Université de Montréal

Ethics in Health Policy for Allergy: A Practical Approach for Decision-Makers

Éthiques en politique en santé concernant les allergies: Une approche pratique pour les décideurs en santé

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RÉSUMÉ

Comme à l'approche d'un tsunami, l'incidence grandissante des allergies affecte maintenant plus de 30% de la population des pays développés. Étant la cause de nombreuses morbidités et un risque significatif de mortalité, les allergies nécessitent des dépenses exorbitantes au système de santé et constituent une des plus importantes sources d'invalidité. Cette thèse a pour but de contribuer à faciliter la prise de décision éclairée dans le développement de politiques en santé en lien avec cette maladie immunitaire chronique en utilisant des principes d'éthique comme outils pour guider le développement de politiques en santé. Le premier chapitre démontre le présent déficit d'analyses des enjeux éthiques en allergologie et démontre de quelle façon les réflexions en éthique peuvent guider le développement de politiques et l'élaboration de stratégies appliquées aux allergies. Les chapitres qui suivront présentent des applications spécifiques des principes d'éthiques ciblant des contextes précis comme des méthodes qui fournissent des outils de réflexion et des cadres théoriques qui peuvent être appliqués par les décideurs pour guider des interventions en santé concernant les allergies et les conditions de co-morbidité reliées. Le second chapitre présente un cadre théorique pour l'évaluation et la priorisation d'interventions en santé publique par la diminution des allergènes présents dans l'environnement basées sur des théories de justice sociale. Les critères entourant les politiques d'évaluation se concentrent sur les enjeux éthiques référant aux populations vulnérables, sur une distribution plus égale des bénéfices pour la santé, et sur le devoir d'éviter la stigmatisation. Le troisième chapitre offre aux administrateurs et au personnel infirmier du réseau scolaire un cadre décisionnel pour guider le développement de politiques efficaces et éthiquement justifiables concernant les allergies alimentaires pour les écoles. Dans ce contexte, les principes de base d'éthique en santé publique et en bioéthique - par exemple, l'*empowerment* des populations vulnérables dans la prise en charge de leur santé et la protection de la confidentialité du dossier médical - servent d'outils pour évaluer les politiques. Le dernier chapitre emploie les principes de base de recherche en éthique comme méthode pour développer un argumentaire en faveur de la réforme des réglementations entourant la production de médicaments immunothérapeutiques. La nécessité éthique d'éviter les risques de méfait à l'endroit du sujet humain dans la

recherche permettra de servir de guide pour structurer de futures politiques en santé publique en égard à la production d'immunothérapeutiques à l'échelle mondiale.

mots clés: Allergies, Bioéthique, Politiques en santé, Santé publique, Analyses de politique, Principes d'éthiques, Cadres théoriques

ABSTRACT

Like a slowly rising wave approaching shore, the growing incidence of allergic disease now afflicts over 30% of the population in the developed world. Being the cause of severe morbidities and a significant risk of mortality, allergy requires huge resource expenditures in health care and is a leading cause of disability. This thesis aims to contribute to ameliorating decision-making capacities in health policy development for this chronic immune disease by employing principles of ethics as tools to help structure policy initiatives. The first chapter will demonstrate the current deficiency of ethical analysis in allergology and show how ethical assessments could have utility in guiding policy developments and treatment strategies for allergy. The subsequent chapters present a focused application of ethical principles within specific contexts as a means to provide reflective tools and theoretical frameworks that could be used by decision-makers to guide health interventions for allergy and co-morbid conditions. The second chapter presents a conceptual framework for evaluating and prioritizing public health interventions in minimizing environmental allergens based on theories of social justice. Policy assessment criteria centre on justice issues pertaining to vulnerable populations, the fair distribution of health benefits, and the imperative to avoid stigma. The third chapter provides school administrators with a framework to guide the development of efficacious and ethically sound food allergy policies for schools. In this context, core principles in public health ethics and bioethics – examples being the empowerment of vulnerable populations in controlling their health and protecting confidentiality of medical information – serve as tools for policy assessments. The final chapter employs core principles from research ethics as a method to argue for regulatory reforms in the production of allergen-immunotherapeutic drugs. The ethical imperative to avoid risks of harm to human subjects in research will serve as a guide to structure future health policies in the global production of immuno-therapeutics.

Keywords: Allergy, Bioethics, Health policy, Public Health, Policy assessment, Principles of ethics, Conceptual frameworks

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LIST OF ABBREVIATIONS

AKA: Also known as

BAU: Bioequivalent Allergen Units

BU: Biological Units

CFCs: Chlorofluorocarbons

CREATE Project: Development of Certified Reference Materials for Allergenic Products and Validation of Methods for their Quantification

CRÉUM: Centre de Recherche en Éthique de l'Université de Montréal

EAACI: The European Academy of Allergy and Clinical Immunology

ECEA: European Committee on Ethics in Allergology

EMEA: European Union European Medicines Agency

EUR: Euros

FDA: American Food and Drug Administration

FRSQ: Les Fonds de Recherche en Santé du Québec

GÉPPS: Group d'Étude sur les Politiques Publiques et la Santé

HFA: Hydofluoroalkane

IHR: In-house reference

IRB: Insitutional Review Board

IRSPUM: Institut de Recherche en Santé Publique de l'Université de Montréal

RAST: Radioallergosorbent test

RID: Radial immunodiffusion

SSHRC: Social Sciences and Humanities Research Council of Canada

UdeM: Université de Montréal

U.K.: United Kingdom

USD: American dollars

WHO: World Health Organization

WWII: World War II

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DEDICATION

To my love, François.

May this thesis serve as inspiration during your future intellectual pursuits.

♥

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INTRODUCTION

The health of our population: many achievements mirrored with new challenges

The deviation of man from the state in which he was originally placed by nature seems to have proved to him a prolific source of diseases

- Edward Jenner

Many people have experienced a feeling where, despite moving forward at a consistent pace, their position seems to remain the same. While this situation may sound like a strange dream, the anecdote of remaining in place despite efforts to progress forward is an accurate description of the current state of population health in many developed nations.

The 20th century was a period of marked health improvement: the average life expectancy rose and rates of child mortality fell dramatically, in part due to significant advances in medicine and nutrition, but also through greater access to clean drinking water and widespread population vaccination programmes, to name but a few public health interventions [1]. By contrast, observations of growing health stagnation – and in some instances, regression [2, 3] – along with mounting concern about a widening of health disparities between population subgroups have become the defining attributes of population health in many industrialized nations [4-8]. In order to help contextualize this epidemiological phenomenon of the 21st century, one can visualize population health as an outcome residing on one side of a revolving door that rotates equally well in either direction.

On the other side of the rotating door reside two forces that are vying to pass through and influence population health achievements; entering from the right are novel health promotion initiatives, while on the left come novel health challenges. Throughout the 20th century, the aforementioned innovations in public health and medicine outpaced the influence of infectious diseases and common medical afflictions, thus health achievements steadily rose. With the rise in life expectancy and changes in society (e.g.,

more sedentary lifestyles, economic globalisation), previous health interventions reached their full capabilities to improve health, and steadily, chronic diseases emerged as the new leading source of pathology. Many chronic diseases entering from the left, such as obesity, cancer, and allergy, have continued to outpace medical and public health initiatives that could effectively prevent or cure these ailments. Now at the point of population health stagnation, researchers and policy makers are seeking new tools in order to improve the efficacy of health promotion initiatives, whether they be in the form of conventional medicine or from fields previously unrelated to health science. One new tool that has recently contributed to the advancement of health initiatives comes from what might appear at first to be an unlikely source: ethics and moral philosophy.

The interdisciplinary melding of ethical analysis and health research emerged from the recognition that the development, enactment, and distribution of health initiatives are intricately linked with many value-based judgements [9-11]. What constitutes as an effective 'treatment' for a given pathology? When bound by resource constraints, which pathologies and ailing populations merit priority for targeted intervention? What duties do individuals, governments, and private corporations have in protecting individual and population health? These questions outline but a few of the many challenging questions raised when devising health policy, and they rarely have easy answers. However, what determines the values and goals that guide our judgements is a matter of *ethics*. Cognizant of the ethical dimensions of health policy, opportunities arise to enhance the decision-making capacities of policy makers through the application of principles of ethics as guides in the development of health initiatives.

This doctoral thesis will present a number of interdisciplinary investigations that merge ethics scholarship and health policy research. The aim of this research project is to employ principles of ethics as a new tool to enhance decision-making capacities and guide the development of health initiatives for a chronic disease that poses a monumental challenge to public health: *allergy*. Before beginning these investigations into ethics and health policy, it will be pertinent to first provide an overview of the aetiology and consequences of this chronic disease.

Caught off-guard: a global pandemic of allergy, and what this entails for our future health

A well-functioning immune system that wages war with the wrong enemy

When there is no enemy within, the enemies outside cannot hurt you.

- African Proverb

Through millions of years of evolution, the immune system has developed into a physiological marvel capable of targeting and eliminating an impressive list of pathogens from our bodies. Though usually a sentinel against disease, if gone awry, the immune system can become a formidable internal enemy. Two general disease categories include *autoimmune* disorders, such as Lupus, where the immune system mistakenly targets elements within the body, and *hypersensitivity* responses to environmental agents, as is the case with allergy.

There are two primary metabolic pathways that orchestrate immune responses, each regulated by distinct classes of antibodies, IgG and IgE. IgG antibodies bind to foreign substances and target them for degradation and elimination by immune cells. IgE antibodies also bind and recruit other immune cells that locally release histamine, a compound that induces inflammation. The inflammation response serves to prevent substances from further infiltrating into the body by inducing swelling and restricted blood flow. In allergy, the immune system perceives common substances, like pollen, as similar to that of a pathogen. However, in allergy the IgE metabolic pathway is favoured. Upon exposure to significant levels of an allergen, an allergic individual releases massive amounts of histamine and severe inflammation results.

Allergic reactions produce a variety of symptoms and morbidities (also defined as *atopic disorders*), with symptoms commonly beginning in early childhood and evolving through specific phases of symptoms until early adulthood. Also known as the *atopic march* [12], allergic sensitivities first manifest in infants as atopic dermatitis, eczema, and urticaria (skin rash, scaly blisters, and hives), and symptoms can later develop into allergic rhinitis (inflamed sinuses) and food allergy. By adolescence, the atopic march culminates in some individuals with the development of allergy-induced asthma. This procession through atopic disorders does not occur with every allergy sufferer; many individuals develop allergy in adulthood and many experience only one disorder. Severe allergic sensitivities

carry a high risk for mortality primarily by inducing anaphylaxis (sudden, severe cardiac and respiratory arrest). Anaphylactic reactions are systemic (delocalised throughout the body) and can arise from exposure to minute quantities of allergens, e.g., when allergic individuals suddenly 'drop dead' following a bee sting or inhaling peanut particles. Some allergy sufferers are fortunate in that their allergic sensitivities can occasionally resolve or attenuate with age, a phenomenon that is likely explained by the maturation and development of the immune and digestive systems [13]. To summarize, allergy can produce a broad variety of morbidities with various degrees of severity. In light of these observations, it is particularly interesting to note that the growth in incidence and variations in allergic symptoms is mirrored by the number of normally benign substances that induce hypersensitivity responses. Moreover, it is common for allergy patients to have sensitivities towards more than one allergenic substance, and sometimes more than seven [14].

Many allergenic compounds are well known; aeroallergens of pollen, dust mite particles, and pet hair are typical examples. However, hypersensitivities exist for hundreds of additional compounds ranging from numerous food proteins, food additives, clothing fibres, certain metals such as nickel, drugs, colouring agents, insect venom, moulds, cockroaches, feathers, and cosmetics. This seemingly endless list of allergenic substances continues to grow as rare case studies of previously unknown allergic sensitivities slowly become well-characterized in larger patient populations. Two notable examples include increasing observations of severe reactions to bed bug bites [15] and from the consumption of red meat [16]. Bizarrely, men have become members of this list of allergenic substances, as a growing number of case studies are reporting women developing allergies towards their male partner's sweat [17] and semen [17-19]. These latter observations are particularly disquieting; not only are we becoming allergic to our environment and common consumer goods, we are also gradually becoming allergic to each other.

A century ago, allergy was virtually unknown. Since then, evidence suggests that a near linear increase in the incidence of allergic sensitivities has accompanied each subsequent birth cohort [20]. Today, the incidence of allergy is approaching almost 50% of the population in several developed countries [21]; in 2005 [22], the results from a population assessment for allergy – accumulated over a period of 18 years – estimated that allergic sensitivities were present in the *majority* of the American population (54%). Due to variations and diversity in methodology, geographical region, and study populations, it is difficult to define which studies provide the most accurate measure of the incidence of

allergic disease. Regardless, the accumulative data indicate that, in the developed world at least, allergy afflicts a very large minority of the population and is comparable to the incidence of other common chronic ailments, such as obesity [23-25]. An even more disturbing observation is that allergies are becoming more common in our *domestic pets*, and born from the recognition of this growing population of allergic dogs and cats is a new industry in hypo-allergenic pet food [26].

What could possibly be the cause of this exploding pandemic?

The (ill-)defined determinants of allergy

Orchestrated by physiological processes of the body, it should come as no surprise that a host of genetic factors correlate with an elevated *predisposition* to the development of immune hypersensitivities and particular atopic disorders (e.g., asthma) [27]. However, genetic predispositions cannot account for the sudden explosion in incidence of allergy since this rapid increase is too abrupt to stem from genetic shifts in the population [28-30]. Such rapid change must originate from socio-environmental and lifestyle transformations.

Too clean, too artificial, or not clean enough? How our living habits prime us for allergy

Disease is not of the body but of the place.

- Seneca (Seneca the Elder)

One long-standing theory for the underlying determinant of allergy is the *hygiene hypothesis* [31]. This widely popular hypothesis suggests that modern day life in the developed world is abnormally clean; we now rarely encounter filth, pathogens, and parasites that were once common in our drinking water, food, and in our urban and home environments. Smaller family sizes, now typical in the developed world, also reduce the transmission of pathogens (e.g., cold and flu) between siblings [32]. While clean living environments provide many benefits to population health, such environments also provide few challenges to our immune systems, which might encourage immune development primed for hypersensitivity responses. An interesting observation that complements this theory is the fact that children who were raised on farms and regularly consumed

unpasteurized milk have exceptionally low levels of allergy [33, 34]. Exposure to the 'less sterile' farm environment and consumption of large amounts of bacteria in milk seem to prevent immune sensitivities towards benign substances.

As is the case with most complicated diseases like allergy, one straightforward unifying theory for its cause is likely an oversimplification. Thus, it is not surprising to see that the link between hygiene and allergy is not definitive and has been widely criticised due to a lack of supporting evidence [28, 35]. There are specific contradictions to theory as well, where prolonged exposure to 'dirty substances' or unclean environments can cause allergy. For example, exposure to dust is a known risk factor for developing allergies towards dust mites [36] and living in substandard housing with poor ventilation and in the presence of vermin and insects, is a significant cause of sensitivities towards cockroaches, mice, rats, and mould [22, 37]. A complementary observation to these findings is that the induction of hypersensitivity responses can occur through exposure to allergenic substances in the work environment. Also known as *occupational allergy*, exposure of workers to aerosol sensitizers, which could – depending on the profession – be anything ranging from enzymes in detergents, to flour dust, to horsehair. In the situation of occupational allergy, the best method to prevent the induction of allergic sensitivities is to enact stringent occupational hygiene protocols that prevent contact between workers and allergenic substances in the workplace [38]. Thus, depending on the circumstances, it appears that a heightened preoccupation with hygiene can either be beneficial or detrimental to preventing allergic hypersensitivities.

Are we victims of our own success? Allergy and economic development

Today's city is the most vulnerable social structure ever conceived by man.

- Martin Oppenheimer

Ask any political leader or economist about their conceptions of an ideal and successful economy and they will likely respond that an ideal economy is one positioned for long-term growth. While economic growth and development is arguably a marker for certain forms of social progress and success, it appears that such development indirectly predisposes society to fall victim to epidemics of allergy and atopic disorders. One fundamental observation that supports this correlation is that allergy predominates in

developed nations; however, as developing nations experience economic growth, so too do they witness a growth in allergy [39, 40].

Interestingly, the fall of communism in the late 1980's enabled researchers to scrutinize the process of economic development and allergy within a reasonably short timeframe. Consider the formally divided nations of East and West Germany [41-45]. Initial hypotheses by allergy specialists reasoned that the impoverished communist East would have elevated levels of atopic disorders due to a higher prevalence of polluting industries and coal-fired power plants in metropolitan centres. Surprisingly, the less polluted and economically advanced West typically had a significantly higher incidence of most forms of allergic sensitisations and co-morbid conditions. Following the fall of Communism and reunification of the country, inequalities in allergy gradually dissipated as the East experienced rapid economic development and a concomitant rise in atopic disorders.

How might economic development cause populations to become prone to allergy? One possible hypothesis is the link between development, increased urbanism, and the acquisition of artificial living habitats. Current economic forces favour the establishment of industries and businesses in urban centres, which in turn motivates a rural exodus of populations into urban areas in order to find more-lucrative employment. However, migrations from rural to urban areas correlate with the development of allergic hypersensitivities [46]. Urban living environments and lifestyles are radically different, or 'artificial', when compared to the natural environments where humanity first evolved. It is theorized [47] that more urban, and thus more artificial, habitats in the form of housing and workplaces with central heating, sealed-off from the exterior natural world, may dysregulate normal immune development. Furthermore, policies concerning the built environment and urban horticulture may also play a role in allergy. Select species of trees and plants appear en masse in parks and along streets, often chosen on the basis of aesthetics. Unfortunately, many of the most popular and aesthetic species produce allergenic pollen, and their monocultivation enables the concentration of allergens in densely populated areas [48].

Environmental degradation: opening the gate to alien allergens and hypersensitivities

The negative influence that environmental degradation inflicts on population health is readily apparent; the detrimental ramifications of polluted air and water are well known examples. Of additional significance, though less well known, is that specific forms of environmental degradation introduce allergenic compounds into novel environments as well as enable conditions that amplify immune hypersensitivity responses. In terms of the latter, high levels of air pollution originating from diesel exhaust is known to bind suspended allergenic particles such as pollen [49, 50]. In addition to compromising the breathing capacities of all people (and especially individuals with respiratory illnesses), smog from diesel exhaust appears to be one mechanism by which aeroallergens become concentrated in the atmosphere and thus raise morbidity levels amongst allergy sufferers, and may also induce hypersensitivities in previously non-sensitized populations [51].

Climate change and the introduction of foreign invasive species are additional factors that induce allergy. Rising global temperatures have lead to new geographical regions that can support the growth of highly allergenic plant species [52]. Moreover, higher average temperatures during the growing season and elevated atmospheric carbon dioxide appear to increase the allergen content of pollen [53]. The accidental introduction of foreign species (e.g., by international trade of consumer goods that unknowingly harbour plants or insects) has caused a sharp rise in previously unknown, severe allergic reactions. A prime example is the surge in anaphylaxis by bites from Red Fire ants, which are indigenous to South America, in the South-eastern United States and in Europe [54, 55].

Common treatment strategies: drugs, immunotherapy, and allergen avoidance

A desperate disease requires a dangerous remedy.

- Guy Fawkes

For many individuals with mild to moderate seasonal allergies, symptom relief is readily available at their local pharmacy in the form of low-cost, over-the-counter anti-histamine drugs, the most common being generic varieties of Diphenhydramine

(*Benadryl*™) and Loratadine (*Claritin*™). More serious atopic disorders, such as asthma, necessitate the administration of potent anti-inflammatory drugs in the form of corticosteroids and anti-leukotriene inhibitors. In the advent of a severe anaphylactic reaction, the immediate injection of epinephrine is the primary means of preventing sudden death by allowing time to obtain necessary medical interventions (e.g., mechanical ventilation to counter respiratory arrest). Nonetheless, these categories of drug treatment only attenuate allergy *symptoms*; they do not contribute towards preventing future allergic reactions or cure hypersensitivity responses (i.e., induce tolerance).

One category of therapeutic is distinct in that it is the only intervention that attends to the root-physiologic determinants of allergy. Allergen-immunotherapy, also known as allergy shots, can induce tolerance, and thus attenuate and sometimes cure allergic hypersensitivities. The treatment regime involves small injections of increasing doses of a problematic allergen over a period ranging from months to years. While it may seem counterintuitive, this controlled exposure of the allergic individual to the allergen can physiologically change their immune functioning, so that the IgG-antibody-mediated immune pathway becomes encouraged and counteracts the IgE-allergy-inducing pathway. Although a tentative cure for certain allergies (i.e., if allergy shots are available for a given allergen), immunotherapy is a less-than-ideal therapeutic strategy. A full course of immunotherapy requires numerous visits to an allergy specialist over an extended period of time. Many patients cannot meet the time commitments required and choose to terminate the therapy prematurely [56]. Furthermore, since the therapy requires exposing allergic individuals to a substance known to induce a hypersensitivity response, immunotherapy carries a small though significant risk of inducing anaphylaxis (recently estimated to occur once for every 1000 administered injections [57]).

Aside from pharmacological interventions, an additional means to minimize allergic reactions is to avoid exposure to allergens. On the basis of “biological rational” [58], methods to eliminate or build barriers to contain allergens are effective means to prevent allergic reactions. Certain allergen elimination or avoidance efforts are relatively simple, such as encasing mattresses and pillows with impermeable covers to provide a barrier against dust mites. However, avoidance of allergens such as seasonal pollen can be extremely difficult or impractical. Overall, numerous treatment strategies exist for allergy and co-morbid conditions. While beneficial, it is worth mentioning that most allergy

sufferers are dependant on pharmaceutical interventions in order to obtain a reasonable quality of life and health security.

A recent legal proceeding concerning refugees epitomizes the absolute necessity of access to pharmaceutical treatments for securing the well-being of many allergy suffers[1]. In April 2011, a Filipino family filed a refugee claim in Canada on the basis of their children's allergies to nuts [59]. The family argued that they could not return to Manila because their sons' severe allergic sensitivities required that they have access to epinephrine auto-injectors (EpiPen), a medication which is not readily available in the Philippines. The Federal Court of Canada concluded that refusal to grant a stay to the family would do irreparable harm to the children.

Societal burden of allergy: from the exhaustion of medical resources to diminished productivity

It is no measure of health to be well adjusted to a profoundly sick society.

- Krishnamurti

The negative consequences of allergic disease are staggering and alarming throughout the world. In Australia, childhood asthma accounts for an estimated 1 million days of school absenteeism each year [60, 61]. In the United States, asthma is the leading source of disability amongst children and is the leading cause of childhood hospitalisations [62]. For adults, allergy is a significant cause of disability amongst the working population and is a leading cause of work-place absenteeism; for example, a survey in the United States found that employees experiencing allergic rhinitis symptoms were absent 3.6 days per year due to the condition, and were unproductive 2.3 hours per workday when experiencing symptoms [63]. In terms of costs due to productivity losses, this same survey estimated allergic rhinitis to be the most costly disease assayed: $593 for allergic rhinitis per employee per year, compared with $518 for high stress and only $40 for coronary heart disease. Mounting evidence suggests that the misery caused by allergy symptoms may be a significant cause of depression and a risk factor for suicide [64, 65]. (Though still a hypothetical association, a possible link between allergies, depression, and suicide provides an explanation as to why suicide rates are higher during periods of the year when pollen

[1] For an interesting case study in public health ethics concerning allergy refugees, see: [66]

levels peak in both the northern and southern hemispheres [64]). Additionally, many people with severe food allergies abstain from dining in restaurants and taking vacations due to an inability to monitor the composition of their meals [67], thus signifying another source of lost economic opportunities, not to mention reduced quality of life.

The main economic burden posed by allergic disease, however, is due to rising resource expenditures for the treatment of allergy and atopic disorders. The following summary of findings presented by Weiss, Haus, and Iikura [60] in a section of a report for the World Allergy Organization exemplifies the exorbitant health care costs of this one chronic immune disease. In 2003, the direct medical expenditures for allergic rhinitis in the United States were estimated at $4.4 billion (USD), *annually*. In Canada, treatment of asthma exceeds $433 million (USD), *annually*. In the United Kingdom, allergic disease accounts for 10% of all primary care prescription costs, *annually*. In Germany, costs associated with the treatment of seasonal allergies exceed EUR 1500 per adult, *annually*. From a global perspective, estimates of the disability burden from asthma are pegged at 15 million disability-adjusted life years (DALYs), *annually*, thus being a level of disability equivalent to that stemming from other common ailments such as diabetes and schizophrenia [68]. Cumulatively, these statistics indicate that the effects of allergic disease far exceed the harm and disability caused to individual allergy sufferers; indeed, this chronic disease is compromising the future sustainability of many social institutions, public health care in particular.

Descriptive versus Normative

The aim of the above informational overview was to demonstrate that allergy is a *very* complex disease, and one that poses an unprecedented challenge to the health of populations of the developed world. Despite over a century of investigation, the exact root determinants of allergy and the physiological mechanisms that initiate hypersensitivities towards normally benign substances still remain to be defined in detail. What is known is that a culmination of multiple genetic, environmental, and social factors is responsible for the current epidemic of allergy. While *descriptive*, this overview of allergic disease contained no *normative* analysis. In other words, judgments, ethical assessments, and proposed moral imperatives concerning the health ramifications of allergy, the population distribution of allergy morbidity, and the legitimacy of treatment strategies, have remained

absent. Such normative reflections will now be the focal point of discussion and will serve to introduce the main problem analysed in this thesis.

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IDENTIFYING THE PROBLEM: ALLERGY RAISES NUMEROUS ETHICAL ISSUES THAT CHALLENGE DECISION-MAKING IN HEALTH

The distribution of allergy morbidity and treatment strategies: a panoply of ethical issues

Any important disease whose causality is murky, and for which treatment is ineffectual, tends to be awash in significance.

- Susan Sontag

Upon initiating this doctoral project, my investigations concerning allergy were approached from a blind or *naïve* normative standpoint. Naïve in this context refers to my having no defined and preconceived moral judgments concerning this disease or its related population distribution of morbidity. Rather, my preliminary analysis centred on conducting a broad literature review in order to acquire knowledge of important issues in the treatment and population incidence of allergy. Concomitantly, training in applied bioethics provided capabilities to analyse observations in allergology and establish normative judgements concerning their ethical significance, in order to be able to propose strategies to address certain problematic aspects of current health policies. Within this analytical strategy, theories and principles of ethics were selected according to their relevance to the particular situation concerning allergy, that is, choosing the right tool for the appropriate task. For example, in the thesis, the implications of health burdens specific to women have been analysed using principles of feminist ethics, while health inequalities were analysed from the perspectives of social justice and methods to define health ineq*ui*ties (unjust inequalities). Below, I present four examples uncovered in this preliminary analysis that pair ethical principles with relevant issues concerning allergy.

Therapeutic developments: ships navigating stormy seas

Access to therapeutics is an indispensable requirement for a normal life for many allergy sufferers. Ethical concerns thus abound when social, legal, and political factors limit

access to life-improving or life-saving drugs. Indeed, numerous challenges exist in terms of access to essential drugs for atopic disorders. One main barrier concerns the elevated costs for therapeutics; namely, the high costs of drugs is a leading cause of medical non-compliance amongst impoverished allergy patients [1]. While this observation alone highlights the need for greater justice in the provision of essential allergy medications, additional questions stem from legal and political factors that encourage elevated drug costs. For one, technological innovation in techniques to administer common generic drugs have enabled pharmaceutical companies to obtain new patents and monopoly rights on previously inexpensive therapeutics [2]. Is this an acceptable business practice given its impact on equitable access and population health? Overall, this situation concerning allergy therapeutics raises questions concerning how to reach an ethical balance between intellectual property rights and innovation, drug costs, and access to essential medicines of great importance for public health [3].

At a broader level, the dichotomy in rates of asthma mortality between the developed and developing world is disquieting. Though the developing world has the lowest population incidence of asthma, asthma mortality predominates in these countries [4]. Thus, the basic medical services that can effectively prevent asthma mortality in the developed world are obviously not available to many impoverished populations of the world. This harsh disparity requires ethical assessment from the perspective of global justice in health.

Children

Unlike most other forms of chronic disease, which primarily afflict adult and elderly populations (e.g., cardiovascular disease, arthritis), allergy predominates in and often first manifests symptoms during childhood [5, 6]. Of greater concern are several observations that children disproportionately experience severe and life-threatening reactions from anaphylaxis and allergen-induced asthma [7, 8]. Since children have little control over their health for which they can be held responsible, several questions arise concerning what duties health officials, childcare workers, and parents ought to have in protecting allergic children from allergic reactions. Furthermore, the onset of allergy in childhood suggests that these allergic individuals may experience significant morbidity throughout their lives, which is not the case with adult-onset diseases. Therefore, questions

arise about whether health interventions and resources for allergy treatment/prevention initiatives in children ought to be prioritized over initiatives for adult-onset diseases.

Women

One prominent critique advanced by feminist scholars in health is that researchers and medical experts tend not to prioritize the specific health needs of women and this in turn aggravates unjust gender-inequalities [9, 10]. Is this true for allergy? Perhaps. Relative to men, women carry a disproportionate burden of allergy morbidity and mortality [11-13], which may suggest that the specific health needs of allergic women are not being met appropriately. Moreover, co-morbid conditions such as asthma complicate many biological processes that are unique to women, namely pregnancy and childbirth [14]. From a feminist ethics perspective, the unique burden experienced by women suggests that the allocation of health resources and interventions for allergy ought not to be distributed equally between both sexes; rather, women merit a higher priority.

Visible and other minority groups

Allergic disease does not discriminate; no individual because of ethnic origin or group identity is secure from developing an allergy. However, the severity and incidence of allergy morbidity is disproportionate amongst ethnic minority groups in developed countries [15]. For example, many new immigrants develop severe allergies five years after immigrating from nations that have a low incidence of allergic disease [16]. Moreover, within indigenous populations of the United States, the incidence of allergy and asthma morbidity is significantly higher amongst minority groups [17], in particular, African Americans [18-20]. While annual deaths from asthma attacks in the United States appear to have stabilized, death rates amongst racial and ethic minorities have shown little improvement [21]. Additional minority groups with elevated incidence of asthma appear to be sexual minorities (gays, lesbians), even amongst members of this minority that do not have risk factors for the disease (e.g., common risk factors such as smoking, low education or socioeconomic status) [22]. These observations raise concerns that factors associated with social exclusion, disenfranchisement, and stigma due to group affiliation may exacerbate allergy and limit access to effective treatments. Ethical policy interventions thus

ought to compensate for the unjust diminished capacities these groups face in terms of their illness and ability to access health services.

When a job determines your allergy, the allergy in turn determines your job

Recall that exposure to sensitizing agents in the work environment can induce debilitating occupational allergic sensitivities. For many workers that develop an occupational allergy, their disease often results in termination of employment and long-term financial insecurity [23-25]. These observations raise several questions concerning what should constitute ethical business practices in the manufacturing of known allergenic substances, and the duties that employers have in protecting the health and employment status of their employees. From a public health perspective, effective health policies to manage occupational allergy will need to address how certain business interests can compromise efforts related to occupational hygiene and health surveillance. While applying stringent occupational hygiene standards and sound health surveillance protocols favour securing the health of employees, these efforts might not be what are most favourable for private interests and profit acquisition. This area requires vigilance and ethical assessment, which could be informed by principles of business ethics in order to provide suitable guides in policy development for occupational allergy.

Humble beginnings as a start, not an end: the aims of this doctoral thesis

The above overview of ethical issues in allergy does not pretend to represent an exhaustive list of topics that would merit further ethical analysis or be the subject of targeted health interventions. Indeed, the following chapters of this thesis that focus on allergic disease (chapters 1-4) will present four additional issues in allergy for ethical inquiry that were not mentioned specifically in the discussion thus far. Due to the vast breath and diversity of ethical issues in allergy and related health policies, it is important to note that the investigations in this thesis are bound by specific limitations. First, this thesis does not aim to outline a comprehensive policy strategy to combat all forms of allergy morbidity. Nor does the analysis aim to develop a universal ethical framework to guide

health policy[2] in dealing with this disease. Instead, this project seeks to reach out to clinical, professional, and regulatory communities that do not specialise in ethics, with the goal of promoting knowledge transfer between the domains of bioethics, health policy, and allergology. This knowledge transfer will take the form of employing principles of ethics to structure policy assessment frameworks that aim to empower 'meso-level' professionals in their daily practice (i.e., the target audience for this thesis are *not* 'macro-level' health policy officials, such as top-level ministers of health in government, but rather professionals typically employed within institutional settings). These frameworks are designed to help strengthen the decision-making capacities of professionals working within a rage of institutional settings (e.g., schools, regional health institutions) who are responsible for the development of health interventions for allergy and co-morbid diseases. The remainder of this chapter will explain these concepts in greater detail.

Unfamiliar territory?: Principles of ethics, decision-frameworks, and health policy development

Before venturing into an analysis and discussion of policy development for allergic disease, certain issues require additional clarification. To begin, it seems reasonable to assume that many health professionals may have modest experience with the field of bioethics, and moreover, the application of ethics in institutional policy development may be for many an unfamiliar methodology [26, 27]. This possibility should come as no surprise since bioethics is a relatively young field of scholarship (originating between the post-war era of the 1950's [28, 29] to the 'technological era in healthcare' of the 1970's [30]), and the specific sub-field or specialty of *health policy ethics* is at a very early stage of development. In 2005, Nuala Kenny and Mita Giacomini, two leaders in health policy studies, described scholarship in health policy ethics to be in its infancy [31]. This expert opinion echoes the views of another ethicist and health policy expert, L. R. Churchill [32]. A 'primordial stage of development' is likewise an apt description of the specialty of *public health ethics*, the origins of which can be traced back to the 1990's [33]. To attend to the likelihood of a reader's unfamiliarity with the application of bioethics in health policy, the

[2] For this thesis, the term *health policy* is in reference to contexts where decisions and analyses centre on establishing regulations or general courses of action without reference to defined individuals. This is distinct from clinical and research contexts, where analyses are more 'narrow and defined' since they typically centre on issues involving interactions between clinicians and patients, or researchers and research subjects.

following discussion will clarify the process of implementing principles of ethics in policy development and the use of ethics frameworks as guides in decision-making processes.

Why is ethics relevant to health policy decisions?

At the outset, the most basic question to ask is why health interventions necessitate an analysis of their ethical implications. The simplest response is that society now demands careful attention to ethics in health contexts [34]. This demand arises from the uncovering of well-known abuses of power in what were blatantly unethical biomedical and epidemiological studies involving human subjects; the Tuskegee [35] and the recently exposed Guatemalan [36] syphilis studies are apt examples, where vulnerable populations (numbering in the thousands of people) were denied treatment for this disease in order to study its transmission and devastating individual and population health effects. Technological innovation in biomedicine is an additional issue of ethical significance because along with the benefits of new technology arise novel risks. Assisted reproductive technologies are a notable example, where along with curing many forms of infertility, science has concomitantly enabled novel means to produce 'designer babies' and the commodification of human reproduction [37]. Further ethical tensions surface from the advent of new challenges to health, as seen with the epidemics of AIDS or allergy; thus, questions abound as to what these emerging problems entail for society as a whole and how we should best address these threats to individual and population health.

In addition to the above societal demands for ethical reflection in health, ethics deliberations and analyses also serve a *practical* function in decision-making and health policy contexts. At the very least, an 'ethics perspective' offers a different way of assessing problems that have long plagued health policy [38, 39, 40 p.4], thus enriching policy discourse by expanding policy development beyond solely monetary, political or evidence-based factors [41]. Health policy development is a complex endeavour that must consider a wide variety of issues ranging from economic, social, cultural, and legal factors, as well as the opinions of diverse stakeholders [42 p.384]. Equally important are the ethical implications[3] of health policy, and in order to have all the 'tools' necessary to achieve the

[3] A detailed overview of ethical issues raised in health policy is provided in the subsequent chapter concerning practical theory in health (*Practical Theory)*. To minimize redundancy, discussion of this topic will be reserved for that chapter.

highest standards in health policy, one tool should arguably be an analysis of the ethical implications [43].

Trevor-Deutsch and colleagues offer an excellent summary of this practical aspect of applying principles of ethics as tools to guide health policy:

> Thoughtful bioethical analysis gives rise to well-reasoned, ethically justifiable solutions based on widely held ethically justifiable moral beliefs that are likely to resonate positively with a society that supports them. It does so by offering solutions that optimize as many ethical considerations as possible, while recognizing that others may be compromised, and explaining why. [44 p.293]

Simply put, by incorporating ethical reflections in health policy assessments, decision-makers are better positioned to determine whether the outcomes of policy are indeed desirable, and if not, are able to identify possible courses of action that could lead to better outcomes [32]. Furthermore, incorporating an ethics analysis into policy development aids decision-makers in being meticulous in their reasoning by requiring decisions to uphold facts and arguments and not merely personal beliefs or self interest [45]. Using widely held principles of ethics as guides helps define goals and core values that should be met by health professionals and the policies put in place. In turn, these guides aid decision-makers to have greater consistency and transparency with their decisions, and as such, they gain additional means to explain how and why they arrived at their decisions [41].

Indeed, the outcomes determined by health policy decisions, such as the structuring of health care systems, undoubtedly have profound ramifications for society. This fact alone highlights the importance that policy decisions be based on important societal values and attend to a range of ethical considerations. How exactly is this done and what strategies can be employed in order to structure ethically sound health policies that complement core social values?

Implementing ethics in health policy development

One common method to plan ethically sound policies is to ensure that policy development is structured according to a *framework* composed of defined ethical principles and theories. These principles and core theories of ethics represent general values that uphold fundamental ‘rules’ (e.g., ensure fairness, avoid harming others, the need to protect

the vulnerable) that orient ethical analysis of specific cases or within specific contexts [46 p.12-18, 47]. Determining which principles should comprise an analytical framework is influenced by many factors (e.g., current knowledge of risks and benefits inherent to a situation, preconceived goals or common social values, general intuitions on how best to handle a dilemma stemming from previous experience). What is most important to note is that each ethical principle focuses consideration towards relevant moral issues, which in turn "establish and define important concepts and can be used to describe important aspects of the positions we hold" [48]. Thus, consider the example of determining whether a health care system should subsidize the implementation of a novel technology [49]. In addition to issues of financial feasibility and medical efficacy, the merits of this technology can also be assessed with regards to its foreseen distribution of benefits and risks across a population. Guidance on this front can surface from a framework structured on the ethical principle of utility maximisation (maximise benefits while minimising harms) along with the need to ensure a fair distribution of utility within society (will certain groups inherently benefit from the technology while others will not?) [44]. Following this assessment, if the technology is expected to produce greater harms than benefits for society, ethical reasoning guided by this framework would suggest that this technology does not merit government subsidies. Another problematic situation would be if the technology could provide a net benefit but these benefits will be unequally distributed (e.g., the technology can only be implemented in urban areas). Once again, ethical reasoning might question whether this unequal distribution of benefits is fair and acceptable, and thus provide valuable insights when debating the merits of this technology.

While exercises in normative ethics are typically 'prescriptive' in nature [31], such that normative conclusions aim to determine (or proclaim) what ought to be done in specific circumstances, decision frameworks should not be perceived as prescriptive tools for health professionals. To expand, decision-making frameworks do not aim to be authoritarian in structure or implementation. That is, these guiding frameworks do not 'order' health professionals to radically change their practice parameters or to conform to the values and ethical principles inherent to each framework. Indeed, ethics frameworks are not the 'rule of law'. The function of these frameworks is instead to help indentify and articulate the issues and values at stake in decisions-making processes, which in turn can empower health professionals so that they may better-evaluate various options and make better-informed choices. Ethics-based frameworks "should therefore be understood less as

norms that are applied, in the model of "applied ethics", and more as guidelines that are *interpreted and made specific* for policy and clinical decision making" (original emphasis) [50 p.182]. Overall, employing ethics frameworks as guides does not imply dictating the content and conclusions drawn from an analysis. Rather, employing frameworks in health policy discourses "encourages broader and more robust moral discussion, requiring personal sensitivity as well as a trained appreciation of the many issues that can be relevant" [48 p.397]. To conclude, frameworks in health policy development serve to improve a professional's decision-making capacities but do not stipulate what these decisions must be.

The development of frameworks to guide decision-making processes in health is now a nearly ubiquitous research activity in bioethics scholarship, and ethics frameworks constitute a primary instrument for ethical analysis in health contexts [44]. A diverse range of frameworks are now available to health professionals as guiding instruments in a breadth of decision-making processes. Notable examples include: frameworks for public health practice [45, 51] and policy [42], frameworks to guide decision processes for nurses [52] and other clinicians [53], and principles that guide professional duties in pandemic flu crises [54, 55] and following acts of bioterrorism [56].

Implementing ethics analyses in health policy: Easier said than done

Though bioethics scholarship is continually developing ethics frameworks as tools to guide policy development, the current implementation of ethics analyses by decision-makers in health faces notable challenges. For instance, though an analysis of ethical issues can provide valuable tools in decision-making processes, Gibson and colleagues [57] question whether such tools are actually available to most decision-makers. This does not appear to be the case since understanding in how to implement ethics analysis appears to be limited amongst most health decision-makers. For example, Gibson et al. note that "[a]lthough healthcare decision-makers are increasingly successful in using clinical evidence and applying economic analyses to set priorities, they are less confident that their priorities are *ethically* sound" [57 p.51] (emphasis added). This current lack of familiarity and confidence in executing ethically sound decisions in healthcare contexts occurs at a period where experts observe a significant and growing demand for practical approaches to incorporate ethics assessments in health service organizations [57].

The above observations are indicative of a broader problem amongst decision-makers in health [41]. Though policy specialists increasingly recognise the utility of ethics analysis in policy development, these specialists remain unfamiliar with ethics as a field of study and lack experience in employing sometimes abstract theories of ethics in day-to-day practice. Therefore, while the targeted end-user for ethics-based frameworks are decision-makers in health (i.e., the professionals that will determine what policy decisions are put forth and implemented in actual, real-world settings), lack of knowledge about the scope and use of ethics frameworks means that these professionals may be incapable of developing these tools on their own. This division between developers of ethics frameworks and actual decision-makers is due to what has been described as a 'two communities' divide between health professionals [58, 59]; the expertise of health professionals has become so specialised that transferring knowledge from one area of expertise to another is often difficult [60]. It is here where the interdisciplinary field of bioethics demonstrates its ability to 'bridge' disparate communities and domains of knowledge.

The role of bioethics: Ethics frameworks in health policy necessitate a knowledge transfer activity

As noted by Jocelyne Saint-Arnaud [61 p.19], the nature of the field of bioethics is one that situates itself not exclusively at a theoretical level, nor at a strictly practical level, but rather at a dialectic space between the two. This 'theoretical level' is in reference to the theory-heavy discipline of Philosophy, where abstract principles and theories of ethics are typically conceived and serve to advance debates centring on questions of 'what ought one do in a hypothetical situation'. The 'practical level' is in reference to real-world health contexts where health professionals face immediate dilemmas and ask questions such as 'what must we do in this immediate situation'. Occupying the space in between, bioethics provides a 'Rosetta Stone' function,[4] and can serve to implement theoretical tools to aid in the resolution of actual dilemmas in health [45]. Being familiar with both philosophical theory and practical challenges in health care, the bioethicist can be a key actor in the

[4] The mere term, *Bio-ethics*, is representative of a field of study aimed at knowledge transfer between theoretical and practical domains of inquiry. As described by Hubert Doucet: "It is clear when looking at the origins of the term [bioethics] that it is was coined with a view to bringing two worlds that normally ignore one another into dialogue" [62 p.14].

translation of knowledge between these two disparate contexts. In turn, this role of 'knowledge translator' enables the systematic incorporation of ethical principles in decision-making processes by uncovering methods to make this process readily tangible to decision-makers in health through the development of ethical frameworks as guides in policy assessment strategies.

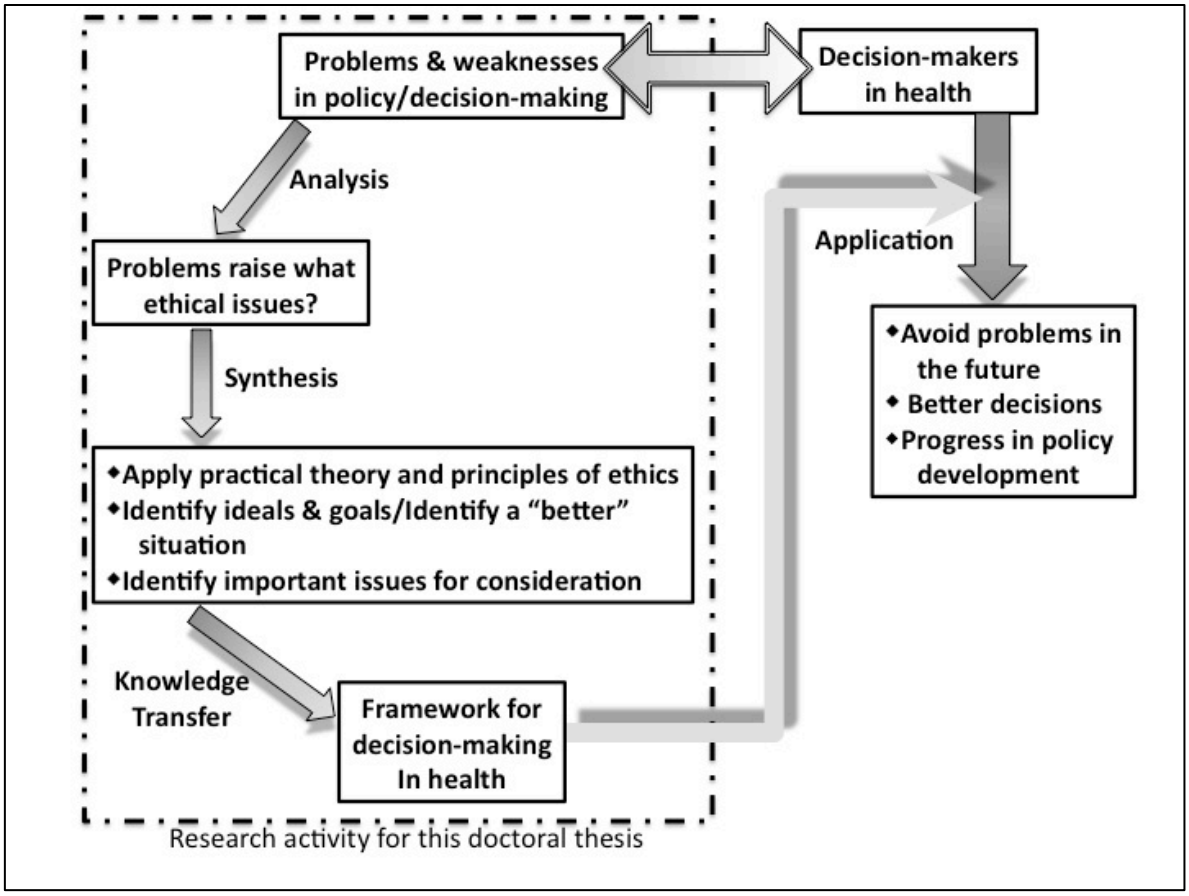
The concluding part of this chapter will provide an overview of the main research goals and analytical methods employed in this thesis, i.e., in relation to the knowledge translation activity of developing decision frameworks for allergic disease. Only a brief explanation will be given here of the research methods, as the broader methodological framework of the thesis will be explained in detail in the subsequent chapter (Methodology).

"An implicit methodology" for analysing allergy

The above title is derived from the work of Hubert Doucet, who offers a description of one form of bioethics methodology [62 p.21]. Described as an "implicit methodology", Doucet illustrates a bioethics analysis executed by a multi-professional health care team as a four-step process. The first step comprises a 'fact finding' activity that consists of gathering relevant information on the ethical dilemma faced by the health care team (e.g., gather all necessary information concerning an end-of-life decision to determine: is the patient competent to provide consent?; what are the treatment options for this patient?; are family members are implicated in this process?; etc.). Having gathered the relevant information, the analysis moves to the second step, which consists in identifying the ethical issues at stake. At this point, evaluations ask 'what exactly is the problem under consideration?' (e.g., does the dilemma arise from new medical technologies?; are ethical tensions due to a clash of values between a patient and a health care professional?). With the main ethical issue identified, the analysis moves on to the third step involving the application of principles of ethics as guides for thinking through the dilemma. To expand, if a dilemma centres on determining what is the best treatment option for a patient, ethical

analysis may reflect upon principles[5] of *beneficence* and *autonomy* in order to assess what is 'good' for the patient — as medicine defines it — and whether a given treatment option will uphold a patient's wishes. The fourth and final step is the *execution*, where the guidance provided by the principles aids the health professionals in identifying a reasonable course of action aimed at resolving the dilemma. Though in reference to ethical deliberations in health care teams, this 'implicit methodology' is typical of thought processes in bioethics (for another example, see: [40 p.204]), and indeed, is a conceptual process that is replicated in this thesis (Figure 1).

Figure 1: Situating the research activities and conceptual methods used in this thesis



The main research questions and activities of this thesis can thus be summarized as a knowledge transfer activity at the nexus of an ethical analysis of allergic disease.

[5] These two principles serve as examples, and certainly additional ethical considerations are relevant to end-of-life decisions that have not been mentioned here. A detailed explanation of these principles is presented in 'Practical theory', through an overview of theory and principles of ethics in health. The following two principles serve as examples; certainly additional ethical considerations are relevant to end-of-life decisions that have not been mentioned here.

Investigation begins with a broad and extensive review of the medical, policy, and public health literature concerning allergy and co-morbid conditions in order to identify challenges faced by health professionals/decision-makers and significant weaknesses in current allergy treatment strategies (i.e., identify challenges and problems concerning allergy that health professionals within institutional settings encounter on a common basis [Figure 1; double headed arrow]). This represents the initial 'fact finding' activity. Identified challenges and weaknesses then become subjects for focused assessment, where a given challenge or weakness is a particular *case* or *context* for ethical analysis. This analysis segment is analogous to the second step in the implicit methodology that serves to identify the main ethical issues that are inherent to the case or context at hand. Moving on, the subsequent research activities centre on identifying principles of ethics that are pertinent to the context. Principles are chosen based on their ability to provide guidance in thinking through the dilemma at hand (step 3). This pairing (or synthesis) of principles to the context is based on whether the principles help identify important issues for consideration, or help define what a 'better' or more 'ethical' outcome would be if the case at hand were to uphold the principle under consideration. These principles are subsequently used to structure decision-making frameworks for the chosen context, with the aim of providing a readily implementable tool to guide health policy interventions for allergy. Research activities end at this stage; thus, how the frameworks established herein are executed (step 4) in actual health policy procedures are not examined in the thesis. However, the overarching aspiration is that these frameworks become applied by health professionals in common practice with the end-result of helping improve decision-making capacities, and thus, health policy development overall within institutions.

Having delineated the research activities and general analytic process employed in this thesis, the discussion will now move to a detailed presentation of the thesis' methodological framework.

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METHODOLOGY: A HYBRID MODEL

Choose always the way that seems the best, however rough it may be. Custom will soon render it easy and agreeable.

- **Pythagoras**

Churchill in 2002 [1] and Kenny and Giacomini in 2005 [2] described health policy ethics as a new sub-field of scholarship in bioethics and policy analysis. Being in its infancy, investigations in health policy ethics present certain challenges, as well as opportunities, when determining the appropriate methodological strategy to employ, and for our purposes, when analysing allergic disease. The main challenge is that there are currently no widely endorsed methods or 'tried-and-true' frameworks for health policy ethics [2]. This is unlike the situation with clinical and research ethics, for example, where decades of scholarship has produced what are now widely accepted — or at least well-known — bioethics frameworks and assessment models (e.g., the framework of *Principlism* [3] for clinical ethics, and the Declaration of Helsinki [4] guidelines for research ethics[6]). This challenge, however, also presents an opportunity to be innovative in this thesis with regards to the application of bioethics frameworks and core principles of ethics. Innovative in this situation is in reference to the opportunity to be 'flexible' when determining the composition of ethical principles to be employed in the development of decision-frameworks for allergy that target a broad range of professionals employed within a diversity of institutional settings. Flexible in this context does not imply random or arbitrary, but instead refers to the fact that a rigid application of one theory or one particular framework of principles would be insufficient, thus signifying the need to consider multiple principles in bioethics and related sub-fields.

This insufficiency is due to one primary reason, namely the broad scope and diversity of dilemmas observed in allergy. Recall from the previous chapter that allergy raises what has been described as a 'panoply' of ethical issues whose contexts vary widely. To expand, challenges inherent to the allergy epidemic implicate contexts ranging from clinical practice, to pharmaceutical innovation, to public health interventions, to the

[6] Both of these frameworks will be described in the subsequent chapter on *practical theory*. To avoid redundancy, core principles of clinical and research ethics are not described in detail here.

distribution of health interventions, and many more. Accordingly, the development of policy assessment frameworks for allergy will target the needs of a diversity of decision-makers in health, ranging from clinicians, to government regulators such as policy analysts, to regional public health officials. While implementing one specific analytical framework of principles within one context might be sufficient for ethical analysis, this framework would likely be ill-equipped for analysis in a different context [3 p.376-377]. For example, it is widely accepted that ethical principles developed for clinical contexts are ill-suited for analysis of population-level contexts in health [5, 6]. Therefore, in order to address the multiple contexts, or 'layers' of complexity, inherent to decision-making for allergy, this thesis will implement a mixed or 'hybrid model' framework of ethical principles. This hybrid model thus includes several core principles of ethics developed for 'individual-level' contexts (namely, core principles of clinical and research ethics) and 'population-level' contexts (namely, core principles of public health ethics and theories of social and distributive justice). Inspiration for implementing a hybrid model in decision-making contexts for health is derived from a similar model published in 2006 by Eileen Morrison in her book, *Ethics in Health Administration: A Practical Approach for Decision Makers* [7]. The remainder of this chapter will explain this 'Morrison-inspired' hybrid model and show how it is adapted to meet the research goals of this thesis.

Individual- and population-level principles: a hybrid model

Written for a target audience of health administrators, Morrison developed a comprehensive ethics framework to help improve the decision-making capacities of administrators in day-to-day practice (health administrators in this context are upper-level management of health care institutions, such as hospitals). It is typical for health administrators to encounter a broad diversity of ethical dilemmas in their careers. These issues range from resolving conflicts between staff and upper-management, to determining what quality of services is appropriate for patients, to establishing what duties should be upheld when serving the needs of the broader community, such as defining what services should be free of charge in order to assure that underprivileged community members have access to necessary health services. Due to this diversity of ethical issues, Morrison does not ascribe to one particular theory (e.g., utilitarianism), or one well-recognised framework of ethical principles (e.g., Principlism), or centre ethical assessments at only one 'level' of

analysis (e.g., community-level). Instead, Morrison describes ethical dilemmas as occupying various levels that influence ethics decisions, and thus constructs a framework that contains principles pertinent to each level of analysis.

The first level of ethical analysis pertains to the personal character of the administrator and ethical nature of their interactions with other staff members. To address ethical issues at this level of analysis, Morrison's framework implements principles of virtue and personal ethics (e.g., Martin Buber's theory to uphold a minimum I-You relationship when interacting with others). Moving one step outwards, the next level of ethical issues centre on policy decisions pertaining to individual patients within clinical contexts. Here, Morrison implements Beauchamp and Childress' framework of Principlism as the basis for ethical assessments, composed of the four cardinal principles autonomy, beneficence, nonmaleficence, and justice. Moving further outwards, the next and broadest level pertains to the organisational structure of the hospital and its interaction with the community. At this level, Morrison centres ethical analysis on issues related to social justice when analysing issues such as the fair access to essential health services. Overall, Morrison's framework constitutes somewhat of a 'toolbox' containing a diverse collection of theories and core principles of ethics. The context (i.e., level of analysis) will determine which 'tools' will be used to help resolve the ethical dilemma at hand.

Morrison's methodological approach and analytical strategy share many similarities with the research question and goals of this thesis. For one, as in health administration, decision-making contexts for allergy implicate a broad range of issues that require ethical assessments at multiple levels, namely individual- and community-level contexts. Thus, in order to have a full set of tools to address ethical issues in allergy, this thesis will take as inspiration Morrison's approach in order to structure a context-specific, hybrid model framework for analysis. To attend to individual-level contexts, this thesis will employ Principlism as a basis for analysis. However, within broader community- or *population*-level contexts, analysis will employ core principles of public health ethics and theories of distributive and social justice. Moreover, Morrison's approach aims to empower health administrators within health care institutions, or what is defined herein as 'meso-level' health professionals implicated in 'institutional-level' policy development. Thus, similar to Morrison, the frameworks proposed in this thesis target meso-level health professionals employed in common institutions, such as childcare facilities, and not 'macro-level' health officials employed with the upper echelons of government, such as ministers of health

tasked with determining broad resource allocation decisions for national health care systems.

While this hybrid framework (i.e., toolbox) will include a diversity of ethical principles (i.e., tools), it is necessary to be clear that these principles are not a random assemblage. Instead, these principles have been selected on the basis of whether they provide valuable insight and the ability to analyse the contexts and cases that will be presented in Chapters 2-4. In other words, these principles have been selected based on their pertinence to the ethical dilemma at hand and their relevance to the epidemic of allergic disease. The following two examples concerning justice theory and virtue ethics will help explain further what is meant by pertinence and relevance, and thus will demarcate important limitations of scope inherent to this framework and subsequent analyses.

As a first example, unlike the case of Morrison's framework, the framework in this thesis does not use virtue ethics or contain any principles pertaining to the moral character of decision-makers in health. Morrison devotes much of her analysis towards the moral character of decision-makers (e.g., does one uphold integrity?) as a means for providing guidance in situations such as conflicts between staff and management. Assessments of this sort are not relevant to the analyses executed in this thesis. As defined in the previous chapter, the research activities of this thesis stop at the level of proposing policy assessment frameworks for institutional decision-makers in health. Thus, attributes of the decision-makers targeted for these frameworks are not relevant to this thesis and therefore, ethical principles pertaining to the moral character of decision-makers are excluded from analysis.

Within the field of health policy, justice assessments are commonly divided into four main categories that define the context and criteria analysed within equity assessments [8, p.30]. One category is *intergenerational* justice, which centres assessments on issues related to the maintenance of resources and health services across generations. An additional category is that of *deliberative* justice, where equity assessments focus on the full and effective participation of affected parties and relevant stakeholders in decision-making processes. A third category is *social* justice, where strategies to minimise health disparities between groups rest at the nexus of equity analysis. The final domain is that of *distributive* justice, which entails analysis of what constitutes a fair distribution of benefits and burdens of health policies across individuals and communities.

An analysis that concentrates on all four categories of justice in health policy would be too expansive for this doctoral project. This thesis will thus limit analysis to two domains, that of distributive and social justice. The reasons for selecting these categories are twofold. Of primary importance is the fact that a recent wave of research has raised concern about the existence of significant health disparities amongst allergy sufferers, disparities that correlate strongly with distinct communities and social determinants [9-13]. These concerns indicate that equity issues associated with health disparities and the distribution of health interventions across various communities are currently of great relevance to decision-making processes for allergy. This does not imply that intergenerational or deliberative justice issues are of no relevance to allergy; however, the latter category is at arms length to the knowledge transfer activities of this thesis and the former is arguably of less significance at this point in the allergy epidemic. To expand, the frameworks developed in this thesis focus on providing guidance directly to decision-makers in allergy. The interactions between decision-makers and relevant stakeholders, or stakeholder deliberations in health policy development, are another area of study altogether, and thus beyond the scope of this doctoral project. And lastly, the incidence of allergic disease has only recently reached epidemic proportions over the course of the past 30 years [14, 15]; this suggests that an intergenerational analysis of allergy may be premature, and as such, theories of intergenerational justice are not included in the analytical framework.

Having explained the methodological approach for this thesis, the following chapter will provide a detailed discussion of the ethical principles and core theories that will be implemented to analyse allergic disease and subsequently develop individual policy assessment frameworks for decision-makers in health. This chapter on *practical theory* will serve two functions, one being to familiarise the reader with these principles prior to their implementation in ethical analyses for allergy. Also included in this 'familiarisation process' are explanations of challenges inherent to the use of specific theories in policy development, such as conflicting accounts of social justice theory. The second function is that this discussion will provide practical examples of how ethics can be used when structuring and assessing health policy so that the link between ethics and meso-level policy assessment parameters will become more apparent for readers unfamiliar with bioethics. Principles of ethics are grouped into two categories as defined by the methodology, namely individual-level and population-level principles.

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PRACTICAL THEORY: PRIMARY PRINCIPLES OF ETHICS IN HEALTH AND THEIR APPLICATIONS IN POLICY DEVELOPMENT

A theory must be tempered with reality.

- Jawaharlal Nehru

Having delineated the main research question and methodological approach employed in this doctoral thesis, this chapter will present a series of ethical principles and concepts that are integral analytical tools employed in this thesis. The application of these principles within the specific context of allergic disease, however, will not be the primary focus at this point in the thesis; a brief summary will be provided by way of conclusion to this chapter, and serve to introduce the subsequent chapters (1-4) that focus on ethical issues in diverse contexts of allergic disease. Instead, the goals of the present chapter are to contextualise principles of ethics relative to general health circumstances (i.e., will not focus on one disease, or one treatment strategy), and show the utility of these principles as guides in decision-making frameworks for health policy that aim to empower a range of professionals working within diverse institutional settings. This chapter thus provides a broad description of practical ethical theories used in analysing issues in health interventions and policies, and explains how these theories can help identify important considerations for structuring policy interventions. With that said, it is important to explain further the main goals of this chapter and the methods chosen to present a set of principles of ethics and their pertinence to health policy.

It is necessary to first state what are *not* the goals of this chapter. The following discussion of ethical principles will not present philosophical debates concerning the strengths and weaknesses of principles and theories, or argue that one principle is superior to another in a specific context. Rather, the principles will each be presented as separate concepts, and a section entitled *Theory application* will then explain the utility of employing the principle or main concepts within decision-making frameworks. The reason for this presentation is twofold. First, this layout replicates the strategy employed by

Morrison in her framework for analysing ethical issues in health administration, written for an audience of health administrators implicated in meso-level policy development for health care institutions [1]. Following Morrison's heuristic approach to applied ethics, the descriptions of abstract principles of ethics will be presented with an array of health professionals in mind as end-users. Knowing that many health professionals have limited knowledge of ethics principles and their application in the context of health policy, these abstract principles need to be explicitly formulated for an audience of 'non-experts'. Second, the utility of this approach is that it promotes knowledge transfer between distinct domains of scholarship and professions. Recall that this dissertation also aims to contribute towards knowledge transfer activities by applying ethical theory in the development and analysis of health policy. Thus it is important to note that the development of additional ethical theories or further advancing philosophical debate about principles of ethics is not the purpose of the current chapter, nor the thesis more generally.

Finally, this chapter does not seek to provide an exhaustive depiction or analysis of all known or popular ethical principles employed within health contexts, which number well over a hundred principles. Rather, the intention is to provide decision-makers in health care and public policy with enough background to be able to understand and evaluate the ethical arguments and decision-frameworks used in this thesis. Recall from the previous chapter that the chosen analytical strategy will include a range of principles and theories that are representative of ethical issues occurring at both the micro-level (*individual*) and macro-level (*population*). Within this chapter, principles of ethics will be presented as two groups based on the individual versus population distinction. The discussion will now begin with an overview of principles developed to help guide decision-making in health where consideration of defined individuals, such as patients, forms the basis for ethical reflection. To conclude, the remaining principles of ethics will expand their focus towards ethical issues related to the health of populations and specific communities.

The basic tenants of Principlism: a guide for 'micro-level' decision-making in health

It would not be an over exaggeration to assert that one of the most important contributions to bioethics scholarship in the late 20th Century was the *Principles of Biomedical Ethics,* by Tom Beauchamp and James Childress [2]. First published in 1979

and now in its 6th edition, this book has become a cornerstone of medical practice, biomedical research, and bioethics[7]. Also known as *Principlism* (or the Four Principles Model), Beauchamp and Childress developed a comprehensive framework for biomedical ethics based on four cardinal principles widely accepted in North America and Europe: respect for autonomy, nonmaleficence, beneficence, and justice. [These principles are very similar to the three principles first enumerated in the influential US Belmont Report [3], *Ethical Principles and Guidelines for the protection of human subjects of research* (autonomy, beneficence, justice; first published in 1979), and reaffirmed in the Canadian *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans* [4] (1998/2010)]. While Beauchamp and Childress do not claim that these four principles constitute a general moral theory, taken together they do provide an effective framework for identifying and reflecting on moral dilemmas in health [2, p. 15]. The primary function of these four principles, in the context of health care service delivery, is to provide clinicians with a relatively simple means ('rules of thumb') to evaluate and deal with ethical challenges arising in a clinical context, particularly with regards to addressing the needs of individual patients and upholding professional duties and responsibilities.

Respect for autonomy

A central tenet and strongly held principle in most Western societies is the need to protect individual liberty, usually inscribed in human rights documents or charters, because every person must have significant freedom to determine their individual life goals and ambitions. While this right to 'self-determination' is virtually undisputed in the Western world, the ability of individuals to exert a significant degree of control over their lives was largely absent (upto the 1970s) in the context of medicine, biomedical research, and health policy [5]. Until the 1970s, clinicians (as well as researchers and public health professionals) typically assumed the role of primary decision-maker with regards to a patient's treatment regimen. This paternalistic approach towards the provision of health care operated from viewpoint that patients are often ill informed concerning the complex details of their treatment, and so it was up to clinicians to decide what was in the best interests of their patients. This presumption, however, came to be recognised as highly

[7] The 5th edition alone is cited in over 1000 publications.

problematic, both in the clinical and research contexts. Clinicians (or researchers) are in fact not best placed to determine what is in the 'best interests' of a patient (or research subject); such assessments necessitate consideration of the personal values and life ambitions of the individual, and only they (or their surrogate) can define what those personal values are and what they wish to accept as treatment (or in the context of research). This recognition that patients should be treated as autonomous individuals empowered to consent to treatment options gradually replaced the prevailing paternalistic culture of medicine (and biomedical research) and reoriented medical practice, professional guidelines, and health law, towards a new focus on the patient as the primary decision-maker in a shared patient-clinician decision-making relationship. It is now standard practice for health professionals to devote time and resources towards educating patients about the risks and benefits of treatment options in order to empower their patients to make free and informed decisions [1, p. 26-29], including the option to refuse all forms of treatment. The mandate to inform and promote voluntary choice – the basis of informed consent – is also now mandatory for participation in clinical trials or research projects involving human subjects [6]. An additional noteworthy aspect of patient autonomy is the notion that provision of truthful and trustworthy information from both the patient *and* clinician are essential to enable truly informed decisions.

Following from the tenet of informed consent and individual choice, respect for autonomy also requires that these choices be kept private or confidential, and that individuals have the power to determine who will know about their medical condition or their participation in research. Also described as "autonomy as confidentiality" [1, p. 29-31], the need to maintain privacy/confidentiality of medical records and health information recognises the fact that such information can be sensitive, and compromise an individual's choice or do harm if confidentiality is breached and information accessed by a third party. For example, most individuals would likely hesitate to seek treatment for stigmatising conditions such as HIV or mental illness if others (e.g., community members, employers) could become cognizant of their condition and/or need for treatment. Indeed, breaches of confidentiality pose significant risks for both individuals and groups since sensitive medical information can be used as a tool to stigmatise and discriminate [2, p. 293-312], notably by denying employment opportunities or eligibility for private health or life insurance.

Moving beyond clinical contexts, the principle of respect for an individual's autonomy also sets out an important guiding principle for health policy development and decision-making frameworks.

Theory Applications

Attention to this first principle, autonomy, can sensitise health professionals and decision-makers to the need to consider an individual's choice as a *primary* and not a secondary concern. At a minimum, it is essential to acknowledge a person's right to hold views, to make choices, and to take actions based on personal values, even if these are contradictory with what a decision-maker might think is the best course of action [2, p. 63]. Thus, when implementing policies that will influence the health of others, decision-makers and professionals need to assess whether such policies are unduly paternalistic or compromise the ability for individuals to make decisions concerning their well-being. If policies are known to limit choice or restrict the ability to give informed consent, this could indicate a need for reform. For example, a standard protocol for an institution might mandate that an individual's consent be given in writing once the individual has been fully informed of their treatment options by a health professional. This protocol undoubtedly aims to protect patient autonomy; however, this policy can be problematic since the individual usually has to give consent in a short timeframe, often when they are in pain or less than fully autonomous. An arguably better approach would be to recognise that written consent is part of an on-going process of information exchange; from this view, it would be completely reasonable to allow individuals to submit their written consent following a few days of reflection, instead of 'on the spot'.

Issues related to confidentiality also require reflection. Respect for autonomy signifies that decision-makers trusted with access to individual health information must ensure that this information remains private. So when, for example, decision-makers analyse medical information in order to determine appropriate policy strategies for a particular health intervention, security measures must be in place to limit access to that information [7] (i.e., accessed only by people that have a legitimate need to know). But policies that invariably result in the identification of people based on a health condition likely indicate a need for reform. Mandating that children at a day camp with a given health condition (e.g., peanut allergies) wear discriminating markers so that they can be easily

recognized in a crowd, or having these children form a separate line in a cafeteria when retrieving their meals, is problematic, even if the aim is to protect public health. In both cases, confidentiality of the children's medical needs is compromised by them being identified as *different*; better policies would seek alternative, more discrete, means to identify individuals in a crowd or distribute specialty meals in the same manner as regular meals.

Beneficence

At the most basic level of interpretation, beneficence signifies a duty to 'do good' and thus act in a way that promotes the well-being of others. Since health is an essential component of well-being [8, 9 p. 16], the connection between promoting the well-being of others through the provision of health services is evident. Beneficence is thus an essential principle in medicine, and doing good and ensuring the well-being of others is a duty for health professionals. This duty is spelled out in codes of ethics that oblige health professionals to: 1) act in the best interests of their patients; 2) care about a patient's health status, and; 3) base treatment decisions on notions of charity and kindness [1, p. 50]. Merely following the basic dictums of best practice guidelines or upholding minimum standards of care is, thus, insufficient. Consider the example of administering an injection to a fearful child. A clinician can simply administer the injection to the child and both can subsequently be on their way. While therapeutically acceptable, this act does not fully respect the principle of beneficence. Rather, the clinician ought to have taken a moment's time to comfort the child and explain that their fears are understandable, but will likely be fleeting after the injection. Caring makes the intervention more than a technical act, but instead part of a therapeutic relationship.

At a more general level of interpretation, beneficence signifies that health professionals have an obligation to be compassionate when making decisions concerning the health of others [1, p. 50]. This obligation can help redirect decision-making strategies away from an exclusive position of impartiality towards a greater consideration of the outcomes a treatment or policy decision will have on others. In other words, the principle of beneficence encourages a 'blurring of the line' between a purely objective assessment of protocols and an empathetic connection to the implications of one's decisions. Employing empathetic approaches towards decision-making in health occur when policy assessments

include questions such as: “What if my decisions would have a direct impact on my own health; would I make the same decisions?”; “Would this proposed health intervention for the elderly be appropriate if it were to implicate my elderly parents?”; “Does this chosen course of action cause unnecessary burdens for people that I would find unacceptable if I were to experience the burden?”. Overall, by asking such questions, decision-makers cease to view those affected by policy interventions as ‘unknown and distant entities’; rather, these ‘nameless individuals’ come to be seen as persons that merit a level of compassion that would be appropriate when making similar decisions for oneself or for those with which we have a close relationship.

Theory applications

Beneficence requires that decision-makers in health ‘go the extra mile’ when developing health policies or making determinations concerning the health of others. This principle of actively doing good or working for the benefit of others helps sensitize decision-makers to the possibility that applying the ‘status quo’ may be insufficient. Rather, an arguably better vision for policy development would be to base decisions with the best interests of others in mind while upholding professional responsibilities to care for those in need. Basing reflections on the above criteria can serve as a guide when evaluating the adequacies of health policies. During assessments, decision-makers should consider whether current policies do indeed meet the best interests of those affected by the policy; if this is not the case, a caring response would be to reform policies to better meet the needs of individuals that may be ‘left behind’. For example, a recently implemented policy may have many observed strengths in that it is effective in improving the health of the majority implicated in the policy intervention. However, a minority may accrue less benefit due to individual challenges (e.g., some may be more socially excluded due to a language barrier). The principle of beneficence would motivate officials to devote extra time and resources to meeting the needs of these disadvantaged individuals (e.g., accommodate those that do not speak the dominant language by providing health services in more than one language). Not only will these efforts likely improve the effectiveness of a policy, such actions are kind and compassionate, which in turn encourages a higher ethical standard when evaluating the true effectiveness of health interventions. In turn, these higher standards provide impetus to question whether the status quo in policy protocols truly employs the best methods

available to meet the needs of others. As a last case in point, decision-making frameworks that include compassionate reflections gain an additional means to evaluate the appropriateness of tentative policies. If a health official would hesitate to implement a chosen intervention if it were to affect themselves or others they care about, this sentiment likely indicates inherent weaknesses that merit attention.

Nonmaleficence

Following the principle of beneficence to 'do good unto others' is the closely related principle of nonmaleficence, or 'do no harm'. On initial reflection it may appear that the two principles are practically the same or a specification of the other. Beauchamp and Childress emphasise, however, that the two principles are distinct due to the fact that nonmaleficence requires specific duties towards protecting individual health (and avoiding harm), in addition to the obligation to do good [2, p. 165]. To clarify this distinction, doing good often involves *actively intervening* to help others, while doing no harm may simply involve *refraining from acts* that are unnecessary and avoidably harmful [2, p. 113].

Here it is important to draw attention to two points. First, the principle of beneficence is most pertinent in situations where one evaluates whether a current situation is 'acceptable enough' or could be 'better' ("did I go the extra mile?"); the moral imperative to do better is a hypothetical possibility. Nonmaleficence is most relevant in situations where a known and unnecessary harm exists or an individual aims to act with malicious intent; the cause of concern in these situations is actual rather than a possibility. The second point pertains to the notions of *unnecessary* and *avoidable* harm [1, p. 46]. Nonmaleficence does not imply that any form of harm in a clinical context is indefensible; many necessary and ethically acceptable medical procedures do inflict various degrees of harm on a patient (e.g., discomfort associated with prostate or pelvic exams, chemotherapy or surgery for cancer treatment). Therefore, the central tenet of nonmaleficence is that the harms stemming from medical treatment must *not outweigh* the expected benefits of the procedure, meaning that the harm or suffering stemming from the medical intervention are a necessary and unavoidable component of the net-beneficial intervention. Nonetheless, the principle of nonmaleficence still obligates clinicians to take all necessary steps to use only the most appropriate forms of treatment and with the least amount of pain and suffering possible [1, p. 46].

The role of nonmaleficence as primary guiding principle in health care has additional significance beyond clinical conduct. The obligation to be attentive to harm also defines standards of scientific excellence and policies for guiding the ethical conduct of biomedical research [6]. It is now standard practice to evaluate the acceptability of research with human subjects on the basis of whether the experiment aims to provide a net benefit to society or advance the well-being of a patient population (i.e., by gaining greater knowledge of disease and possible treatments). Obligations to avoid harm also mandate that experimental procedures use the best methods and that the chosen procedure cause the least amount of pain and suffering possible to research subjects.

Theory applications

When faced with two choices, the most basic level of interpretation of the principle of nonmaleficence dictates that the less harmful choice ought to be chosen. However, this principle has many additional interpretations that can offer valuable guides in decision-making and policy development contexts. First, interventions that are known to carry risks of harm should not continue to be viewed as favourable if viable and less harmful policy alternatives are or become available. This obligation applies regardless of whether the previous, more harmful policy, was effective in achieving its desired health goals. This obligation is of particular importance in light of technological progress and research innovation, for example. With new technology and knowledge come novel means to treat pathologies and execute policy interventions, which can include novel methods to avoid harm, say, through the development of safer methods in clinical trials. Indeed, the presence of known harms often signifies a weakness in a given policy or intervention; following the principle of nonmaleficence, the actions of decision-makers may even be judged as reprehensible if they do not minimize these harms if reasonable and less harmful methods exist.

At a broader level, incorporating reflections concerning nonmaleficence in decision-making processes can also sensitize health officials to the importance of questioning whether harms may arise as a result of their decisions, and if so, whether these harms are justified. By extension, obligations of nonmaleficence emphasise the importance of assessing an intervention or policy in terms of harm prevention versus treatment or reparation. In other words, risk or harm assessments should be done *before* enacting the

policy, rather than merely observing whether any harms become evident in the future; indeed, attending to harms once they arise is morally inferior to *preventing* harm to persons in the first place [10, p. 140].

Justice

The principle of 'justice' has many possible definitions that vary depending on the context of the normative assessment – i.e., judgement – being made (e.g., legal notions of justice, the 'fair' distribution of resources, ensuring equal rights for all persons). For the current discussion, a 'narrow' interpretation of justice that centres on the treatment of individual patients in a clinical setting will be the focus of this section. This narrow focus does not signify that Principlism is not relevant to (or does not consider) macro-level interpretations of justice, such as social or distributive justice; on the contrary, Beauchamp and Childress devote much discussion towards distributive justice when presenting Principlism [2, p. 226-239]. The broader and various definitions for distributive justice – and why these diverse approaches are relevant in health policy – are reserved for a later discussion near the end of this chapter.

So, what do notions of justice entail for individual patients? Morrison interprets patient-centred considerations as an obligation to treat those with fairness, where personal characteristics of patients, such as lifestyle or financial circumstances, ought not to influence the level of professionalism of a clinician in their interactions with a patient [1 p.64]. Simply put, equals should be treated equally, and unequals should be treated unequally [2 p.227], meaning that patients presenting the same health problems ought to be treated according to equivalent standards of care. If clinicians choose not to treat patients with equivalent standards, this choice requires detailed justification.

Upholding this patient-centred principle of justice is important in a variety of circumstances. For instance, justice can serve as an appropriate guide when attempting to treat patients that demonstrate unpleasant behaviour, are dirty, or are simply rude [1 p.64]. While these patient characteristics may offend a clinician or even compromise their professionalism, the principle of justice obligates the clinician to assess whether they are treating the patient as well as they would treat more pleasant patients. Another example concerns how attention to justice can help identify weaknesses in medical practice by questioning the legitimacy of inequalities in care. Ethnic differences are a case in point,

where in the United States, the quality of care provided to ethnic minorities has long been known to be substandard compared to patients of the ethnic 'White' majority [11]; e.g., clinicians are less likely to recommend influenza vaccination to Hispanic and African-American patients, regardless of whether these people have health insurance [12]. Considering justice for patients raises significant concerns about whether these ethnic differentials in standards of care can ever be justified; it also points to the need to raise clinicians' awareness about the possibility for ethnic bias in their medical decisions.

Though it may at first appear contradictory, the principle of justice can also provide guidance when justifying the *unequal* treatment of patients in specific contexts. Consider patient triage in the emergency department, where gravely ill patients are prioritized and thus 'jump the queue' in front of less ill patients that may have been waiting lengthy periods. Moderately ill patients left waiting may conclude that their situation is unfair [1 p.64]. However, providing immediate service to those with more urgent (severe) medical needs supports one aspect of patient justice, namely that urgency is more important than waiting time. Furthermore, *if* the moderately ill patients were in fact seriously ill, they would reasonably expect the emergency department to prioritize services to them first as well. In other contexts, e.g., where urgency is less an issue, "first come / first served" or even lottery approaches may be just means of organising/rationing access to a service.

Theory applications

Simply put, within clinical contexts, 'like-patients' should be treated 'alike'. This basic interpretation of justice, however, is a germane concept for decision-makers in health. First off, this principle provides guidance when assessing what standards ought to be upheld when devising policies in light of understandable variations in characteristics of individuals. Decision-makers should question whether their standards are equivalent for all individuals targeted by the health policy; for instance, by assessing whether a policy will treat certain individuals differently than others. Consider the case of an administrator tasked with devising a meal programme for an institution (e.g., an old-age residence). The administrator is aware that certain individuals attending the institution have food intolerances, thus the meal programme must provide alternatives, and so the administrator decides to provide gluten-free substitutes since these alternatives are readily available and well known by the administrator. However, food intolerances can arise from other foods,

such as milk (i.e., lactose-intolerance). The administrator's choice to provide gluten-free alternatives is arguably unfair since consideration is paid to only one form of food intolerance and not others. A more just alternative would be to consider the needs of all food intolerant individuals and thus provide a wide variety of meal alternatives, including milk-free substitutes. Here, the needs of all food intolerant individuals are treated alike. This situation clearly also has practical and economic implications, that also lead to (distributive) justice concerns if there are insufficient resources (personnel, financial) to meet all needs of the population.

Individual-centred justice also provides means for decision-makers to assess whether their decisions may be biased and encourage undue favouritism. Are policies and interventions developed more quickly or made more accessible for people with health conditions that are viewed with greater sympathy (e.g., patients with leukaemia versus smoking-related lung cancer)? Are policy decisions delayed due to the fact that they will mostly implicate a specific and less socially valued group of people (e.g., individuals with that health complaint tend to be 'annoying', 'poor', or less politically active)? If the answer to the above questions is 'yes', justice signifies an obligation to reconsider the validity of this choice. Overall, justice considerations denote that if there is need to treat individuals targeted by a policy differently, decision-makers must explain and justify why any differences are warranted. By incorporating justice considerations as 'checks and balances', decision-making frameworks are more likely to provide consistent and fair assessments that are more aware of and able to mitigate possible bias. Therefore, individual-centred justice reminds decision-makers that individual characteristics that are irrelevant to health or to the given health intervention should remain irrelevant to the decision at hand.

At the level of populations: A new ethics for the public's health

The incorporation of Principlism within the professional practice and training of health professionals and decision-makers continues to have an important impact on the quality and provision of patient services. Though this impact is profound, one must be conscious of important limitations inherent with the four cardinal principles of bioethics. The limitations of Principlism derive from the fact that these principles were specifically developed for application at the level of individuals ('micro focus'), namely interactions between individuals, and specifically clinician-patient interactions. Attempts to

subsequently apply the four principles at a collective level ('macro focus'), where assessments focus on populations or communities as in the case of public health, can at times prove challenging and even deficient [13, 14 p.26, 15, 16 p.25-27, 17, 18]. In clinical medicine, clinicians aim to *treat* or cure an ailment at the request of the patient, while public health generally aims to *prevent* the spread of communicable disease or the onset of chronic disease amongst the population. With this distinction in mind, it should become clear that the best interests of a sick individual can be very different from the best interests of the community. The former situation centres ethical assessment on issues related to individual access to and quality of care, while the latter raises ethical duties to counter social and environmental risk factors that may culminate in elevated incidences of illness in 'statistical populations' of typically undefined/unidentified individuals. At the most basic level of interpretation, the ethical priorities in medicine and public health may be divergent [18].

Consider first the principles of informed consent and autonomy [13, 14 p.27]. Questions arise as to whether populations can consent to public health interventions, and furthermore, whether the best interests of the population should override an individual's autonomous decisions (which they often do in public health interventions, for example, with the imposition of a quarantine on an individual or group to prevent the spread of infectious disease amongst community members). In terms of beneficence and nonmaleficence, should decisions in public health favour doing good and avoiding harm towards individuals, or the community [16 p.26]? For instance, public health regulations can deny the employment of a pregnant woman in a job that requires manipulation of known teratogens. Though this policy aims for the greater good of the community by avoiding risks of harm to women and to future generations (not to mention the foreseen health care expenses accrued from foetal malformations), this policy may impose a harmful burden of unemployment on pregnant woman. Moreover, notions of justice to treat *like* individuals *alike* appear distant to the broader needs of populations. As will be described in further detail below, population-level justice issues typically focus debate towards: 1) how limited health resources will be allocated in society; 2) what interventions ought to be targeted towards communities in need, and; 3) what constitutes a fair distribution of benefits and burdens stemming from a public health intervention [2 p.226, 19]. As a final point, the domain of public health raises a host of new moral considerations that are alien to medicine, namely that public health practice often involves the use of governmental, or

even ‘police’, powers on populations through the enactment of laws and regulations that restrict individual liberties in order to control risk factors for disease [15]. What ethical standards should dictate the limits of these powers?

Despite the pronounced distinctions and differences, clinical medicine and public health share many core moral values (e.g., securing and promoting good health), and accordingly, the general values inherent to Principlism are not necessarily antagonistic with common values of public health. Indeed, much scholarship into the delineation of core ethical principles for public health has used Principlism as a foundation to ‘build upon’, where the four cardinal principles become inspirational in the development of core values for population, or ‘macro’, assessments. The core values for assessment of public health interventions proposed by Massé and Saint-Arnaud are one case in point [17]. Principles based on notions of justice, nonmaleficence, beneficence, and autonomy are integral to their analytic framework, along with additional values, including utility, precaution, and uncertainty; however, these principles are adapted to be representative of populations. For example, beneficence remains rooted in the duty to ‘do good’. Yet this duty is in reference to the *common good* of the community, and thus emphasises doing good through communal acts that demonstrate solidarity or uphold individual responsibilities towards the advancement of health for the population as a whole. As another example, Massé and Saint-Arnaud emphasise notions of ‘autonomy as confidentiality’. Even though the ultimate aim of a policy may be to protect population health, the authors reiterate that there is a duty for policies to respect the private lives of community members. The laudable goals of public health ought not provide a carte blanche for health officials to invade individuals’ private lives or release personal information. Rather, public health initiatives should find means to protect health via the least intrusive means possible, thereby balancing the needs of the community with the basic rights of individuals. Similar conclusions are drawn by other experts in public health ethics in terms of balancing individual freedoms and liberties in order to protect the population’s health [15, 20, 21]. For instance, a primary guiding principle for public health policy is that interventions should aim to be the least intrusive in people’s private lives as well as aim to be the least restrictive in terms of individual liberties. Accordingly, when assessing if policies are sufficiently tempered in terms of their use of ‘police powers’, decision-makers ought to determine whether the restrictions imposed by the policy are “proportional to the risk of public harm and … necessary and relevant to protecting the public good” [22 p.6].

Theory applications

Generally speaking, scholarship in bioethics has evolved from numerous founding theories of moral philosophy into a broad range of principles (values and theories) that can help guide decision-making in health. During the course of this evolution, core theories of ethics have been applied to specific contexts and have subsequently been 'adapted' into principles that identify and define issues of moral significance. However, this adaptation has lead to the formulation of principles that are best suited for ethical analysis within specific contexts. Thus, direct application of principles within novel contexts can prove deficient in representing and upholding the priorities and concerns within these novel situations. The context-specific adaptation of principles is made apparent when attempting to apply micro-level, or individual-focused, ethical principles in health to macro-level, population-focused frameworks – i.e., a direct application of Principlism is simply not well adapted for the domain of public health ethics. In spite of the initial disjunction between population/public health and individual/medicine frameworks, previous ethical principles for the latter have served as a foundation for further evolution and adaptation. The result has been an expansion of principles and frameworks in order to better represent the health of communities.

Armed with conceptual 'tools' for both micro- and macro-level ethical assessments, decision-makers in health have a broad set of principles that can serve as guides in policy development, which is significant since decisions in health often require consideration of the needs of both individuals *and* communities. In addition to providing a wider range of ethical frameworks for policy analysis, the distinctions between micro- and macro-level contexts clarify the need to seek *balance* between obligations towards communities and individuals. Simply overlooking the needs of one or the other may signify an ethical analysis that is overly focused on one context, and thus insufficient. Thus, decision-makers in public health must question whether their choices are "too extreme, too much in favour of the [needs] of the individual, or of the [needs] of the community" [14 p.35]. Through such questions, decisions can be more 'tempered' and so better suited to meeting the ethical obligations that are pertinent within a range of contexts.

Having outlined important differences, as well as similarities, between ethical principles relevant to both individual- and population-level assessments, the remaining

sections of this chapter will now provide an in-depth discussion of prominent principles in public health ethics, beginning with a proposed *code of ethics* for public health.

Deontological guides for health professionals: Codes of ethics in decision-making frameworks

In his book, *Everyday Ethics for Career and Personal Development* [23, Chapter 7], J. R. Jones presents what he describes as "quite simple and straightforward" [p.138] tools for ethical decision-making. One such tool is termed 'The Bell, the Book, the Candle'[8], which figuratively represents a decision framework that may prove useful when encountering ethically problematic situations. The *bell* represents the metaphorical 'warning bells' that go off in one's head when faced with an ethical dilemma (i.e., what many refer to as an uncomfortable and hesitant sentiment or instinct associated with making a decision). When they arise, these sentiments should not be disregarded or underestimated. Rather, these sentiments suggest that the dilemma at hand has significant implications, and as such, decisions concerning this matter merit greater consideration. Now conscious of the need for reflection, decision-makers should then turn to the *book* for guidance, which refers to existing deontological codes for professionals, laws, regulations, as well as departmental policies, standards and procedures. After referring to these resources, decision-makers should determine which choices concerning the ethical dilemma would best meet these guidelines for professional conduct. If a chosen course of action violates prominent laws, standards, codes of ethics, etc., one should reconsider the validity of this choice. The final step in the framework, the *candle*, serves to verify the soundness of the chosen decision by imaging how the choice would be perceived if 'exposed to the light of day', that is, exposed to public scrutiny or evaluated by colleagues. Would others view this decision as admirable or as contentious? If the latter, one should question whether the chosen course of action is still justified relative to other options.

On initial assessment, this decision framework is indeed simple and practical; note that the *bell* and the *candle* are thought processes that virtually every individual is capable of making. However, the true strength of this step-wise thought process resides in the application of deontological codes of ethics in decision-making.

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[8] Jones identifies Michael Josephson of The Josephson Ethics Institute as the originator of the framework.

Embracing a new arrival: A code of ethics for public health

Until 2002, public health institutions in the United States were unlike most other medical institutions, having not yet published a code of ethics for their professionals [24] (abbreviated hereon as *the code*). Following the formation of a working group of public health professionals, numerous experts in public health and bioethics were consulted in order to develop a consensus concerning what principles should compose a code of ethics for US public health practitioners (table 1; reprinted from: [24]). To date, this code comprises 12 principles deemed as essential guiding values that outline duties for public health professionals. Since public health professionals come from numerous different professions with a diversity of backgrounds and perspectives (e.g., epidemiologists, nurses, physicians, and people with social science backgrounds), it is not surprising that the code reflects this diversity through a collection of ethical concepts that target a broad range of ethical imperatives related to population health. For example, the second principle reflects well the previous discussion concerning the need to balance individual rights and concerns for the health of the community. Additional familiar concepts in this code are the duties to protect the personal information of community members (principle 10) and to promote justice through a fair implementation of public health initiatives amongst diverse communities (principle 4). Other principles reinforce professional duties to secure the public's trust through transparency (#6), encouraging public engagement in policy development (#8 & 12), and ensuring the competency of public health officials (#11).

Table 1: Principles of the ethical practice of public health

1	Public health should address principally the fundamental causes of disease and requirements for health, aiming to prevent adverse health outcomes.
2	Public health should achieve community health in a way that respects the rights of individuals in the community.
3	Public health policies, programs, and priorities should be developed and evaluated through processes that ensure an opportunity for input from community members.
4	Public health should advocate for, or work for the empowerment of, disenfranchised community members, ensuring that the basic resources and conditions necessary for health are accessible to all people in the community.
5	Public health should seek the information needed to implement effective policies and programs that protect and promote health.
6	Public health institutions should provide communities with the information they have that is needed for decisions on policies or programs and should obtain the community's consent for their implementation.
7	Public health institutions should act in a timely manner on the information they have within the resources and the mandate given to them by the public.
8	Public health programs and policies should incorporate a variety of approaches that anticipate and respect diverse values, beliefs, and cultures in the community.
9	Public health programs and policies should be implemented in a manner that most enhances the physical and social environment.
10	Public health institutions should protect the confidentiality of information that can bring harm to an individual or community if made public. Exceptions must be justified on the basis of the high likelihood of significant harm to the individual or others.
11	Public health institutions should ensure the professional competence of their employees.
12	Public health institutions and their employees should engage in collaborations and affiliations in ways that build the public's trust and the institution's effectiveness.

This début code of ethics for public health practice has many qualities. At the very least, the code makes explicit the need to uphold specific standards when devising health policies. Moreover, the 12 principles define an exemplary long-term vision for public health initiatives, while at the same time providing the diversity of professionals working in pubic health with a readily comprehensible 'moral compass' [24] to help orient their decision-making processes.

Theory application

Though developed primarily by experts in public health ethics as a deontological tool for public health practitioners, the above code of ethics is a noteworthy addition to the domains of health policy and decision-making as a whole. Recall that a diverse range of health professionals were consulted during the drafting of the code, and as such, the accumulative knowledge represented in the 12 principles may provide useful guides in decision-making frameworks beyond the borders of public health practice [24]. So in the event that a decision-maker experiences the proverbial 'ringing bell' when devising health policies, this code of ethics can serve as one of many 'books' to reference for ethical guidance.

For example, decision-makers might have reservations when assessing whether or not their choices meet professional standards of excellence. Such reservations are expected when, for instance, a health professional is tasked with executing interventions that are unfamiliar to their daily practice (e.g., a school nurse must collate the medical records of students with serious health conditions so that necessary information is available during an emergency; but what does this activity entail?). In such circumstances of uncertainty, the health professional can verify whether their decisions are up to par with relevant principles of the code [e.g., Are these medical records sufficiently detailed so that they can be later used as a tool to prevent adverse health outcomes in the school environment? (Principle 1); Have I consulted with the group of students implicated by this intervention so that I have their consent for its implementation? (Principle 6); These records contain confidential information – have I ensured that it will remain confidential? (Principle 10)]. If upon referring to the code the health official observes that their choices do not meet professional standards of excellence, this likely signifies the need for reforms, or to obtain further guidance. If their choices do coincide with ethical standards set by professional orders in health, this fact should provide a degree of reassurance. At the very least, the decisions made by the health official will meet the final criteria of 'the bell, the book, and *the candle*', meaning that when 'exposed to the light of day', their decisions are more likely to be viewed as ethically legitimate by fellow health professionals.

Thanks, but no thanks: policies that stigmatise

A popular expression in the English language is, "The road to hell is paved with good intentions". This expression captures one of many ironies of life: while we may base our actions on the premise of doing what is good and right, our actions can cause unintentional and even significant harm to others. Decisions in health policy are not immune to this irony, where even the best intended policies [25] require vigilance towards unintended consequences. A well-known unintended harm that may arise from policy decisions is the ability to stigmatise recognisable groups of people [14 p.120]. Stigmatisation is a social construct that is "characterized by exclusion, rejection, blame or devaluation that results from experience, perception or reasonable anticipation of an adverse social judgement about a person or group" [26 p.441]. More simply put, stigma involves the association of a 'negative and shameful label' with a particular community that can become a defining, though mistaken, attribute of that group within society.

Stigmatisation has long had a significant association with health, where for example, specific pathologies and 'unhealthy behaviours' have been associated with particular communities, or have been used to promote and perpetuate negative stereotypes and the denigration of groups of people. For example, a recent study [27] observed a high incidence of tuberculosis amongst illegal immigrants in the United States. Given the current political climate and hostility towards illegal immigrants, health officials fear that these findings may encourage draconian extradition policies and promote amongst the public undue alarm and hostility towards this already vulnerable population [28]. Specific health policies and public health interventions can also inculcate stigma. North American policies that impose a life-long ban on all gay and bisexual men as eligible blood donors – due to a higher incidence of HIV within this population – are notable examples. The fact that such policies target sexual orientation and not unsafe sexual practices[9] has raised fierce criticisms that current policies simply perpetuate the misconception that HIV/AIDS is a 'gay disease' [29].

Health-related stigma has several negative ramifications for population health, contributing as it does to health disparities by discouraging stigmatised and thus 'shamed' people from seeking health care [30]. But why is stigma an important topic for *ethical*

[9] For example, monogamous gay men in long-term relationships remain ineligible for life, while heterosexuals with multiple sex partners that do not practice safe sex are eligible blood donors.

reflection? It is readily apparent that addressing stigma arising from health policies fits with the principle of nonmaleficence, though in this situation the harms are mostly in reference to communities and not defined individuals. By extension to a macro-level then, the duty to avoid harms as much as feasibly possible signifies an obligation for decision-makers to seek less harmful alternatives to pre-existing stigmatising policies [13]. What if non-stigmatising alternatives are not possible? Duties to minimize harms remain, so health officials might enact measures to minimize public misconceptions concerning communities targeted for health interventions by, for example, promoting public education campaigns that correct misconceptions about disease incidence and offset misattribution of blame to particular communities [22].

Here it should also be apparent that the principles of *avoiding stigmatisation* (non-maleficence) and *autonomy as confidentiality* are in many aspects complementary. Indeed, the need to respect confidentiality in health has been inspirational in the development of ethical frameworks aimed at attenuating the risks of stigmatisation in public health [13]. A recent example that links the concepts of confidentiality and stigma is contained within the decision framework proposed by Thompson and colleagues, developed following the SARS epidemic in Toronto [22]. A main source of criticism concerning how public health officials and the media handled the influenza epidemic centred on an overemphasis in associating the disease with ethnic minorities, namely the Chinese community. SARS posed significant risks to all members of the population; therefore, Thompson et al. question the utility of health officials informing the public that those infected were primarily Asian minorities. Surely identifying the ethnicity of a small collection of those infected serves little benefit in controlling the epidemic? From these observations, Thompson and colleagues propose the following guiding principle for public health: "Disclose only private information that is relevant to achieve legitimate and necessary public health goals" [22 p.6]. This principle seeks to balance the need to protect the public (by informing them of a known risk factor) with the duty to protect private information of individuals, which in turn can avoid unnecessary stigma.

As a closing point, failure to avoid stigma is not solely an ethical concern in health policy, but also a question of efficacy. Policies perceived as stigmatising become easy targets for criticism by members of the public as well as other health professionals [31], criticisms that in turn may erode public trust and thus compliance, while also creating divisions in professional values amongst health officials. Certainly, the effectiveness of a

given health policy hinges on the ability for the policy intervention to be embraced, not shunned, by society, which is also contingent on the willingness for health officials to unite efforts to ensure its comprehensive implementation.

Theory applications

Even with the best of intentions, decisions made with the laudable goal of protecting health can have unwanted consequences. In many cases, stigmatisation can originate from poor judgements made during the structuring of health policies, such as by targeting interventions towards specific *communities* rather than specific health *conditions* [14 p.13]. In other situations, stigma is an unintended consequence of the public being misinformed of a health condition. Regardless of origin, decision-makers have a duty to avoid this unwanted and detrimental outcome. By being sensitive to the possibility that health decisions can inadvertently stigmatise a defined group of people, decision-makers gain a valuable tool to evaluate possible weaknesses and the ethical legitimacy of policy interventions.

Indeed, attention to stigma provides a guide for a 'step-wise' assessment framework. First, greater awareness of stigma should motivate decision-makers to be critical of the ramifications associated with targeting health interventions towards specific communities [13]. If interventions do require targeted health efforts, decision-makers should then assess whether this policy may confer a negative label to an identifiable group or community. If risks of this harm appear likely, the next step in policy development should determine means to minimise or avoid stigma. Reconfiguring policies so that they target *conditions* rather than *groups* of people, for example, might be a more useful and less stigmatising strategy (e.g., policies for sexually transmitted diseases that target high risk sexual practices rather than individual sexual orientations). Limiting the provision of personal health information of communities is also a valid strategy if such information is not essential for the effectiveness of a given health intervention (e.g., when informing parents to be vigilant towards head lice, school administrators do not need to inform parents which students already have head lice, or the fact that most of these students come from a particular neighbourhood). Finally, if stigma cannot be avoided, decision-makers have an obligation to implement public education campaigns alongside the chosen health

intervention in order to break negative stereotypes (e.g., educate the public that bed bugs can infest any residence, not just those of 'unclean people').

Beyond feminism: Empathy and the ethics of care for 'statistical populations'

Due to a prolonged history of the near exclusion of women from academia, scholarship in most domains of inquiry – including ethics [32, p. 154] – has largely overlooked or trivialized the specific life experiences, needs, and intellectual perspectives of women. Much has changed following the gradual inclusion of women in academic research, and one notable case in point has been the identification of a significant divide, and thus distinction, between traditional ethics (i.e., 'mainstream', male-dominated moral theory) and feminist ethics [33]. Without aiming to be overly simplistic, feminist scholars have – amongst many other achievements – demonstrated that there is more than one perspective by which to evaluate ethical dilemmas [32, p. 154-169]. Traditional ethical theories (e.g., Utilitarianism, Kantian ethics) typically assert only one perspective, centring on the need for *impartiality* during moral deliberations. Impartiality signifies that ethics-based assessments should be impersonal and free of bias as a necessary means to ensure that decisions are truly fair, and thus ethically legitimate. Concluding that a given decision is the most ethical choice because that choice suits the best needs of the person making the decision is obviously suspect; rather than impartial, this decision is clearly egoist and self-serving. Favouring decisions so that they prioritise the needs of family or close friends over the needs of strangers would also exemplify partial judgements, and thus be interpreted as unacceptably biased decisions according to traditional ethics theories.

Feminist ethics theory has lead to strong critiques of the previously unquestioned assertion for impartiality and impersonality as an ideal in decision-making. It is unlikely that absolute impartiality in ethical assessments is feasible, for one, but furthermore, feminist scholars question whether it is fundamentally against human nature not to favour consideration for those with which we have close relationships, such as family [2, p.371]. Surely under certain circumstances it would be reasonable (and even admirable) to give greater moral weight to family obligations than obligations to strangers, for instance [32, p. 155]? It is through our interactions and relationships with others that we develop unique attachments that are fundamental to our identities. In times of need, we turn for help to

those with whom we have our closest, most caring, relationships. The realisation that at some point in our lives we will either provide or need care and support by those close to us has lead to the view that ethical deliberations must consider an 'ethics of care' [34]. The obvious good that arises through these forms of social cooperation between family and friends signifies that these caring relationships hold moral significance, so it is argued that by incorporating notions of care, compassion, interdependence through support, and empathy towards the needs of others can provide moral guidance in decision-making [34].

Notions of care, compassion, and empathy in decision-making are reminiscent of the previous exposé of the principle of beneficence; indeed, many aspects of feminist theory and Beauchamp and Childress' explanation of beneficence are complementary [35, 36]. Recall that obligations of beneficence include the need to feel empathy towards each individual. While the notion of having an empathetic interaction with a defined individual should be evident in the context of patient-clinician relationships, such interactions are impossible (or at least extremely challenging) when orchestrating health interventions for populations or communities. No personal connection exists between the health official or decision-maker and the population that will be targeted by a given policy; the members of that population are in a sense, a faceless, 'statistical population'. Maintaining this impersonal perception of populations targeted by health policies is arguably far from ideal. At the very least, conceptions of divisions or 'one step removed' from the implications of health policy run contrary to the ideals of public health initiatives [24, 37], which instead reinforce notions of promoting health through social solidarity, thereby acknowledging the importance of interdependence between humans in communities and a collective empathy towards those in need of aid [17 p.140-142, 38]. Feminist ethics theories can provide ways to bridge this divide between 'statistical populations' and the goals of public health by informing decision-makers of the need to develop policies built upon premises of care and interdependence [38], much like how one would base decisions concerning family members. Thus, decision-makers gain guidance through implementing thought experiments where they imagine themselves as 'caring parents' providing support to fellow 'family members' of society (e.g., "How would you want to treat everyone in society if you imagined yourself as everyone's parent?" [39, p.1058]). Overall, by orienting policy development away from disconnected, impartial, views of 'statistical populations' towards ideals of interconnectedness and social solidarity, decision-makers are primed to develop

more empathetic policies that superimpose well with duties to promote the health of communities.

Theory applications

The primary utility of feminist ethics theory in policy development is the ability to refocus the underlying motives of decisions executed by health professionals. By incorporating the most basic interpretations of feminist critiques in decision-making processes, health professionals raise their awareness and sensitivity towards the fact that health policies will have a direct impact on the lives of others, whether this impact will be observed by the health professional or not. In other words, feminist notions of *connectedness* and the need to maintain strong *relationships* between people can serve as guides when implementing policy decisions for 'statistical populations'. Rather than viewing this population as a group of individuals of no personal acquaintance, decision-makers should instead imagine what their responsibilities would be as a caring parent for this population (a justified paternalism). For example, when determining the minimum level of health services should be available to *community X*, such determinations can be guided by asking what services, protections, and basic needs are necessary to uphold duties of caring for *family members* that comprise community X. On the whole, by considering how a policy may impact actual people, and whether imposition of such policies would be acceptable if applied towards those with which we have close relationships, this compassionate mind-set will arguably encourage the development of more ethically legitimate decisions in health.

Empowerment of vulnerable populations

Upon observation of any given population, it should become readily apparent that many distinct communities and sub-populations exist within the whole; there are inevitably 'haves' and 'have-nots'. Common factors that draw distinctions between communities include differing levels of power, social exclusion, and disenfranchisement, all of which relate to the vulnerability of a community and its members [40, 41]. The concept of vulnerability has increasingly become a subject of analysis and concern in public health due to its strong correlation with poor health outcomes [42, 43]. Vulnerability of

communities denotes social groups that, "because of shared social characteristics, [are] at higher risk of risks" [44, p.218]. For example, high rates of violent crime and pollution are known risks to health, risks that are more prevalent in impoverished neighbourhoods [45, 46] with the result that members of impoverished communities are at higher risk of encountering these health risks. Well known vulnerable populations in Canada include aboriginals, people 'surviving' below the poverty threshold, adults without a high school degree [47], and sexual minorities [48].

The vulnerabilities that define particular communities are due to numerous factors [42], but they have in common aspects of social exclusion, disempowerment, and the reduced ability of people to protect their own health. The following three examples will help make these correlations more explicit.

1) The current economic crisis and resulting collapse of the housing market in the United States has disproportionally lead to homelessness amongst once lower-middle class citizens; it is now common for these Americans to have to make tough choices concerning whether they will devote scarce resources towards health care (e.g., pharmaceuticals) or minimally acceptable standards of housing [49].
2) People suffering from mental illness frequently encounter significant public stigma that motivates many to become introverted, isolated, and thus less inclined to seek out appropriate health services [50].
3) Adolescents that do not accommodate to norms imposed by their peers are often ostracised [51], which in turn can make them the target of bullying, a troubling phenomena that has recently resulted in a wave of teen suicides in North America [52, 53].

A shared trait in these three examples is that they involve groups with particular vulnerabilities that often produce a 'downward spiral' in population health. These observations have encouraged the development of the ethical principle of *empowerment* as a guiding ideal for policies targeting the health needs of vulnerable people [54, 55].

As the word denotes, em*power*ment in health aims to help individuals and communities gain power and control of their lives through interventions that redress social problems related to their oppression and exclusion, as well as the attenuation of factors that result in the concentration of health risks. The notion of designing health interventions as tools for empowerment has marked an important transition in health policy, where analysis has advanced beyond principles of beneficence (i.e., the duty to do more for those with

special needs), to include consideration of whether policies contribute towards emancipating people from inequities and oppression [14, p.xii]. Indeed, this concept is integral to the above mentioned Code of Ethics for Public Health, where the fourth clause stipulates that *"public health should advocate for, or work for the empowerment of, disenfranchised community members, ensuring that the basic resources and conditions necessary for health are accessible to all people in the community"*. With the need for empowerment of the vulnerable in mind, health promotion efforts are then primed to reflect on, and work to reform, wider social structures associated with vulnerability and not focus only on changing individual behaviour [14, p.116].

Notions of empowerment and vulnerability can guide health policy development on several fronts. First of all, they raise awareness to the possibility that a universal application of a particular health intervention is likely insufficient since a 'one-size-fits-all' strategy does not take into account differing levels of disenfranchisement within society [41, 56]. An arguably better strategy would incorporate methods to redress factors that diminish opportunities for vulnerable populations to fully benefit from health promotion activities. Thus, policies that support the provision of mental health services are insufficient if policy makers do not also include measures that work to help break the social stigma associated with mental illness. Similarly, suicide prevention efforts aimed at adolescents require more than the provision of counselling services at secondary schools, and should also include mechanisms to counter pervasive bullying and harassment. Finally, orienting treatment strategies towards the use of pharmaceuticals will do little to help those people who are forced to choose between paying for medical treatment or paying their rent; alleviating poverty must also be an essential component in such strategy. At the most basic level, the above examples demonstrate that policy development must consider the differing needs of various communities targeted by a health intervention. Communities will differ in their degree of opportunities and abilities to accrue health benefits due to various factors, including vulnerability. By incorporating strategies to counter vulnerability through diverse empowerment interventions, health policies can be better structured to meet goals of promoting health benefits amongst the 'have-nots' as well as the 'haves'.

Theory application

Helping communities that are consistently subject to social deprivation is no longer a question of pity or charity [57] but rather of efficacy and due diligence in public health [58]. Diligence in this circumstance signifies that decision-makers must evaluate potential health interventions within a broader context that includes consideration of how social factors related to vulnerability can impede the success of a chosen policy proposal. By overlooking the reality of differentials in power and risk factors for poor health amongst different communities, decision-makers miss opportunities to structure interventions that can attenuate these differences [40]. Disparities in opportunities, social exclusion, and power impose limits on the extent to which a health intervention will benefit some communities but not others. However, by attending specifically to such disparities and incorporating methods to empower the disadvantaged members of society, decision-makers are more inclined to develop interventions that will be of broader benefit across communities.

For many decision-makers in health, attending to social factors that concentrate risks for poor health – such as poverty and violent crime – may appear to be beyond their jurisdiction or scope of intervention [56]. Indeed, addressing social determinants of health and vulnerabilities will require major political changes that alter the structure of society by, for example, reducing unemployment [59]. Regardless, the principle of empowerment is still useful as a guide in smaller-scale health interventions since sources of vulnerability are many fold and include tangible factors that health professionals encounter in their daily practice. For example, work environments that permit harassment compromise the health and well-being of employees in general, and not only those that are the target of harassment [60]. In addition to reprimanding employees that create such hostile work environments, decision-makers should assess what factors allow employees to be harassed in the first place [1, p.56]. Thus with empowerment in mind, decision-makers can question what aspects of the work environment need reform so that employees can avoid hostility and undue influence by others, such as by offering organisational support (e.g., guidelines on what behaviour is unacceptable) and job security for individuals that complain about substandard working conditions (so-called “whistle-blower” protection) [61]. This shifts power towards employees that need it most and offers methods to break free from oppressive working relationships.

On the whole, the concepts of vulnerable populations and the duty to empower those who are most vulnerable provide a valuable guide when designing health interventions. At the onset, decision-makers should question whether a universal application of a policy would be sufficient to address the needs of all members targeted by the intervention. Are there particular groups that are less likely to benefit from the intervention due to avoidable factors that diminish their opportunities to protect their health? If so these groups require due diligence, and decision-makers should then ask, "within my professional sphere of influence, what measures can I enact to dispel factors of domination and oppression, and in turn enable all people to have a greater degree of self-determination in relation to their health?". By addressing these questions, decision-makers take the first step towards ensuring health interventions will be effective for the 'have-nots' as well as the 'haves'. At the very least, this premise is arguably a more equitable, or just, position for policy development.

The final segment of this chapter on practical theory will now return to the topic of justice or equity in health. The initial presentation of justice limited discussion to the fourth tenet of Principlism, where micro-level assessments highlight the duty to care for individuals fairly by treating 'like' circumstances 'alike'. The concluding sections will now focus on macro-level justice assessments that are prominent in debates concerning population health, especially in terms of pressing health policy issues related to resource allocation in health care, priority setting in policy development, and evaluating the fair distribution of benefits and burdens in population health interventions. The theoretical basis for these debates in health policy rest on theories of *distributive* and *social* justice, debates which are made rich and complex by the fact that numerous theories of justice are relevant to macro-level policy decisions in health. The following discussion will thus begin by describing this complexity and diversity of theories of justice in order to show why each theory identifies important concepts to consider when analysing notions of equity in health policy. Though this diversity of theoretical frameworks pose certain challenges for policy development (i.e., which theories are most relevant?), the following analysis will demonstrate the utility of one prominent theory in the development of decision frameworks in health, namely Norman Daniels' adaptation of Rawlsian social justice.

Multiple theories of social justice in health: A challenge in policy development and decision-making

Determining whether a given situation is just or fair can be a surprisingly complex task; especially when one aims to define the 'just nature' or 'fairness' of a given health policy decision in terms of macro-level distribution of resources, setting priorities in population health, or targeting initiatives towards specific communities. But before addressing issues of justice in health policy, it is necessary to first ask what makes notions of justice difficult to implement in decision-making, and accordingly, why is it that defining justice presents specific challenges. Amartya Sen, a prominent figure in social justice theory, highlights the inherent challenges of employing theories of justice in decision-making (whether in health or other contexts) by identifying the disagreements that arise when trying to define *inequality* and *inequity.* Specifically, Sen asserts that difficulties become apparent when attempting to answer the following question: justice determinations ought to centre on "equality of *what*?" [62, p. 4, 63].

To clarify, justice-centred assessments begin with the observation of an unequal distribution of a chosen measure (income, happiness, wealth, life expectancy, etc.) between defined groups or individuals. A group having a deficiency or inequality of the chosen measure (e.g., income) leads to an inequity when this situation would ameliorate (depending on what constitutes as an 'improvement') if the inequality of the measure between the groups were lessened or eliminated. Sen argues convincingly that the chosen measure for justice assessments is itself a value-based judgement (what criteria for equality does one value most?) and that striving to achieve greater equality in one measure may not coincide with equality in scale of another measure [62, p. 2, 63] (in fact, promoting equality in one measure may exacerbate inequality in another) and thus greater equity from another perspective. For example, equalizing the wealth between two groups of individuals may not equalize their levels of happiness; thus, would equalizing the distribution of wealth produce a truly just outcome?

At this point, it should become clear that choosing "equality of what" for analysis is a matter of profound and longstanding philosophical debate (for an overview the numerous theories of social justice developed by philosophers, see: [64]). A review of *all* prominent theories of social justice is beyond the scope of this chapter (and thesis), and so this thesis will limit analysis to a select set of theories or principles of justice relevant for decision-

making in health. It is nonetheless important to clarify how employing various theories of social justice can produce conflicting analyses in decision-making. The following discussion will present a brief overview of three prominent principles of justice employed in health policy, in order to show how each principle focuses justice assessments towards a different measure. Following this overview, the discussion of social justice in health will conclude with a detailed presentation of a fourth and final theory, that of Rawlsian social justice theory applied to health contexts, which will be the focus of health policy proposals presented in Chapter 2.

Why not strive to maximize utility and efficiency?

What could be better than striving to maximise the greatest amount of health improvement with limited resources? Indeed, in these times of severe economic hardship, it seems logical that what is most fair for society is to ensure that public resources get the greatest 'bang for the buck', and accordingly, policies should prioritise efforts to provide the greatest accumulative improvement in health for the population. This perspective of resource distribution in health originates from theoretical frameworks of Utilitarianism, where the basis for ethical analysis resides in determining which action will provide the greatest 'utility' or 'welfare' for the greatest number [64]. However, measuring 'utility' or 'welfare' can be somewhat vague concepts in health policy analysis (e.g., what is a unit of utility in health?). To address the vague character of these concepts, scholarship in health policy has since developed quantifiable measures to calculate the efficacy of health interventions, such as Disability-Adjusted Life Years (DALYs).

Endorsed by the World Bank [65] and the World Health Organisation [66], DALY is a combined measure of morbidity and mortality that quantifies the burden of a given pathology. In brief, DALYs combine "time lived with a disability and the time lost due to premature mortality" [67] (for a detailed explanation of DALY measurements, see: [67-69]). Upon establishing DALY units for pathologies, these units can be implemented in resource allocation exercises, where a defined goal can be to minimize the disease burden in society within budgetary limits (i.e., in terms of cost-effectiveness: with x dollars, what is the greatest number of DALYs that can be eliminated?). Minimising DALYs signifies maximising utility in health; thus health interventions can be prioritised according to their expected utility per unit cost.

Though a well-developed and popular metric employed in health policy around the world [70], maximizing the utility of health interventions through DALY measurements is hotly contested and viewed by many as an ethically questionable basis to fairly prioritise health interventions [69, 71]. One primary source of criticism is that priority frameworks based on utilitarian principles often neglect the needs of those in the worst state of health.

Maximising utility will leave the vulnerable 'out in the cold'

As demonstrated in the previous discussion concerning vulnerable populations, each society will inevitably contain a heterogeneous assemblage of communities where some fair better, and others worse, in their abilities to secure good health. Recall that a defining feature of vulnerable populations is the concentration of health risks within these communities, which encourages the compounding of social, economic, environmental, etc. factors that challenge the broad efficacy of health interventions (e.g., smoking cessation campaigns are less effective for lower socioeconomic classes due to factors ranging from lower literacy rates to high unemployment [72, 73]). Understandably, achieving an equivalent measure of utility or benefit from a health intervention employed amongst deprived and particularly vulnerable populations will likely require greater initiative and resources than that needed for more 'well-off' populations [68, 74]. In a sense, these vulnerable populations are more 'costly' and so less 'cost-effective'. A similar observation is made within the context of severely ill or disabled patient populations [68, 74]. For instance, an intervention may accrue little health benefit amongst the frail elderly but produce great benefit amongst the working adult population (e.g., according to a utilitarian perspective, a health programme that aims to extend life expectancy will be of little 'utility' to those nearing the end of their lives; thus, this programme should be reserved for younger populations). Broadly speaking then, adherence to Utilitarian frameworks as an ideal for resource allocation can thus give less priority, and thus direct fewer benefits, towards communities that are systematically disadvantaged in securing health [9, p.150-158].

Many scholars view this situation as discriminatory and unfair [68, 71, 74, 75] because strategies based on maximising cost-effectiveness in resource distribution might, over the long term, compound and perpetuate a range of disadvantages experienced by vulnerable segments of society [9, p.157]. At the very least, compounding disadvantage in society is contradictory to many fundamental values of public health (see principles 1-4 &

9 of the code of ethics for public health, table 1, above). In response to these concerns, alternative theories of justice in health policy have centred assessments on the needs of the most disadvantaged members of society, such that their needs should be prioritised over the 'healthier majority' [9, 19, 76, 77]. To exemplify one such theory of justice in health policy, Madison Powers and Ruth Faden [9] develop a framework for prioritisation in health policy based upon measures of systematic disadvantage across multiple categories of well-being; communities observed to have a compounding of disadvantages in well-being receive highest priority.

Though strategies that focus on promoting the health status of the most disadvantaged will likely be less efficient according to strict financial measures [64], frameworks for targeted interventions will arguably promote equity by raising the bottom segment of health achievers towards the average level of health achievement attained by the majority of the population [44]. However, in addition to questions of inefficiency, favouring the needs of the 'worst-off' have been criticised on numerous grounds ranging from libertarian objections[10] to a disregard of individual responsibility in health [64].

Will someone take responsibility for his or her actions?

While notions of efficiency and acts of solidarity to help the vulnerable have great appeal, an additional concept raised in health equity debates is the notion of 'just desert' [64]. Just desert signifies 'receiving what one deserves' based on merit and personal choice, and thus justice assessments from this perspective focus on notions of personal responsibility in health. Personal responsibility in health has long been a central topic in public health policy; the publication of the Lalonde Report [78] in 1974 is an example, where a primary determinant of health achievement is attributed to lifestyle choices.

At the core of the just desert premise is that the unhealthy choices people make (e.g., smoking despite knowing its negative health effects, choosing to practice unsafe sex) should be seen as a personal rather than a social responsibility and as such should not have priority over unavoidable health needs when establishing resource distribution strategies

[10] Libertarian philosophy focuses justice assessments on individual freedoms and typically opposes government interference in individual control over their resources [64]. Libertarian proponents often contest frameworks that favour the needs of the disadvantaged since these usually entail redistributing resources away from the privileged (those "who have earned their rewards") towards those in need. If imposed by governments, this redistribution diminishes individual freedom in resource utilisation, which runs counter to Libertarian ideals.

[79]. However, it is important to define what is meant by *choice* in unhealthy lifestyles. It is well known that certain individuals, due to mere bad luck, live in environments that are unfavourable to making healthy choices, and thus these choices are not actually avoidable (e.g., individuals living in neighbourhoods that do not provide access to fresh fruits and vegetables, AKA 'food deserts', should not be held responsible for unhealthy eating habits [80, 81]). Allocating health resources towards vulnerable communities is therefore justified under many circumstances if such decisions aim to redress the "lack of opportunit[ies] that some may have to achieve good health because of inadequate social arrangements, as opposed to, say, a personal decision not to worry about health in particular" [63, p.660].

While allocating health resources on the basis of giving to those that which they deserve has a degree of appeal, many policy experts criticise this framework as being socially divisive and impractical in terms of epidemiological evidence [82]. In terms of divisiveness, some policy analysts raise concerns that frameworks based on judgements of lifestyle choices could lead to undue 'victim blaming' in health policy decisions [83]. Health priorities might become overly focussed on determining who in society is 'at fault' for poor health rather than providing care to those in need, and when taken to the extreme, such moral judgements may incline health officials to abandon the needs of those judged to have been imprudent in their lifestyle choices [84 p.3]. From an epidemiological perspective, determining whether or not unhealthy behaviours are a matter of choice is often very complex since a wide array of socio-environmental and psychological factors influence individual lifestyles. This complexity suggests that justice assessments based on just desert are to some extent, or even inevitably, arbitrary [82]. For instance, would it be appropriate to blame an individual for heavy drinking following a messy divorce; or how about the stressed-out workaholic who is desperately striving to obtain better employment opportunities? In both cases it is difficult to determine whether such unhealthy choices are readily avoidable, unreasonable, or based on imprudent decisions.

Theory applications

Without a doubt, "explicating the demands of justice in allocating public health resources and in setting priorities for public health policies, or in determining whom they should target, remain among the most daunting challenges in [policy development]" [15 p.171]. This challenge is obviously not the result of a paucity of philosophical debate or

scholarly analysis concerning equity in health contexts. Rather, a wealth of scholarship has identified a wide variety of issues that are integral to debates pertaining to health equity and what rights and responsibilities should be important considerations in population health interventions and policy. Whether it be efficiency, lifestyle choices, favouring the needs of the vulnerable, or ensuring equal capabilities for health, these issues – which have each been the focus of theories of social justice – are all relevant in health policy discourse. This signifies, as stated by Beauchamp and Childress, that "no single principle can address all problems of justice" [2 p.227] in health. Employing one theory of justice in policy will inevitably result in a difficult trade-off in equity criteria defended by contrasting theories.

At this point it may seem that employing any given theory of social justice in decision frameworks will inevitably collide and so lead to an impasse. If each theory identifies important concepts in health equity, it is difficult – likely impossible – to define which perspective of social justice should have precedence over others. Nevertheless, these conflicts in theory do not mean that principles of social justice have little utility in health policy development or as tools in decision-making by health professionals. On the contrary, different theories of social justice provide insight into a *range of considerations* that are important when considering health inequalities and the pursuit of equity. Therefore, decision-makers need to first view "health equity as a very broad discipline which has to accommodate quite diverse and disparate considerations", and accordantly, "appreciate that health enters the arena of social justice in several distinct ways, and they do not all yield exactly the same reading of particular social arrangements" [63, p.660]. No one theory of social justice will offer a complete analysis of the equitable nature of a given health policy strategy if employed in exclusivity. Instead, assessments made with each theory can arguably provide a partial contribution towards a better understanding of equity in population health and the associated complex realities that come with these assessments.

Overall, when implementing principles of social justice as a guide in policy development, decision-makers need to be 1) *transparent,* and 2) *considerate* towards opposing opinions. Transparency here denotes the need for decision-makers to be explicit about their choice of equity criteria that will guide a given policy agenda. Decision-makers should be prepared to advance solid arguments as to why these equity criteria are most appropriate in addressing health inequalities or in setting priorities. At the very least, these arguments should provide insight into questions such as "this intervention aims to promote equality of *what*?" and "why do these principles of social justice identify important issues

in this context?". As such, decision-makers must be humble and open minded, and accept that their arguments may be criticised from other perspectives of social justice. Upon considering any differences in opinion, decision-makers should then assess means to incorporate within the policy development process the additional social justice considerations identified through debate. Such actions will encourage the development of more accommodating policies that are more attuned to the complex reality of health equity assessments.

To summarise, decision-making frameworks centring assessment on justice require openness to debate and consideration of multiple perspectives of equity in health. Abstract principles of justice will "provide only rough guidelines for forming specific policies or taking concrete actions" and so each theory will "succeed only partially in bringing coherence and comprehensiveness to our fragmented visions of social justice" [2, p.230]. However, rough as these guidelines may be, all debates require an *initiator* of discussion, a foundation upon which to build. Therefore, many philosophers would argue that "principles of justice can offer little help until they have been integrated into a systematic framework" [2, p.230]. Indeed, it is logical to assume that much insight into the strengths and weaknesses of given principles of justice can be derived from the actual application of these principles in health policy development by health professionals. In other words, in order to advance debate, it is essential to transfer the knowledge inherent to social justice theory into the realm of practical application. The following discussion will aim to contribute towards such an initiative by proposing one prominent theory of social justice as a guide in policy development. The following presentation of Rawlsian social justice theory will serve as an introduction to a later application of this theory as a foundation for decision-making frameworks for priority setting in public health.

A theory for targeted application: equality of opportunity in population health

Consider for the moment the following thought experiment. Imagine that your memory has been temporarily and selectively erased so that you no longer have any recollection about your age, gender, social class, degree of power in the social order, family history... nothing. One area where your memory does not forsake you is your observations

of the society to which you belong. You can recall that many people are fortunate in that they have access to all the necessities to live well and be content. However, many people fare far worse, where for some, life is a constant struggle. Those less fortunate are burdened by many factors, such as extreme poverty, substandard housing, discrimination, a collective disregard for the needs of the disadvantaged, and so forth. Worst of all, you can recall that those experiencing severe burdens have few opportunities to escape this disadvantaged state; their condition is often hopeless. Your temporary amnesia prevents you from knowing whether you are a member of the fortunate or unfortunate segments of society. At this point, a simple question is posed to you: *if you had the power to change society*, *how would you amend it so that it will suit your best interests*? Would you want the current social arrangements to remain, or would you be better off if social institutions ensured that all people have equal opportunities for achievement? Knowing that the possibility exists that you are a member of the less fortunate in society, it appears that your safest bet would be to reform society so that it would enable all people to escape such forms of destitution.

The above scenario is a variation of John Rawls' [85] famous thought experiment, known as the *veil of ignorance*. Rawls argues that any self-interested individual who cannot foresee their future well-being would want society to ensure fair opportunities to achieve one's goals in life for all citizens, rather than allow social inequalities to form based on biological and social lotteries to which individuals have no control over (e.g., being born with or without 'healthy' genetics; being born into a rich or poor family; possessing – or not – talents that are in high demand within society [e.g., virtuoso musical abilities]). Rawls' conception of justice, entitled *justice as fairness*, derives from two core concepts: equality in opportunity and the allocation of primary resources based on the difference principle.

Rawls proposed that social institutions have the duty to redress social inequalities in abilities and disabilities, and a guiding rule for such redress is to instate a social system that will ensure equality of opportunity for all. An essential duty for social institutions is therefore to ensure equal rights, protect liberties, and provide conditions for self-respect to all citizens, independent of factors such as wealth, gender or ethnicity [85, p.477]. Discrimination in any form is understandably counterproductive and so social institutions must safeguard human rights and foster citizen participation in political discourse so that everyone is guaranteed equivalent protections, and thus abilities to achieve. In addition to the non-material goods of rights, freedoms and feelings of self-worth, Rawls proposed that

social institutions should also ensure a fair distribution of primary resources amongst all citizens. Primary resources can assume many forms, such as minimum standards for housing, nutrition, and equal access to education. Consider the latter example of education. The ideals advanced by Rawls would uphold the duty for society to provide equal access to education so that all citizens may educate themselves to the fullest of their abilities and desires, and not be limited by factors such as the ability to pay for these services. Furthermore, those people unfortunate in the biological lottery, such as those born with learning disabilities, should have access to specialised training in order to overcome these disabilities as much as possible, regardless of whether such services would cost more [2, p.236].

However, to ensure a true equal distribution of opportunities amongst all citizens, Rawls advanced the argument that the distribution of primary resources *cannot* be equal. Rather, distribution of resources must follow the difference principle, where resources are directed first towards those in greatest need. More specifically, Rawls proposed that the best method to eliminate unacceptable inequalities in opportunities was for resources to be directed towards the most vulnerable and disadvantaged members of society (i.e., those who are the 'worst-off'). By targeting resources towards those in greatest need, Rawls argued that this strategy would be the best method to eliminate inequalities in opportunity that serve no benefit to society as a whole.

Uniting Rawls with health policy

The initial conception of *justice as fairness* advanced by Rawls pertained to the structuring of society and was not designed specifically in terms of population health inequalities [85]. Only later did scholarship begin to apply Rawls' theory within the specific context of health, a notable example being the work of Norman Daniels [10, 76, 77, 86]. Daniels argues that health services are an essential component of social justice since disease will diminish an individual's capacity to function normally. This signifies that individuals in a poor state of health have reduced opportunities in life compared to others in healthier states. Accordingly, if society aims to promote equality of opportunity amongst its population, health institutions must aim to restore individuals to the level of functioning they would have enjoyed if they were healthy [10, 76]. Here we see that by applying Rawlsian conceptions of social justice, health care should not be viewed like any other

service available through the free-market. Instead, health care is best viewed as a special kind of good that enables greater equality of opportunity if a reasonable level of care is made available to all members of society.

Following the thesis that securing health is an essential component of equality of opportunity, Daniels, in collaboration with the epidemiologists Ichiro Kawachi and Bruce Kennedy, advanced the thesis that upholding Rawlsian principles of justice can be a strategy for improving population health [77]. Their argument rests in part on an observed trend in population health. While relatively wealthy, developed nations achieve the highest levels of life expectancy, health measures plateau when per capita GDP reaches $9000 (US$). Therefore, population health does not necessarily follow a linear relationship with respect to the net wealth of a nation. From this observation, Daniels and colleagues propose the hypothesis that net wealth is not the sole determinant of health achievement; rather, how evenly wealth is distributed in society can play an equally important role. Daniels and colleagues correlate this hypothesis by examining nations such as Japan and Sweden, which have more equal income distributions and higher life expectancies than the US, despite having less net wealth [87]. Daniels and coauthors also refer to longitudinal studies demonstrating that in the US, states with the highest income inequalities between social classes have slower rates of improvement in average life expectancy when compared to states with more equitable income distributions [88]. Recent nation-wide assessments of other developed countries, such as Canada [89], continue to substantiate the existence of socio-economic gradients in population health that do not correlate with differentials in access to health care [90, 91]. Overall, empirical findings suggest that the degree of income and resource equity may have dramatic effects on population health. For Daniels and colleagues, a solution to observed health differentials between social classes is to an extent, straightforward: one must reduce gradients in income and available resource between socio-economic strata within currently inequitable societies. Rawlsian social justice theory is thus proposed as one framework to guide government institutions in the development of social safety nets and income redistribution strategies as a broad public health intervention that address the needs of worse-off members in society [77, 91].

In addition to the work of Daniels and collaborators, Andrew Courtwright [30] recently questioned whether Rawlsian social justice theory could help identify important considerations in health policy outside the context of resource distribution. Courtwright has focused on the distribution of non-material goods, specifically liberties and ability for self-

respect, and examined the significance that these non-material goods have in terms of health disparities. He notes that stigmatisation of vulnerable community groups can exacerbate health inequalities, because feelings of shame and diminished self-respect discourage stigmatised individuals from seeking appropriate health services and following healthy lifestyle choices [30]. From these observations, Courtwright argues that efforts aimed at reducing health inequalities entail more than addressing questions of resource distribution; they must also include specifying the duties for government institutions to ensure a social environment that fosters self-respect and feelings of self-worth. On the whole, Courtwright recommends that upholding Rawlsian principles of equality of opportunity in relation to non-material goods could serve as a useful guide towards reducing health inequalities related to stigmatised health conditions.

Theory applications

Are the central tenets proposed by Rawls *the* ultimate and best theory of social justice to guide health policy development? No. Just like all other theories of social justice, the principles upheld by Rawls address a select set of a broad range of considerations that are pertinent to health equity assessments. However, many health officials will likely share the general intuition that the central tenets proposed by Rawls will do more to advance, rather than impede, efforts to achieve greater justice in population health [92]. Regardless, one does not need to adhere strictly to this theory if one agrees that the promotion of equality of opportunity and improvement of the situation of the worst-off members of society are two concepts that require consideration when designing policy agendas. Thus, rather than a philosophical conviction, Rawlsian principles should be viewed as one of many knowledge foundations that can help structure decision-making frameworks in health.

Even in the absence of debate, it is reasonable to conclude that decision-making frameworks gain an advantage if they include, rather than overlook, an assessment of equal opportunities in health. Indeed, merely being aware of the potential for certain communities to have reduced opportunities in securing health is a valuable asset for decision-makers. In addition to this awareness, assessments that incorporate analysis of opportunities in health can help identify inadequacies in proposed health services and programmes. Consider a situation where a diverse group of people all suffer from a given pathology, which, for the

most part, is treatable via a pharmaceutical regimen. However, a minority of individuals do not respond well to the therapeutic regimen or experience adverse drug reactions. A decision-maker may conclude in this situation that the health benefits accrued by the majority would justify the provision of the pharmaceutical treatment to all those that could benefit. Though the aims of this decision are laudable, attending to the principle of equality of opportunity would show that this policy is inadequate. By focusing the health intervention on the provision of pharmaceuticals, the majority of people suffering from the pathology gain opportunities to improve their health while a minority does not. This situation will predictably exacerbate inequalities in opportunities amongst this population, which runs counter to ideals of promoting health equity. An arguably better strategy would be one that incorporates additional treatment options so that all individuals gain means to treat their affliction.

It is understandable that policy development will often focus on issues pertaining to the equitable provision of material goods, such as pharmaceuticals. However, the principle of equality of opportunity shows that non-material goods should also be included in health equity assessments. Decision-makers must be aware that non-material goods, such as basic human rights, dignity, and feelings of self-worth play an equally important role in securing population health [93, 94] and should therefore be important factors for consideration in health policy. Yet many decision-makers in health might regard issues pertaining to rights as being beyond their remit, or consider issues of dignity and self-worth are solely personal matters. Yet, recall that Courtwright delineated how stigma impinges on feelings of dignity and self-worth, which in turn can undermine efforts to achieve equity in population health. Also recall that decision-makers do have a degree of control over structuring policies so that they avoid stigmatising vulnerable populations. Thus by merging these two concepts, we observe how decision-makers can promote equal opportunities in health in relation to non-material goods by avoiding the development of stigmatising health interventions. Overall, the choices made by health officials within their professional jurisdiction are actions that can contribute towards ensuring a social environment that fosters self-respect and feelings of self-worth.

Another tangible example concerns non-material goods in the form of power or influence, key factors that form the crux of lobbying or political pragmatism in health policy development [95]. Communities and organisational bodies (e.g., patient advocacy groups, industry representatives) differ in their opportunities to attract attention and direct

political action towards addressing their health needs. Differences in abilities to successfully lobby for a cause (e.g., funding for a given treatment) may be due to many factors [96] (e.g., of particular importance being financial support and political influence from the pharmaceutical industry [95, 97, 98]). Regardless of the source, these differentials in lobbying power and political influence should raise concern since, at the very least, they likely undermine equal opportunity in addressing population health concerns. Thus, with the principle of equality of opportunity in mind, decision-makers should question whether lobbying efforts might unduly bias their decisions in policy development. If this appears to be the case, this situation should encourage decision-makers to amend their decisions so that they are more inclusive of the needs of other groups that are unable to deploy equivalent levels of influence on decision-making processes. Overall, a more ethical and democratic approach to decision-making is one that bases choices on the premise of providing equal consideration to the interests of all members of the community.

An additional challenging situation faced in health policy relates to priority setting. Since it is often impossible to meet the health requirements of all communities all at once, decision-makers will need to justify their choice in executing certain interventions before others and explain why these interventions should favour the needs of defined groups in society. A growing consensus amongst scholars is that the poor health measures amongst systematically disenfranchised communities are of primary concern in health equity discourses [19, 24, 76, 99, 100]. Arising from these concerns are arguments that prioritising the needs of the worst-off is ethically justified since, at the very least, such efforts will avoid exacerbating the already disadvantaged state of these communities relative to those that are better-off [101, p.214]. If decision-makers share these convictions, upholding Rawlsian principles to favour the needs of the worst-off within priority-setting frameworks can provide guidance and means to ethically justify the targeting of health interventions to particular groups.

General conceptions of distributive justice in health policy

Analysis of health equity is not exclusive to situations concerning health inequalities between population groups. In addition to social justice issues, health policy interventions inevitably also raise many distributive justice issues. Unlike the multiple and sometimes conflicting perspectives of social justice, a primary tenet of distributive justice

has emerged and appears to have attained widespread consensus amongst health scholars, namely the principle of the fair distribution of benefits and burdens [2, p.326-394, 13, 19, 102, 103, p.30, 104].

At the heart of distributive justice assessments is an analysis of the positive and negative outcomes or features of health policy interventions. Positive attributes are broadly termed as 'benefits', which signify the advantages gained by policy initiatives, such as a health intervention's success in reducing or preventing morbidity and mortality (within the context of health research, benefits are typically in reference to the knowledge gained from biomedical investigations). Negative attributes fall under the heading of 'burdens', which refer to any disadvantages that arise from health initiatives, such as risks of harm, hardship or restrictions in civil liberties. Recall that population health interventions may require the imposition of hardships or restrictions on individuals and communities [19, 20], for instance, by restricting freedom of movement and association due to quarantine, or requiring citizens to pay taxes on 'unhealthy' products (e.g., tobacco tax) in order to dissuade consumption, or by introducing risks of harm from breaches in personal privacy.

Previous sections of this chapter have identified why benefits and burdens in health policy are main concerns in ethical assessments: the duty to minimise harms through acts of nonmaleficence and the duty to implement the least restrictive or invasive health policies being apt examples. In addition to consideration of the relative amounts of advantages versus disadvantages in health policy outcomes, justice assessments move one-step further by focusing assessments on whether the allocation of benefits and burdens across individuals and communities are fair [103, p.30]. But what is meant by fair?

Fairness in distributive contexts does not imply that benefits and burdens must always be distributed equally [102]; rather, justice assessments raise concerns when the benefits and burdens of health interventions appear concentrated towards some communities (or individuals) and not others. Reliance on mere intuition would likely lead one to question whether such a concentration of benefits and burdens is suggestive of undue favouritism, or indicative of double standards in policy development (i.e., upholding professional standards in some contexts but not others). Duties to promote health equity appear particularly compromised if benefits or burdens are *exclusive* to certain communities while comparable communities remain *excluded*. The following examples will help place these concepts into context.

Consider a situation where a health intervention, say a vaccine, is made available to a paediatric population; however, health officials conclude that the most efficient means to distribute the vaccine would be to limit its distribution to urban areas. This situation seems fundamentally unfair since this policy decision will inevitably exclude people in rural areas from benefiting directly from this intervention. From the perspective of burdens, many would likely agree that justice is compromised if health regulations impose disproportionate burdens on particular segments of society [13]. Such criticisms arise, for instance, concerning taxes on sweetened beverages as a means to curb rising rates of obesity [105]. Concerns centre on whether such taxes would be regressive in that they would impose a disproportionate burden on the poor, since this population segment allocates a higher percentage of annual income to food (thus, relative to more wealthy groups, the poor will loose a greater percentage of their income due to this tax).

Gostin and Powers [19] offer another example in relation to crisis situations, as would be the case with a natural disaster. Government officials may direct a population to evacuate or seek shelter in safe areas. Though rational, this evacuation order is deficient from a justice perspective: health officials did not consider that disabled and impoverished citizens will not have equivalent mobility and access to private transport as would the majority of citizens. A more fair evacuation strategy would devise plans to ensure these vulnerable members are not left behind. This example identifies how notions of justice encourage health officials to question whether a policy can be of benefit to all, including those disadvantaged members of society.

A third example pertains to issues of exploitation, a concern when specific communities are exposed to risks of harm, but taking these risks will provide no net benefit. Conducting clinical trials for experimental medications in the developing world is a notable example [106]. Clinical trials for experimental drugs carry risks of harm to research participants (e.g., unforeseen adverse drug reactions), risks that most would find acceptable if outweighed by the expected benefits from the research endeavour (e.g., the development of a novel treatment). This arguably just balance of risks and benefits would not be obtained if clinical trials conducted in the developing world would serve to produce medications that will only be made available to developed world populations. Overall, it is becoming widely accepted [6] that it is fundamentally unfair to inflict significant risks on populations that are unlikely to enjoy the benefits from health research. By extension, equivalent conclusions can be made for public health interventions.

Theory applications

Decision-making in health policy will undoubtedly raise issues pertaining to distributive justice. Assessing whether or not a given health intervention is effective at reducing morbidity and mortality is only one component of a larger analysis. Equally important to questions of efficacy are issues pertaining to the fair distribution of benefits accrued from health policy agendas. A complimentary issue in policy analysis concerns burdens; merely designing health interventions to avoid burdens as much as feasible is insufficient. Decision-makers must also assess whether their chosen strategies in policy development will disproportionally impose burdens on specific population segments. Overall, if benefits or burdens must be targeted towards particular groups, this requires strong justification. At the very least, those who must bear the burdens from a policy intervention should also accrue a net benefit. Thus, standard equity assessments should ask *who stands to benefit or be harmed when implementing strategic decisions?* If the distribution of these factors appears unduly exclusive to some and not others, this likely indicates the need for reforms.

Applying practical theory in decision-making frameworks for allergy: A synopsis

Having provided a general overview of principles of ethics and their utility in health policy contexts, the following chapters of this thesis will apply these principles within a novel context: allergy. These principles will serve two functions: first as analytical tools to assess the ethical implications of allergic disease, and second, to structure decision-making frameworks to help guide health professionals in the development of health policies for allergy. Rather than focus on policy officials employed within the upper echelons of government, these frameworks specifically target 'meso-level' health professionals employed within common institutions (such as schools or regional public health departments).

Chapter 1 provides an overview of existing research concerning ethical issues in allergy. Written for a target audience of allergologists, this chapter is in preparation for submission to the journal, *Clinical and Experimental Allergy*. This investigation involved a preliminary literature review of academic articles that discuss ethical issues in allergology

or employ principles of ethics to guide decision-making in allergy health policy. Thus far, this literature search retrieved *fewer* than 35 academic articles that contain a significant ethical analysis concerning allergic disease, which suggests that ethical analysis in allergology is a largely overlooked area of investigation. In raising attention to this apparent paucity of ethical analysis concerning allergy, the article argues that the allergology community should engage in further ethical analysis within their specialization, in order to improve health policy and promote research innovation. This chapter also serves a more indirect purpose, that is, it demonstrates the novelty of this doctoral research and how this project contributes to advancing research in the largely overlooked and underdeveloped domain of ethics in allergology.

Defining the unequal distribution of allergy morbidity amongst socioeconomic classes and minority groups as a social injustice frames the debate in Chapter 2. Published in a special edition on public health ethics in the journal, *Les ateliers de l'éthique/The Ethics Forum* [107], this chapter was inspired by the work of Daniels, Kennedy, and Kawachi [73] and the use of Rawlsian theories of social justice to analyse population health inequalities. However, for this chapter, Rawlsian principles of social justice are not employed within resource allocation discourses. Rather, such principles serve to structure a step-wise assessment framework to prioritize and assess the ethical legitimacy of public health policies that reduce environmental allergens. This assessment framework calls attention to the diversity that exists within the allergic population and the unequal morbidity levels experienced amongst sub-populations of allergy sufferers. In terms of justice, policies should reflect this diversity and aim to provide equal opportunities in health to all members of the allergic population. In situations where targeted policies are merited, the allergic sub-population selected for a particular public health intervention should constitute a particularly disadvantaged group in their abilities to control their allergy morbidity. Additionally, such interventions must have built-in safeguards that ensure policies do not inadvertently stigmatize the population targeted by the public health intervention.

School nurses and administrators of childcare institutions are the target audience in Chapter 3. Published in the *Journal of School Nursing* [108], this chapter aims to address known weaknesses in food allergy policies for schools and childcare settings. To this end, core principles in bioethics and public health ethics are used to develop a framework to assess the adequacy and ethical legitimacy of food allergy prevention efforts. Principles

such as the protection of confidentiality, fair provision of health benefits and burdens, avoiding stigmatization, and empowerment all serve as points for assessment. This policy assessment protocol, in turn, provides a reflexive tool to aid administrators and school nurses in their decision-making capacities when structuring food allergy policies for childcare and educational institutions.

The final chapter investigates ethical issues inherent in current drug regulations concerning the production of allergen vaccines used in allergen-immunotherapy. Published in the *Journal of Asthma and Allergy Educators* [109], this chapter raises questions about the need to assess the potency of these drugs in highly allergic human test subjects. Human subject testing is a necessary procedure in prominent drug regulations that aim to standardize the batch-to-batch consistency of allergen vaccines. Though beneficial, in that this testing enables the production of higher quality therapeutics, such testing is not free of risks, risks that ought to be avoided as much as possible. Following an overview of innovation in in-vitro testing methods, this chapter argues that capabilities in reducing or eliminating human subject testing are rapidly approaching fruition. Thus allergy educators and drug regulators should prepare to reform current standardization guidelines to phase-out human subject testing. To guide this regulatory transition, the article concludes with a reflexive framework to structure drug regulatory policies based on principles of nonmaleficence, beneficence and the fair distribution of benefits and burdens stemming from research.

The following chapter (1), will now aim to answer two basic questions: *What is known in terms of ethics in allergology*, and *why is this domain of inquiry important*?

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CHAPTER 1: ISLANDS SEPARATED BY VAST OCEANS: THE PAUCITY OF ETHICAL ANALYSIS IN ALLERGOLOGY

The following chapter is in preparation for submission to the journal *Clinical and Experimental Allergy*. The analysis herein is thus preliminary, oriented specifically to this thesis, and subject to further modifications prior to submission for peer-review.

Abstract

While a growing body of research is uncovering the aetiology and effective treatments for allergy, research that assess the broader ethical implications of this disease is virtually non-existent. This article will demonstrate both the paucity of academic research concerning ethical implications in allergy – especially in terms of policy and public health issues – and explain why ethical analysis is integral to formulating effective health strategies for allergic disease. An exhaustive literature search identified less than 35 academic articles focussed on the topic of ethics and allergy; this is a miniscule number when compared to the amount of articles published on ethical issues related to other chronic illnesses, such as obesity. It is important to demonstrate to allergy specialists the need for, and utility of, further incorporating ethical analyses in allergology, and in the development of health policies for allergy. Indeed, health policy and public health interventions will undoubtedly encounter ethical dilemmas and the allergology community should play a significant role in helping to address these issues. However, incorporating ethical analyses in allergology does not imply that the allergology community must acquire extensive knowledge in bioethics; instead, interdisciplinary research that incorporates expertise from allergology, public health, and bioethics would enable allergy specialists to advance critical knowledge development in this largely overlooked domain of study.

Introduction

Without a doubt, the sudden development of an epidemic of a chronic disease would garner significant concern amongst the public, clinicians and health officials. It is reasonable to assume that such concern would then motivate the conduct of empirical studies to identify the underlying mechanisms of the disease in order to then evaluate possible health interventions. With such knowledge, value-based judgements and thorough debate centring on how best to prioritize and disseminate treatment options and preventive efforts would likely follow. While logical, this sequence of events appears to be less-than-ideal with regards to the treatment of allergy and atopic conditions.

A seeming weakness in allergology is how the field has addressed debates concerning the implementation of treatment strategies, and the justification of value-based judgements about particular health policies. Or in other words, there is a considerable lack of analysis concerning the ethics and legitimacy of allergy research initiatives, treatments, and health policies. A recent editorial written by prominent researchers in allergology and published in the journal *Allergy* is a prime example [1]. This editorial provides an overview of several global allergy research networks and future research areas that are of foremost interest. Rather surprisingly, only investigations centring on physiological aspects of allergy were deemed of importance; no mention is made of the need for future analyses that serve to identify the broader social, political, and ethical factors that significantly influence allergy treatment strategies and the population distribution of morbidity. The omission of the latter should not be misconstrued to imply that the broader and "less technocratic" socio-environmental and ethical issues of allergy have been investigated in depth and thus merit little, if any, priority. In fact, this article will demonstrate that concerted ethical analysis in allergology has barely begun.

Should the global community of allergy specialists care about this arguably underdeveloped sub-domain of allergology? This article will contend that indeed, they should. However, these arguments will not claim that allergologists should tear-off their lab coats and then focus on philosophical debates concerning "how many allergens can one fit on the head of a pin?". Rather, the aim here is to further sensitize allergy

specialists to the range of social and political factors that influence clinical practice and the implementation of research findings, and the contexts in which such research raises important ethical issues. With greater awareness of such issues, allergy specialists will be better positioned to engage in interdisciplinary research with members of the bioethics community in order to advance ethical analysis and debate in allergology. More generally, interdisciplinary research between these communities will help define the values that ought to guide decisions in health policy and public health interventions for allergy.

Scientific research and clinical experience serve to inform us of the underlying causes of disease, what the risks and benefits are concerning known treatment strategies, and whether emerging treatment modalities show promise in further reducing morbidity. It is wrong, however, to assume that scientific investigation and clinical practice in allergology – and the influence of both on health policy – exist within a purely objective, value-free space. Rather, all of these domains in health are interlinked and raise ethical questions in need of consideration [2-4]. What are the goals of allergy research, and how ought these goals define how resulting medical innovation is implemented and distributed amongst the population? Which forms of allergy morbidity are most significant and, under inevitable conditions of limited resources, which populations of allergy sufferers merit priority in targeted health interventions? What constitutes an effective treatment of atopic disorders, and what proportion of treatment strategies ought to comprise disease prevention efforts? The above are but a brief list of important ethical questions – with no simple answers – that must be subject to ethical reflection and analysis in order to achieve a measure of consensus and recognition of legitimacy, as well as to enable political action (i.e., public policy). It is evident that the voice of the allergology community is essential to these discussions, and in turn, will determine society's success in attenuating the devastating health consequences of the expanding epidemic of allergy.

But first, this chapter will now demonstrate the current (limited) extent of ethical analysis in allergology.

Methodology

An exhaustive literature search was conducted during the months of January to March 2012, via the Internet using the following academic search engines and online databases: GoogleScholar (www.googlescholar.com), PubMed (www.ncbi.nlm.nih.gov/pubmed), Web of Knowledge (Thompson Reuters; www.webofknowledge.com), CAIRN.info (www.cairn.info), Érudit (www.erudit.org), and Refdoc.fr (www.refdoc.fr). Manuscripts in the form of publications in academic journals written in English or French were included in the analysis; publications other than manuscripts appearing in academic journals or books (e.g., theses, institutional newsletters, conference proceedings, news articles) were excluded from the analysis.

An exhaustive search for ethics analyses concerning allergic disease and common atopic disorders was conducted using the keywords: 'allergy', 'atopy', 'atopic', 'urticaria', 'rhinitis', 'dermatitis', 'anaphylaxis', and 'asthma', which were paired with 'bioethics', 'ethics', 'ethical', 'moral', and 'unethical' to enable independent searches for each possible pairing of terms (e.g., 'asthma ethics', 'atopy moral', etc.). An equivalent search was repeated using the same key words in French (uticaire, rhinite, dermatite, atopie, atopique, allergie, anaphylaxie; éthique, bioéthique, morale, moraux). Manuscripts retrieved for each pair of search terms were assessed for content and inclusion in this study. Manuscripts were further excluded from analysis if they met the following criteria: 1) ethics terminology was mentioned only in passing (e.g., appear in two or fewer sentences) *and* the analytical content of the manuscript did not focus discussion on ethical issues; 2) the manuscript *only* mentioned ethics in relation to the research project having passed ethical review by an Insitutional Review Board (e.g., IRB, ethics advisory board, protocols for the ethical conduct of human subjects in research, etc.); 3) provided titles and abstracts in English or French but the text of the manuscript is of another language. The remaining manuscripts were read and categorized by content in relation to sub-specialisations in Bioethics, that is, relating to clinical, research, health policy, and public health ethics. (To expand: clinical ethics pertains to ethical issues arising in clinical contexts, often involving interactions between health professionals and individual patients/families; research ethics concerns the ethical conduct of human subjects research; health policy ethics concerns the

structuring, implementation, organisation, and provision of health services; and public health ethics pertains to health interventions targeting populations rather than individual patients). These manuscript were further divided into two categories which determined their inclusion in the primary analysis or whether they were delegated to annex of this chapter: 1) manuscripts comprising academic articles of several pages are included in the primary analysis; 2) manuscripts comprising short works, such as correspondences, letters to the editor, commentaries of fewer than 3 printed pages, and editorials are listed in the annex only and are not included in the main analysis herein. Manuscripts were deemed to be of particular interest (marked with an 'X') if they devote a significant discussion of ethics *in relation to* allergy (rather than limit discussion of ethical issues to a paragraph or only a short section heading within the manuscript, or if ethical issues are delegated as a distinct topic for analysis such that ethical issues are not framed particularly within the context of allergy).

In order to provide a simple comparison in the amount of ethics research available for chronic diseases other than allergy, the parameters of the literature search were repeated for obesity. However, this literature review was limited to the term 'obesity' (e.g., using search terms 'obesity ethics', 'obesity moral', etc.), and did not include searches employing terms for common co-morbid conditions (e.g., metabolic disorder, diabetes).

Results and Analysis: The paucity of academic articles concerning ethics and allergy

If time is represented anecdotally as 'water' and academic investigations as 'land', the accumulated knowledge concerning ethics and allergy is accurately described as "islands separated by vast oceans" (Table 2). The results from the exhaustive literature search identified fewer than 50 academic articles on the subject of ethics and allergy, which spans 31 years of academic research (1980-2012). The majority of articles retrieved from this search (approximately 90%) have been published within the last ten years alone (2002-2012). Of these 50 articles, fewer than 35 contain a significant analysis of ethical issues in allergology (i.e., articles in which the authors

provide a detailed description of ethical issues concerning allergy, rather than merely mention ethical issues within a paragraph or brief section within the manuscript; in Table 2, these articles are indentified with an ‘X’). This publication history indicates that most investigations centring on ethical issues in allergy are exceptionally recent and not representative a significant effort to advance knowledge in this interdisciplinary domain of study; that is to say, ethical concerns do not appear to “be on the radar” of the international allergology community.

Table 2: Summary of results from the literature search for ethical analysis in allergy

	Year of publication	Author(s)	Bioethics sub-domain	Notable ethics analysis--of particular interest	Reference
Articles in English	2011	Kreger et al	Health policy, Public health	X	[5]
		Behrmann	Health policy, Research	X	[6]
		Master et al.	Research	X	[7]
	2010	Landrigan et al.	Public health		[8]
		Behrmann	Health Policy, Public Health	X	[9]
		Behrmann	Health Policy	X	[10]
		Ellwood et al.	Research	X	[11]
	2009	Engler et al	Clinical	X	[12]
		Brody et al.	Research	X	[13]
	2008	Park, Grayson	Research	X	[14]
		Craner	Research, Health policy	X	[15]
	2007	Scherer et al.	Research	X	[16]
		Canonica	Research		[17]
		Wise	Research	X	[18]
	2006	Liss	Research	X	[19]
		O'Lonergan, Milgrom	Research	X	[20]
		Brody et al.	Research	X	[21]
		Clark et al.	Research		[22]
	2005	O'Lonergan, Milgrom	Research	X	[23]
		Brody et al.	Research	X	[24]
		Roberts	Clinical		[25]
		Scherer et al.	Research	X	[26]
		Resnik et al.	Research	X	[27]
		Onder	Research	X	[28]
	2004	Rous, Hunt	Health Policy	X	[29]
		Sutherland	Research		[30]
		Dolen	Research		[31]
		Coffey et al.	Research	X	[32]
		Annett et al.	Research	X	[33]
		Brown et al.	Health policy, Public health	X	[34]
	2003	Brown et al.	Health policy, Public Health	X	[35]
		Midulla	Clinical, Research		[36]
		Brody et al.	Research	X	[37]
	2002	Miller, Shorr	Research	X	[38]
		Miller, Shorr	Research	X	[39]
	2001	Payne et al.	Clinical		[40]
		Holley et al.	Research		[41]
	2000	Holt, Sly	Research		[42]
	1996	Storrs	Clinical		[43]
	1995	Harth, Thong	Research	X	[44]
		Feingold	Clinical		[45]
		Gibson et al.	Clinical		[46]
	1994	Holt	Clinical		[47]
	1990	Olivier	Clinical	X	[48]
French	2009	Piette, Demoly	Clinical	X	[49]
	2001	Duguet et al.	Clinical		[50]
	1999	Del Volgo	Clinical		[51]
	1996	Lacronique	Clinical		[52]

While the ‘water’ is vast, the ‘land’ is minimal at best and largely represents one form of ‘landscape’. Of the less than 35 articles which do devote significant ethical analysis to issues in allergology, approximately 70% of these articles target ethical issues within research contexts. Of these articles concerning research ethics, the vast majority (nearly 75%) concern research on asthma. Only 8 articles identified in this literature search conduct a significant ethical analysis on issues pertaining to public health and health policy in allergology, 3 of which are articles presented in subsequent chapters of this thesis. No books devoting chapters to ethical issues in allergy treatment or the distribution of atopic morbidities were found. The small collection of articles identified are also representative of ‘islands’ of knowledge, where most articles remain separate from the others in terms of subject for ethical scrutiny. In other words, there are few links between these research publications, such that the information provided in earlier publications rarely cites or ‘builds upon’ in subsequent works concerning ethics and allergy. However, there are notable exceptions to this observation, being the publications by Brown and colleagues [34, 35] concerning environmental justice and asthma, as well as the publications concerning research subjects in asthma studies conducted by Brody and colleagues [13, 21, 24, 37].

Though the results from this literature review indicate ethical analysis in allergology appears quite limited, these results are not necessarily indicative of a true deficiency of knowledge or a lack of initiative in this area of study. It could be argued that ethical analysis in health science and policy (i.e., different from clinical or research ethics) is a relatively new domain of scholarship; thus, it is unsurprising that investigations concerning ethical issues pertaining to the particular disease of allergy are still in their infancy. Indeed, research in biomedical ethics only began to develop prominence in the 1960’s, and the sub-specialization of public health ethics gained notoriety at the beginning of the 1990’s [53, p. vi-viii]. To address this possibility, the parameters of the literature search were replicated for the chronic disease of obesity in order to enable a simple comparison between the amount of ethics scholarship in relation to both diseases.

Obesity is a useful disease for comparison due to its similarities with allergy. Namely, both are chronic diseases that predominate in the developed world, both have a

high population incidence (>25% of populations in developed countries), and both have *recently* exploded into epidemic proportions that pose a significant challenge to public health [54-56]. From this less expansive literature search, over 60 manuscripts pertaining to obesity and ethics were identified, and accumulatively represent several hundreds of pages of published material on the subject (data not shown). Between 2007 and 2010, alone, 23 research articles were published on ethics and obesity [57-79]. Moreover, unlike allergy where retrieved manuscripts were exclusive to academic articles, analysis of ethical issues related to obesity has been the focus of a book [80] and the subject of several book sections [81-88]. Comparing obesity to allergy, a reasonable conclusion derived from both literature searches is that ethical analysis concerning allergy is very limited and at an embryonic stage of academic development. Arguments that ethics in health policy and public health is too new a field of study for there to be extensive application when analysing recent epidemics of disease are not supported by these findings. Instead, the wealth of scholarship available for ethics and obesity should serve as inspiration concerning the future potential for ethics in allergology. Overall, the paucity of ethical scrutiny for allergy likely stems from other factors, such as lack of awareness, interest, or capacities to engage in interdisciplinary research that integrates ethical reflection with allergy research and clinical practice [89]. The following section will attempt to address these potential inhibitors to an applied bioethics in allergology.

Discussion: Adding ethics to the arsenal starts with greater awareness

The provision of a broad argument supporting the need for, and utility in, applying ethical principles to aid decision-making capacities in the domain of health is not necessary for this article. For one, the vast majority of clinicians and researchers – including those specialising in allergology – are probably already well familiar with basic principles of clinical and research ethics that are now a mandatory component of most medical training curricula and that regulate practice in scientific research. The groundbreaking work by Beauchamp and Childress [90], *Principles of Biomedical Ethics* is likely familiar since it has been incorporated into numerous best practice

medical guidelines. Without question, attending to principles of patient autonomy, beneficence, non-malevolence, and justice support good clinical practice and patient care. In terms of research, most health scientists will be familiar with the need to submit research proposals for institutional ethics review, and core principles for the protection of human subjects in research are essential elements of international laws governing human experimentation [91].

Ethical issues unique to allergology

While the above safeguards are well established in legislation, in professional codes of ethics and in medical practice guidelines, these documents are not all-encompassing. There are circumstances unique to allergology that require greater awareness, scrutiny, and debate in order to 'fine-tune' the decision-making capacities of clinicians and researchers. Consider the observation that visible minority patients in the United States, such as African Americans, are less likely to receive asthma treatment according to best practice guidelines and are less likely to receive adequate education concerning how to properly administer their asthma medication [92]. These inequalities in treatment provision do not necessarily arise because of endemic racism in medicine; instead, these inequalities might stem from patient characteristics such as socioeconomic status [93], where patients possessing a higher education level are more inclined to ask their physician necessary questions concerning their treatment [94]. Regardless, clinical allergists must be aware of the potential for inadvertent bias and thus strive to uphold principles of justice in the provision of appropriate information and asthma treatments to all patients.

Another example pertains to research, where emerging clinical trials show promise in the development of immunotherapy for food sensitivities [95]. The expected success of these trials will encourage further development of additional food allergen vaccines and novel treatment modalities. Yet, how ought future clinical trials be constructed to investigate these novel drugs and treatments, and what population(s) ought to compose the primary study group? Since food allergy and associated risks of anaphylaxis disproportionately afflicts children [96, 97], ought trials focus on

establishing appropriate dosing schemes for this population? While children will stand to benefit most from clinical developments from these trials, including this vulnerable population in research is typically discouraged and often encounters significant ethical challenges (e.g., informed consent with young children is often impossible) [23, 98]. The allergy research community will need to debate these ethical issues. At the very least, such ethical reflection will help avoid possible challenges concerning innovation in immunotherapy and assist in securing public, academic, and political support for these research endeavours. Overall, these two examples of ethical issues in allergology demonstrate the need for specific ethical analysis in this field of health science. Greater ethical scrutiny in allergology will undoubtedly uncover numerous additional issues of interest.

The importance of health policy and public health

Whereas clinical and research matters are readily tangible to allergologists, a focal point for greater scrutiny and ethical analysis must include the broader social, political, and legal factors that impact treatment provision and the translation of scientific knowledge into health interventions. Greater sensitivity towards these broader issues is arguably in the best interests of allergy specialists. Allergologists should, without a doubt, play a significant role in contributing to policy debates concerning how best to address the public health consequences of allergy; but the potential of health policy and public health developments in controlling allergy morbidity cannot be overestimated.

The alarmingly high incidence of allergic sensitivities in the developed world – a conservative estimate being 30% of the population [99-101] – signifies that well-coordinated policy proposals that motivate political action and social change will determine what medical treatment strategies are available to the growing number of allergy sufferers. While indispensable, the provision of affective treatments is not the sole moral imperative. Rather, greater ingenuity must also be directed towards public health prevention efforts in order to quell this growing epidemic and address the root determinants that cause allergic sensitivities in the first place. The sudden rise of atopic

disorders cannot be explained by genetic changes in the population, but rather are linked to environmental factors and life-style habits of Western society [102, 103]. Addressing these determinants falls within the jurisdiction of public health, thus indicating that many achievements in allergology will likely come from effective public health efforts [104]. The moral values held by the allergology community can and should guide future treatment and prevention efforts, due in part to the growing recognition of the responsibility for investigators and clinicians "to be accountable to the public and to answer questions about the implications of their work for health care, society, and policy" [89, p.1].

Given the identified paucity of ethical analysis in allergology, there is a need for more ethical discourse in order to define the moral values that will guide health policy and public health interventions.

Principles of ethics as tools to define values in public health and policy for allergy

"[W]e are scientists. How are we supposed to know what society wants from us? That is something for others to debate and formulate; we are perfectly willing to listen and respond."

- Daniel Cohen, in [63, p. 50]

The statement by Cohen is likely a familiar sentiment shared by many specialists in health science and clinical practice, where researchers and clinicians feel somewhat removed from the process of health policy development and designing public health campaigns; that task is typically reserved for another group of specialists, namely public health professionals. Further, Cohen describes a 'top-down' approach to policy, where the values held by investigators are not necessarily *essential* components that guide policy debates and determine what evidence will serve as justification for health interventions. This situation is arguably less-than-ideal. For one, this one-step-removed position from matters of public policy runs counter to growing calls for health researchers to bear a social responsibility to ensuring that the knowledge gained in their roles as scientists is used to achieve societal betterment [106]. An arguably better policy

development strategy would be to embrace the specialized knowledge and experience of allergologists at the start, where their values concerning optimal treatment and preventative efforts can guide health policy and public health initiatives, not the other way around. But how might the allergology community best define these values?

Defining values: The utility of ethical principles

Defining goals and values, in health policy or otherwise, requires ethical reflection and debate, which in turn can be guided by core principles in ethics. One of the best and most concise explanations of the utility of employing principles of ethics as guides in health policy can be found in the recent work by Churchill [4]. Churchill notes how ethical reflection allows individuals (or groups) to identify, clarify, and define the aims and goals of health policy. Once goals are defined, a broader and more stable basis for health policy initiatives can be developed through ethical debate. These debates can enable consensus building which in turn provides a stable foundation of support for policy initiatives. Determining which policy goals constitute as "ethical" depends on whether policies support principles of ethics that are valued by decision-makers and the population that will be affected by such policy interventions. The application of principles of ethics in health policy is best demonstrated through pertinent examples.

First, consider the ethical implications of vast national disparities in the number of allergy specialists. Though most developed nations have a similar incidence of allergy, clinicians specializing in the treatment of this disease vary substantially across regions, ranging from 1:16,000 allergist per capita of the population in Germany, 1:65,546 in the United States, 1:135,000 in Denmark, to 1:1,083,333 in the United Kingdom [107]. An even more unbalanced situation pertains to paediatric specialists in allergy. For example, in 2003 the Royal College of Physicians reported that the United Kingdom had fewer than 10 paediatric allergy specialists, compared to 96 in Sweden, and approximately 2000 in Japan [108]. Broad disparities and significant deficiencies in paediatric specialists exist despite the fact that allergic disease disproportionately afflicts children, and treatment of paediatric populations requires specific expertise. At the most basic level of ethical analysis, such vast inequalities raise questions as to whether

clinical allergists in many regions of the world can fulfil core values of providing adequate and essential care to the allergic population.

Despite all efforts and good intentions by clinicians, clinical allergists will not be able to provide optimal care under political conditions that lead to a chronic deficiency of certain specialists in medicine, but enable a more adequate provision of others. While these inequalities and shortages alone identify a need for change, clinical allergists need to define what would constitute a more ideal distribution of allergy practitioners. Utilizing principles of equity with respect to health outcomes would be a reasonable guide in recommending reforms in public policies that currently permit such vast inequalities in clinical expertise. Moreover, the allergology community will need to define which subspecialisations in clinical allergy policy reforms should be prioritized in order to best uphold values of optimal care. Being cognizant of the needs of children and why their health should be given priority [93], ethical principles that uphold and prioritize the protection of vulnerable populations would have utility in determining what constitutes a more appropriate proportion of paediatric specialists in clinical allergy.

As a second example, consider the link between technological innovation, the commercialization of novel therapies, and access to essential drugs. For many people with allergies and related atopic disorders, uninhibited access to therapeutic interventions is indispensable to achieving an appreciable quality of life. It is therefore disquieting that numerous social, legal, and political factors limit access to essential therapies. Consider recent innovations that enabled the transition to chlorofluorocarbon (CFC)-free asthma inhalers. Ozone depleting CFCs were banned in manufacturing except for the production of essential products, such as metered dose inhalers of drugs used in the treatment of chronic lung disease [109, 110]. The purpose for this exception, however, was to allow time for research to uncover suitable replacements. Indeed, the discovery of novel, non-aerosol administration techniques and the propellant hydofluoroalkane (HFA) enabled a gradual phase-out of CFCs in asthma medications [111-113]. But these cumulative innovations have not been exclusively beneficial. The patenting of these novel drug administration methods has resulted in pharmaceutical companies regaining monopoly rights in the production of once common, and

inexpensive, generic asthma drugs [114]. Such monopoly privileges restrict access and impose cost-barriers [115, 116] to medications that many impoverished people require to live free of severe disability (elevated costs of treatment are a major factor in patient non-compliance to therapy [117]).

Surely these turn of events were not the intended goals of the academic researchers that contributed towards developing these CFC-free drug varieties. Moreover, inadvertent restrictions in access to essential drugs runs counter to core values that the application of research knowledge should serve to benefit society while avoiding the potential for harm whenever possible. Now cognizant of these contradictions in values, researchers must ask whether there are more ethical strategies to transfer research knowledge into clinical application. Such strategies would likely uphold and be guided by principles of benefit maximization, harm reduction, and justice in the provision of treatment; indeed, the choices made by senior investigators and directors of research institutions can help determine the success of these laudable strategies. For one, investigators and directors of research institutes could re-evaluate conditions that define patents on innovations developed through their efforts or at their institutions. Recent policies concerning the patenting of innovations discovered at the University of British Columbia (Canada) is a notable example [118]. Known as the *Global Access Initiative*, some university polices mandate that patent rights are transferred to corporations under the condition that products commercialized from patented technology will be available to populations of the developing world. To enable such access, corporations must provide discount pricing of products destined for developing world markets. Allergy researchers should consider adopting similar policies concerning patenting and whether these models will uphold their core values of maximizing access to, and the benefits of, medical innovations made at their institutes.

Building knowledge in ethics in allergology will require interdisciplinary collaborations

Merging the terms ‘ethics’ and ‘allergology’ is a straightforward indication that advancing scholarship in this hybrid domain will necessitate interdisciplinary research,

and thus collaborative initiatives are likely inevitable (e.g., the combination of neuroscience and ethics to form the field of *neuroethics* [119]). Undeniably, it would be an overly demanding claim that specialists in allergy become equally specialized in another, unrelated domain of scholarship, that is applied ethics. The need for expertise beyond a level of general awareness and interest concerning ethical issues, however, is not essential. This expertise is already available through specialists in fields such as business ethics, bioethics or environmental ethics. Having raised arguments for greater awareness and interest in ethical analysis in the previous sections, this section will now discuss issues pertaining to establishing capacities to promote cross-disciplinary investigations in allergology.

With the realization of the complex aetiologies of most pathologies that challenge public health, experts agree that effective policy strategies for these diseases will require knowledge sharing between multiple disciplines in health research [120, 121]. A growing call for training in health sciences to become more interdisciplinary and inclusive of academic disciplines outside of science are also voiced as strategies to improve academic training of new scientists and clinicians [122-124]. Overall, encouraging interdisciplinary research that integrates ethics and allergology would be consonant with this more general movement. Indeed, establishing greater ties between the biomedical and applied ethics communities sounds simple enough, though it does require a sustained initiative to bridge divides and build capacities that enable real collaboration. In practice, establishing the groundwork for interdisciplinary research is not simple and many experts voice the need for greater support to foster communication and interactions across disciplines [89, 120, 122, 125]. In particular, numerous administrative, cultural, funding allocation, and geographical factors favour research specialising in one discipline. However, there exist means to break down barriers to interdisciplinary research [120]; as noted by Robillard and colleagues [89], the establishment of dedicated ethical, legal and social implications (ELSI) programs, such as those fully integrated into genetics and regenerative medicine, provide models for reforms in other domains in the biomedical sciences. The take-home message here is that individual clinicians and researchers do not have the sole responsibility to establish contacts and build capacities in interdisciplinary research. Rather, research institutes and

departments in allergology have an equally important responsibility to establish programmes and administrative infrastructure that will favour fruitful collaborations with other domains, including applied ethics.

Despite administrative, cultural, and geographical barriers to interdisciplinary research, members of the allergology community do not need to wait for broad administrative changes in the structure of their organisations and research institutes before initiating interactions with specialists in applied ethics. For one, most allergy specialists will likely have had some association and familiarity with ethicists in their place of work through evaluations of research protocols by institutional review boards, or ethics consultations in the clinical context. This established professional network should not be underestimated, but rather seen as an opportunity. Merely engaging in conversations with these colleagues – outside contexts of evaluating research proposals or participating in ethical consults for particular dilemmas – would be a simple means to exchange ideas, and initiate future collaborations and shared learning opportunities.

Conclusion

The paucity of ethical scrutiny in allergology described in this article does not aim to denote solely a weakness in this particular field of biomedical science. Rather, this analysis aims to advance the argument that fostering the development of applied ethics in allergology would enable many *strengths* and opportunities in allergy research and in the optimal design of treatment and prevention efforts. However, the fact that this preliminary literature search retrieved fewer than 35 articles on ethics and allergy signifies that much work remains to be done. The rapid development of bioethics scholarship over the past decade in relation to diseases like obesity should serve as inspiration of the potential that lies ahead for the allergology community.

The growing awareness [2, 4, 53, 126] that initiatives in public health and decisions in health policy are laden with ethical dilemmas and political tensions signifies that decision-makers in health would benefit from enhanced skills in applied ethics. A greater awareness and sensitivity towards the broader ethical, social, and political factors in health research would also be of benefit for clinicians and

investigators, including those specialising in allergy. At the very least, having the ability to identify and verbalize ethical issues in allergy would prove beneficial when members of the allergology community are called forth to provide their expert opinion concerning policy initiatives and public health interventions. In the absence of ethical reflection, one must question whether decision-makers in health are employing all the tools necessary to design optimal treatment and prevention strategies. Furthermore, a lack of academic publications that outline ethical issues that are specific to allergy raise questions as to whether policy makers are cognizant of important ethical tensions that affect clinical practice and abilities to transfer research knowledge into effective health interventions. Thus, the current paucity of academic work in ethics in allergology signifies that future imperatives in allergology should include greater collaborative efforts with members of the applied ethics community in order to advance knowledge in this largely overlooked domain of inquiry.

On a positive note, the seeming divide between ethics and allergy research and clinical practice appears to be on the cusp of change. In 2001, The European Academy of Allergy and Clinical Immunology (EAACI) called attention to major areas in clinical and research ethics that merited future intervention [127], and recommended the establishment of a European Committee on Ethics in Allergology (ECEA). The Canadian research network, AllerGen, which provides support for interdisciplinary training and research in allergy, states that one its three specific research goals is to advance knowledge in the domain of "Public Health, Ethics, Policy and Society" [128]. It is unfortunate that these capacity building efforts in ethics and allergology appear to have not yet reached their full potential; this author did not find evidence (e.g., a webpage) that the ECEA has been established, and the exhaustive literature search retrieved only one article where the authors were affiliated with AllerGen [7]. Regardless, the positive position concerning ethics scholarship put forth by these prominent organizations indicates, at the very least, a nascent recognition of the need for greater knowledge in this largely overlooked area of allergology.

One can hope that the preliminary efforts towards capacity building in interdisciplinary research made by these prominent allergy organizations will provide impetus for others to follow suit. This article aims to contribute to this process by

encouraging greater awareness of the untapped ethical resources that await their application towards addressing key dilemmas in allergology. Once awareness grows, it is only a matter of time before current islands separated by vast oceans will grow into mountains of knowledge and expertise. This is not a question of if, but when; the future success in developing effective policies and public health interventions for the epidemic of allergic disease depend on it.

Annex to Chapter 1

Table 3: Manuscripts other than articles excluded from primary analysis

Year of publication	Author(s)	Bioethics sub-discipline	Of interest	Reference
2011	Murphy, Sandel	Health policy, Public health	X	[93]
	Kling	Clinical	X	[129]
2010	Kling	Clinical, Research	X	[130]
	Wolf et al.	Clinical		[131]
	Bleecker et al.	Research		[132]
	Martinez, Fabbri	Research		[133]
	Naspitz, Warner	Research	X	[134]
2007	Payne	Research		[135]
	Hourihane, Beirne	Research	X	[136]
2006	Coffey, Ross	Research		[137]
2004	Kling, Pead	Clinical	X	[127]
2002	Carter	Research		[138]
	Bisgaard et al.	Research		[139]
	Savulescu, Spriggs	Research		[140]
2001	Bonetta	Research		[141]
	Bush	Research		[142]
	Warmer	Research		[143]
1999	Ferdman, Church	Research		[144]
1998	Kelso	Research		[145]
1995	Mansmann	Clinical		[146]
	Eaton, Downing	Clinical, Health policy	X	[147]
	Reisman	Research		[148]
1994	Smith, Burton	Clinical		[149]
1993	Reisman	Clinical		[150]
	Schmidt	Research		[151]
	Frew	Clinical, Research		[152]
1987	Sly	Research		[153]
1980	Rubenstein	Clinical		[154]
2007	**Revuz**	**Clinical**		**[155]**

Bold font indicates a manuscript written in French.

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Prelude to Chapter 2

Having identified the paucity of ethical analysis concerning allergy, the remaining chapters of this thesis will aim to support one of the main arguments put forth in Chapter 1. That is, Chapters 2 to 4 will defend the argument that merging knowledge between the disciplines of ethics and allergology can help clinician-scientists and policy makers in better structuring health policies for this chronic disease. Moreover, using principles of ethics as a guide in health policy development could serve as a means to ameliorate the decision-making capacities of officials involved in designing health interventions for allergy. The following chapter will begin a focused application of ethics within allergy policy developments by centring attention on justice in the distribution of health achievements amongst the population of allergy sufferers.

The Introduction of this thesis made note of the significant body of recent epidemiologic evidence that demonstrates the existence of large gaps in health achievements, particularly with regards to differences in average life expectancy between population subgroups, such as members of different socioeconomic classes [1]. The observation that social determinants, such as social class hierarchies, correlate with vast inequalities in health raise questions as to whether this inequality is fair or *just*. Indeed, in *Justice is Good for our Health* [2], Daniels, Kennedy, and Kawachi argue convincingly that such health inequalities do represent a profound injustice. These authors then propose tentative policies that are derived from philosophical theories of social justice to help attenuate health inequalities. For example, if health inequalities correlate with differences in socioeconomic classes, Daniels and colleagues suggest that policies that promote the more-equitable distribution of resources between classes, such as income, could improve the health of citizens in the lower and middle-classes.

While analysing health inequalities within a framework of social justice has utility in defining such inequalities as unfair and thus meriting targeted health intervention, the use of theories of social justice to guide 'real-world' public health interventions is not free of criticism. Due to a current lack of evidence that supports income redistribution as a valid health intervention, Barbara Starfield [3, p.67-70] questions whether such 'pro-justice' policies will be effective, feasible, and practical.

This lack of evidence also signifies that policies that aim to promote social justice as a health intervention are too abstract and hard to justify politically.

Despite these criticisms, employing principles of social justice in health policy is intriguing; perhaps the application of these theories within a different context could address some of the above criticisms and still have utility in guiding real-world policy developments. The following chapter will demonstrate one such possibility, that is, an application of the theories of social justice employed by Daniels and colleagues. The goal is not to propose specific policies – that task is left up to public health officials – but instead to show that principles of social justice can be used to develop a framework to assess: 1) the ethical acceptability of tentative public health interventions for allergy and asthma, and 2) help prioritize their implementation. This assessment framework calls attention to the need for public health interventions to provide equal benefit to all members of the allergic population. In situations where interventions aim to improve the health of a *specific* group of allergy sufferers, the population targeted in the public health intervention should be exceptionally vulnerable to allergy morbidity. Such an assessment framework, structured on principles of social justice, is arguably far less controversial than other approaches. Surely it would not be hard to justify politically the enactment of public health policies that aim to provide fair and equal benefit to all members suffering from disease? Rather, would it not be politically contentious for health policies to favour the needs of some while neglecting the needs of others? If a public health intervention must target a specific population, a reasonable argument is that this intervention ought to aim to improve the health of a population that is particularly deprived and disadvantaged in securing good health.

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CHAPTER 2: ALLERGIES AND ASTHMA: EMPLOYING PRINCIPLES OF SOCIAL JUSTICE AS A GUIDE IN PUBLIC HEALTH POLICY DEVELOPMENT

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Abstract

The growing epidemic of allergy and allergy-induced asthma poses a significant challenge to population health. This article, written for a target audience of policy-makers in public health, aims to contribute to the development of policies to counter allergy morbidities by demonstrating how principles of social justice can guide public health initiatives in reducing allergy and asthma triggers. Following a discussion of why theories of social justice have utility in analyzing allergy, a step-wise policy assessment protocol formulated on Rawlsian principles of social justice is presented. This protocol can serve as a tool to aid in prioritizing public health initiatives and identifying ethically problematic policies that necessitate reform. Criteria for policy assessment include: 1) whether a tentative public health intervention would provide equal health benefit to a range of allergy and asthma sufferers, 2) whether targeting initiatives towards particular societal groups is merited based on the notion of 'worst-off status' of certain population segments, and 3) whether targeted policies have the potential for stigmatization. The article concludes by analyzing three examples of policies used in reducing allergy and asthma triggers in order to convey the general thought process underlying the use of the assessment protocol, which public health officials could replicate as a guide in actual, region-specific policy development.

Résumé

L'épidémie en croissance d'allergie et d'asthme pose un défi important en matière de santé des populations. Cet article a pour but de contribuer au développement de politiques pour contrer la mortalité due à ces maladies en démontrant comment les principes de justice sociale peuvent guider les initiatives en santé publique par la réduction des causes d'allergies et de l'asthme. À partir des principes rawlsiens de justice sociale, il devient possible d'élaborer un protocole d'évaluation de ces politiques à l'attention des décideurs en santé publique. Ce protocole peut être utilisé comme un outil dans l'évaluation des priorités d'initiatives en santé publique et dans l'identification de problèmes éthiques des politiques mises en place. Les critères d'évaluation de ces politiques comprennent les points suivants : 1) une intervention spécifique en santé publique doit procurer un bénéfice en santé également réparti dans une population de patients atteints d'allergie ou d'asthme ; 2) si les initiatives ciblent un groupe particulier, ce groupe doit comporter principalement des populations défavorisées, et 3) les politiques ciblées ne doivent pas avoir un effet stigmatisant. L'analyse de trois politiques différentes en charge de lutter contre les déclencheurs des allergies et de l'asthme sera présentée dans le but de tester l'efficacité du protocole présenté dans cette étude.

Introduction

Throughout the 20th century, the developed world has achieved vast improvements in population health, most notable in the dramatic increase in average life expectancy and decrease in infant mortality. The beginning of the 21st century, however, is seeing mounting evidence of stagnation—and sometimes regression—in previous population health achievements [1, p.2], which stem from the increasing prevalence of chronic diseases. The chronic disease of allergy is exemplary; the incidence of allergic sensitivities towards common substances within our environment is now of epidemic proportions and continues to rise [2, 3].

Endemic allergic sensitivities do not imply a mere increase in the number of people with itchy eyes and runny noses. Rather, this chronic illness produces a multitude of morbidities ranging from irritable disorders such as dermatitis, to disabling conditions that have a high risk for mortality, such as asthma and anaphylaxis (sudden cardiac and respiratory arrest). These morbidities pose a significant challenge to public health. For one, they dramatically lower a person's quality of life [4, 5]; they also result in huge costs for national health care systems in terms of pharmaceutical expenses and hospitalizations due to asthma and anaphylaxis [6-8]. Of further significance, allergies are a main cause of disability; for example, asthma is the leading source of disability amongst American children [9]. Indeed, there is pressing need for coordinated efforts to counter this escalating source of pathology.

This article aims to contribute to efforts aimed at countering allergy morbidity by demonstrating the utility of incorporating ethical analysis within the development of public health policy. The discussion will centre on adapting Rawlsian principles of 'justice as fairness' – with the aid of work by Daniels, Kennedy, and Kawachi [10] – as a means to identify the strengths and weaknesses inherent in policies aimed at reducing allergy and asthma triggers within the environment. Specifically, I use these principles of social justice as criteria for policy assessment, to help policy makers decide whether a tentative public health intervention would provide equal health benefit to a range of allergy and asthma sufferers, and whether targeting initiatives towards particular societal groups is merited based on the notion of 'worst-off status' of certain population

segments. In relation to the latter assessment, a concomitant criterion for evaluation will include analysis of whether a policy may have the negative consequence of stigmatizing the population targeted for the public health intervention.

These principles of social justice will serve as a framework for the design of a step-wise assessment protocol that can aid public health officials in prioritizing policy initiatives. Furthermore, this protocol will also provide a means to identify ethical challenges inherent in some policies, thus signalling the need for specific reforms such as including measures to avoid possible stigmatization. After outlining the assessment protocol, three policies for the reduction of allergy and asthma triggers will serve as examples for assessment. These include policies of reducing air pollution, reducing allergens in automobiles, and reforming food labels to better indicate the presence of food allergens. The aim of this assessment is not to determine which are the ideal policies for reducing allergy morbidity. Rather, this analysis seeks to demonstrate the utility of the general thought process underlying the proposed assessment protocol – that is, one based on *principles of social justice* – which public health officials could replicate as a guide in actual policy development at the regional level.

Before presenting the policy assessment protocol, an overview of the aetiology, treatment, and social determinants of allergy is necessary in order to demonstrate why Rawlsian principles of social justice are relevant within the context of this chronic disease. Furthermore, this overview provides information necessary for the final analysis of example policies for the reduction of allergy and asthma triggers.

Aetiology of allergy and asthma

Physiological and biomedical factors of allergy and asthma

Allergy is a chronic disease of the immune system where the body overreacts to common, typically non-pathogenic, substances in the environment, such as pollen, mould, and certain food proteins. Simply stated, immune responses normally target pathogens (i.e. bacteria), where the binding of antibodies induce its elimination and the localized release of histamine. Histamine produces inflammation that prevents further infiltration of the pathogen into the body by causing a reduction in blood flow and

swelling. In allergy, the mistaken targeting of benign substances by the immune system results in a surge of histamine release where the resultant inflammation produces pathological conditions varying from skin rash, respiratory impairment (i.e. asthma), and in some cases, sudden death (i.e. anaphylactic shock). Allergy-induced asthma is a particularly noteworthy pathology in terms of prevalence and physical impairment. Up to 80% of certain allergic populations develop asthma [11], a burdensome disorder that is one of the leading causes of worker disability [12], and a major contributor to total population disability levels [9] in industrialized nations.

Many chronic diseases, such as diabetes and arthritis, predominate in middle-aged and elderly populations. Allergy is unusual since it is prevalent across a broad spectrum of the population (i.e. all age groups, both sexes, all socioeconomic classes, and all ethnicities), while young children in particular have the highest incidence of allergic sensitivities. For example, in the United Kingdom – a nation with a particularly high incidence of allergy – 39% of children and 30% of adults have been diagnosed with one or more allergic conditions [6]. The reason why *some* individuals develop tolerance to allergens with age is likely associated with the maturation of the immune and digestive systems [13].

There are three main categories of treatment strategies for allergic sensitivities. The first and most common is pharmacotherapy, which involves the administration of drugs such as antihistamines that attenuate allergy symptoms. Immunotherapy is another strategy, and involves the injection of gradually larger doses of extracts of the problematic allergen, to physiologically induce tolerance in a sensitized patient. Immunotherapy is only available for treating sensitivities where medical extracts for that given allergen exists, and is largely unavailable for the treatment of food allergies due to elevated risks of adverse reactions to food allergen extracts [14]. A final strategy aims to prevent allergic reactions by reducing or eliminating altogether a person's exposure to allergens. An example of an avoidance effort is the removal of carpets from living environments as a means to reduce exposure to dust. Allergen elimination is an extreme form of avoidance commonly employed in situations where no other medical options are available, as is the case with severe food allergies that necessitate the elimination of food allergens from a person's diet [15].

While certain genetic factors associated with immune function can elevate the risk of developing and severity of allergy and asthma [16], there is clear evidence that the incidence of allergic sensitivities correlates strongly with social and environmental determinants.

Social determinants of allergy and asthma

There are several hypotheses as to why the developed world, and increasingly the developing world [17, 18], is witnessing an epidemic of allergy and concomitant asthma. It appears that increased urbanization is associated with a greater incidence of allergic sensitivities [19]. Exactly how urbanism in industrialized societies promotes allergic sensitivities, however, remains poorly understood. Yet evidence suggests that our current 'artificial living habitats' [20] – artificial in the sense that many individuals distance themselves from nature by spending large amounts of time indoors – may encourage the immune system to overreact towards substances common in nature, such as pollen. Further, living within buildings and employing transport vehicles also permits exposure to abnormally high levels of allergenic substances, such as dust mites, a known risk factor for the development of allergy towards dust [21]. Another purported cause of allergy has been termed the 'hygiene hypothesis' [22], where the reduced exposure to infectious agents in our society – due to improved urban sanitation, vaccination, and the use of antibiotics – may interfere with the development of the immune system and promote allergic hypersensitivities.

The incidence of allergy has additional associations with the structuring and organisation of society. For instance, Isolauri and colleagues [2] assessed the incidence of allergy within populations of different birth cohorts born between the years of 1923 to 1990. They observed that while physiological attributes of the immune system remained roughly constant, the incidence of food allergy rose linearly in later cohorts, with one exception. Those people born during and immediately after World War II (WWII) had a significantly lower incidence of allergic sensitivities. The authors conclude that the mass disruption of society from WWII caused an unusual protective effect from allergic disease.

Another factor in allergy concerns the societal constructs of socioeconomic classes and ethnic minority groups. While allergic sensitivities exist within all ethnicities and social classes, the distribution of pathology is *uneven*. To expand, morbidity from allergic disease follows a steep socioeconomic gradient [23], exemplified by the fact that hospitalizations for asthma predominate amongst low and middle socioeconomic classes [24], and that asthma morbidity rates are higher amongst ethnic minorities [9, 25]. It is interesting to note that the socioeconomic gradient in asthma morbidity remains even in nations such as Canada [24] that provide universal access to comprehensive health care services, thus indicating that unequal access to health services is unlikely to be the cause of these elevated morbidity levels. Additionally, allergic sensitivities are distinct amongst socioeconomic classes, where lower classes often display allergies to environmental allergens associated with factors of socioeconomic deprivation. For example, impoverished inner-city children commonly have sensitivities to cockroaches, rodents, mould, and dust, the root cause of which is living in substandard housing [26-28].

The social determinants of allergy and allergy-induced asthma demonstrate an important fact concerning these chronic illnesses. For one, allergy sufferers are a diverse population of various ages and ethnicities. Of greater significance is the fact that certain populations, such as children, ethnic minorities, and members of lower socioeconomic classes are particular vulnerable to allergy and asthma morbidity.

The pertinence of social justice in assessing allergy and asthma morbidity

Social justice and population health

Justice centres on determining what is ‘fair’, focussing on philosophical notions of what ought to constitute a rightful distribution of resources, outcomes of deliberations, and the provision of just-deserts (rewards), amongst others. The focal point of deliberations concerning *social* justice concerns philosophical notions of the ideal, just society. There are numerous theories of social justice with varying focal points in assessing what constitutes the fair distribution of societal factors [29]. As a

general example (which relates to the subsequent discussion on Rawlsian social justice theory), certain social justice theories aim to define ideals such as the roles social institutions ought to have in ensuring an equitable distribution, amongst societal members, of protections, liberties, resources, and opportunities in achieving one's ambitions in life.

Theories of social justice are relevant in the context of population health, especially since health (defined here as *normal functioning and the absence of pathology*) is essential in providing individuals with the freedom and opportunity to achieve their chosen ambitions or goals in life [30, p.29-31]. Theories of social justice can provide useful tools for defining morally problematic, unequal distributions of health achievements, and arguments for the associated moral responsibility of governments to rectify these inequalities through social reforms. For example, malnutrition may predominate within a defined societal group, thus inhibiting some members of society from achieving their full potential. But is this unjust? If malnutrition is the result of the unequal distribution of resources that is beyond the control of deprived societal members, this situation would arguably be an unjust social arrangement. Furthermore, certain theories of social justice would affirm that social institutions, or societal reform, ought to provide additional protections and resources for this deprived population segment. To conclude, the application of theories of social justice in evaluating population health is a growing field of inquiry [31], and assessing health inequalities within ethical frameworks of justice provides additional means for identifying morally problematic deficiencies in population health that necessitate policy intervention.

Social justice, allergy, and asthma

The previous discussion of the social determinants of allergy and asthma is a helpful case study with which to explain why public policy reforms based on theories of social justice are relevant within the context of these diseases. The observation that these illnesses predominate in industrialized nations suggest that social structures and the state of living environments are significant determinants of allergic disease. The fact

that allergy and asthma have emerged as a recent burden to population health, and continue to increase in prevalence, also confirms that these illnesses are due mainly to socio-environmental factors and not genetic factors that are beyond the remit of social reforms. The observation that sudden disruptions of society, by events such as war, can influence the incidence of allergic disease is of additional interest. For one, it suggests that social reforms, orchestrated by positive means such as public health initiatives, hold promise in significantly countering allergy morbidity.

While allergy and asthma are associated with attributes of a society, can their presence in a population constitute an *injustice*, where theories of social justice would have utility in guiding public health policy development? Current levels of morbidity are arguably an injustice in certain groups of allergy and asthma sufferers. It is unjust that factors beyond the control of an individual, such as being a member of an ethnic minority, place some members of society at an increased risk of allergy and asthma morbidity. The same rationale applies to impoverished children – who obviously have little control over their living environments – develop allergic sensitivities because of substandard living conditions.

As a final note, the observation that allergy and asthma morbidity levels follow a socioeconomic *gradient*, where morbidity increases as one moves down the socioeconomic ladder, suggests that differentials in health correlate with the current means by which society allocates resources across the population. Differentials in wealth and divisions amongst social classes are arguably social constructs, constructs that can be changed through policy developments. As an example, policies that encourage a more even distribution of resources between socioeconomic classes could improve the health prospects of many impoverished population segments suffering from allergy and asthma. Overall, morbidity levels amongst lower socioeconomic classes are elevated, unnecessary, avoidable, and thus unjust. Therefore, orienting public health policy towards enacting social reforms is a possible strategy to alleviate a significant proportion of allergy and asthma morbidity.

A policy assessment protocol based on Rawlsian principles of social justice

Why Rawlsian principles of social justice?

To quote Amartya Sen [32, p.75], "[b]y far the most influential theory of justice to be presented in this century has been John Rawls's 'justice as fairness'". Indeed, Rawlsian principles of social justice continue to have significant influence in numerous academic fields, including health policy [30]. The policy discussion presented in this article will be yet another example of the continuing applicability of Rawls' philosophical contributions. However, before describing some of the key principles of 'justice as fairness' presented in *A Theory of Justice* [33], a short explanation is required as to why these particular principles have been chosen.

Rawlsian social justice theory was determined as a relevant framework to analyze allergic disease from observations of its utility in analyzing macro-level population health inequalities. For example, in their chapter in the edited collection *Is Inequality Bad For Our Health?* [10], Daniels, Kennedy, and Kawachi analyze differentials in population health measures in terms of life expectancy, both globally and within particular nations. They note the existence in many societies of a socio-economic gradient in life expectancy, where lower classes consistently fair worse in health achievements than higher classes. Subsequently, the authors analyze these inequalities from a social justice perspective where they argue that because such health inequalities are elevated, unnecessary, and avoidable, they constitute an injustice. Daniels and colleagues conclude their paper by formulating tentative policy initiatives, based on Rawlsian principles of social justice, which may be used to counter these health inequalities. They argue for the use of Rawlsian principles as an appropriate framework for the assessment of health inequalities on the basis the attention that Rawls' theory gives to guaranteeing fair equality of opportunity for all individuals. Opportunities in this context refer to the abilities that individuals have in fulfilling their chosen life course and achievements. Since securing good health would significantly protect the range of opportunities available to individuals, employing principles that aim to provide equality of opportunity are an appropriate guide for health policy development to

counter health inequalities. The policy proposals put forward by Daniels and colleagues are grounded on the notion that a more just or even distribution of resources between socio-economic classes would raise the life expectancy of lower income groups. Additionally, they suggest that policies which would provide greater opportunities for members of lower income brackets to improve their socioeconomic status, such as enabling greater access to higher education, could uncouple the social determinants that produce lower life expectancies in these population segments.

The thesis presented by Daniels, Kennedy, and Kawachi has many similarities with the assessment of allergic disease presented in this article. For one, as is the case with life expectancy, a significant degree of allergy morbidity is arguably an injustice since it follows a socio-economic gradient. This suggests that the elevated allergic morbidities in low and middle social classes are unnecessary and likely avoidable if these groups had equivalent opportunities to those of higher social classes. The observation that allergy morbidity is significantly higher amongst visible minorities and the poor indicate that their opportunities are limited by allergic disease. Thus, public health initiatives that aim to provide equality in the opportunity to avoid allergy morbidity between all groups of allergy sufferers is an appropriate framework to guide policy development in minimizing allergic disease. This article, however, will not re-iterate the broader health policy reforms put forth by Daniels and colleagues. Rather, the discussion will focus exclusively on policy proposals implemented at the regional level in order to reduce environmental allergy and asthma triggers. Therefore, the context here is brought down a notch, so that the application of Rawlsian principles of social justice is implemented as a guide within regional public health policy development for a specific chronic ailment.

Overview of Rawlsian principles of social justice used to formulate a policy assessment protocol

Rawls' theory of social justice centres on the premise of *equality of opportunity*. According to Rawls, an ideal society is one that is organized to be fair and free where all people possess equal basic liberties and equal potential to achieve their defined

prospects in life. Discrimination in any form is counterproductive to promoting opportunity, and so social institutions ought to safeguard human rights such that everyone is guaranteed equivalent protections. Two main principles here are of significance to policy development. The first concerns the notion of equality of opportunity. This principle signifies the importance for social institutions to enact policies and social reforms that will provide equal opportunity for benefit to all diverse members of society. In relation to public health, this implies that policies directed towards a disease ought to be formulated upon the goal of ameliorating the health of all individuals afflicted by that given ailment. Recall that allergy sufferers form a diverse group of various ages, ethnicities, and allergic sensitivities. Thus, from a Rawlsian perspective, ethical public health policies would be those that aim to reduce allergy morbidity amongst the broad spectrum of allergy sufferers. Furthermore, promoting equality of opportunity implies that the health needs of certain groups of allergy suffers ought not to be ignored due to influences such as lobbying for health resources by another segment of allergy sufferers.

The second principle concerns protections against discrimination. The ethical imperative for social institutions to protect against discrimination is relevant to public health policy in terms of stigmatization. The incidence of illness within a defined population segment can inadvertently promote the misconceived idea that *all* individuals within this group have the negative attribute of being 'diseased'. Therefore, public health officials need to be sensitive to stigmatization and so have a responsibility to employ methods that minimize this possibility. But public health initiatives themselves may play a role in promoting stigmatization. For example, targeted policies could aim to reduce allergy morbidity amongst impoverished children through educational campaigns in low-income areas that encourage people to remove dust and mould from their homes. This targeted policy carries a risk of stigmatizing those of lower socio-economic status by conveying the idea that they live in 'dirty' conditions. Public health officials thus have a responsibility to enact measures to protect these people from inadvertently acquiring the misconceived label of 'being unclean'.

Now we face a contradiction. How can we justify targeting public health initiatives to a particular group of people (as in the example above concerning

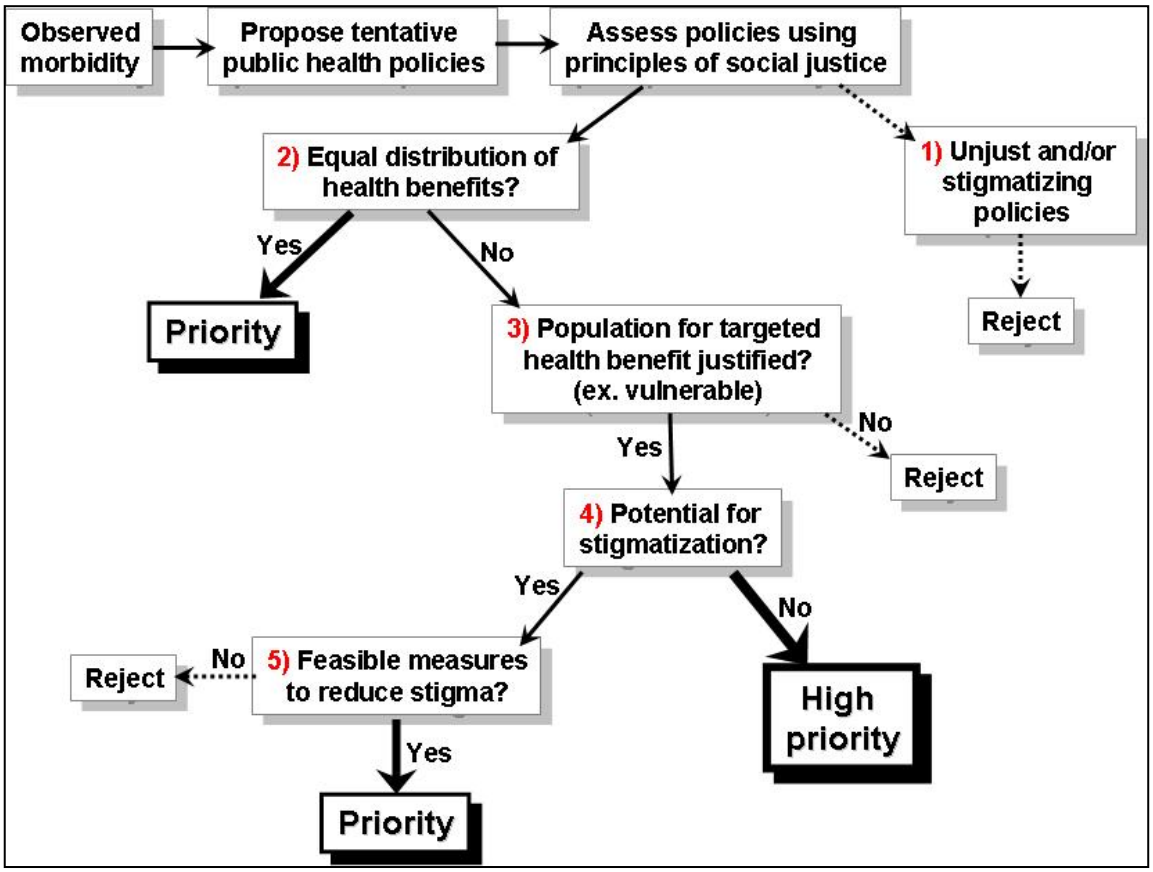
impoverished children) when the principle of equality of opportunity requires that policy initiatives ought to provide equal health benefit to all? Rawlsian social justice theory can provide guidance in this situation according to the *difference principle*. As a further requirement of equality of opportunity, Rawls argued that social institutions ought to mitigate the effects of socio-economic inequalities that prevent less fortunate members of society from having equal opportunities in life. This entails implementing policies for directing resources towards those that are 'worst-off'. Overall, Rawls claims that *priority* ought to be directed towards promoting betterment within particularly deprived, vulnerable populations in order to raise their level of opportunity to a level that is achieved by more privileged population members. In other words, social institutions are justified in favouring the distribution of resources towards 'worst-off' population groups in order to decrease differences in opportunities between societal members.

The difference principle thus provides guidance in determining whether targeted public health policies are justified. It would be justifiable to place priority in directing public health initiatives, and thus health benefit, towards a specific population if this group meets criteria of being particularly vulnerable and deprived. The previous example concerning impoverished children would meet such criteria. These children are vulnerable in the sense that they have little control over their health, and their low socio-economic status suggests that they are deprived.

A step-wise assessment protocol for public health policies

I will now present a policy assessment protocol formulated on the previous discussed principles of equality of opportunity, ensuring protections against discrimination, and the difference principle of favouring the redistribution of resources towards the 'worst-off' members in a population. A summary of the protocol appears in Figure 2.

Figure 2: Schematic overview of a policy assessment protocol formulated upon Rawlsian principles of social justice



Numerous factors influence regional population health, including culture, climate, distribution of wealth, and access to health care. These multiple influences on health signify that regional as well as individual variations in morbidity and mortality are to be expected. Thus, in the context of public health, the beginning of policy development starts with identifying morbidity within regions and population groups. Upon identifying morbidity, preliminary public health policies aimed at countering the root determinants of disease then follow. Of those policies deemed feasible in reducing disease, subsequent evaluations centre on prioritizing policies and determining whether particular policies pose ethical challenges that require specific reforms or protections.

The first step in policy assessment (step 1) centres on determining whether a tentative policy is blatantly unjust and defies the principle of equality of opportunity. These would include policies that carry a high risk for stigmatization, where the efficacy of the policy *requires* that certain groups be associated with a negative label. Another

category of unjust policies is those that provide betterment to some to the *adversity* of others, which completely counters the notion of equality of opportunity. A final example of unjust policies includes those that are pushed forward due to unjustified lobbying and pragmatism. All policies meeting such criteria of assessment are ethically unsound and ought to be rejected.

If the tentative policy passes the initial ethical assessment, the subsequent steps aid in determining what general level of priority the policy should have relative to other policies. This is particularly important in situations of resource constraints that permit the limited implementation of public health initiatives. The first priority assessment (step 2) asks whether the proposed policy aims to provide equal health benefit to all members that compose the population requiring the public health intervention. Policies that meet this criterion support the principle of equality of opportunity and should thus receive priority in implementation.

If the policy aims to focus health benefit to a defined sub-group of a population experiencing morbidity, subsequent priority assessments (step 3) ask whether the targeting of resources towards this group is justified. If the targeted population does not possess characteristics of being particularly vulnerable, deprived, and thus 'worst-off', the policy is not justified for it does not support the difference principle. These policies ought to be rejected.

Subsequent assessments (step 4) must focus on reassessing whether if by targeting policy initiatives towards a specific, vulnerable group, the policy initiative may inadvertently stigmatize that population. If there is minimal risk for stigmatization, this policy proposal should receive high priority since it will likely bring health benefits to a 'worst-off' population that is in greatest need of aid. However, if there is a risk for stigmatization, the final assessment (step 5) should determine whether it is feasible to incorporate within the policy additional protections to minimize or circumvent this problem. There are various methods to minimize harms from stigmatization in public health; which Thompson et al. [34] argue centre on: 1) the need to protect privacy, and 2) the provision of public education to correct misconceptions about disease incidence and to offset misattribution of blame to particular communities (a full detailed description of such mechanisms is beyond the scope of this article). If harm reduction

strategies such as these cannot be incorporated within the targeted public health policy, then the policy ought to be rejected.

Applying the protocol: assessing policies in the reduction of allergy and asthma triggers

To recapitulate, avoidance and elimination treatment strategies are common strategies for reducing exposure to environmental allergens and asthma triggers. These treatment strategies require regional reforms in social and environmental factors, and thus fall largely within the jurisdiction of public health policy. Therefore, these strategies will be the focus of the current policy analysis rather than the biomedical-focussed treatment strategies of pharmacotherapy and immunotherapy, which fall more within the jurisdiction of the acute care health system. Analysis of three policies will serve as examples to demonstrate the step-by-step thought process underlying the use of the assessment protocol presented above, which public health officials could replicate as a guide in regional policy development.

Reducing air pollution

Outdoor pollutants – smog, ozone, and sulphur dioxide – negatively affects everyone, yet places a particularly heavy burden on those inflicted with respiratory illnesses like asthma [26]. Of additional consideration is the fact that residential areas located proximal to regions of high air pollution, such as busy highways, are often low cost housing inhabited by low-income earners. Recall that factors of substandard housing and low socio-economic status correlate with elevated asthma morbidity. Overall, health policies aimed at reducing air pollution are potential strategies to reduce asthma triggers. Therefore, feasible policies could centre on decreasing automotive emissions through encouraging public transit and redirecting heavy traffic away from residential areas. How might these policy initiatives fare in terms of assessment by the above protocol?

Reducing air pollution via public transit or the redirection of traffic does not carry an overt risk for stigmatizing a particular group of people. Since the policy focuses

on pollution due to traffic congestion, it does not convey a negative label towards asthma sufferers. Furthermore, policies aimed at reducing air pollution do not appear to contradict principles of equality of opportunity. The health benefits that would be achieved by this policy do not depend on denying certain opportunities to other population groups.

Advancing from step 1, the next assessment concerns the distribution of health benefits. This policy appears sound in terms of providing equal health benefit to all asthma sufferers. Yet, it could be argued that this public health intervention would have added benefit to asthma sufferers residing in low-income neighbourhoods since they are often living in regions containing elevated levels of pollution. This is not problematic since providing added benefit to this socio-economically deprived population is justifiable in terms of the difference principle. Overall, this policy should receive priority in implementation.

Normally the assessment process would end here, however this example contains a hidden complication. Asthma is but one of many morbidities that arise from allergic sensitivities. Thus, policies for reducing air pollution will be primarily of benefit to those with allergy-induced asthma and less so for those experiencing other allergy morbidities. Is this justified? Such a policy does nonetheless appear to be justified in light of an aforementioned fact concerning asthma, that is, that asthma is a leading cause of disability, especially amongst children. Therefore, asthma sufferers fit criteria of being a particularly disadvantaged, 'worst-off', segment of allergy sufferers. Upon further analysis, it appears that policies for reducing air pollution should receive high priority in implementation.

Reducing allergens in automobiles

Efforts to minimize exposure to allergens typically focus on living environments. With a general upward trend in commute times, a significant segment of the population is spending an increasing amount of time in their cars, thus making the car somewhat of a 'living environment'. Indeed, one study indicates that car interiors can develop high concentrations of allergens [35]. Therefore, public health initiatives

that reduce the build-up of allergens within automobiles may be an effective means to lower allergy and asthma morbidity.

A tentative public health intervention aimed at reducing allergens within automobiles could involve lobbying car manufacturers to change the structure of automobiles so that they are less likely collect allergens. For example, upholstered car seats, which are excellent at trapping a variety of allergens such as pet hair, could be redesigned so that they are easier to clean or are impermeable to common allergens. Now we turn to the assessment.

Early steps within the assessment protocol indicate inherent weaknesses in these policy proposals. While there is a small risk of stigmatizing certain allergy sufferers as having poor cleaning habits, this problem could be avoided by incorporating public education campaigns within the policy. For example, the public could be informed that allergen accumulation in cars is primarily due to the ability for car seats to trap allergens rather than poor cleaning habits. The main problems arise at step 2.

Such policies would primarily benefit allergy sufferers that are also vehicle owners. Being a policy that targets a specific sub-population, further analysis should determine whether this is justified. There does not appear to be evidence indicating that this population group is particularly vulnerable or is heavily disadvantaged by elevated levels of morbidity. Furthermore, their ability to own and operate a vehicle suggests that they are less likely to be socio-economically deprived, or at least not amongst the most disadvantaged. Therefore, the reduction of allergens within automobiles should not have priority relative to other initiatives, such as the aforementioned example of reducing air pollution.

This does not mean that this policy is not of any value; the policy assessment simply indicates that public health officials should not be *aggressive* in implementing this policy, especially if it would direct resources away from policies deemed as more ethically sound by the assessment protocol. In situations such as this, public health officials should then assess whether it is possible to implement the policy in a more ‘hands-off’ manner that would require few resources. For example, merely informing car manufacturers that current car interiors trap allergens may be sufficient in initiating reforms to car interiors.

Reforming food labels to better indicate the presence of food allergens

There are several important issues related to food allergy. First, people with allergic sensitivities to food allergens compose a large segment of the population of allergy sufferers. Second, food sensitivities are more common amongst children than in adults. Of those with food allergy, many experience life-threatening reactions upon exposure to a given food allergen and this is a source for psychological stress and heightened caution surrounding the daily activity of eating [36]. Of particular importance, and as previously noted, there are virtually no biomedical interventions to prevent severe reactions to food allergens, so food allergic individuals must employ strict measures to eliminate the problematic allergen from their diet and environment.

People with food sensitivities therefore rely on ingredient listings on food labels to indicate the presence of allergens. Current regulations concerning food labels, however, are less than ideal. For example, ingredient listings such as 'natural flavours' may not indicate the fact that a food product contains milk products, milk being a common allergen [37]. Therefore, current regulations concerning food labels allow certain common allergens not to be clearly listed on food labels, and this can place food sensitive individuals at unnecessary risk. Thus, a tentative public health initiative could focus on reforming food labels to better indicate the presence of common allergens.

Upon analysis, this tentative policy does not appear to carry risks for stigmatization. A clearer listing of food ingredients (e.g., from 'natural flavours' to 'natural flavours, including milk') would not imply any negative connotations towards food allergic individuals. Nor does this policy appear to counter principles of equal opportunity since reformed food labels would not disadvantage any particular group of the population.

Legislating reforms to food labels is an example of a targeted policy intervention since it will be of exclusive health benefit to food allergic individuals. Therefore, the assessment of this policy advances from step 2 to step 3. Is targeting health benefits to this particular group justified? Such initiatives are justified since food allergic individuals fit criteria of being a particularly disadvantaged group of allergy sufferers.

For one, many food allergic individuals experience elevated morbidity since food allergies commonly induce severe reactions, and food allergies predominate amongst children, a particularly vulnerable population group. Furthermore, unlike other allergic sensitivities, there are virtually no other treatment strategies, such as pharmacotherapy or immunotherapy, for severe food allergies. Therefore, many food allergic individuals could be classified as being particularly restrained, and thus disadvantaged, in their ability to minimize morbidity from their allergic sensitivity. Overall, the following analysis indicates that policies for reforming food labels should receive high priority in implementation.

Summary

The analysis above of initiatives in reducing allergy and asthma triggers aims to highlight a key issue concerning public health policy. For one, it aims to show how ethical analysis can serve as a general guide in determining preliminary strengths and weaknesses inherent in particular health policies. Within the context of allergy and asthma, Rawlsian principles of social justice focus attention on determining if public health interventions are ethically sound in terms of the provision of equal benefit to all allergy sufferers. Rawlsian principles also focus scrutiny on the provision of protections from stigmatization. In addition, these principles provide rational to justify the targeting of health benefits towards particularly disadvantaged groups of allergy sufferers. Overall, the protocol for ethical analysis of policies presented here outlines a systematic thought process useful in priority setting. Relative to the above three examples, ethical analysis indicates that public health officials should place preference towards policies aimed at reforming food labels and reducing air pollution, while reducing allergens in automobiles should receive lower priority. This systematic thought process can be replicated as guide within regional development of various strategies in reducing allergy and asthma triggers, and thus allergy morbidity.

Conclusion

The increasing incidence of chronic diseases is raising a fundamental challenge for policy makers seeking to secure population health. This article focuses on the particular health burden caused by allergy and concomitant asthma and proposes tools for public health policy development that will hopefully contribute to countering current morbidity levels originating from these ailments.

This article demonstrates how Rawlsian principles of social justice have utility in formulating an assessment protocol for policies of reducing morbidities associated with environmental allergens. The Rawlsian principles of equality of opportunity, ensuring protections against discrimination, and priority in the redistribution of resources towards the 'worst-off' members in a population have particular relevance in policy analysis. These principles translate into criteria that are directly pertinent for policy assessment. In practice, this means testing public health initiatives to see if they would provide equal benefit to the range of allergy suffers, and whether the targeting of health benefits to a particular group of allergy sufferers is justified. Additionally, analyzing these policies from a social justice perspective provides means to identify early on whether a policy is ethically unsound and requires rejection or reforms, such as including provisions to minimize the harms of stigmatization. Overall, this article demonstrates the utility of applying Rawlsian principles of social justice in regional-level public health policy development.

While the proposed policy assessment protocol was designed specifically within the context of allergic disease, it is possible that it may have utility in guiding policy development for several other pathologies. Namely, this protocol may have utility in guiding public health strategies in countering other chronic illnesses that exist within a wide spectrum of the population that includes segments of particularly vulnerable and deprived peoples.

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Prelude to Chapter 3

In 1946, the World Health Organization (WHO) proposed a new and broader definition for 'health', as "*a state of complete physical, mental, and social well-being and not merely the absence of disease or infirmity*" [1]. This definition has notable strengths, namely that it recognises that health is not just determined by the inner workings of the body. Rather, many additional determinants in an individual's environment and social network play an equally important role. In turn, this more expansive vision of health signifies that all members of society can have an important role in securing the health and well-being of others, whether or not they play a direct or active role in the healthcare system. Moreover, policies unrelated to the provision of medical interventions, or ones that do not target directly a particular morbidity, may still be of great significance in contributing to the health and well-being of a population.

As was the case with the previous chapter, the following chapter will reflect on approaches to policy development that are conducive to the above expansive vision of health by presenting a framework to structure food allergy policies for childcare institutions. While some of the policy proposals in this chapter will focus upon medical intervention (e.g., availability of epinephrine for anaphylaxis), others will not. These will include policies based on ideals of empowerment, confidentiality, and the emotional bond between parents and children. Though not directly 'medical' in nature, these factors will be shown to be relevant to the health and well-being of allergy sufferers.

An additional recurrent theme will be the need for recognition of distinct populations that are vulnerable to allergy morbidity; however, unlike the previous chapter that centred attention towards large segments of society (such as lower socioeconomic classes), this analysis focuses on the specific population of children within the school environment. This chapter will once again demonstrate how factors related to stigmatization are important issues necessitating consideration in health policy for allergy. Yet another familiar theme in this chapter will be attention to the need to distribute health benefits equally amongst the school population of food allergic children. However, unlike the target audience in the previous chapter, i.e., being public health officials, this chapter aims to help improve the decision-making capacities of

officials that indirectly play significant roles in protecting the health of allergy sufferers, that is, school administrators and school nurses.

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CHAPTER 3: ETHICAL PRINCIPLES AS A GUIDE IN IMPLEMENTING POLICIES FOR THE MANAGEMENT OF FOOD ALLERGIES IN SCHOOLS

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Abstract

Food allergy in children is a growing public health problem that carries a significant risk of anaphylaxis such that schools and child care facilities have enacted emergency preparedness policies for anaphylaxis and methods to prevent the inadvertent consumption of allergens. However, studies indicate that many facilities are poorly prepared to handle the advent of anaphylaxis and policies for the prevention of allergen exposure are missing essential components. Furthermore, certain policies are inappropriate because they are blatantly discriminatory. This article aims to provide further guidance for school health officials involved in creating food allergy policies. By structuring policies around ethical principles of confidentiality and anonymity, fairness, avoiding stigmatization, and empowerment, policy makers gain another method to support better policy making. The main ethical principles discussed are adapted from key values in the bioethics and public health ethics literatures and will be framed within the specific context of food allergy policies for schools.

Introduction

The industrialized world is witnessing a growing incidence of allergy [2-4]. Allergy is a chronic disease wherein the immune system becomes hyper-responsive (also described as hypersensitive) to common substances in the environment, such as allergenic components in pollen, dust, and animal dander. Typical allergic reactions produce watery eyes, nasal congestion and skin irritations such as hives. However, certain allergic individuals experience severe allergic reactions that carry a significant risk for mortality. Of particular concern are allergic responses that induce asthma or anaphylactic reactions. Anaphylaxis is a systemic allergic reaction resulting in extreme cardiac and respiratory impairment and is typically fatal if medical attention is not sought immediately.

One major category of allergic disease is food allergy. Food allergies are prevalent in the industrialized world and it is estimated that eight percent of children under the age of three have a food allergy [5], with approximately 1.5 percent of the population being allergic to peanuts [6]. Studies also indicate that the incidence of food allergic disease is increasing dramatically [7, 8]. The most common allergenic foods include peanuts, nuts, egg, milk, soy, and fish; yet hypersensitivities are also observed for a variety of other food products, including many fruits, vegetables, food colouring agents, and spices [9].

Food allergies have certain particularities relative to other forms of allergic disease. Therapeutic interventions of pharmacotherapy and immunotherapy provide treatment for most forms of allergy. These therapeutic options are typically not applicable with food allergy, where the primary means to avoid a food reaction is to eliminate the allergenic substance from one's diet [10]. Furthermore, the risk of experiencing a severe reaction or anaphylaxis is generally higher with allergic reactions to food [11]. Another characteristic of food allergy is that it is particularly prevalent in children and adolescents [10].

The widespread incidence of food allergy in children, and thus risk for anaphylaxis, poses a significant challenge to those individuals (i.e., parents, educational and health professionals) that oversee their wellbeing. A large amount of responsibility in the management of severe food allergic reactions has fallen on administrators and health professionals of childcare settings, such as schools and daycares, locations where reactions to food commonly occur. Eighty-four percent of food-allergic children will experience an allergic reaction while at school [12], and one quarter of *initial* allergic reactions to food arise in the school environment [13]. The presence of at least one food allergic student

within a childcare setting or school appears to be nearly inevitable, with one American study finding that 55 percent of elementary schools surveyed reported having 10 or more affected students [14]. The high number of food allergic students has resulted in numerous schools implementing policies that aim to prevent allergic reactions and reduce the risk of mortality should an anaphylactic reaction occur.

To aid schools and childcare settings in developing appropriate policy responses, several allergy medical organizations and experts have published guidelines on preventative strategies for food allergen exposure and anaphylaxis [10, 15-20][11] (hereon cited as simply, "Guidelines"). These guidelines typically describe factors such as emergency action plans for anaphylactic reactions, provide templates of medical information files for allergic students, and propose guidelines on how to minimize the risk of accidental ingestion of problematic foods. While such recommendations have been available for many years, studies demonstrate various (often limited) degrees of compliance, much heterogeneity in the application of policies, and a highly variable ability of many school officials to respond appropriately to severe food reactions [12, 14, 21]. Furthermore, certain policies employed in schools are arguably unethical and place undue psychosocial stress on food allergic students. For example, some policies inadvertently cause food allergic students to be separated from "normal" students, thus encouraging stigmatization and even discrimination [22]. These are significant problems. If schools and childcare settings are to fully address the needs of food allergic students, they must employ a more thorough application of guidelines, have better emergency preparedness, and avoid stigmatizing policies.

This article provides further guidance for school nurses and administrators to take a lead in the oversight and protection of food allergic children. Many school nurses likely face difficulties when determining which strategies will best address the needs of students. Indeed, depending on factors such as student population, age, variety of food allergy, and availability of food services, food allergy policies will have to be adapted to meet the specific contexts of educational facilities. How can this be done and how is one to determine if the resulting policies are most appropriate? Certain ethical principles can aid school nurses in this process. By basing policy decisions on sound ethics, school nurses and

[11] Several of these guidelines and mission statements date from the 1990's and represent foundational policy documents on food allergy in relation to childcare settings. Though they may appear dated, these documents remain relevant within current food allergy policy developments.

administrators gain a valuable tool that can help them in determining which policies are best for their institution. This article will present the ethical principles of confidentiality and anonymity, the fair distribution of benefits and burdens, and empowerment. Key principles in the public health ethics literature will also be presented. These principles are placed within context of common food allergy policies where through ethical reasoning, good policies can be made *better* and the appropriateness of policies can be identified relative to alternatives[12]. For example, paying attention to the principle of anonymity can help prevent the enactment of stigmatizing policies, while attention to the fair distribution of benefits can guide decision-making in determining whether to ban certain food ingredients from a cafeteria menu. Before commencing the discussion of how to integrate ethical principles into food allergy policies, it will be helpful to have an overview of common recommendations and policies, and the key problems observed with the implementation of such policies.

Common guidelines and policies for the management of food allergies in childcare settings

Several guidelines and recommendations have been proposed by various experts and committees, including paediatricians specializing in food allergy as well as the American Academy of Allergy, Asthma, and Immunology (as previously cited: Guidelines). Most guidelines provide information on two main issues for food allergic students. One topic pertains to emergency preparedness, which refers to how facilities ready themselves before a severe food reaction occurs in a child and what childcare administrators are to do immediately following the onset of an anaphylactic reaction (Emergency Action Plans for food allergy are available online; see Young et al. [23] for a recent example). The other main issue is one of prevention, where strategies are provided

[12] Within the United States, several national and regional laws and regulations mandate certain practice parameters and policies concerning food allergic children within the school environment (e.g., national regulations include statutes within section 504 of the Rehabilitation Act, Americans with Disabilities Act [ADA], and the Family Educational Rights Privacy Act [FERPA]). This article will not focus discussion towards such legislation, which will likely be already familiar to school nurses and administrators. Rather, this discussion aims to advance knowledge on food allergy policy developments and thus focuses on ethical frameworks, exclusively – ethics being a subject that is currently absent within the academic literature concerning food allergy.

on how childcare facilities can minimize the risk of accidental consumption and exposure to food allergens.

The first step recommended for emergency preparedness is for facilities to maintain medical information files on allergic students that are readily accessible to school heath professionals. The American-based Food Allergy and Anaphylaxis Network provided a template medical file that is endorsed by several experts [10, 12, 24]. The template – which is to be completed in conjunction with the child's primary care provider – contains sections that allow for listing of the child's allergic triggers and the medication to be administered depending on the degree of allergic reaction. Also present are emergency contacts for the child and diagrams on how to administer epinephrine (adrenaline) if an anaphylactic reaction should occur. To clarify, the administration of epinephrine is the first line of defence in countering anaphylaxis prior to seeking medical attention at a healthcare facility. The general function of health records is to give health professionals at educational facilities the opportunity to assess periodically the particular needs of food allergic students. These documents also provide a resource that school nurses and administrators can turn to in the advent of an allergic reaction. The availability of epinephrine in childcare facilities and educational settings is essential in strategies aimed at reducing the risk of fatalities from severe allergic reactions. Recommendations of multiple professional organizations (as previously cited: Guidelines) state that epinephrine should be easily accessible and stored in a known location. Staff members that commonly work with food allergic students should be trained in identifying an allergic reaction and know how to administer epinephrine when necessary. Therefore, emergency preparedness for severe food reactions can be viewed as a three component initiative: 1) accessible medical information files on allergic children, 2) availability of epinephrine in the advent of an anaphylactic reaction, and 3) training of staff in the appropriate administration of epinephrine.

The underlying cause of severe food reactions is the inadvertent consumption by individuals of food not known to contain a problematic allergen. Policies that have as their goals the prevention of food allergy reactions focus on preventing children from consuming food that is unfamiliar to them. One common method is to enforce strict "no food sharing" policies that prohibit the sharing (or trading) among students of food, utensils, and food containers [20, 25]. When food services, namely cafeterias, are available at a school, efforts are to be made to ensure the safety of the food provided and that allergen-free alternatives

are available. To this end, it is recommended that food service staff be educated in methods to avoid the cross-contamination of prepared meals through the proper washing of surfaces and utensils [20]. Food service staff should also be educated in the reading of food labels in order to identify the presence of allergens [14]. Other common strategies in preventing the inadvertent consumption of allergen-containing food are for facilities to restrict the consumption of certain foods to specific areas, or to ban the presence of some foods altogether. Such methods can include having a designated "allergen-free" table in the cafeteria where products that contain common allergens, like peanuts, are not to be consumed. It should be noted that "allergen-free" does not imply a dining area that is only of use for food allergic children. Rather, the area should be available to all children that choose not to consume common allergens within that space. Many experts note that administrators of schools and childcare facilities must be vigilant to ensure that the presence of a food allergy does not result in the segregation of the food allergic child from other children (as previously cited: Guidelines). While children with food allergy have a serious medical condition, their allergy should not result in their exclusion from events, such as field trips, or in their isolation during meal times.

With regards to food bans, most experts do not endorse such policies [20, 26]. Many argue that broad food bans are largely ineffective, provide a false sense of security, and are burdensome on families that do not have food allergic children [10]. Some studies have demonstrated that peanut bans in schools do decrease substantially the presence of peanuts in school lunches [27]. The complete elimination of peanuts, however, appears to be next to impossible. Despite criticisms, policies for the banning of certain foods from schools are relatively widespread [28]. In settings with particularly young children that are incapable of objectively selecting the food they eat, such as preschools, food bans are recommended for major allergens [20]. The general principle in preventing severe food reactions is to prevent the inadvertent consumption of the allergen.

It should also be noted that additional policies not related to eating habits have been developed to prevent severe food reactions. Anaphylactic reactions have been induced in children due to arts and crafts activities and science projects [13]. In these situations, allergenic components were part of the project (e.g., the use of peanut butter in the making of birdfeeders). It is recommended that schools and childcare facilities avoid the use of common allergenic compounds during such learning activities.

A curious fact concerning food allergic children is that their medical condition can make them the target of bullying and harassment. There have been documented incidents of fellow students, perhaps not understanding the seriousness of food allergies, forcing allergic students to consume allergen containing food, with dire consequences [24]. Because of this threat, some experts recommend the promotion of anti-bullying policies as an essential component in the prevention of accidental allergen exposure [20, 28]. Furthermore, most relevant guidelines strongly endorse the need for the education of staff and *all* students on the issue of food allergy [20]. Only once administrators, teachers and students fully understand the severity of food allergy, and the best methods for the prevention of severe reactions, can precautionary policies be enforced, appreciated and thus effective.

To summarise, efforts to prevent severe food reactions must go beyond discussions about eating habits to also include broad education initiatives concerning food allergy, the promotion of respect for food allergic children (e.g., by preventing bullying and harassment), and the avoidance of allergenic compounds in school activities.

Weaknesses observed in policies for the management of food allergies in childcare settings

While the availability of guidelines for managing food allergy have provided valuable resources for administrators and school nurses, many challenges are observed when food allergy policies are executed in real-world settings. Studies conducted in the US have shown that many schools are inconsistent in their application of guidelines and that policies vary widely among facilities [12, 14, 28]. Heterogeneity in policy application is not problematic *per se* – depending on the specificity of a given educational facility (e.g., size, variety of food allergies, the availability of food services), some policies will not apply or will need to be adapted to fit the particular needs of a given facility.

This heterogeneity becomes problematic, however, when the inconsistent application of guideline recommendations compromises an educational facility's ability to manage appropriately the risks of childhood food allergy. For example, Rhim and McMorris [14] observed that some schools do not keep medical information files on food allergic students, thus compromising the ability of school health professionals to address

the health and safety needs of these students. Furthermore, the authors noted that some schools did not keep emergency epinephrine (two percent of schools surveyed), while a significant proportion (10 percent of schools surveyed) did not have staff trained in the administration of this life saving drug. These observations demonstrate important gaps in emergency preparedness strategies within certain educational facilities. Similar observations have been made by Powers, Bergren, and Finnegan [12], who found that numerous schools did not have written food allergy emergency plans, and many school personnel felt unsure with regard to how and when to administer epinephrine.

The presence of gaps is also observed in policies aimed at preventing the inadvertent consumption of food allergens. Rhim and McMorris [14] found that while many schools offered food substitution and meal replacements in cafeterias, most did not educate food service staff on the reading of food labels in order to identify the presence of hidden allergens. Another problem that has been voiced by children concerning policies for the management of food allergy is that certain measures are blatantly discriminatory. In some facilities, food allergic students are required to leave the general queue in order to collect their meal from another location, thus branding them as distinct and different from other students [22]. Furthermore, students have complained about the poor quality of meal replacements and allergen-free alternatives provided in school [22]. The poor quality of these meals was attributed to a lack of knowledge and interest on the part of cafeteria personnel in preparing tasty allergen-free meals.

The above observations indicate that many educational facilities need to review the current strengths and weaknesses within their policies for the management of food allergy. Particular vigilance is needed to eliminate gaps in emergency preparedness and allergen avoidance policies. It also appears that a degree of poor judgement can be present during the formulation of certain policies, such as those that inadvertently promote discrimination. Ethical principles can be used to both help school nurses in their role to support administrators in decision-making, and provide guidance on how to make acceptable policies *better* by having them meet minimum ethical standards.

Ethical principles as a guide in developing food allergy policies

Preventing severe food reactions in children is a matter of public health, and numerous resources are available that can aid officials in implementing effective public

health initiatives. One resource is the 2002 publication of a code of ethics for public health [29]. The first clause of this code of ethics is particularly pertinent to beginning an ethical dialogue on food allergy policies: "*Public health should address principally the fundamental causes of disease and requirements for health, aiming to prevent adverse health outcomes*" [29, p.1058]. This clause is important, because in the context of schooling and childcare, it means that facilities cannot permit the partial enactment of guidelines or allow for gaps in efforts to prevent anaphylaxis. If school nurses are to prevent the adverse health outcomes of food-induced anaphylaxis, they must ensure the policies are sound, robust, and follow the standards set forth by experts, even if these recommendations are not enforced through legislation. For example, school nurses must ensure that their emergency preparedness plans are complete: having epinephrine available is not sufficient if staff are not trained on how this potentially life saving medication is to be administered; having medical information files readily available is not sufficient unless all students with food allergy are included in this registry. This first principle of public health ethics affirms that the goal of proper management of food allergy is the prevention of anaphylaxis, and thus, the complete enactment of emergency preparedness plans and avoidance policies is essential.

Another general principle that can aid school nurses and administrators in policy decisions is to pay attention to their professional and fiduciary responsibilities, that is, the trust or care relationship they have with food allergic children requiring assistance. To expand, many feminist scholars argue that our relationships with others are not impartial since they are linked to responsibilities of care for others that play a role in our daily lives [30]. Decision makers in public health – including school health – should thus imagine themselves as "caring parents" for members of society under their responsibility, and they should ask themselves the following question: "*what resources and level of protection would you expect if it were your food-allergic child?*". The answer to this question can prove valuable in informing choices about which policies to enact within a given school or childcare facility.

Confidentiality and anonymity

Respect for confidentiality and protection of privacy are core ethical principles in health care, as well as prominent core values upheld in many social democratic societies,

especially in North America and Europe. Individuals afflicted with a given ailment – something that may have a significant impact on their personal lives – have the right to keep this fact private if they so choose. The right for individuals to choose to keep their medical needs confidential stems from both a respect for their autonomy as individuals, and recognition of the very real risks that the inappropriate disclosure of health information may entail. These risks may include, among others, unjust discrimination in employment, the loss of health or life insurance coverage, and stigmatization on the basis of a particular medical condition [31]. Thus, it is important that sensitive health or medical information be dealt with carefully, treated as confidential, and be disclosed only to those professionals that need such personal information in order to protect the health of the individual. Any documentation, such as personal medical files, that are formulated during interactions with medical professionals should be secured to ensure these documents remain confidential.

The principle of confidentiality is particularly relevant for food allergic children. Interviews with children with food allergies confirm that occasionally, their food allergy results in discrimination and stigmatization by other students, and this produces significant psychosocial stress [22]. Furthermore, being labelled as "food allergic" carries an increased risk to a child's wellbeing since this can make them the target of bullying and harassment, and has already been mentioned, resulted in instances of children being force-fed food to which they were allergic [24]. Therefore, when school nurses and administrators are formulating policies for food allergy, *they must be vigilant that policies do not cause food allergic children to become identified as different from other children*. For example, having allergic children line up in a different line in order to collect their meal alternatives is unacceptable. Similarly, guidelines that recommend the provision of an "allergen-free" eating area, such as peanut and milk-free cafeteria table, can be problematic. This policy would only be appropriate if food allergic students do not exclusively occupy this table. To prevent exclusion and assure anonymity of the allergic condition, policies ought to include efforts that encourage friends of the allergic student to also bring in allergen-free lunches, thus allowing for inclusion of all students. Of course, it is recommended that use of allergen-free areas not be mandatory for food allergic children [24].

The principle of confidentiality is pertinent to food allergy policies in relation to emergency preparedness. An essential component of emergency preparedness is the ready availability of medical information files so that school health professionals have easily at hand the information necessary to help a child should they experience an allergic reaction.

However, this policy ought to be employed alongside efforts that ensure these files remain confidential. Any additional staff members (e.g., secretarial or computer maintenance staff) that might view such files must also be informed that these files contain medical information and thus must be treated as confidential. After viewing a child's file, school health professionals must inform staff members that they are not to provide information found in that file to anyone else.

At times, keeping an absolute stance on anonymity may prove impractical. For example, if school administrators choose to impose a food ban, they need to inform parents of the food to be banned and the reasons for the policy. A dilemma surfaces in determining how much specific information should be divulged when informing others (parents), while maintaining confidentiality and anonymity of the affected children. Thompson and colleagues address this issue with an ethical value concerning privacy: "*Disclose only private information that is relevant to achieve legitimate and necessary public health goals*" [32, p. 6]. By applying this principle, school nurses can help administrators inform others of food allergy and their efforts in preventing anaphylaxis without violating the privacy of food allergic children. For example, it is appropriate to inform others that an educational facility has several students with severe food allergies that carry a significant risk for anaphylaxis. Additional information, like identifying characteristics and the medical requirements of food allergic students are irrelevant and ought not to be divulged.

Additional challenges may arise when communicating the health needs of allergic students to other children. Imagine the situation where a child unknowingly sits at an "allergen-free" table with a meal that may possibly contain allergens. Rather than inform the child that that they are not permitted at the table because of the needs of a specific, identified student, the school nurse should inform school officials to explain that the student's nutritious meal might be harmful to other students *and staff* (emphasis added) at that given table. School health professionals should then communicate to the parents or guardian of that child to consider preparing allergen-free meals as a means to ensure their child's safe inclusion at any table within the school setting.

Fair distribution of benefits and burdens

Another core ethical principle is justice or fairness; that is, that all individuals have equal access to resources that ensure their happiness and wellbeing. From a public health

perspective, this implies that policy initiatives will be of broad health benefit to all applicable members of society. Fairness also implies that if policies require a certain degree of restrictions on behaviour or liberties, these burdens ought not to be discriminatory and ought to be applied evenly throughout society.

The value of fairness is applicable to food allergy policies on several levels. For one, when formulating policies, administrators ought to ensure that *policies will be of benefit to all, and not for only certain food allergic students*. For example, administrators should ensure that policies do not focus on a given allergen, to the exclusion of others. Peanuts are commonly scrutinized during discussions on food allergy as peanut allergy is notoriously associated with anaphylaxis [13]. Therefore, it is common for policies to focus on peanuts, and implement peanut food bans or peanut free classrooms. However, other allergens, like milk, are also common inducers of anaphylaxis [33]. Therefore, for policies to be of equal benefit for all food allergic students, policies such as "no food sharing" ought to be favoured over specific bans of one particular allergen. Furthermore, it is generally agreed that food allergy policies should be age appropriate, so that as children mature, they can and should acquire a greater responsibility in managing their allergy [20]. However, this does not imply that food allergy policies should focus exclusively on the needs of young children while leaving those of adolescents unaddressed. Indeed, it is known that the majority of severe food reactions occur in children over the age of 5 and are especially prevalent in food allergic adolescents [22, 24]. So in applying the principle of fairness, policies ought not to benefit only young children or assume that the needs of more mature students can be met by their own efforts. For example, school health officials should not assume that more mature, adolescent students would consistently carry emergency epinephrine and thus only provide emergency epinephrine in settings for the care of young children that are understandably less capable of upholding such a responsibility.

Additionally, when formulating food allergy policies, school nurses ought to ensure that *food allergic students have access to the same opportunities and resources as other students*. For example, it is recommended that common allergens not be included in science or art projects, therefore permitting the participation of all students. However, this policy ought to be extended so that food products are not used as rewards for academic performance or during classroom celebrations [24]. Rather, to allow all students to participate, these items ought to be replaced with non-edible items like sports cards or colourful school materials (pens, pencils) [24]. Another example pertains to allergen-

elimination meals provided at school cafeterias. Food allergic students note that these meals can be of lower quality and less palatable than regular meals. Food preparation staff should be supported to ensure they are knowledgeable in preparing allergen elimination-diet meals that are of the same quality as regular meals served at the educational facility. Additionally, the meals ought not to be provided at extra costs to the allergic child [15]. To avoid possibilities for stigmatization, the meals could be demarcated subtly with a small sticker or pen mark placed on the cellophane wrapping or at the edge of a serving plate.

Another issue of fairness pertains to the fair distribution of burdens that may arise from certain food allergy policies. In general, school nurses and administrators must ensure that policies *do not unduly burden the eating habits of certain children*. For example, food bans ought to be avoided for they can significantly compromise the daily eating habits of many children not affected by food allergy. Take the example of a broad food ban on soy, a common allergen. Such a ban will unduly burden the eating habits of children that are vegetarian or members of certain ethnic communities, where soy is a common protein replacement or staple food. However, under certain circumstances, policies may be justified in restricting the eating habits of certain children. For example, specific food bans can be deemed appropriate in facilities with very young children that are incapable of objectively deciding which food they can consume [20]. Determining whether restricting specific eating habits is appropriate can be resolved by applying Thompson and colleague's ethical values on restricting liberties. They state that restricting liberties is appropriate if "*the restriction is proportional to the risk of public harm and is necessary and relevant to protecting the public good*" [32, p. 6]. Thus, by applying this principle, it would be appropriate that school nurses inform administrators to apply food bans in the preschool setting where the risk for the accidental consumption of allergens is high. However, such bans might not be appropriate in a cafeteria where policies such as allergen-free dining tables and the provision of allergen-free meal alternatives are appropriate measures that do not involve restricting a child's liberties.

Empowerment

There are two ways to orient initiatives for securing the health and wellbeing of a community. One method, which may be overly or unreasonably paternalistic, involves the imposition of policies and regulatory efforts on others without providing alternatives or

explanations as to why such rules are important. The other, arguably more ethical approach (i.e., less coercive), involves empowering people in the control of their health and wellbeing. Examples of empowerment include educating the public on sound health choices and the provision of resources so that people are more able to protect their wellbeing. The notion of empowerment is integral to the code of ethics for public health proposed by Thomas and colleagues; the fourth clause states that: "*Public health should advocate for, or work for the empowerment of, disenfranchised community members, ensuring that the basic resources and conditions necessary for health are accessible to all people in the community*" [29, p. 1058]. But how do notions of empowerment apply to food allergy?

Munoz-Furlong states that empowerment of food allergic children is essential since "[e]mpowering a child to participate in food allergy management strategies will yield a confident child who is less likely to make mistakes or take unnecessary risks and who can rebound after an allergic reaction" [24 p. 1654]. Thus, when school health professionals are formulating policies for food allergy, an essential component should be the empowerment of all students and staff. Primary methods to achieve empowerment include the broad education of all students and faculty on food allergy, anaphylaxis, and methods to avoid food reactions [15, 20, 27]. Other means to empower food allergic children include encouraging them to carry, and be knowledgeable in the administration of, emergency epinephrine. Of course, this will only be appropriate with older children and it does not absolve educational facilities of the responsibility for keeping their own supplies of epinephrine available. Additionally, administrators should take threats to the safety and wellbeing of food allergic children seriously, as would be the case with bullying and harassment. Overall, school nurses and administrators should strive to ensure that their efforts in the management of food allergy include elements of empowerment by providing children and staff with resources that will enable them to gain better control of the children's health and wellbeing.

Conclusion

The industrialized world is witnessing a growing incidence of allergic disease and food allergy in children and this poses a significant challenge to public health. The main concern with food allergy is the possibility for the inducement of life-threatening

anaphylactic reactions due to the inadvertent consumption of a food allergen. To address this concern, most schools have enacted policies to prepare for the sudden onset of anaphylaxis in food allergic children. Such efforts include the provision of emergency epinephrine and the training of staff in its administration. Additionally, schools and childcare facilities commonly employ policies that aim to prevent food allergic children from mistakenly consuming allergen containing foods. Such efforts include employing "no food sharing" policies or the provision of "allergen-free" tables in dining areas.

Despite these efforts, numerous studies have demonstrated that many schools are ill prepared to effectively prevent severe food-induced allergic reactions. This is due to incomplete emergency preparedness plans and gaps in methods for the avoidance of food allergens. Furthermore, some policies require reform because they allow (or even encourage) the discrimination and stigmatization of food allergic children. Thus, many educational facilities need to review and reformulate their policies concerning food allergy. When doing so, school health officials and administrators should follow some basic ethical principles to guide decision-making and policy development. The ethical principles of confidentiality and anonymity, the fair distribution of benefits and burdens, and empowerment can guide policy decisions for food allergy (summarized in Table 4).

Table 4: Key ethical principles to aid in implementing policies for food allergic children

Ethical principles	Policy response or areas of particular vigilance	Examples
Underlying principles	• Policies should address the fundamental causes of disease and requirements for health, aiming to prevent adverse health outcomes. • Imagine if the food allergic child was your own. What level of protection would you expect for your child?	• Enact appropriate, and complete, emergency preparedness and allergen avoidance policies.
Confidentiality and Anonymity	• Do policies cause a food allergic child to become distinct from others? • Are medical files confidential and does staff respect confidentiality? • Only disclose private information that is necessary for protecting health.	• Do not make allergic children form a separate queue when collecting their meals. • Do not disclose identifying characteristics of allergic children or their specific medical needs.
Equal benefits and burdens	• Avoid unduly burdening the eating habits of certain children. • Enact policies that will be of benefit to all food allergic students. • Ensure food allergic students have access to the same opportunities and resources as others.	• Provide allergen-free meals that are of the same quality as regular meals. • Focus policies on all allergens (no food sharing), not one allergen (e.g., peanuts).
Empowerment	• Ensure the education of staff and students on allergic reactions to food. • Provide resources so that food allergic children can gain further control over their health	• Take threats of bullying seriously. • Encourage allergic children to carry epinephrine.

By employing these principles, school nurses can aid administrators in policy making and gain another means to ensure that food safety policies are complete and ethical, while avoiding problems seen with discriminatory polices that place undue psychosocial stress on food allergic children. With a greater concerted effort and the endorsement of effective and ethical policies, the threat of fatalities from severe food reactions in childcare settings can be made virtually non-existent.

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Conflicts of interest

None declared.

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Prelude to chapter 4

As to diseases, make a habit of two things –to help, or at least, to do no harm.

- Hippocrates

In the previous two chapters we observed how factors related to ethnicity, lower socioeconomic status, bullying, and the unequal distribution of health burdens and benefits could cause individuals to become exceptionally vulnerable to disease. Conversely, these two chapters also demonstrated how policies that counter individual vulnerability, such as by promoting ethical imperatives of empowerment and protection from harm, can have significant utility in securing health for the population. Without question, vulnerability and susceptibility to harm are typically defined as something 'negative' and 'unwanted', and those in power to enact necessary protections from harm likely have a duty to do so. This is especially true in cases where an individual's vulnerability to harm is imposed and beyond their control.

However, is it possible that in certain situations the underlying reasons that cause an individual to become vulnerable to harm could enable greater benefits to society as a whole? And if such a situation exists, do we still have a moral duty to minimize this specific vulnerability and risk of harm? What if an individual voluntarily consents to being placed at risk because they know that their sacrifice will help minimize risks to others? Does this situation merit reform? Indeed, as the final chapter of this thesis will demonstrate, the above circumstances and related ethical questions do exist in a heretofore ignored context: the production of allergen-immunotherapeutic drugs, also termed *allergenic extracts*.

The following chapter focuses attention on the use of human subjects to assess the potency of immunotherapeutic drugs, which in turn enables patients to benefit from the production of higher quality allergenic extracts. However, potency testing is not a risk-free procedure. Despite the fact that human subjects voluntarily engage in this testing and that this procedure enables benefits in the treatment of allergy, this chapter will argue that there is an ethical imperative for future drug legislation to eliminate human subject testing for potency. This is in spite of the fact that testing procedures

implementing human subjects are currently the *best* method currently available to regulate the production of these drugs. Biomedical innovation will likely provide alternatives to this testing in the near future. Thus, ought drug regulations for allergenic extracts strive to phase-out human subject testing as soon as possible? Several arguments concerning how to best structure future regulations will once again centre on issues related to the fair distribution of health benefits and burdens.

CHAPTER 4: HAVE TECHNOLOGICAL INNOVATIONS MADE UNETHICAL THE USE OF HUMAN SUBJECTS FOR POTENCY ASSESSMENTS OF ALLERGENIC EXTRACTS?

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Abstract

Since the 1990's, production batch consistency and the standardization of potency units of allergenic extracts used in allergen-immunotherapy has been the focus of drug regulatory reforms and much academic debate. This article seeks to expand the current debate by identifying ethical arguments in support of regulatory reforms to eliminate the use of human subjects for potency assessments of these therapeutics. While human subject testing is the best method to assess biological potency, it also exposes subjects to significant risks, risks that ought to be avoided as much as possible. Innovation in in-vitro immunoassays will soon provide feasible alternatives to biological assessments. This article will argue that the allergology community must now consider eliminating human subjects in standardization and potency assessment methods as an ethical imperative in regulatory reforms. Moreover, the allergology community will soon need to reach consensus regarding when *in-vitro* tests are 'good-enough' in replicating biological potency assessments, so that human subject testing could be avoided without compromising the safety and efficacy of allergen-immunotherapy. Overall, this discussion will provide an overview on how to structure global standardization regulations for allergenic extracts based on the principle of minimizing human subject testing, a topic which, to date, has been largely overlooked in relation to extract standardization policies.

Introduction

Allergen-immunotherapy will soon mark an important milestone: the 100th anniversary of its use in recorded clinical practice. Much has changed since immunotherapy was first described by Dr. Leonard Noon in 1911 (London, U.K.) [1], where administration of pollen extracts was observed to minimize hay fever symptoms. For one, the incidence of allergic disease is exploding into pandemic proportions and will afflict roughly one quarter of the population of several nations (e.g., Canada, United Kingdom, United States) [2]. In addition to the growing clinical importance of allergen-immunotherapy in securing public health, biotechnology-derived allergens may soon be added to complement the current therapeutic arsenal [3], thereby expanding a therapeutic base that is currently comprised of allergenic extracts (AKA *allergen vaccines*) that are obtained through the extraction of biological source materials. Though primarily administered via subcutaneous or intra-dermal injection, sublingually administered forms of allergenic extracts are another recent revolution in allergen-immunotherapy [4]. Of arguably greatest importance are the growing standardization efforts for allergenic extracts that are significantly improving the quality and safety of immunotherapy by ensuring a more consistent potency and composition of therapeutics around the globe [5].

This article focuses attention on future regulatory developments that aim to encourage a more global standardization of allergenic extracts. Current regulatory reforms by the American Food and Drug Administration (FDA) [6, 7] and the European Union European Medicines Agency (EMEA) [8-11] have made improvements in the quality and safety of certain varieties of these drugs. However, despite these regulations, several important weaknesses remain, the most notable being that the FDA and EMEA each recommend different standardization procedures. The result is that standardized products of the same allergen from either continent often have large discrepancies in their potency and composition.

This situation has motivated the allergology community to call for improved regulatory measures, and most importantly, the development of a universal standardization procedure for all allergenic extracts [12]. Exactly how to develop such a universal standardization protocol remains a matter of debate, one that has largely

centered on the general technological feasibility of various proposed strategies [13, 14]. An important and closely related issue, but one that has been largely overlooked in this debate, is whether there is still a need for human subjects to be used in biological potency assessments of this class of therapeutics. The use of human subjects in routine biological potency assessments is currently an important component of standardization policies. However, routine biological potency assessments expose human subjects to significant risks, such as severe allergic reactions, risks that should be avoided as much as possible. Thus, the allergology community will soon face an ethically contentious issue. Encouraging standardization efforts will increase risks to human subjects around the globe if additional nations choose to apply regulations that employ human subject testing as a "gold-standard" in biological potency assessments. Must this be so, or is innovation in in-vitro immunological testing providing acceptable alternatives to biological tests? Moreover, if alternatives become available, this availability does not affirm why regulators *should* choose novel in-vitro methods if human subject testing is the most accurate and reliable method to measure biological potency.

This article aims to expand current, rather 'techno-centric', debates on regulatory reforms for allergenic extracts by analyzing the legitimacy of employing human subject testing in standardization efforts. Following a brief overview of current potency assessment and standardization methods, this article will describe proposed regulatory reforms and recent technological innovations in *in-vitro* potency assessments that may one day eliminate the need for human *in-vivo* testing. This overview will support the main arguments that: 1) eliminating human subjects in standardization and potency assessment methods should be an ethical imperative in regulatory reforms; and, 2) that the allergology community should reach consensus regarding when *in-vitro* tests are 'good-enough' in replicating biological potency assessments, so that *in-vivo* tests could be avoided without compromising the safety and efficacy of allergen-immunotherapy. By analyzing the ethics of human subject potency assessments, this article aims to encourage the development of regulatory policy developments by value-based judgments that are not overly or exclusively focused on issues of technological feasibility. Indeed, an equally important issue in this debate is whether it is unethical to encourage human subject testing in standardization efforts throughout the globe.

A unique class of drugs: extracted allergens and their challenging standardization

Allergenic extracts

To describe allergenic extracts as a particularly *distinct* class of drug would be an understatement. While the vast majority of pharmaceuticals contain one well-defined, synthetic active moiety that is easily manufactured as a final product of consistent potency, allergenic extracts are known best for their complexity and irregularities in their composition. This complexity and irregularity is due to the fact that the active ingredients for these drugs are not synthetic, but of biologic origin.

As their name implies, allergenic extracts are composed of allergens extracted from a given biological compound. While this may appear as a relatively simple process, the vast biological diversity that exists amongst members of the same species means that, depending on the biological source materials used in the extraction process, there will be radical differences in the composition and potency of allergenic extracts between production batches and manufacturers [15]. Numerous environmental conditions can also influence the allergen content of a biological source [15, 16]; for example, a particularly rainy growing season can reduce the allergen content of pollens. Further, the allergenicity of a substance is often due to multiple components, each representing distinct allergens with unique physiochemical properties; and these physiochemical differences can result in variations in the amount of allergens extracted during the manufacturing process [15, 16]. Therefore, manufacturers employing distinct production procedures will invariably produce allergen vaccines that are non-equivalent in terms of concentration of active ingredients. To conclude, unlike most pharmaceutical products, the composition of active moieties in allergenic extract preparations can be radically different.

The complexities of allergenic extracts extend beyond issues of pharmaceutical composition. Most classes of pharmaceuticals employ a common measurement to denote potency (e.g., mg/tablet), making the potency of a given drug easy to compare

between different manufacturers. The same situation does not exist for most allergenic extracts. Rather, manufacturers can present the potency of their products using one of a variety of units that cannot be inter-converted (e.g., BAU, AU, LU, JAU, PNU, Noon, etc.) [12]. Certain units are archaic, dating back to the clinical beginnings of immunotherapy (e.g., Noon, PNU), yet are still in current use despite the fact that they do not accurately reflect the potency of the therapeutic [15]. For example, Noon units represent a given mass of allergenic material extracted with a volume of extraction fluid (mg/ml). Due to the aforementioned variations in allergen source materials, extracts of the same allergen source labelled as containing equivalent Noon units of potency can in fact vary substantially in their actual therapeutic potencies.

Allergen-immunotherapy

Indeed, allergenic extracts are a pharmaceutical oddity. The unique attributes of these therapeutics are made all the more significant when employed in allergen-immunotherapy. A typical immunotherapy regimen involves the subcutaneous injection of the offending allergen in a series of increasing potencies over the course of months, sometimes years. The controlled exposure to the allergen induces tolerance by physiologically altering the patient's immune system [17]. Since the therapy necessitates the administration of a substance known to illicit a hypersensitivity response, it is imperative that the allergenic extract not be *over*-administered in order to avoid severe systemic and life-threatening reactions, such as anaphylaxis [18]. Conversely, the under-administration of the therapeutic compound will compromise treatment efficacy.

Discrepancies in the potency of administered allergenic extracts are thus a critical factor in the safe and effective use of immunotherapy. Confusion stemming from multiple units of measure and unforeseeable fluctuations in allergen content between production batches and manufacturers are significant sources of clinician error and adverse reactions to immunotherapy [19]. Fortunately, death from allergen-immunotherapy is exceedingly rare. Nonetheless, even the low incidence of anaphylaxis – recently estimated to occur at 6 events per 1000 injections [20] – is still significant.

Current standardization protocols

A logical solution to improve the safety and efficacy of immunotherapy is to enact regulations that ensure the production of allergy vaccines of a consistent or 'standard' composition and potency. Two government regulatory agencies, the FDA Center for Biologics Evaluation and Research and the EMEA, have pioneered standardization efforts for allergen-immunotherapy [21]. The FDA base their regulatory strategy on the development and distribution of well-characterized allergen reference standards [22]. These reference standards are essentially a mock vaccine made by the extraction of allergens through a consistent production process and from restricted sources that are controlled for biological variability. Each reference standard is assessed for their composition of major allergens and biological potency, measured in terms of Bioequivalent Allergen Units (BAU). The potency of final standards is set at a specific BAU per millilitre concentration for each category of allergen. Manufacturers must then perform a comparative analysis between production batches of their allergenic extracts and the FDA standard in order to demonstrate that the potency of the two are equivalent. This standardization procedure has notable strengths. The FDA determines a constant potency with a universal unit for an entire allergen category, thereby eliminating potency variations between drug brands and production batches. The main weakness with the FDA standardization strategy, however, is that only 19 reference standards have been developed for a few select allergen sources (e.g., cat, dog, stinging insect venom) [23]. Since there are numerous additional allergens employed in immunotherapy, a significant amount of allergenic extracts remains exempt from FDA standardization efforts.

The EMEA employs a separate standardization strategy that focuses on the production processes of individual manufacturers. EMEA regulations recommend that each manufacturer produce their own extensively characterized in-house reference (IHR) vaccine [11] (for the sake of simplicity, the term 'reference standard' is used in this article to denote both FDA and EMEA standard extracts). For some manufacturers the reference standard is assessed in terms of biological potency, but unlike the FDA

standards, potency is typically recorded in Biological Units (BU). Manufacturers employ their reference standard in final quality assessments of allergenic extract batches much like the FDA standards, where the final composition of major allergens and potency must be equivalent to that of their standard. The main benefit of the EMEA strategy is that, technically, *all* extracts can be standardized for batch-to-batch consistency. However, most allergenic extract products were commercialized before the establishment of the European Union and are therefore exempt from EMEA regulations [21]. And even the minority of EMEA standardized products are not without significant problems. As each manufacturer determines the final potency and unit of measure for their products, it is very difficult to compare extracts between manufacturers; different products of the same allergen are typically not interchangeable and a multitude of confusing units are still used to denote allergenic potency.

Biological potency assessments: the need for human subjects

Despite the weaknesses inherent in both strategies, these standardization efforts have resulted in safer and higher quality allergen-immunotherapeutic drugs [5], as well as the development of methods to accurately measure the *biological* potency (i.e., 'allergenicity') of this class of therapeutics. Recall that allergenic extracts are complex mixtures of biological material that contain several allergenic compounds that are both known and well characterized and others that remain to be defined. All allergenic compounds in an extract constitute therapeutically relevant active moieties, and together they determine the allergic response induced when administered to a patient, better known as its biological potency.

The multitude of known and unknown allergens makes potency assessments of extracts challenging, such that most in-vitro analytical tests provide only rough estimates of true allergenicity. For example, certain in-vitro immunological tests using synthetic antibodies measure specific known allergens by quantifying their association with antibodies. Potency quantifications by this method are by default an estimate of true allergenicity since unknown allergens are not measured with this test; the binding of antibodies is not equivalent to quantifying an allergic reaction. The inherent

deficiencies in in-vitro assessments can be circumvented by quantifying the actual allergic immune response induced in human subjects. Unsurprisingly, the complex human immune system is superior to in-vitro assessments since it will recognize all allergenic compounds in an extract, regardless of how complex the mixture may be.

In general, the methods used in Europe and the United States to test immune response are relatively straightforward, comparable to skin prick tests commonly employed in the diagnosis of an allergic sensitivity. In America[13] a population of 15-20 highly allergic adults is administered intradermally serial dilutions of the extract, while in Europe[14], 20 or more allergic adults can comprise the test subject population. In both situations, the visible allergic reaction observed on the skin's surface (in the form of an inflamed welt) is proportional to the biological and therapeutic potency of the extract [24].

The consequence of using human subjects in standardization efforts

The above overview of allergenic extract standardization and human subject potency assessments identifies several issues of particular significance. First, the *best* assessment of an allergenic extract's potency involves inducing an allergic reaction, which is *best* determined by in-vivo methods. Allergenic extracts assessed for biological potency are in turn more predictive in the severity of reaction induced when administered to the average allergic patient. Thus, biological units of potency can help reduce clinician error due to the inadvertent over-administration of the extract during immunotherapy. Overall, these benefits demonstrate that the use of human subjects is the 'gold-standard' in potency assessments of reference standards and therefore is inextricably linked with extract standardization efforts by the FDA and EMEA. It is important to note that reference standard extracts are made of labile biological materials

[13] Also known as the $ID_{50}EAL$ method [24], subjects are administered intradermally with 3-fold dilutions of the allergenic extract. This in turn produces a visible allergic reaction on the skin's surface, known as an 'erythema response' (i.e., an inflamed circular welt or 'wheal'). The diameter of the resultant welt is a function of the concentration of the extract, which is assigned a biological potency in terms of BAU.

[14] Also known as the Nordic method, subjects are also administered serial dilutions of a given extract, however, the resultant allergic response is compared to the welt produced from the percutaneous administration of a known amount of histamine (histamine constitutes as a control that mimics an allergic response). Comparisons between welt diameters of the extract and the histamine control determine biological potency in terms of BU.

that have a limited shelf-life, thus each renewal of a reference standard will require yet another round of human subject potency assessments. As current regulatory strategies strive to standardize a growing number of products, an increasing number of allergic individuals will likely be implicated in the production of immunotherapeutic drugs.

This need for human subjects could very well become common worldwide. Recall that allergic disease is a growing global pandemic, and as such, allergen-immunotherapy is conducted in many countries around the world, in addition to Europe and the United States [2]. Furthermore, due to ecological and geographical factors, many allergenic plant and animal species are region-specific, thus immunotherapeutic drugs need to be produced at a regional level in order to cater to the health needs of local populations. As a result, individual nations will likely in the near future develop their own regulations for extract standardization, undoubtedly using the FDA and EMEA strategies as models, or simply adopt one of these standards in their entirety (e.g., Australia has adopted the EMEA regulations [25, 26]).

While a more concerted effort to standardize allergenic extracts worldwide is laudable – and endorsed by the World Health Organization [12] – the need to involve an increasing number of human subjects in this process raises significant practical and ethical concerns. From the perspective of efficient drug development, the growing need for human subjects for routine potency assessments of reference standards could counter standardization efforts due to shortages in research participants willing to undergo such testing, thus making the whole process impractical. Indeed, similar shortages in research participants have slowed the completion of numerous clinical drug trials [27]. It is important to note, however, that biological potency assessments of allergenic extracts are not benign procedures or free from risk; they can be painful and even induce severe systemic allergic reactions. These and additional examples will form the basis of the argument that future regulatory efforts around the globe ought to avoid implicating human subjects in this process as much as possible. Effective means to eliminate the use of human subjects should be sought-out despite the fact that this in-vivo testing strategy is currently the most accurate and reliable method to measure biological potency. However, this argument carries little weight so long as there are no technologically feasible alternatives to human testing. The following section will provide an overview

of technological innovations in in-vitro potency tests that may provide the analytical tools necessary to replace human testing without compromising the safety of allergen-immunotherapy.

Future directions in allergen extract standardization: examples of recent innovations

Quantification of one major allergen is reliable for some extracts

No matter how revolutionary scientific innovation may be it is unlikely, at least in the near future, that technology will be able to reproduce all the complex details of the human immune system. But that does not signify that science has not made considerable improvements in measuring the allergen content of complex mixtures and in replicating allergic responses *in-vitro*. For example, the radial immunodiffusion (RID) technique has been adapted to measure the allergen content of allergenic extracts [13]. This assay quantifies the binding of synthetic antibodies to the major allergen in the extract mixture. Recall that for most allergenic extracts this quantification typically provides an *estimate* of actual biological potency; however, studies have demonstrated that certain extracts are exceptions. RID quantifications of the major allergen content of short ragweed pollen [28], ryegrass pollen [29], and cat [29, 30] extracts were determined to correlate significantly with their biological potency. Such observations suggest that future regulatory reforms might replace human potency assessments with RID methods for the standardization of these particular allergenic extracts [13]. While potency measures by RID may not provide accurate assessments of the biological potency for *all* extracts, being able to do so for *some* suggests that future research will uncover additional extracts for which this correlation applies [31].

Complex extracts require quantification of several allergens

The main weakness with the RID technique is that this analysis focuses on quantifying one major allergen by one antibody in an extract that typically contains several allergenic components that are all therapeutically relevant. Expanding the

number of synthetic antibodies employed in a given immunoassay would correct for this deficiency since each additional antibody included in an analysis would detect an additional allergenic component. The FDA Center for Biologics Evaluation and Research is in the process of developing such a multi-antibody testing strategy specifically for the purpose of extract standardization [32]. Known as the multiplex microbead antibody method, preliminary findings demonstrate that this in-vitro testing strategy can measure potency with an appreciable level of accuracy to that of biological assessments for cat and ragweed extracts [33, 34]. Being in the preliminary stages of development, it is unknown how applicable this immunoassay will be for the standardization of all allergenic extracts. However, the fact that it is being developed by a leading drug regulator specifically for standardization efforts suggests that this in-vitro test may soon be employed in routine potency assessments, thus providing a feasible alternative to human subject testing of FDA reference standards.

Developing biotechnology-derived allergens as 'ideal' reference standards

In addition to FDA innovations, a European network of public sector drug regulators, academic researchers, and private pharmaceutical companies have made significant progress in the global standardization of allergenic extracts. This network, known as the CREATE Project [35, 36] (acronym for the *Development of Certified Reference Materials for Allergenic Products and Validation of Methods for their Quantification*), initiated the development of reference standards and a common set of in-vitro analytical tests to assess the potency of extracts. The availability of these reference standards and consistent testing methods would address many of the aforementioned weaknesses in current EMEA standardization protocols [35]; however, the CREATE Project also aspires to develop a common set of reference standards that could be implemented by manufacturers around the world.

Revolutionary in terms of its aspiration for global drug regulatory reform, the CREATE standardization strategy has additional attributes of interest. For one, their efforts have focused on the development of reference standards composed of

biotechnology-derived allergens. Unlike extracts from biological sources, biotech-allergens can be purified to near homogeneity and produced in a consistent form with relative ease, thus providing an ideal, unchanging reference standard. The predictable and homogeneous consistency of CREATE Project standards also signifies that common in-vitro immunoassays could provide potency quantifications of these purified allergens with appreciable accuracy. Indeed, in-vitro quantification of a collection of pollen and dust mite standards using the in-vitro radioallergosorbent test (RAST) was recently observed to correlate with biological potency assessments of these common allergens [14].

Replicating human immune responses in-vitro

The final example of an emerging revolution in in-vitro immunological testing merits particular attention. As mentioned previously, the human allergic response is a complex physiological reaction involving numerous metabolic processes. The majority of in-vitro immunological assays do not reflect this complexity since they focus on only one aspect of an allergic reaction, i.e., the association of an antibody with an allergen. Therefore, a logical strategy for improving current immunoassays is to develop a system that mimics human allergic reactions in-vitro. Vogel and colleagues [37] have made promising developments in replicating this complex physiological process. Their strategy involves ‘humanizing’ a rat basophilic leukemia cell line by transferring genes for human cell membrane receptors that associate with IgE antibodies. Upon mixing an allergenic extract with IgE antibodies obtained from the sera of allergic patients (obtained from a blood sample), these humanized cells will then associate with the antibody-allergen complexes in the solution. This final association induces metabolic changes within the cells which are quantifiable, and in turn, more representative of immune processes that initiate an allergic response. Though still in early development, as well as a highly simplified representation of a human allergic reaction, this in-vitro assay represents an innovative step forward in producing a ‘test-tube immune response’ that could eliminate the need for human subject potency assessments of allergenic extracts.

Innovation does not guarantee future standardization efforts free of human subject testing

This brief overview of technological innovation in in-vitro immunological testing demonstrates that feasible alternatives to the 'gold-standard' of human subject potency assessment are emerging. Further, current immunoassays are sure to become increasingly more sophisticated and representative of human allergic reactions [38]. Thus, the possibility of government regulators reforming current standardization guidelines so that human subject potency assessments are gradually phased-out and replaced with suitable in-vitro methods appears foreseeable. Indeed, the above examples indicate that both American and European drug regulators are making efforts to execute such a transition. Moreover, as the allergology community encourages standardization efforts around the globe, government regulators will have the option to enact standardization guidelines that minimize or avoid altogether the use of human subjects in their future regulatory process. However, the key word in these tentative standardization policies is *option*, meaning that eliminating human subjects from standardization efforts is a value-based decision and by no means definitive.

Government regulators around the world could choose to continue employing human subject potency assessments based on justifiable rationales. For instance, in-vivo potency assessments have a proven track record of efficacy and are considered to be the most accurate method to quantify the biological potency of allergenic extracts. So why adopt a new strategy when current testing methods already work extremely well? Correspondingly, replacing human subject assessments with any in-vitro test will inevitably involve a compromise, where any decreases in the accuracy of the recorded biological potency by an in-vitro test may raise the risk for adverse reactions to immunotherapy amongst the general patient population. Opting for regulatory protocols that may raise the risk of adverse drug reactions seems counterintuitive. There are also practical issues with employing innovative in-vitro tests, which include the possibility that novel testing methods may not be considered as cost-effective in certain regions, most notably in developing countries. The following section will respond to these

critiques by arguing that avoiding human subjects in standardization efforts ought to be an ethical imperative despite the aforementioned justifications.

Why *not* use human subjects for potency assessments of allergenic extracts?

Ethical arguments that explain *why* the use of human subjects in this particular context ought to be eliminated when possible will centre on two main issues: the practicality of such tests and the ability to avoid harm to persons.

Testing practicality

To begin, it is important to note the many similarities between routine biological potency assessments and clinical drug trials. Clinical trials of experimental therapies typically progress through four phases of assessment in terms of their toxicity and efficacy. Phase one clinical trials centre on the controlled administration of an experimental drug to small populations of volunteer (usually healthy) subjects in order to determine possible adverse reactions, and correspondingly, determine a rough dosing profile for the drug in terms of toxicity. Though biological potency assessments of allergenic extracts are conducted on commercialized therapies and reference standards that have passed experimental clinical assessment, the procedure still relies on exposing a select number of volunteers to a therapeutic compound in order to assess its dosing profile, which is directly related to its toxicity/risk of inducing an adverse reaction. While distinct, the similarities shared by human subject potency assessments and phase I clinical trials help contextualize the broader methodological complexity of such potency assessments.

For instance, conducting clinical trials requires independent oversight to ensure such testing and volunteer recruitment procedures meet international standards for ethics in research (e.g., the Declaration of Helsinki [39]). While these ethical standards are essential tools in protecting human subjects from harm and coercion, such standards have made finding suitable volunteers for clinical trials an arduous procedure that commonly results in delays in conducting analyses [27]. In terms of standardizing

allergenic extracts, potency assessments involving human subjects also need to follow international ethical standards and require independent oversight to ensure such routine testing is safe and conducted in an appropriate setting. Thus, similar challenges seen with the execution of clinical trials may arise as a growing number of governments attempt to standardize allergen-immunotherapeutic drugs. This is not a purely hypothetical possibility since experts in allergen standardization have previously described the recruitment of human subjects for potency assessments as "laborious and time-consuming" [40, p.66]. A shortage of suitable volunteers is also a real possibility. Recall that biological potency assessments often require patients that are *highly* sensitive to the allergen source being tested. Therefore, despite the high incidence of allergic disease, only a subgroup of the allergic population is appropriate for testing, and identifying and recruiting highly sensitive individuals is known to be very difficult [24].

Drug regulatory schemes that are inextricably linked with human subject potency assessments may encounter significant tensions as regulators aim to standardize a growing number of allergenic extracts both nationally and internationally. Within a given nation, the possible shortage in volunteers willing to undergo such testing could delay the availability of essential reference standards for an entire industry. At an international level, the necessary government and corporate oversight needed to ensure that such testing meets accepted standards of safety and ethical conduct may dissuade governments from initiating standardization efforts in the first place. This is especially true for resource-poor nations with limited government infrastructure. Either situation will be ethically problematic; an inefficient standardization strategy will delay access to needed therapeutics, and the abandonment of such efforts will prevent the production of high quality therapeutics for an entire patient population.

Risks associated with biological potency assessments

The aforementioned practical difficulties with human subject potency assessments are not insurmountable; indeed, European and American regulators are able to sustain standardization efforts despite these challenges. Regardless, standardization efforts face additional considerations in terms of exposing human subjects to foreseeable

risks of harm that must be considered when developing drug regulations for allergenic extracts. Without over-inflating the risks associated with human subject potency assessments, it is important to recognize that the risks are *not negligible* and thus ought to be avoided as much as possible.

Problems associated with human subject potency assessments arise even before executing the actual test. Given that the test aims to measure an allergic reaction, research subjects must forego treatment for their allergies prior to the potency assessment [41-43]. This makes sense since administration of common allergy medications such as antihistamines will attenuate an allergic response. Though good for test results, withdrawal of treatment is not ideal for the allergic individual who must endure higher levels of allergy morbidity in order to participate in potency assessments. In terms of the actual test, recall that biological potency assessments require the administration of the allergenic extract into the skin in order to produce inflamed welts that are readily measurable. At the very least, the induced allergic response can be painful and itchy, with the associated natural tendency to scratch the irritated skin thereby raising the possibility of infection. At the very worst, the allergic response can become systemic and induce a life threatening anaphylactic reaction.

The possibility of allergenic extracts inducing severe systemic reactions is well known. Correspondingly, the allergology communities of several nations [17, 19, 44, 45] stipulate in best practice guidelines that immunotherapy should be conducted with appropriate medical supervision in a facility that is equipped to treat severe allergic reactions. High levels of compliance with such best practice guidelines has meant that anaphylaxis in the clinical setting is increasingly rare, but still significant (6 events per 1000 injections). Death from anaphylaxis is exceedingly rare; nonetheless, deaths from the administration of allergenic extracts have been documented despite being conducted by competent clinicians in medically supervised environments [46, 47]. Even in situations where swift medical intervention prevents a fatality, experiencing an anaphylactic reaction can produce long-term psychological distress [48] (anaphylaxis is commonly described as a near death experience where its onset induces “feelings of impending doom” [49, p. 703]). Taken as a whole, the risk associated with the administration of allergenic extracts is significant since the degree of harm from such a

reaction (death or psychological scarring) is very high, even though the incidence of severe adverse reactions may be quite low. Note that this risk assessment pertains to the administration of allergenic extracts within the clinical setting, which is distinct from biological potency assessments within the regulatory and drug manufacturing settings. How, then, do the risk profiles compare between each venue?

On initial reflection, it may appear reasonable to assume that the risks are roughly equivalent. It is highly unlikely that biological potency assessments, which require stringent technical and statistical protocols [13], would ever be conducted by individuals other than skilled medical researchers in appropriate testing facilities. Critical distinctions in risk of harm do arise, however, in relation to the human test subjects and the administered allergenic extract. Unlike the average patient undergoing immunotherapy, potency assessments are typically conducted on *highly allergic* individuals, a population known to be at much higher risk for anaphylaxis and death [46]. Moreover, unlike a commercialized extract used in immunotherapy that is labeled with a given potency, biological potency assessments aim to assess the *unknown concentration* of a reference standard extract. Thus by default, it is unknown how much of an allergic response these reference standards will induce in highly allergic subjects; as such, there is a risk of administering an amount of allergenic material capable of inducing a severe systemic reaction. To conclude, drug regulators should not assume that routine human subject potency assessments will be spared of any adverse events. The probability of adverse outcomes from biological potency assessments will only increase if additional standardization efforts around the globe remain inextricably linked with the need for human subject testing. A better situation would be to develop standardization protocols that minimize human subject testing as much as possible.

Eliminating human subjects is a question of ethics

At this point it should be clear that the foreseeable risks associated with allergenic extract standardization efforts are not a result of negligence but rather an ethically debatable issue. The use of human subject potency assessments is, without question, necessary since these assessments enable the production of quality

therapeutics, which in turn lower the risk of severe adverse reactions to allergen-immunotherapy amongst the general patient population. From a risk-benefit perspective, biological potency assessments focus 'reasonable' and 'unavoidable' risks on a small group of human subjects for the greater benefit of society. This risk-benefit profile is the basic justification for exposing volunteers to potentially significant risks in phase I clinical trials, and correspondingly is a premise supported by prominent research ethics guidelines (for example, see section 21 of the Declaration of Helsinki [50]). However, innovation in in-vitro immunological tests is providing feasible alternatives to biological testing methods and this fact must raise questions about whether the risk to human subjects from potency assessments remain reasonable and unavoidable. Since the main guiding principle in research ethics involving human subjects is to minimize risks and harms as much as possible [51], it is apparent that global standardization efforts of allergenic extracts that maintain the status quo of human subjects for routine potency assessments will eventually become an unethical practice in pharmaceutical regulation.

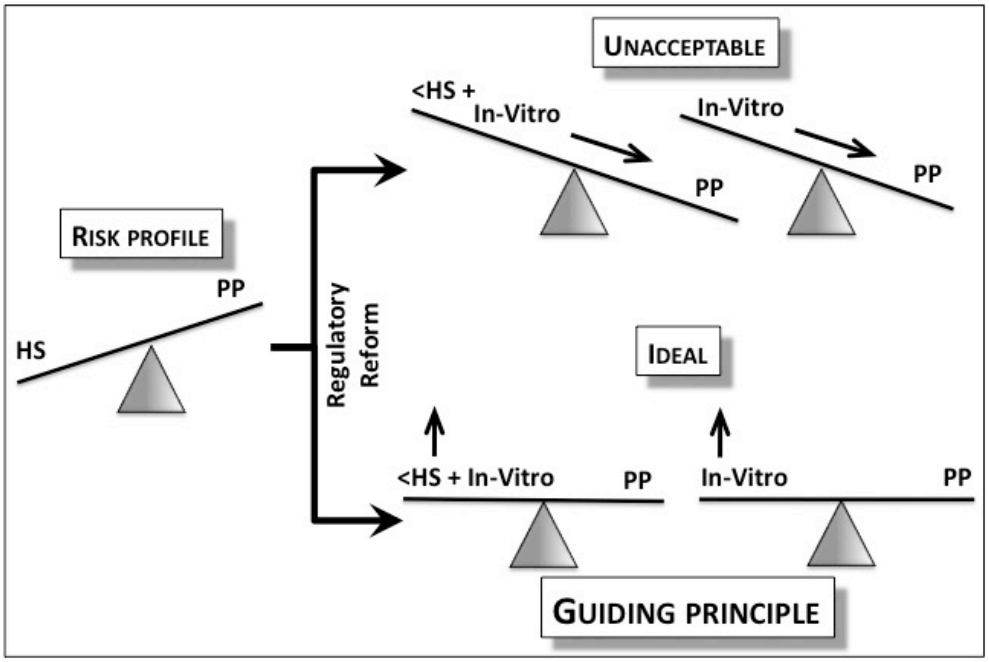
As the use of allergen-immunotherapy approaches its 100th anniversary in clinical practice, the allergology and drug regulatory communities will need to engage in a more intricate debate concerning how to encourage a greater standardization of allergenic extracts around the world. Rather than debating the strengths and weaknesses of the current FDA and EMEA standardization strategies, which could be adopted in some form or another in various nations, regulators ought to consider a novel regulatory structure that breaks away from a dependence on human subject testing as a gold-standard in potency assessments. But how ought such a novel standardization strategy be structured, and based on what justifications? The concluding section of this article will now aim to answer this question by providing an overview of preliminary value-based judgments to support the development of ethically sound standardization protocols.

Framing the debate concerning standardization reforms relative to human subject testing and innovative in-vitro assays

Regulatory reforms that centre on the issue of biological potency assessments will require extensive debate on two interrelated, yet distinct, issues concerning technological innovation and risk of harm to persons. The first issue must address the main critique of what degree of compromise – if any – is acceptable in terms of avoiding the risks and impracticalities of human subject testing and possible increases in the risk of adverse drug reactions amongst the general patient population. From this initial debate, the second issue will need to assess what in-vitro-replacement testing strategy will meet an acceptable risk profile for individual categories of allergenic extracts with the aim of avoiding human subject testing as much as possible.

To begin the discussion concerning any possible compromise in risk distribution, it is necessary to define the main principle that ought to guide value-based decisions (Figure 3). The ability to avoid risks from human subject testing is essential; however, this laudable goal is unacceptable if it is achieved by placing greater risks on the general patient population due to less accurate potency assessments of reference standards. In other words, ideal regulatory reforms ought to diminish risks towards human subjects while maintaining an equivalent quality and safety profile for standardized allergenic extracts.

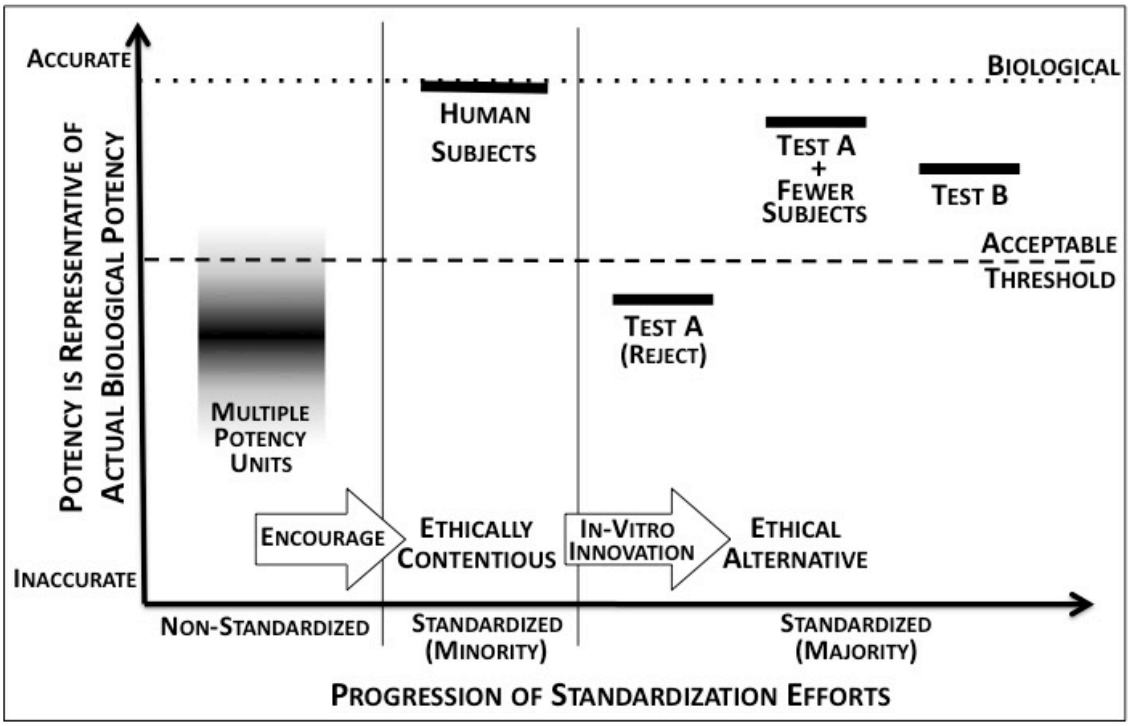
Figure 3: Main guiding principle in regulatory reforms



Reforms that reduce risks to human subjects, yet shift greater risks towards the general patient population (e.g., potency assessments that require fewer human subjects but are less accurate), are unacceptable. Reforms must aim to reduce the need of human subjects (e.g., employ in-vitro testing) while maintaining an equivalent level of safety of immunotherapeutics for the patient population. HS: human subjects; PP: patient population; In-vitro: In-vitro immunoassays.

This situation is achievable if in-vitro assays alone can provide reliable measures of biological potency, or if less reliable in-vitro measures can be cross-checked for accuracy by employing fewer human subjects in the process (e.g., 5 human subjects rather than the norm of 20). From this main guiding principle, debate on possible regulatory reforms will then need to define when, or to what acceptable degree, this *ideal* situation can be achieved in *actual* (i.e., 'real world') standardization efforts (Figure 4).

Figure 4: Defining an acceptable threshold for in-vitro testing



Human subject testing provides the most accurate assessment of biological potency, yet is ethically contentious. Minimizing human testing with in-vitro assays ought to be encouraged. Not all in-vitro tests can provide accurate potency assessments. Drug regulators will need to reach consensus concerning what constitutes as an acceptable threshold in the accuracy of novel testing strategies that minimize the use of human subjects, yet provide appropriate measures of potency relative to biological potency assessments.

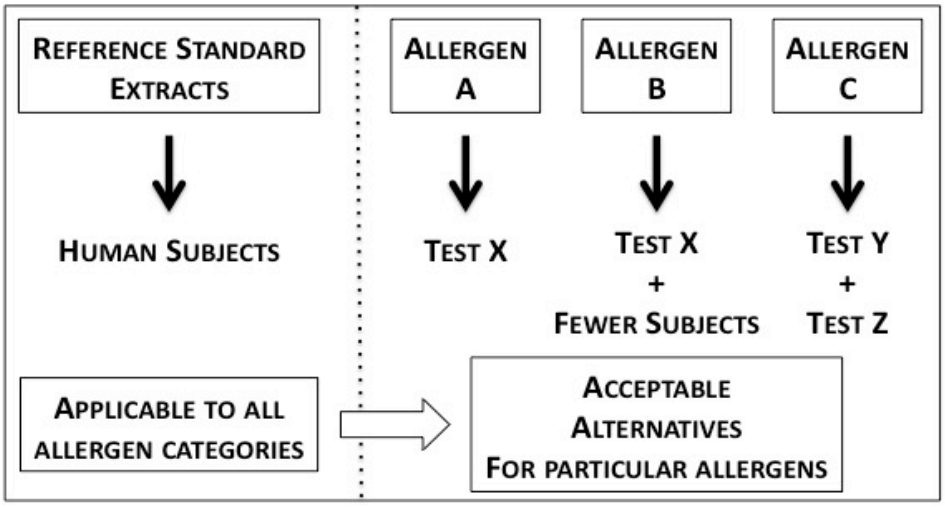
At this point, it is important to recapitulate specific regulatory challenges in real world standardization efforts. First, the majority of the global supplies of allergen-immunotherapeutic drugs are not standardized; as such, these drugs can have considerable fluctuations in their composition and are labelled with potency units that are not necessarily representative of their ability to induce an allergic response when administered to the average patient. The main priority is thus to encourage standardized production of these drugs with concomitant labelling of their biological potency. While innovative in-vitro immunoassays can measure potency with a high degree of precision, human subject testing remains the most accurate means of defining the potency of immunotherapeutics in terms of biological allergenicity. Therefore, the allergology and drug regulatory communities will need to reach consensus on what constitutes a

reasonable threshold for when novel potency assessment protocols are ‘good enough’ relative to the human subject gold standard.

For instance, an exclusive application of the in-vitro test ‘A’ could provide potency measures that are on average 80% representative of biological potency relative to conventional testing involving 20 subjects. This discrepancy may be considered too high in terms of potentially increasing adverse drug reactions amongst the general patient population. However, coupling test ‘A’ with fewer human subjects (say, 10) could be 90% representative. This situation could constitute a fair middle ground since the 10% discrepancy would minimize the number of human subjects yet result in a negligible increase in risk for patients. Furthermore, the fewer human subjects needed in this standardization strategy would help reduce the aforementioned impracticalities with human subject testing (e.g., shortage of volunteers), and thus could increase the efficiency of standardization efforts (a benefit that should be considered when determining what constitutes as an appropriate threshold in potency assessments). Of course, an even better situation would be identifying an in-vitro test that when applied in exclusivity would have a negligible discrepancy in potency assessments.

Upon deciding what constitutes an appropriate threshold for assessing biological potency, it is important to recognize that regulatory experts will then need to evaluate what in-vitro-replacement testing strategy will be applicable to particular categories of allergenic extracts (Figure 5). Recall that all categories of allergenic extracts have distinct physiochemical properties; for example, allergic sensitivities to many biological materials (e.g., dog) is often due to multiple allergens (i.e., ‘major’ and ‘minor’ dog allergens), some of which are well-known and others that remain to be defined. Human subject testing can account for the intrinsic complexity of analyzing the content of allergenic extracts since the human immune system will recognize all allergenic compounds, regardless of the complexity of the extract. Correspondingly, individual in-vitro immunoassays will vary in the degree to which their potency quantifications are representative of actual biological potency, and thus particular testing methods or combinations of methods will likely be better suited for certain allergen categories and not others.

Figure 5: Regulatory reforms should foresee the need for multiple testing strategies



While human subject testing is applicable to all classes of allergenic extracts, physiochemical differences between allergens signify that appropriate in-vitro testing alternatives may be unique to each allergen category.

To expand, recall that for a minority of allergen categories, such as ragweed, quantification of the major allergen from this biological source correlates with the biological potency of extracts. In the minority of situations where this correlation applies, quantification of the major allergen content by, for example, the RID immunoassay, could meet the minimum threshold in potency assessment required by regulatory experts. For allergenic extracts of greater complexity, it likely will be necessary to conduct a RID analysis in tandem with an additional assay (e.g., "In-vitro humanized immune system" in development by Vogel *et al.* [37]), which could also include a smaller number of human subjects as a means to ensure that potency assessments are accurate. In conclusion, while human subject testing is applicable to all categories of allergenic extracts, it unlikely that drug regulators will be able to rely on only one in-vitro testing strategy in future standardization efforts. Rather, the ethical imperative to transition to standardization strategies that minimize the use of human subjects will require extensive debate and empirical research in order to determine which 'shoe' (allergen category) will fit the right 'foot' (testing method).

Conclusion

From a pharmacological perspective, allergenic extracts are surprisingly complex therapeutics, and routine drug analyses, such as potency assessments, remain difficult despite a century of use in clinical practice. Coupled with the fact that the incidence of allergic sensitivities are rising at alarming rates and there is thus increasing demand for allergen-immunotherapy, it is now all the more important to establish comprehensive international regulatory guidelines to ensure that allergenic extracts are produced at the highest level of quality and safety.

However, a continued application and expansion of current regulations that aim to standardize this category of therapeutics will face growing critique if regulations remain inextricably associated with the "gold-standard" of human subject potency assessments. This should come as no surprise since all forms of pharmaceutical research involving human subjects involve risks of harm in various forms. As described in this article, it is apparent that the risks associated with routine human subject potency assessments are significant, ranging from the possibility of compromising the overall efficiency of standardization efforts to causing severe morbidities, which includes the very low risk of mortality, among test subjects. These risks are morally defensible as long as there are no feasible alternatives that will provide equal benefit to the general patient population when applied in drug regulatory strategies. Indeed, while human subject testing has long been the best method for assessing the allergen content of complex mixtures, rapid innovation in in-vitro immunoassays means that feasible alternatives to current standardization guidelines may soon become a reality.

This article has provided a focused discussion on the legitimacy of current standardization strategies in terms of ethically contentious attributes of potency assessments. While very specific, it is curious that this topic has been largely overlooked in the academic literature pertaining to allergen-immunotherapy. Thus, in addition to being the underlying motivation for this manuscript, the analysis herein will hopefully encourage further debate on this pertinent topic within the allergology and drug regulatory communities. Furthermore, the framework and overview of value-based judgments can hopefully provide guidance in future debates concerning how best to reform drug regulation policies for allergenic extracts. On a final note, we have much to

look forward to as we celebrate the 100th anniversary of allergen-immunotherapy in clinical practice. Much pride is due to the innumerable technological innovations that have dramatically improved the safety, efficacy, and availability of this therapeutic regimen. With confidence, it appears that we too will soon celebrate another revolution, being the ability to provide high-quality allergenic extracts to patients without placing risks on volunteers that, in the past, have graciously enabled the production of these therapeutics.

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Conflicts of Interest

The author declares no conflicts of interest.

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DISCUSSION—A PRACTICAL APPLICATION OF ETHICAL THEORIES TO AID DECISION-MAKERS IN ALLERGY

Real knowledge is to know the extent of one's ignorance.

- Confucius

Despite the phenomenal surge in the incidence of allergic sensitivities these recent years, those fortunate not to have an allergy may underestimate[15] the significance and severity of this chronic disease [1-3]. Common misconceptions include that allergy symptoms are psychosomatic, or are representative of an overly frail individual, or are claimed as an excuse to avoid participating in specific activities such as culinary events. These negative preconceptions of individuals with allergic sensitivities are simply not true, but rather suggest that many members of the public who claim such disregard towards the actual social and medical ramifications of this chronic immune disorder possess a significant degree of ignorance concerning allergy.

Now at the concluding segment of this doctoral thesis, I feel the need to confess my own profound ignorance that influenced my former preconceptions of allergy. Prior to immersing myself into the study of this disease, I would often roll my eyes when hearing people speak about their allergies. Thoughts of, "*Oh, get over it already*", or "*What's wrong with you? It's just a cat*", would often cross my mind. I can also recall attending a stand-up comedy performance where a comedian jokingly ridiculed food allergic children as being weak, where death from consuming a single peanut was purported as Nature's way of ensuring that only 'strong' children live to reproduce. I found the performance to be quite humorous—at the time.

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[15] It is interesting to note that the growing notoriety of allergy also has the opposite effect. Population surveys [4] note that a proportion of the public mistakenly associate or assume a variety of common disease symptoms, such as digestive disturbances, are due to allergic sensitivities. This self-diagnosis of allergy is often due to a completely unrelated medical condition, such as food intolerance (e.g., intolerance to the milk sugar, lactose, stems from a deficiency of the digestive enzyme, lactase, a condition which is unrelated to milk allergy).

Now armed with a robust understanding of allergy, these false preconceptions have evolved into convictions of concern and respect for allergic afflictions. Furthermore, recognition of the real suffering experienced by many allergic patients has instilled personal motivations that this doctoral research project should not only serve as a means for academic training, but also contribute towards a social responsibility to enact change. Below is a summary of the efforts presented herein that aim to contribute towards minimizing the health burden of allergy.

Synopsis: breaking new ground in allergology while providing new tools for decision-makers

The overarching goal of this research project aims to encourage—and in many cases, initiate—further research attention towards a domain in allergology that remains underdeveloped. But first, initial investigations sought to answer one fundamental question: *What is the extent of analysis devoted towards assessing the ethical implications of allergy morbidity and treatment provision?* The results from an exhaustive literature review identified fewer than 35 academic articles address ethical issues in detail concerning allergy, three of which are articles originating from this doctoral project. This paucity of ethical analysis exists despite the fact that numerous ethical issues surface from the toll this chronic disease imposes on population health. The observed deficiency of employing principles of ethics within allergology then served to advance the argument that this research domain represents a wealth of opportunity for future interdisciplinary investigations.

The subsequent goal of this thesis was then to contribute towards developing reflective tools and theoretical frameworks that could be used by decision-makers to guide health policy interventions for allergy and co-morbid conditions. The aim of this research initiative was to develop practical tools for a *broad range of health professionals* implicated in allergy. With that said, it is important to assert that the theoretical frameworks proposed herein aim to empower ‘meso-level’ health professionals in their daily practice. Thus, rather than target ‘macro-level’ health professionals, such as national ministers of health that are responsible in determining complex resource allocation strategies for national health care systems, this thesis centres analysis down one level towards health professionals employed within institutions and not the upper echelons of government. As

demonstrated throughout Chapters 2 to 4, such meso-level health professionals include public health officials tasked with developing regional health interventions (e.g., for cities or specific neighbourhoods), administrators of child care settings and nurses employed within educational institutions, and policy analysts working within specific jurisdictions of drug regulatory bodies. A common analytical theme that unites the theoretical frameworks proposed in this thesis include a focused attention towards issues concerning: 1) populations particularly vulnerable to allergy morbidity; 2) the duty for decision-makers to minimize risks of individuals experiencing an allergic reaction and how their disease might be source of stigma, and; 3) ensuring the fair distribution of health benefits and burdens arising from tentative policy interventions. By employing core principles of ethics in health policy, public health, and bioethics, policy recommendations from this thesis will aid decision-making capacities within three specific contexts.

First, Norman Daniels' application of Rawlsian theories of social justice in health inspired the use of these same theories as a guide in public health policy development for allergy and asthma. Rather than replicate Daniels' analysis—where Rawls' theory served as a framework to critique unjust distributions of health achievements—principles of social justice were used to define focal points for assessment in the development and prioritization of policies targeting environmental allergens and asthma triggers. The step-wise assessment protocol presented herein focuses evaluation on: 1) whether a tentative public health intervention would provide equal health benefit to a range of allergy and asthma sufferers, 2) whether targeting initiatives towards particular societal groups is merited based on the notion of 'worst-off status' of certain population segments, and 3) whether targeted policies have the potential for stigmatization.

Investigations then centred on current weaknesses and deficiencies observed in the structuring of food allergy policies for school children. In this context, ethical principles that uphold the duty to protect confidentiality and anonymity, fairness, avoiding stigmatization, and empowerment, served as guides in the development of a theoretical framework to define the adequacy and legitimacy of food allergy prevention efforts. This policy assessment protocol, in turn, provides a reflective tool to aid administrators and school nurses in their decision-making capacities when structuring food allergy policies for childcare and educational institutions.

The final chapter placed scrutiny on regulations and global standardization efforts for allergenic extracts used in immunotherapy. Research centring on current regulatory

protocols identified questions regarding whether emerging technical capacities in immunology will obviate the use of allergic patients as human subjects for potency assessments of these drugs. Despite human subject potency assessments being a reasonable and accurate testing method, the fact that this testing is not free of risks advances the argument that such testing ought to be avoided when possible. Core principles of research ethics concerning harm prevention and the fair distribution of research benefits and burdens then served as a guide concerning how to reform standardization efforts in light of technological advances that may enable the primary application of in-vitro testing strategies.

The application of a select set of ethical principles within specific contexts proved useful in the formulation of frameworks to guide health policy development. However, the select focus of this project also signifies that the analysis herein is bound by inherent limitations.

Limitations of this research project: A question of scope

The first limitation of this thesis project concerns issues of the reach (scope) and applicability of this research in allergic populations others than the allergic populations targeted herein. Namely, it is worth questioning whether the health policy frameworks presented in these latter chapters could be of equal utility in other regions of the globe. Note that this analysis focussed exclusively on the allergy epidemic within the *developed world* where allergy predominates. However, as a significant component of the developing world is now experiencing rapid economic growth and is becoming "Westernized", the allergy epidemic is expanding its reach into populations once 'immune' to this disease [5-7]. Thus, while the allergy policy proposals in this thesis were defined as ethical imperatives for Western countries, such policies might be over-demanding in areas of prolonged conflict, severe resource constraints, and a limited development of social institutions. In these locales, inability to meet, or disinterest in following, certain ethical principles in health policy might not be a morally reprehensible act.

Consider enacting school food allergy policies in a resource poor nation[16] as an example. In Chapter 3, a main duty stated for school administrators was the need to have epinephrine available on hand should an anaphylactic reaction arise. Would this duty be reasonable at a school that barely has enough resources to provide books to its students, let alone the refrigerator needed to store the epinephrine? From this example it is apparent that, overall, the moral arguments that could guide pertinent allergy policies in the developing world would be different from many guiding principles presented in this thesis.

Another apparent limitation of this research project is that it does not demonstrate the vast breath and diversity of ethical principles and ethics scholarship that has emerged recently from the Philosophy and Bioethics communities (recent examples of prominent scholarship concerning ethics and health include: [9-14]). Without a doubt, these additional ethical principles and theories could have equal utility in health policy development, and if applied to relevant research questions, could serve as essential tools in guiding policy initiatives for allergy as well. A brief description of one prominent theory of social justice recently applied to analyse population health, yet not employed in this thesis, will exemplify this claim.

The theory refers to the recent work by Powers and Faden [15], where the authors develop a framework using six "core dimensions" [p.16] of well-being as means to prioritize public health interventions and assess key justice issues in the distribution of health achievements amongst population sub-groups. These six core dimensions, defined as being essential components for well-being, are categorized as the following: health, personal security, reasoning, respect, attachment, and self-determination. (For the sake of brevity, a detailed definition for each dimension will not be provided). Powers & Faden argue that "a life substantially lacking in any one of these [dimensions] is a life seriously deficient" [p. 29], where by identifying the degree by which morbidity negatively affects each dimension serves as a framework to determine which health inequalities constitute the most significant forms of social injustice, and thus, merit priority in public health intervention. Moreover, analysing how current health interventions directed towards ailing populations fail to ameliorate multiple dimensions of well-being could serve another function. Namely, it provides a means to define weaknesses inherent in health policies and

[16] Just prior to submitting this thesis, Hossny and colleagues [8] published the population incidence of food allergy to peanuts in a sample of Egyptian school children. 3% of children were confirmed to have peanut food allergy, an incidence that is roughly equivalent to that seen in the developed world.

thus why certain populations remain vulnerable to morbidity despite the availability of health interventions. Indeed, Powers & Faden's framework is appealing, especially considering how the topic of vulnerable populations is a central subject in this thesis.

Rather than negative, the limitations of this research project should be viewed in more positive light. For one, they indicate that many principles of ethics have yet to be employed as tools in policy developments for allergy. This in turn signifies that there are additional means to improve decision-making capacities in health interventions, each representing pertinent avenues to advance research.

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CONCLUSION

Building upon foundations: Future directions in research

Never let the future disturb you. You will meet it, if you have to, with the same weapons of reason which today arm you against the present.

- Marcus Aurelius Antoninus

The final segment of this thesis will now provide three examples of promising areas of future research. The following proposed research projects are a selection of pertinent topics that would build upon the knowledge foundations developed in the previous three published research articles that compose this academic work. We begin this discussion in relation to Chapter 2, where further attention centres on issues of social justice in the provision of allergy treatment to disenfranchised population segments.

Alleviating allergy morbidity necessitates a greater focus on justice and the promotion of equal capabilities in health achievements

The need for greater equity in abilities to control allergy morbidity within disenfranchised populations cannot be overemphasized. It is particularly disquieting that, to this day, factors related to race and poverty continue to significantly hamper the health of populations in the developed world. This must change.

There are several issues related to allergy treatments and health inequalities that require ethical scrutiny. One problem with current treatment regimens is that they are notoriously expensive—in fact, prescription medications account for the largest direct medical expenditure in asthma treatment [1]. In addition, annual pharmaceutical expenses are typically over $1300 for patients with particularly aggressive forms of allergy and asthma, patients which tend to predominate in lower socioeconomic classes [2]. Because of these costs, many patients are unable to afford needed pharmaceuticals and thus non-adhere to treatment [3], which in turn produces elevated morbidity levels and frequent visits to emergency departments in order to receive care [4]. In addition to social factors related to socioeconomic deprivation, racial factors are known to compromise the efficacy of biomedical interventions for allergy and asthma. Even when controlling for factors related

to income, patients of African descent are less likely to receive prescriptions for medications recommended by best practice medical guidelines, and are less likely to receive training in how best to use inhalers commonly employed in the treatment of asthma [5].

It is apparent that one integral component missing from current biomedical and public health interventions is to couple these treatment strategies with policies that promote social justice. If current interventions work well for middle, and even better for upper classes, as well as the racial majority, it seems logical that we need to raise the lowest strata upwards and promote the opportunities of minorities in order for these interventions to work well for *all* population segments. It is apparent that future commitments to reducing allergic disease cannot champion public health and biomedical interventions while excluding broader social reforms that would better position these interventions for success in all societal groups. The allergology community needs to be made more aware of this fact.

Having reaffirmed the importance of justice in allergy treatment strategies, we now return to policy dilemmas within the specific context of childcare settings and the population of food allergic children.

Foreseeable challenges for administrators of childcare settings: balancing the rights of the disabled with the needs of parents, children, and childcare institutions

Where until recently only avoidance and elimination efforts were the best strategy to prevent food-induced anaphylaxis [6], treatments for childhood food allergy, primarily in the form of immunotherapy, are gradually becoming more accepted by allergists and available to the average patient [7]. While such therapeutic innovation is arguably long overdue and will be of significant benefit, the availability of this health intervention will likely raise several contentious issues that require extensive debate. Foreseeable tensions will centre on whether childcare settings should continue to be held responsible in protecting the health of food allergic children, or whether immunotherapy should be obligatory for this minority of children attending the institution.

Mandating that children undergo specific medical assessments or interventions as a contingency for admittance at a childcare institution is not uncommon; for example, many

districts in the United States mandate childhood vaccinations as a prerequisite for school enrolment [8]. It is therefore a possibility that officials could require immunotherapy for children with severe food allergies on the basis of several justifications. As described in Chapter 3, effective food allergen avoidance policies are complicated, burdensome, and require significant time and resource expenditures. Certain policies also require restricting the activities of parents and non-allergic children, and also impose specific duties on staff and faculty members. It is thus not irrational to want to avoid these challenges by directing greater responsibility in health protection towards food allergic children and their parents.

The benefits accrued to the majority in this situation, however, may be met with strong opposition by the minority targeted by these policy decisions. As is the current situation concerning mandatory vaccination programmes [9], many parents and members of the public fiercely oppose the imposition of medical treatments upon their children. This opposition can stem from unfounded fears (e.g., the thoroughly debunked, yet continuing fear, that vaccines cause autism [10]), as well as reasonable concerns of possible adverse reactions to therapy, and most importantly, philosophical convictions that such policies are an affront to one's civil liberties and autonomy in individual determinism.

It is highly likely that mandated immunotherapy for severely food allergic children would be met with similar philosophical convictions and concerns [11, 12]. School officials and policy-makers must be made aware of this possibility. However, unlike policies such as vaccination, which aim to prevent illness, immunotherapy aims to cure an *ailment*. This ailment can be viewed as a "contextual" disability, where food allergy is made problematic when childcare settings do not establish appropriate safeguards for these disabled children. We now see how ethical issues concerning the mandated treatment of food allergy will require an analysis of the rights of the disabled, as well as debate concerning the duties school officials and policy-makers have to protect and uphold these much valued rights. Without question, this debate must be initiated in the near future in order to avoid foreseeable conflicts between children, parents and administrative officials.

Indeed, allergen-immunotherapy for food sensitivities will raise several challenging policy-related questions concerning the broader benefits and risks of this medical intervention. Because of the undeniable importance allergen immunotherapy will have in contemporary medicine, future research developments concerning the production of quality immunotherapeutic drugs is a pertinent subject requiring further investigation.

Shot-in-the-arm: pharmaceutical companies have a duty to further standardize allergen-immunotherapeutic drugs

The final chapter of the thesis described in detail specific duties that *government regulators* have in terms of encouraging the standardization of allergen-immunotherapeutic drugs. This chapter, however, made little mention of another key stakeholder that undoubtedly plays a vital role in this process, being pharmaceutical manufacturers. Indeed, what role ought pharmaceutical companies have in global allergenic extract standardization efforts? Do the private corporations that manufacture these drugs have a duty of their own—also phrased as a *corporate social responsibility* [13]—to standardize their products, regardless of whether government legislation mandates such production methods? Moreover, is it morally acceptable that, despite having standardization protocols readily available, companies continue to produce substandard therapeutics that unnecessarily complicate allergy treatment regimens and thus raise risks of adverse reactions for patients?

Unequal application of drug regulations also raises important questions of whether corporations share duties amongst themselves. Namely, is it fair that certain companies—but not others—are exempt from regulations, and thus the costs associated with standardizing their extracts, since their products were commercialized before the advent of drug regulations for allergenic extracts? These regulatory exemptions and resultant cost savings are arguably not fair and not favourable to the needs of patients. For one, emerging forms of immunotherapeutic drugs have novel benefits over age-old allergic extracts, which include improved safety and shortened treatment intervals [14]. However, the additional costs due to regulatory oversight of these novel drugs may provide a competitive advantage for substandard allergenic extracts and thus impede innovation.

Overall, a significant extension to the work presented in the final chapter of this thesis would be to define and analyse the ethical and policy implications of the above questions. The goal of this project should not be to point an overly accusatory finger at the private sector. A more receptive approach would be to argue that when all stakeholders (e.g., regulators, companies, patient representatives) are onside and aim for the same goal, initiatives achieve their desired goals with greater ease. And what could be a better goal than enabling the production of the best therapeutics on offer that can cure patients of a debilitating and sometimes life-threatening disease?

The unexpected benefits are often the best

The rewards of this doctoral training extend far beyond the acquired knowledge and analytical capabilities developed during this training experience. Instead, the greatest rewards from this doctoral training were made apparent through unexpected events that demonstrated how this research might have the capability to make a positive difference in the lives of allergy sufferers. This was made apparent after receiving emails from deeply concerned parents requesting copies of the article pertaining to food allergy policies for schools. Their correspondence conveyed emotional stories of having severely allergic children that they feared were at risk of a fatal reaction due to inaction on the part of school administrators. Other concerns voiced by these parents were that school allergy policies placed a heavy burden on food-allergic students, and this in turn compromised their learning experience. They hoped that my article could help guide them in their fight to make their school a safer learning environment for their children. I am honoured to have contributed to this fight.

There are many more worth fighting.

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