen
Pen Cap
Rubber Pusher (in pen)
Aluminum Top
Rubber Stop (beneath Top)
Glass Container- In Pen
Lorry from Frankfurth to Port...
Rotterdam Port to New York Port
Lorry from New York Port to...
Insulin Production Components- US Scenario

12.9 Metformin Use – United States Scenario

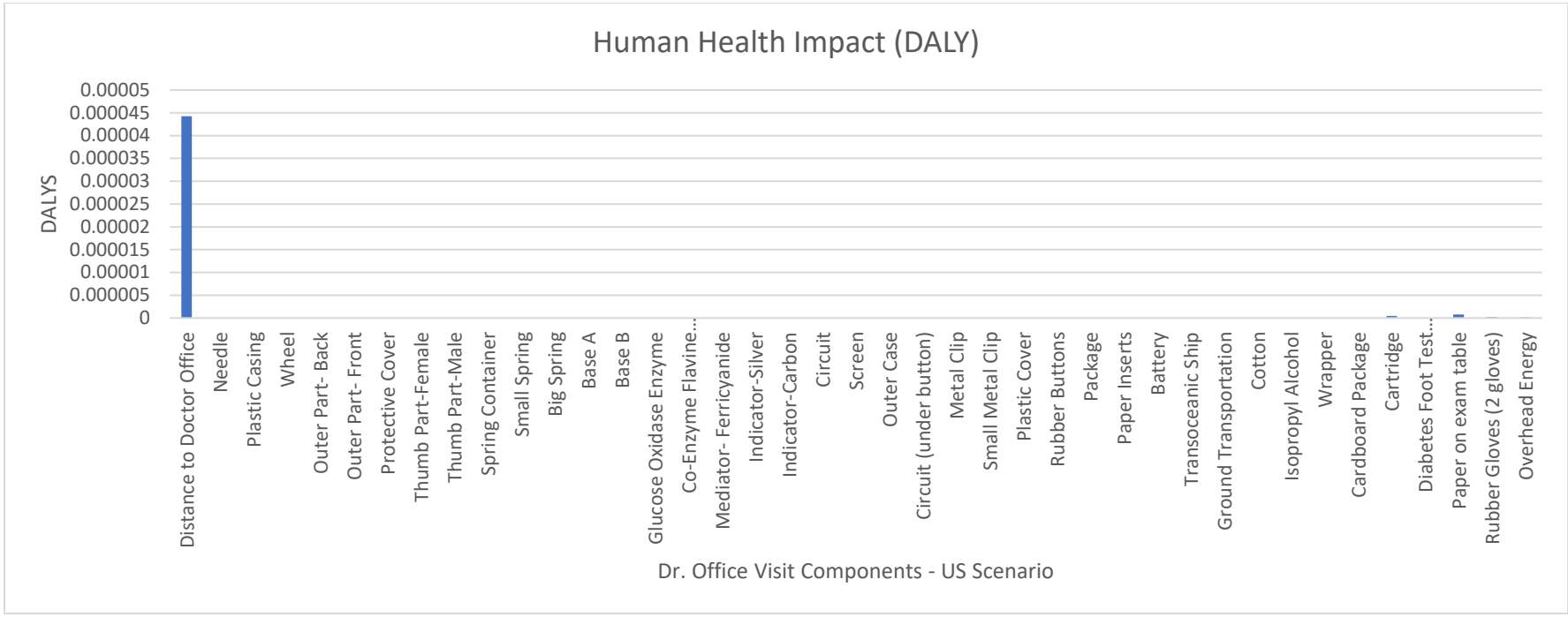


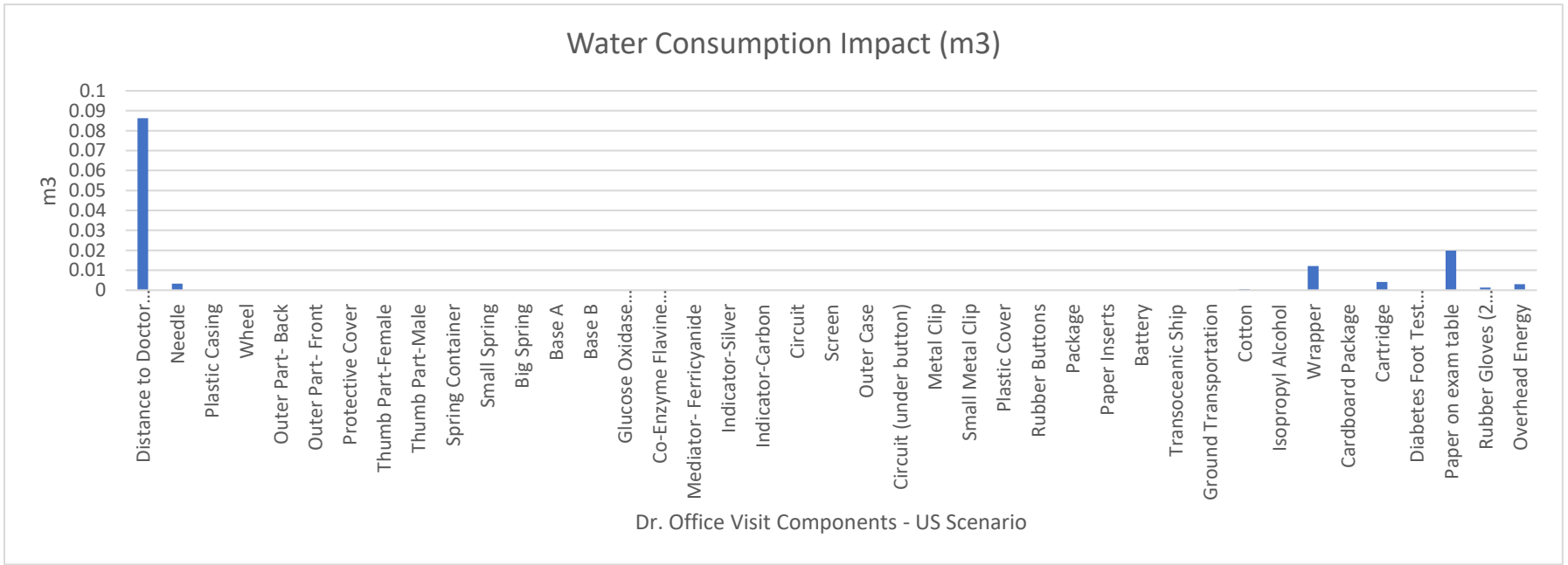


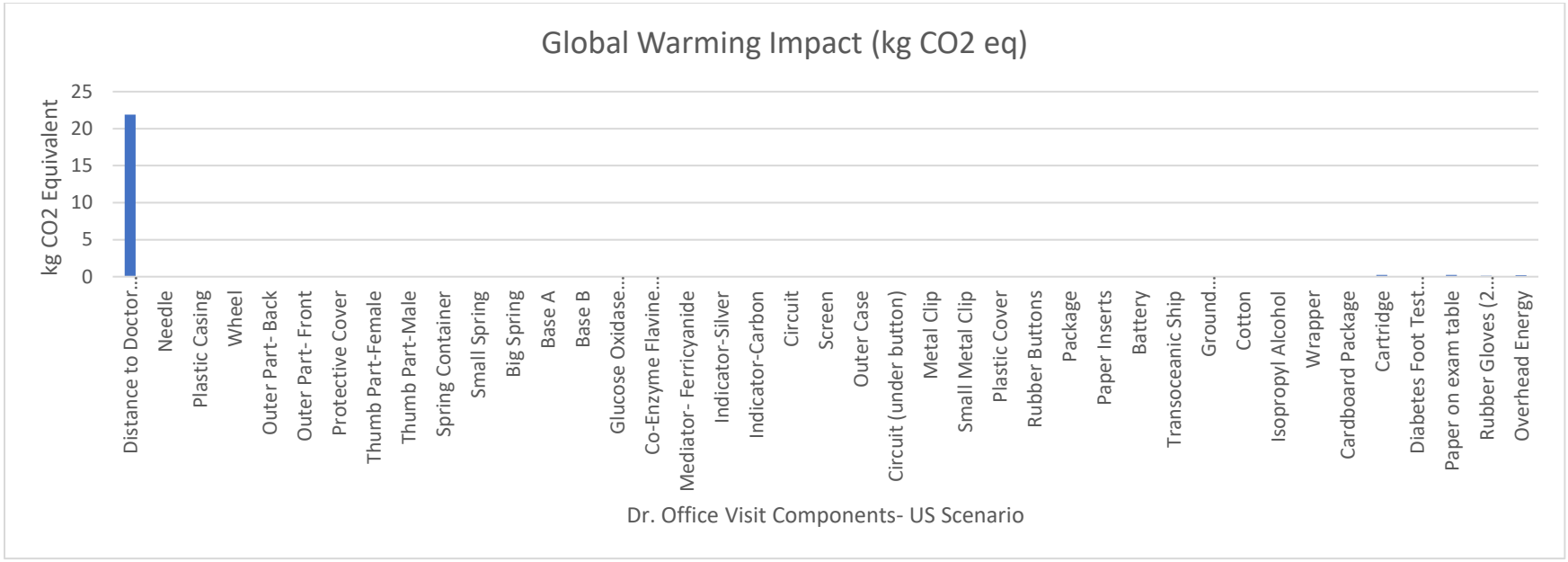




12.10 Doctor Visit – US Scenario



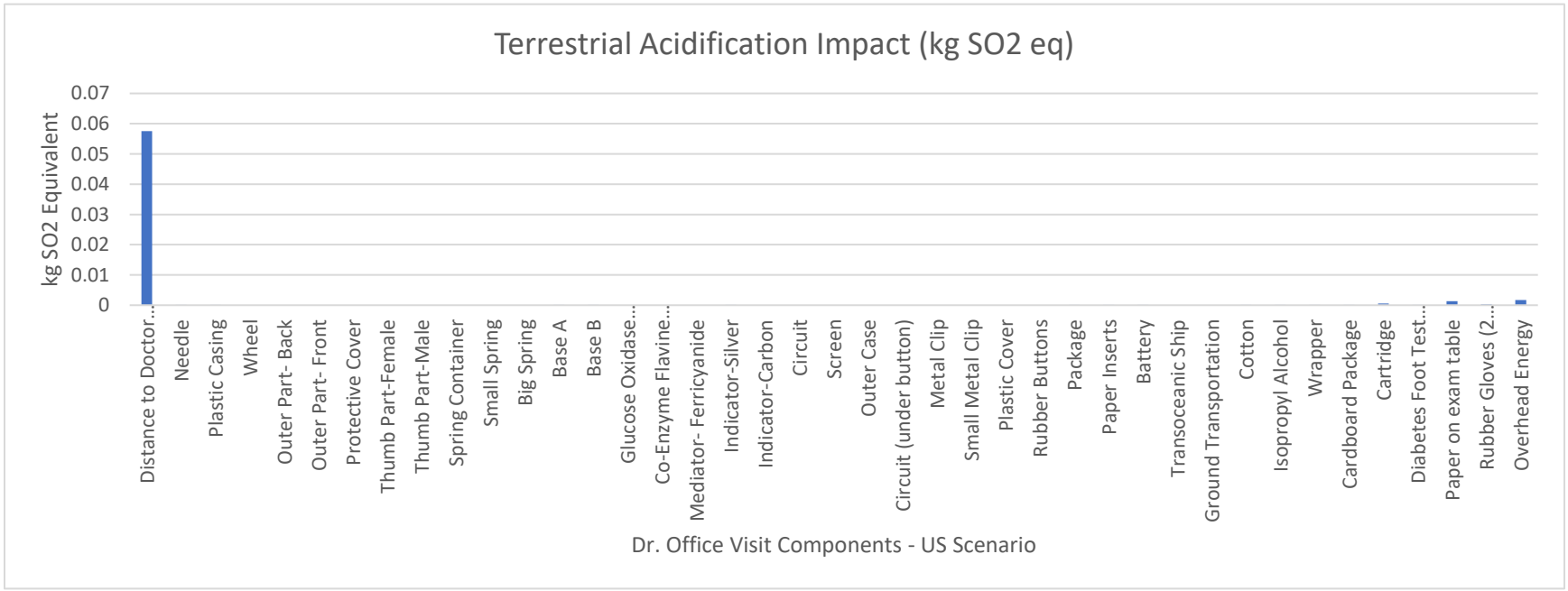



Global Warming Impact (kg CO2 eq)
kg CO2 Equivalent
25
20
15
10
5
0
Distance to Doctor...
Needle
Plastic Casing
Wheel
Outer Part- Back
Outer Part- Front
Protective Cover
Thumb Part-Female
Thumb Part-Male
Spring Container
Small Spring
Big Spring
Base A
Base B
Glucose Oxidase...
Co-Enzyme Flavine...
Mediator- Ferricyanide
Indicator-Silver
Indicator-Carbon
Circuit
Screen
Outer Case
Circuit (under button)
Metal Clip
Small Metal Clip
Plastic Cover
Rubber Buttons
Package
Paper Inserts
Battery
Transoceanic Ship
Ground...
Cotton
Isopropyl Alcohol
Wrapper
Cardboard Package
Cartridge
Diabetes Foot Test...
Paper on exam table
Rubber Gloves (2...
Overhead Energy
Dr. Office Visit Components- US Scenario

11

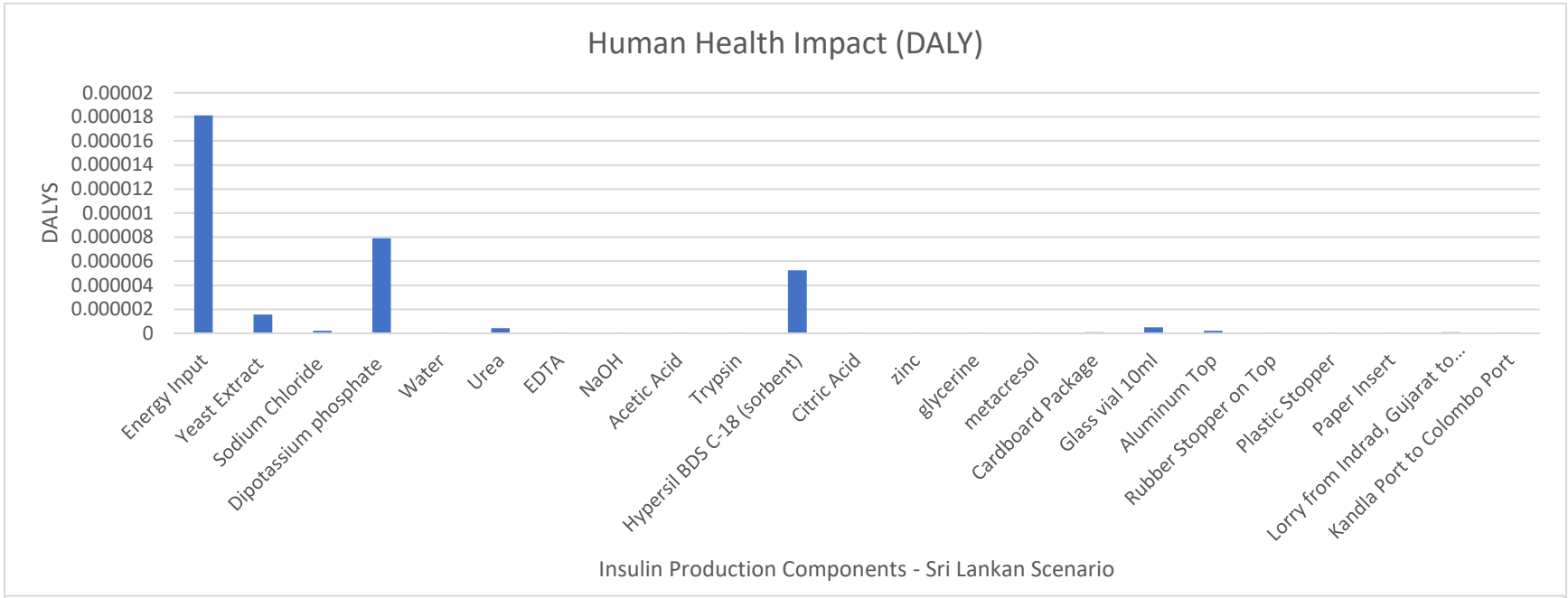
12

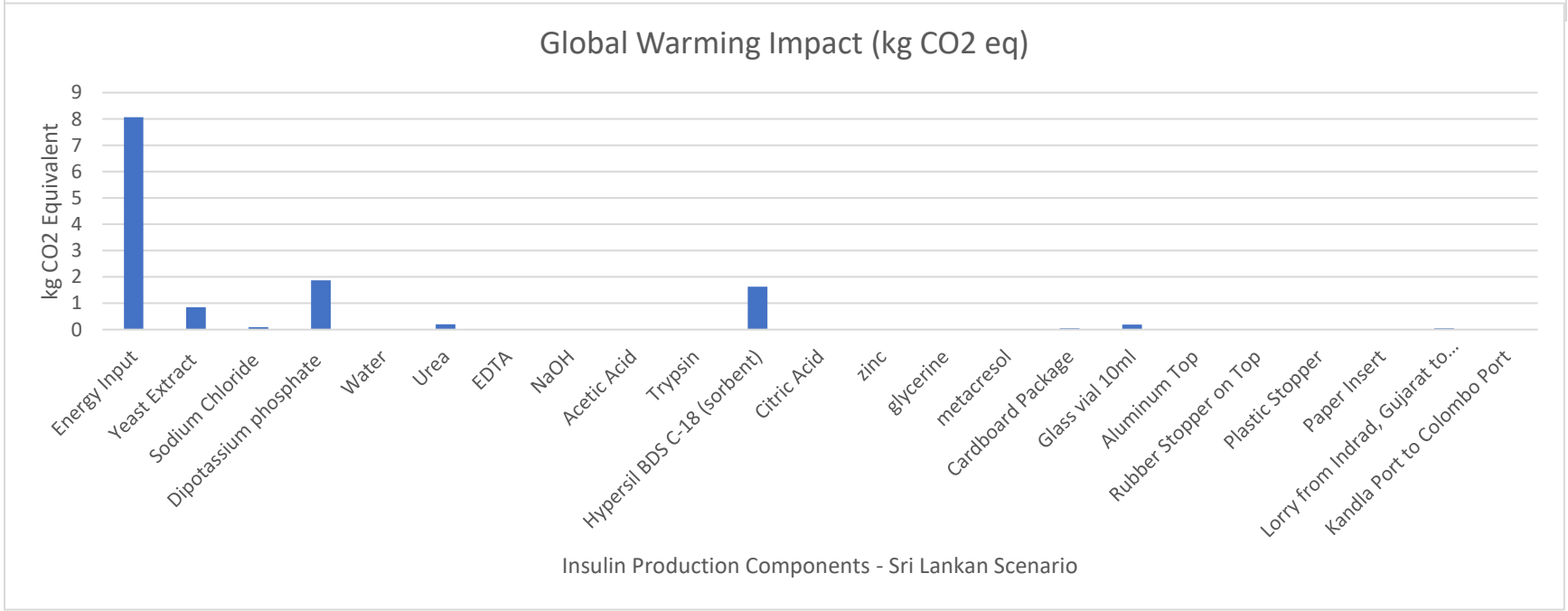
13


Terrestrial Acidification Impact (kg SO2 eq)
kg SO2 Equivalent
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0
Distance to Doctor...
Needle
Plastic Casing
Wheel
Outer Part- Back
Outer Part- Front
Protective Cover
Thumb Part-Female
Thumb Part-Male
Spring Container
Small Spring
Big Spring
Base A
Base B
Glucose Oxidase...
Co-Enzyme Flavine...
Mediator- Ferricyanide
Indicator-Silver
Indicator-Carbon
Circuit
Screen
Outer Case
Circuit (under button)
Metal Clip
Small Metal Clip
Plastic Cover
Rubber Buttons
Package
Paper Inserts
Battery
Transoceanic Ship
Ground Transportation
Cotton
Isopropyl Alcohol
Wrapper
Cardboard Package
Cartridge
Diabetes Foot Test...
Paper on exam table
Rubber Gloves (2...
Overhead Energy
Dr. Office Visit Components - US Scenario

14 *12.11 Insulin Production – Sri Lanka*

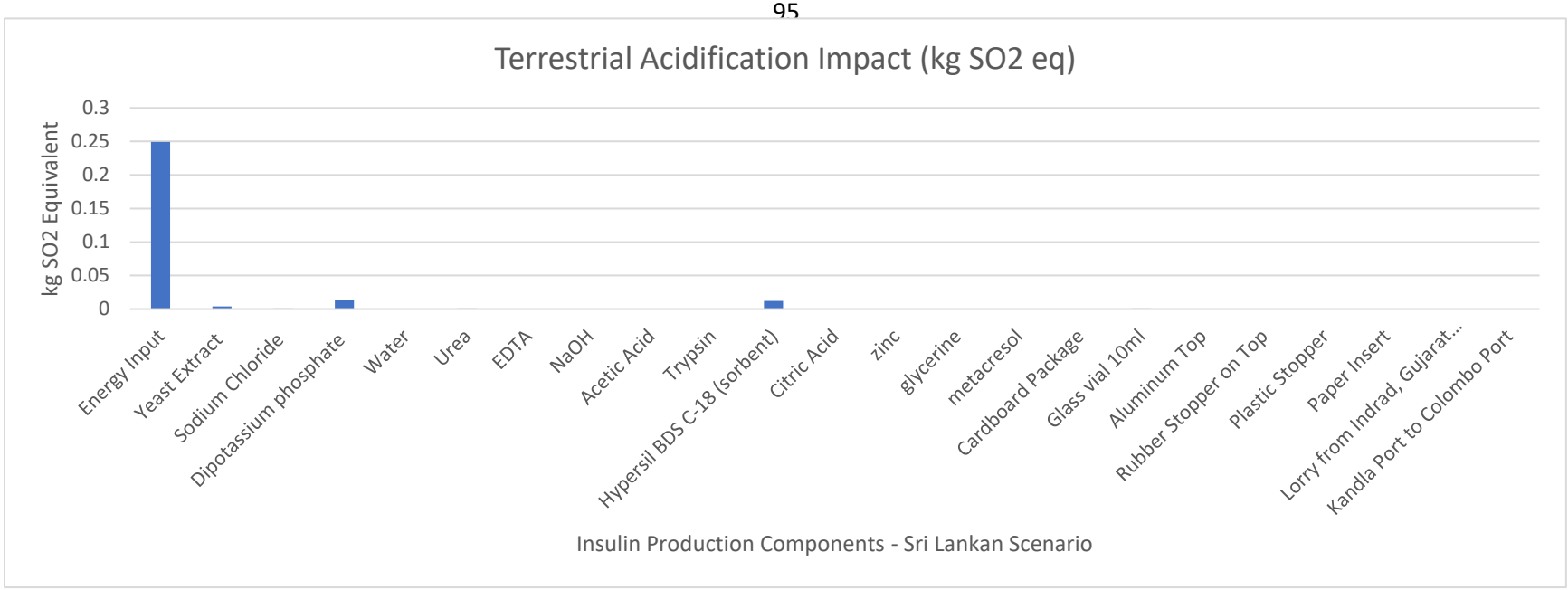
15

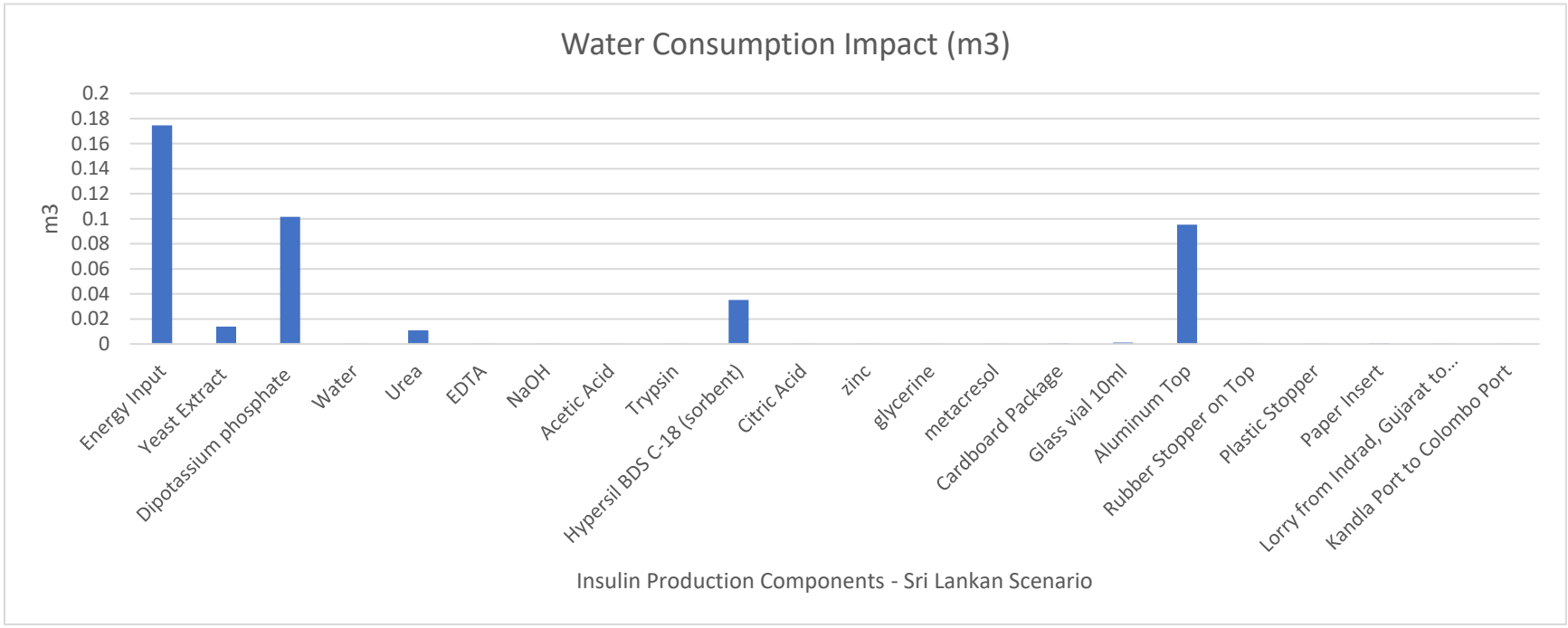




16

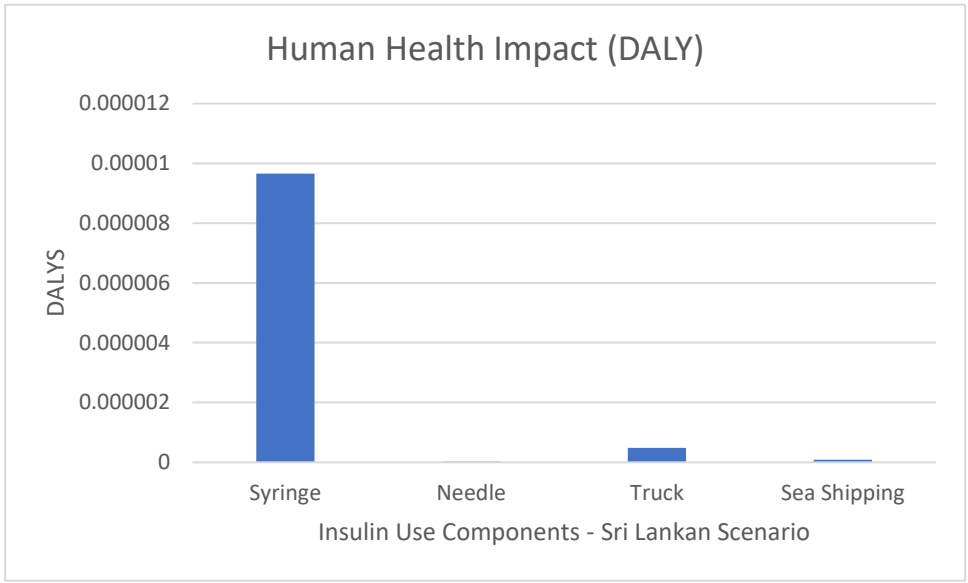
17

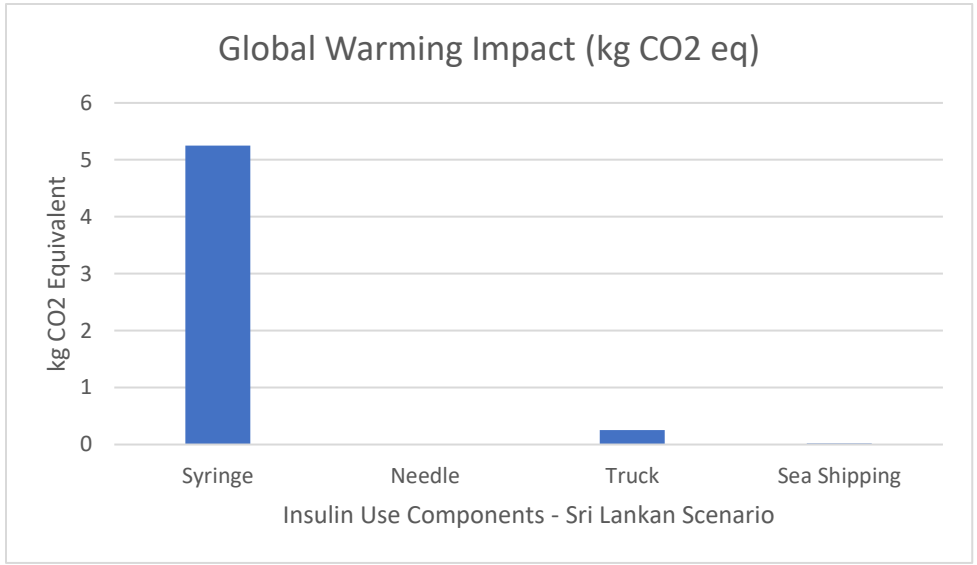

Terrestrial Acidification Impact (kg SO2 eq)
kg SO2 Equivalent
0.3
0.25
0.2
0.15
0.1
0.05
0
Energy Input
Yeast Extract
Sodium Chloride
Dipotassium phosphate
Water
Urea
EDTA
NaOH
Acetic Acid
Trypsin
Hypersil BDS C-18 (sorbent)
Citric Acid
zinc
glycerine
metacresol
Cardboard Package
Glass vial 10ml
Aluminum Top
Rubber Stopper on Top
Plastic Stopper
Paper Insert
Lorry from Indrad, Gujarat...
Kandla Port to Colombo Port
Insulin Production Components - Sri Lankan Scenario

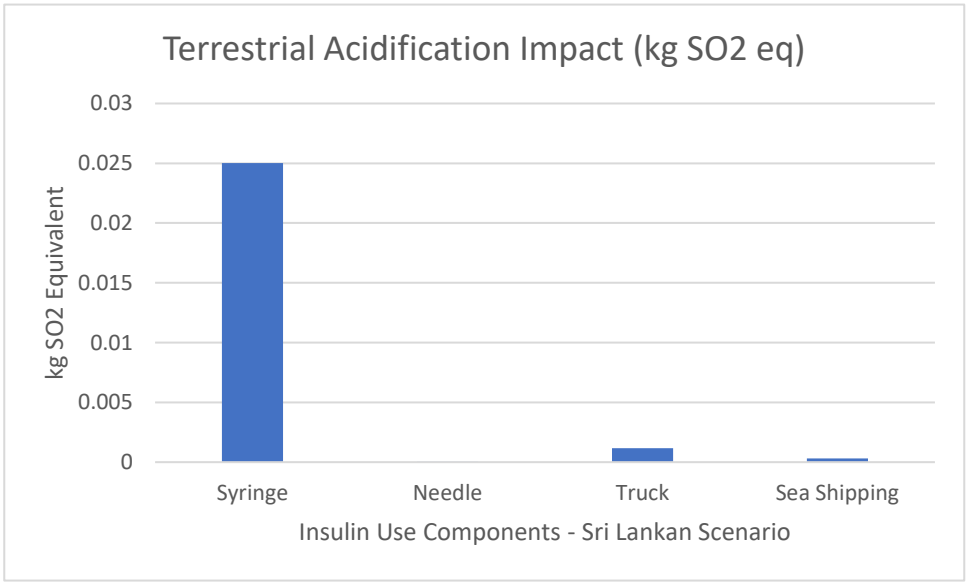

Water Consumption Impact (m3)
m3
0.2
0.18
0.16
0.14
0.12
0.1
0.08
0.06
0.04
0.02
0
Energy Input
Yeast Extract
Dipotassium phosphate
Water
Urea
EDTA
NaOH
Acetic Acid
Trypsin
Hypersil BDS C-18 (sorbent)
Citric Acid
zinc
glycerine
metacresol
Cardboard Package
Glass vial 10ml
Aluminum Top
Rubber Stopper on Top
Plastic Stopper
Paper Insert
Lorry from Indrad, Gujarat to...
Kandla Port to Colombo Port
Insulin Production Components - Sri Lankan Scenario

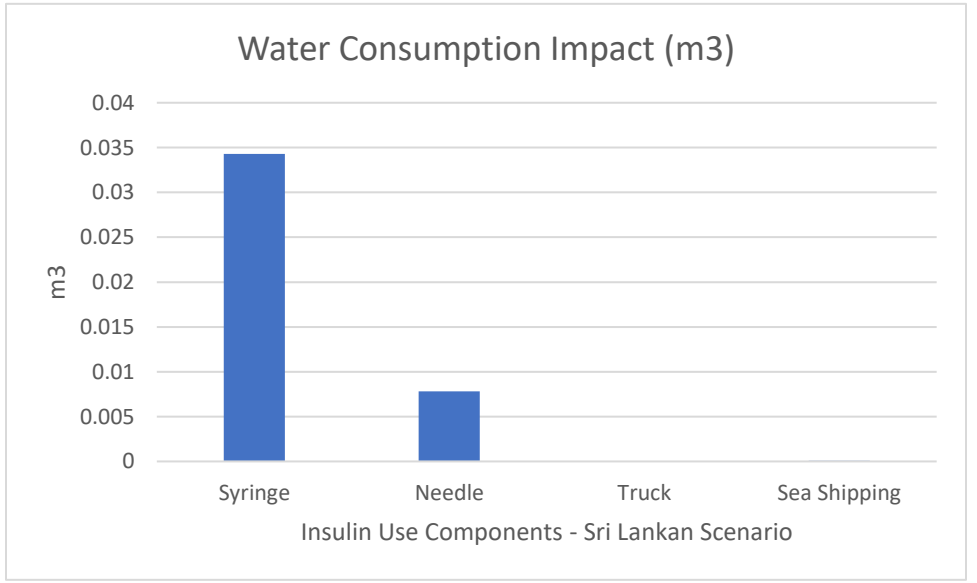
18 *12.12 Insulin Use – Sri Lanka*

19



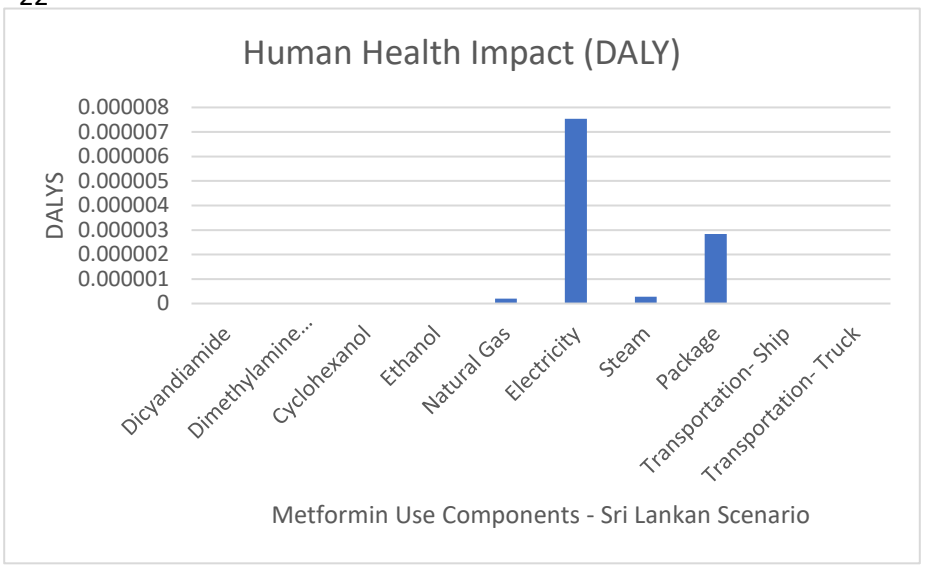


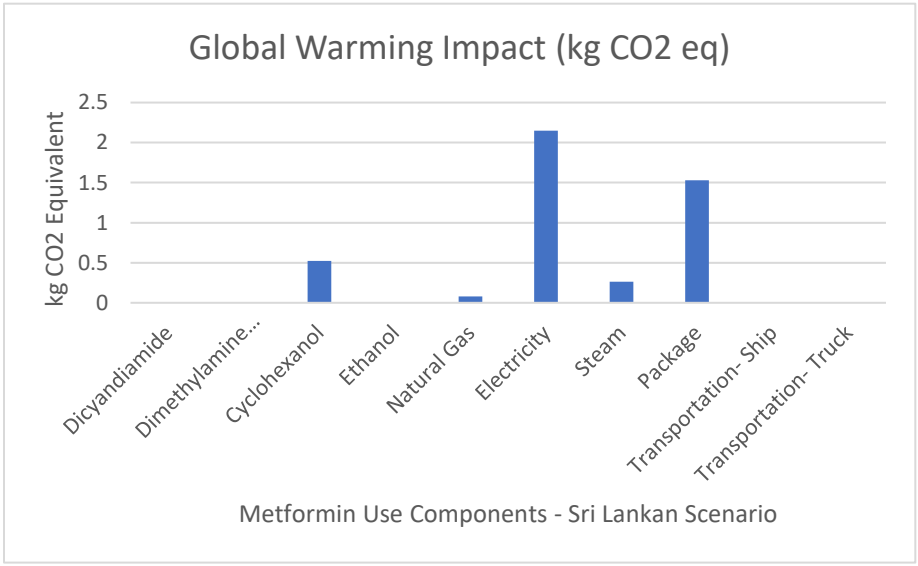


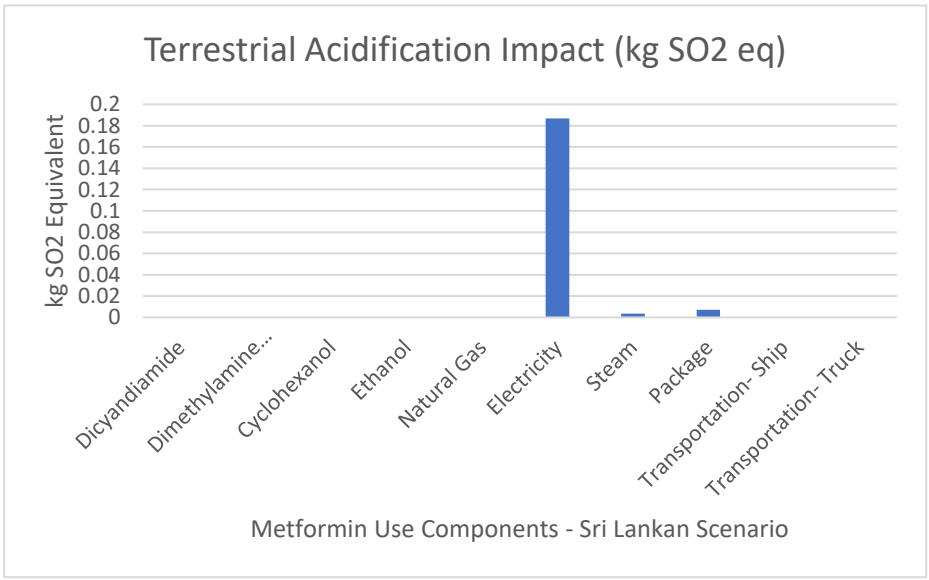


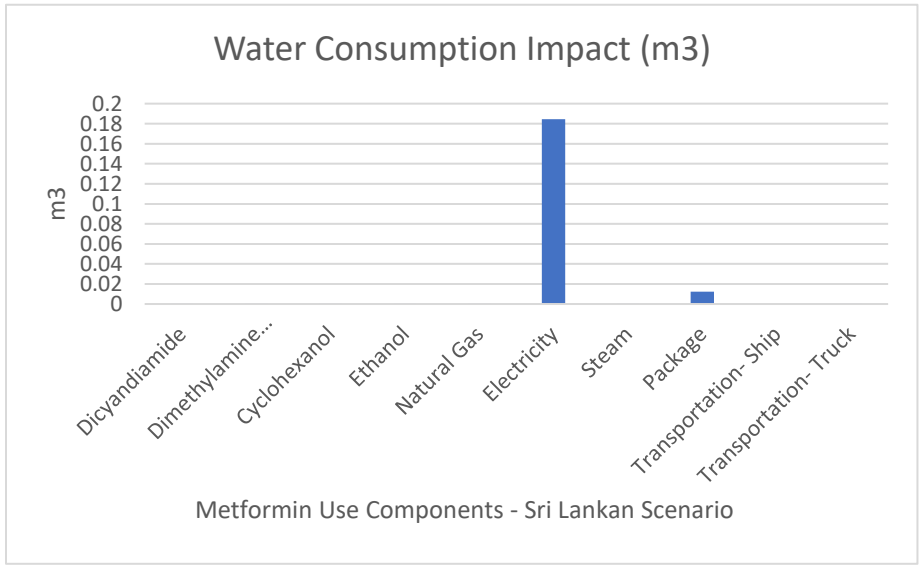
21 *12.13 Metformin Use – Sri Lanka*

22

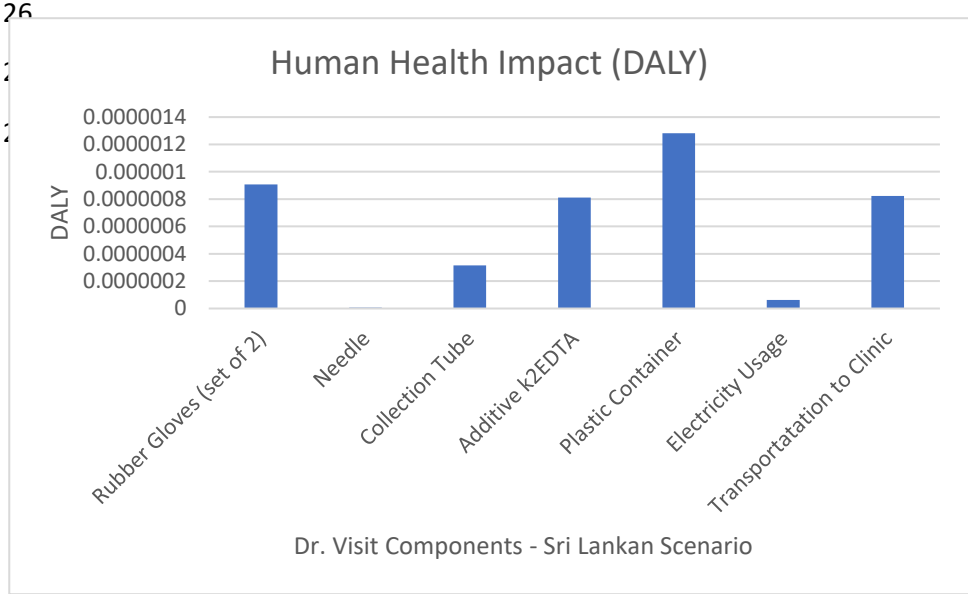


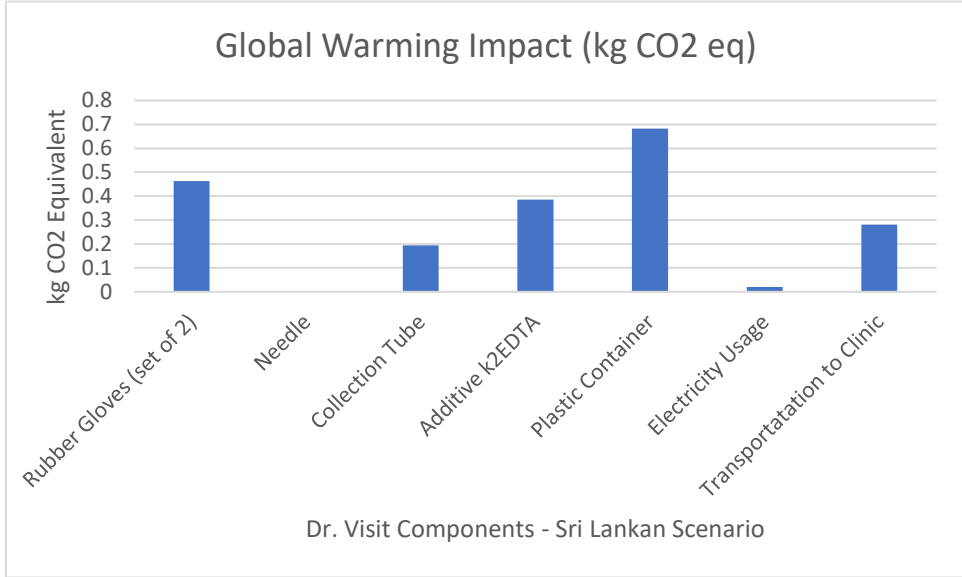


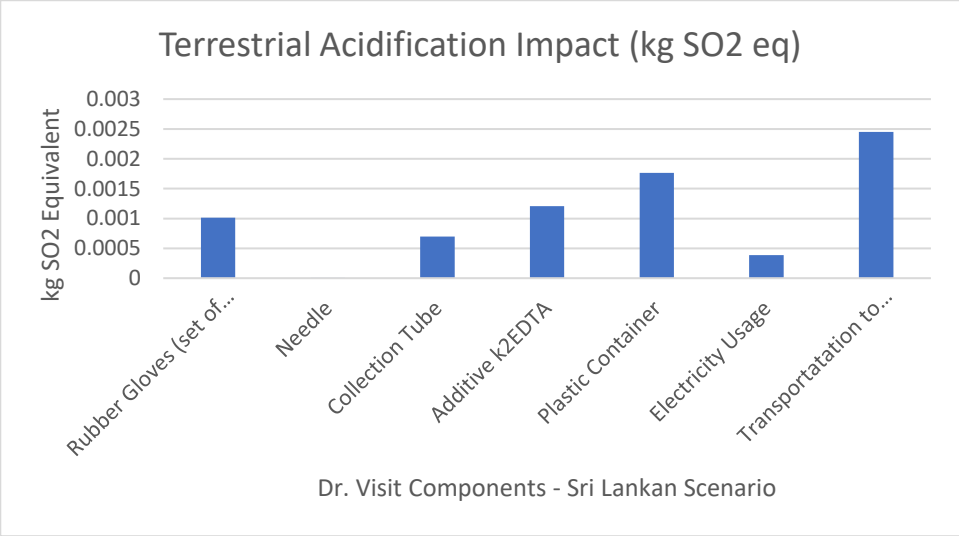


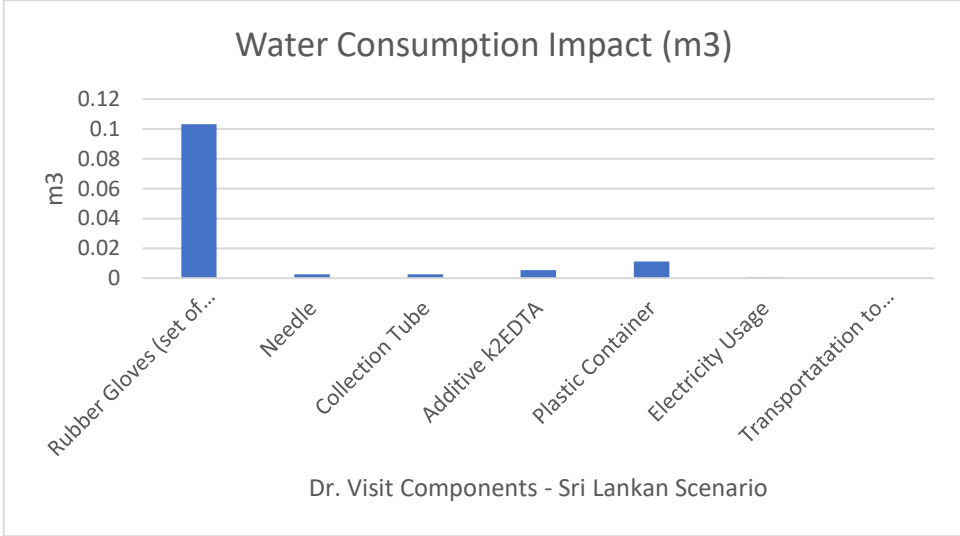


12.14 Dr. Visit – Sri Lanka









13 Appendix D: Additional Environmental Impact Indicator Results

All information regarding indicator and unit descriptions are sourced from: Huijbregts, M.A.J., Steinmann, Z.J.N., Elshout, P.M.F. et al. Int J Life Cycle Assess (2017) 22: 138. https://doi.org/10.1007/s11367-016-1246-

The data tables provided under each impact indicator section highlight the direct outputs associated with each system component for the indicator being analyzed.

13.1 Ozone Depletion

Indicator: Stratospheric ozone decrease

Characterization Factor: Ozone depletion potential (ODP)

Unit: kg CFC-11-eq to air

Damage Pathway: Human Health- years of life lost and disabled related to increased skin cancer and cataract due to UV-exposure

Study's Impact Indicator Results:

	Insulin Use: USA	**Metformin Use: USA**	**Insulin Use: Sri Lanka**	**Metformin Use: Sri Lanka**
Total	3.10215E-05	3.13439E-05	3.25179E-05	1.51227E-05
Standard Deviation	5.79138E-06	4.1228E-05	2.86838E-05	2.94377E-05
Min	2.52301E-05	-9.88E-06	3.83E-06	-1.4315E-05
Max	3.68129E-05	7.25719E-05	6.12017E-05	4.45603E-05
	Insulin Use: USA	**Metformin Use: USA**	**Insulin Use: Sri Lanka**	**Metformin Use: Sri Lanka**
Glucose Meter	9.76E-07	9.76E-07		
Test Strips	5.99E-06	2.00E-06		
Lancet	1.64E-06	5.46E-07		
Lancing Device	3.20E-08	3.20E-08		
Insulin Use	4.14696E-06		3.67183E-07	
Insulin Production	7.24873E-06		3.13585E-05	
Metformin Production		1.68E-05		1.43304E-05
Doctor Visit	1.10E-05	1.10E-05	7.92269E-07	7.92269E-07

13.2 Ionizing Radiation

Indicator: Absorbed dose increase

Characterization Factor: Ionizing radiation potential (IRP)

Unit: kBq Co-60-eq to air

Damage Pathway: Human Health- Years of life lost and disabled related to an increase in cancer and hereditary diseases due to exposure to radiation.

Study's Impact Indicator Results:

	Insulin Use: USA	**Metformin Use: USA**	**Insulin Use: Sri Lanka**	**Metformin Use: Sri Lanka**
Total	2.819831399	8.010720375	1.67358365	2.116836913
Standard Deviation	0.796350359	2.959172121	0.756361404	2.88116E-05
Min	2.023481041	5.05E+00	9.17E-01	2.116808102
Max	3.616181758	10.9698925	2.429945054	2.116865725
	Insulin Use: USA	**Metformin Use: USA**	**Insulin Use: Sri Lanka**	**Metformin Use: Sri Lanka**
Glucose Meter	0.147256012	0.147256012		
Test Strips	2.03E-01	6.77E-02		
Lancet	7.60E-02	2.53E-02		
Lancing Device	3.57E-03	3.57E-03		
Insulin Use	0.66357775		0.001041629	
Insulin Production	0.450843479		1.544538766	
Metformin Production		6.49E+00		1.988833659
Doctor Visit	1.28E+00	1.28E+00	0.128003254	0.128003254

13.3 Ozone Formulation- Human Health

Indicator: Tropospheric Ozone population intake increase

Characterization Factor: Photochemical oxidant formation potential: humans (HOFP)

Unit: kg NOx-eq to air

Damage Pathway: Human Health- Years of life lost related to an increase in respiratory diseases caused by exposure to ozone.

Study's Impact Indicator Results:

	Insulin Use: USA	**Metformin Use: USA**	**Insulin Use: Sri Lanka**	**Metformin Use: Sri Lanka**
Total	0.084834732	0.121958094	0.189157229	0.126997768
Standard Deviation	0.556514058	2.87642345	0.281205618	0.287996594
Min	-0.471679326	-2.75E+00	-9.20E-02	-0.160998826
Max	0.64134879	2.998381544	0.470362846	0.414994362
	Insulin Use: USA	**Metformin Use: USA**	**Insulin Use: Sri Lanka**	**Metformin Use: Sri Lanka**
Glucose Meter	0.003346774	0.003346774		
Test Strips	3.19E-03	1.06E-03		
Lancet	5.12E-03	1.71E-03		
Lancing Device	2.55E-04	2.55E-04		
Insulin Use	0.014709225		0.00995572	
Insulin Production	0.005770795		0.170653411	
Metformin Production		6.31E-02		0.11844967
Doctor Visit	5.24E-02	5.24E-02	0.008548098	0.008548098

13.4 Fine Particulate Matter

Indicator: PM2.5 population intake increase

Characterization Factor: Particulate matter formation potential

Unit: kg PM2.5-eq to air

Damage Pathway: Human Health- Years of life lost related to an increase in cardiopulmonary and lung cancer caused by exposure to primary and secondary aerosols.

Study's Impact Indicator Results:

	Insulin Use: USA	**Metformin Use: USA**	**Insulin Use: Sri Lanka**	**Metformin Use: Sri Lanka**
Total	0.059459425	0.225444349	0.356504073	0.003046593
Standard Deviation	0.039775546	0.289839571	0.29147002	0.287923954
Min	0.019683879	-6.44E-02	6.50E-02	-0.28487736
Max	0.099234971	0.515283921	0.647974092	0.290970547
	Insulin Use: USA	**Metformin Use: USA**	**Insulin Use: Sri Lanka**	**Metformin Use: Sri Lanka**
Glucose Meter	0.00303416	0.00303416		
Test Strips	2.26E-03	7.53E-04		
Lancet	3.62E-03	1.21E-03		
Lancing Device	1.15E-04	1.15E-04		
Insulin Use	0.01508088		0.007878243	
Insulin Production	0.006764503		0.200142291	
Metformin Production		1.92E-01		0.003046593
Doctor Visit	2.86E-02	2.86E-02	0.148483538	0.148483538

13.5 Terrestrial Ozone Formation

Indicator: Tropospheric ozone increase

Characterization Factor: Photochemical oxidant formation potential: ecosystems (EOFP)

Unit: kg NOx-eq to air

Damage Pathway: Loss of plant species due to increase in ozone exposure.

Study's Impact Indicator Results:

	Insulin Use: USA	**Metformin Use: USA**	**Insulin Use: Sri Lanka**	**Metformin Use: Sri Lanka**
Total	0.088741085	0.125134799	0.191501047	0.128252609
Standard Deviation	0.040247475	0.040250191	0.287688212	0.281196934
Min	0.04849361	8.49E-02	-9.62E-02	-0.152944325
Max	0.128988559	0.16538499	0.479189259	0.409449543
	Insulin Use: USA	**Metformin Use: USA**	**Insulin Use: Sri Lanka**	**Metformin Use: Sri Lanka**
Glucose Meter	0.003384613	0.003384613		
Test Strips	3.56E-03	1.19E-03		
Lancet	5.48E-03	1.83E-03		
Lancing Device	2.61E-04	2.61E-04		
Insulin Use	0.015158249		0.010663508	
Insulin Production	0.006223061		0.172095319	
Metformin Production		6.38E-02		0.119510388
Doctor Visit	5.47E-02	5.47E-02	0.008742221	0.008742221

13.6 Freshwater Eutrophication

Indicator: Phosphorous increase in freshwater

Characterization Factor: Freshwater eutrophication potential (FEP)

Unit: kg P-eq to freshwater

Damage Pathway: Loss of aquatic species due to increased phosphorous concentrations.

Study's Impact Indicator Results:

	Insulin Use: USA	**Metformin Use: USA**	**Insulin Use: Sri Lanka**	**Metformin Use: Sri Lanka**
Total	0.014701966	0.037881608	0.038333496	0.035022055
Standard Deviation	0.005753379	0.02925206	0.028413653	0.028451482
Min	0.008948587	8.63E-03	9.92E-03	0.006570574
Max	0.020455344	0.067133667	0.066747149	0.063473537
	Insulin Use: USA	**Metformin Use: USA**	**Insulin Use: Sri Lanka**	**Metformin Use: Sri Lanka**
Glucose Meter	0.002611356	0.002611356		
Test Strips	5.71E-04	1.90E-04		
Lancet	5.68E-04	1.89E-04		
Lancing Device	1.17E-05	1.17E-05		
Insulin Use	0.003008309		0.000179649	
Insulin Production	0.002721097		0.037749512	
Metformin Production		2.97E-02		0.03461772
Doctor Visit	5.21E-03	5.21E-03	0.000404335	0.000404335

13.7 Terrestrial Ecotoxicity

Indicator: Hazard-weighted increase in natural soils

Characterization Factor: Terrestrial ecotoxicity potential (TETP)

Unit: kg 1,4-DCB-eq to industrial soil

Damage Pathway: Species loss due to chemical exposure in soils.

Study's Impact Indicator Results:

	Insulin Use: USA	**Metformin Use: USA**	**Insulin Use: Sri Lanka**	**Metformin Use: Sri Lanka**
Total	110.0487295	114.362229	66.30324704	52.37202575
Standard Deviation	8.5547203	8.553169496	28.64163732	29.33322515
Min	101.4940092	1.06E+02	3.77E+01	23.0388006
Max	118.6034498	122.9153985	94.94488436	81.70525089
	Insulin Use: USA	**Metformin Use: USA**	**Insulin Use: Sri Lanka**	**Metformin Use: Sri Lanka**
Glucose Meter	3.96E+00	3.96E+00		
Test Strips	2.63E+00	8.75E-01		
Lancet	2.28E+00	7.59E-01		
Lancing Device	2.02E-01	2.02E-01		
Insulin Use	4.909164615		0.219093817	
Insulin Production	2.377762703		64.38071438	
Metformin Production		1.49E+01		50.6685869
Doctor Visit	9.37E+01	9.37E+01	1.70343885	1.70343885

13.8 Freshwater Ecotoxicity

Indicator: Hazard-weighted increase in freshwaters

Characterization Factor: Freshwater ecotoxicity potential

Unit: kg 1,4-DCB-eq to freshwater

Damage Pathway: Species loss due to chemical exposure in freshwater

Study's Impact Indicator Results:

	Insulin Use: USA	**Metformin Use: USA**	**Insulin Use: Sri Lanka**	**Metformin Use: Sri Lanka**
Total	110.0487295	114.362229	66.30324704	52.37202575
Standard Deviation	8.5547203	8.553169496	28.64163732	29.33322515
Min	101.4940092	1.06E+02	3.77E+01	23.0388006
Max	118.6034498	122.9153985	94.94488436	81.70525089
	Insulin Use: USA	**Metformin Use: USA**	**Insulin Use: Sri Lanka**	**Metformin Use: Sri Lanka**
Glucose Meter	3.96E+00	3.96E+00		
Test Strips	2.63E+00	8.75E-01		
Lancet	2.28E+00	7.59E-01		
Lancing Device	2.02E-01	2.02E-01		
Insulin Use	4.909164615		0.219093817	
Insulin Production	2.377762703		64.38071438	
Metformin Production		1.49E+01		50.6685869
Doctor Visit	9.37E+01	9.37E+01	1.70343885	1.70343885

13.9 Marine Ecotoxicity

Indicator: Hazard weighted increase in marine water

Characterization Factor: Marine ecotoxicity potential (METP)

Unit: kg 1,4-DCB-eq to marine water

Damage Pathway: Species loss due to chemical exposure in marine waters.

Study's Impact Indicator Results:

	Insulin Use: USA	**Metformin Use: USA**	**Insulin Use: Sri Lanka**	**Metformin Use: Sri Lanka**
Total	3.554710646	4.522037604	2.26167749	2.929959994
Standard Deviation	2.863117567	4.004094471	2.864624374	2.863117567
Min	0.691593079	5.18E-01	-6.03E-01	0.066842427
Max	6.417828213	8.526132074	5.126301864	5.793077561
	Insulin Use: USA	**Metformin Use: USA**	**Insulin Use: Sri Lanka**	**Metformin Use: Sri Lanka**
Glucose Meter	0.558579812	0.558579812		
Test Strips	6.31E-02	2.10E-02		
Lancet	5.15E-02	1.72E-02		
Lancing Device	1.13E-03	1.13E-03		
Insulin Use	0.254290094		0.008912987	
Insulin Production	0.136907657		2.252764503	
Metformin Production		1.43E+00		2.895072239
Doctor Visit	2.49E+00	2.49E+00		0.034887755

13.10 Carcinogenic Toxicity

Indicator: Risk increase of cancer disease incidence

Characterization Factor: Human toxicity potential (HTPc)

Unit: kg 1,4-DCB-eq to urban air

Damage Pathway: Years of life lost and disabled due to cancer and non-cancer effects due to ingestion and inhalation of toxic substances.

Study's Impact Indicator Results:

	Insulin Use: USA	**Metformin Use: USA**	**Insulin Use: Sri Lanka**	**Metformin Use: Sri Lanka**
Total	1.687783122	2.852317376	3.999154009	2.904759146
Standard Deviation	2.852836159	4.037404688	2.88726964	2.897589305
Min	-1.165053036	-1.19E+00	1.11E+00	0.007169841
Max	4.540619281	6.889722064	6.886423649	5.802348451
	Insulin Use: USA	**Metformin Use: USA**	**Insulin Use: Sri Lanka**	**Metformin Use: Sri Lanka**
Glucose Meter	0.120697021	0.120697021		
Test Strips	4.99E-02	1.66E-02		
Lancet	7.55E-02	2.52E-02		
Lancing Device	2.88E-03	2.88E-03		
Insulin Use	0.222423207		0.001941356	
Insulin Production	0.155759852		3.958807757	
Metformin Production		1.63E+00		2.866354249
Doctor Visit	1.06E+00	1.06E+00	0.038404897	0.038404897

13.11 Non-Human Carcinogenic Toxicity

Indicator: Risk increase of non-cancer disease incidence

Characterization Factor: Human toxicity potential (HTPnc)

Unit: kg 1,4-DCB-eq to urban air

Damage Pathway: Years of life lost and disabled due to cancer and non-cancer effects due to ingestion and inhalation of toxic substances.

Study's Impact Indicator Results:

	Insulin Use: USA	**Metformin Use: USA**	**Insulin Use: Sri Lanka**	**Metformin Use: Sri Lanka**
Total	42.59898876	62.36803309	42.07277858	36.40300221
Standard Deviation	9.521008532	9.53823039	28.78549315	28.9048213
Min	33.07798023	5.28E+01	1.33E+01	7.498180905
Max	52.11999729	71.90626348	70.85827173	65.30782351
	Insulin Use: USA	**Metformin Use: USA**	**Insulin Use: Sri Lanka**	**Metformin Use: Sri Lanka**
Glucose Meter	13.42399528	13.42399528		
Test Strips	1.19E+00	3.97E-01		
Lancet	1.02E+00	3.40E-01		
Lancing Device	2.65E-02	2.65E-02		
Insulin Use	3.200866126		0.285452572	
Insulin Production	2.564014343		41.09502606	
Metformin Production		2.70E+01		35.71070226
Doctor Visit	2.12E+01	2.12E+01	0.692299948	0.692299948

14 Appendix B: Detailed Sensitivity Analysis Findings

The following section details the results of the individual sensitivity analysis assessments.

14.1 U.S. Treatment Pathway: Number of Doctor Visits

This analysis assessed the impact of number of visits to the doctor's office on the four impact indicators. The intent was to investigate if there were significant differences in the final impact of the scenario assessment if patients were to increase or decrease their in-person interactions with healthcare providers. Table 3 shows the impact indicator totals attributable to the number of doctor visits. Tables 4 and 5 shows how the overall T2d treatment totals are impacted by tested variability of doctor visits with regards to the United States Insulin Use scenario and the United States Metformin Use scenario, respectively.

Table 9: Impacts associated with tested number of In-Person Doctor Visits according to the assumed components of a doctor visit specified in the Data Inventor section.

# of Doctor Visits	Climate Impact (kg CO2 Equiv./Functional Unit)	Total Terrestrial Acidification Impact (kg SO2 eq)	Total Water Consumption Impact (m3)	Health Impact (DALY/Functional Unit)
12	142.095098	0.420971329	0.877484929	0.000281107
11	127.0947571	0.35778119	0.753627107	0.000254749
10	114.5833904	0.316737689	0.669741589	0.000230702
9	102.6942674	0.281230848	0.595849147	0.000207232
8	91.05404174	0.247938671	0.525953935	0.000183993
7	79.60527567	0.216350081	0.459133516	1.61E-04
6	68.1182177	0.184420774	0.391698138	0.000137835
5	56.71731652	0.153258082	0.325646417	0.000114818
4	45.25897748	0.121584313	0.258672258	9.17E-05
3	33.87243577	0.090549389	0.192851146	6.87E-05
2	79.60527567	0.06164395	0.130873525	4.60E-05
1	11.27166597	0.030012771	0.063976236	2.29E-05

157

158 *Table 10: Final Functional Unit Impacts Associated with Alternative Values for Number of In-Person Doctor Visits in the U.S. Insulin Use Scenario*

# of Doctor Visits	Climate Impact (kg CO2 Equiv./Functional Unit)	Total Terrestrial Acidification Impact (kg SO2 eq)	Total Water Consumption Impact (m3)	Health Impact (DALY/Functional Unit)
12	154.1698852	0.489327379	4.686611404	0.000335144
11	139.1695442	0.42613724	4.562753582	0.000308787
10	126.6581776	0.385093739	4.478868064	0.000284739
9	114.7690545	0.349586898	4.404975622	0.000261269
8	103.1288289	0.316294721	4.33508041	0.00023803
7	91.68006282	0.284706131	4.268259991	0.000214969
6	80.19300485	0.252776824	4.200824613	0.000191872
5	68.79210367	0.221614132	4.134772892	0.000168855
4	57.33376463	0.189940363	4.067798733	0.000145785
3	45.94722292	0.158905439	4.001977621	0.000122781
2	34.8	0.13	3.94	0.0001
1	23.34645312	0.098368821	3.873102711	7.69343E-05

159

160

161

162

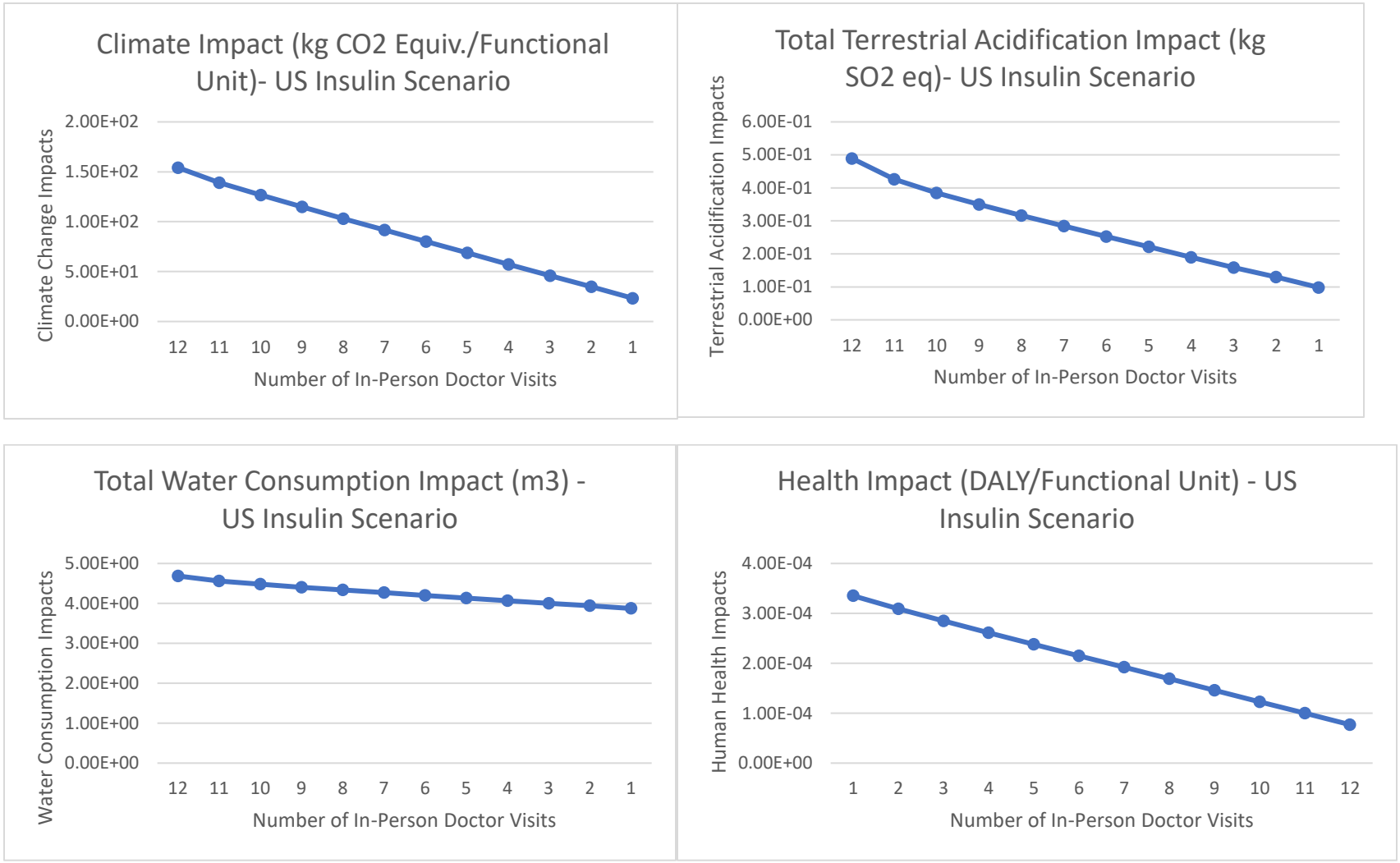
163

164

165

166

Figure 12: In-Person Dr. Visit Impact Sensitivity Analysis- US Insulin Use Scenario

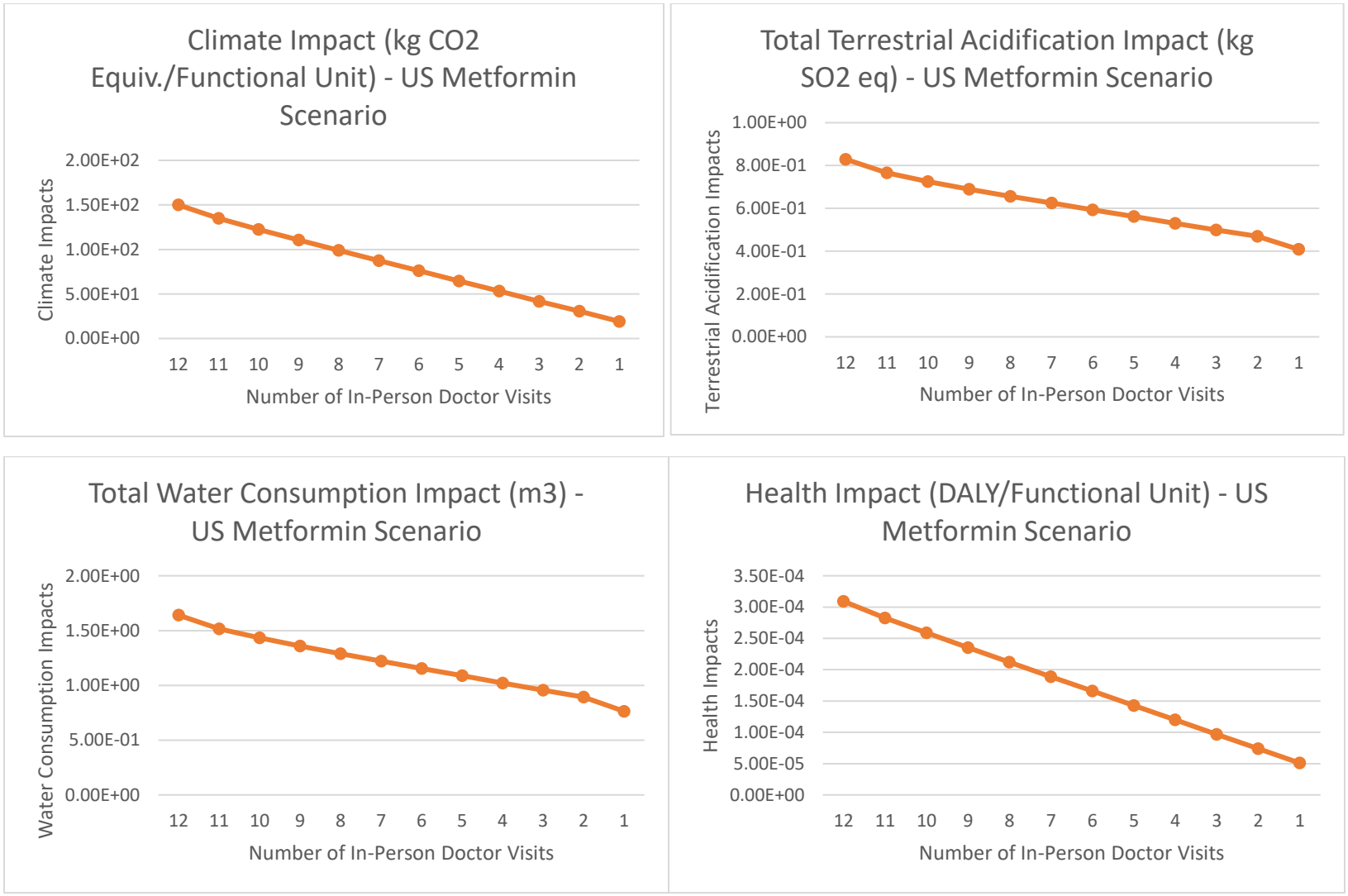


179 *Table 11: Final Functional Unit Impacts Associated with Alternative Values for number of in-person doctor visits in the U.S. Metformin Use Scenario*

# of Doctor Visits	Climate Impact (kg CO2 Equiv./Functional Unit)	Total Terrestrial Acidification Impact (kg SO2 eq)	Total Water Consumption Impact (m3)	Health Impact (DALY/Functional Unit)
12	1.50E+02	8.29E-01	1.64E+00	3.09E-04
11	1.35E+02	7.66E-01	1.52E+00	2.83E-04
10	1.22E+02	7.25E-01	1.43E+00	2.59E-04
9	1.11E+02	6.90E-01	1.36E+00	2.35E-04
8	9.89E+01	6.56E-01	1.29E+00	2.12E-04
7	8.75E+01	6.25E-01	1.22E+00	1.89E-04
6	7.60E+01	5.93E-01	1.15E+00	1.66E-04
5	6.46E+01	5.62E-01	1.09E+00	1.43E-04
4	5.31E+01	5.30E-01	1.02E+00	1.20E-04
3	4.17E+01	4.99E-01	9.56E-01	9.68E-05
2	3.06E+01	4.70E-01	8.94E-01	7.40E-05
1	1.91E+01	4.08E-01	7.63E-01	5.09E-05

180

Figure 13: In-Person Dr. Visit Impact Sensitivity Analysis- US Metformin Use Scenario



185

186 *14.2 Doctor's Visit Overhead Energy Sensitivity Analysis*

187 The variable Doctor's Visit Overhead Energy is designed to assess the effects of energy use during in-person doctor visits on the overall impacts
188 associated with T2d treatments. The variable is only assessed in the context of the US treatment scenarios. Sri Lankan treatment scenarios were
189 not considered given the low energy intensity of public medical buildings.

190

191 *Table 12:Impact values attributed to the Overhead Energy Use of a Doctor's Office per Functional Unit. Functional Unit assumes two doctor visits per year.*

	MJ/Functional unit	Climate Impact (kg CO2 Equivalent/Functional Unit)	Total Terrestrial Acidification Impact (kg SO2 eq)	Total Water Consumption Impact (m3)	Health Impact (DALY/Functional Unit)
Baseline	51.45823906	0.191459564	0.001703588	0.003074792	1.77674E-07
Scenario 1	308.7494344	1.148757382	0.010221526	0.018448756	1.06604E-06
Scenario 2	154.3747172	0.574378692	0.005110762	0.009224378	5.33022E-07
Scenario 3	102.9164781	0.382919128	0.003407176	0.006149586	3.55348E-07
Scenario 4	77.1873586	0.287189346	0.002555382	0.004612188	2.6651E-07
Scenario 5	61.74988688	0.229751476	0.002044306	0.003689752	2.13208E-07
Scenario 6	56.60406296	0.21060552	0.001873946	0.003382272	1.95441E-07
Scenario 7	46.31241516	0.172313608	0.001533228	0.002767314	1.59907E-07
Scenario 8	41.16659124	0.15316765	0.00136287	0.002459834	1.42139E-07
Scenario 9	25.72911954	0.095729782	0.000851794	0.001537396	8.8837E-08
Scenario 10	12.86455977	0.04786489	0.000425896	0.000768698	4.44E-08
Scenario 11	2.572911954	0.00958	0.0000852	0.0001538	8.88E-09

192

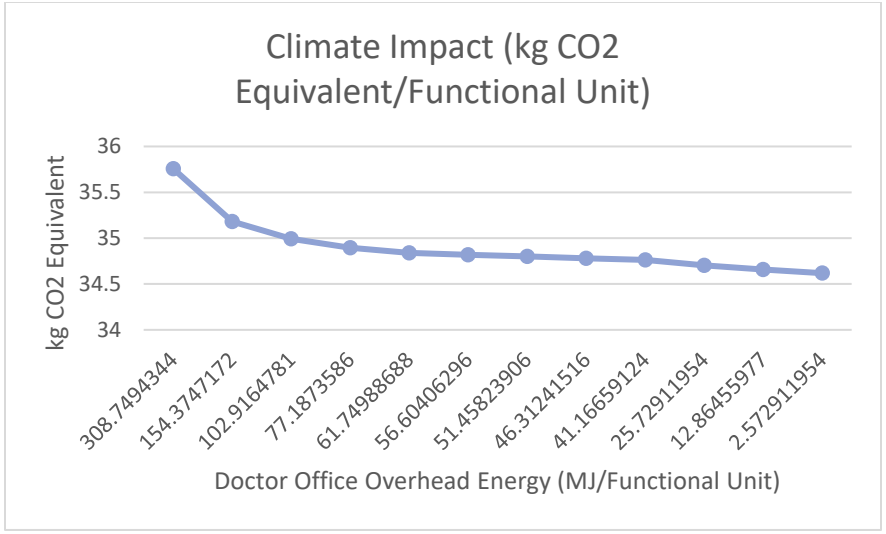
193

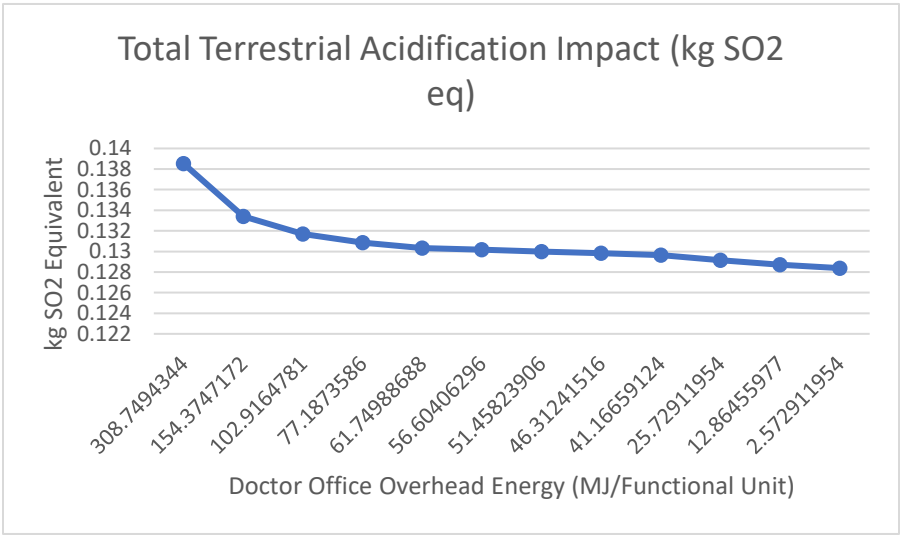
194

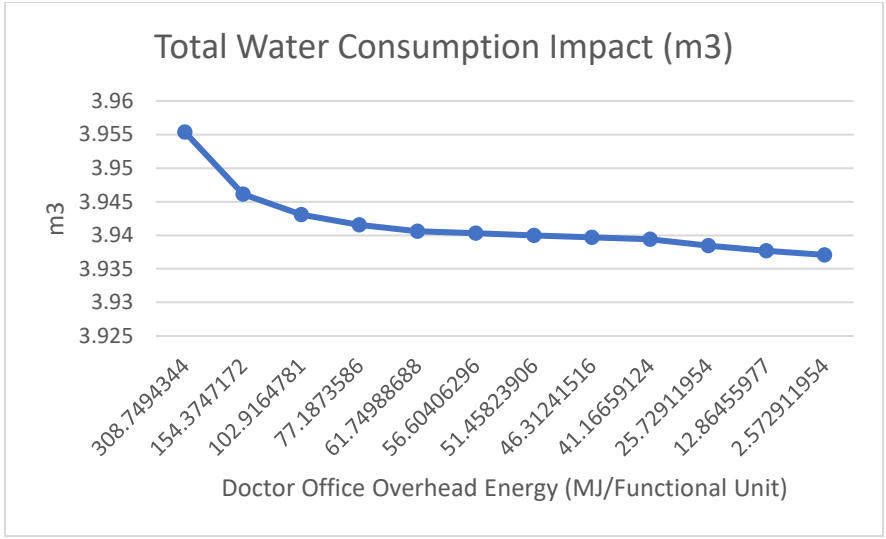
Table 13: Total T2d Treatment Impacts per sensitivity analysis scenario for overhead energy used during a doctor visit in the US Insulin Use Scenario. All values are calculated by Functional Unit, which assumes two in-person doctor visits per year.

	MJ/Functional Unit	Climate Impact (kg CO2 Equivalent/Functional Unit)	Total Terrestrial Acidification Impact (kg SO2 eq)	Total Water Consumption Impact (m3)	Health Impact (DALY/Functional Unit)
Scenario 1	308.7494344	35.75729782	0.138517938	3.955373964	0.000100888
Scenario 2	154.3747172	35.18291913	0.133407174	3.946149586	0.000100355
Scenario 3	102.9164781	34.99145956	0.131703588	3.943074794	0.000100178
Scenario 4	77.1873586	34.89572978	0.130851794	3.941537396	0.000100089
Scenario 5	61.74988688	34.83829191	0.130340718	3.94061496	0.000100036
Scenario 6	56.60406296	34.81914596	0.130170358	3.94030748	0.000100018
Baseline	51.45823906	34.8	0.13	3.94	0.0001
Scenario 7	46.31241516	34.78085404	0.12982964	3.939692522	9.99822E-05
Scenario 8	41.16659124	34.76170809	0.129659282	3.939385042	9.99645E-05
Scenario 9	25.72911954	34.70427022	0.129148206	3.938462604	9.99112E-05
Scenario 10	12.86455977	34.65640533	0.128722308	3.937693906	9.98667E-05
Scenario 11	2.572911954	34.61812044	0.128381612	3.937079008	9.98312E-05

Figure 14: Dr. Office Overhead Energy Variable Scenario Results for Total T2 Impacts- US Insulin Use







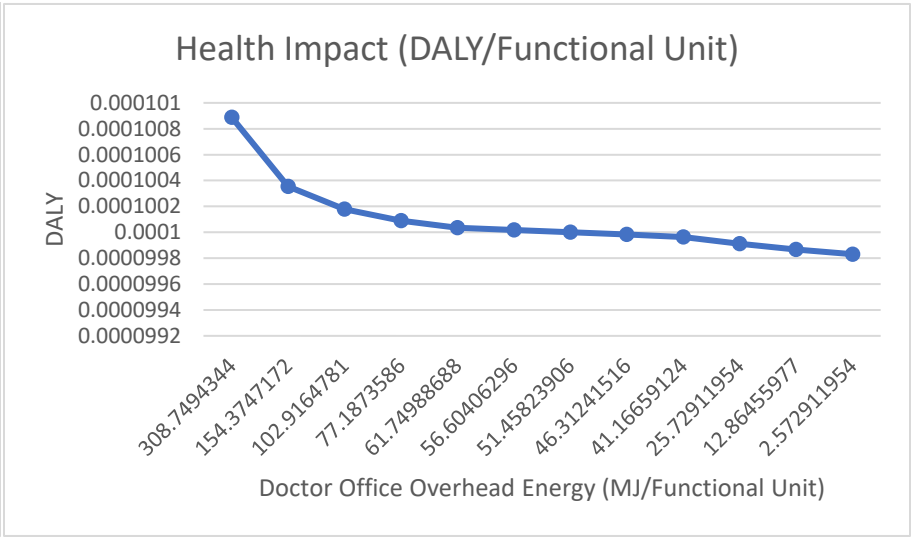
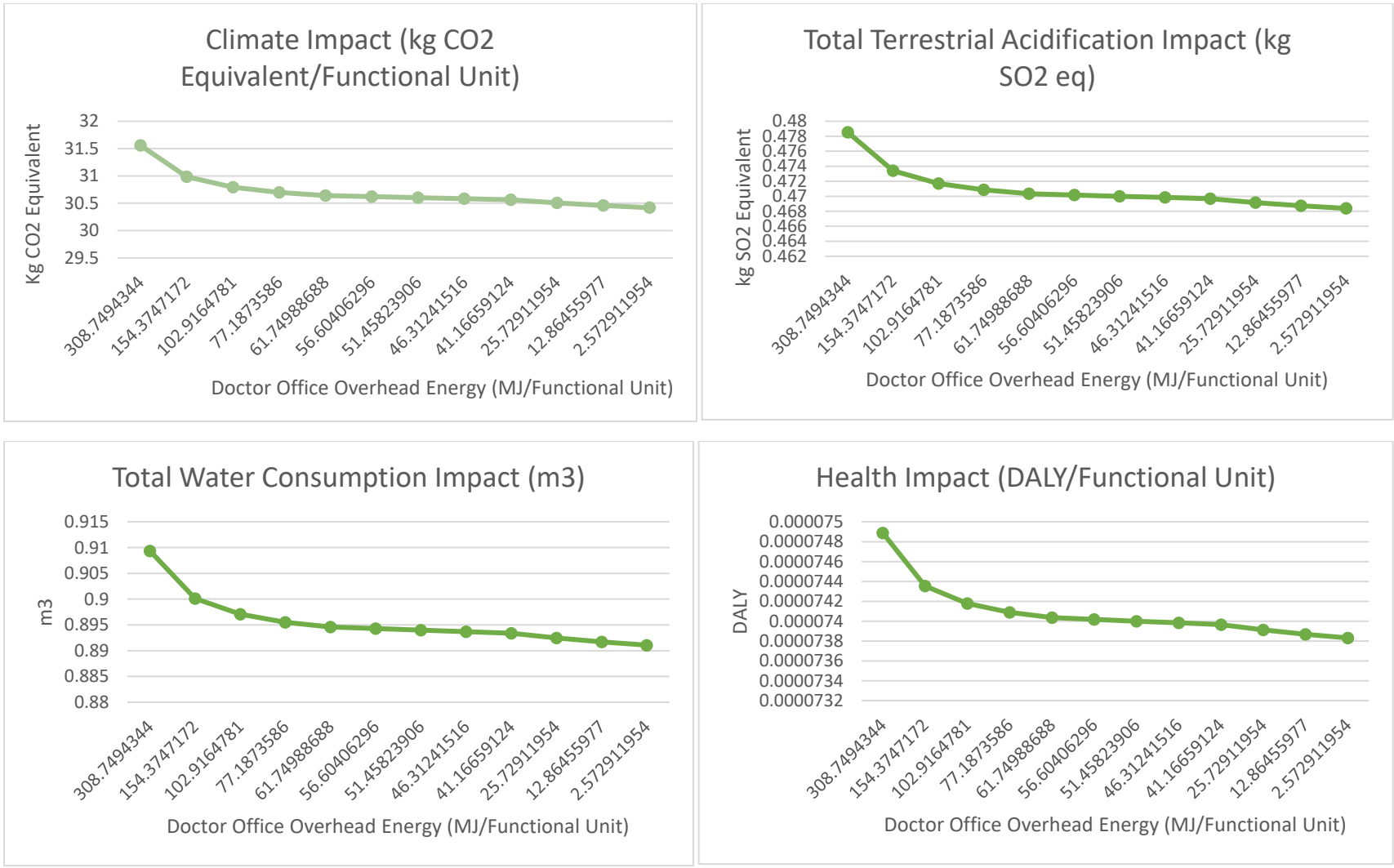


Table 14: Total T2d treatment Impacts associated with sensitivity analysis adjusted variables for overhead energy used during a doctor visit in the US Metformin Use Scenario. All values are calculated by Functional Unit, which assumes two in-person doctor visits per year.

		Climate Impact (kg CO2 Equivalent/Functional Unit)	Total Terrestrial Acidification Impact (kg SO2 eq)	Total Water Consumption Impact (m3)	Health Impact (DALY/Functional Unit)
Scenario 1	308.7494344	31.55729782	0.478517938	0.909373964	7.48884E-05
Scenario 2	154.3747172	30.98291913	0.473407174	0.900149586	7.43553E-05
Scenario 3	102.9164781	30.79145956	0.471703588	0.897074794	7.41777E-05
Scenario 4	77.1873586	30.69572978	0.470851794	0.895537396	7.40888E-05
Scenario 5	61.74988688	30.63829191	0.470340718	0.89461496	7.40355E-05
Scenario 6	56.60406296	30.61914596	0.470170358	0.89430748	7.40178E-05
Baseline	51.45823906	30.6	0.47	0.894	0.000074
Scenario 7	46.31241516	30.58085404	0.46982964	0.893692522	7.39822E-05
Scenario 8	41.16659124	30.56170809	0.469659282	0.893385042	7.39645E-05
Scenario 9	25.72911954	30.50427022	0.469148206	0.892462604	7.39112E-05
Scenario 10	12.86455977	30.45640533	0.468722308	0.891693906	7.38667E-05
Scenario 11	2.572911954	30.41812044	0.468381612	0.891079008	7.38312E-05

Figure 15: Dr. Office Overhead Energy Variable Scenario Results for Total T2 Impacts- US Metformin



14.3 Distance to Doctor's Office in the United States

Distance to the doctor's office is a measure of the environmental and human health emissions associated with the round-trip distance required to journey to and from a doctor appointment. The calculations assume that the patient will be traveling in a gasoline-powered, single occupancy vehicle.

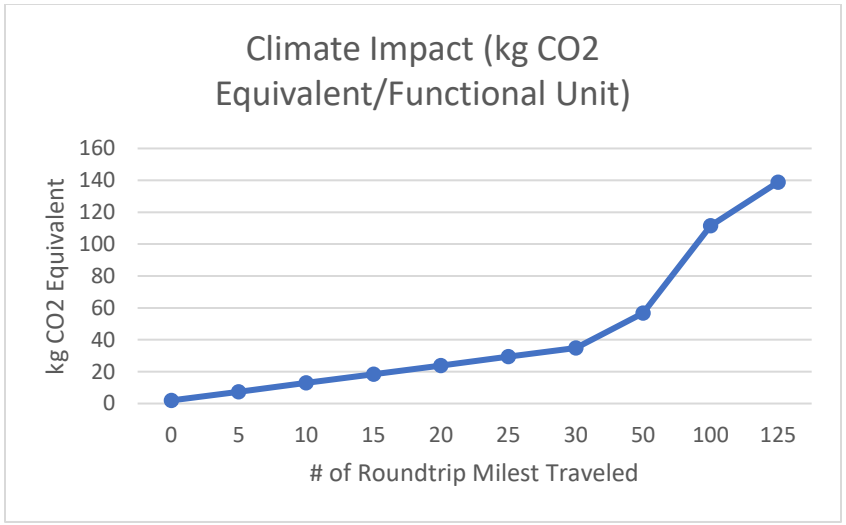
Table 15: Impact values of sensitivity analysis scenarios for the round-trip distance required by a T2d patient to visit a doctor in the US treatment scenarios.

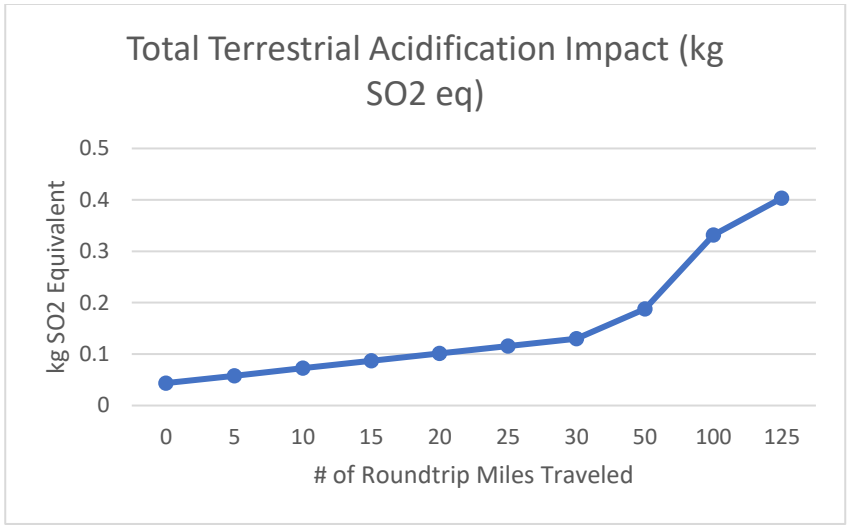
	# of Roundtrip Miles Traveled	Climate Impact (kg CO2 Equivalent/Functional Unit)	Total Terrestrial Acidification Impact (kg SO2 eq)	Total Water Consumption Impact (m3)	Health Impact (DALY/Functional Unit)
Scenario 1	0	0.833034978	0.004102816	0.044594458	1.70383E-06
Scenario 2	5	6.306080864	0.0184881	0.066164225	1.27686E-05
Scenario 3	10	11.77912675	0.032873383	0.087733992	2.38333E-05
Scenario 4	15	17.25217264	0.047258667	0.109303758	3.4898E-05
Scenario 5	20	22.72521852	0.06164395	0.130873525	4.59627E-05
Scenario 6	25	28.19826441	0.076029234	0.152443292	5.70274E-05
Baseline	30	33.67131029	0.090414517	0.174013059	6.80922E-05
Scenario 7	50	55.56349384	0.147955651	0.260292126	0.000112351
Scenario 8	100	110.2939527	0.291808487	0.475989793	0.000222998
Scenario 9	125	137.6591821	0.363734905	0.583838627	0.000278322

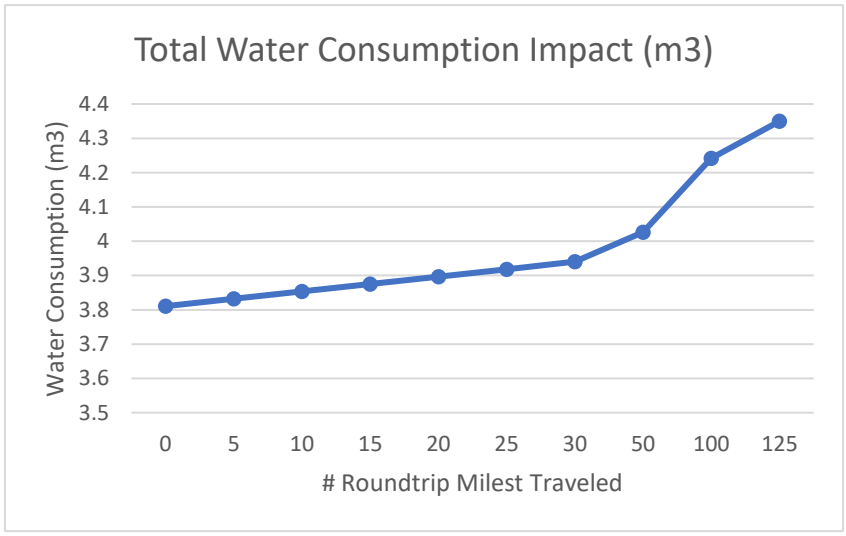
Table 16: Total T2d treatment impacts after including scenario sensitivity analysis assessments of roundtrip distances traveled to the doctor in the U.S. Insulin Use Scenario

	# of Roundtrip Miles Traveled	Climate Impact (kg CO2 Equivalent/Functional Unit)	Total Terrestrial Acidification Impact (kg SO2 eq)	Total Water Consumption Impact (m3)	Health Impact (DALY/Functional Unit)
Scenario 1	0	1.961724684	0.043688299	3.810581399	3.36117E-05
Scenario 2	5	7.43477057	0.058073582	3.832151166	4.46764E-05
Scenario 3	10	12.90781646	0.072458866	3.853720933	5.57411E-05
Scenario 4	15	18.38086234	0.086844149	3.8752907	6.68058E-05
Scenario 5	20	23.85390823	0.101229433	3.896860466	7.78706E-05
Scenario 6	25	29.32695411	0.115614716	3.918430233	8.89353E-05
Baseline	30	34.8	0.13	3.94	0.0001
Scenario 7	50	56.69218354	0.187541134	4.026279067	0.000144259
Scenario 8	100	111.4226424	0.33139397	4.241976735	0.000254906
Scenario 9	125	138.7878718	0.403320387	4.349825568	0.00031023

Figure 16: Sensitivity Analysis Results of Impacts Associated with Distance to Doctor Office Variable Scenarios- US Insulin Use







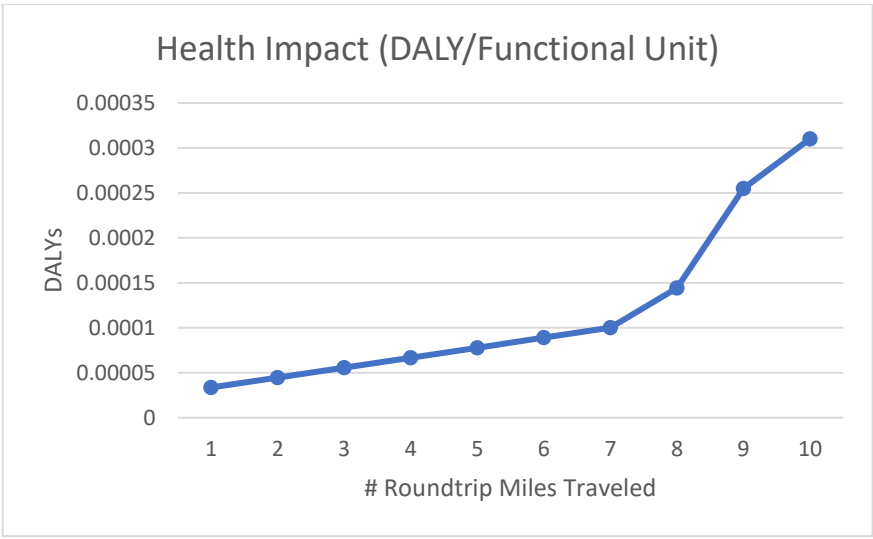
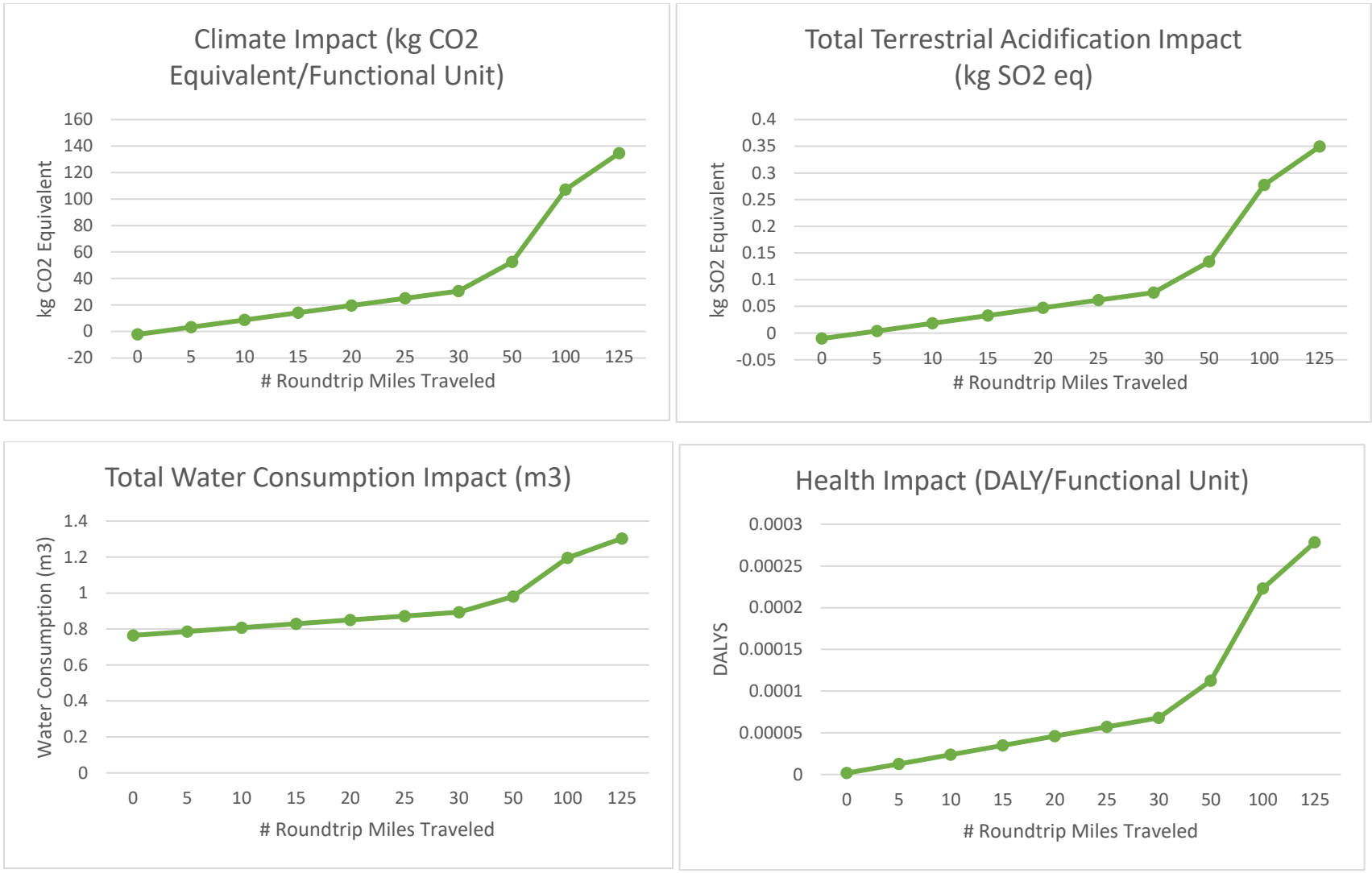


Table 17: Total T2d treatment impacts after including scenario sensitivity analysis assessments of roundtrip distances traveled to the doctor in the U.S. Metformin Use Scenario

	# of Roundtrip Miles Traveled	Climate Impact (kg CO2 Equivalent/Functional Unit)	Total Terrestrial Acidification Impact (kg SO2 eq)	Total Water Consumption Impact (m3)	Health Impact (DALY/Functional Unit)
Scenario 1	0	-2.238275316	-0.010282467	0.764581399	1.70383E-06
Scenario 2	5	3.23477057	0.004102816	0.786151166	1.27686E-05
Scenario 3	10	8.707816456	0.0184881	0.807720933	2.38333E-05
Scenario 4	15	14.18086234	0.032873383	0.8292907	3.4898E-05
Scenario 5	20	19.65390823	0.047258667	0.850860466	4.59627E-05
Scenario 6	25	25.12695411	0.06164395	0.872430233	5.70274E-05
Baseline	30	30.6	0.076029234	0.894	6.80922E-05
Scenario 7	50	52.49218354	0.133570368	0.980279067	0.000112351
Scenario 8	100	107.2226424	0.277423203	1.195976735	0.000222998
Scenario 9	125	134.5878718	0.349349621	1.303825568	0.000278322

Figure 17: Sensitivity Analysis Results of Impacts Associated with Distance to Doctor Office Variable Scenarios- US Metformin Use



14.4 Insulin Dosage- United States

The US Insulin Dosage variable assesses the different impacts associated with different dosages of insulin when used in the context of the U.S. Insulin-Use scenario model. The variables assessed range from 5 to 25. The assessed variables sought to cover a range of patient scenarios from those with relatively high insulin production and sensitivity rates to those patients with relatively low insulin production and sensitivity rates.

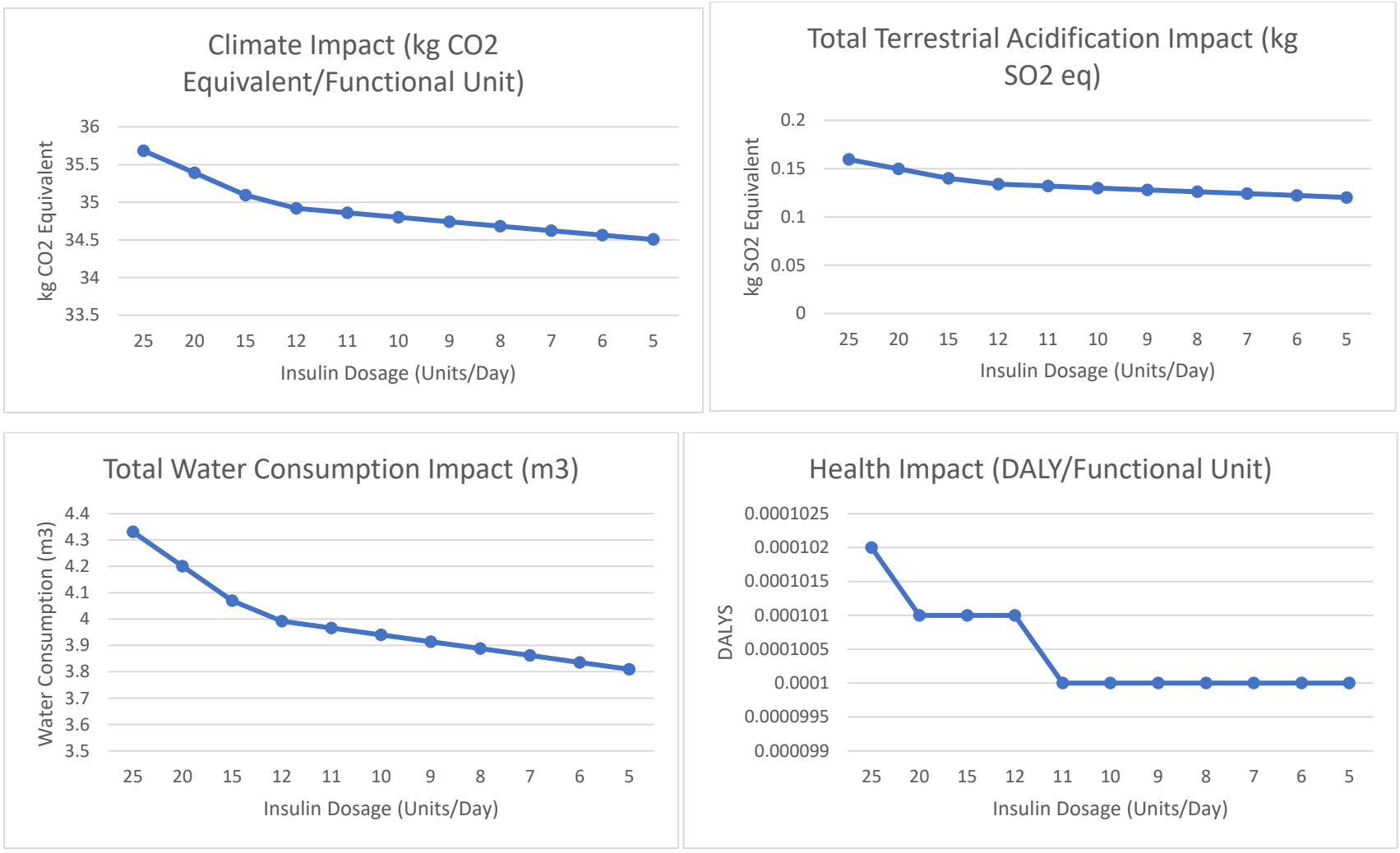
Table 18: Insulin Dosage Sensitivity Analysis Impact Results

	# Units/Day	Climate Impact (kg CO2 Equivalent/Functional Unit)	Total Terrestrial Acidification Impact (kg SO2 eq)	Total Water Consumption Impact (m3)	Health Impact (DALY/Functional Unit)
Scenario 1	25	42.76427331	0.266653547	0.899278126	0.000104
Scenario 2	20	42.46950149	0.256830836	0.769015663	0.000103
Scenario 3	15	42.17472967	0.247008125	0.638753201	0.000103
Scenario 4	12	41.99786658	0.241114498	0.560595723	0.000103
Scenario 5	11	41.93891222	0.239149956	0.534543231	0.000102
Baseline	10	41.87995786	0.237185414	0.508490738	0.000102
Scenario 6	9	41.82100349	0.235220872	0.482438246	0.000102
Scenario 7	8	41.76204913	0.233256329	0.456385753	0.000102
Scenario 8	7	41.70309477	0.231291787	0.430333261	0.000102
Scenario 9	6	41.6441404	0.229327245	0.404280768	0.000102
Scenario 10	5	41.58518604	0.227362703	0.378228276	0.000102

Table 19: Total T2d Impact Treatment Results for Insulin Dosage Variable Sensitivity Analysis. Each Scenario is Assessed in the Context of the US Insulin Use Model.

	# Units/Day	Climate Impact (kg CO2 Equivalent/Functional Unit)	Total Terrestrial Acidification Impact (kg SO2 eq)	Total Water Consumption Impact (m3)	Health Impact (DALY/Functional Unit)
Scenario 1	25	35.68431545	0.159468133	4.330787388	0.000102
Scenario 2	20	35.38954363	0.149645422	4.200524925	0.000101
Scenario 3	15	35.09477181	0.139822711	4.070262463	0.000101
Scenario 4	12	34.91790872	0.133929084	3.992104985	0.000101
Scenario 5	11	34.85895436	0.131964542	3.966052493	0.0001
Baseline	10	34.8	0.13	3.94	0.0001
Scenario 6	9	34.74104563	0.128035458	3.913947508	0.0001
Scenario 7	8	34.68209127	0.126070915	3.887895015	0.0001
Scenario 8	7	34.62313691	0.124106373	3.861842523	0.0001
Scenario 9	6	34.56418254	0.122141831	3.83579003	0.0001
Scenario 10	5	34.50522818	0.120177289	3.809737538	0.0001

Figure 18: Sensitivity Analysis Results of Impacts Associated with Insulin Dosage Variable Scenarios- US Insulin Use Model



14.5 Insulin Production Energy- United States Scenario

The Insulin Production Energy variable seeks to assess the impacts associated with different amounts of energy used in the insulin production process. This assessment does not investigate the impacts associated with a different energy mix. The assessment is confined to the impacts associated with overall production energy increases or decreases, distributed across a standard mix of electrical, steam and gas energy sources.

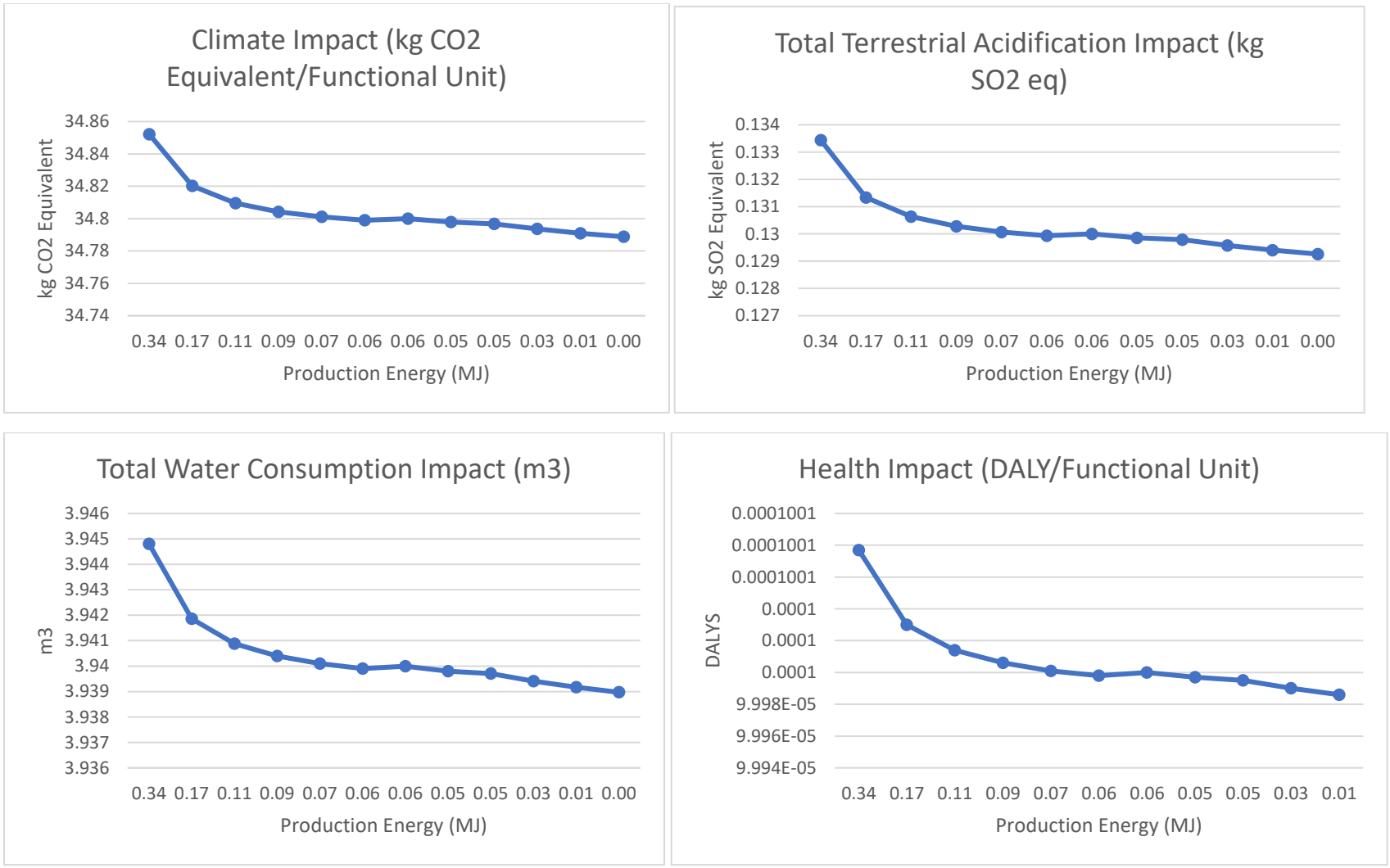
Table 20: Insulin Production Energy Variable Sensitivity Results

	MJ/Functional Unit	Climate Impact (kg CO2 Equivalent/Functional Unit)	Total Terrestrial Acidification Impact (kg SO2 eq)	Total Water Consumption Impact (m3)	Health Impact (DALY/Functional Unit)
Scenario 1	0.344	41.40858335	0.222064136	0.255872186	0.000101851
Scenario 2	0.172	41.37664271	0.219957659	0.252930305	0.000101804
Scenario 3	0.115	41.36599584	0.2192555	0.251949677	0.000101788
Scenario 4	0.086	41.3606724	0.218904421	0.251459364	0.00010178
Scenario 5	0.069	41.35747834	0.218693773	0.251165176	0.000101775
Scenario 6	0.063	41.35534896	0.218553341	0.25096905	0.000101772
Baseline	0.057	41.35641365	0.218623557	0.251067113	0.000101774
Scenario 7	0.052	41.35428427	0.218483126	0.250870987	0.000101771
Scenario 8	0.046	41.35321959	0.21841291	0.250772925	0.000101769
Scenario 9	0.029	41.35002552	0.218202262	0.250478736	0.000101764
Scenario 10	0.014	41.3473638	0.218026722	0.25023358	0.00010176
Scenario 11	0.003	41.34523443	0.21788629	0.250037454	0.000101757

Table 21: Total T2d Impact Treatment Results for Insulin Production Energy Variable Sensitivity Analysis. Each Scenario is Assessed in the Context of the US Insulin Use Model.

	MJ/Functional Unit	Climate Impact (kg CO2 Equivalent/Functional Unit)	Total Terrestrial Acidification Impact (kg SO2 eq)	Total Water Consumption Impact (m3)	Health Impact (DALY/Functional Unit)
Scenario 1	0.344	34.8521697	0.133440579	3.944805073	0.000100077
Scenario 2	0.172	34.82022906	0.131334102	3.941863192	0.00010003
Scenario 3	0.115	34.80958219	0.130631943	3.940882564	0.000100014
Scenario 4	0.086	34.80425875	0.130280864	3.940392251	0.000100006
Scenario 5	0.069	34.80106469	0.130070216	3.940098063	0.000100001
Scenario 6	0.063	34.79893531	0.129929784	3.939901937	0.000099998
Baseline	0.057	34.8	0.13	3.94	0.0001
Scenario 7	0.052	34.79787062	0.129859569	3.939803874	0.000099997
Scenario 8	0.046	34.79680594	0.129789353	3.939705812	0.000099995
Scenario 9	0.029	34.79361187	0.129578705	3.939411623	0.00009999
Scenario 10	0.014	34.79095015	0.129403165	3.939166467	0.000099986
Scenario 11	0.003	34.78882078	0.129262733	3.938970341	0.000099983

Figure 19: Sensitivity Analysis Results of Impacts Associated with Insulin Production Energy Variable Scenarios- US Insulin Use Model



14.6 Metformin Dosage - United States Scenario

The Metformin Dosage variable is designed to assess changes to impacts resulting from different medication dosages of the drug Metformin. As this is a very widely prescribed medication with patients using a large variety of dosages, this analysis is particularly relevant to this study. The selected dosage scenarios are the result of conversations with medical doctors regarding frequent dosage amounts their patients receive. Low dosages are common among newly diagnosed patients and those with high insulin sensitivity. High dosages are common among patients who have had the disease for some time and/or have reduced insulin sensitivity.

Table 22: Metformin Dosage Variable Impact Results

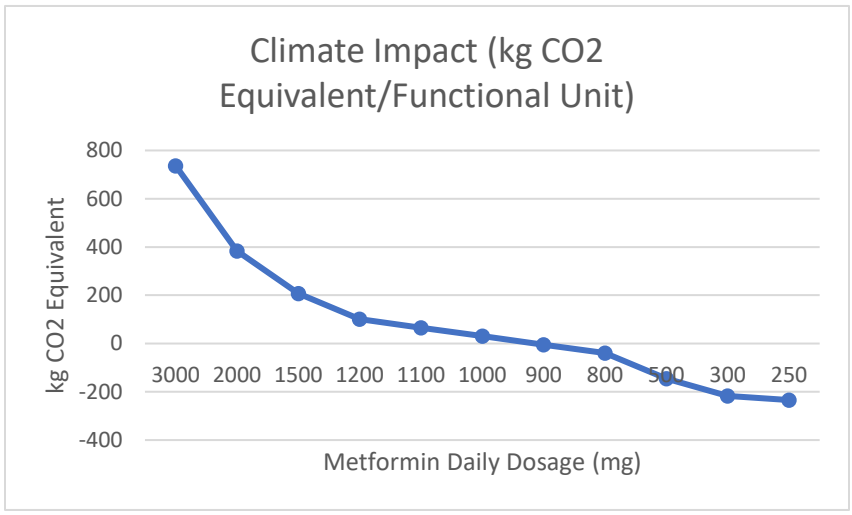
	mg/Day	Climate Impact (kg CO2 Equivalent/Functional Unit)	Total Terrestrial Acidification Impact (kg SO2 eq)	Total Water Consumption Impact (m3)	Health Impact (DALY/Functional Unit)
Scenario 1	3000	1059.216777	0.144788413	0.162375726	0.000047369
Scenario 2	2000	706.1445177	0.096525609	0.108250484	3.15794E-05
Scenario 3	1500	529.6083883	0.072394206	0.081187863	2.36845E-05
Scenario 4	1200	423.6867106	0.057915365	0.064950291	1.89476E-05
Scenario 5	1100	388.3794848	0.053089085	0.059537766	1.73686E-05
Baseline	1000	353.0722589	0.048262804	0.054125242	1.57897E-05
Scenario 6	900	317.765033	0.043436524	0.048712718	1.42107E-05
Scenario 7	800	282.4578071	0.038610243	0.043300194	1.26317E-05
Scenario 8	500	176.5361294	0.024131402	0.027062621	7.89484E-06
Scenario 9	300	105.9216777	0.014478841	0.016237573	4.7369E-06
Scenario 10	250	88.26806472	0.012065701	0.013531311	3.94742E-06

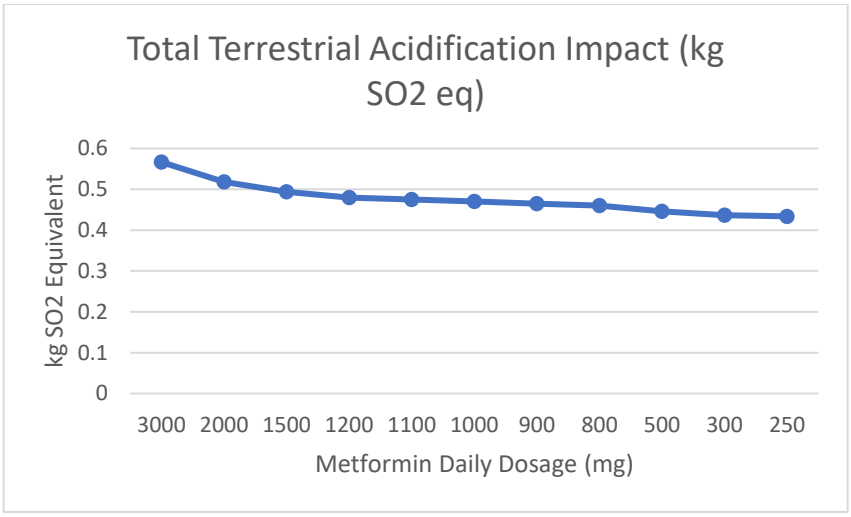
291 *Table 23: Total T2d Impact Results Per Metformin Dosage Variable. Results are calculated by functional unit (assumes 365 days) and in the US Metformin Use Model.*

	mg/Day	Climate Impact (kg CO2 Equivalent/Functional Unit)	Total Terrestrial Acidification Impact (kg SO2 eq)	Total Water Consumption Impact (m3)	Health Impact (DALY/Functional Unit)
Scenario 1	3000	736.7445181	0.566525609	1.002250484	0.000105579
Scenario 2	2000	383.6722588	0.518262805	0.948125242	8.97897E-05
Scenario 3	1500	207.1361294	0.494131402	0.921062621	8.18948E-05
Scenario 4	1200	101.2144517	0.479652561	0.904825049	7.71579E-05
Scenario 5	1100	65.9072259	0.474826281	0.899412524	7.55789E-05
Baseline	1000	30.6	0.47	0.894	0.000074
Scenario 6	900	-4.7072259	0.46517372	0.888587476	0.000072421
Scenario 7	800	-40.0144518	0.460347439	0.883174952	0.000070842
Scenario 8	500	-145.9361295	0.445868598	0.866937379	6.61051E-05
Scenario 9	300	-216.5505812	0.436216037	0.856112331	6.29472E-05
Scenario 10	250	-234.2041942	0.433802897	0.853406069	6.21577E-05

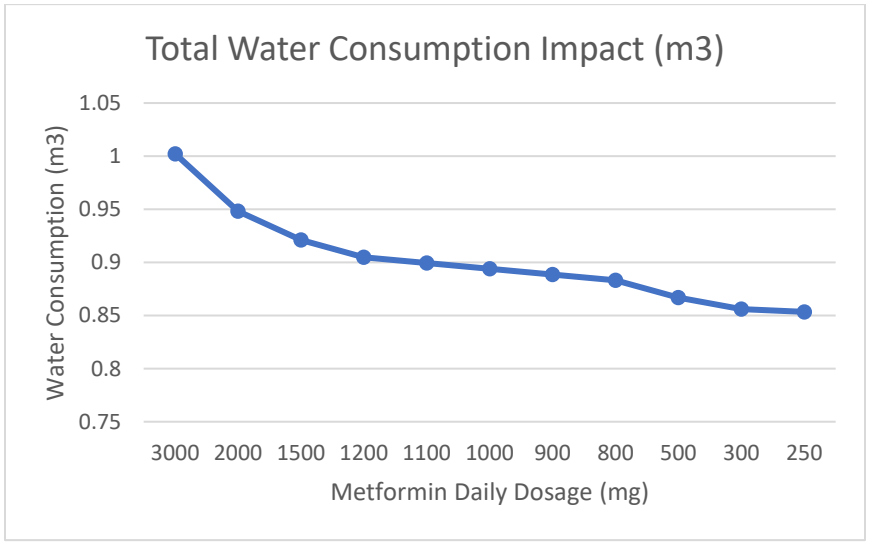
292

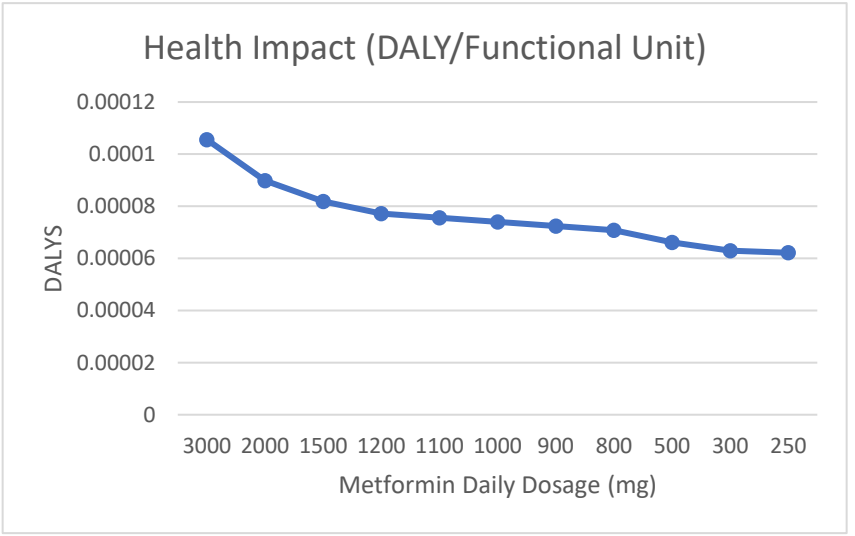
293 *Figure 20: Sensitivity Analysis Results of Impacts Associated with Metformin Dosage Variable Scenarios- US Metformin Use Model*





294





295

296

14.7 Metformin Production Energy Use - United States

The Metformin Production Energy Use variable seeks to understand the effects of different amounts of energy used in the production process. Whether or not energy efficiency in the production process offers substantive impacts on the overall impacts of treating T2d. The variable does not consider changes to the energy mix in the production process, merely to the overall energy input as measured in MJ.

Table 24: Impacts of Metformin Production Energy Use Variable Scenarios

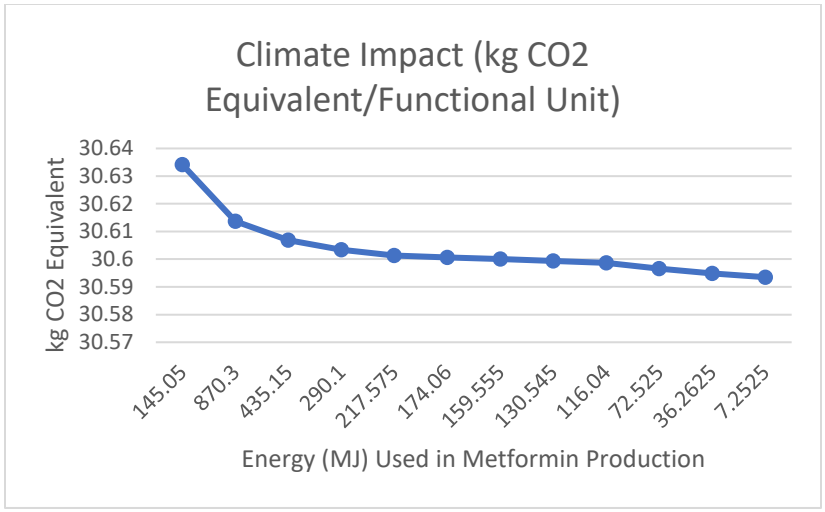
	MJ/Functional Unit	Climate Impact (kg CO2 Equivalent/Functional Unit)	Total Terrestrial Acidification Impact (kg SO2 eq)	Total Water Consumption Impact (m3)	Health Impact (DALY/Functional Unit)
Scenario 1	496	353.1064342	0.049571415	0.055049415	1.58814E-05
Scenario 2	248	353.085929	0.048786249	0.054494911	1.58264E-05
Scenario 3	165	353.0790939	0.048524526	0.054310077	0.000015808
Scenario 4	124	353.0756764	0.048393665	0.054217659	1.57989E-05
Scenario 5	99	353.0736259	0.048315149	0.054162209	1.57933E-05
Scenario 6	91	353.0729424	0.048288977	0.054143726	1.57915E-05
Baseline	83	353.0722589	0.048262804	0.054125242	1.57897E-05
Scenario 7	74	353.0715754	0.048236632	0.054106759	1.57878E-05
Scenario 8	66	353.0708919	0.04821046	0.054088275	0.000015786
Scenario 9	41	353.0688413	0.048131943	0.054032825	1.57805E-05
Scenario 10	21	353.0671326	0.048066513	0.053986616	1.57759E-05
Scenario 11	4	353.0657656	0.048014168	0.053949649	1.57722E-05

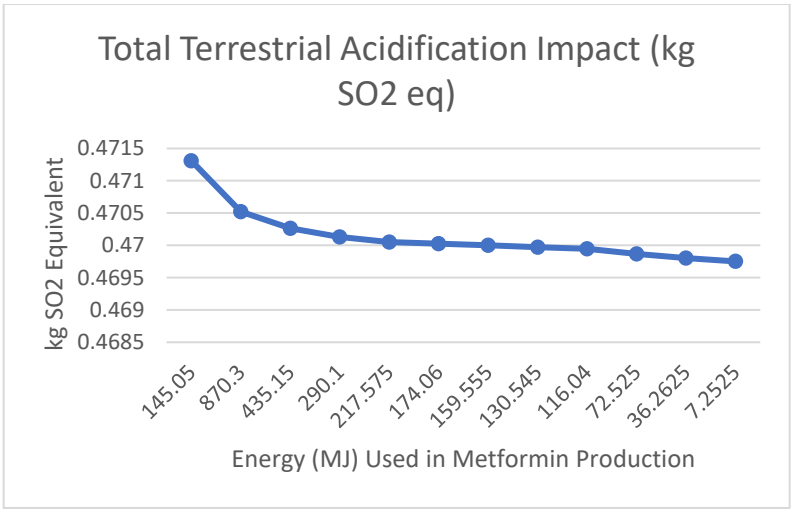
306 *Table 25: Total T2d Impact Results Per Metformin Production Energy Use Variable. Results are calculated by functional unit (assumes medications for 365 days) and in the US*
307 *Metformin Use Model.*

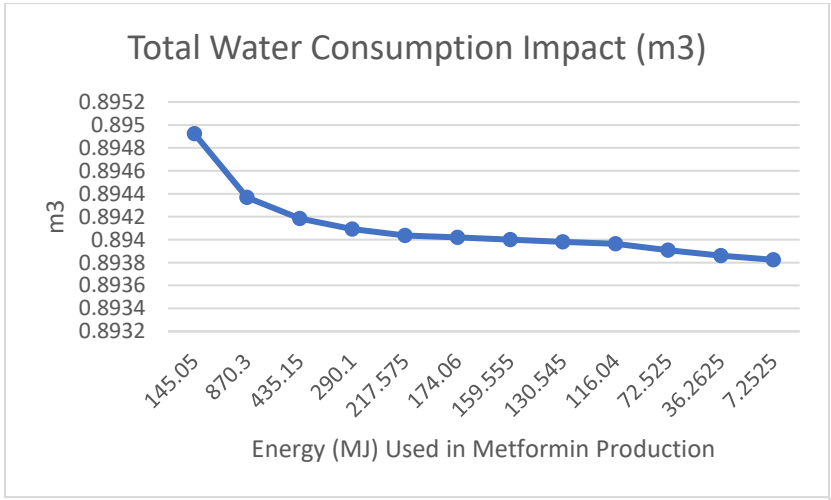
	MJ/Functional Unit	Climate Impact (kg CO2 Equivalent/Functional Unit)	Total Terrestrial Acidification Impact (kg SO2 eq)	Total Water Consumption Impact (m3)	Health Impact (DALY/Functional Unit)
Scenario 1	496	30.6341753	0.471308611	0.894924173	7.40917E-05
Scenario 2	248	30.6136701	0.470523445	0.894369669	7.40367E-05
Scenario 3	165	30.606835	0.470261722	0.894184835	7.40183E-05
Scenario 4	124	30.6034175	0.470130861	0.894092417	7.40092E-05
Scenario 5	99	30.601367	0.470052345	0.894036967	7.40036E-05
Scenario 6	91	30.6006835	0.470026173	0.894018484	7.40018E-05
Baseline	83	30.6	0.47	0.894	0.000074
Scenario 7	74	30.5993165	0.469973828	0.893981517	7.39981E-05
Scenario 8	66	30.598633	0.469947656	0.893963033	7.39963E-05
Scenario 9	41	30.5965824	0.469869139	0.893907583	7.39908E-05
Scenario 10	21	30.5948737	0.469803709	0.893861374	7.39862E-05
Scenario 11	4	30.5935067	0.469751364	0.893824407	7.39825E-05

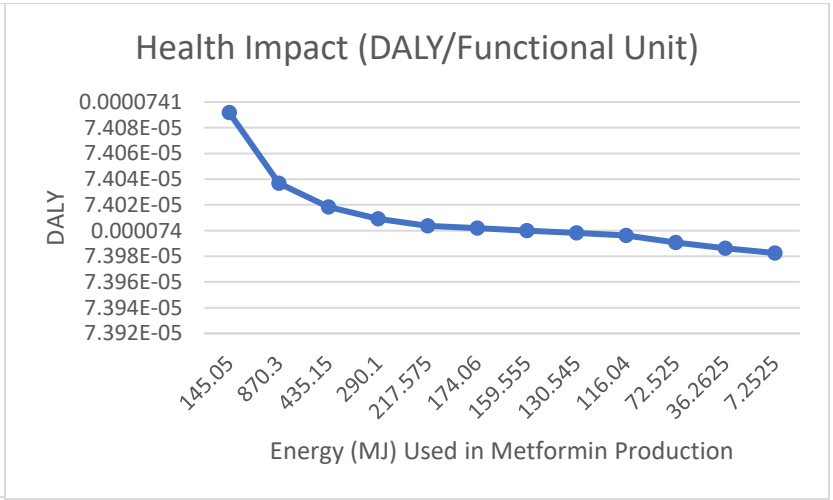
308

Figure 21: Sensitivity Analysis Results of Impacts Associated with Metformin Production Energy Use Variable Scenarios- US Metformin Use Model









14.8 Insulin Dosage- Sri Lanka

The Insulin Dosage variable is the same as that assessed for the United States Insulin Use model, with the distinction that the dosage variability is adjusted to reflect estimated dosage variability among Sri Lankan patients. Additionally, the impacts are assessed within the Sri Lankan Insulin Use model.

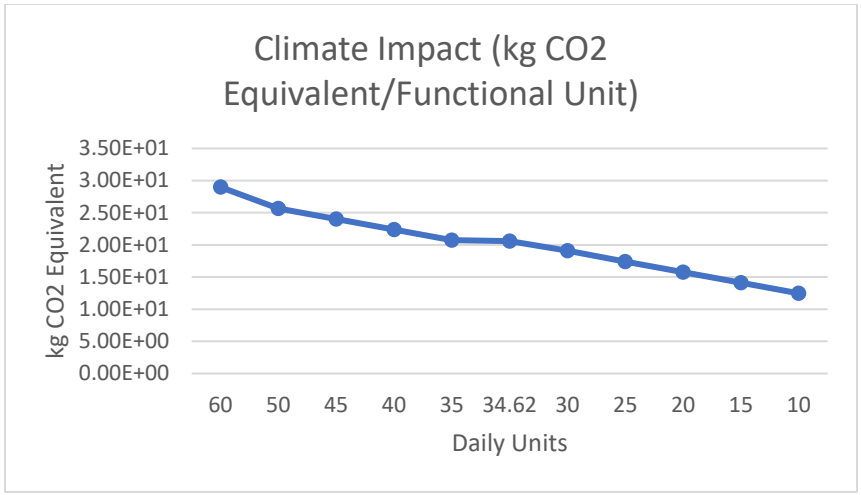
Table 26: Impacts of Insulin Dosage Variable Scenarios

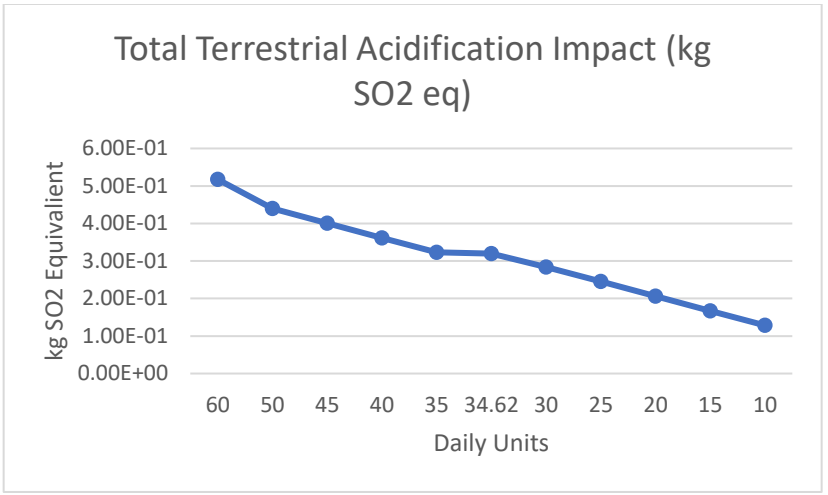
	Units/ Day	Climate Impact (kg CO2 Equivalent/Functional Unit)	Total Terrestrial Acidification Impact (kg SO2 eq)	Total Water Consumption Impact (m3)	Health Impact (DALY/Functional Unit)
Scenario 1	60	21.44175176	0.479266977	0.727943208	5.61E-05
Scenario 2	50	18.14020688	0.401445809	0.612478311	4.76E-05
Scenario 3	45	16.48943444	0.362535224	0.554745863	4.34E-05
Scenario 4	40	14.83866201	0.32362464	0.497013414	3.91E-05
Scenario 5	35	13.18788957	0.284714055	0.439280966	3.49E-05
Baseline	34.62	13.06243086	0.281756851	0.4348933	3.46E-05
Scenario 6	30	11.53711713	0.245803471	0.381548517	3.07E-05
Scenario 7	25	9.886344695	0.206892886	0.323816069	2.64E-05
Scenario 8	20	8.235572257	0.167982302	0.26608362	2.22E-05
Scenario 9	15	6.58479982	0.129071717	0.208351172	1.79E-05
Scenario 10	10	4.934027382	0.090161133	0.150618723	1.37E-05

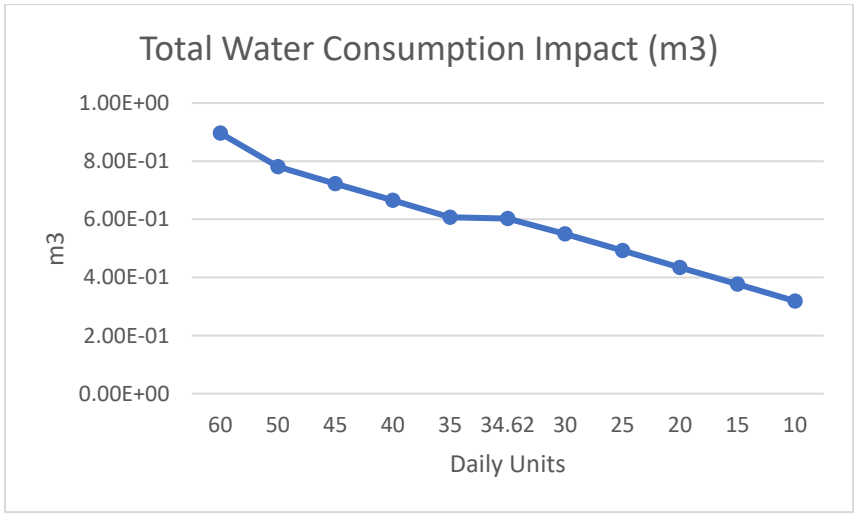
Table 27: T2d overall treatment impacts with variable scenario inputs. These results are per functional unit (assumes daily medication for 365 days) and modeled in the Sri Lanka Insulin Use model.

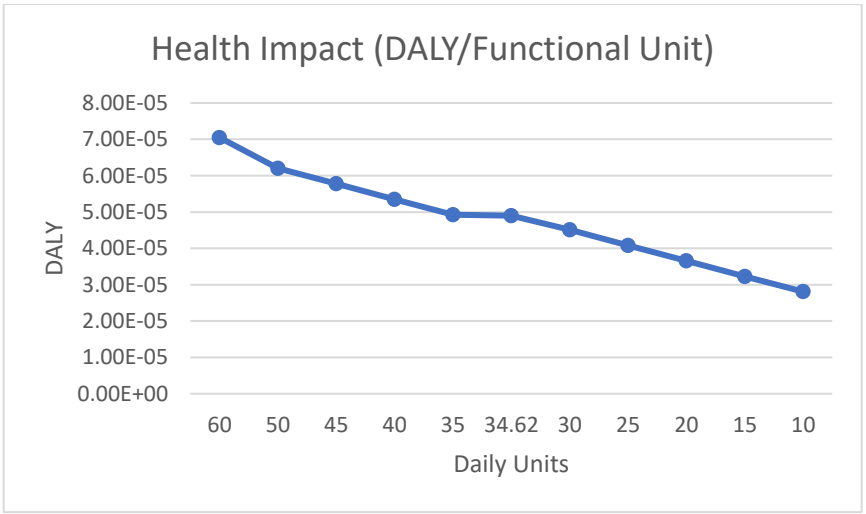
	# Units/ Day	Climate Impact (kg CO2 Equivalent/Functional Unit)	Total Terrestrial Acidification Impact (kg SO2 eq)	Total Water Consumption Impact (m3)	Health Impact (DALY/Functional Unit)
Scenario 1	60	28.9793209	0.517510126	0.896049908	0.0000705
Scenario 2	50	25.67777602	0.439688958	0.780585011	0.000062
Scenario 3	45	24.02700358	0.400778373	0.722852563	0.0000578
Scenario 4	40	22.37623115	0.361867789	0.665120114	0.0000535
Scenario 5	35	20.72545871	0.322957204	0.607387666	0.0000493
Baseline	34.62	20.6	0.32	0.603	0.000049
Scenario 6	30	19.07468627	0.28404662	0.549655217	0.0000451
Scenario 7	25	17.42391384	0.245136035	0.491922769	0.0000408
Scenario 8	20	15.7731414	0.206225451	0.43419032	0.0000366
Scenario 9	15	14.12236896	0.167314866	0.376457872	0.0000323
Scenario 10	10	12.47159652	0.128404282	0.318725423	0.0000281

Table 28: Sensitivity Analysis Results of Total T2d Impacts Associated with Insulin Dosage Variable Scenarios- Sri Lankan Insulin Use Model









14.9 Insulin Production Energy Use - Sri Lanka

The Insulin Production Energy Use variable, similar to the Insulin Production Energy Use variable described in the U.S. Insulin Use scenario, is used to assess the impacts energy use reduction in the insulin production process. These findings may indicate if investments in improved efficiencies in the production process have a measurable effect on environmental and human health impacts. Energy inputs are measured overall, and the variable does not account for any fluctuations in the energy mix of the production process. The scenarios are modeled within the Sri Lanka Insulin Use model.

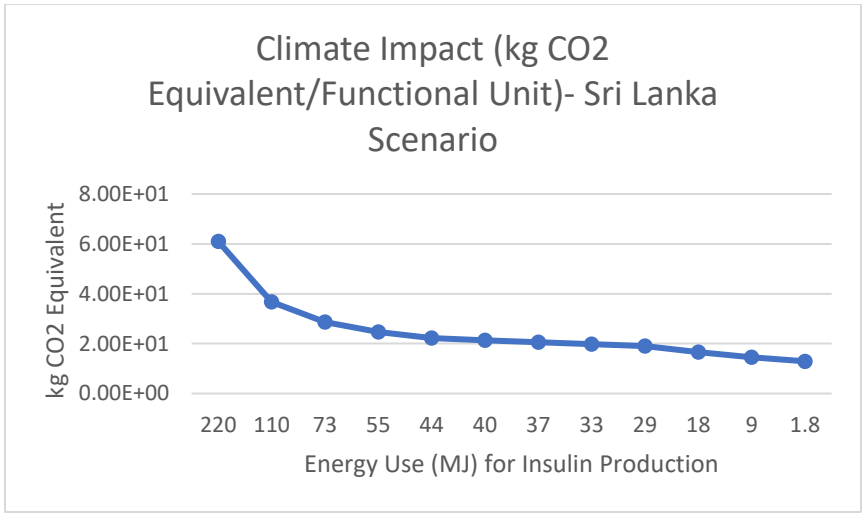
Table 29: Impacts of Insulin Production Energy Use Sensitivity Analysis- Sri Lankan Model

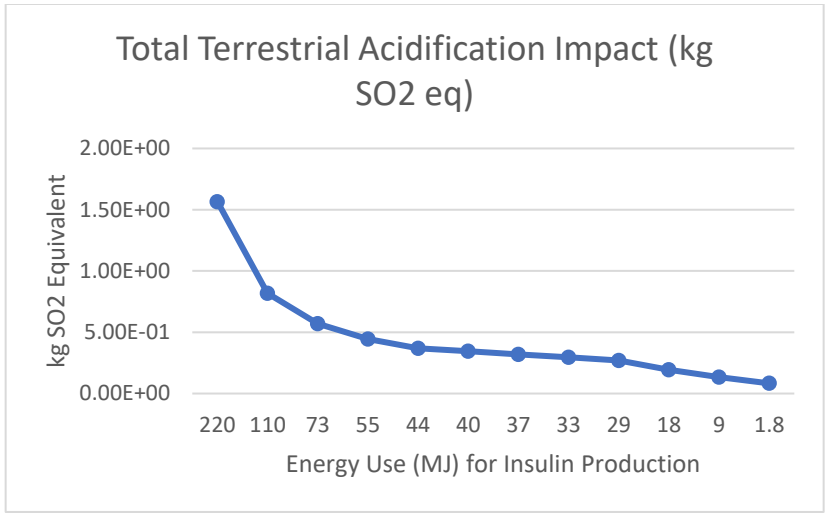
	MJ/Functional Unit	Climate Impact (kg CO2 Equivalent/Functional Unit)	Total Terrestrial Acidification Impact (kg SO2 eq)	Total Water Consumption Impact (m3)	Health Impact (DALY/Functional Unit)
Scenario 1	220	53.41957213	1.527948377	1.308138788	0.000125
Scenario 2	110	29.20528737	0.780233461	0.784191495	0.0000708
Scenario 3	73	21.13385912	0.530995156	0.609542397	0.0000527
Scenario 4	55	17.09814499	0.406376003	0.522217848	0.0000436
Scenario 5	44	14.67671652	0.331604512	0.469823119	0.0000382
Scenario 6	40	13.86957369	0.306680681	0.452358209	0.0000364
Baseline	37	13.06243086	0.281756851	0.4348933	0.0000346
Scenario 7	33	12.25528804	0.25683302	0.41742839	0.0000328
Scenario 8	29	11.44814521	0.23190919	0.39996348	0.0000309
Scenario 9	18	9.026716737	0.157137698	0.347568751	0.0000255
Scenario 10	9	7.008859674	0.094828122	0.303906476	0.000021
Scenario 11	1.8	5.394574023	0.044980461	0.268976657	0.0000174

Table 30: T2d Overall Treatment Impacts as affected by Insulin Production Energy Use variable scenarios. The resulting impacts are calculated by functional unit (which assumes daily medication for 365 days) and according to the Sri Lanka Insulin Use model.

	MJ/Functional Unit	Climate Impact (kg CO2 Equivalent/Functional Unit)	Total Terrestrial Acidification Impact (kg SO2 eq)	Total Water Consumption Impact (m3)	Health Impact (DALY/Functional Unit)
Scenario 1	220	60.95714127	1.566191526	1.476245488	0.0001394
Scenario 2	110	36.74285651	0.81847661	0.952298195	0.0000852
Scenario 3	73	28.67142826	0.569238305	0.777649097	0.0000671
Scenario 4	55	24.63571413	0.444619152	0.690324548	0.000058
Scenario 5	44	22.21428566	0.369847661	0.637929819	0.0000526
Scenario 6	40	21.40714283	0.34492383	0.620464909	0.0000508
Baseline	37	20.6	0.32	0.603	0.000049
Scenario 7	33	19.79285718	0.295076169	0.58553509	0.0000472
Scenario 8	29	18.98571435	0.270152339	0.56807018	0.0000453
Scenario 9	18	16.56428588	0.195380847	0.515675451	0.0000399
Scenario 10	9	14.54642881	0.133071271	0.472013176	0.0000354
Scenario 11	1.8	12.93214316	0.08322361	0.437083357	0.0000318

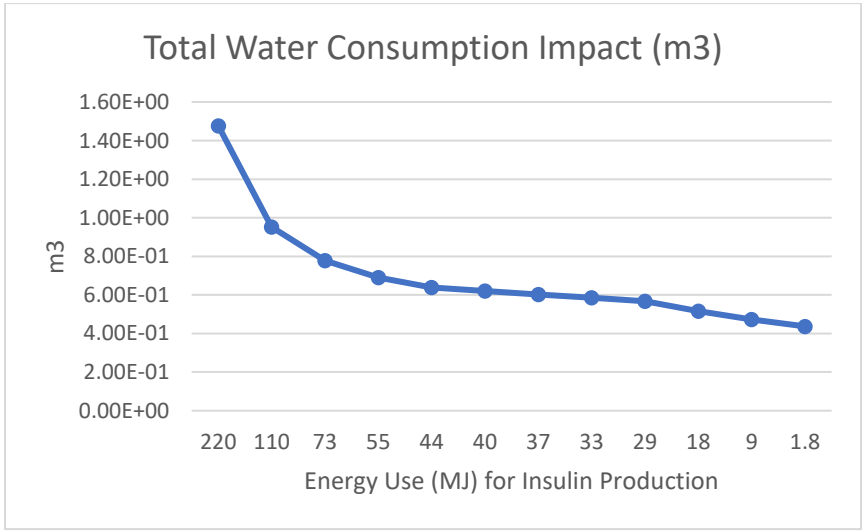
345 *Figure 22: Sensitivity Analysis Results of Total T2d Impacts Associated with Insulin Production Energy Use Variable Scenarios- Sri Lankan Insulin Use Model*

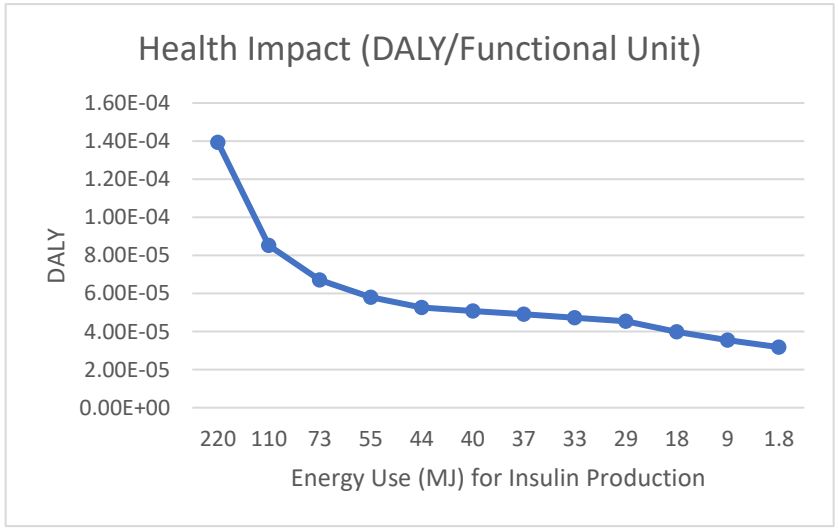




346

347





348

349

14.10 Metformin Dosage Sensitivity Analysis- Sri Lanka

The Metformin Dosage variable is designed to assess changes to impacts resulting from different medication dosages of the drug Metformin. As this is a very widely prescribed medication with patients using a large variety of dosages, this analysis is particularly relevant to this study. The selected dosage scenarios are the result of conversations with medical doctors regarding frequent dosage amounts their patients receive. Low dosages are common among newly diagnosed patients and those with high insulin sensitivity. High dosages are common among patients who have had the disease for some time and/or have reduced insulin sensitivity. This variable is assessed according the Sri Lankan Metformin Use model.

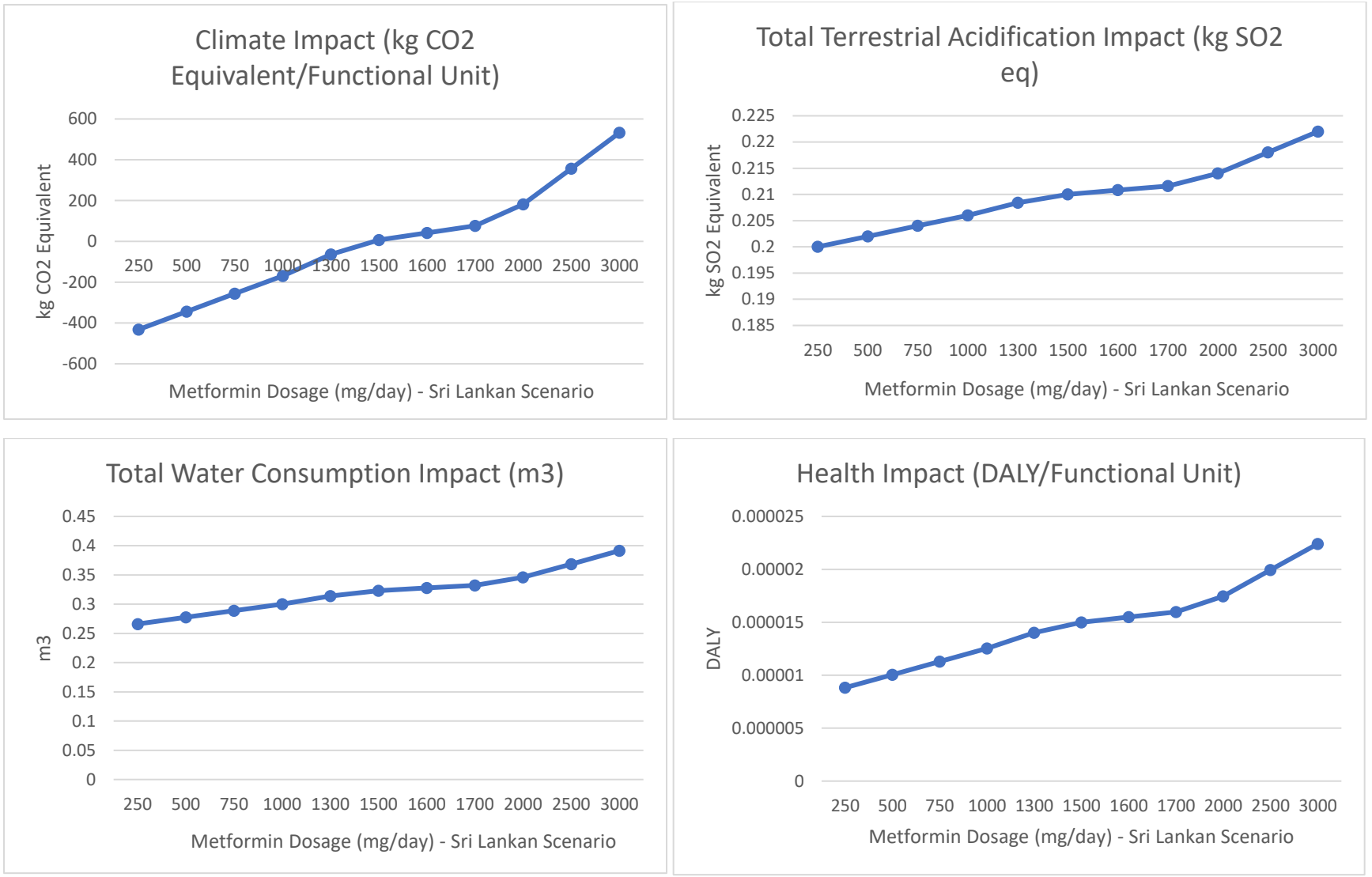
Table 31: Impacts of Metformin Dosage Variable Sensitivity Analysis- Sri Lankan Model

	# mg/Day	Climate Impact (kg CO2 Equivalent/Functional Unit)	Total Terrestrial Acidification Impact (kg SO2 eq)	Total Water Consumption Impact (m3)	Health Impact (DALY/Functional Unit)
Scenario 1	250	91.17121962	0.059843092	0.023663	1.68212E-05
Scenario 2	500	178.8276099	0.061842437	0.035059	1.80562E-05
Scenario 3	750	266.4840001	0.063841782	0.046456	1.92912E-05
Scenario 4	1000	354.1403903	0.065841127	0.057853	2.05262E-05
Scenario 5	1300	459.3280586	0.06824034	0.071529	2.20082E-05
Baseline	1500	529.4531708	0.069839816	0.080646	2.29962E-05
Scenario 6	1600	564.5157269	0.070639554	0.085205	2.34902E-05
Scenario 7	1700	599.578283	0.071439292	0.089764	2.39842E-05
Scenario 8	2000	704.7659512	0.073838506	0.10344	2.54662E-05
Scenario 9	2500	880.0787317	0.077837195	0.126233	2.79362E-05
Scenario 10	3000	1055.391512	0.081835885	0.149027	3.04062E-05

Table 32: T2d Overall Treatment Impacts as affected by Metformin Dosage variable scenarios. The resulting impacts are calculated by functional unit (which assumes daily medication for 365 days) and according to the Sri Lanka Metformin Use model.

	# mg/Day	Climate Impact (kg CO2 Equivalent/Functional Unit)	Total Terrestrial Acidification Impact (kg SO2 eq)	Total Water Consumption Impact (m3)	Health Impact (DALY/Functional Unit)
Scenario 1	250	-431.7019512	0.200003276	0.266017	0.000008825
Scenario 2	500	-344.0455609	0.202002621	0.277413	0.00001006
Scenario 3	750	-256.3891707	0.204001966	0.28881	0.000011295
Scenario 4	1000	-168.7327805	0.206001311	0.300207	0.00001253
Scenario 5	1300	-63.5451122	0.208400524	0.313883	0.000014012
Baseline	1500	6.58	0.21	0.323	0.000015
Scenario 6	1600	41.6425561	0.210799738	0.327559	0.000015494
Scenario 7	1700	76.7051122	0.211599476	0.332118	0.000015988
Scenario 8	2000	181.8927804	0.21399869	0.345794	0.00001747
Scenario 9	2500	357.2055609	0.217997379	0.368587	0.00001994
Scenario 10	3000	532.5183412	0.221996069	0.391381	0.00002241

364 *Figure 23: Sensitivity Analysis Results of Total T2d Impacts Associated with Metformin Dosage Variable Scenarios- Sri Lankan Metformin Use Model*



365

366

367

14.11 Metformin Production Energy- Sri Lanka

The Metformin Production Energy Use variable seeks to understand the effects of different amounts of energy used in the production process. Whether or not energy efficiency in the production process offers substantive impacts on the overall impacts of treating T2d. The variable does not consider changes to the energy mix in the production process, merely to the overall energy input as measured in MJ. This variable is considered in the context of the Sri Lankan Metformin Use model.

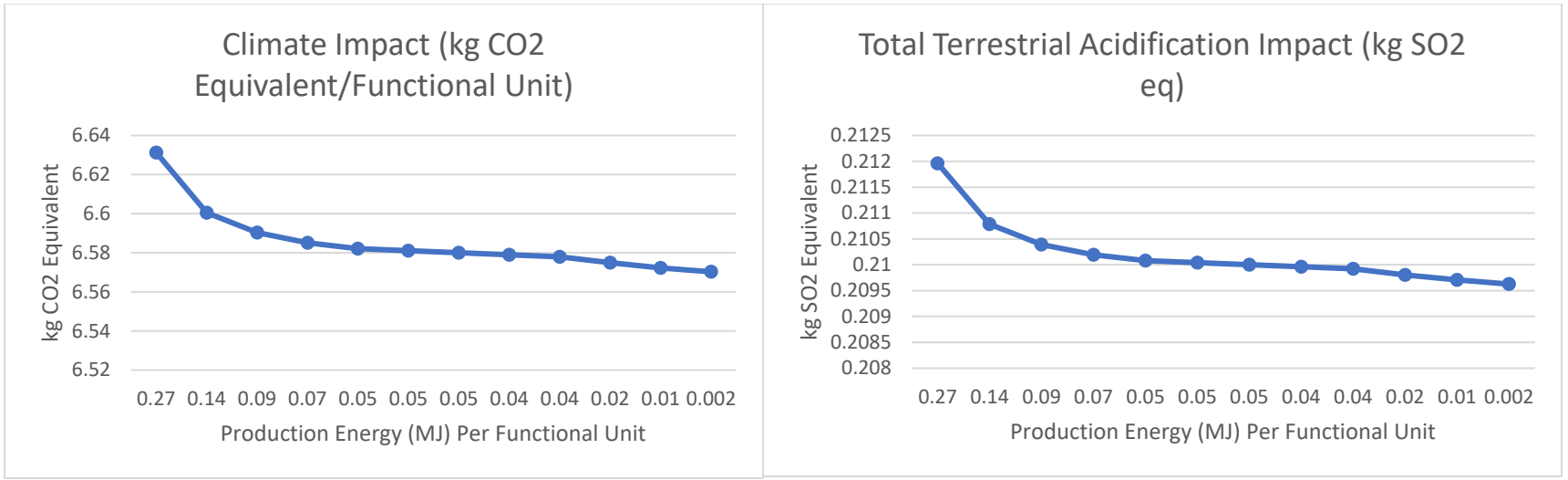
Table 33: Impacts of Metformin Production Energy Use Variable Sensitivity Analysis- Sri Lankan Model

	MJ/Functional Unit	Climate Impact (kg CO2 Equivalent/Functional Unit)	Total Terrestrial Acidification Impact (kg SO2 eq)	Total Water Consumption Impact (m3)	Health Impact (DALY/Functional Unit)
Scenario 1	496	6.631263	0.211962916	0.324386	1.51377E-05
Scenario 2	248	6.6005052	0.210785166	0.323555	1.50551E-05
Scenario 3	165	6.5902526	0.210392583	0.323277	1.50275E-05
Scenario 4	124	6.5851263	0.210196292	0.323139	1.50138E-05
Scenario 5	99	6.5820505	0.210078517	0.323056	1.50055E-05
Scenario 6	91	6.5810252	0.210039258	0.323028	1.50028E-05
Baseline	83	6.58	0.21	0.323	0.000015
Scenario 7	74	6.5789747	0.209960742	0.322972	1.49973E-05
Scenario 8	66	6.5779495	0.209921483	0.322945	1.49945E-05
Scenario 9	41	6.5748737	0.209803708	0.322862	1.49862E-05
Scenario 10	21	6.5723105	0.209705563	0.322792	1.49794E-05
Scenario 11	4	6.57026	0.209627046	0.322737	1.49739E-05

Table 34: T2d Overall Treatment Impacts as affected by Metformin Production Energy Use variable scenarios. The resulting impacts are calculated by functional unit (which assumes daily medication for 365 days) and according to the Sri Lanka Metformin Use model

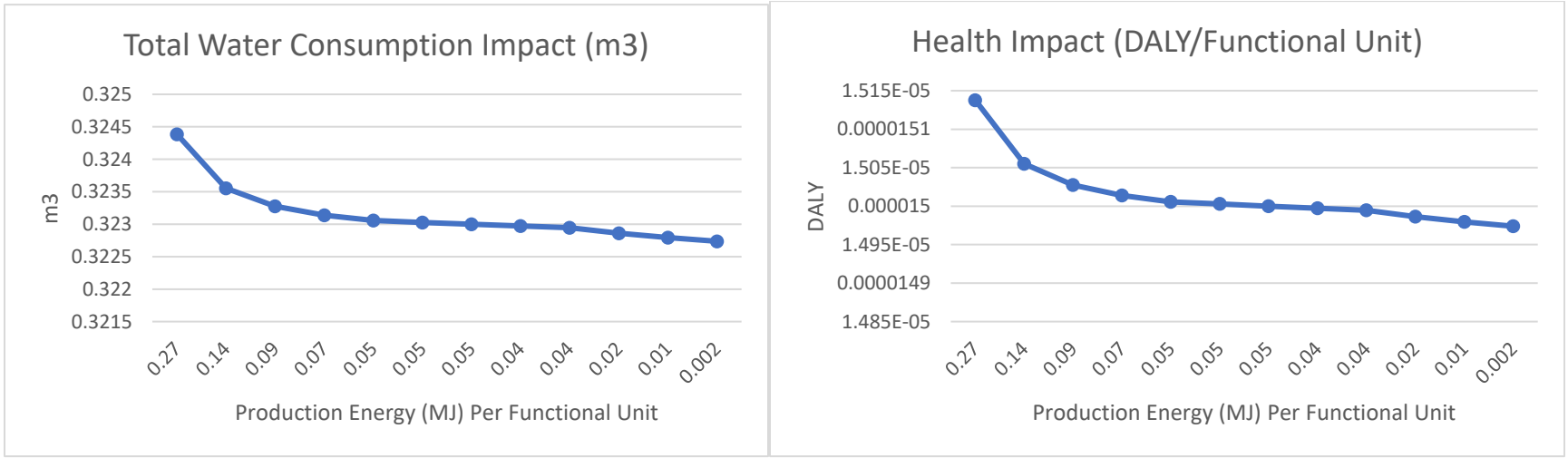
	MJ/Functional Unit	Climate Impact (kg CO2 Equivalent/Functional Unit)	Total Terrestrial Acidification Impact (kg SO2 eq)	Total Water Consumption Impact (m3)	Health Impact (DALY/Functional Unit)
Scenario 1	496	6.631263	0.211962916	0.324386	1.51377E-05
Scenario 2	248	6.6005052	0.210785166	0.323555	1.50551E-05
Scenario 3	165	6.5902526	0.210392583	0.323277	1.50275E-05
Scenario 4	124	6.5851263	0.210196292	0.323139	1.50138E-05
Scenario 5	99	6.5820505	0.210078517	0.323056	1.50055E-05
Scenario 6	91	6.5810252	0.210039258	0.323028	1.50028E-05
Baseline	83	6.58	0.21	0.323	0.000015
Scenario 7	74	6.5789747	0.209960742	0.322972	1.49973E-05
Scenario 8	66	6.5779495	0.209921483	0.322945	1.49945E-05
Scenario 9	41	6.5748737	0.209803708	0.322862	1.49862E-05
Scenario 10	21	6.5723105	0.209705563	0.322792	1.49794E-05
Scenario 11	4	6.57026	0.209627046	0.322737	1.49739E-05

383 *Figure 24: Sensitivity Analysis Results of Total T2d Impacts Associated with Metformin Production Energy Use Variable Scenarios- Sri Lankan Metformin Use Model*



384

385



386

387