The Disability-Adjusted Life Year (DALY) and Influenza in Ireland

An evaluation of the suitability of the DALY as a metric for measuring and managing the burden of influenza in Ireland

by

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Candidate Declaration

Candidate Name: Roisin Quigley

I certify that the dissertation titled The Disability-Adjusted Life Year (DALY) and Influenza in Ireland: An evaluation of the suitability of the DALY as a metric for measuring and managing the burden of influenza in Ireland submitted to the department of Pharmaceutical Business and Technology, Griffith College Dublin is the result of my work, and that where reference is made to the work of others, due acknowledgement is given.

Conflict of interest

I declare a potential conflict of interest as I am currently an employee of AstraZeneca, whose childhood influenza vaccination is currently the vaccine of choice by the HSE for childhood influenza vaccination in Ireland. AstraZeneca also partially funded my participation in this programme. The result of this research could highlight the burden of influenza in Ireland and therefore indirectly suggest that increased vaccination uptake could be of benefit to Irish society. This has the potential influence sales of the AstraZeneca.

AstraZeneca had no influence or input into the research in any way, including in the chosen topic, research methods or resulting outcomes. The topic chosen was entirely my choice and all opinions expressed in this research are entirely my own.

Candidate Signature: 

Date: 21/05/2023

Supervisor: Mark Campbell

Signature:

Date:

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Abstract

The burden of influenza in Ireland in insufficiently characterised. Quantifying the burden of influenza could lead to benefits such as informed decision-making on policy, effective healthcare planning and preparation and prioritisation of health research investments and healthcare interventions. These benefits are particularly pertinent in today's Irish setting, as it is facing chronic resource shortages. The Disability Adjusted Life Year (DALY) is proposed as a useful metric for quantifying the burden of influenza. It is a measure of overall reduction in health due to disability before death and the decline in life expectancy due to death. This research aimed to use this metric to estimate the burden of influenza in Ireland and to investigate the feasibility, suitability, utility and validity of the estimate in practice in the Irish healthcare and health policy setting. A mixed-method approach with an overall interpretivist philosophy was employed. Using a quantitative method, the DALY calculation was performed to estimate the burden of influenza in Ireland in DALYs and to explore variability of the calculation. A qualitative method was then used to gain the views of subject matter experts on the validity, feasibility, suitability and utility of the DALY to them in practice. Both methods were combined via abduction to arrive at a conclusion. Results showed that per 100,000 population, influenza contributed 87.75 DALYs in the 2018/2019 season and 38.8 DALYs in the 2017/2018 season. The utility of this estimate depends upon the DALY's function as a "common currency" for comparison. It would be suitable and useful to inform HSE policy and highlight the burden of influenza; however, few other appropriate DALY estimates exist for comparison. Therefore, the estimate cannot be used to arrive at a conclusion regarding the burden of influenza and it is not yet feasible to be used for its intended purpose. This estimate will provide a useful comparator to future studies. The wider adoption of the DALY in Ireland is required for its utility to be realised and benefits gained.

1. Keywords

Influenza, disease burden, DALY, summary measure, infectious disease, virology

The Disability-Adjusted Life Year (DALY) and Influenza in Ireland

An evaluation of the suitability of the DALY as a metric for measuring and managing the burden of influenza in Ireland

1. Introduction

1.1. Overview

This research is an investigation, based on a combination of secondary research and stakeholder interviews, into the suitability of the Disability-Adjusted Life Year (DALY) as a metric for measuring and managing the burden of influenza in the Republic of Ireland. The burden of influenza in this study refers to the impact of influenza in terms of illness and mortality. Economic and social burden are out of scope. The DALY is a summary measure of disease burden representing loss due to both death and ill-health. The term “disability” refers to a state of less than perfect health. The “suitability of the DALY” is to say whether the DALY is fitting and useful for target groups in Ireland as a measure of the burden of influenza. This research will add to the body of evidence supporting, or opposing, the DALY method and will indicate whether it could be applied to the Irish healthcare and health policy setting.

The burden of influenza globally is well-accepted among the scientific community. However, recent studies suggest that its impact in terms of morbidity and mortality may be more severe than previously estimated. According to a multinational survey conducted by the Centres for Disease Control (CDC), up to 646,000 people worldwide die from seasonal influenza-like illness (ILI) each year, of whom up to 105, 690 are children younger than 5 years (Centers for Disease Control, 2022a). This is higher than the previous estimates. These findings renew the urgency surrounding influenza prevention and control—a topic that was forced to take a position of lower priority during the COVID19 pandemic.

To make informed decisions on health priorities such as these, policymakers need access to reliable measures of the comparative burdens of disease on populations. An example of a standardised measure of disease burden is the Disability-Adjusted Life Year (DALY), which is a measure of healthy life lost due to an illness or risk factor. This method is increasingly cited as a powerful tool for decision-making, including by the World Health Organisation (WHO) (Arnesen & Kapiriri, 2004; World Health Organisation, 2022).

The methodology behind calculating DALYs continues to evolve; however, some methodological challenges remain. Thus, this study aims to use this method to estimate the DALYs associated with influenza in Ireland to investigating its feasibility, suitability, utility and validity as a method of estimating the burden of influenza in Ireland.

This research is particularly pertinent in the current Irish healthcare setting as it is facing chronic resource shortages. There is a nationwide shortage of hospital beds, ICU beds and medical staff (Prospect, 2020). Therefore, it is particularly important in this setting to be able to make good, evidence-based decisions on healthcare resource allocation.

The practical contribution of this study is two-fold. Firstly, it will for the first time highlight the estimated degree of disease burden attributed to influenza in Ireland. This information may form an evidence base for healthcare priorities. It may also inform the wider public of the burden of the commonly circulating disease, influencing behaviour in terms of vaccination uptake and seasonal vigilance. Secondly, it informs researchers and policymakers of the feasibility, suitability, utility and validity of the DALY for measuring and managing the burden of Influenza in Ireland. This could lead to the DALY being more readily adopted in research and policymaking, leading to improved health outcomes.

The theoretical contribution of the study is also two-fold. Firstly, it creates new knowledge of the burden of influenza in Ireland, building on the body of knowledge surrounding the burden of Influenza globally. Secondly, it provides further analysis of the suitability and validity of the DALY methodology when used in varying contexts. Academically, this research will expand the discussion around the methodology used for calculating DALYs.

Initially, this research aimed to calculate the burden of Influenza in Ireland using surveillance data from the Health Protection Surveillance Centre (HPSC)—Irelands specialist agency for surveillance of communicable disease. During the initial discovery stage, it emerged that the data collected by the HPSC represents only a small subset of ~6.9% of the population. This meant that the BoD could not be *calculated*, but rather *estimated*. The aims and objectives of the study were amended accordingly.

1.2. Background

1.2.1. Estimating the burden of influenza in Ireland using DALYs

Globally, influenza is estimated to cause up to 646,000 deaths annually, with this figure expected to rise as further surveillance and laboratory studies take place (Luliano et al.,

2018). In Ireland, it causes a significant number of illnesses, hospitalisations, ICU admissions and deaths almost every year (HPSC, 2022).

Aside from its impact on human health and wellbeing, influenza circulation also results in significant uptake of scarce healthcare resources such as hospital beds, ICU beds and healthcare professional capacity (HPSC, 2022). This is particularly important in today's Irish setting, as there is an ongoing hospital overcrowding crisis due to chronic lack of resources including the abovementioned (Prospect, 2022). In times like these, careful consideration and planning must go into healthcare resource allocation.

Healthcare decision-makers require a consistent, reliable method of comparing the relative burdens of disease to determine priority areas for intervention. Widely used for this purpose are summary measures of population health such as DALYs. Summary measures provide simple representations of complex epidemiology that can be used to develop efficient preventive or interventive strategies.

This study investigates the DALY method of estimating BoD. The DALY method is attractive because rather than simply estimating mortality or incidence rates, which was commonly done in the past, DALYs account for the reduced health state due to disability before death, the time spent in that health state and the decline in life expectancy (LE) due to death. Estimating the burden of influenza in Ireland using DALYs has not yet been formally conducted nor published and could form valuable data for health policymakers.

1.2.2. Challenges associated with estimating DALYs

For DALYs to be fit for purpose, outputs of the calculation should be standardised, requiring standardised inputs. However, it is recognised that variation exists in the approaches used to estimate the calculation's inputs including mortality rates, incident cases, disability duration, disability weight (DW) and life expectancy (Nomura et al., 2021), which contributes to variability in output.

Additionally, surveillance data for infectious diseases such as influenza are inherently imprecise (Brammer et al., 2009). This is because a significant proportion of cases are managed within the community without reporting to any health facility, and therefore go unaccounted for. Even cases which are clinically suspected by general practitioners (GPs) may not be serologically confirmed because this does not usually affect the treatment course. Often, non-serologically confirmed cases will also not be reported. These issues lead to questions over the validity and reliability of surveillance data for use to inform decision-making.

Some methodological issues may also be associated with the method proposed for the calculation of DALYs. Some have concerns over the 'universal' approach to weighting the severity of diseases, arguing that the severity of each individual disease fundamentally depends on the context (Fox-Rushby, 2002). Concerns such as these lead to uncertainties with regard to the metric's validity.

This research investigates the reliability and validity of the DALY as a measure of Influenza in Ireland by performing the calculation, exploring its variability and seeking the views of subject matter experts on the outputs, outcomes and implications.

There is no published evidence of the use of DALYs by stakeholders as a measure of burden of influenza in Ireland. Therefore, this research will also explore the feasibility and potential utility of such a measure to various stakeholders.

1.3. Research aims and objectives

1.3.1. Aims

The purpose of this research is to estimate the burden of influenza in Ireland in terms of DALYs and to investigate the feasibility, suitability, utility and validity of this measurement in practice in the Irish healthcare and health policy setting.

Specifically, its aims are to:

1. Determine an appropriate methodological approach to estimating DALYs attributed to influenza
2. Estimate the burden of disease (BoD) attributed to influenza in Ireland[1]
3. Investigate the feasibility, utility, suitability and validity of DALYs as a measure of the burden of influenza in Ireland

This exploration is pertinent as it may facilitate more accurate measurements of BoD and thus enhance the understanding of diseases, improve health policy decisions and monitor health trends over time. A valid method of estimating of the burden of influenza could provide a useful tool to many stakeholders including healthcare professionals, health policymakers and other industry leaders. An exploration into the applicability of the DALY

[1] This aim was originally to *calculate* the burden, but was changed to *estimate* the burden due to the discovery that the surveillance data was insufficient

to influenza in Ireland has not yet been formally conducted and published; therefore, this research will elucidate the matter for the first time.

1.3.2. Objectives

The specific objectives of this research are to:

1. Estimate the DALYs attributed to influenza in Ireland during the 2017/2018 and 2018/2019 seasons using publicly available influenza surveillance data[2]
2. Calculate DALYs attributed to Influenza in Ireland using various disability weights and life expectancies to explore variability in output
3. Determine whether the estimation of DALYs based on surveillance data is a suitable and valid metric for the burden of Influenza in Ireland by interviewing a panel of subject matter experts and other stakeholders
4. Investigate in which capacity (if any) the calculation of DALYs attributed to Influenza in Ireland will be most feasible and useful in practice by interviewing a panel of subject matter experts and other stakeholders

Achievement of these objectives will highlight the burden of Influenza in Ireland, a topic which is often underappreciated due to its ever-presence. This may renew efforts surrounding influenza prevention and control which could lead to reduced seasonal burden on the healthcare system and wider society. Achievement of these aims will also highlight the potential of the DALY as a tool for evidence-based healthcare decision making in Ireland. This tool is not yet widely used in Ireland but is promoted by the WHO. Clarity as to whether it forms a valid, useful, suitable and feasible tool will be of value to target groups.

The surveillance data referred to in these objectives is the data gathered by the HPSC—Irelands disease surveillance centre. The term ‘surveillance’ in this context refers to the collection, collation, analysis and communication of data related to the prevalence of influenza in Ireland. During the course of the secondary research for this study, it was noted that the quality of the influenza surveillance data in Ireland is of concern. This is because the surveillance reports were found, unexpectedly, to be based on serologically confirmed influenza cases, with only 6.9% of GPs recruited to report presentations of influenza-like-illness. This omits a large portion of influenza cases in the population and

[2] The surveillance available data from the HPSC was found to be more limited than expected at project outset, so data from the literature was also utilised

led to questions regarding the impact of that data quality on summary measures such as the DALY. Exploring this further became a secondary aim of the research.

1.3.3. Research questions (RQs)

Four specific RQs are addressed in this research:

1. What number of DALYs is estimated to be attributed to influenza in Ireland during the 2017/2018 and 2018/2019 seasons?
2. What degree of variability can be associated with the estimation of DALYs?
3. Is the estimation of DALYs a suitable and valid metric for burden of influenza in Ireland?
4. Is the estimation of DALYs attributed to influenza in Ireland feasible for and useful to stakeholders in practice?

Answering these RQs will build on the body of knowledge surrounding the burden of influenza in Ireland and globally. This is important information as it allows for informed healthcare policy decision-making on a local and global level. This type of data, where available, generally leads to implementation of health campaigns with improved outcomes and impacts, such as vaccination programmes and governmental reimbursement of medicines. These RQs will also address the potential of the DALY as a tool for better evidence-based healthcare decision making in Ireland. The DALY is not yet widely used for this purpose in Ireland but is strongly supported by the WHO. Therefore, clarity as to whether it is a valid, useful, suitable and feasible tool is of value to target groups in Ireland.

1.3.4. Intended outcomes

There are four intended outcomes of this study. Firstly, to devise a method for applying the global DALY calculation to the Irish population and healthcare setting. This method could then be used by future researchers to estimate the burden again after a period of time or an intervention, or in different populations.

A second intended outcome is for the burden of influenza in Ireland to be highlighted in terms of incidence, severity and decline in life expectancy in a single measure. The result can be used to compare the burden of influenza to that of other diseases and risk factors such as alcohol abuse, type 2 diabetes and COVID19. This may then form the basis of evidence-based health policy decisions.

Thirdly, to expand the methodological discussion on the way DALYs are estimated, and gain insights from target groups of the metric in Ireland as to its suitability and feasibility for them in practice.

Finally, a recommendation as to whether estimating DALYs associated with influenza in Ireland, based on available surveillance data, is a method that can and should be used in healthcare policy and life-science industry settings.

1.3.5. Conceptual framework

The intended outcomes described above are a product, and key element, of the conceptual framework for this research. The conceptual framework began with preliminary research into the potential cost-effectiveness of a school-based influenza vaccination programme in Ireland. During preliminary reading on the topic, the concept of DALYs emerged. The metric appeared to offer great value to healthcare and society, spurring the key concept of the research “Suitable use of DALYs as a feasible, reliable, and valid metric for calculating BoD in Ireland could assist/improve decision making around influenza prevention and control.”. Key concepts from the literature were then reviewed to provide supporting information to the research itself and to support the justification for the research project. Following the literature review, the abovementioned aims, objectives and RQs emerged. This informed the methodological framework required to address those questions which is described in chapter 3. This, in turn, informed the analytical framework described in section 3.3.5 and 3.4.6. It is expected that result of the analysis will align with the intended outcomes mentioned above and will add to the literature on the topic.

1.4. Practical and theoretical contribution of the study

The practical contribution of this study is two-fold. Firstly, it will highlight the estimated degree of disease burden attributed to influenza in Ireland. This may inform priorities for policymakers and healthcare professionals and inform the wider public of the burden of the commonly circulating disease—influencing behaviour such as vaccination uptake and seasonal vigilance. Secondly, it will inform researchers and policymakers of the feasibility, suitability, utility and validity of the DALY for measuring and managing the burden of Influenza in Ireland. This could lead to the DALY being more readily adopted in research and policymaking. This is particularly important as for the metric to be fit for purpose, i.e., to be used as a comparison tool, competing conditions must also be represented in the same format. The more widely adopted the metric, the more useful it is.

The theoretical contribution of the study is also two-fold. Firstly, it creates new knowledge of the burden of influenza in Ireland, and consequently builds on the body of knowledge of the global burden. Secondly, it provides further analysis of the suitability and validity of the DALY methodology when used in varying contexts.

1.5. Potential difficulties with the study

Potential difficulties with the study are planned for and mitigated where possible. It is recognised that research ethics must be considered during the primary research (interviews with subject matter experts and other industry leaders and stakeholders). During these interviews, it must be ensured that participation in the research is voluntary, informed consent is attained, PAC (privacy, anonymity, confidentiality) principles are followed and no harm, physical or psychological, comes to any participant.

An additional ethical issue is the potential conflict of interest as the principal researcher is an employee of AstraZeneca, whose childhood influenza vaccine is the current vaccine of choice for childhood influenza in Ireland. To acknowledge this issue, full disclosure of the potential conflict is made in the candidate declaration in the preliminary pages.

During initial secondary discovery for this study, it was noted that the quality of the current gold-standard surveillance data used in Ireland is of concern. This is because the current HPSC surveillance reports use a small sample size of 6.9% of the total population. This led to early consideration of the impact of the data quality on the results supporting the answer to RQ 1. For this reason, the original question (which was originally '*calculate* the DALYs associated with influenza in Ireland during the 2017/2018 and 2018/2019 seasons') was revised to 'What number of DALYs is *estimated* to be attributed to influenza in Ireland during the 2017/2018 and 2018/2019 seasons?'. The aims and objectives were revised accordingly.

1.6. Structure and contents of the document

This document consists of 5 chapters, beginning with this introduction (Chapter 1).

The next chapter, Chapter 2, comprises a literature review on the topic of measuring burden of Influenza using DALYs. Three main concepts are reviewed: The burden of influenza (2.1.1), quantifying the burden of disease (2.1.2) and the DALY method for quantifying the burden of disease (2.1.3). In these sections, current estimates of the burden of influenza globally and locally in Ireland are reviewed, followed by current efforts

in its prevention and control. Current attitudes and approaches to quantifying BoD are then reviewed, focussing particularly on the largest systemic effort thus far to do so—the Global Burden of Disease (GBD) study. The foundation, evolution and adoption of the DALY method is reviewed and challenges/limitations associated with the method are discussed.

Chapter 3, 'Research Methodology', details the conceptual framework, research methodology and methods used to obtain primary and secondary data and the data analysis techniques. This is a mixed-methods study using both quantitative and qualitative methods. Methods used to generate primary data include performing the DALY calculation (quantitative) and interviews with key stakeholders and industry leaders in infectious disease in Ireland (qualitative). The combination of both methods to arrive at the final theory is also described. This section also describes ethical considerations for this research.

Chapter 4, 'Findings and Analysis' describes and analyses the findings. The findings are discussed in the context of the published literature, highlighting issues, trends, consistencies and anomalies.

Chapter 5, 'Conclusions and Recommendations' offers conclusions and recommendations as to the burden of influenza in Ireland and whether the calculation of DALYs as a measure of this is a valid, feasible and useful method. It also recognises some limitations of the research and offers suggestions for further research on the topic.

The document ends with a list of references and appendices which include a glossary of definitions, ethical procedure documents, interview materials used, calculation materials used and a progress report summary.

1.7. Chapter conclusion

In conclusion, as methods of BoD estimation are becoming more comprehensive, the burden of influenza globally is appearing to be more significant than previously thought. This renews the urgency surrounding influenza prevention and control—a topic that was forced to take a position of lower priority during the COVID19 pandemic. To make informed decisions on health priorities such as these, policymakers need access to reliable measures of the comparative burdens of disease on populations. The DALY has been proposed for this purpose.

This is particularly important in the current Irish healthcare setting which is facing chronic resource shortages. This research aims to estimate the burden of influenza in Ireland in

terms of DALYs and investigate the feasibility, suitability, utility and validity of this measurement in this context.

Ultimately, the research highlights the burden of influenza using a summary measure (the DALY) which can be compared across different diseases and populations. Based on interviews with key target groups a recommendation is made as to whether estimating DALYs associated with influenza in Ireland based on available surveillance data is a method that can and should be used in health policy and life-science industry settings. The study expands the methodological discussion around the way DALYs are measured and calculated to support optimisation of the method.

2.0 Literature review

2.1 Overview

This research is an investigation, based on a combination of secondary research and stakeholder interviews, into the suitability of the DALY as a metric for measuring and managing the burden of influenza in Ireland. The preceding chapter outlined the potential utility of this metric to health policymakers for making evidence-based decisions on the prevention and control of influenza. This is significant in the current Irish healthcare setting due to chronic resource shortages. Based on this, aims, objectives and RQs were introduced providing the purpose of the research which is to estimate the burden of influenza in Ireland based on data collected during the 2017/2018 and 2018/2019 seasons and to investigate the feasibility, utility, suitability and validity of it as a measure of the burden of influenza in Ireland.

The following literature review identifies and discusses key components of the conceptual framework for this research (detailed in section 3.2). It summarises existing knowledge on the key concepts of the research, introduces existing theories and frameworks and highlights the gaps in literature that this research intends to fill.

The first part of this chapter (2.1.1 The burden of influenza) provides an overview of influenza and its related burden. Influenza is a highly contagious disease which circulates each year due to frequent antigenic drift despite efforts in its prevention. The burden in Ireland and globally is substantial but remains insufficiently characterised due to deficient surveillance systems and analysis. The role and extent of vaccinations in preventing the spread of the virus is examined by reviewing vaccine efficacy and coverage in Ireland. This section provides context for the study and adds perspective to later findings.

The following section (2.1.2 Quantifying the burden of disease) goes on to review the benefits and criticisms of quantifying BoD, particularly of using more holistic methods than traditional prevalence and mortality rates. Benefits and criticisms of holistic BoD methods are reviewed, focussing particularly on the conception, evolution and current status of the Global Burden of Disease (GBD) project, from which the DALY originated. The extend of adoption of such holistic measures of BoD in Ireland is then reviewed. This provides the setting for the DALY, its intended function and its empirically established benefits and limitations.

Finally, the DALY method for quantifying the BoD is described (section 2.1.3), reviewing the evolution of the method and the current proposed method. Challenges and methodological weaknesses are of particular interest. Evidence of its use in practice to date it then reviewed.

This review provides justification for the key concept of this literature – "Suitable use of DALYs as a feasible, reliable, and valid metric for calculating BoD in Ireland could assist/improve decision making around influenza prevention and control". It also identifies the gap in knowledge the research intends to fill, leading to the key research questions. This process is described in full in the conceptual framework for this study which appears in section 3.2.

2.1.1 The burden of influenza

Influenza is a highly contagious acute respiratory virus which continues to impact global populations despite efforts in its prevention and control. The following section reviews the burden associated with infuenza in terms of mortality and morbidity, both globally and in Ireland. It also reviews efforts for its prevention and control.

Influenza

Influenza is a highly contagious acute respiratory virus which circulates worldwide every year. In Ireland and other temperate regions, it circulates almost every Autumn/Winter season. It spreads via aerosolised droplets from the mouth or nose in addition to contaminated hands and surfaces. It infects all age groups, causing a range of outcomes from asymptomatic infection and mild respiratory illness to severe systemic disease and death (Vanderven et al., 2017).

Typically, symptoms occur abruptly and include high fever, chills, headache, generalised weakness, severe aches in muscles and joints, red eyes and respiratory signs such as

sore throat, dry cough and rhinitis (Gibson et al., 2013). However, it can affect any organ and may manifest as more unusual and severe complications such as pneumonia, hepatic encephalopathy, myocarditis and severe neurological conditions (Gibson et al., 2013; Baral et al., 2020).

Influenza viruses evolve quickly by frequent antigenic variation, resulting in the circulation of different strains each year (Kim et al., 2018). As a result, influenza continues to be a communicable disease despite ongoing efforts in its prevention and control. There are four distinct antigenic types of influenza called types A, B, C and D. Type A is further subdivided based on antigenic variant (H1N1, H5N1 etc.). Usually, no more than two dominant strains circulate simultaneously. Influenza type A is the most common to circulate in humans, followed by influneza B (Kim et al., 2018). The severity of the influenza season is dependent upon circulating strains.

The burden of influenza globally

Although most individuals infected with influenza will recover within a week without requiring medical treatment, mortality associated with influenza globally is significant. According to estimates by CDC, WHO and their global health partners, influenza causes up to 650,000 deaths per year (Luliano et al., 2018). This estimate, however, accounts for death from respiratory disease alone, and does not account for deaths from other diseases such as cardiovascular disease, which can also be influenza related (Madjid et al., 2004). Thus, improved surveillance methods and laboratory studies of all influenza-related diseases is expected to yield higher mortality estimates.

In a study of the impact of 31 infectious diseases on EU population health from 2009 to 2013, Influenza ranked highest in terms of DALYs, contributing 30% of total burden measured (Cassini et al., 2018). It must be noted that, in the absence of adequate surveillance data, this study used a single incidence data source, the Flu Watch cohort study in the United Kingdom (UK) (Hayward et al., 2014), to represent influenza incidence in Europe. The population studied in the Flu Watch cohort study may have a different epidemiological profile and vaccination coverage than the rest of EU and therefore does not represent an ideal data source. However, it appears to be the most appropriate source available.

In addition to excess mortality, influenza infection causes significant hospitalisation each year. In a publication by Troeger et al. (2017) for the 2017 Global Burden of Disease (GBD) study, it was estimated that 54.5 million lower respiratory tract infections

attributable to influenza occurred in that year alone, of which 8.2 million were severe (defined as infections resulting in pneumonia, or which required inpatient admission or oxygen therapy). These estimates must be interpreted with caution due to the inherent impreciseness of influenza surveillance data resulting from the variability in its availability and quality. Nonetheless, it is widely accepted among the scientific community that the burden of influenza globally is substantial (WHO, 2017).

The burden of influenza in Ireland

Ireland is no exception to the burden of influenza described above; however, the severity of the impact changes each year with differing circulation of strains. The 2018/2019 season was described by the HPSC as 'moderate', with 7,943 notified influenza cases, 3,244 hospitalisations, 159 ICU admissions and 97 deaths reported that year. Whereas the previous season, 2017/2018, was described as 'severe', with 11,889 notified cases, 4,713 hospitalisations, 191 ICU admissions and 255 deaths reported. These figures must be interpreted with caution, as they are likely gross underestimations. Influenza cases are generally only notified in Ireland if they are serologically confirmed, which omits the majority of true influenza cases as most are never serologically confirmed. Non-serologically confirmed influenza cases are known as cases of influenza-like-illness (ILI), and most GPs in Ireland are not required to report these to HPSC. Therefore, 'notified cases' is not representative of the true incidence rate and could be misleading.

Moreover, ICU admission and mortality rates are likely also underestimations as these are commonly misclassified and attributed to other comorbidities or secondary infections (Aziz et al., 2021). The relative severity of both seasons is illustrated below in Figure 1 for comparison of season severity only.

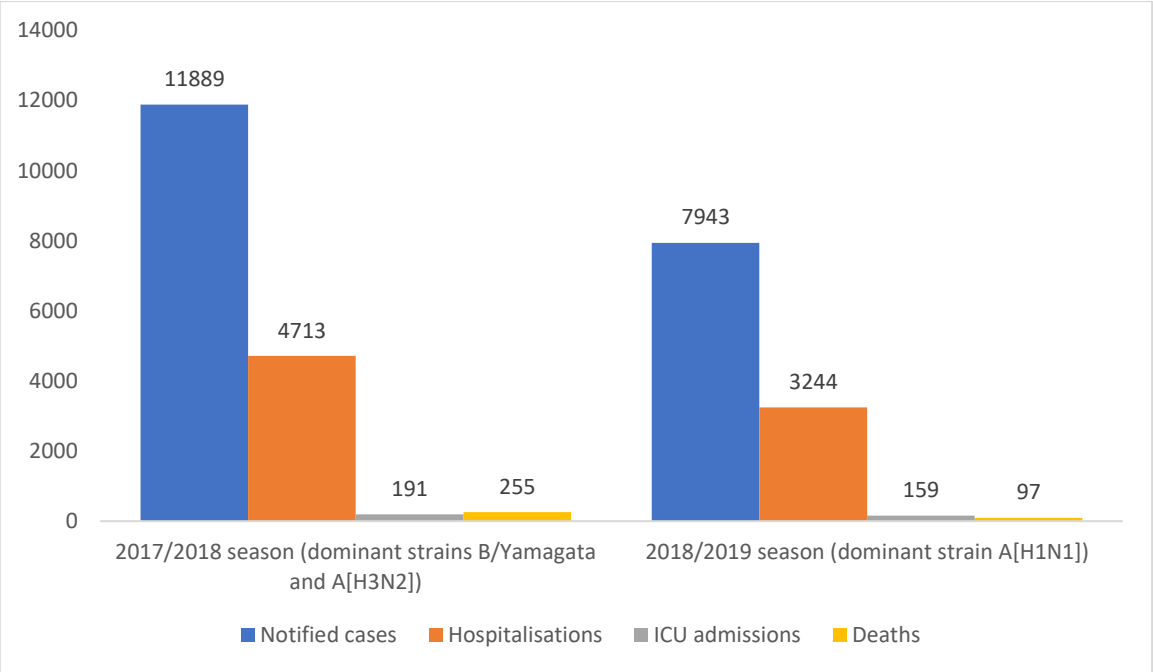

Figure 1: Relative severity of influenza during the 2017/2018 and 2018/2019 seasons in terms of notified cases, hospitalisations, ICU admissions and deaths. Figure is for comparison of season severity only. Data are not representative of true burden. Figure created by the author (2023) with data source: HPSC (2023)

The burden of paediatric influenza is also well recognised by the Irish national health service, the Health Service Executive (HSE). In a pre-season briefing in November 2022, it reported that up to 10% of all children under the age of 15 (a total population of about one million as of 2022) attend a GP with symptomatic ILI each influenza season. Strikingly, it also reported that the highest rate of hospitalisation occurs in children <5 years. This is illustrated in Figure 2 (HSE, 2022) which displays confirmed cases, hospitalisations and ICU admissions stratified by age group in the 2018/2019 season.

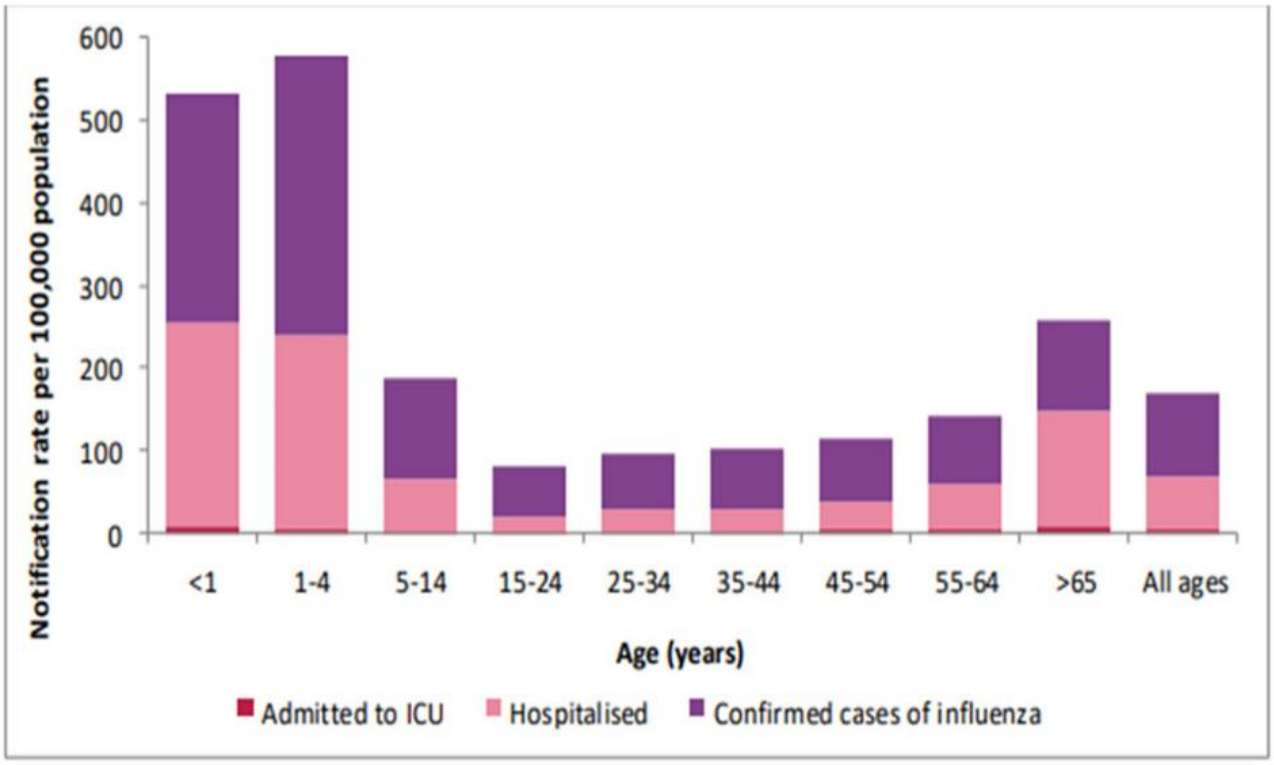

Figure 2: (HSE, 2022) Age-specific notification rates/100,000 Irish population for influenza, by hospitalisation status, during the 2018/2019 season, in Ireland. Data source: HPSC

Although useful in some respects, data in the form of incidence, hospital admissions and mortality cannot be used as a valid basis for comparison to other diseases competing for the limited healthcare resources. A measure of the overall number of years of life lost due to mortality, plus the amount of time spent in a state of ill health and the relative severity of that health state may be more meaningful and useful. It may be more meaningful as it represents more closely the true burden of the illness of society. It may be more useful as expressing the burden in a summary measure which can be applied to any disease or risk factor allows it to be used for making valid comparisons.

In light of this, this research aims to estimate the burden of influenza in Ireland using the DALY, which is a summary measure of both morbidity and mortality. Given good quality underlying data, illustrating the burden using a summary measure such as the DALY could bring new understanding of the burden and facilitate more direct comparison of this health matter versus others.

Influenza vaccination

Vaccination remains the most effective means of preventing influenza disease and complications. It is widely employed to reduce the burden on the healthcare system and society in developed countries (Gross, 1995; Nichol et al., 1995; Bridges et al., 2000). Influvac Tetra, the influenza vaccine manufactured by pharmaceutical company Mylan, and the current vaccine of choice for adults in Ireland, is reported to have prevented up to 68% of influenza cases during the 2019/2020 season (Leroux-Roels et al., 2022). The competing influenza vaccine developed by Sanofi was reported to have prevented 52% of infections in the same season (Gresset-Bourgeois et al., 2017).

Still, vaccine efficacy varies each year with differing virus strains and can often be quite poor (Rolfes et al., 2019). This is because, to allow time to manufacture and deliver vaccines before the season begins, vaccine manufacturers must predict the strains most likely to circulate ~9 months before the season begins. The efficacy of the vaccine therefore depends on the accuracy of this prediction.

Furthermore, varying characteristics of vaccine recipients also contributes to variability in efficacy. This is mainly due to the phenomenon of reduced immunogenicity of vaccines in the elderly population due to age-related immunosenescence (Fuentes et al., 2017). Figure 3 provides an illustration of the variability in influenza vaccine efficacy year-to-year in the US using data obtained from the CDC (Centres for disease control, 2022b). The figures used to represent efficacy refer to the prevention of laboratory-confirmed influenza infection. However, vaccine efficacy can be measured using a range of outcomes, such as prevention of GP visits, hospitalisations, ICU admissions and deaths, some of which may provide more clinically and societally meaningful results than simply number of cases.

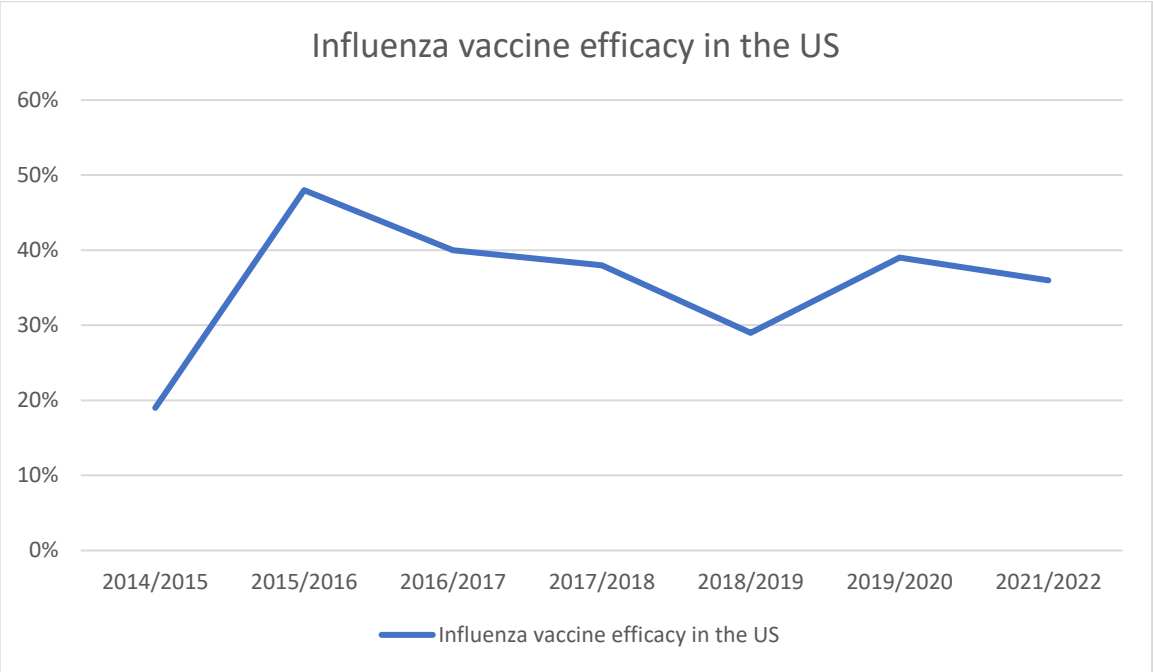

Figure 3: Influenza vaccine effectiveness in the US from 2014 - 2022. The 2020/2021 season is not applicable as influenza circulated in very low numbers due to restrictions put in place during the COVID19 pandemic. Figure by the author with data source: CDC (2022b)

Influenza vaccination efforts in Ireland

The WHO endeavours to reduce global burden of influenza by increasing vaccination uptake (WHO, 2022a). This goal has been supported by the European Parliament and all European countries are therefore expected to have a national vaccination policy in place (European Comission, 2022). The vaccination campaign in Ireland has been expanding steadily since 2004 (HPSC, 2022). The current strategy (as of 2023) is to provide the vaccine free of charge to at-risk groups, children aged 2 – 17 years, all adults over 50 years of age and health and care workers. Mobile vaccination teams attend nursing homes to provide vaccines to residents and carers. Additionally, healthcare workers can receive a vaccine in their workplace. All other cohorts must attend a participating GP or pharmacy to avail of the vaccine. Uptake in the 2021/2022 season was 16.6% in children, 26.9% in those aged 50-64 years and 75.4% in those aged 65 years and over (Health Service Executive, 2023). Ireland met its target of vaccination uptake of 75% in those aged >65 years, but uptake remains low in the remaining cohorts.

If deemed beneficial, further efforts could be employed to improve vaccination uptake. For example, the United Kingdom (UK) has employed a school-based influenza vaccination

programme which sees mobile vaccination teams visit all participating primary and secondary schools in the UK offering vaccinations. This has significantly increased vaccine uptake among children, which has in turn had a positive effect on influenza-related outcomes (Pebody et al., 2013; Kassianos et al., 2020). Introducing such a campaign in Ireland would be expected to achieve similar results; however, such a campaign would require additional funding and resources which are in high demand in Ireland at the time of writing (Prospect, 2020). Thus, health policymakers require accurate, reliable and meaningful information relating to the burden of influenza, in addition to the potential benefit of further intervention, to make informed decisions on whether resources should be allocated to such interventions. This research aims to explore the potential of the DALY for this purpose.

In summary, influenza is a highly contagious virus which can cause serious illness and evades immunity by evolving into new antigenic variants each Autumn/Winter season. As a result, the burden of influenza remains significant despite global efforts in its prevention and control. This is a key element of the conceptual framework of this study (described in section 3.2). The following section reviews literature on the concept of quantifying the BoD, and specifically the burden of influenza, for purposes such as the abovementioned.

2.1.2 Quantifying the burden of disease (BoD)

Quantifying the BoD is the process of measuring the impact of a particular health problem in a given population. This can involve assessing the incidence and prevalence of a disease, estimating mortality rates or calculating the economic and social costs associated with the disease. The need to quantify the BoD has been increasingly recognised over the last two decades (Institute for Health Metrics and Evaluation, 2023) as it allows healthcare decision makers to make evidence-based decisions on priority areas and resource allocation. Assessment of interventions in the areas of immunisation, food and water safety and clinical care are some of the examples where BoD data can be useful. It also allows the evolution of the burden of a disease to be tracked over time, for example pre- and post- intervention, and across various populations.

A key benefit of quantifying the BoD is that it facilitates direct comparison between different diseases and populations, creating an evidence-based foundation for decision-making. Traditionally, and oftentimes still, data limited to prevalence and mortality rates are used to inform healthcare decisions (World Health Organisation, 2004); however, the elucidation of the complexity of healthcare over time has led to the conception of more holistic and complex measurements of health and disease which incorporate not only the

presence/absence of disease or life but also the *severity* of the disease, the *quality* of life gained and the impact of those health states on mental wellbeing (Ezzati et al., 2006).

Elements such as severity of disease and quality of life are measured using the concept of the 'utility score', which is a score that reflects the preference the general population gives to one health state over another (Gold et al., 1996). These scores are usually qualitatively generated using surveys of large samples of the public, which is seen as a reliable source (Yin et al., 2016). However, some critics are of the view that the subjectivity of the utility scoring system leads to a lack of sensitivity for the metric (Sacristán, 2003). The 'universality' of such scores has also been called into question, with some arguing that the severity of each individual disease fundamentally depends on the context (Fox-Rushby, 2002).

Clearly, there is much to consider when it comes to adopting such methodologies in practice. This research will explore the suitability of this method when applied to the Irish population and healthcare setting relating to influenza. It will further gather the opinions of subject matter experts and industry leaders on the potential utility, validity, suitability and feasibility of quantifying the burden of influenza in terms of DALYs. This will either support or refute the use of the metric for better healthcare decision-making.

The Global Burden of Disease (GBD) Project and the DALY

In the words of its founder, the GBD project is "a systematic, scientific effort to quantify the comparative magnitude of health loss due to diseases, injuries, and risk factors by age, sex and geographies for specific points in time'' (Murray et al. 2012). The framework was first developed by the World Bank in the 1990s and is now coordinated by the Institute for Health Metrics and Evaluation (IHME) at the University of Washington. The project endeavours to develop comprehensive estimates of mortality and morbidity associated with major diseases and injuries to inform decision-making in health and social policy, assist efficient allocation of resources and track progress towards health goals (Institute for Health Metrics and Evaluation, 2021). The GBD framework cites three specific aims:

i. To systematically incorporate information on non-fatal outcomes into the assessment of the health status (using a time-based measure of healthy years of life lost due either to premature mortality or to years lived with a disability, weighted by the severity of that disability)
ii. To ensure that all estimates and projections were derived on the basis of objective epidemiological and demographic methods, which were not influenced by advocates.

iii. To measure the BoD using a metric that could also be used to assess the cost-effectiveness of interventions. The metric developed was the DALY.

The launch of the GBD project was significant as it was the first formal, comprehensive estimation of global disease burden in terms of prevalence, severity and years of life lost using a single metric (the DALY). It was also the first time a common holistic metric was used to measure disease burden across varying diseases and geographical locations, allowing comparison between them (Murray, Lopez and Jamison, 1994). For example, the impact of both depression and breast cancer on a particular population could be represented in a common 'currency', demonstrating which disease had a greater adverse impact on the population. Furthermore, the impact of certain diseases such as cancer in one geographical location could be compared to its impact in another. The publication of the first GBD study in 1990 uncovered many otherwise hidden or neglected health challenges such as mental illness and the burden of road injuries (Murray, Lopez and Jamison, 1994).

GBD studies have been published intermittently since 1990, incorporating a wider scope and methodological refinements each time. Each time the method is refined, new estimates are generated for the entire time series from 1990 to maintain comparative ability (IHME, 2017). Since 2015, GBD updates have been published annually.

Although the framework is viewed positively overall, limitations remain such as poor data quality in some cases, questions over the methodological validity of the DW and, more recently, data privacy concerns (Chen et al., 2015; Murray, 2022). Many of these issues are inherent to epidemiology and are recognised by the leaders of the GBD study. In this regard, Christopher Murray (2022)—founder and director of GBD—stated "we have made an increasingly robust effort to obtain wide-ranging feedback on the processing and results of each GBD estimation" (Murray, 2022). This is reflected in the 40-person scientific council convened for the GBD framework comprising leading experts who evaluate criticisms and recommendations of the GBD processes and methods (including the DALY). This is in addition to the Independent Advisory Committee which is another 13-person team which meets twice annually to discuss and advise on the GBD processes and methods (IHME, 2022a). Minutes and actions of all advisory meetings are published, inviting further peer commentary. This demonstrates their commitment to optimising the GBD methods using wide-ranging and diverse opinions of scientific experts around the world.

Th GBD framework brought forth the DALY method and the team behind it is responsible for ensuring its validity. Based on the above information, the GBD committee endeavour

to make the DALY method as valid and suitable for its purpose as possible. This research will explore the validity and feasibility of this method for measuring burden of influenza in Ireland by applying it to Irish demographics using available data. It will also explore the views of subject matter experts on the validity of this metric for quantifying the burden of influenza in Ireland.

BoD quantification in Ireland

Healthcare and research institutions in Ireland are actively developing the infrastructure necessary to record and analyse data for quantifying the national BoD. In fact, the European Union mandates a certain extent of disease surveillance in all member states, particularly in communicable disease (European Parliament, 2021). Ireland is further bound by WHO Regulations which aim to prevent, protect against, control and provide a public health response to the international spread of disease (WHO, 2022a). The HPSC is the Irish national focal point for these responsibilities and collaborates with national research institutions in an attempt to gather the necessary data.

Many independent researchers have also published studies on the burden of various diseases in Ireland including cardiovascular disease, COVID19, hepatitis C, fungal disease and osteoarthritis (Rayner et al., 2009; Thornton et al., 2011; French et al., 2015; Moran et al., 2022). Interestingly, of these studies only two used the DALY as a measure of BoD—the study on cardiovascular disease and that on COVID19. The three other studies relied on national prevalence as a metric for BoD.

Healthy Ireland (HI)—one of the largest population health surveys in Ireland driven by central Government bodies—also opts out of using a summary measure such as the DALY and instead presents findings primarily as prevalence estimates (Ipsos MRBI, 2017). Another of the largest epidemiological studies in Ireland, The Irish Longitudinal Study on Ageing (TILDA), also presents findings in terms of prevalence (Trinity College Dublin, 2023).

The creators of the DALY would argue that BoD is better quantified as an overall reduction in health state due to both disability before death and the decline in life expectancy due to death, rather than simply prevalence or mortality alone. As an example, back pain as a condition in Ireland is not as prevalent or deadly as heart disease (IHME, 2017). However, those with back pain may live in a state of chronic disability for many years. The aim of the DALY is to account for this time lived in disability, the degree

of disability and the reduction in life expectancy. Burden expressed in DALYs is more reflective of societal reality than prevalence or mortality. Therefore, using such methods to aid decision-making may maximise the benefit to society.

A barrier to the implementation of summary measures such as the DALY is the validity and reliability of data. The effectiveness of these measures is entirely dependent upon the quality of the underlying data. If the disease surveillance data collected is subject to biases, based on an insufficient sample size or subject to inaccurate modelling etc., then the summary metrics may not be valid or reliable. This would counteract the purpose of the metric, which is to aid evidence-based decision-making. Therefore, ensuring the quality of the underlying data is key to the concept of quantifying the BoD. It is possible that concerns over the quality of surveillance data is part of the reason why the method has not yet been widely adopted in Ireland. This research will explore the feasibility of utilising the DALY for measuring the burden of influenza in Ireland by applying the method to Irish demographics and available data. It will triangulate these findings by exploring the views of subject matter experts on the suitability, feasibility and validity of this metric for this purpose.

Estimating the burden of Influenza in Ireland

Active efforts are ongoing to estimate the burden of influenza in Ireland. In fact, to comply with European standards, all medical practitioners in Ireland are required under legislation to notify the HPSC of influenza cases. The HPSC is Ireland's specialist agency for the surveillance of disease. It works in partnership with health service providers and other organisations in Ireland to carry out nationwide disease surveillance, epidemiological investigation, and related research (HPSC, 2020). The term ‘surveillance’ in this context refers to the collection, collation, analysis and communication of data related to the prevalence of influenza in Ireland. The HPSC gathers data annually on notified influenza cases, dominant circulating strains, rates of hospitalisation and ICU admissions and number of deaths.

During the early stage of this research it emerged that the HPSC’s surveillance methods are more limited than originally assumed. This was surprising, as the legislation states that all medical practitioners are required to notify the HPSC of notifiable disease (influenza included) (Government of Ireland, 2004). Although this is true, it is applied only to serologically confirmed influenza cases, which omits the majority of true influenza cases as most are never serologically confirmed. Non-serologically confirmed influenza

cases are known as cases of influenza-like-illness (ILI), and most GPs in Ireland are not required to report these to HPSC.

Instead, HPSC recruits a subset of ~6.9% of GPs to report presentation of ILI as an 'early warning system' for circulation of the virus (personal communication, Miriam Kelly, January 2023). In effect, this means that the number of influenza cases occurring in Ireland in any one season is unknown. This approach is common among most European countries (Cassini et al., 2018). In contrast, approximately 98% of all GP practices in Scotland routinely report ILI presentations to Public Health Scotland (PHS)—their HPSC equivalent.

With that said, all hospitals in ROI are required to report cases of ILI in addition to ICU admissions and deaths caused by influenza. Therefore, data from hospitals will be more robust than that from the public.

This discovery made clear that based on these data, the burden of influenza in Ireland cannot be *calculated*; but instead, may only be *estimated*. The questionable data quality also reduces the validity and reliability of the calculation output. Ultimately, this erodes the base for using DALYs for evidence-based intervention—one of its primary functions. As a result of this discovery, the estimation of the burden of influenza in Ireland during the 2017/2018 and 2018/2019 seasons will be interpreted with caution.

In summary, quantifying the BoD allows policymakers to make evidence-based decisions to maximise societal benefit from finite healthcare resources. Methods used to quantify BoD have evolved in recent years, becoming more holistic by accounting not only for the presence/absence of disease/life but also the degree of disability incurred and the quality of life gained. The DALY is one such measure, conceptualised for the GBD project launched in 1990 to quantify the global BoD. This measure, although promoted by the WHO, is not much in evidence in the BoD literature in Ireland, which is a key factor in the conceptual framework of this research (figure 5). This research intends to address whether the DALY *can* and *should* be used for measuring and managing the burden of influenza in Ireland. The following section reviews the DALY in detail, describing the current method, its evolution and associated challenges.

2.1.3 The DALY method

The calculation of DALYs has evolved significantly since its conception in 1990 to overcome criticisms, methodological challenges and increase overall validity. The

following section reviews the current method to calculate DALYs, the evolution of the method, its remaining challenges and its use in practice today. This provides insight into the methodological framework of metric as a baseline for the application of the method to Irish demographics and data in this research as is described further in Chapter 3 (Research Methodology).

The calculation

A DALY is a numerical figure representing BoD. It is a time-based measure that combines years of life lost (YLL) due to premature mortality and years of life lost due to time lived in disability (YLD), measured using the below formula (WHO, 2020).

DALY = YLL + YLD

The YLL corresponds to the number of deaths at a given age multiplied by the remaining life expectancy at that age, as shown below. This is performed for each age-group.

$$\mathrm{YLL} = \sum_{a=1}^{n} \mathrm{YLL}_a = \sum_{a=1}^{n} \mathrm{Number\,of\,deaths}_a \times \mathrm{Remaining\,life\,expectanc}$$

where *a* = age-group, *n* = number of age-groups.

The YLD is derived by multiplying the number of cases (prevalence or incidence cases) by the average duration of the disability state (e.g. mild, moderate, severe etc.) and a weight factor that reflects the severity of the disability on a scale from 0 (perfect health) to 1 (dead). This is the DW (Salomon et al., 2012). As health states may differ in terms of DW and duration, the calculation is performed for each health state.

$$\mathrm{YLD} = \sum_{h=1}^{l} \mathrm{YLD}_h = \sum_{h=1}^{l} \mathrm{Number\,of\,cases}_h \times \mathrm{duration}_h \times \mathrm{disability\,weight}_h,$$

with *h* = health state and *l* = number of health states.

This research adopts this method, published by the WHO, to estimate the burden of influenza in Ireland based on surveillance data collected during the 2017/2018 and 2018/2019 seasons. It also explores its feasibility, utility, suitability and validity as a measure of burden of influenza in Ireland.

Methods used to determine DWs

DWs are generated by researchers conducting DW studies. Many of these researchers are GBD collaborators and conduct their research according to agreed methods. However, some disability studies are conducted using other methods, for example if nation specific DWs are preferred (Haagsma et al., 2015; Nomura et al., 2021) or to generate DWs for diseases not yet studied by GBD collaborators (Nanjan Chandran et al., 2021). Variability in the way DWs are generated can lead to non-standardised outputs of the DALY calculation, which erodes the ability of the DALY to be used for comparative purposes. This research aims to investigate the degree of variability caused by differing methods of DW estimation.

DWs generated for GBD studies nowadays are based on surveys of large samples of the general public (Vos et al., 2015). The most-cited method, published by Vos et al. (2015), briefly comprises respondents being presented with a series of randomly selected comparisons of health states and asked to indicate which health state is ‘healthier’ than the other. A statistical model is then applied to yield DWs from these pairwise comparisons on a scale from 0 (no health loss) to 1 (equivalent to death). This is a type of utility score. In total, responses were gathered from 30,230 people in 167 countries to yield these DWs (Vos et al., 2015), and they are therefore proposed to be ‘universal’. The DWs generated in this study appear to be those of current choice for GBD studies (Solomon et al., 2015; James et al., 2018; Vos et al., 2020).

Challenges

Since its conception, GBD methodology has been subject to much criticism and is continuously being improved based on these critiques. Below are some brief examples of

previous issues with the methodology of the DALY which have since been resolved and some of which remain.

Challenges overcome

Age-weighting

Age-weighting was previously a part of the calculation of the DALY. It incorporated the weighting of age according to social roles played by people of different ages. For example, it was thought that as an infant or an elderly person does not play a major role in society's workforce, these ages should not contribute as much of a loss to the overall BoD. This concept is illustrated in the below graph by Roing (2015). This approach was subject to heavy criticism, particularly on ethical grounds, and was removed from the method in 2010. The current DALY method focuses only on 'health' loss, rather than any loss in social value.

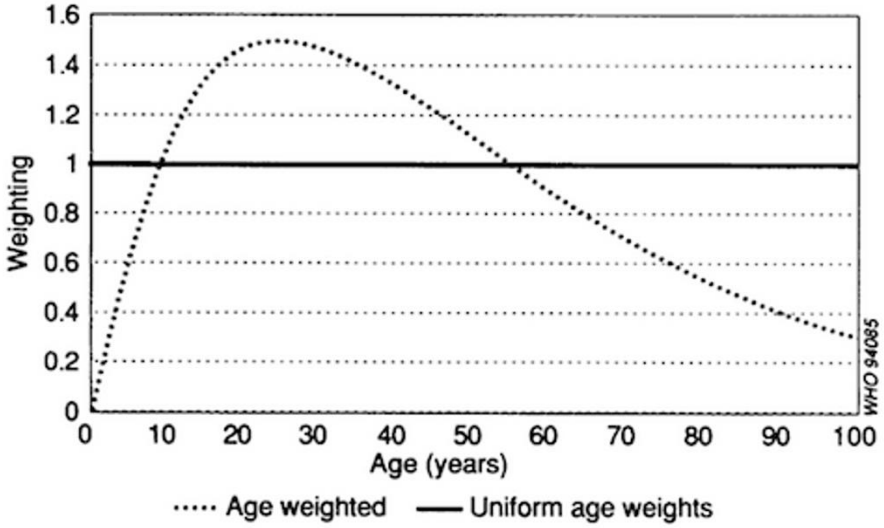

Figure 4: A diagram of the age-weighting previously used for the calculation of DALYs (Roing, 2015)

Future-discounting

Another issue similar to the above was future-discounting which is the practice of applying higher weights to benefits that arise in the present relative to the future. The anticipated effect of this was to incentivise policymakers and practitioners to focus on health interventions that could be implemented right away for immediate benefit. Critics argued that there was no valid reason to value health benefits now more than those in the future (Lyttkens, 2004), and it was removed from the calculation in 2010.

DW generation methods

As alluded to in section 2.1.2, the approach to generating DWs for use in DALY calculations has also evolved over time. The first DALY studies relied solely on the survey of a small number of medical experts to inform on the non-desirability of certain health states. This approach was replaced with society-based surveys which was deemed more appropriate as the function of the DALY was to inform on societal decision-making (Charalampous et al., 2022).

Challenges remaining

Disability weights

Concerns remain around the validity of DWs. One concern is whether the DWs generated for the GBD project can be removed from their societal context to be considered universal. Questions have been raised, for example, over whether the decrease in quality of life associated with paraplegia can be considered equal in a low-income country as in an urban area of a high-income country where assistive technologies and public transportation are available (Chen et al., 2015). For this reason, some researchers feel it is appropriate to generate national/regional DWs (Schwarzinger et al., 2003). Despite such concerns, however, disability-weight studies based on population surveys in different countries do show generally consistent results (Üstün et al., 1999; Solomon et al., 2012).

Poor quality data

Oftentimes, the data that estimations such as the DALY are based on is sparce or of low quality. For example, many low-income countries may not have the resources to monitor disease prevalence, incidence, mortality rates and mortality causes. It's been discovered that even some high-income countries like Ireland have limited disease surveillance methods as outlined in section 2.1.2. Despite these issues, it is generally agreed that providing a best estimate using the data available and assumptions where necessary is preferable to providing no estimate at all.

Data on common infectious diseases such as influenza in particular are inherently unprecise. This is because many cases will be managed in the community and therefore go undetected and unreported. Many cases which do require medical intervention will still go unreported as serological testing is often not required to treat the illness. Furthermore, it is difficult to determine deaths attributed to influenza as many of the deaths occur due to

secondary infections or co-morbidities (Aziz et al., 2021). This underestimation is recognised as a limitation in infectious disease surveillance. Some researchers have attempted to develop multiplication factors which can be applied to account for this (Gibbson et al., 2014). However, these multiplication factors must be disease-, country-, age-, and sex-specific, which is not that practical.

One of the biggest challenges is to ensure that data inputs from different sources and countries are standardised and of the same quality. If the inputs are not standardised, then the validity of the DALY as a mode of comparison is reduced. This concept is demonstrated by Arneesen and Kapiriri, (2004) in their publication on the influence different value choices have on DALY outputs. They found that changing the value choices (of DWs, age-weights and future discounting) within reasonable limits lead to striking changes in the relative burden attributed to different diseases. Recognising that age-weights and future discounting have since been omitted from the calculation, the effect of varying DW values on the calculation output remains of interest and will be further explored in this research.

The GBD recognises these issues and endeavours to overcome them by expanding the uptake of gold-standard methodologies in global health research. It does this by offering education and training opportunities for policymakers and scholars engaged in population health research. The training promotes the use of GBD data, results and tools as the gold-standard in academic, research and professional settings (IHME, 2022b). They also adhere to and promote the Guideline for Accurate and Transparent Health Estimates Reporting (GATHER) which is a checklist of 18 items that should be reported every time new global health estimates are published, including descriptions of input data and estimation methods. GATHER aims to promote the generation of coherent estimates based on disparate sources of data. Wide adoption of these methods is a potential solution for the issue of non-standardised inputs.

This research investigates the reliability and validity of the DALY as a measure of Influenza in Ireland by exploring the variability of the calculation given varying data inputs and seeking opinions of subject matter experts. There is no published evidence of the use of DALYs by stakeholders as a measure of burden of influenza in Ireland. Thus, this research will for the first time explore the feasibility and potential utility of such a measure to various stakeholders.

The DALY method in practice

Despite the above issues, many researchers and policymakers recognise the DALY method as a useful tool (Shah et al., 2019). It has been applied to a variety of global and national health initiatives, including the Global Vaccine Action Plan and the Geneva Negotiations on Global Health (WHO, 2013; WHO, 2023a). Its utility was demonstrated during the COVID19 pandemic when it was used to inform the global approach to optimally and equitably allocating the limited initial doses of the COVID19 vaccine to those at highest risk (WHO, 2023a).

In Ireland specifically, the number of researchers who have adopted the DALY method to estimate national BoD is limited (Chakraborty, 2020; Moran et al., 2022; Kabir et al., 2022). Healthy Ireland (HI), one of the largest population health surveys in Ireland driven by central Government bodies, opts to present its findings primarily as prevalence estimates (Ipsos MRBI, 2017). Another major epidemiological study in Ireland, The Irish Longitudinal Study on Ageing (TILDA), also presents findings in terms of prevalence primarily (Trinity College Dublin, 2023). No evidence was found of the DALY method being used in national health policy decisions.

In summary, The DALY is a time-based measure that combines years of life lost (YLL) due to premature mortality and years of life lost due to time lived in disability (YLD). A key element of the calculation is the DW, which is a pre-defined number on a scale representing the non-desirability of a health state generated using public surveys. The calculation itself has evolved to omit age-weighting and future-discounting, but challenges remain around the validity of the DWs and the quality of data inputs. Use of the metric is not much in evidence for quantifying the BoD in Ireland. This is a key factor in the conceptual framework for this research (figure 5), which aims to explore the DALY as a tool for policymakers, researchers and other healthcare decision-makers to make informed, evidence-based decisions on health policies in Ireland. The result of the research will indicate whether the DALY can and should be used as a metric to inform health policy in Ireland.

2.2 Chapter conclusion

Influenza presents a significant burden in Ireland and globally, and efforts in its prevention and control should be renewed following the end of the COVID19 pandemic. Prevention and control efforts thus far have mainly centred around influenza vaccination, which provides varying levels of protection each season. Influenza vaccination uptake in Ireland remains relatively modest and may benefit from increased resources for vaccination campaigns. To make informed decisions on allocation of resources, health policymakers

and industry professionals require accurate, reliable, comparable information relating to the burden of influenza.

Efforts to quantify the BoD are underway to provide this type of information. The DALY is one example of a method to quantify the BoD to inform decision-making. This method was created through a large collaboration of researchers for the GBD project, is continuously being revised and improved, and is strongly supported by the WHO. Its benefit is that it combines time lived with disability with years of life lost to summarise the overall burden of the disease. However, the literature reports that issues remain with its validity and reliability, and a review of research papers and health sector documents shows that it is not yet widely used for research nor policy in Ireland. This formed a key concept for the conceptual framework for this research, which can be viewed in section 3.2. This research proceeds (in the Research Methodology Chapter) to explore and examine the suitability, validity, utility and feasibility of the DALY as a method of estimating the burden in Ireland by developing and performing a method of applying the DALY calculation to the Irish population and healthcare setting and conducting interviews with a panel of experts.

3.0 Research methodology

3.1 Overview

The WHO and other organisations have previously measured the number of DALYs attributed to influenza at a global level, but to date no equivalent calculation has been carried out in Ireland. A primary aim of this research is to apply the method of calculation most commonly used globally to data available in Ireland during the 2017/2018 and 2018/2019 seasons.

Additional calculations using various alternative variables are used to explore and examine the degree of variability that can be associated with the calculation of DALYs.

Using the above calculation and evaluation of alternative methods as a base, and through a series of interviews with stakeholders in the health and pharma sectors in Ireland, the research then focuses on whether the calculation of DALYs is a suitable and valid metric for burden of influenza in Ireland. The interview data are used to consider the suitability and practical use of the calculation.

The research philosophy which is dominant in this research is interpretivism; however, it employs a mixed-method approach. One approach to gather primary data is positivist

using a deductive approach involving the application of mathematical equations. This approach is used to address RQs 1 and 2 (see below for a reminder). The other approach is interpretivist, inductive and has a grounded-theory strategy involving collection and analysis of data through interviews of subject matter experts. This strategy is employed to address RQs 3 and 4. Both methods differ significantly in philosophy, approach, strategy and process, and will therefore be separated from eachother in the body of this chapter. The research philosophy, approach, strategy and process for RQs 1 and 2 will first be described in its entirety in section 3.3, followed by same for questions 3 and 4 in section 3.4.

When combining these two disparate elements at the analysis stage (Chapter 4) an abductive approach is taken to allow the grounded theory to emerge and address the research aims.

3.1.1 Research Questions (RQs)

1. What number of DALYs is estimated to be attributed to influenza in Ireland during the 2017/2018 and 2018/2019 seasons?
2. What degree of variability can be associated with the estimation of DALYs?
3. Is the estimation of DALYs a suitable and valid metric for burden of influenza in Ireland?
4. Is the estimation of DALYs attributed to influenza in Ireland feasible for and useful to stakeholders in practice?

3.2 Conceptual framework

The below diagram (figure 5) depicts the conceptual framework for this study. It positions this research within the context of the existing theory and empirical research by showing the link between the key concepts identified in the literature, the gap in literature this research aims to address and how it will be done.

Box 1 states the key concept giving rise to this research (which is phrased as a hypothesis for the purposes of the conceptual framework); “Suitable use of DALYs as a feasible, reliable, and valid metric for calculating BoD in Ireland could assist/improve decision making around influenza prevention and control”. The justification for this research concept, stated in box 2, is that the standardised use of DALYs across all diseases and populations is required for the metric to reach its full potential value. Although the metric is strongly supported by the WHO, it is still not widely used for measuring BoD in Ireland. Additionally, the burden of influenza in Ireland is insufficiently

characterised. Thus, this study will estimate the BoD of influenza using the DALY, and investigate whether this metric is valid, useful, suitable and feasible for use for this purpose in Ireland.

A search of the relevant literature unveiled further key concepts to support the research as depicted in box 3. It was determined that the burden of influenza in Ireland has not been sufficiently characterised and that DALYs are not widely used in Ireland for BoD studies, except for one recent study on the burden of COVID19 which may indicate the early stages of adoption of the DALY. It was also determined that the DALY method has evolved significantly since its conception, but issues remain around validity and suitability which may be giving rise to hesitancy in its use.

The review of literature supported the key concept for the research and uncovered a knowledge gap which is addressed using 4 key research questions as seen in box 4. The burden of influenza in Ireland in the most recent pre-COVID19 seasons could be estimated using DALYs; the degree of variability associated with the estimation of DALYs would be explored; and the suitability, validity, utility and feasibility of the metric for burden of influenza in Ireland would be investigated for the first time.

In order to address these questions, the methodological framework, as seen in box 5, comprises applying the GBD framework method for estimating DALYs to the Irish demographics and healthcare setting, exploring the variability associated with this method, and interviewing stakeholders about the implementation of the DALY in practice. This gave rise to two specific and appropriate data collection methods (depicted in box 6) which are 1: to collect surveillance data on 2017/2018 and 2018/2019 influenza seasons from suitable sources HPSC and CSO[3], and 2: to generate data on attitudes, interests, views and opinions via semi-structured interviews with individuals in target groups. By doing both, the results are triangulated to strengthen the findings.

The analytical framework (box 7) which accompanied these data collection methods respectively are 1: ‘calculation’ of DALYs using collected data and GBD method and 2: narrative-thematic analysis of interview data.

The intended outcome of the above is stated in box 8. These outcomes serve to address the key concept for the research and build on the existing body of knowledge on the topic in the literature.

[3] During the data collection phase, significant gaps in the data required meant that data adapted from the literature was also required to generate an estimate for burden of influenza in Ireland.

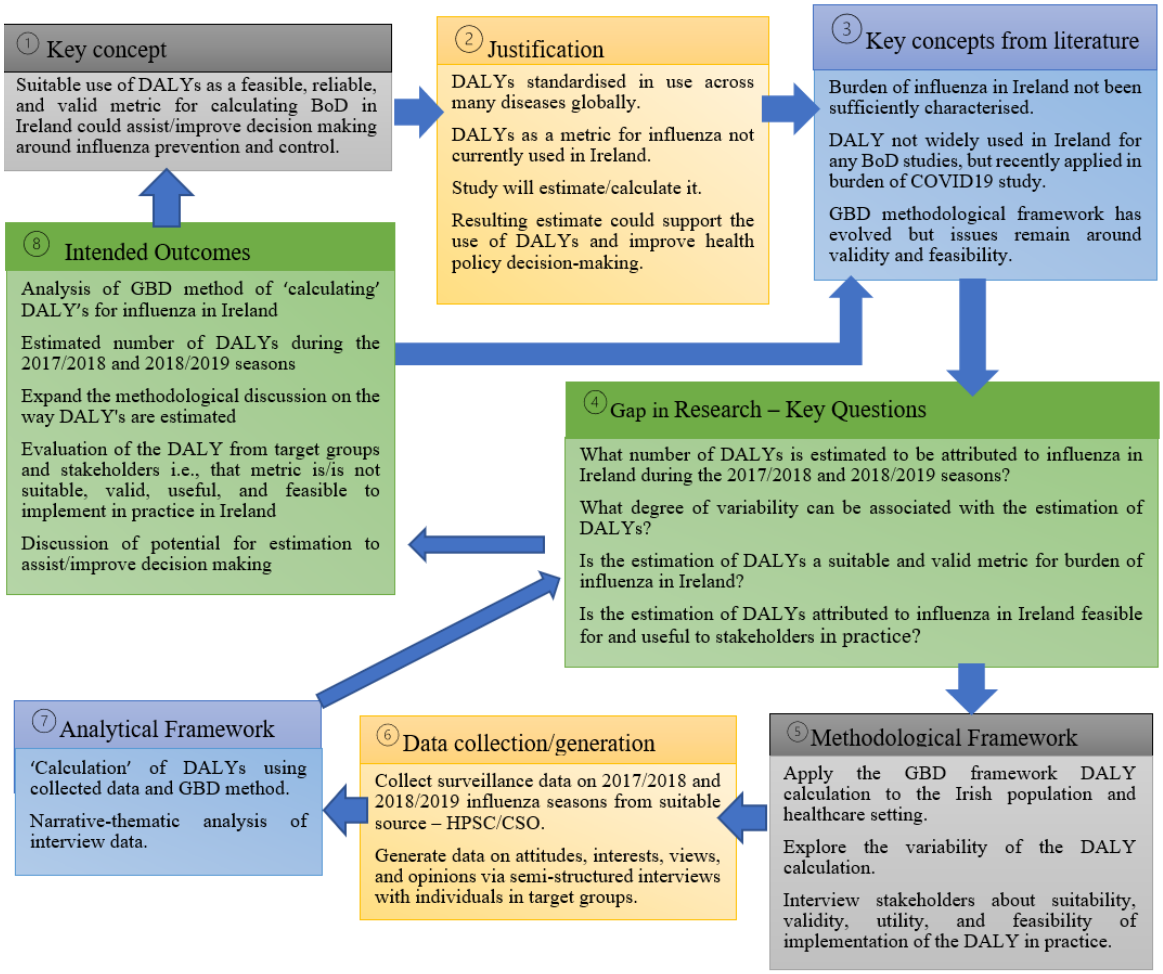

Figure 5: Conceptual framework for this research (devised by Author, 2023)

3.3 Primary research methodology for DALY estimation

This section describes the methodology employed to address RQs 1 and 2— to estimate the number of DALYs associated with influenza in seasons 2017/2018 and 2018/2019 and explore the variability in the calculation. Later, in section 3.4, the views of a panel of experts on the metric are gathered to triangulate the data and strengthen the findings. This follows the methodological framework set out in the conceptual framework for this research detailed in section 3.2 above.

3.3.1 Research philosophy

The optimal way to address RQ 1—to determine the DALYs associated with influenza in Ireland for the two seasons specified—is to perform the calculation based on influenza surveillance data published by the HPSC and CSO. In essence, a 'measurement' of the burden of influenza in quantitative terms is required, which is entirely deductive in nature. Addressing this RQ involves collecting data from the HPSC/CSO and interpreting and analysing it to generate new meaning.

The expected result is the estimated number of DALYs, expressed in years, representing the burden of influenza in Ireland during the two seasons. This part of the research will also serve to test the suitability and feasibility of the equation itself for the Irish population and current healthcare setting, and for comparison to the alternative methods of DALY calculation which will be used to address RQ2. This type of research is born out of a positivist research philosophy.

Similarly, exploring the variability of the calculation is best done by performing the calculation given varying data inputs and observing the effect on output. This, too, is objective, deductive and quantitative and is therefore of positivist philosophy. The concept of the DALY itself—transforming the BoD into a quantifiable and measurable metric—is primarily of positivist philosophy. However, the DW element of the calculation is of interpretivist philosophy, as DWs are generated using surveys of public opinion.

An advantage of the positivist approach is that assigning a numerical measurement to a complex concept such as the BoD allows the burden to be estimated, illuminating a phenomenon which is otherwise difficult to observe. Importantly, it also acts as a "common currency" which allows the burden to be compared across different diseases and populations—bringing new meaning and understanding to the burden of the disease.

A disadvantage associated with this approach is that it is not always possible to rely on quantitative data. Occasionally, it is difficult to accurately measure worldly phenomena

and without accurate measurement, positivist research can be less reliable. This was highlighted when a member of the HPSC, Ireland's gold-standard surveillance centre, confirmed that the figures they report annually are based only on a small portion of the Irish population, as further explained in section 2.1.2. In this case, *measurement* of the burden of influenza is not be feasible and instead the burden may only be *estimated,* which is a significant limitation both in terms of reliability and suitability for use. Nevertheless, a best estimate may bring new understanding and meaning to the burden of influenza in Ireland.

3.3.2 Research approach

Despite the absence of any hypothesis in this research, a deductive approach is taken to address RQs 1 and 2. This is because there is a wealth of literature on the topic and upon review a dominant theory emerged that influenza causes significant BoD globally. This theory is generally accepted in the medical science literature, is often overlooked by the public and professionals alike. The burden has not been sufficiently characterised in Ireland. From this, a proto hypothesis is formed which is "Significant burden was associated with influenza in Ireland in seasons 2017/2018 and 2018/2019". This is instead phrased as a research question (RQ1) in the early chapters to better amalgamate the positivist and interpretivist elements of the research (as alluded to in section 1.1). This hypothesis is tested by performing the calculation of DALYs associated with influenza in Ireland during those seasons to either accept of refute the hypothesis. To estimate the burden of influenza in numerical terms, the deductive approach is optimal (Wilson, 2010).

Similarly, you could say that a proto-hypothesis emerged around the variability associated with the estimation of DALYs which is "The estimation of DALYs varies significantly based on variable data inputs". This is translated to RQ 2 in the early chapters. To test this hypothesis, the calculation is performed using varying data inputs to determine the effect on output and, in turn, the variability of the overall calculation. Again, a deductive approach is optimal to clarify this matter.

This research ultimately combines data gained from a deductive approach (calculation), inductive approach (interviews) to become an abductive approach overall. This is discussed further in later sections of this chapter.

3.3.3 Research strategy

The strategy used for this portion of the research is a mathematical calculation of DALYs using the WHO method published in 2020 (WHO, 2020). DALYs associated with

influenza in Ireland in seasons 2017/2018 and 2018/2019 are estimated using the calculation based on existing HPSC data, CSO data and published literature. Confining the scope to two seasons is necessary due to resource constraints. Therefore, the two most recent seasons pre-COVID19 were chosen as influenza circulation patterns were impacted by public health measures during the COVID19 pandemic from 2020 to 2022.

The aim is not to examine how the burden of influenza changed from one season to the next, rather to estimate the burden at both points in time to account for variability in season severity. Therefore, the research is primarily cross-sectional. This applies to both research strategies employed in this study.

As described in section 2.1.2, the HPSC is Ireland's health surveillance centre and publishes influenza surveillance data weekly. This data, if of sufficient quality, may form useful inputs to the DALY calculation (described in section 2.1.3). By generating a number representing the burden of influenza, it is expected that new meaning and understanding of the burden of influenza in Ireland could be obtained. If found valid, it could also allow the burden of this disease in Ireland to be compared to different diseases and populations in a new way.

The strategy for RQ 2 is similar—to perform the mathematical calculation, based on data from HPSC, CSO and published literature. The output of the calculation could illustrate the potential variability in output given slight variations in input and therefore indicate the potential validity of the metric. Interviews of a panel of experts are also performed (see section 3.4) to gain a human perspective on this aspect of the study by gathering viewpoints on the likely validity and suitability of the output.

During the course of this research, it emerged that the HPSC's surveillance methods are more limited than originally assumed. Although all medical practitioners are required to notify the HPSC of influenza, this is applied only to serologically confirmed influenza cases, which omits the majority of true influenza cases as most are never serologically confirmed. Non-serologically confirmed influenza cases are known as cases of influenza-like-illness (ILI), and most GPs in Ireland are not required to report these to HPSC. Instead, HPSC recruits a subset of ~6.9% of GPs to report presentation of ILI as an 'early warning system' for circulation of the virus. Due to the small sample size of 6.9% of the GPs, inaccuracy of the modelling became a significant limitation to testing the accuracy and reliability of the calculation. Despite this, the HPSC remains the gold-standard for such data.

Research aims were subsequently refined from a *calculation* of the burden of influenza to an *estimation,* as this is the best possible method to deploy within the constraints of the available data. To obtain a sufficient sample size to *calculate* the burden of influenza, a

large-scale survey of all households, GPs and health centres in Ireland would be required, similar to the 'Flu Watch' Cohort study which was performed in the UK (Hayward, 2014).

3.3.4 Data generation for estimation

The overall procedure to estimate the DALYs involves performing the published GBD method using 3 health states as per the GBD DW tables (WHO, 2020) – mild, moderate and severe acute infection. Below is the calculation performed to estimate DALYs associated with influenza. This method was devised by a committee of experts with input from peer review over 20 years since its conception and is therefore considered the optimal method to follow. However, gathering the appropriate data required to perform this method from publicly available sources in Ireland may be a significant challenge. The GBD method will be amended according to available data inputs.

$$DALY = YLL + YLD$$

Required data are gathered from multiple sources including the HPSC database, the Central Statistics Office (CSO) and published literature. The calculation is made using data from seasons 2018/2019 and 2017/2018 to account for variability in season severity. As per current GBD methods, future discounting and age weighting are not included in the calculation (WHO, 2020). The calculation using the GBD method and 2018/2019 data is hereafter referred to as the "original calculation".

To calculate YLL:

When estimating YLL, two inputs are required: the number of deaths; and conditional life expectancy, both of which must be defined at age-group level. YLL is estimated as:

$$\mathrm{YLL} = \sum_{a=1}^{n} \mathrm{YLL}_a = \sum_{a=1}^{n} \mathrm{Number\ of\ deaths}_a \times \mathrm{Remaining\ life\ expectanc}$$

where *a* = age-group, *n* = number of age-groups.

Mortality data stratified by age group is available from the HPSC; however, it is not stratified by sex. Therefore, the YLL calculation can only be based on the whole cohort.

The average life expectancy of males and females based on the Irish life tables available from the CSO is used (CSO, 2020). The HPSC provide mortality data stratified by 5 age groups: 5-14 years, 15-25 years, 25-44 years, 45-64 years and 65+ years. The median age of each group is used as the age of death i.e., the age used to represent the age group 45-64 years is 54.5 years.

This element of the calculation could be more accurate if the available mortality data was categorised with a greater number of distinct age groups and by sex. This will be considered during the interpretation of the results in chapter 4: Findings & Analysis.

To calculate YLD:

As per the GBD DW tables (see A4), three health states associated with acute infection are included in the calculation: mild, moderate and severe. The below calculation is performed for each health state as each had differing DW and duration.

$$\mathrm{YLD} = \sum_{h=1}^{l} \mathrm{YLD}_h = \sum_{h=1}^{l} \mathrm{Number\,of\,cases}_h \times \mathrm{duration}_h \times \mathrm{disability\,weight}_h,$$

with *h* = health state and *l* = number of health states.

Severe infection is defined as infection requiring hospitalisation (Cassini et al., 2018). This data are sourced from the HPSC annual influenza reports.

Moderate infection is defined as infection requiring medical attention less the number of hospitalisations. The number of infections requiring medical attention is estimated by adjusting the estimated occurrences based on results from a large community study on influenza in the UK, the Flu Watch cohort study (Hayward, 2014). This study estimated rates of infection and rates of medically attended infection in the UK from seasons 2006 – 2011 using household surveys.

This method for estimating moderate infection is the most appropriate as no such data based on the Irish population is available. The number of influenza infections occurring in Ireland is not tracked and the number of GP consultations due to influenza-like-illness is also not known. The UK population is similar in demographics to the Irish population and is therefore an appropriate sample to use. This data may even be more accurate in some respects than the equivalent Irish figures, as GP consultation in the UK is free of charge, whereas in Ireland must be paid for. This could influence medical attendance by those ill with influenza in Ireland.

Mild is defined as symptomatic influenza infection not requiring medical attention. The rate of symptomatic infection is estimated using results from the Flu Watch cohort study (2014), as surveillance data in Ireland is insufficient to estimate such figures on a population level.

It must be noted that the influenza case rates in the Flu Watch Cohort Study are of unvaccinated individuals. In Ireland, vaccination uptake is high among the elderly and moderate-low among the remaining population (see section 2.1.1). Therefore, the rates of infection identified in the Flu Watch Cohort study cannot accurately be applied to the Irish population. Despite this, no better data exists for use in this calculation. This limitation will be accounted for in the Findings & Analysis chapter.

A fourth health state for acute infection is included in the GBD DW tables; “Infectious disease, post-acute consequences (fatigue, emotional lability, insomnia)”. This health state is omitted in this calculation as the number of influenza cases resulting in long-term consequences is negligible (Cassini et al., 2018).

The duration of mild and moderate infection for this estimate is five days, based on a definition set out by Nicholson, Wood and Zambon, (2003) in their paper on Influenza. The duration of severe infection, which is defined in this research as requiring hospitalisation, is estimated to be 8 days based on a study of clinical outcomes of influenza by Ludwig et al. (2020).

To examine variability in the calculation

It is recognised that variability in for example, severity definitions, DWs and life expectancy can lead to variability in the results of BoD studies using the DALY as a metric. Therefore, the original calculation used for section 3.3.4 above is performed a further three times using different variables; two different sets of DWs and one different set of Irish life tables (see A4). DWs from a European-specific DW study performed in 2015 (Haagsma et al., 2015) are first applied, then DWs from Japan-specific DW study conducted in 2021 (Nomura et al., 2021). The DW as a variable was chosen as it appears from the literature to be the most problematic element of the calculation in terms of validity (see section 2.1.3). The original calculation is performed again using the Irish life tables No. 15 from 2005-2007 (CSO, 2009), when the average life expectancy was 2 years shorter than in 2015-2017. This is another problematic element of the calculation, as life expectancy varies significantly between populations and over time.

3.3.5 Data analysis

Following the calculations, the results are analysed by expression in terms of rate per 100,000 population and percentage change from the original calculation. This method of analysis is appropriate for the methodological framework, and follows the analytical framework set out in the conceptual framework detailed in section 3.2.

When addressing RQ 1, the number of DALYs each season per 100,000 population is estimated. This rate is then used to compare the output of the calculation to that of similar studies performed in Ireland and the EU. This is to assess the accuracy of the calculation when applied to Irish parameters. Additionally, the percentage of total DALYs comprising YLLs and YLDs is determined. These rates are also compared to the published literature.

When addressing RQ 2—exploring the variability in the calculation given varying inputs—the percentage change in output compared to the original calculation for each change in variable is calculated. The percentages comprising YLLs and YLDs are also determined for each variable.

In summary, answers to RQs 1 and 2 are expected following the application of the above methods. The number of DALYs estimated to be attributed to influenza in Ireland during the 2017/2018 and 2018/2019 seasons will be generated and analysed with two purposes; to potentially highlight the burden of influenza in Ireland, and to test the currently approved method for calculation of DALYs when applied to the Irish population and healthcare setting. The degree of variability associated with the estimation of DALYs will also be explored to further examine whether this metric can and should be employed by policymakers in Ireland.

3.3.6 Summary

In summary, the above methodology is employed to address RQs 1 and 2— to estimate the number of DALYs associated with influenza in seasons 2017/2018 and 2018/2019 and explore the variability of the calculation. This element of the research is multifunctional; it may potentially highlight the burden of influenza in Ireland and it tests the suitability of the currently approved method for calculation of DALYs when applied to the Irish population and healthcare setting. This ultimately serves to address the key concept of this research– whether this metric can and should be employed by policymakers in Ireland.

The results of the above method will be triangulated by gaining the opinions of a panel of experts on the validity and suitability of the calculation when applied to the Irish setting. The method for this is outlined in the following section.

3.4 Primary research methodology for determining DALY validity, suitability, utility and feasibility

This section describes the methodology employed to address RQs 3 and 4— to determine the validity, suitability, utility and feasibility of the DALY in practice in Ireland based on the views of a panel of experts. This is of interest because during the early stage of the research it became apparent that the DALY is not yet widely used in Ireland for research nor health policy purposes, but if adopted could provide a useful tool for health policy decisions and for understanding better the BoDs across time and populations.

3.4.1 Research philosophy

The feasibility and validity of the DALY will be somewhat indicated by the result of the calculation performed as part of the above methods. These results will be further explored in an interpretive fashion by gaining the views of subject matter experts on the feasibility, validity, utility and suitability of using the metric in practice. The optimal approach to do this is to gain insights into the views of target groups such as health policymakers, health policy consultants and researchers. Certainly, the suitability and utility of this metric is entirely determined by these individual's perception of the metric, and how it fits into their everyday reality. Therefore, interviews with these stakeholders is the optimal data collection method, which is a naturalistic method of interpretivist philosophy. In employing this approach, two layers of interpretation apply—each interviewee's interpretation of the metric and its utility, and the author's interpretation of the interviewee's responses. This double layer of interpretivism provides depth to the findings, and is likely to result in data which is honest and trustworthy, and therefore valid. It also doubles the degree of subjectivity of the data and may leave more room for bias. Caution will be taken when interpreting the findings in this regard.

3.4.2 Research approach

Following the deductive approach employed in making the calculations/estimations (section 3.3.2), an inductive approach is then employed to gain human perspective on the validity and suitability of the calculation in practice. An inductive approach is typical of interpretivist philosophy. The responses to interview questions are collectively analysed

for themes and patterns, and thus used to form broader generalisations and theories around the use of the DALY in practice in a typical inductive fashion.

A distinct advantage of this approach over the purely deductive approach employed for RQs 1 and 2, is its flexibility. There are no firm guidelines or specific procedures which need to be followed with induction because the research is forming novel theory as it progresses. This is an interesting element of the research as it provides the potential to uncover unexpected insights.

Some critics of this method would argue that any inductive research is subject to researcher and subject bias and therefore may not be relied upon (Henderson, 2022). Conversely, the opposition views this as a strength, seeing value in the interpretation of the perspectives of both subject and researcher to generate new meaning (Corbin, 2015). In this respect, the interviewees can be viewed as co-researchers who use their lived experiences to assist in identifying the suitability, reliability and validity of utilising the proposed equation and resulting estimation in practice. The interviewees are likely to answer questions honestly and therefore add validity to the findings.

This research ultimately combines data gained from a deductive approach (calculation), inductive approach (interviews) to become an abductive approach overall. This is further discussed in section 3.5.

3.4.3 Research strategy

The strategy chosen for this section of the research is grounded theory based on data collected through semi-structured interviews. This strategy is employed as the medium because the intent is to learn from the perspectives of the participants through 1:1 conversations in which the participants can freely express their views. In addition to their verbal responses to questions, participant's body language and tone and pitch of voice are observed, providing further depth to the data.

3.4.4 Sampling

Purposive sampling is used as the sampling strategy for this section of the research. Subjects are purposefully targeted and chosen to take part, rather than randomly chosen as is the case with random sampling. This is appropriate as the views of the specific population 'target users of the metric' are of most value when addressing whether a metric is useful, suitable and feasible for stakeholders. Additionally, the views of the specific population 'subject matter experts on the topic' are of value as they are in the best

position to provide rich, well-informed responses. This results in a relatively small sample size being possible, but also required. This approach to sampling is more appropriate for qualitative research (van Rijnsoever, 2017) due to the depth of analysis that is required for such studies (Plümper et al., 2019).

The ideal target participant profile became apparent following the identification of the key concept of this research; “Suitable use of DALYs as a feasible, reliable, and valid metric for calculating BoD in Ireland could assist/improve decision making around influenza prevention and control.”. Based on this, the opinions of senior, competent professionals from target groups of the DALY are of most value for addressing the proto hypothesis. Such participants are professionals forming parts of the cross-functional committees involved in healthcare decision-making around influenza in Ireland; for example, senior members of the HPSC, Senior Epidemiologist with the HSE, members of the Department of Health within the Irish Government, Health Data Analysts employed by the Department of Health, Senior Researchers in Virology or Public Health in Ireland etc.

These target participants are intended as subject matter experts and target groups for likely future use of the metric. The metric’s suitability and utility is entirely dependent on the views of these types of individuals, and their opinions of the validity and feasibility of employing the metric would be most accurate.

Invites are sent via email to 14 target participants (see A3 for invite template). Due to the nature of the target participants as busy, senior professionals, a short interview comprising 5 questions with an estimated run time of 20 minutes is used to encourage participation. A total of 5 recipients (35%) agreed to partake. The participation rate of 35% gives confidence that a sufficient quantity and quality of data are provided to enable an interpretivist analysis in the small health system Ireland has relative to other countries. Once the 5 interviews are complete, the researcher reassesses whether further interviews are required based on the quality of the data collected.

3.4.5 Data collection

The procedure for collection of the data for RQs 3 and 4 is to gain ethical approval, formulate and send interview invites to target participants and then schedule and perform the interviews. The data gathered is then thematically analysed. These steps are detailed further in the below sections.

Ethical approval

Prior to any interviews taking place, ethical approval is gained by completing the Griffith College ethics procedure. This includes submitting an ethics application form, an informed consent form for participants, a participant information leaflet (PIL), proposed interview questions and an ethics declaration to the faculty for approval (see A2 for submitted materials). This research is deemed low risk as responses to questions are anonymised and limited to attitudes and opinions in the participant's capacity regarding their professional activities only. No ethical issues were raised in response.

Prior to each interview the participant is emailed a copy of the PIL and a consent form to sign and return.

Interviews

Pilot interview

A pilot interview is conducted to test whether the design of the research is appropriate. Changes made following this are outlined below.

Initially, the interview consisted of 7 questions. However, following the pilot interview it became apparent that the first question "*Are you aware of the DALY as a metric for BoD?"* is not necessary as it is usually clear from preliminary conversation whether the participant is familiar with the metric. Additionally, it was noted that the questions "*Would this metric be useful to you in practice?"* and "*Would this metric be suitable for you in your practice?"* usually results in the same answer, so these questions were combined to "*Would this metric be useful/suitable to you in practice?".* No other amendments are implemented at this stage.

Remaining interviews

Video interviews take place virtually over Microsoft (MS) Teams using a PowerPoint presentation as the medium. The interviews start with a brief overview of the research and an explanation of the DALY before moving onto the 5/6 interview questions. The PowerPoint presentation and interview questions can be found in A3.

It must be noted that the brief overview of the DALY given by the researcher at the beginning of each interview is a potential source of bias, especially if interview participants are unfamiliar with the metric prior to the interview. If this is the case, their opinion of the

metric would likely be influenced by the way the researcher described the metric. If it is described in a positive manner, the interview participant may view the metric positively, and vice versa. This is a limitation of qualitative research, particularly of narrative interviews. The researcher is not independent of the results, and the results are therefore subjective. Conversely, some view this as a strength of the qualitative method, seeing value in the perspectives of both subject and researcher to generate new meaning (Corbin, 2015). Future researchers employing similar methods should limit bias by ensuring introductory overviews are as neutral as possible.

Due to constraints with permissions for MS Teams, the interviews are not recorded. Instead, notes recording verbal answers, reactions, body language and anything else noteworthy are taken on a Microsoft Word document (see A3 for sample). The requirement to quickly transcribe the conversations is an issue with this data collection process, as it meant the researcher's full attention is not with the interviewee during the conversation. This may hinder the conversation slightly. Additionally, the extent of the conversation which is recorded is limited by the speed at which the researcher can type. This may result in partial recording of some responses.

3.4.6 Data analysis method for interviews

Narrative thematic analysis is used to analyse the views, opinions, knowledge, experiences and values of the interview participants captured in the interview transcripts. This approach is inductive and follows the analytical framework set out in the conceptual framework for this research detailed in section 3.2 above.

Verbal and non-verbal communication is in scope of the analysis. This includes the words spoken by the participants, their facial expressions, pitch and tone of voice and body language. This type of data is not analyzed in isolation, but rather within the context in which it occurs (outlined in Chapter 1 of this document). This is a form of discourse analysis and adds depth to the findings (Willig., 2014).

Inspiration is taken from the method for thematic analysis developed by Braun and Clarke (2010) and the below five steps are followed. In Braun and Clarkes original method (2010), coding is included as step 2; however, this step was not necessary for this research as the data set is manageable in its absence.

Prior to the below steps taking place, the data are 'cleansed' by translating the short-hand notes taken during the interviews into legible text. This is performed directly after each interview to maintain accuracy, though still has potential for discussion bias.

1. **Familiarisation**

   First, the researcher becomes familiar with the data. This step begins during the interviews when the researcher listens to and watches the responses of the participants. The researcher gains insights and begins developing theories as the conversations occur. The process continues as the researcher revisits and reads the interview transcripts several times following the interviews. Any concepts or theories of interest upon initial analysis are highlighted. This leads to the next step which is generating themes.

2. **Generating themes**

   This step comprises identifying any themes present in the data. Again, this step begins during the interviews and is formalised when the themes are captured and written down. The themes identified by the researcher are influenced by what has been read in the literature. This is accounted for by discourse analysis. Recurring themes, points of contrast or agreement between interviewees and any themes which are common, or in contrast, to the literature are of particular interest.

3. **Reviewing themes**

   Themes are reviewed to ensure they are useful, valid and accurate representations of the data. The interview transcripts are revisited to validate the themes.

4. **Defining and naming themes**

   Once validated, the next step involves defining and naming the themes. Figure 7 in the following section illustrates the names of the themes and how they relate to the interview questions and RQs.

5. **Writing up**

   The final step is to write up the analysis, which is found in section 4.2 below. Each theme is described, noting how often is arises and its significance in the wider literature.

   This analytical method uses the specific views and opinions of a panel of experts to make generalisations, which is typical of inductive research. This provides a distinct advantage, which is the potential to uncover new and unexpected insights from the data.

Narrative thematic analysis is the most suitable approach for analysing a small number of short verbal transcripts of interviews (Mihas, 2023). It also allows flexibility in interpreting the data as there are no firm guidelines or specific procedures which need to be followed because the research is forming novel theory as it progresses.

However, thematic analysis is also subjective and relies on the researcher's judgement. Therefore, care must be taken in its analysis and interpretation to avoid missing nuances in the data and identifying themes which are not there.

3.4.7 Summary

In summary, the above methodology is employed to address RQs 3 and 4— to explore the validity, suitability, utility and feasibility of the DALY for measuring and managing the burden of influenza in Ireland. An interpretivist approach is taken, conducting semi-structured interviews with a panel of experts/target users of the DALY to gather their views and opinions on its value in practice. These target participants are in the best position to provide rich, well-informed information on the topic. The results of the interviews are analysed for themes and patterns to form broader generalisations and theories around the use of the DALY in practice in Ireland, in a typical inductive fashion. This ultimately serves to address the key concept of this research–whether this metric can and should be employed by policymakers in Ireland.

3.5 Abductive approach: Combining both methods

This research ultimately combines data gained from a deductive approach (calculation) and inductive approach (interviews) to become an abductive approach overall. The results of the calculation and interviews are combined and analysed in an iterative fashion to produce a grounded theory addressing the key aim of this research: "To estimate the burden of influenza in Ireland in terms of DALYs and to investigate the feasibility, suitability, utility and validity of this measurement in practice in the Irish healthcare and health policy setting". This theory is presented in Chapter 5, the Conclusion. The process followed for combining both methods is described below.

3.5.1 Complementarity of both methods

The inductive and deductive methods used to address the research aim are complimentary in that they have opposing strengths. The strength of induction is forming

novel theory as the research progresses, providing the potential to uncover new and unexpected insights. The strength of deduction is more certainty in conclusions. By using both, the benefits of both are realised and findings are strengthened.

Looking more closely at the data collection methods, further complementarity can be seen. Performing the DALY calculation provides initial insights into its feasibility and validity and, to a lesser extent, utility and suitability. The initial theories are then strengthened by asking experts for their opinion on the matter. Inversely, the insights gathered from the experts inform how best to perform the calculation; for example, by providing insights into the availability of surveillance data and the meaning of the data. Another example is the emergence of a theme of concern regarding the validity of DWs through the interviews, which leads to the DW being chosen to explore for variability in the calculation. In this way, both methods inform one another and must therefore be performed in parallel, iterating between both methods as they progress. This process is further outlined and visually depicted below.

3.5.2 The process of combination of both methods

The below diagram depicts the way in which both methods combine to arrive at the final theory. The sequence in which key data generation/collection steps took place is depicted, with curved arrows demonstrating how some steps iterated back and forth throughout the process. The results of both methods combine at the end via abduction to arrive at the final theory.

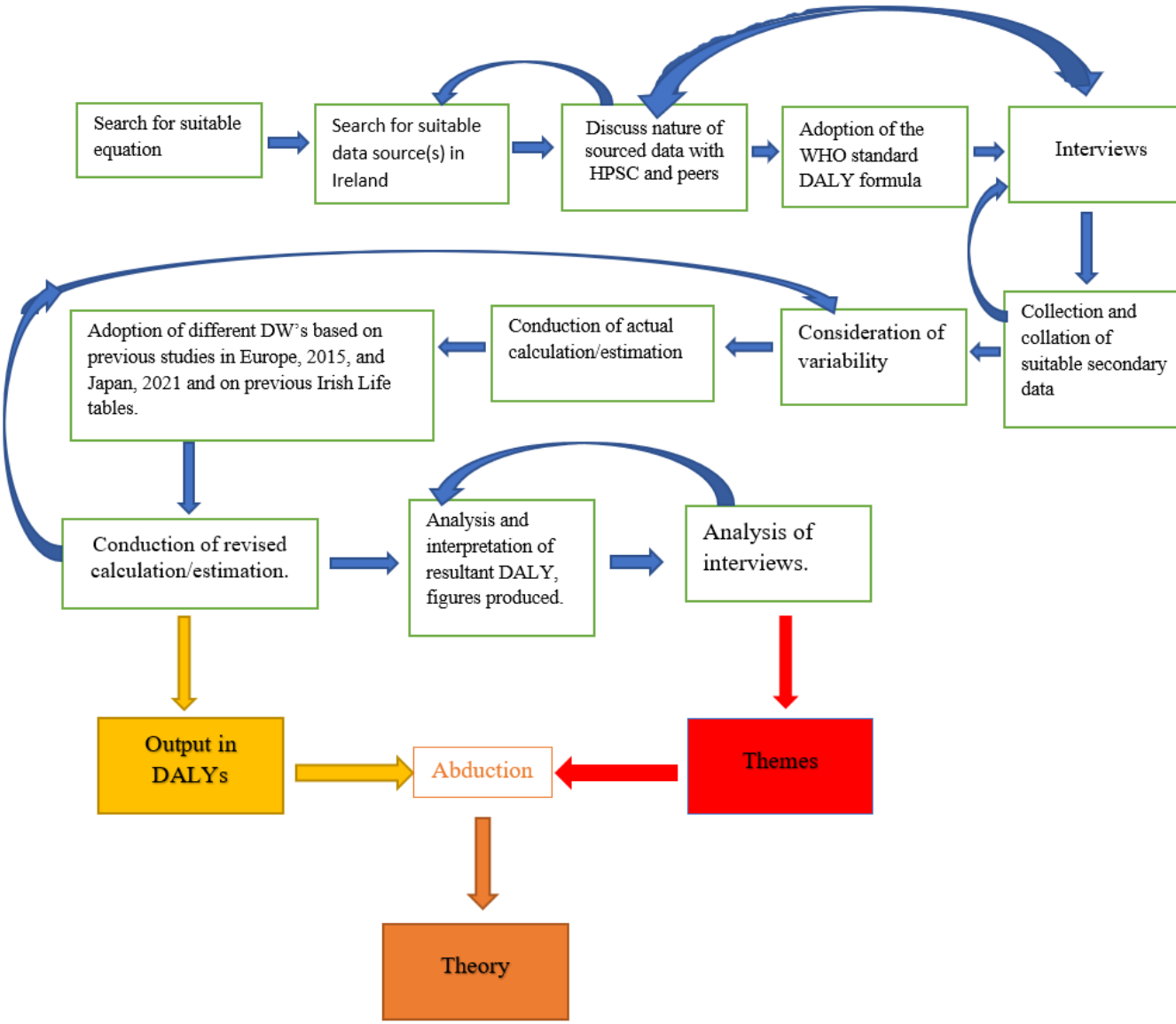

Figure 6: The process of combination of both research methods to arrive at the final theory (created by author, 2023).

In summary, both methods intertwine and complement each other throughout the research. Insights gained from interviewee responses influenced the equation, and performing the equation influences conversations had in interviews. Overall, both methods work together in tandem resulting in abductive reasoning to address the key research aims.

3.6 Chapter summary

In summary, this research, although dominantly interpretivist in philosophy, employs a mixed-method approach using both mathematical equations and subject matter expert interviews to gather primary data. The mathematical equation is used to address RQs 1

and 2, while interviews of subject matter experts are required to address questions 3 and 4. The completion of these methods results in findings which address the overall key concept of the research (box 1 of the conceptual framework). The next chapter describes and analyses the findings in the context of the wider literature.

4.0 Findings and analysis

The purpose of this research is to estimate the burden of influenza in Ireland in terms of DALYs and to investigate the feasibility, suitability, utility and validity of this measurement in practice in the Irish healthcare and health policy setting. RQ1 attempts to estimate the DALYs associated with influenza in Ireland by performing the WHO method for its calculation using Irish data. RQ2 explores the variability of the calculation given varying data inputs to inform on its reliability. RQ3 and 4 investigate the feasibility, suitability, utility and validity of this measurement in practice by interviewing a panel of experts.

This chapter describes and analyses the findings of the four RQs set forth at the beginning of this document (section 1.3.3). Each RQ is reintroduced, followed by a description of the findings associated with it under the heading Findings. Each of these findings are then analysed in the context of the wider literature and implications in the Analysis section which follows. The chapter ends with a concluding summary.

4.1 The DALY calculation (RQ1 and RQ2)

RQ 1 and 2 were addressed using a positivist methodology, as outlined in the previous chapter. A calculation was performed to first estimate the number of DALYs associated with influenza in Ireland across two seasons (RQ1). The purpose of this was to potentially highlight the burden of influenza in Ireland. It also served two other purposes; 1. as a pilot to test whether the calculation was applicable to the Irish population and healthcare setting, and 2; as a basis for comparison to explore the variability of the calculation for RQ2. For this reason, the calculation of DALYs in the 2018/2019 season is referred to as the ‘original calculation’. The original calculation is then performed using differing ad specific variables (DWs, life expectancies) to explore the variability associated with the calculation (RQ2) and indicate its validity. The results of these calculations are presented and discussed below.

4.1.1 RQ1: What number of DALYs is estimated to be attributed to influenza in Ireland during the 2017/2018 and 2018/2019 seasons?

The calculation for DALYs published by the WHO was performed to estimate the number of DALYs associated with influenza in Ireland across two seasons. This was to potentially highlight the burden of influenza in Ireland and was also used as a pilot to test whether the calculation was applicable to the Irish setting and as a basis for comparison to explore the variability in RQ2. The results of the calculation are described below and are discussed in the context of the wider literature and implications in the following Analysis section (4.1.1.2).

4.1.1.1 Findings

Finding 1: Gaps in required data had little effect on calculation output

Gaps in the data required to calculate DALYs associated with influenza in Ireland were found. However, in the case of influenza, these gaps had a minor effect on calculation validity. The data unavailable were influenza incidence and rates of medically attended illness which were required to estimate rates of “mild” and “moderate” infection. This data is required to calculate YLD (see section 2.2.3), which only contributes 2-3% to the overall DALY figure (see next finding). Therefore, inaccuracies in the calculation of YLD will have a minor effect on the validity of the final estimate.

Supplementary data from the Flu Watch Cohort Study conducted by Hayward et al. (2014) in the UK were used as inputs to complete the calculation. This supplementary data was deemed appropriate as the epidemiology of influenza is expected to be similar in the UK and Irish populations. Moreover, similar studies in New Zealand and the Netherlands found similar results, (van Lier et al., 2016; Cassini et al., 2018) providing confidence in its validity.

Importantly, rates for hospitalisation, ICU admission and mortality per season are available from HPSC. This is positive as these are the data required to calculate YLLs (see section 2.1.3), which contributes 97-98% to the final DALY figure for influenza. Mortality data was stratified by age group, but not stratified by sex. As LE differs per sex, calculation of YLL would be more accurate if this information was included. In lieu of this, the average LE of both sexes must be used. This likely had a minor effect on the calculation output.

Finding 2: Estimate DALYs associated with influenza in Ireland in 2017/2018 and 2018/2019

Using the methods outlined in chapter 3, it is estimated that influenza contributed approximately 4271.17 DALYs to the Irish population in the 2017/2018 influenza season. This is equivalent to 87.75 DALYs per 100,000 population. The vast majority (98%) of DALYs comprised YLL, with only 2% comprising YLD.

The following season (2018/2019) was less severe, resulting in an estimated total of 1891.72 DALYs, or 38.8 DALYs per 100,000 population. A total of 97% that season comprised YLL, with 3% comprising YLD. This indicates that the majority of the burden attributed to influenza is due to premature mortality.

In summary, RQ1 aimed to estimate the number of DALYs associated with influenza in Ireland across two seasons. Gaps in the data required to perform the calculation were found. However, these gaps had a negligible effect on calculation output and validity. Appropriate supplementary data from the literature were used to perform the calculation and arrive at an estimate. It is estimated that in Ireland influenza caused 4271.17 DALYs in 2017/2018 and 1891.72 DALYs in 2018/2019. The validity of these findings and their implications are discussed in the context of the literature in the following section.

4.1.1.2 Analysis

RQ1 aimed to estimate the number of DALYs associated with influenza in Ireland across two seasons. This was to potentially highlight the burden of influenza in Ireland and was also used as a pilot to test whether the calculation was applicable to the Irish setting and as a basis for comparison to explore the variability in RQ2. The findings of the calculation are described in the previous section and are now discussed in the context of the literature and wider implications.

Finding 1: Gaps in required data had little effect on calculation output

The findings show that gaps exist in the data required to calculate YLDs associated with influenza in Ireland. However, these gaps had a minor effect on overall calculation validity as, in the case of influenza, YLD contributes only 2-3% to the overall DALY figure (see next finding).

Supplementary data from the Flu Watch Cohort Study conducted by Hayward et al. (2014) in the UK were required as inputs to calculate YLD. This supplementary data was appropriate as the epidemiology of influenza is expected to be similar in the UK and Irish

populations. Moreover, similar studies in New Zealand and the Netherlands found similar results, (van Lier et al., 2016; Cassini et al., 2018) providing confidence in its validity.

The majority of the data required for calculating YLLs, which contributes 97-98% to the final DALY figure, was available from HPSC. This provides confidence in the validity of the resulting estimate (see next finding). One issue with the data required for YLLs was that mortality data was not stratified by sex. As LE differs per sex, calculation of YLL would be more accurate if this information was included. In lieu of this, the average LE of both sexes must be used. This adds or removes approximately 1.5 years to the LE used in the calculation, which on its own can significantly impact the calculation output (as demonstrated in section 4.1.2). In this case, as it is an average of two, it is unlikely to have had a significant effect on output.

The issue of the gaps in data required to calculate the YLD associated with influenza is echoed by findings from the interviews (see section 4.2.1.1). During these interviews, a common theme was concern surrounding the availability of the data required. This was subsequently confirmed by a senior member of the HPSC who stated definitively "*we don't at any point in time know how many people have the flu*".

Similarly, results from the Burden of Communicable Diseases in Europe study published by Cassini et al. in 2018 found that the surveillance system used in the EU is generally not population based, but rather aims to capture the magnitude and the rate of change of influenza activity, to identify the start and end of the season and circulating strains. Because of this, influenza surveillance data in the EU cannot be used to identify the true incidence of influenza. This group instead used the Flu Watch Cohort Study as their main source of data as this is the only large community study published and appears to be valid. Again, this had little adverse effect on the overall estimate as surveillance data are required to calculate YLD, and YLD contributes only 2-3% to DALY estimations for influenza.

Influenza surveillance methods in the UK are more robust than in the EU. The UK health system, the NHS, employs multiple different approaches to monitor influenza activity including reporting of ILI, 'FluSurvey' in which participants electronically report household influenza activity each week, 'FluDetector' which is a system for monitoring internet-based search queries as a surveillance method for ILI, and many more initiatives (Gov.uk, 2019).

The employment of more robust surveillance methods such as those mentioned above would increase the accuracy of the DALY estimate for influenza in Ireland. However, the improvement in accuracy would be limited to <1% and therefore should not represent a priority for the Irish health policy makers.

Finding 2: Estimate DALYs associated with influenza in Ireland in 2017/2018 and 2018/2019

Epidemiology generally accepts that not all estimates will be exact, but usually a genuine estimate is better than no estimate. This is seen with many estimates made for developing countries which often don't have any surveillance systems in place (Bray et al., 2022). Reasonable assumptions are made to arrive at a best estimate to help guide decision-making. This was the approach taken in this research in response to some data being unavailable.

The estimate arrived at for the DALYs associated with influenza in Ireland in the 2017/2018 season is 4271.17 DALYs, and in the 2018/2019 season is 1891.72 DALYs. These figures come with some caveats. The incidence rate of infection used to calculate YLD was adapted from the Flu Watch Cohort study which studies unvaccinated individuals. In Ireland, vaccination uptake is high among the elderly and moderate-low among the remaining population (see section 2.1.1). Therefore, this rate of incidence is probably an overestimation. With that said, the effect of this on the resulting figure is negligible as YLD contributed just 2-3% to the overall figure. Additionally, this overestimate is somewhat offset by the non-inclusion of post-acute consequences in the calculation of YLD. This assumption is supported by the alignment of this estimate to that of similar studies performed in the EU and the Netherlands, as further outlined below.

Inaccuracies with the calculation of YLLs has more of an impact on the accuracy of the final figure, as YLL contributes 97-98% of the overall DALYs. The prevailing issue with influenza mortality data is that many influenza deaths are misclassified and attributed to other comorbidities or secondary infections, resulting in underreporting (Gibbons et al., 2014). Therefore, the mortality figures reported by HPSC, and thus the estimated DALYs, are likely to be underestimates.

The Burden of Communicable Diseases in Europe study reported a rate of 81.8 DALYs per 100,000 population (Cassini et al., 2018). This is an annual average based on years 2009 – 2013. Another study on burden of influenza in the Netherlands reported an average annual burden of 52.6 DALYs per 100,000 population in the period 2007 to 2011 (van Lier et al., 2016). Our estimate for the year 2017/2018 in Ireland is similar, at 87.75 DALYs per 100,000 population. The 2017/2018 was classified a 'severe' season by HPSC. Our figure for 2018/2019 season is slightly lower, at 38.8 DALYs per 100,000 population; however, all findings are approximately in line. This is to be expected as Ireland and the Netherlands are part of the EU and provides confidence in the estimate.

To put these figures into perspective, other estimates of BoD in Ireland using the DALY are required. However, as mentioned in section 2.1.2, few exist. The most appropriate comparator available is the results of a BoD study performed for a PhD thesis measuring the burden of non-communicable diseases in Ireland (Chakraborty, 2020). This study followed the WHO/GBD methods and provides a useful comparator; however, it has not been peer reviewed and will therefore not be used to draw any conclusions.

This study found that in 2017, DALYs per 100,000 population attributed to diabetes and cancer were 37.6 and 25.4 respectively. Estimates for influenza ranged from 38.8 – 87.75 DALYs. This indicates that, depending on season severity, the burden of influenza may exceed the burden of diabetes and cancer in Ireland. Based on this and conversations had during interviews, the burden of influenza is grossly underestimated by the public and professionals. One interview participant stated that there is a "*lack of understanding and awareness*" around the mortality associated with influenza. The ability to express it like this, in a format which is common across all diseases and risk factors, helps to highlight the otherwise underappreciated burden.

For the figures generated for burden of influenza in this study to be fit for purpose, i.e. to be used as a comparison tool to inform health policy decision-making, competing conditions must also be represented in terms of DALYs. As described in section 2.1.2, few other BoD studies in Ireland utilise this metric. Therefore, the result of this study cannot be used presently to make a recommendation on the extent of intervention required. It may, however, be utilised as a means of comparison by future researchers conducting BoD studies using DALYs.

In summary**,** RQ1 aimed to estimate the number of DALYs associated with influenza in Ireland across two seasons. Although gaps in the required data were present, these had little impact on the calculation. Using HPSC data and supplementary data from the literature, it is estimated that influenza caused approximately 4271.17 DALYs in 2017/2018 and 1891.72 DALYs in 2018/2019. These estimates are approximately in line with similar estimates made for the populations of the Netherlands and wider EU (van Lier et al., 2016; Cassini et al., 2018).

Interestingly, these estimates exceed the DALY estimates for diabetes and cancer in Ireland in 2017 (Chakraborty, 2020) and may indicate that influenza contributes more burden to the Irish population than previously understood. However, for this estimate to be used as a comparison tool to inform health policy decision-making, competing conditions must also be represented in terms of DALYs. At present, few BoD studies in Ireland utilise this metric. Therefore, the result cannot be used to make a recommendation. It may,

however, be utilised as a means of comparison by future researchers conducting BoD studies using DALYs.

4.1.2 RQ2: What degree of variability can be associated with the estimation of DALYs?

It is recognised that variability in for example, disease severity definitions, DWs and life expectancy can lead to variability in the results of BoD studies using the DALY. Exploring the degree of variability associated with the DALY is a key aim of this study. To do this, the original calculation used for section 4.1.1 above is performed a further three times using different and specific variables; two sets of national DWs and one different set of Irish life tables. This was done to assess whether this would result in considerable variability. Findings are described and analysed below.

4.1.2.1 Findings

RQ2 aimed to determine the variability that can be associated with the calculation of DALYs. Varying data inputs including DWs, and Life Tables were used as inputs to the calculation to determine their impact on the calculation. The findings are described below and are discussed in the context of the literature and implications in the following Analysis section (4.1.2.2).

Finding 3: Use of EU-specific DWs did not result in a significant change to DALY output

The original calculation was performed using 2018/2019 data with the DWs generated by Haagsma et al. (2015) for an EU population burden of disease study (EUBD), rather than the global DWs listed in the GBD database. This resulted in a total of 1892.83 DALYs—a negligible increase of 1.11 DALY, or 0.05%. The percentage comprising YLL and YLD stayed the same at 98% and 2% YLD respectively.

Finding 4: Use of Japan-specific DWs resulted in a significant change to DALY output

Performing the original calculation with DWs generated by Nomura et al. (2021) for the Japanese population resulted in a total of 2080.82 DALYs—a significant increase of +189.1 DALYs, or +10%.

Finding 5: Use of Irish Life Tables No. 15 resulted in a significant change to DALY output

Performing the original calculation with the 2005 Irish Life Tables (when LE was 2 years shorter) resulted in a total of 1697.72 DALYs—a significant decrease of 192 DALYs, or -11%. The percentage comprising YLL decreased slightly to 97% and YLD comprised the remaining 3%.

In summary, varying data inputs can result in significant variation to the calculation output. EU-specific DWs did not differ significantly from the global DWs, and therefore resulted in a negligible impact (+0.05%) on DALY output. In contrast, using Japan-specific DWs did result in a significant impact (+10%) on DALY output, despite YLD comprising only 2% of overall DALYs. Using Irish Life Tables No. 15, in which Irish LE was 2 years shorter, also resulted in a significant change to DALY output.

4.1.2.2 Analysis

RQ2 aimed to determine the variability that can be associated with the calculation of DALYs. Varying data inputs including DWs, and Life Tables were used as inputs to the calculation to determine their impact on the calculation. The findings are described in the previous section and are now discussed in the context of the literature and wider implications.

Finding 3: Use of EU-specific DWs did not result in a significant change to DALY output

It is unsurprising that using EU-specific DWs did not result in a significant change to DALY output compared to using global DWs. This is because the European DWs and global DWs did not differ significantly (see A4 for all three DW tables used). Severity descriptions for the majority of health states, including infectious disease, remained the same. The DW increased very slightly for mild infection (0.006 for GBD and 0.007 for EUBD), remained the same for moderate infection, and decreased slightly for severe infection (0.133 for GBD and 0.125 for EUBD). Both variations offset each other somewhat leading to a negligible variation in output. This is consistent with the theory described in section 2.1.3 that large disability-weight studies based on population surveys in different territories often show generally consistent results (Üstün et al., 1999; Solomon et al., 2012). This theory supports the use of globally generated DWs in the calculation of DALYs for developed

countries such as those in the EU. However, the applicability of globally generated DWs to developing countries with limited illness supports and amenities remains unclear.

Finding 4: Use of Japan-specific DWs resulted in a significant change to DALY output

In contrast to the above, using Japan-specific DWs did result in a significant change to DALY output. The Japanese population weighted mild infection twice as burdensome as the global average (0.012 versus 0.006). They weighted moderate infection eight times more burdensome (0.424 versus 0.051), and severe infection approximately twice as burdensome as the global average (0.242 versus 0.133). Cultural differences in perceptions of the severity of ill health was cited as the reason for this disagreement (Nomura et al., 2023).

This serves to illustrate the effect a change in one variable can have on the output of the calculation. If the GBD DWs are not closely representative of any one country's population—as we see is the case with Japan—then the validity of the method for generating national disease burdens may be reduced. On the other hand, without using standardised methods the outputs of the calculation may not be accurately used for comparison purposes. A potential solution to preserve validity in both scenarios is to use nationally generated DWs for national resource allocation decision-making, but to use global GBD DWs for international comparisons.

Finding 5: Use of Irish Life Tables No. 15 resulted in a significant change to DALY output

Interestingly, performing the calculation using Irish Life Tables No. 15, which details what the LE of Irish people was in 2005-2007, also resulted in a significant change to DALY output. LE was approximately 2 years shorter at this time so fewer years of life were lost following death. This translated to an 11% decrease in DALYs associated with influenza. This change would have been standardised across all conditions and risk factors in Ireland at that time, so does not have any notable implications in and of itself. However, it serves to highlight the variability in DALYs according to the life tables used, which differ significantly across populations and over time.

There are differing methods to estimating LE, giving rise to a debate in the literature as to which is best to use in BoD estimates. The GBD method for calculating DALYs employs a life table which is independent of the mortality risks experienced by the population being assessed, whereas other methods take into account those risks. Some critics believe this

approach is more appropriate for predicting life-years lost from premature mortality in any given country (Anand and Reddy, 2019). Similar to national DWs, for the calculation to be most accurate the latest population-specific life tables should be used for population-specific decisions on resource, but global life tables should be used for international comparisons.

In summary, RQ2 aimed to determine the degree of variability that may be associated with the calculation of DALYs associated with influenza. It was found that the DALY calculation can be variable given varying data inputs. Therefore, care must be taken when choosing input variables such as DWs and LEs. The choice of DW tables and life tables should be made based on the proposed function of the DALY in that circumstance. To inform national health policy decisions, DALYs generated using nationally generated DWs and national LEs are most valid. To be used for international comparison, standard GBD DWs and global LEs should be used.

4.2 The interviews (RQ3 and RQ4)

To address RQ3 and RQ4, an interpretivist approach was taken by conducting interviews with subject matter experts and target groups of the metric. The interview questions (IQs) asked are listed in figure 7 according to which RQ they originally intended address. Narrative thematic analysis is performed on the results of the interviews to identify themes, also included in figure 7. The findings are then discussed in the context of the wider literature and society.

The IQs were designed to address RQ3 and/or RQ4, which are seen in the first column in figure 7. The IQs asked are listed in the second column, according to which RQ they intended address. IQ2 was designed to address both RQ3 and 4. Themes resulting from the IQs are shown in the third column. These themes were arrived at following an iterative process to collate, locate and analyse key data points, as described in section 3.5. There is significant overlap of themes among IQs and RQs. Often, themes that arose in response to one IQ were also pertinent to other IQs and therefore other RQs. Therefore, many themes are repeated for multiple IQs, as shown in column three of the below table.

The themes resulting from the interviews are further described and analysed below.

Research Questions (RQs)	Interview Questions (IQs)	Themes

RQ3: Is the estimation of DALYs a suitable and valid metric for burden of influenza in Ireland?	IQ1: Do you think this metric, based on influenza surveillance data, is valid?	Scepticism towards validity of DWs DALY applicability to acute influenza Positive view on qualitative approaches to measure burden Concerns about availability of underlying data
	IQ3: Would this metric be suitable for use in your practice?	Concerns about availability of underlying data
	IQ2: Do you see any value in this metric for estimating the burden of influenza in Ireland?	DALY applicability to acute influenza Positive view on qualitative approaches to measure burden Useful to highlight disease burden for disease awareness
RQ4: Is the estimation of DALYs attributed to influenza in Ireland feasible for and useful to stakeholders in practice?	IQ4: Would this metric be useful to you in practice?	Positive view on qualitative approaches to measure burden Concerns about availability of underlying data Useful to inform HSE policy Useful to highlight disease burden for disease awareness
	IQ5: How could you implement this metric into your field?	Concerns about availability of underlying data
	IQ6: Is this feasible?	

	Feasibility of generating the estimate is dependent upon availability of data
	Feasibility of using the metric is dependent upon wider adoption
	Useful to highlight disease burden for disease awareness

Figure 7: Relationships between the Research Questions (RQs), Interview Questions (IQs) and resulting themes.

4.2.1 RQ3: Is the estimation of DALYs a suitable and valid metric for burden of influenza in Ireland?

To explore whether the DALY metric can and should be considered for use in Ireland, interviews were conducted with a panel of experts to determine their views on the metric for measuring and managing the burden of influenza in Ireland. Interview questions 1, 2, 3 and 5 were specifically designed to address whether the metric is suitable and valid for use for this purpose (RQ3). The main themes arising from the interviews are described and analysed below.

4.2.1.1 Findings

Finding 6: Scepticism towards validity of DWs

Overall, the panel of experts looked positively on the DALY as a metric for measuring and managing burden of influenza in Ireland. However, when asked whether the metric was valid (IQ1), some participants demonstrated scepticism towards the validity of the DWs used for the estimation. One participant began by saying that the metric appears valid, but they would "*need to know how they [the DWs] are weighted to be sure*". Another participant demonstrated scepticism in their facial expression following this question and questioned the DW validity with regard to children. This participant's work is primarily with children, and he understands that children can be affected by diseases differently to adults and the elderly. Therefore, he wasn't convinced that one DW could apply to all. He asked, "*are they [the DWs] generated just for adults?*". This theme provides insight into

the views of the subject matter experts on the validity of the DALY metric for use in Ireland (RQ3).

Finding 7: Applicability of the DALY to acute influenza

In discussing the applicability of the DALY to measuring and managing influenza following IQ1 and 2, some participants alluded to the acute nature of influenza and how most people who get infected don't become 'disabled' in the traditional sense. They questioned the applicability of the metric to an acute illness such as influenza. One participant stated that the DALY may not be as suitable to an acute disease as for chronic diseases such as cancer. As though in response, the other participant stated, "*I do recognise where some people are coming from by saying influenza doesn't translate into disability so therefore the metric mightn't be valid; but even so it can still be used to highlight differences in disability because influenza causes so little of it".* This theme provides insight into the views of the subject matter experts on the suitability of the DALY to influenza (RQ3).

Finding 8: Positive view on qualitative approaches

Overall, there was a positive reaction from participants around the validity and suitability of the metric for measuring and managing influenza in Ireland. In particular, two participants looked positively on the apparent movement to more qualitative methods to measure BoD, rather than simply mortality or morbidity. Methods which encompass the patient's quality of life were seen as suitable, valid and useful by these two participants in response to IQ1, 2 and 4. One noted "*A lot of health metrics are going towards a more qualitative approach so 'how does it make you feel' which is valid because what a lot of health authorities are looking at quality of life rather than just mortality and morbidity*". The other participant referred to this as "*richer data*" than the traditional methods mortality and morbidity. This theme provides insight into the views of the subject matter experts on the validity and suitability of the DALY to influenza (RQ3).

Finding 9: Concerns about availability of underlying data

Four of the five participants demonstrated concerns surrounding the data required for the calculation. The concern was whether the data was available and was of sufficient quality. This theme arose in response to IQs 1, 2 and 6, but was echoed by the researcher throughout the research process when the data in the correct form could not be found. One participant, an Economic Advisor who performs similar calculations to determine

cost-effectiveness of medications, noted that a lot of their calculations require "*a bunch of assumptions*" due to lack of data availability. Another senior member of the HPSC demonstrated scepticism as to whether this calculation was possible given the current availability of the data required. He stated, "*we don't at any point in time know how many people have the flu*". Two other participants alluded briefly to the dependence of the metric's validity on the quality of the underlying data. One stated that the metrics suitability "*depends on the completeness of data available and analysis*". This theme provides insight into the views of the subject matter experts on the validity and feasibility of the DALY to influenza (RQ3-4).

In summary, RQ3 aimed to determine whether the estimation of DALYs is a suitable and valid metric for burden of influenza in Ireland. Interviews with a panel of experts were conducted to address this question. Themes of scepticism towards validity of DWs, applicability of the DALY to acute infection, positive views on qualitative approaches and concerns about availability of underlying data were induced from the interviews. These findings are discussed in the context of the literature and implications in the following section.

4.2.1.2 Analysis

RQ3 aimed to determine whether the estimation of DALYs is a suitable and valid metric for burden of influenza in Ireland. Interviews were conducted with a panel of experts to determine their views on the matter. The main findings in the form of key themes are described in the previous section and are now discussed in the context of the literature and wider implications.

Finding 6: Scepticism towards validity of DWs

Overall, the panel of experts looked positively on the DALY as a metric for measuring and managing burden of influenza in Ireland. However, when asked whether the metric was valid, some interview participants demonstrated scepticism towards the validity of the DWs used for the estimation.

As mentioned in section 2.1.2, the first set of DWs was established for the GBD 1996 study. The method used to generate DWs was flawed then but has evolved substantially in response to recommendations from global experts. The current GBD DWs were generated in 2015 by Vos et al. using public surveys of 30,230 people in 167 countries. This is seen by GBD collaborators as the most valid method to generate DWs to date.

Such collaborators include a 40-person scientific council comprising leading experts who evaluate criticisms and recommendations of the GBD processes and methods (including generating DWs), an Independent Advisory Committee which advises on the GBD processes and methods (IHME, 2022a), and peer review by other leading experts. This demonstrates the GBD's commitment to optimising the methods used for the GBD project using wide-ranging and diverse opinions of scientific experts around the world (IHME, 2022a). This process for creating the methods is robust and provides confidence in the validity of the GBD DWs.

Yet, inherently the DWs will not be valid in every scenario. As mentioned in section 2.1.3, a prevailing concern regarding DWs is whether they can be removed from their societal context to be considered universal. Questions have been raised, for example, as to whether the decrease in quality of life associated with paraplegia can be considered equal in a low-income country as in an urban area of a high-income country where assistive technologies and public transportation are available (Chen et al., 2015). This theory was supported by the study by Nomura et al. (2023) which generated DWs for the Japanese population which differed significantly in some cases from the global DWs. However, the DWs generated by the study on European participants were similar to the global DWs. To preserve validity, nationally generated DWs are most accurately used for decisions on national resource allocation, but global DWs are best used for international comparisons.

In terms of influenza specifically, issues with validity of DWs have a negligible effect on the validity of the calculation as YLD contributed just 2-3% of DALYs. Any variation between the DWs used for the calculation and the 'true' DWs would have a small effect on this 2-3%, likely resulting in an impact of <0.05%. Therefore, any concerns with validity of DWs does not significantly impact the suitability, validity, utility and feasibility of its implementation for measuring and managing influenza in Ireland.

Finding 7: Applicability of the DALY to acute influenza

During the interviews, two participants referred to the acute nature of influenza implying that people who are infected don't become 'disabled' in the traditional sense. One participant stated that the DALY "*may not be as suitable to an acute disease as for chronic diseases such as cancer*". Consistently, section 4.1.1.1 shows that the proportion of DALYs from influenza attributed to YLDs is negligible at 2-3%. This supports the observation that influenza does not cause significant 'disability' in the population. Its burden stems mostly from premature mortality.

Still, the low YLD attributed to influenza remains relevant as a means of comparison. This was highlighted by another interview participant, who stated "*I do recognise where some people are coming from by saying influenza doesn't translate into disability so therefore the metric mightn't be valid; but even so, it can still be used to highlight differences in disability because influenza causes so little of it.".* This participant also clarified that the metric can be used for any disease or risk factor, stating that the metric "*can be used for comparisons agnostic to disease or even field of working (e.g. healthcare versus housin*g)".

The misunderstanding in the applicability of the DALY to acute illnesses could be one of the reasons for the slow adoption of the metric in Ireland and should be clarified. The DALY remains a valid metric to apply to all illnesses, including acute, as a means of comparison.

Finding 8: Positive view on qualitative approaches

Overall, there was a positive reaction from participants around the validity and suitability of the metric for measuring and managing influenza in Ireland. In particular, two participants looked positively on the apparent movement to more qualitative methods to measure BoD, rather than simply mortality or morbidity. One noted "*A lot of health metrics are going towards a more qualitative approach so 'how does it make you feel' which is valid because what a lot of health authorities are looking at quality of life rather than simply mortality and morbidity*". The other referred to this as "*richer data*" than the traditional methods mortality and morbidity.

There is a general consensus in the literature that more holistic methods for measuring disease burden, which encompass the quality of life gained rather than simply the presence of absence of it, are more reflective of, and meaningful to, society (see section 2.1.2). Nowadays, health is seen by the public health community as a multidimensional construct that includes physical, mental and social elements. The DALY succeeds in capturing the physical and mental elements of health. It historically tried to include the social aspect, but this was met with too many challenges and has since been removed from scope. This holistic method is more reflective of societal reality. Therefore, using such methods to aid decision-making should maximise the benefit to society.

The issue with the move to more qualitative methods for measuring health and disease is that it is difficult to assign numbers to qualitative data. The DALY attempts to do this using the DWs, by surveying large samples of the global population on their perception of different health states and applying statistical models to translate the results into a scale

of 0 to 1. It became clear from secondary research (see section 2.1.3) and was supported by primary research (see finding 6), that challenges remain around the validity of these DWs.

With that said, the method used for generating the current GBD DWs appears to be a valid approach, and confidence may be placed in their use. The option to create population specific DWs if deemed necessary is also available, which could increase validity of the DALY for specific purposes. Ultimately, the use of summary measures such as DALYs, QALYs etc. provides information which is reflective of societal reality and their use in aiding healthcare policy should maximise benefit to society.

Finding 9: Concerns about availability of underlying data

Concerns surrounding the data required for calculating DALYs has been a common theme throughout this research. The majority of interview participants demonstrated concern as to whether the required data was available and was of sufficient quality. This theme was echoed by the researcher as the project progressed and the data in the correct form could not be found.

Finding number 1 of RQ1, confirms this concern. The finding shows that data were unavailable in Ireland for influenza incidence, rates of moderate influenza illness and mortality data stratified by sex. To fill these gaps data from the Flu Watch Cohort Study (Hayward et al., 2014) was adapted. Interestingly, one interview participant, an Economic Advisor who performs similar calculations to determine cost-effectiveness of medications, noted that a lot of their calculations require "*a bunch of assumptions*" due to lack of data availability. It appears this is a common issue in making such estimations.

Luckily, the gaps in data exist mostly in the data required to calculate YLD, which comprises only 2-3% of the overall estimate for influenza. This means that although the interview participants were correct in their doubt that some of the data required exists, the impact of this on the estimate is negligible.

In summary, RQ3 aimed to determine whether the estimation of DALYs is a suitable and valid metric for burden of influenza in Ireland. Overall, the panel of experts looked positively on the theory of the DALY as a metric for measuring and managing burden of influenza in Ireland. Holistic BoD metrics which encompass the patient's quality of life were seen as suitable, valid and useful. The metric is also suitable for measuring and managing influenza despite its acute nature. Some hesitancy towards the validity of DWs remained but this has little impact in practice on the validity of DALY estimations for influenza, as YLD contributes on 2-3% to the estimate. Participant's concern over the

availability of the data required to estimate DALYs associated with influenza was justified, as gaps in data do exist. However, these gaps had a negligible impact on the overall validity of the estimate.

4.2.2 RQ4: Is the estimation of DALYs attributed to influenza in Ireland feasible for and useful to stakeholders in practice?

To explore whether the DALY metric can and should be considered for use in Ireland, interviews were conducted with a panel of experts to determine their views on the metric for measuring and managing the burden of influenza in Ireland. Interview questions 2, 4, 5 and 6 were specifically designed to address whether the metric is feasible for and useful to stakeholders in practice (RQ4). Most of the findings relating to this were in response to these IQs; however, some useful information pertaining to this RQ was also provided following some of the other interview questions. The main themes arising from the interviews are described and analysed below.

4.2.2.1 Findings

RQ4 aimed to determine whether using the DALY is feasible for and useful to stakeholders in practice. Interviews were conducted with a panel of experts to determine their views on the matter. The findings in the form of key themes resulting from the interview questions are described below. The findings are discussed in the context of the literature and implications in the following Analysis section (4.2.2.2).

Finding 10: Feasibility of generating the estimate is dependent upon availability of data

When asked whether the implementation of this metric into the participant's industries would be feasible (IQ5 and 6), three participants stated that this is dependent upon the availability of the underlying data. One stated "*it depends on the completeness of data available and analysis*". If data are insufficiently complete, it is not yet feasible to perform calculation and use the resulting information. One participant—a senior member of the HPSC—stated that he does not think the data on influenza which is required to make this calculation is available. In this regard, he stated definitively "*we don't at any point in time know how many people have the flu*". It was agreed by most participants that if the data are available, the metric can be easily performed and integrated into reports and

campaigns. This theme provides insight into the views of the subject matter experts on the feasibility of the DALY for application to influenza in Ireland (RQ4).

Finding 11: Feasibility of using the metric is dependent upon wider adoption

When asked whether the implementation of this metric into the participant's industries would be feasible (IQ5 and 6), one participant stated that this is dependent upon the widespread use of the DALY for BoD studies. In response to whether its implementation would be feasible, this participant stated, "*only if it was well-recognised and widely used*". When asked whether it is a suitable metric, he stated, "*Yes but you would need a large sample to be using it for it to make sense*". He believed that its feasibility for use is limited without a means of comparison. This is to say, unless the burden of other diseases and risk factors are expressed in DALYs, the number of DALYs associated with influenza is meaningless. This theme was echoed by another interview participant, who believed that the fundamental utility of the DALY is as a means of comparison. In response to whether the metric would be useful, he stated, "*its real utility would be with its comparison*". Accordingly, without the ability to be compared to other diseases in the same format, it's not feasible for use. This theme provides insight into the views of the subject matter experts on the feasibility of the DALY for application to influenza in Ireland (RQ4).

Finding 12: The DALY is useful to inform HSE policy

When asked if the metric would be useful to them in practice (IQ4), three participants stated that it would be mainly useful to inform HSE policy. For example, to indicate whether influenza vaccination efforts should increase or if more hospital beds and ICU equipment is required. One participant stated that knowing the annual burden of influenza could allow the HSE to "*prepare and prevent*" by incentivising vaccination and preparing GPs and hospitals for the seasonal increase in activity. Another participant stated that it would be useful for "*evaluating the effectiveness of interventions such as vaccination campaigns by estimating the DALYs before the campaign and again afterwards*". This theme provides insight into the views of the subject matter experts on utility of the DALY for application to influenza in Ireland (RQ4).

Finding 13: The DALY is useful for disease awareness

Another theme that arose during the interviews in response to multiple questions was the utility of the DALY to highlight the burden of the disease for disease awareness purposes.

The calculation is disease-agnostic, meaning it can be applied to any disease or risk factor. This provides a common currency for comparison of disease burden. The ability to compare the burden of one disease versus another is a useful tool to highlight disease burden within populations. Some participants saw this as a useful tool within their industries for disease awareness purposes. For example, one participant stated that there is a "*lack of understanding and awareness* [of the burden of influenza]" and that this metric could create awareness of the burden. Another participant was of a similar opinion, stating that using the metric "*as a comparative tool in* [vaccination] *campaigns or as part of a social media campaign would make the problem real in patients' eyes*". This theme provides insight into the views of the subject matter experts on utility and feasibility of the DALY for application to influenza in Ireland (RQ4).

In summary, RQ4 aimed to determine whether using the DALY is feasible for and useful to stakeholders in practice. Interviews were conducted with a panel of experts to determine their views on the matter. It appears that feasibility of adopting this metric for measuring and managing influenza in Ireland is dependent upon availability of data and the metric's wider adoption. Additionally, it appears the DALY would be useful to inform HSE policy and for disease awareness. These findings are discussed in the context of the literature and implications in the following section.

4.2.2.2 Analysis

RQ4 aimed to determine whether using the DALY is feasible for and useful to stakeholders in practice. Interviews were conducted with a panel of experts to determine their views on the matter. The findings in the form of key themes resulting from the interview questions were described in the previous section and are now discussed in the context of the literature and wider implications below.

Finding 10: Feasibility of generating the estimate is dependent on availability of data

A common theme resulting from the interviews was that the feasibility of implementing the DALY for influenza in Ireland is dependent upon the availability of the underlying data. As described in section 4.1.1.1, the majority of the data required for calculating DALYs associated with influenza is available from HPSC. Some gaps in data required do exist; however, these gaps have a negligible impact on the overall validity of this particular estimate (as described in section 4.1.1). Therefore, in response to RQ4, it is feasible to calculate DALYs for influenza in Ireland.

The feasibility of using this information for its intended purpose is another issue, which is analysed further in the next finding.

Finding 11: Feasibility of using the metric is dependent upon wider adoption

Based on the literature and results of the interviews, the feasibility of implementing the metric into practice in Ireland is dependent upon the widespread adoption of the DALY for BoD studies. This is to say, unless the burden of other diseases and risk factors are expressed in the same format, the number of DALYs associated with influenza is meaningless. The metric's utility is derived from its ability to be applied to any disease or risk factor. This provides a common "currency" through which the burdens can be directly compared. This is intended to form the basis of decisions on resource allocation, to highlight the burden of the disease compared to others, and to provide baseline data to monitor trends over time.

However, as described in section 2.1.2, few BoD studies in Ireland utilise this metric. One PhD thesis titled "*Attributable burden, life expectancy and income loss to non-communicable diseases in Ireland: from evidence to policy-making*" (Chakraborty, 2020) did utilise the DALY to generate national burden estimates for diabetes and cancer, and these estimates are used as the only comparator to this research's estimates in section 4.1.1. However, as this study is not peer-reviewed, it is not used to draw any conclusions on the relative burden of influenza in Ireland. Therefore, no such conclusions can be made.

More widespread use of the metric is required for it to perform its intended function as a comparative tool to inform health policy decisions, highlight the BoD and monitor health trends over time.

Finding 12: The DALY is useful to inform HSE policy

When exploring the potential usefulness of the DALY to stakeholders in the interviews, a common theme which emerged was that it would be mainly useful to inform HSE policy. One participant stated that knowing the annual burden of influenza could allow the HSE to "*prepare and prevent*" by incentivising vaccination and preparing GPs and hospitals for the seasonal increase in activity. Another participant stated that it would be useful for evaluating the effectiveness of interventions such as vaccination campaigns by estimating the DALYs before and after the campaign.

These suggestions are commonly cited benefits associated with using the DALY metric for measuring and managing influenza. The WHO lists some of the benefits as follows (WHO, 2015):

1. *Assist healthcare planners in informed decision-making and in the planning process by providing them with a comprehensive and comparable assessment of death, and severe disease. This is particularly relevant for augmenting vaccine manufacturing capacity in low and middle-income countries and targeted use of antivirals for reducing influenza-related severe morbidity and mortality.*
2. *Assist donor agencies and national governments in prioritizing health research investments and healthcare interventions.*
3. *Guide healthcare planners and multilateral agencies in demand-side planning for healthcare services during outbreaks and epidemics.*
4. *Assist the pharmaceutical industry in planning for novel low-cost and effective interventions for the prevention and treatment of influenza.*
5. *Provide baseline data with which to compare data from annual influenza outbreaks and new events, such as an influenza pandemic*

Implementing the DALY into HSE policymaking could result in some of the above listed benefits which would improve the approach to healthcare and maximise benefit to patients and society.

However, as mentioned in finding 12: “Feasibility of using the metric is dependent upon wider adoption”, the use of the DALY for comparison purposes is not yet feasible in Ireland. The first step is for the metric to be more widely adopted by researchers generating BoD estimates. This research indicates that the metric is valid, useful, feasible and suitable for use in Ireland, but its scope is limited to influenza. Further research is required into whether this metric maintains validity, suitability, feasibility and utility when applied to other illnesses. If so, the metric should be more widely adopted to realise its full potential.

Finding 13: The DALY is potentially useful for disease awareness

Another theme which arose when exploring the potential utility of the DALY was its utility for disease awareness purposes. This is an interesting theme as it’s a function of the metric rarely mentioned in the literature. The theory is that the ability to measure the burden of the disease, and the ability to compare the burdens of diseases and risk factors, could highlight the true importance of the disease. Highlighting the burden to patients may lead to changes in behaviour such as increased vaccination uptake and increased

vigilance during the influenza season to avoid spreading infection. Which could result in a reduction in seasonal burden. Highlighting the burden to healthcare providers may lead to increased prescribing of vaccinations and improved care of those infected—also leading to societal benefit.

This serves as an important secondary benefit of using the DALY for measuring and managing burden of influenza in Ireland, and further supports its implementation. However, as mentioned in finding 12: “Feasibility of using the metric is dependent upon wider adoption”, the use of the DALY for comparison purposes is not yet feasible in Ireland. The first step is for the metric to be more widely adopted by researchers generating BoD estimates. Once this is the case, the DALY may begin to perform its purpose of aiding evidence-based decisions, and secondarily, highlighting the burden of influenza in Ireland to positively influence behaviour.

In summary, RQ4 aimed to determine whether using the DALY is feasible for and useful to stakeholders in practice. The findings suggest that the calculation of DALYs associated with influenza is feasible; however, the use of this metric in practice is not, as there are few comparators available. Without standardised comparators, the number of DALYs associated with influenza is meaningless. More widespread adoption of the metric in Ireland is required for it to realise its full potential.

If more BoD estimates expressed in DALYs become available, the metric would be useful mainly to improve HSE decision-making by providing an evidence base. This could maximise benefit to patients and society. Another secondary benefit would be highlighting the burden of the disease to society and HCPs to positively influence behaviour surrounding influenza prevention and control.

4.3 Chapter summary

The results of this research provide a well-rounded understanding of the current position of the DALY as a potential metric for measuring and managing the burden of infuenza in Ireland. Results for RQs 1 and 2 were based on performing the calculation using available data to explore its feasibility, validity and reliability first-hand. Key findings showed that generating a valid estimate using Irish parameters is possible, despite minor gaps in the data required. Influenza is estimated to have caused 4271.17 DALYs in 2017/2018 and 1891.72 DALYs in 2018/2019. The calculation was found to be variable depending on data inputs. Therefore, care should be taken when choosing input variables.

RQs 3 and 4 aimed to further examine the feasibility, validity, suitability and utility of the metric by interviewing a panel of subject matter experts. The research found that it is

feasible to generate an estimate for DALYs associated with influenza in Ireland, but it is not feasible to implement this metric into practice as very few appropriate comparators exist. Without the possibility of comparison, the DALY is futile. However, if the metric became more widely used in Ireland it would likely be useful and suitable for stakeholders. Therefore, more widespread adoption of the metric is required for it to realise its potential for aiding evidence-based decisions and highlighting the burden of influenza in Ireland. This would maximise benefit to society.

The below table summarises the key findings to all four RQs.

Table 1: Summary of findings

Research question (RQ)	**Finding**
RQ1: What number of DALYs is estimated to be attributed to influenza in Ireland during the 2017/2018 and 2018/2019 seasons?	Although gaps in required data exist, supplementary data could be used to arrive at a valid estimate of DALYs associated with influenza in Ireland. This estimate is 4271.17 DALYs in 2017/2018 and 1891.72 DALYs in 2018/2019.
RQ2: What degree of variability can be associated with the estimation of DALYs?	Varying data inputs can result in significant (~10%) variation to the calculation output.
RQ3: Is the estimation of DALYs a suitable and valid metric for burden of influenza in Ireland?	While there is some scepticism towards the validity of DWs, the findings show that the DALY is a suitable and valid metric for measuring and managing the burden of influenza. However, its feasibility for use in practice is dependent upon its wider adoption.
RQ4: Is the estimation of DALYs attributed to influenza in Ireland feasible for and useful to stakeholders in practice?	The findings show that the DALY would be useful to inform HSE policy and highlight the burden of influenza. They also show that it is feasible to calculate DALYs associated with influenza. However, its utility is dependent upon its wider adoption.

The next chapter concludes this research, offering a final summary of conclusions and their implications. Practical and academic recommendations are made, limitations are listed and suggestions for future work are put forward.

5.0 Conclusions and recommendations

This research set out to estimate the DALYs attributed to influenza in Ireland, explore whether calculation is variable, and investigate whether its use in practice in Ireland is feasible, suitable and useful. These objectives were addressed using a mixed-method approach. Using a quantitative method, the DALY calculation was performed to estimate the burden of influenza in Ireland and to explore the variability of the calculation. A qualitative method was then used to gain the views of subject matter experts on the validity, feasibility, suitability and utility of the DALY in practice. Below, the research objectives are restated with the results provided and their implications. Some limitations of the research are disclosed, and the chapter ends with final comments.

Estimate the DALYs attributed to influenza in Ireland during the 2017/2018 and 2018/2019 seasons using publicly available influenza surveillance data

A valid estimate for the number of DALYs attributed to influenza in Ireland during the 2017/2018 and 2018/2019 seasons (RQ1) was achieved. We estimate that in Ireland influenza caused 4271.17 DALYs in 2017/2018 and 1891.72 DALYs in 2018/2019. Per 100,000 population, this translates to 87.75 DALYs and 38.8 DALYs respectively. Issues with data availability was a concern throughout the research and was echoed by subject matter experts in interviews. Although gaps do exist, in the case of influenza they had little impact on the validity of the calculation. Appropriate supplementary data from the literature was used to complete the calculation to sufficient validity. The final estimates were approximately in line with estimates from EU and the Netherlands, providing confidence in their validity (van Lier et al., 2016; Cassini et al., 2018).

For these figures to be fit for purpose, i.e. to be used as a comparison tool to inform health policy decision-making, competing conditions must also be represented in terms of DALYs. Few other BoD studies in Ireland utilise this metric. Therefore, the result of this study cannot be used to make a recommendation on the extent of intervention required. It

may, however, be utilised as a means of comparison by future researchers conducting BoD studies using DALYs.

We recommend that researchers consider the adoption of this metric to measure BoD in Ireland. Sufficient adoption of the metric could result in benefits such as informed decision-making on policy, effective healthcare planning and preparation and prioritisation of health research investments and healthcare interventions. These benefits are particularly pertinent in today's Irish setting, as it is facing chronic resource shortages.

Academically, the result of this research question has provided a validated method for estimating DALYs associated with influenza in Ireland. Researchers in the future may use the same method to generate estimates that can be compared to those generated for this study. For example, by generating estimates for the 2023/2024 season and comparing to the estimate of this study to examine the impact of the COVID19 pandemic (2020-2022) on the burden of influenza.

This research has also expanded the methodological discussion surrounding the calculation of DALYs by providing insight on variability of the metric given varying inputs and exploring the views of experts on the validity of the metric.

Calculate DALYs attributed to Influenza in Ireland using various disability weights and life expectancies to explore variability in output

It was found that DALY estimations can be variable depending on what kind of variables you choose. This is echoed in the literature. Therefore, care must be taken when choosing input variables such as DWs and LEs. We propose that the choice of DW tables and life tables should be made based on the proposed function of the DALY in that circumstance. To inform national health policy decisions, DALYs generated using nationally generated DWs and national LEs are most valid. To be used for international comparison, standard GBD DWs and global LEs should be used. This study provides additional evidence to add to the academic discussion on the DALY methodology.

Determine whether the estimation of DALYs based on surveillance data is a suitable and valid metric for the burden of Influenza in Ireland

This objective was initially addressed by gathering the required data from appropriate public sources and performing the calculation. Based on this, it was discovered that the calculation can be performed with confidence to estimate DALYs with influenza in Ireland. Although gaps in the data do exist, these had little impact on the validity of the calculation (<0.05%). The panel of experts looked positively on the theory of the DALY as a metric for

measuring and managing burden of influenza in Ireland. Some hesitancy towards the validity of DWs remained but this has little impact in practice on the validity of DALY estimations for influenza, as YLD contributes on 2-3% to the estimate. Participant's concern over the availability of the data required to estimate DALYs associated with influenza was justified, as gaps in data do exist. However, these gaps had a negligible impact on the overall validity of the estimate.

Therefore, it appears the metric is valid for measuring influenza in Ireland. However, to be suitable for their purpose, competing conditions must also be represented in terms of DALYs and few are. We recommend that researchers and policymakers consider the adoption of this metric to measure and manage BoD in Ireland. Sufficient adoption of the metric could result in benefits such as informed decision-making on policy, effective healthcare planning and preparation, prioritisation of health research investments and healthcare interventions and to provide baseline data to measure effectiveness of interventions. These benefits are particularly pertinent in today's Irish setting, as it is facing chronic resource shortages.

Investigate in which capacity (if any) the calculation of DALYs attributed to Influenza in Ireland will be most feasible and useful in practice

Based on interviews with subject matter experts, the *calculation* of DALYs associated with influenza is feasible; however, the *use* of this metric in practice is not, as there are few comparators available. Without standardised comparators, the number of DALYs associated with influenza is meaningless. More widespread adoption of the metric in Ireland is required for it to realise its full potential.

If more BoD estimates expressed in DALYs become available, the metric would be useful mainly to improve HSE decision-making by providing an evidence base. This could maximise benefit to patients and society. Another secondary benefit which would also benefits patients and society would be highlighting the burden of the disease to positively influence behaviour surrounding influenza prevention and control. Therefore, we recommend that researchers and policymakers consider the adoption of this metric to generate BoD estimates in Ireland.

5.1 Limitations

Some limitations associated with this research must be noted. First, the data used as inputs to the calculation is incomplete. No influenza incidence rates or information on rates of 'mild' and 'moderate' ILI in Ireland were available. Appropriate supplementary

data from the literature was used instead, but this is not an ideal source. The effect of this on the validity of the calculation is likely minimal (<0.05%), but the estimate would be more accurate if the required data was available.

Additionally, mortality associated with influenza is not available stratified by sex. Instead, an average of both male and female life expectancies was used. This reduced accuracy of the estimation very slightly. It is also widely cited that mortality rates associated with influenza are often underestimates (Gibbson et al., 2014). Therefore, it is possible that the estimates generated for this study are underestimates. However, they were approximately in line, if not higher, than similar estimates made for the EU and the Netherlands (van Lier et al., 2016; Cassini et al., 2018).

Finally, in this research a total of 5 participants agreed to take part in interviews. This participation rate was accepted as it was expected that a sufficient quantity and quality of data would be provided to enable an interpretivist analysis in the small health system Ireland has relative to other countries. We believe this was the case; however, more interview participants would have provided further depth and reliability to the findings. In particular, an interviewee from the Department of Health would have provided valuable input into the findings.

5.2 Suggestions for further research

To gain a valid answer as to whether the metric is useful for managing BoD in Ireland, further research is required into this metric's validity, suitability, feasibility and utility when applied to other illnesses. If it is valid, BoD studies should be conducted using the metric to generate DALY estimates for multiple illnesses and risk factors to allow comparison between them. This is where the true value of the DALY lies.

5.3 Final comments

This research generated a valid estimate for DALYs associated with influenza in Ireland. Therefore, calculation of the DALYs associated with influenza is feasible. However, the estimate cannot be used at present to arrive at a conclusion regarding the burden of influenza. This is because to do so it must be compared to other DALY estimates and few appropriate estimates exist in Ireland. This is also the reason why it is not feasible for the estimate to be used for its intended purpose.

This estimate will, however, provide a useful comparator to future studies. If more studies in Ireland adopt the DALY as a metric, its utility in informing HSE policy and highlighting the burden of disease may be realised.

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Appendices

A1. Definitions and glossary

Term	Definition
Ireland	Republic of Ireland
BoD	The burden of disease
True burden of influenza	Actual burden, irrespective of surveillance, of influenza on the population in terms of mortality and morbidity.
Disability	A state of less than perfect health
Irish population	Everyone who was present in the State on the night of Sunday, 03 April 2022'', the third of April 2022 being the most recent census night (CSO, 2022).
ILI	Influenza-like-illness. Sudden onset of symptoms with a temperature of 38°C or more, in the absence of any other disease, with at least two of the following: dry cough, headache, sore muscles and a sore throat (HPSC, 2022).
HSE	Health Service Executive. The government-funded, public health system in Ireland. Excludes private healthcare services.
Feasibility of DALYs	The feasibility of implementing the calculation of DALYs into common practice to determine the true burden of influenza.
Utility of DALYs	The usefulness of DALYs as a measure of true burden of influenza to various stakeholders in Ireland
Suitability of DALYs	The suitability of DALYs as a measure of the true burden of influenza in Ireland.
Validity of DALYs	The reliability of the output of the calculation as a measure of the true burden of influenza in Ireland.
WHO	World Health Organization
DALY	Disability Adjusted Life Year
YLL	Years of Life Lost
YLD	Years Lived with Disability
GATHER	Guideline for Accurate and Transparent Health Estimates Reporting

LE	Life expectancy
DW	Disability weight
CDC	Centres for Disease Control
ICU	Intensive Care Unit
HPSC	Health Protection Surveillance Centre. Ireland's disease surveillance centre.
CSO	Central Statistics Office
GP	General practitioner
QALY	Quality-adjusted life year
GBD	Global Burden of Disease (project)
RQ	Research question
CF	Conceptual framework
IQ	Interview question
EU	European Union
EUBD	The burden of disease in Europe study (Cassini et al., 2018)
UK	United Kingdom
IHME	Institute for Health Metrics and Evaluation
TILDA	The Irish Longitudinal Study on Ageing
HI	Health Ireland (study)

A2. Ethical procedure

Sample Participant consent form

Consent to take part in research

The Disability-Adjusted Life Year (DALY) and Influenza in Ireland: An evaluation of the suitability of the DALY as a metric for measuring and managing the burden of influenza in Ireland

- I <participant> voluntarily agree to participate in this research study
- I understand that even if I agree to participate now, I can withdraw at any time or refuse to answer any question without any consequences of any kind
- I understand that I can withdraw permission to use data from my interview within two weeks after the interview, in which case the material will be deleted.
- I have had the purpose and nature of the study explained to me in writing and I have had the opportunity to ask questions about the study

- I understand that participation involves answering a series of questions regarding the use of the DALY in my work and my industry.
- I understand that I will not benefit directly from participating in this research
- I understand that all information I provide for this study will be treated confidentially
- I understand that in any report on the results of this research my identity will remain anonymous. This will be done by changing my name and disguising any details of my interview which may reveal my identity or the identity of people I speak about.
- I agree to my interview being audio-recorded.
- I understand that disguised extracts from my interview may be quoted in the dissertation named at the top of this form.
- I understand that if I inform the researcher that myself or someone else is at risk of harm, they may have to report this to the relevant authorities - they will discuss this with me first but may be required to report with or without my permission
- I understand that signed consent forms and original audio recordings will be retained locally on the researcher's laptop hard drive, to which only the researcher has access, until approximately November 2023.
- I understand that a transcript of my interview in which all identifying information has been removed will be retained for two years following November 2023.
- I understand that under freedom of information legalisation I am entitled to access the information I have provided at any time while it is in storage as specified above.
- I understand that I am free to contact any of the people involved in the research to seek further clarification and information.

Researcher Details

Name: Roisin Quigley

Degree Programme: Msc Pharmaceutical Business and Technology

College Details: Griffith College Dublin and Innopharma

Contact number:

Contact mail:

Signature of participant

Name

Signature of participant

---------- ---------- Date

Signature of researcher

I believe the participant is giving informed consent to participate in this study

---------- ---------- Date

Signature of researcher

Sample participant information letter (PIL)

Participant Information Letter

The Disability-Adjusted Life Year (DALY) and Influenza in Ireland An evaluation of the suitability of the DALY as a metric for measuring and managing the burden of influenza in Ireland

I would like to invite you to take part in a research study. Before you decide if you will participate you need to understand why the research is taking place and what it would involve for you. Please take time to read the following information carefully. Don't hesitate to ask questions if anything you read is not clear or if you would like more information. Take time to decide whether or not to take part.

WHO I AM AND WHAT THIS STUDY IS ABOUT

My name is Roisin Quigley, I am a part-time student of Griffith College studying a masters degree in Pharmaceutical Business and Technology, alongside working in Pharmaceutical Regulatory Affairs. I am completing this research as part of my final dissertation for my master's degree.

The aim of this research is to estimate the burden of influenza in Ireland in terms of Disability-Adjusted Life Years (DALYs) and to investigate the feasibility, suitability, utility and validity of this measurement in practice in the Irish healthcare and health policy setting.

WHAT WOULD TAKING PART INVOLVE?

I am conducting a number of interviews with subject matter experts in the Irish healthcare and health policy setting. Interview participants are asked to sign a consent form prior to the interview. Interviews will involve approximately 7-8 questions on the participants opinion of the DALY and its applicability to their work and industry. It is expected interviews will take approximately 20 minutes and may be done in person or over Zoom/MS Teams (whichever is preferable). Interviews will be recorded for the purposes of transcription unless specifically requested otherwise.

WHY HAVE YOU BEEN INVITED TO TAKE PART?

You have been asked to take part as you have been identified by my colleague Barry Morris, Business Unit Director in AstraZeneca Ireland, as a subject matter expert in the field of infectious disease health policy (vaccination campaigns).

DO YOU HAVE TO TAKE PART?

Your participation is voluntary and you have the right to refuse participation, refuse any question and withdraw at any time (including after the interview has taken place) without any consequence.

POSSIBLE RISKS, BENEFITS AND CONFIDENTIALITY

From a participant's perspective this research project represents a low risk as responses to questions will be anonymised and limited to attitudes and opinions in your capacity

regarding your professional activities only. Your responses will benefit you and other professionals working in the health care and health policy settings. If you have any concerns about this please ask the interviewer before signing the consent form.

HOW WILL INFORMATION YOU PROVIDE BE STORED AND PROTECTED?

Signed consent forms and original audio recordings will be retained on the researcher's laptop hard drive. The laptop requires a password to gain access, therefore only the researcher should have access until submission to the college. The files will be stored locally until after my degree has been conferred in November 2023. A transcript of interviews in which all identifying information has been removed will be retained by the college for a further two years after this. Under freedom of information legalisation you are entitled to access the information you have provided at any time.

WHAT WILL HAPPEN TO THE RESULTS OF THE STUDY?

My plan for this research is limited to submitting to the college for my dissertation. It will therefore be accessible in the college library and could potentially be made available in online e-journals or repository.

WHO SHOULD YOU CONTACT FOR FURTHER INFORMATION?

Primary Researcher:

Roisin Quigley

THANK YOU

Submitted ethics application & declaration form

Innopharma education

GRIFFITH COLLEGE

Ethics Application & Declaration Form

DISSERTATION TITLE: The Disability-Adjusted Life Year (DALY) and Influenza in Ireland: An evaluation of the suitability of the DALY as a metric for measuring and managing the burden of influenza in Ireland

RESEARCHER'S NAME: Roisin Quigley

PROGRAMME OF STUDY: MSc Pharmaceutical Business and Technology

SUPERVISOR'S NAME: Mark Campbell

DECLARATION:

The information in this application form is accurate to the best of my knowledge. I undertake to abide by the principles outlined by Innopharma/Griffith College ethics policy in my research dissertation. I confirm that I have completed a full ethics assessment for my research dissertation as per the college guidelines. I will not begin my primary research until such approval from my supervisor and/or ethics Committee has been obtained.

I pledge to carry out my research according to the Innopharma/Griffith College academic integrity standards. Any results presented in my dissertation will be from my own, original research, I will reference and/or acknowledge any material or sources used in its preparation and I will not plagiarise the work of anyone else.

For Student:

STUDENT SIGNATURE:

DATE:

The research contained within this research dissertation proposal has been approved.

For Supervisor:

Ethics Committee Approval Required: ☐ Yes ☐ No

SUPERVISOR SIGNATURE:

DATE:

For Ethics Committee (if required):

Ethics Committee Approval Given: ☐ Yes ☐ No

ETHICS COMMITTEE MEMBER SIGNATURE:

DATE:

NOTE: Supervisors are responsible for ensuring their students fill in this form correctly and that all ethical areas have been considered.

SECTION 1: DESCRIPTION OF RESEARCH STUDY

1.1 Purpose and objectives of research *[300 words maximum/ use literature review findings to guide]*

The aim of this research is to estimate the burden of influenza in Ireland in terms of DALYs and to investigate the feasibility, suitability, utility and validity of this measurement in practice in the Irish healthcare and health policy setting.

Specifically, I aim to:

4. Explore various methodological approaches to estimating DALYs attributed to influenza
5. Estimate the burden of disease (BoD) attributed to influenza in Ireland.
6. Investigate the feasibility, utility, suitability and validity of DALYs as a measure of the BoD of influenza in Ireland

This exploration is necessary as it may facilitate more accurate measurements of BoD and thus enhance the understanding of and policy-making utility of DALYs. An accurate method of estimating of the BoD of influenza would provide a useful tool to many

stakeholders including healthcare professionals, health policymakers and other industry leaders. An exploration into the applicability of this metric to influenza in Ireland has not yet been formally conducted and published; therefore, this research will elucidate the matter for the first time.

The specific objectives of this research are to:

1. Estimate the DALYs attributed to influenza in Ireland during the 2017/2018 and 2018/2019 seasons using publicly available influenza surveillance data[4]
2. Calculate DALYs attributed to Influenza in Ireland using various disability weights and life expectancies to explore variability in output
3. Determine whether the estimation of DALYs based on surveillance data is a suitable and valid metric for the burden of Influenza in Ireland by interviewing a panel of subject matter experts and other stakeholders
4. Investigate in which capacity (if any) the calculation of DALYs attributed to Influenza in Ireland will be most feasible and useful in practice by interviewing a panel of subject matter experts and other stakeholders

1.2 Research methodology: [***300 words maximum/ detail how you will acquire your primary data (focus groups/interviews/online surveys etc). Proposed questions for questionnaires and/or interviews must be included in the appendix].***

The primary data required for this research is the opinions of subject matter experts and other stakeholders on the suitability, utility, validity and feasibility of using the DALY as a measure of influenza in Ireland. This will require interviews with approximately 8 participants. Interviews will be undertaken in person where possible and virtually otherwise. Interviews will be approximately 20 minutes long. Example of the types of questions that will be asked are listed as follows:

1 **Are you aware of the DALY as a metric of burden of disease?**
2 **Do you think this metric is valid?**
3 **Do you see any value in this metric for estimating the burden of influenza in Ireland?**
4 **Would this metric be useful to you in practice?**
5 **Would this metric be suitable for use in your practice?**
6 **How could you implement this metric into your field?**

7 **Is this feasible?**

SECTION 2: POSSIBLE ETHICAL ISSUES

Answer 'yes' or 'no' to the following questions.

SUBJECT MATTER

Does the research proposal involve:

Research into specific company activities that would be deemed sensitive or confidential

No

Research into politically and/or racially/ethnically and/or commercially sensitive areas

No

Sensitive, personal, professional or corporate issues

No

RESEARCH PROCEDURES

Does the research proposal involve:

Research that might damage the reputation of companies or participants

No

Research that may negatively affect the reputation of Griffith College/Innopharma

No

Use of personal records without consent No

Use of company data without consent

No

The offer of any inducements to participate No

Audio or visual recording without consent No

Using a language other than English No

PARTICIPANTS

Does the research proposal involve:

People who are not competent and/or fluent in English

No

Does your research group include any of the following vulnerable groups

No

(Adults with psychological impairments; Adults with learning difficulties; Adults under the protection/control /influence of others (e.g. in care/prison); Relatives of ill people (e.g. parents of sick children); Hospital or GP participants recruited in a medical facility; persons under the age of 18)

If you have answered NO to ALL questions, please go straight to Section 4.

If you have answered YES to ANY question in SECTION 2, you must fill in SECTION 3.

SECTION 3: STEPS TAKEN TO AVOID ETHICAL ISSUES

[Only fill in this section if you answered YES to ANY of the questions in Section 3. For example, if you answered yes to including participants who are not fluent in English, you might put forward a plan that offers your survey in two languages to take this into account. Another example could be a study where the researcher wants to include information about the care received by children with a long-term condition but it would not be ethical to approach the children directly but it might be acceptable to instead ask parents questions about their child's care. If these plans are acceptable to your supervisor, you may not need to apply for ethical approval from the Ethics Committee].

3.1. If your ethics relates to ***Subject Matter***, outline your action plan to work around any sensitive issues.
3.2. If your ethics relates to ***Research Procedures***, outline your action plan to deal with possible ethical issues in your research procedures.
3.3. If your ethics relates to ***Participants***, outline how you will protect vulnerable persons or those that do not have English as their first language.

SECTION 4: ABOUT YOUR PARTICIPANTS

4.1. Outline your participant profile and why you have chosen them for this study *[Do not provide names except where it is deemed impossible to conceal identity].*

Subject matter experts and other stakeholders in the field of health policy around infectious disease. The typical profile would be a chief pharmacist for the main medicines wholesaler in Ireland. Business unit director for one of the main influenza vaccine company in Ireland. Academic researchers in the field of infectious disease. Personnel involved in health policy making.

4.2 How do you plan to gain access to/contact/approach your participant(s).

I work for AstraZeneca, a manufacturer for one of the main influenza vaccines in Ireland. I can interview my colleagues in work and ask them for connections to health policy makers.

I will contact academic researchers by email to request interviews. I am acquainted with two researchers in the field already and hope to be granted an interview with at least one more.

I will contact health policy personnel by email requesting their participation in a short interview for academic purposes.

SECTION 5: INFORMATION, CONSENT AND CONFIDENTIALITY

5.1 **Participant Information Letter (PIL) for participants**

[You must submit an information letter for participants with this application, as part of your appendices document. For online surveys, it is sufficient to include a paragraph summarising and explaining the purpose of the research at the beginning of the survey. In all other research e.g. interviews, phonecalls, a PIL should be provided to each participant before they are asked for their consent to take part. A template PIL is available in Moodle].

Please confirm below that your information letter covers:

Description of the research topic and method

Yes

Details of what participation will involve

Yes

Rights to anonymity Yes

Confidentiality Yes

Rights to withdraw from the research

Yes

The contact details of the researcher and supervisor (if necessary)

Yes

5.2 **Informed Consent Form (ICF) for participants**

[Informed consent is required for most research. For online surveys, it is sufficient to get the participant to tick two boxes at the beginning of the survey – one to state they understand the research and one to give consent. In all other research e.g. interviews, phonecalls, a signed consent form is required. If the data is gathered online e.g. zoom, a signed consent form can be scanned and sent to the researcher. A template ICF is available in Moodle. The signed ICFs, along with the surveys, audio files or interview notes etc. must be stored in the primary data folder on moodle and can be accessed by Innopharma staff for the purposes of verifying the authenticity of the research carried out and the data collected].

Please indicate below if your research requires a signed consent form by selecting the relevant option only:

Yes: my research requires signed consent and I have attached an ICF in the appendices of my application.

SECTION 6: STORAGE OF DATA

[Please ensure that you are abiding by GDPR and the national Data protection laws https://www.hrb.ie/funding/gdpr-guidance-for-researchers/gdpr-and-health-research/).

*The student is responsible for storage of data and this will be handed over to the college in an electronic format as part of the thesis submission i.e. primary data and completed ICFs where applicable will be added to the primary data folder on moodle. The rationale is to keep data **as long as it is still useful** and there is an intention to use it further **for research** so if this is not the case then this can be stipulated here and a shorter retention period given.]*

6.1. How will you store the research data and for how long? How will you manage data protection issues?

Interview transcripts will be written into word documents and saved locally on my laptop hard drive until thesis submission, after which I will delete the files.

SECTION 7: NON-DISCLOSURE AGREEMENT & STUDENT CONSENT

7.1 **Non-Disclosure Agreement (NDA)**

Will the final dissertation contain any information pertaining to any source what would warrant the use of a Non-Disclosure Agreement (NDA) e.g. industry-based research?

No

7.2 **Student consent**

If a Non-Disclosure Agreement (NDA) is not required, does the Student consent to allow their completed dissertation to be held/published by Innopharma/Griffith College?

Yes

SECTION 8: RECORDING AND RETENTION OF DISSERTATION VIVA

8.1 **Viva Recording**

The Dissertation viva will be recorded. This recording may be used to facilitate assessment by Innopharma staff, a third reader if necessary and/or if requested by the external examiner for the Programme. The recording will be held in line with current GDPR guidelines and will not be made publicly available.

SECTION 9: DOCUMENT CHECKLIST

NOTE: Applicants must attach the following documents in electronic format to the appendix.

Which documents are added to the appendix? Please tick N/A if not applicable:

9.1 Participant Information Letter (PIL) for participant

Yes

9.2 Informed Consent Form (ICF) for participant

Yes

9.3 Questions/survey for interviewees/focus groups etc *(can be in draft form)*

Yes

9.4 Any other documents e.g. Non-Disclosure Agreement

N/A

I confirm that this application is complete and all required documents are included in the appendix.

For Student:

STUDENT SIGNATURE:

DATE:

SECTION 10: APPENDIX

A3. Interview materials

PowerPoint slides used for interviews

The Disability-Adjusted Life Year (DALY) and Influenza in Ireland

An evaluation of the suitability of the DALY as a metric for measuring and managing the burden of influenza in Ireland

Primary Research Interview

The Disability-Adjusted Life Year (DALY) and Influenza in Ireland
An evaluation of the suitability of the DALY as a metric for measuring and managing the burden of influenza in Ireland

The DALY calculation:

DALY = YLL (years of life lost) + YLD (years lives with disability)

YLL = N (number of deaths) x L (average life expectancy)

YLD = I (incidence) x DW (disability weight) x L (length lived in disability)

Key principles

- A metric developed in 1990 by the World Bank to quantify burden of disease; its now coordinated by the Institute for Health Metrics and Evaluation (IHME)
- To inform health and social policy, to monitor health trends over time and across different populations

Main advantages:

- More holistic than mortality/prevalence
- Combines mortality and morbidity into one metric
- Accounts for non-fatal outcomes
- Accounts for time spent in a state less than health
- Accounts for degree of disability

My Research

- Is the estimation of DALYs a suitable and valid metric for burden of influenza in Ireland?
- Is the estimation of DALYs attributed to influenza feasible for and useful to stakeholders in practice?

1. Do you think this metric, based on influenza surveillance data, is valid?

Logically/factually sound

- Answer:

2. Do you see any value in this metric for estimating the burden of influenza in Ireland?

- Answer:

3. Would this metric be useful to you in practice?

• Answer:

4. How could you implement this metric into your field?

• Answer:

5. Is this feasible?

• Answer:

Interview Invite

Dear <recipient>,

I would like to invite you to take part in a research project that I am conducting into the suitability of a metric called the Disability-Adjusted Life Year (DALY) for measuring burden of disease in Ireland. Please see below for further details on myself, the research and what the interview would entail.

Myself

My name is Roisin Quigley. I am a part-time master's student with Griffith College Dublin studying Pharmaceutical Business and Technology. As part of my degree I am required to conduct primary research on an area related to the Life Sciences.

My research

My research is based on the suitability of the Disability-Adjusted Life Year (DALY) as a metric for measuring burden of disease. This metric combines both mortality and morbidity into one metric while also accounting for length of life lost and length of time spent in a

disease state. It is proposed as a much more meaningful and valuable metric for burden of disease, but is not yet implemented in Ireland. If implemented, it could provide a great evidence-base for health policy decisions going forward.

My ask

As part of the research, I want to find out whether health policy-makers in Ireland think this metric would be suitable and feasible for them in practice. This would involve a short (appox 15 minute) virtual or in-person interview comprising 5 simple questions on their opinion of the suitability of the metric for their industry. I would be most grateful if you could take part in this interview, as your opinions on the matter would be of great value.

When

The 20-minute interview can take place any time that suits you between now and the 28th of April.

Once again, I would be extremely grateful if you could take part in this interview for educational purposes. Please let me know if this would be possible and we can arrange a date.

Many thanks and kind regards,

Roisin Quigley

Example of interview transcript

8 **Are you aware of the DALY as a metric of burden of disease?**

No

9 **Do you think this metric, based on influenza surveillance data, is valid?**

Yes but you would need a large sample to be using it for it to make sense. A lot of health metrics are going towards a more qualitative approach so 'how does it make you feel' which is valid because what a lot of health authorities are looking at *quality* of life rather than simply mortality and morbidity. He would need to know how they are weighted it to be sure of validity because one disease for one person could affect them far worse or less than others.

10 **Do you see any value in this metric for estimating the burden of influenza in Ireland?**

Yeah – he and his team just did a white paper for flu for economic burden – as part of that they looked at days lost to work – having to cover childcare – teachers being out of work – whereas nobody really looks at quality of life burden – how did it make you feel? Mental health etc – using this to come at it from a different angle would be of value

11 **Would this metric be useful to you in practice?**

Yeah from a commercial perspective for AZ – if they can get the message out that flu can make you feel bad and have long-term implications – the burden of it – along with the economic side – it would be good for their business

12 **Would this metric be suitable for use in your practice?**

Only if it was well-recognised and widely used

13 **How could you implement this metric into your field?**

From commercial point of view – driving awareness of how challenging flu can be – mortality rates are high with flu – lack of understanding and awareness – using this metric to justify and create awareness

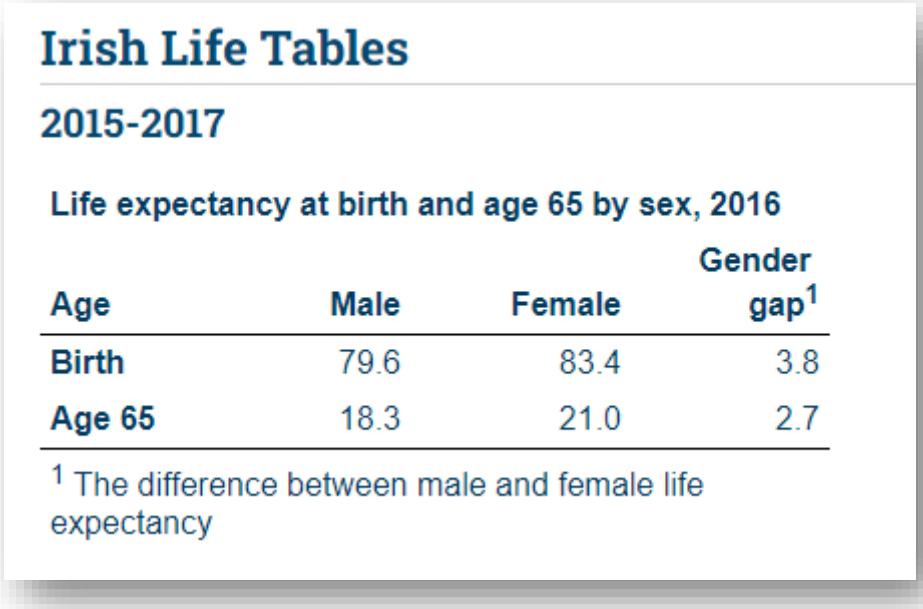
14 **Is this feasible?**

It would be feasible but would require investment and time

AOB: We then spoke briefly about the burden of flu in children, that the burden of flu in children is much higher than for covid, and I informed the participant that the HPSC figures are actually a gross underestimation of population estimates. He said there's not much awareness around the burden of flu.

A4. Calculation materials

Summary of Irish Life tables No. 17 (2015 – 2017) (CSO, 2020)



Irish Life Tables

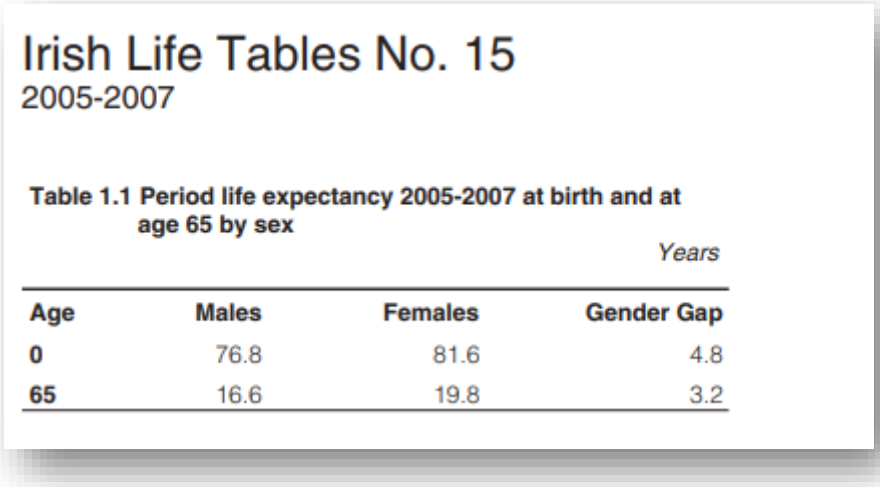
2015-2017

Life expectancy at birth and age 65 by sex, 2016

Age	Male	Female	Gender gap[1]
Birth	79.6	83.4	3.8
Age 65	18.3	21.0	2.7

[1] The difference between male and female life expectancy

Summary of Irish Life tables No. 15 (2005 – 2007) (CSO, 2009)



Irish Life Tables No. 15

2005-2007

Table 1.1 Period life expectancy 2005-2007 at birth and at age 65 by sex

Years

Age	Males	Females	Gender Gap
0	76.8	81.6	4.8
65	16.6	19.8	3.2

Disability Weight tables used from GBD 2019 methods 2000 – 2019 (WHO, 2020)

Annex Table C Health state weights used in WHO Global Health Estimates

Health state	GHE2019	GBD 2019	GBD 2010	GBD 2004
Infectious disease				
Infectious disease: acute episode, mild	0.006	0.006	0.005	0.005
Infectious disease: acute episode, moderate	0.051	0.051	0.053	0.137
Infectious disease: acute episode, severe	0.133	0.133	0.210	0.615
Infectious disease: post-acute consequences (fatigue, emotional lability, insomnia)	0.219	0.219	0.254	

Disability Weight tables used from Japanese DW study (Nomura et al., 2021)

Table 2 Estimated Japanese disability weights (95% uncertainty interval), compared to the GBD 2013 disability weights

From: How do Japanese rate the severity of different diseases and injuries?—an assessment of disability weights for 231 health states by 37,318 Japanese respondents

Id	Health state	Japanese DW	GBD 2013 DW [11]	Factor of two or greater difference	Factor of three or greater difference
Infectious disease					
1	Infectious disease, acute episode, mild	0.012 (0.005–0.022)	0.006 (0.002–0.012)		
2	Infectious disease, acute episode, moderate	0.424 (0.289–0.577)	0.051 (0.032–0.074)	Japan > GBD	Japan > GBD
3	Infectious disease, acute episode, severe	0.242 (0.163–0.340)	0.133 (0.088–0.190)		
4	Infectious disease, post-acute consequences (fatigue, emotional lability, insomnia)	0.074 (0.047–0.106)	0.219 (0.148–0.308)	Japan < GBD	

Disability Weight tables used from European DW study (Haagsma et al., 2015)

Table 3 Estimated disability weights with uncertainty intervals (UI)

From: Assessing disability weights based on the responses of 30,660 people from four European countries

		Disability weight (+ UI)		
Category[1]		Mean	2.5%	97.5%
	Infectious diseases			
Original	Infectious disease, acute episode, mild	0.007	0.005	0.01
Original	Infectious disease, acute episode, moderate	0.051	0.039	0.06
Original	Infectious disease, acute episode, severe	0.125	0.104	0.152
Original	Infectious disease, post-acute consequences (fatigue, emotional lability, insomnia)	0.217	0.179	0.251

Sample of handwritten calculation of DALYs

A5. Dissertation progress report summary

Dissertation Progress Report Summary

14 May 2023

Student Name	Roisin Quigley
Student Number	3065290
Programme	MSc PT
Cohort	10
Module	Dissertation
Supervisor/First Marker	Mark Campbell
Second Reader/Marker	Kathy Clarke
Dissertation Title	The Disability-Adjusted Life Year (DALY) and Influenza in Ireland: An evaluation of the suitability of the DALY as a metric for measuring and managing the burden of influenza in Ireland

Week	**Date**	**Activities for Previous Week**
1-2	31/10/22	Read Dissertation Handbook on 2/11/2022 Submit Proposal part A by 04/11/2022 Started a Draft Dissertation document (using template) by 04/11/2022
3-4	14/11/22	Downloaded Sample Proposal B from Moodle by 11/11/22 Developed draft Proposal Part B by 11/11/22
5-6	28/11/22	Appointed Supervisor on 09/12/22 Contacted Supervisor on 09/12/22 Emailed Proposal B to Supervisor on 12/12/22 Met with Supervisor (online) on 12/12/22
7-8	12/12/22	Received Feedback on Proposal B from Supervisor on 15/12/22

		Began drafting dissertation chapter 1 by 20/12/22
9-10	26/12/22	Continued drafting chapter 1 over Christmas
11-12	9/01/23	Met with supervisor to discuss possibility of revising research topic on 6/01/23 Revised proposal part B in light of new research topic by 9/01/23
12-13	23/01/23	Received feedback on second revision of proposal part B from supervisor on 14/01/23 Met with supervisor online to discuss new approach on 16/01/23 Restarted introduction chapter by 17/01/23 Met with supervisor online to discuss introduction chapter on 31/01/23
13-14	6/02/23	Received Feedback on Preliminary Pages and Introduction Chapter on 02/02/23 Amended introduction chapter in light of feedback by 6/02/23
15-16	20/02/23	Began drafting literature review by 12/02/23 Sent supervisor a copy of literature review for review by 20/02/23
17-18	06/03/23	Received feedback on literature review on 23/02/23 Amended literature review based on feedback and continued drafting the chapter by 06/03/23
19-20	20/03/23	Met with supervisor online on 09/03/23 to discuss literature review Sent supervisor finished introduction chapter for formal review using grading grid on 20/03/23
21-22	03/04/23	Prepared ethics submission and submit by 31/03/23 Sent interview invites to target participants by 03/04/23 Continued drafting literature review
23-24	17/04/23	Completed 6 interviews by 17/04/23 Met with supervisor on 12/04/23 Sent final literature review to supervisor for formal review using the grading grid by 17/04/23

25-26	1/05/23	Revised literature review based on feedback in grading grid by 21/04/23 Began research methods section by 24/04/23 Watched last year's Viva workshop on 26/04/23 Completed mini viva with supervisor on 28/04/23
27-28	15/05/23	Completed research methods section and submit for formal review by supervisor on 02/05/23 Completed the calculation portion of the research by 05/05/23 Completed Findings & Analysis section by 12/05/23 Completed abstract, made adjustments to all chapters by 12/05/23 Met with supervisor on 12/05/23 Implemented final feedback suggestions and produced final draft of dissertation by 19/05/23 Submitted completed dissertation on 19/05/23 Completed full Viva by 26/05/23