Recognizing contemporary determinants of public health: human rights, armed conflict and genetics

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Overview

This chapter considers a number of determinants of health that have become recognized as significant to public health practice. Whilst these are certainly not new, their relevance to public health research and practice has only relatively recently become acknowledged by mainstream practitioners. The determinants selected for inclusion in this chapter are considered especially pertinent to contemporary and future public health practice in the UK and globally, namely: human rights, armed conflict and genetics.

Overall learning objectives:

For each of these emerging determinants the reader will learn how the fundamental building blocks of public health may be applied in novel areas of knowledge, research and practice. By the end of this chapter you will have learned that basic public health principles and methods prove just as relevant in understanding these new contexts as in more traditional areas.

Further learning objectives are provided for each section in this chapter.

Key terms are also described in each section in this chapter.

HUMAN RIGHTS

Human rights as a tool for public health

Nineteenth-century public health interventions, and the emerging public health acts that underpinned those interventions, were predicated on the assumption that the public good justified infringement of individual liberties. Measures such as quarantine, detention, compulsory medical examination and vaccination were commonly employed weapons for disease control in the armoury of most states (see Chapter 1). Such powers were wide ranging; there were few obligations to review decisions or rights of appeal against them. However, with the emergence of a body of health ethics in the

second half of the twentieth century, and the increasing prominence of the doctrine of human rights, the assumption that the public good always overrides individual rights and liberties came to be questioned. This section will examine how the recognition of human rights has influenced attitudes to public health interventions, and how public health legislation has been amended to reflect this growing recognition of human rights. It will also consider how the recognition of human rights might assist rather than constrain the exercise of public health practice.

Human rights are viewed as a tool for the better implementation of public health rather than as an obstacle to public health, because:

- human rights ensure that all public health measures are carried out with respect for the dignity and worth of communities and their members;
- by this, they encourage public confidence in, and increase the legitimate authority of, health measures;
- human rights recognize that to live in an environment conducive to public health is a fundamental right.

However, it might be argued that human rights can act contrary to public health. This tension is explored next.

Learning objectives

By the end of this section you will be able to:

- describe the emergence of human rights arguments in public health
- recognize and explain legal frameworks for protection of rights relevant to public health
- describe the public health measures that might potentially infringe acknowledged rights
- recognize ways in which compliance with human rights might benefit public health

Key terms

Human rights The Universal Declaration of Human Rights states that:

'All human beings are born free and equal in dignity and rights. They are endowed with reason and conscience and should act towards one another in a spirit of brotherhood' (Article 1), and that:

> Everyone is entitled to all the rights and freedoms set forth in this Declaration, without distinction of any kind, such as race, colour, sex, language, religion, political or other opinion, national or social origin, property, birth or other status. Furthermore, no distinction shall be made on the basis of the political, jurisdictional or international status of the country or territory to which a person belongs, whether it be independent, trust, non-self-governing or under any other limitation of sovereignty (Article 2).

The interrelationship of human rights and public health

The Universal Declaration of Human Rights, cited above, provides a basis for protection of human rights everywhere, although in a far from perfect world there are too many examples of states that violate these rights. The principles set out in the Declaration have been transposed into many national and international laws. In a single chapter it is not possible to look at the many nationally specific provisions; instead we illustrate the key issues by reference to one international legal instrument, the European Convention on Human Rights. First, however, we examine the evolution of public health law and how it has been informed by human rights issues in one typical country, England.

England's first national Public Health Act in 1848 provided a model for public health legislation around the world, not just in Britain and its colonies but in other countries, such as Japan. The Act provided powers to intervene in relation to both places (water supplies, sewerage, housing, rubbish, etc.) and people. In relation to people, the Act provided a range of compulsory powers including compulsory medical examination and compulsory detention in a hospital for an unlimited time, with no review or appeal procedures. Reforms were introduced in the 1936 version of the Public Health Act, providing protections for civil liberties, for example by establishing limits on the time people could be detained and the rights to seek a review of a detention order, but these protections were abandoned in 1968 when a range of public health measures were consolidated into a single Act. They were not reinstated in the Public Health Act of 1984.

The development of public health legislation took place against a background of legal provisions recognizing the rights of individuals against interventions by the state. The Universal Declaration of Human Rights was adopted and proclaimed in 1948, and the European Convention on Human Rights came into force in 1953. While several of the rights listed in these documents had relevance for public health interventions, it was some time before states and public health communities recognized that commonly accepted public health measures might be constrained by the provisions of these human rights instruments.

The revised International Health Regulations (IHR 2005), produced by WHO, have enshrined the importance of human rights in the exercise of public health. The requirement that WHO members states comply with the IHR has prompted countries around the world to revise their public health legislation.

In England and Wales, the Health and Social Care Act 2008, Part 3, amending the 1984 Public Health Act, introduces some human rights constraints on public health measures, particularly procedural protections against abuse of quarantine and isolation powers. For example, a public health measure imposed on an individual must now be proportionate to what it seeks to achieve (section 45D), compulsory medical treatment and vaccination are prohibited (section 45E), and there are provisions for review and appeals against compulsory power orders (section 45F).

The European Convention on Human Rights (ECHR) and how it might constrain public health measures

The ECHR lists rights that signatories, including all EU member states, must comply with the exercise of governmental powers. Some of the rights in the ECHR are 'qualified', which means that restrictive measures can be justified in certain circumstances.

Examples are Article 8 (right to respect for private and family life), Article 9 (freedom of thought, conscience and religion), Article 10 (right to freedom of expression) and Article 11 (freedom of assembly and association). Article 5 (the right to liberty and security) is a 'limited' right and restrictions can only be imposed in certain specified circumstances. The ECHR also sets out 'absolute' rights that cannot be interfered with under any circumstances, such as Article 3 (prohibition on torture, inhuman or degrading treatment), Article 4(1) (prohibition on slavery) and, arguably, Article 6 (right to a fair trial).

Compulsory vaccination, treatment or medical examination

Interventions such as compulsory vaccination, examination and treatment raise issues in relation to Article 3 (inhuman and degrading treatment), Article 8 (the right to private and family life) and Article 9 (freedom of thought, conscience and religion) of the ECHR.

If Article 3, an absolute right allowing for no exceptions, is to be invoked, it must first be determined whether the medial intervention in question amounts to inhuman and degrading treatment. Ill treatment must be of at least a minimum level of severity to fall within the scope of the Article and factors taken into account include the duration of the treatment, its physical or mental effects and the sex, age and state of health of the victim (Abdulaziz 2005). The European Court has in the past stated that there must be an element of humiliation to count as ill treatment (Labita 1995), going beyond the 'inevitable element of suffering or humiliation connected with a given form of legitimate treatment or punishment'. In the case of *Jalloh v. Germany* (Jalloh 2000) for example, the administration of emetics (to cause vomiting) against a patient's will was held to be a violation of Article 3.

The courts are generally quicker to rule that inhuman or degrading treatment has taken place where a citizen is detained by the state. 'Where a person is deprived of his liberty, the State must ensure that he is detained under conditions which are compatible with respect for his human dignity and that the manner and method of the execution of the measure do not subject him to distress or hardship exceeding the unavoidable level of suffering inherent in detention (A and others 2005). Concerns might arise where a citizen is detained under a compulsory quarantine power and, on the word of a single doctor, subjected to an invasive medical examination. Where a patient refuses to consent to invasive medical examination or treatment, there is often an underlying religious or cultural reason for doing so. In these circumstances forced medical examination could be seen as disrespectful and humiliating to the individual.

Where the intervention does not amount to inhuman and degrading treatment, Articles 8 or 9 could come into play and, as these are both qualified rights, the proposed infringement would be subject to the balances set out in the Convention. These balances consider whether the measure is in accordance with the law, in pursuit of a legitimate aim and necessary and proportionate in a democratic society. The doctrine of patient consent is a core value in medical law and the European Court is reluctant to interfere with a competent patient's decision to refuse treatment, even where such refusal might harm the patient (re AK 2001). However, the harm being considered in the context of disease control is harm not only to the patient him/herself, but also harm to the wider public.

There have been surprisingly few challenges to the use of compulsory powers in this way, perhaps because the diseases where such powers are most commonly

exercised, for example in relation to tuberculosis, often arise in migrant, poor and insular communities who might have limited access to legal knowledge or assistance.

Quarantine and detention

These measures may potentially infringe Article 5: 'Everyone has the right to liberty and security of person. No one shall be deprived of his liberty save in the following cases and in accordance with a procedure prescribed by law.'

As Article 5 is a limited right, restrictions on liberty and security will only be lawful if they are for a purpose listed in the ECHR. One such purpose does relate specifically to public health: *(e) the lawful detention of persons for the prevention of the spreading of infectious diseases*.

In the case of *Enhorn v Sweden* (Enhorn 2000), an HIV positive man who had transmitted the virus to another was held in isolation by the Swedish public health authorities. He challenged his detention in the European Court of Human Rights, arguing that his ECHR rights had been breached (Martin 2006). The Court held that in order for a detention to be lawful:

- the measure must be proportionate;
- there must be an absence of arbitrariness;
- the detention must be a last resort measure;
- the detained person must be suffering from an infectious disease;
- the spread of disease must be dangerous to public safety *and*;
- the detention must have as its objective not only protection of the healthy but also care of the ill.

The Court found that the Swedish Government had failed to consider whether any lesser measures could have achieved the same outcome of protecting public health and thus the measure was not a last resort. Accordingly, there had been a breach of Article 5.

The legality of the quarantine or isolation, and in particular large-scale programmes envisaged in many national pandemic preparedness plans, would need to be judged under the conditions set out in the *Enhorn* judgement. It is important to note that HIV is not transmitted in the same way as influenza, which is spread considerably more easily and is usually airborne (Health and Safety 2009). The European Court, therefore, might be inclined to allow detention on health grounds more readily than in the *Enhorn* case. The counter argument is that the speed of transmission makes isolation almost redundant, as transmission may well have occurred before an infected person enters quarantine or detention.

It is likely that quarantine will be more difficult to justify than simple isolation. Although both measures potentially infringe human rights, there is a stronger public health argument for containing those infected in isolation. Article 12(1) of the *International Covenant on Economic, Social and Cultural Rights* recognizes 'the right of everyone to the enjoyment of the highest attainable standard of physical and mental health'. Isolation of people displaying symptoms is arguably necessary both for the health of the public at large and in the interests of society in controlling the spread of the virus (Boggio et al. 2008). Quarantine, however, envisages the detention of those not yet displaying symptoms, on the basis that some of those detained are at risk of developing the disease and thus may pose a risk to others. This can mean detaining those who might develop symptoms together with those who might not, putting the

health of some persons at risk for the benefit of others. Concerns were raised by the Nuffield Council on Bioethics (2007) that quarantine might be implemented inappropriately or abused. At issue also is whether the measure is actually effective. In the SARS outbreak some 1200 people were quarantined in Hong Kong and 131,000 in Taiwan (Gostin and Berkman 2007). Quarantine was later considered of limited effect due to the difficulty in diagnosing mild cases, the raised level of panic that the measure created, and the number of violations of it (Rothstein et al. 2003).

Fear of quarantine can make people reluctant to seek diagnosis and can result in stigmatization of groups or individuals (Murphy and Whitty 2009). If quarantine is not considered effective, any benefit in terms of protecting the public will be reduced and it will be harder to demonstrate proportionality. The WHO guidelines on preparedness planning state that the use of social distancing measures such as isolation and quarantine 'must be carefully circumscribed and limited to circumstances where they are reasonably expected to provide an important public health benefit' (World Health Organization 2007) and that isolation should be voluntary to the greatest extent possible.

Relevant factors would include whether the period of quarantine or isolation is time limited and whether the detention is subject to regular review. Other considerations, related to proportionality and arbitrariness, include the degree of due process (such as whether the detained person is allowed a right of appeal) and whether plans are in place to detain separately those displaying symptoms from those who might only potentially be infected (Gostin and Berkman 2007).

Rights of review and appeal

Article 6 of the ECHR provides that, 'In the determination of his civil rights and obligations or of any criminal charge against him, everyone is entitled to a fair and public hearing within a reasonable time by an independent and impartial tribunal established by law.'

This is arguably an absolute right (Brown v Stott 2001), entitling citizens to a fair trial including the right to take court proceedings to settle a civil dispute. The courts have held that the right includes access to a court; adequate notice of a hearing and time to prepare a defence; and a proper opportunity to present one's case (Dombo Beheer 1993). There is also an obligation on the state to provide legal assistance for persons that have been isolated or put in quarantine, as they are not able to arrange adequate defence for themselves (Megyeri v Germany 1992). Many states in Europe and elsewhere, including until recently England and Wales, do not provide procedures for review or appeal of compulsory orders such as for quarantine or detention (Martin et al. 2010).

Medical information sharing

Systems of surveillance to track the spread of infections and isolate those infected are vital in containing disease (Gostin and Berkman 2007). However, such systems have implications for the right to privacy under Article 8 of the ECHR. As with medical interventions, an important consideration will be whether control could be achieved by lesser means. The Home Affairs Select Committee in the United Kingdom Parliament considered the issue of data collection in 2008 (Home Affairs Committee 2008) and suggested a move towards 'data minimalization' – collecting only necessary data and storing it for the shortest amount of time possible.

Human rights and non-communicable diseases

Issues of human rights are less likely to arise in the context of public health measures to prevent or control non-communicable diseases. Despite arguments by the pro-tobacco or pro-alcohol lobbies, there is no legally recognized right to smoke or to drink alcohol. What is at issue here are not *rights* but *freedoms* – individuals arguing that their freedom or autonomy is being constrained by tobacco or alcohol restrictions and taxes, or on controls on fast food advertising. The counter argument is that our freedom or autonomy to choose has been deliberately eroded by intensive advertising, and by the availability and use of addictive substances, such that public health interventions, for example, prohibition on advertising or protection of smoke-free public places, are necessary to restore our freedom to choose a healthy lifestyle rather than eroding it.

One issue that has raised human rights arguments is the fluoridation of water supplies. This is complex because someone living in an area where there is fluoridation does not have a realistic freedom to choose not to drink fluoridated water. In many countries, arguments based on public benefit and utilitarianism (the greatest benefit for the greatest number) have prevailed. There have also been claims that fluoridation is harmful to health (it is, but only at levels far higher than those in fluoridated drinking water), but if such arguments were true then human rights might become an issue in the context of fluoridation.

The 2005 International Health Regulations (IHR) and human rights

The revised IHR 2005 explicitly requires that human rights be taken into account in the exercise of public health measures, stating that 'the implementation of the IHR shall be with full respect for the dignity, human rights and fundamental freedoms of all persons.' The IHR make clear that states must recognize principles of human rights in that

- state responses must be appropriate;
- any measures taken must be no more intrusive than available alternatives;
- consent should be obtained for measures unless compulsory measures are warranted;
- there is an obligation to preserve the confidentiality of identifiable information.

These provisions place a responsibility on nations to ensure both that their public health laws incorporate human rights principles, and that public health practice is exercised in accordance with these principles.

Human rights recognition can benefit public health

The protection by the state of rights and freedoms is fundamental for public trust in government initiatives, and if the public is to cooperate with public health measures. Enforcement of measures is not always easy or practical. A population-wide refusal to comply with anti-smoking legislation or with prohibitions on public gatherings to control spread of disease, could severely damage public health objectives (although it is important to ascertain the true level of support, as one may argue that the tobacco industry, for instance, has under-played the widespread support for bans on smoking in public places – see Chapter 8 for more on this topic). This is especially so in circumstances of a disease pandemic. Indeed pandemic preparedness plans rely heavily on volunteers, on home nursing, on neighbours taking food to the sick and on care for the

children of the sick. We can see this from the pandemic simulation exercises that have taken place for assessing the feasibility of plans.

The success or failure of disease control measures lies not with enforcement mechanisms but with the willingness of the population to behave responsibly and in accordance with communitarian values. Where the state fails to recognize either limits on its powers or the need not to sacrifice the rights of individuals for the public benefit, then trust and cooperation are less likely. The objective of public health practice is care and protection of the population against all threats to health. It is not law enforcement for the sake of it. Countries with the most draconian public health powers are rarely those with the highest level of public trust or the best population health. The recognition by the state of individual rights is a good starting point to creating the public trust necessary to achieve effective public health.

Of course the achievement of public support for public health initiatives is not just about rights. It is also about justice in the distribution of public health burdens, and about social justice in access to opportunities and goods. It concerns normative responsibilities to redress inequalities, to care for those most at risk of public health harms, and to redistribute goods so that all members of the population have an equal opportunity to survive a threat to public health. While rights documents often focus on what states must not do, rather than on responsibilities of states to take positive action for the protection of their populations, some human rights instruments have attempted to impose positive obligations on states to assist in the achievement of conditions for health. The Universal Declaration of Human Rights, for example, states the following in Article 25:

- Everyone has the right to a standard of living adequate for the health and well-being of himself and of his family, including food, clothing, housing and medical care and necessary social services, and the right to security in the event of unemployment, sickness, disability, widowhood, old age or other lack of livelihood in circumstances beyond his control.
- Motherhood and childhood are entitled to special care and assistance. All children, whether born in or out of wedlock, shall enjoy the same social protection.

And Article 12(1) of the International Covenant on Economic, Social and Cultural Rights recognizes 'the right of everyone to the enjoyment of the highest attainable standard of physical and mental health'.

One thing that can be achieved by an enforceable legal framework of human rights is to make clear that everyone has a right to the minimum conditions necessary to attain health, and that the state has an obligation to work towards the attainment of these conditions. This supports an expectation by the population of a healthy environment, and supports the work of individuals and lobby groups working to improve public health.

Activity 9.1

The following Open Access paper can be found at: http://medicine.plosjournals.org/perlserv/?request=get-document&doi=10.1371/journal.pmed.0040050

Singh JA, Upshur R and Padayatchi N (2007) XDR-TB in South Africa: no time for denial or complacency. *PLoS Med* **4**(1): e50.

Commenting on this paper, Coker et al. wrote (Coker R, Thomas M, Lock K and Martin R (2007) Detention and the evolving threat of tuberculosis: evidence, ethics and law. *J Law Med Ethics* **35**(4): 609–15, 512.

> Singh et al.'s paper on the challenge posed by XDR-TB in South Africa stimulated afresh the debate around the use of detention in order to protect public health. The debate originated a decade earlier when New York City, responding to its epidemic of drug resistant tuberculosis in the early 1990s, passed laws facilitating the detention of non-infectious individuals and shifting the burden of proof from an assessment of risk posed to public health to an assessment of likely treatment compliance. In relation to XDR-TB in South Africa, the authors propose that under some circumstances individuals might be isolated whilst awaiting susceptibility results. They advocate initial voluntary isolation of patients with drug resistant tuberculosis, separating those with multi-drug resistance from those with extensive drug resistance, and recommend coercive measures where voluntary isolation is declined, acknowledging that the duration of isolation may potentially be indefinite or until death in some cases of XDR-TB. The authors conclude: 'Although such an approach might interfere with the patient's right to autonomy and will undoubtedly have human rights implications, such measures are reasonable and justifiable, and must be seen in a utilitarian perspective. Ultimately in such cases, the interests of public health must prevail over the rights of the individual.'

After reading the paper by Singh et al. consider the following questions in the context of Europe, where the European Convention on Human Rights applies:

1 What human rights issues arise in relation to involuntary detention of persons who have not yet been confirmed as having MDRTB or XDRTB?
2 Where an individual has been confirmed as suffering from multi-drug resistant tuberculosis, what human rights concerns might arise where a decision is made to detain that person on grounds that his/her personal or social circumstances suggest that he/she might not comply with a treatment regime?
3 Would it infringe a person's human rights to detain that person without specifying the length of the detention?
4 Could compulsory treatment of a person with MDR/XDR tuberculosis be justified on public health grounds?
5 Is it the case that, as Singh et al. suggest, 'Ultimately in such cases, the interests of public health must prevail over the rights of the individual'?
6 Should we take in to account, in considering the questions above, the differing disease context in Africa? Would it be justifiable to accept differing levels of human rights protection in different countries?

Feedback

1 There is a prima facie breach of the detained person's right to liberty and security, and right to family life, by them being detained. Detention is only justified if it is imposed for the purpose of protection of public health, if it is the least restrictive alternative measure, if the choice of whom to detain is not discriminatory, if the risk posed by the detained person outweighs the harm done by the detention, and if the place of detention is appropriate to the health of the detained person.

   There is also a prima facie breach of the person's right to a fair trial if the decision to detain has not been made in accordance with the law, if the person has had no opportunity to challenge the detention, if there is no time limit given to the period of detention and if there is no appeal or review process.

The detention of someone who has not yet been confirmed as infectious is problematic as the person may pose no risk at all to public health. Quarantine procedures with time limits accompanied by regular medical examination to confirm infectiousness would be more appropriate.

2 A person suffering from MDRTB can potentially create a public health risk. Where that person complies with a treatment regime and with advice on limiting contact with others, there is no need to compulsorily detain. Hence it might be arguable that it is justified to take into account that person's capacity to comply. However such an assessment involves passing judgement not on the person's physical state of health but on psychological and social factors. Public health officials may not have the necessary skills to undertake these judgments. It would be easy for judgments to be made on social or racial stereotyping rather than on the attributes of the individual. The history of the exercise of public health powers tells us that attribution of irresponsible disease behaviours to particular sections of society has been common, especially in the context of disease epidemics and pandemics. Any such judgment must be made on concrete evidence of the person's previous health behaviours and not on an assumption of non-compliance based on ethnicity or socioeconomic status.

3 This would amount to a breach of the right to a fair trial. Wherever a person is detained, be it for the commission of a criminal offence or for the protection of public health, the infringement of the person's right to liberty cannot be indefinite or infinite. The person is entitled to know the proposed length of detention, and that time period must be justifiable on public health grounds and must be challengeable. The detention time need not be specified in terms of days or months, but could be predicated on an event, such as a confirmation that the person is no longer infectious.

4 Western legal systems support the notion of autonomy. Every person with capacity to make decisions about their health is entitled to choose whether to consent to, or refuse, medical treatment. The fact that someone is suffering from an infectious disease does not lesson that person's capacity to make an autonomous decision. However, refusal of treatment, and failure to treat, could result in the detention of a person indefinitely if the person continues to be infectious. Such a person would need to be monitored regularly to determine continued infectiousness, as continuation of detention must be justified on grounds that the risk of that person to the health of the public outweighs the infringement of their rights.

5 Singh's comments were made in the context of a different culture, with different beliefs, ethics and legal culture. Western health ethics, and laws, assume the autonomy of the individual and prioritize autonomy over other values such as communitarianism, family or tribal loyalty, etc. The African Charter on Human and People's Rights for example, unlike the European Convention on Human Rights, makes clear that individuals owe duties to their family and their community, and that rights do not prevail over the public good. Asian values based on Confucianism and Buddhist beliefs would take a similar approach. Hence the answer to this question will depend on the culture and ethics beliefs of the population of the state.

6 The level of disease risk in each state will be relevant to the assessment of risk. The compulsory detention or treatment of a person with disease must be justified by an assessment that on balance, the risk created by the infectious person outweighs the infringement of rights. So seriousness of the level of disease, access to medical resources, closeness of living quarters etc. will all input into the assessment of risk that person creates to the health of others. This is not to say there are differing levels of human rights. The rights remain the same, and the

principles for assessment of protection of those rights remain the same, but the facts on which those principles are to be determined differ. It is also the case that the culture and ethics of the society will be relevant in determination of the balance between public good and private right. Imposition of western interpretations of human rights on African and Asian states has been rejected as 'cultural imperialism'. African and Asian values, so long as they are debated and supported by the public, should be taken into account in the determination of how rights are to be protected and enforced.

ARMED CONFLICT

Armed conflict and public health

The deaths, injuries and illness attributable to armed conflict are major contributors to the global burden of disease (Murray et al. 2002). The discipline of public health plays a crucial role in mitigating the impact of armed conflict on health. In this section you will learn how conflict can have an impact on the health of civilian populations, and then examine key epidemiological approaches that should be used by humanitarian organizations to help understand the scale of health needs and the impact of the humanitarian response.

Learning objectives

By the end of this section you should be able to:

- describe how armed conflict can influence health
- explain the direct and indirect effects of armed conflict on health
- discuss the key epidemiological approaches used to measure the health status of conflict-affected populations

Key terms

Armed conflict There are various definitions of armed conflict, but a commonly used definition of major armed conflict is one that has over a 1,000 battle-related deaths in one year.

Household surveys Collection of information from a representative sample of households on health events.

Mortality rate The number of deaths occurring in a given population at risk during a specified time period. In conflict-affected settings, this is usually expressed as deaths per 10,000 persons per day.

Surveillance The systematic collection and analysis of information over time to regularly monitor changes in health.

Background on armed conflict

There was an overall rise in the number of armed conflicts globally since the 1950s, with the majority being protracted civil conflicts between a national government and irregular armed groups, rather than international conflicts between countries. Civil wars are extremely complex in nature and often have many causes. These include: grievances over exclusion from economic resources, the scope to gain from potential spoils of war; entrenched economic and social inequalities, extreme poverty, economic stagnation and high unemployment; environmental degradation and scarcity of resources; political exclusion, weak governance, high militarization and a history of conflict; and ethnicity and religion (often exploited by political leaders) (Stewart 2002).

Although international law provides legal protection for civilians in times of war (Box 9.1), many conflicts are characterized by the deliberate targeting of civilians who may be killed, raped, maimed and abducted (Bruderlein and Leaning 1999). Civilian populations may also be forcibly displaced from their homes by violence and insecurity. These forcibly displaced populations currently include around 27 million internally displaced persons (IDPs) who have fled their homes but remain within the national borders of their own country and around 15 million refugees who have fled across an international border into a neighbouring country.

Refugees and IDPs have most commonly lived in camp settings but a relative majority now reside in urban areas, a phenomenon that presents new challenges for the way in which health services are provided (Spiegel et al. 2010). Another sizeable proportion lives in rural areas. There are also many people in conflict zones who, though not displaced, have low access to essential health services, food and other basic needs due to surrounding insecurity.

Box 9.1 International law in conflict-affected settings

There are a number of international treaties that seek specifically to protect civilians and the humanitarian organizations providing relief services in times of war. International Humanitarian Law (notably the 1949 Geneva Conventions and their two 1977 Additional Protocols) includes the obligation for all parties to collect and care for the sick and the wounded, as well as the obligation to respect and protect hospitals, ambulances, and medical personnel, and to provide protection against rape and indecent assault. However, many instruments within International Humanitarian Law are primarily intended to cover international wars and their application and enforcement in civil wars is limited. This increases the challenge of providing health care in civil wars.

Refugee Law (The 1951 Refugee Convention and related 1967 Protocol) addresses the specific rights of refugees. The Convention requires participating countries to provide refugees protection and social support, including for their health. It also created the post of United Nations High Commissioner for Refugees to manage protection and support services for refugees. However, Refugee Law does not cover IDPs. Although IDPs are guaranteed certain basic rights under the Geneva Conventions, ensuring these rights is often the responsibility of those national governments that were responsible for their displacement in the first place. As a result, protection and support provided for IDPs can be severely lacking, including access to health care.

The influence of armed conflict on health

The ways in which armed conflicts influence health are specific to the individual contexts. Hence, it is necessary to take account of the underlying pre-conflict conditions, the characteristics of the conflict, and the impact of the conflict itself (Figure 9.1). The underlying pre-conflict risk factors include poverty and socioeconomic vulnerability ('distal' factors) which reduce the ability to withstand the impact of the conflict. The underlying epidemiological conditions are also critical, with younger populations living in areas with a high burden of communicable disease (mainly sub-Saharan Africa and Asia) generally at higher risk. Weaker health systems are also less able to withstand conflict than stronger systems, further reducing the availability of health services during the conflict.

Conflicts where there is a high intensity of violence towards civilians inevitably have a profound impact on health. Civilians may be attacked directly, forcibly displaced from

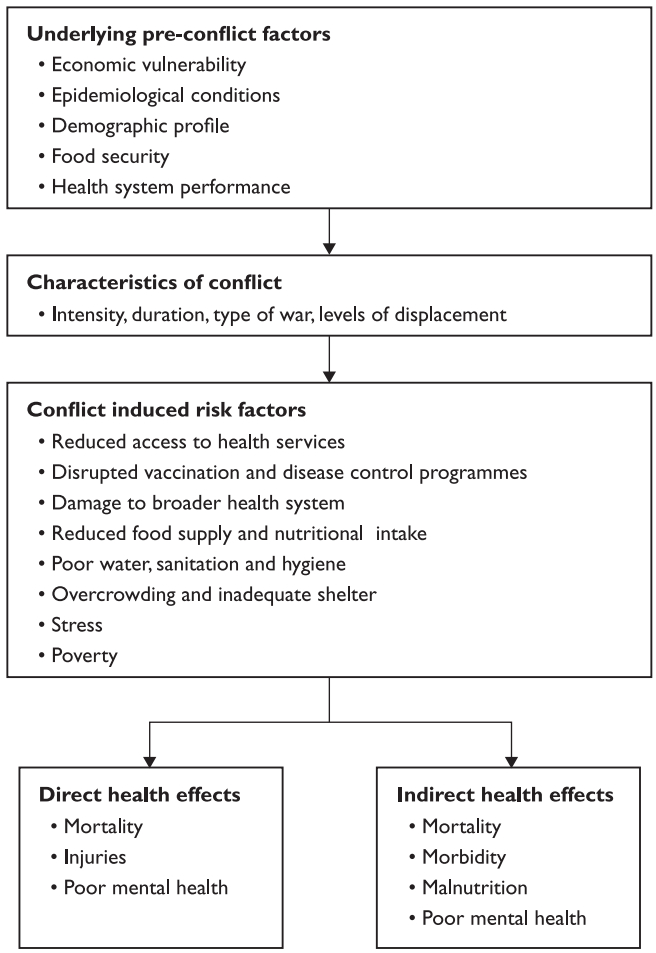


Figure 9.1 Ways in which conflict can influence health

their homes, and suffer from destruction of health facilities. Similarly, longer durations of conflict increase the impact on population health. Civil conflicts are frequently characterized by little adherence to human rights principles and International Humanitarian Law by combatants (see Box 9.1), leading to targeting of civilians and humanitarian organizations. Entrapped populations may be particularly vulnerable to such violence and loss of access to health services. Forced displacement can also have extremely detrimental consequences for health, particularly for IDPs living in very overcrowded camp conditions (for example, the camps in northern Uganda, Darfur and Somalia in the 2000s), and refugees who move into areas where support services are not yet available (for example, about ten per cent of the 500,000 to 800,000 Rwandan Hutu refugees who fled into Goma, Zaire in 1994 died within one month – mainly due to cholera). However, it should be noted that long-established and well-organized refugee camps are generally characterized by good health outcomes with mortality rates usually well below those of even the surrounding host community.

Armed conflict influences the risk factors for ill health in a number of ways. It can delay or prevent access to health services due to the insecurity involved in travelling to health facilities, destruction of health facilities, health workers being forced to flee, and vital medicine and supply chains being disrupted. Importantly, it frequently disrupts vaccination and disease control programmes resulting in outbreaks of infectious disease. Already poor nutritional status may worsen due to inability to grow or purchase food because of insecurity, displacement and impoverishment. Rising malnutrition increases vulnerability to infection, especially among children and elderly people. Conflict and displacement commonly result in worsening living conditions as people are forced to flee into makeshift settlements which are often characterized by limited access to clean water, adequate sanitation and thus poor hygiene (increasing the risk of diarrhoeal diseases, such as cholera and typhoid), inadequate shelter (increasing the risk of diseases such as pneumonia and other respiratory infections) and overcrowding (increasing the risk of diseases such as measles, acute respiratory infections and tuberculosis).

Direct and indirect health effects

Civil conflicts are often extremely protracted (lasting on average for ten years) and so have extremely long-term effects on health, both during the war and long after it. These health effects can be divided into direct effects sustained in the fighting, such as deaths and injuries, and indirect effects resulting from an increase in the risk of infectious and non-infectious disease and poor nutrition. As noted above, the majority of indirect deaths occur among children and elderly people, and arise from preventable communicable diseases such as acute respiratory infections, diarrhoeal diseases, tuberculosis and malaria (with malnutrition, measles and HIV as common underlying conditions).

The ratio between direct and indirect effects depends on the timing and context of the conflict. It is common for the direct effects to predominate in the early stages of conflict as people die from the violence (particularly young men), but indirect effects take over as living conditions, health services and nutritional status deteriorate.

The burden of indirect effects is substantially higher in conflict-affected populations living in tropical and very poor settings because of underlying endemic communicable diseases and limited access to health services, food, and income. It is estimated that between 70 and 98 per cent of war-related mortality in nine major conflicts in

sub-Saharan Africa since 1945 was due to the indirect effects of preventable and treatable diseases (Human Security Centre 2005).

Armed conflict also affects reproductive health because of the lack of access to health services, impoverishment and exposure to violence. Extremely high rates of sexual violence by combatants against civilians have been reported during wartime but also increasingly by civilians against other civilians in long-term chronically insecure situations such as those in the eastern part of the Democratic Republic of Congo. High rates of mental illness have also been recorded among conflict-affected populations as a result of exposure to violent and traumatic events, poor living conditions, insecurity, impoverishment, disrupted social norms, and the loss of livelihoods (Miller and Rasmussen 2010). There is also growing awareness of the impact of conflict on chronic diseases such as diabetes and heart disease among displaced persons in middle-income settings, such as IDPs in Georgia (Spiegel et al. 2010). The damage caused to health by civil conflicts extends well beyond the period of active warfare, with women and children the most affected by their prolonged effects (Human Security Centre 2005).

The role of public health in conflict-affected settings

There is broad consensus on the types of public health interventions required in conflict-affected situations. This consensus is formalized in the Sphere Guidelines and Handbook which provide the main standards for humanitarian interventions (see Box 9.2).

Box 9.2 Sphere Guidelines – key health interventions

- Initial assessment
- Sufficient and safe water, adequate sanitation facilities
- Sufficient food and nutrition supplements
- Mass vaccination
- Disease surveillance, outbreak preparedness and control
- Primary health care and referral hospital services for severe cases
- Shelter and site planning
- Reproductive health services
- Mental health and psycho-social care

Public health disciplines are essential in guiding decision-making to prioritize optimal activities within the agreed interventions outlined in Sphere and to ensure they are: (i) addressing the main health problems (e.g. high risk diseases); (ii) providing adequate coverage to meet health needs; and (iii) effective (and cost-effective) in addressing health needs. However, a fundamental challenge in quantifying the health impacts of conflict is that health information systems, particularly registration systems that record deaths and the causes of death, often cease to function in conflict-affected areas (indeed in many low-income conflict-prone countries they may not have been functioning before the conflict). In the absence of functioning standard health information systems, the methods commonly used to obtain health information to guide decision-making are rapid assessments, surveillance and surveys. This data collection is commonly carried by humanitarian organizations.

Rapid assessments

Rapid assessments provide a quick means of informing decision-making at the onset of a crisis. Types of information include: the characteristics of the conflict, such as general levels of insecurity and targeting of civilians; demographic and socioeconomic characteristics of the affected populations; health profiles of the affected area, in terms of endemic and epidemic-prone diseases; availability and functionality of health services; and living conditions and availability of food and clean water. Potential sources of information include:

- existing situational reports;
- media reports;
- databases and maps of global distribution of specific diseases;
- records of past disease outbreaks in the affected area or similar areas;
- past reports from health information system.

However, rapid assessments do have limitations due to the quantity and quality of available data and the trade-off between rapidity and quality of data collection. These reports are unlikely to provide accurate data on mortality rates, prevalence or incidence of diseases and acute malnutrition, or the impact of health interventions.

Surveillance systems

Surveillance systems provide the most important means of monitoring population health effectively in crisis-affected settings, providing trends in mortality, prevalence of acute malnutrition and enabling detection of epidemics (i.e. monitoring the burden of disease and the impact of interventions). Surveillance systems in conflict-affected settings may include: (i) health-facility based surveillance of epidemic-prone diseases, either from an exhaustive list of facilities or a few sentinel sites; (ii) demographic surveillance to monitor trends in mortality rates, by collecting information on births and deaths from all households by means of home visitors; and (iii) more specialized systems consisting of repeat surveys to monitor HIV at risk behaviours and prevalence, acute food insecurity and malnutrition prevalence. Surveillance systems should be established in the affected area as soon as is possible.

Household surveys

Cross-sectional household surveys are commonly used to collect data at a single point in time on crude and under-5 mortality rates (see Box 9.3) and on prevalence of acute malnutrition, in places where functioning surveillance systems do not exist. Follow-up surveys can then be used to identify any changes in these outcomes (so indicating the possible impact of interventions). A range of other health outcomes are also measured by household surveys (albeit far less frequently) such as maternal mortality, mental health conditions such as post-traumatic stress disorder and depression, HIV-related behaviour, and experience of sexual and gender-based violence. Surveys are also used to provide essential information on the coverage of interventions (e.g. vaccinations, therapeutic feeding, water and sanitation, and access to health care).

Box 9.3 Mortality data in conflict-affected settings

The primary goal of any comprehensive humanitarian programme should be to reduce loss of life. Crude and under-5 mortality rates are therefore crucial indicators to understand the nature and severity of the crisis, and the Sphere Guidelines use mortality rates to categorize whether there is an emergency or not (stating that a doubling of pre-conflict baseline mortality can be considered an emergency situation). Mortality rates are also essential in understanding the impact of humanitarian relief (i.e. in reducing the loss of life).

The difference between the observed mortality rate during the conflict and the mortality rate in the pre-conflict baseline period represents the excess mortality rate caused by the conflict. The excess mortality rate can be applied to the population and period it refers to in order to estimate the absolute number of excess deaths caused by the conflict. For example, it was estimated that there were 5.4 million war-related excess deaths (the vast majority from disease) in the Democratic Republic of Congo between 2000 and 2007. This represents a catastrophic combination of elevated mortality rates for a very large population over a long period of time (Coghlan et al. 2007).

Very approximate causes of mortality (e.g. disease, violence, pregnancy-related) can be collected by home visitors and lay data collectors. More specific and accurate causes of death can be recorded by using verbal autopsy questionnaires administered by trained clinical personnel.

Challenges for public health

Despite general agreement on the key interventions required in humanitarian settings, there has often been a failure to deliver them (United Nations 2005). Recent measures seek to strengthen coordination and accountability within the global humanitarian community, including the development of sectoral guidelines for the health sector (IASC 2009); a major obstacle to effective delivery of appropriate services remains the lack of detailed knowledge of health needs in particular contexts. This is largely due to a failure of humanitarian organizations (and country governments where they are still functioning) to conduct surveillance and surveys. As a result, essential information on health needs and the impact of interventions is missing. This also impedes global comparisons on the extent of humanitarian need, so risking inequitable targeting of aid and other resources. Instead there is a tendency for humanitarian organizations to collect process information (e.g. the number of health services provided) rather than information on outputs (e.g. coverage of interventions) or impact (e.g. changes in mortality rates). Even when surveillance and surveys are conducted, many are of a poor standard, often with low sensitivity for deaths that may have occurred. Household surveys very frequently feature inadequate sampling and insufficient sample sizes as well as multiple other biases, which can result in erroneous findings and imprecise results, and lead to potentially ineffective humanitarian responses (Prudhon and Spiegel 2007; Working Group for Mortality Estimation in Emergencies 2007).

There are several reasons for the failure to collect adequate surveillance and survey data. Insecurity and logistical challenges inhibit data collection, particularly for surveillance systems among dispersed populations. Donor agencies tend to favour process rather than impact indicators and are reluctant to pay for resource-intensive

surveillance systems. Donors may be reluctant to fund collection of data that do not relate specifically to the activities they are undertaking. Importantly, there is limited capacity within many humanitarian organizations to conduct field epidemiology to a sufficiently rigorous standard, sometimes coupled with a failure to recognize its value. These reasons need to be addressed so that the quantity and quality of data collected among conflict-affected populations can be improved (Roberts and Hofmann 2004).

Activity 9.2

Figure 9.2 shows crude mortality rates (CMR) (per 10,000 persons per day) over a 12-month period in a conflict-affected population in sub-Saharan Africa. What factors do you think may explain the changes in the crude mortality rate?

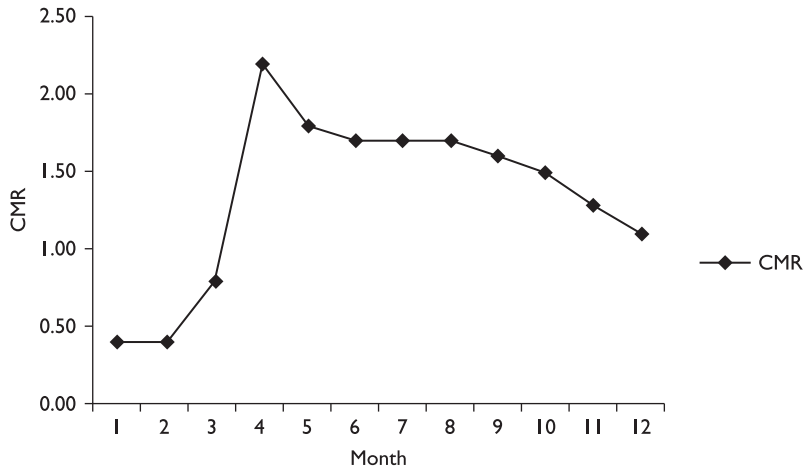


Figure 9.2 Mortality rates over a 12-month period in a conflict-affected population in sub-Saharan Africa

Feedback

Months 1 to 2 show a stable baseline rate fairly typical of the region (i.e. pre-conflict). Months 3 to 4 show a substantial increase in CMR, well above the baseline rate (therefore an emergency according to Sphere Guidelines). This increase could be attributable mainly to the direct effects of an outbreak of armed conflict (i.e. violence-related deaths). The slight fall in month 5 could be as violence reduces. The continuation of the high CMR in months 5 to 8 could be attributable to the indirect effects of the conflict such as increases in communicable diseases. The decrease in CMR in months 9 to 12 could be due to improved security and humanitarian interventions resulting in better access to health services, food, shelter, clean water and sanitation. However, the CMR in month 12 remains above double the baseline rate and so it should still be considered an emergency situation and further interventions are required to continue reducing the CMR.

Conclusion

In this section you have learnt about the ways in which armed conflict can influence health and key public health priorities in conflict-affected settings. You also learnt about the essential need for good epidemiological research in conflict-affected settings.

GENETICS

The emerging relevance of public health genetics

By its nature, our genome has influenced the health of the human population since the origins of mankind. Predisposition to, or causation of disease spanning all aetiologies and organ systems is, to varying degrees, mediated by our genes. Whilst the most potent effects of genetic variation on human health (Mendelian diseases such as Huntington's chorea or cystic fibrosis) were among the first to be recognized, these are rare and a comprehensive examination of the more subtle genetic influences on common diseases has taken decades to develop. In recent years, knowledge of the human genome sequence has permitted a much wider and more detailed investigation of genetic determinants of disease.

Here we illustrate some ways in which genetic information has influenced population health, and the wide range of opportunities for intervention to improve public health emerging from this rapidly developing area.

Learning objectives

By the end of this section you should be able to:

- understand key concepts in genetic epidemiology and how the unique features of the genome make it a valuable tool for investigating and influencing population health
- appreciate the importance of the human genome sequence to recent developments in genetic epidemiology and how it has facilitated research that has implications for population health
- understand the role of contemporary genetic research in identifying novel opportunities for improving population health and the potential for incorporating genetics into mainstream clinical care, therapeutics and prevention
- appreciate differences in the implications of genetics and genomics for the health of individuals and of populations

Key terms

Complex disease Conditions occurring frequently in the population, often with multi-factorial aetiologies (thus there is often an interplay between genes and environment). Examples are coronary heart disease and type II diabetes.

Genome The sum of all of an individual's genetic information.

Genome-wide association study (GWAS) Large epidemiological study comparing frequencies of SNPs across the entire genome between groups with, and without a particular phenotype (e.g. type II diabetes or a circulating biomarker, e.g. blood cholesterol).

Genotype The composition of an individual's DNA at a particular point (locus) or area of the genome.

Linkage study Epidemiological study designed to identify sequences of DNA shared by individuals with a common phenotype, often a disease.

Locus A defined point in the genome, which may be a single base (e.g. a SNP), a whole gene, a cluster of genes or another, larger area that may or may not contain any genes.

Mendelian disease Diseases where a single mutation gives rise to a major, deleterious phenotype and is inherited in a Mendelian pattern through a family. Examples include Duchenne muscular dystrophy and some familial hyperlipidaemias.

Mutation Usually refers to a larger change in genotype with more substantial phenotypic consequences, such as a large insertion or deletion of nucleotide bases.

Phenotype The physical, biological manifestation of a gene, which may be simple (e.g. the concentration of a protein in the bloodstream) or complex (a personality or behaviour). Phenotype is also determined by environment.

Polymorphism A small change in an individual's DNA sequence, usually limited to a few nucleotide bases, that may or may not influence the individual's phenotype: for example, a single nucleotide polymorphism (SNP).

Single nucleotide polymorphism (SNP) A change from one nucleotide base to another at a particular location in the genome; SNPs accounts for the majority of genetic variation between individuals.

The pre-genome era

A key question in investigating the genetic architecture of disease is the degree to which risk of developing that disease (e.g. coronary heart disease, CHD) or variation in a risk factor associated with it (e.g. blood pressure, BP) is determined by genetic variation. Much of the research has used studies of identical (monozygotic) twins, who have the same genes but, especially where separated at birth, may have been exposed to different environments. The resulting heritability estimates vary considerably between traits (e.g. 50 per cent for CHD, 80 per cent for height). Scientists have gone on to try to identify the individual genes underlying this genetic component of disease, with results being harnessed for interventions in population health, including (i) improved disease prediction; (ii) elucidating novel pathogenic pathways and uncovering potential therapeutic and preventive targets; (iii) so-called 'personalized' medicine.

Before today's technological capacity to genotype many thousands of genetic variants rapidly, genetic studies to investigate disease causation in humans were typically performed using either linkage or candidate gene studies. Linkage analysis involves the investigation of an individual with a disease (e.g. familial hypercholesterolaemia) and

their close relatives, both affected and unaffected by the disease, in order to identify DNA sequences shared by the affected individuals. Candidate gene studies investigate variation at a single genetic locus, typically in a case-control study design. However, this approach requires an *a priori* hypothesis that the genetic variant is implicated in disease, yielding several potential sources of error. First, genetic variation underpinning disease that is not already known – and which may yield important information about previously unknown aspects of a disease – will not be detected. Second, candidate gene studies are prone to bias in study design, which has led to many years of inconsistent results.

Identifying the majority of genetic determinants of disease required an approach for identifying variants without an *a priori* hypothesis. This hypothesis-free approach (the genome-wide association study, GWAS) performs multiple tests of association between several hundred thousand genotyped single nucleotide polymorphisms (SNPs) and disease status and employs statistical techniques to minimize false positive associations (Type 1 errors) likely to arise from such a large number of tests.

Sequencing the genome

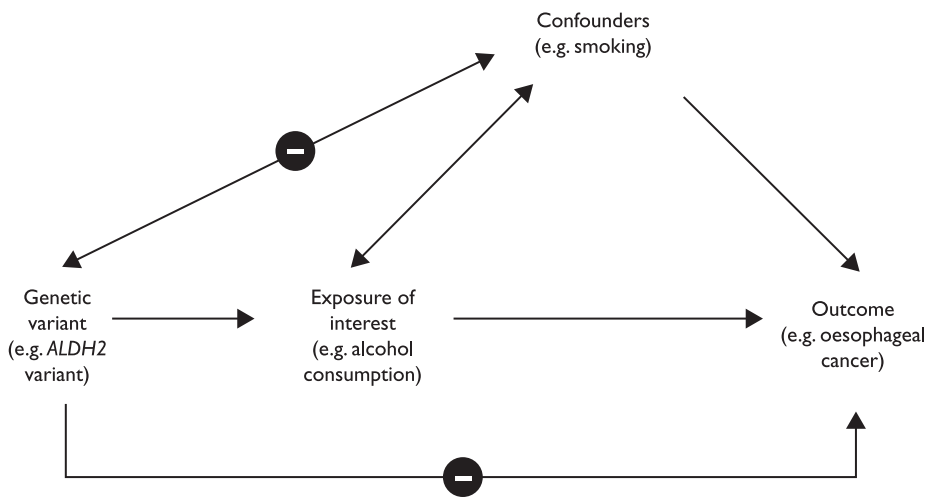
Completed in 2003, the sequencing of the entire human genome was a task of unprecedented size. Composed of over 3 billion base-pairs and containing around 25,000 genes, the genome took a large, international collaboration 13 years to construct and laid out for the first time the full blueprint of the human body, providing opportunities for insights into its function in health and disease. Since 2003, technological advances have been a major catalyst in exploiting and applying the genome sequence data. Identification of SNPs across the genome and their cataloguing by the International HapMap Project have permitted a large-scale, quantitative approach to assessing genetic associations with many diseases and other traits, notably in the form of genome-wide association studies (GWAS).

Although many new loci have emerged from the growth of GWAS (catalogued at www.genome.gov/gwastudies), the resulting biomedical revolution predicted by some has not fully materialized. Expectations of the potential of GWAS to provide groundbreaking insights into the pathophysiology of the world's great diseases have been disproportionately high and several features limit their direct translation into clinical use. SNPs identified by GWAS studies appear to account for only a small amount of the heritability of traits estimated from monozygotic twin studies and the inference has been drawn that we have yet to discover all of the genetic determinants of many diseases. However, given the influence of natural selection on the genome, whereby the most harmful genetic variants are least likely to persist across generations (unless their effects only manifest after reproductive age, for example, Huntington's disease), genetic variants causing large differences in disease susceptibility are unlikely to be found commonly in the population. The most likely variants to be found by a method such as GWAS are common ones with modest effects. Although this may be seen as a limitation of GWAS, SNPs of modest effect can have a substantial effect on population health.

The post-genome era

Much research using the genome sequence has examined genetic determinants, identified by GWAS studies, of pathophysiology, therapeutics and prevention in a range of disorders. Identification of variants associated with a complex disease such as type II diabetes has propelled investigation of the role of these genes in disease aetiology; the

translational potential of this investigation for population health is substantial. Mendelian randomization (MR) is a tool that exploits genetic information (often from GWAS) to this end, permitting causal inference that minimizes confounding and obviates reverse causation – two major limitations of traditional epidemiology (Figure 9.3). For example, using Mendelian randomization, the causal role of alcohol consumption in oesophageal cancer has been confirmed. Previous non-genetic observational studies were limited by confounding – since alcohol consumption is strongly correlated with smoking, and smoking is strongly associated with oesophageal cancer, it had been difficult to disentangle the role of alcohol using only non-genetic observational data. Furthermore, a randomized controlled trial of alcohol exposure would be difficult and perhaps unethical to implement. Using the *ALDH2* gene as an instrumental variable of alcohol exposure, because different variants of the gene influence an individual's tolerance, and thus consumption of alcohol, researchers were able to demonstrate that gene variants associated with higher alcohol intake were also associated with greater risk of oesophageal cancer, providing evidence of the causal role of alcohol that was free from confounding by tobacco.



In MR analysis, polymorphisms are used as proxies for a risk factor or exposure and their association with risk of a disease is estimated. Robust causal inference from MR analysis is used to evaluate the 'true' causal impact of established and emerginig risk factors in disease and to evaluate potential targets for prevention and therapy.

Figure 9.3 The use of Mendelian randomization in epidemiology

Activity 9.3

List three examples of potentially causal exposures in common disease that could be investigated through Mendelian randomization. List the benefits of MR over (i) observational (non-genetic) research and (ii) randomized controlled trials, which are both conventional sources of evidence for causality in such conditions.

Feedback

Large numbers of putative risk factors are frequently reported by the lay press for conditions such as cancers. Examples are easily found in national daily newspapers. You might have included the following examples, although there are many other possibilities:

(i) coffee and cancer
(ii) artificial sweeteners and heart disease
(iii) aluminium and Alzheimer's disease

Advantages of MR over

(i) observational studies
  - MR minimizes confounding.
  - MR eliminates reverse confounding.
  - The genetic 'exposure' in MR studies is very robustly characterized, whilst exposures in observational epidemiology may be more difficult to measure. For example, a gene associated with intolerance to a particular food may influence intake over a lifetime, providing a better measure than a food diary kept for a week several decades earlier.

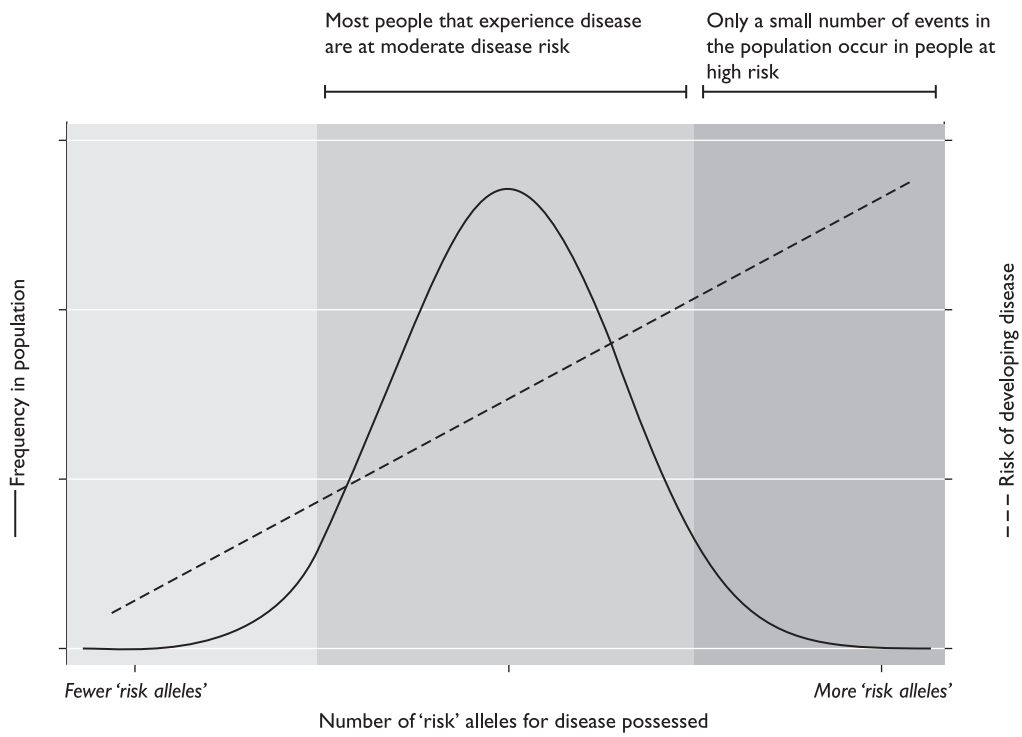
(ii) Randomized controlled trial
  - MR studies cost less and take less time than RCTs.
  - MR studies can easily be performed on a very large scale (i.e. not limited by the number of individuals recruited to a RCT).
  - Using a genetic 'exposure' may prevent exposure to a potential drug or therapy.
  - Large amounts of available data in MR studies allow investigation of a wide range of phenotypic associations with the genetic variant in question.
  - Genetic studies avoid ethical difficulties of exposing individuals to potentially harmful exposures.
  - Genetic variation reflects lifetime exposure to the phenotype altered by the genetic variant. In contrast, most randomized trials have durations of weeks or months, and, very rarely, years. Hence, through MR studies, differences in disease risk arising from lifetime exposure to phenotypes can be measured.

Predicting risk of common disease

Predicting which individuals in a population will develop a serious disease has long been a goal in individual and population health care, so as to be able to intervene to prevent cases from developing (primary prevention). Coronary heart disease (CHD) is a good candidate for prediction, since it is a common condition with a long preclinical phase, and well-established evidence for the causal roles of high blood pressure and elevated levels of circulating blood lipids. Moreover, effective behavioural and pharmacological interventions allow these risk factors to be modified early to reduce the risk of future disease.

At present, physicians calculate an individual's absolute risk of developing CHD within 10 years using models like the Framingham Risk Equation (Score) that take into account familiar risk factors such as smoking, cholesterol levels and age. The predicted risk from these models is used to decide whether, and how, to reduce a person's risk of developing CHD, based on agreed thresholds. However, these non-genetic risk equations are not perfect predictors of disease risk. It is well recognized that genes

influence risk of disease, thus it may be possible to incorporate genetic information into risk scores. Furthermore, genotype is becoming increasingly cheap to measure and, in comparison to non-genetic risk factors (e.g. smoking), it is fixed at conception. However, whilst genotype appears a panacea for prediction, its clinical translation has been hampered for several reasons. First, genetic variation accounts for only a small proportion of the variance of the risk of diseases like CHD, and the effects of commonly measured variants on disease risk are modest. Second, since the architecture of genetic variation differs between ethnic groups, a variant predicting disease in one group may be unusable in another. Furthermore, and most importantly, Geoffrey Rose's '**Prevention Paradox**' (Rose et al. 2008) extends to genetics – because risk **alleles** are inherited independently (under Mendel's law), most individuals with a common disease such as CHD are exposed to average, and not markedly unusual, risk alleles (Figure 9.4). Hence, setting a threshold for high-risk genotype (as one might in conventional risk prediction) to distinguish people likely to develop CHD from those that are not, is unlikely to be very helpful. Indeed, epidemiological studies that have incorporated genetic information into established risk equations have reported only very small or no improvement in predicting disease events. It is possible that emerging technologies will uncover rarer alleles that have greater effect estimates though their rarity



Since alleles are allocated randomly at conception, and thus risk associated with them is distributed approximately normally in a population, the majority of individuals in that population are at moderate risk. Most of the cases of disease therefore occur in individuals with average levels of risk alleles. This is analagous to Roses' 'prevention paradox'.

Figure 9.4 The prevention paradox analogy

may render population screening to detect them inefficient. Nonetheless, as more loci are associated with disease development, genetic information may gain utility when incorporated in disease prediction.

Activity 9.4

List the characteristics of an ideal predictive test for a chronic disease, such as CHD, that has a major impact on population health. Briefly, browse the literature available online to find any currently available or proposed tests that fit your criteria. What are the benefits and limitations of genetics for predicting diseases like CHD?

Feedback

Ideal features of a predictive test include the examples below. Many of these characteristics also apply to conventional screening tests.

- The test should be cost-effective to perform and must be able to be used on a large, population scale.
- The marker measured by the test should not change markedly with time.
- Measurement of the marker should not be operator-dependent (which can introduce error).
- The test should accurately designate individuals as high or low risk, or as cases or non-cases of the outcome in question (i.e. perfect discrimination – this is only rarely possible).
- A treatment for the condition in question should be available that is acceptable to patients, efficacious (i.e. prevents recurrence or occurence of disease), has no major adverse effects and is cost effective in the prevailing health care system.
- Treatment of those identified as 'at risk' reduces risk of disease to nil (NB this is unlikely at present for most genetic disorders).
- The test should be acceptable to the individual.
- The disease has a major impact on public health.
- The natural clinical course of the disease is well understood.

Pharmacogenomics

One of the most widely anticipated applications of genetic information is to predict response to treatment or prevention interventions – an example of 'personalized medicine'. A person's genotype may influence how they respond to therapeutic substances. You can identify whether your genes code for the fast of slow variants of the enzyme that breaks down drugs by acetylation in the liver by whether coffee at night keeps you awake (slow) or not (fast). Such a response could be either an intended effect (for example, the degree to which a statin reduces cholesterol) or an undesired, harmful effect. Pharmacogenetics is growing rapidly, with a surge in research articles published since the 1990s. However, only a few pharmacogenetic tests – predominantly in cancer medicine – are currently used, owing principally to an inadequate evidence base. Here we briefly contrast two pharmacogenetic tests that have shown different utility for clinical use: abacavir and *HLA-B*5701* and warfarin and *CYP2C9/VKORC1*.

Abacavir – a drug used in the treatment of HIV – is effective in controlling HIV infection but can cause a life-threatening hypersensitivity reaction in some individuals. A variant has been identified in the *HLA-B*5701* gene that predisposes individuals to this adverse reaction and consequently abacavir is not prescribed to people with the high-risk genotype in order to avoid this serious side effect – a pharmacogenetic success story.

Warfarin, a widely prescribed anticoagulant (blood-thinning agent) used in treating cardiovascular disease, presents a contrasting scenario. Warfarin is only effective in preventing harmful blood clots at a narrow range of doses, which is close to the range of drug levels that cause harm. Polymorphisms in the *CYP2C9* and *VKORC1* genes have been associated with the therapeutic response to warfarin. However, the studies concerned mostly investigated surrogates for warfarin efficacy rather than major clinical events associated with it and the real utility of genotype in predicting warfarin treatment response is, therefore, still uncertain.

Activity 9.5

What would be the key benefits to population health of an effective pharmacogenetic test?

Feedback

Key benefits include:

- substantial reductions in the incidence of adverse drug reactions;
- optimization of the intended effects of therapy; together, these will increase the therapeutic and preventive benefits of drug therapy, minimize the burden of disease caused by drugs, thus reducing costs to health care systems, maximizing cost-efficacy and optimizing the benefit of the intervention in the population;
- increased drug concordance (i.e. with knowledge that the drug prescription is 'personalized' to an individual, they may be more likely to take it as prescribed).

A substantial, and familiar, limitation of pharmacogenetics is that common genetic variants are unlikely to explain much of the variability in drug response in a population. Many non-genetic factors such as drug dosing, concomitant drug use and the degree to which patients take their medications as prescribed by their doctor (concordance) are likely to play a role. If we are to use genetic information to predict therapeutic response more accurately, it will probably need to be incorporated with non-genetic information. As with risk prediction, an ability to predict response to a preventive or therapeutic intervention has important consequences for the efficacy of prevention and treatment strategies in the population.

Population genomics vs personal genomics

It is important to distinguish between the applications of genetic research for individuals and for populations. Common genetic variants tend to have small effects, which are, consequently, only detectable in very large samples; indeed, it is not uncommon

for collaborative genetic studies to include hundreds of thousands of participants. The identification of a genetic variant associated with increased risk of myocardial infarction in such a study is likely to be of greater value in influencing the health of a whole population than of an individual since it may suggest a novel risk factor or an opportunity for pharmacological or behavioural prevention. Nonetheless, the vogue for personal genetic testing for such variants is growing. Marketed principally by commercial companies at prices that are falling rapidly, personalized genetic tests for a range of SNPs identified by GWAS studies for their association with many common, and several rarer conditions are offered to consumers. At present the clinical value of these tests to either the individual or the population has not been demonstrated, although future research may increase their utility in risk assessment and drug prescription. However, there is ongoing debate about the need to 'protect' the public from direct-to-consumer advertising of genetic tests, as their utility is not known.

The entry of genomics into public consciousness may, it has been suggested, have important implications for public health and health behaviours. As more associations between genes and common risk factors emerge, such as obesity, physical inactivity and smoking, and those findings become increasingly newsworthy, it is possible that obese individuals or smokers may begin to attribute risk factors increasingly to their genotype, believing them to be outside their control and therefore not amenable to modification for risk reduction. Important questions are therefore raised about appropriate marketing and publicity surrounding genetic information, particularly in an increasingly health-literate and information-driven society.

Genetics offers many powerful tools for investigating how common diseases develop and how they might be prevented or treated. While the field of population genomics is moving rapidly, it has yet to have a material impact on the population's health. The potential it holds, however, in risk assessment, risk factor identification and better targeting of prevention and treatment is great and is likely to eventually bear fruit.

Activity 9.6

Use the Internet to identify two direct-to-consumer genetic testing services. Consider the ethical implications of this type of marketing and service provision. List the advantages and disadvantages of direct-to-consumer genetic testing in general, paying particular attention to:

- benefits to individual health;
- benefits to public health;
- cost-effectiveness;
- viability for use in mainstream health care.

Feedback

Several companies, including 23andMe (https://www.23andme.com) and deCODEme provide such services, offering information on risk of around 95 diseases, and providing genetic information to predict drug response; the cost of testing your genome is currently approximately US$400. Table 9.1 illustrates the main advantages and disadvantages of direct-to-consumar testing.

Table 9.1 Advantages and disadvantages of direct-to-consumer genetic testing

	Advantages	*Disadvantages*
Individual health	• Knowledge of one's genome can aid motivation in adopting risk-reducing behaviours	• Genomic futility (rather than motivate lifestyle modification, individuals with 'bad' genes may decide such action is futile) • Most SNPs have small effect and therefore individually will not yield much information
Public health	• Can be incorporated into a prediction model • Individuals who pay for genetic testing may subsequently participate in research studies	• Widening the spectrum of inequality (at least initially, it is likely that only the well-off will pay for their genome sequence)
Cost-effectiveness	• Cost is relatively low, and decreasing	• Is the genetic information of sufficient clinical value to yield value-for-money?
Mainstream health care	• Rapid, low cost testing for a large number of genetic markers may, in the future, yield more information more quickly than conventional laboratory tests. • Patients may hold their genetic data indefinitely, compared to time-limited conventional test results.	• Superiority over conventional testing and prediction methods may take some time to be proven. • Health care workers will need extensive training in the application and interpretation of many genetic testing techniques.

Summary

This chapter introduced you to three of the newest areas of public health research and practice, which are doubtless going to become more prominent in the years to come. You are encouraged to keep up to date with the emerging evidence from each of these areas, regardless of where your public health career takes you, as a reminder of the ever-expanding role of public health and its importance to the future of mankind and of civilization.

References

Human rights

A. and Others v the United Kingdom Application no. 3455/05.

Abdulaziz, Cabales and Balkandali v UK [1985] Application nos. 9214/80; 9473/81; 9474/81.

Boggio A, Zignol M, Jaramillo E et al. (2008) Limitations on human rights: are they justifiable to reduce the burden of TB in the Era of MDR and XDR-TB? **Health and Human Rights 10**(1): 121–6.

Brown v Stott [2001] 2 WLR 817.

Dombo Beheer BV v Netherlands [1993] 18 EHRR 213.

Enhorn v Sweden Application no. 56529/00.
Gostin L and Berkman B (2007) Pandemic influenza: ethics, law, and the public's health. *Administrative Law Review* **59**: 121.
Health and Safety (2009) *Health and Safety Laboratory Annual Report & Accounts 2008/2009*.
Home Affairs Committee Publications (2008) 'A Surveillance Society'. Fifth Report of Session 2007–2008 8 June.
Jalloh v Germany Application no. 54810/00.
Labita v Italy Application no. 26772/95.
Martin R (2006) The exercise of Public Health Powers in cases of infectious disease: human rights implications. *Medical Law Review* **14**(1): 132–43.
Martin R, Conseil A, Longstaff A et al. (2010) Pandemic influenza control in Europe and the constraints resulting from incoherent public health laws. *BMC Public Health* **10**: 532.
Megyeri v Germany [1992] 15 EHRR 584.
Murphy T and Whitty N (2009) Is human rights prepared? Risk, rights and public health emergencies. *Medical Law Review* **17**(2): 219–44.
Nuffield Council on Bio-Ethics (2007) *Public Health: Ethical Issue*s. London: Nuffield Council on Bio-Ethics.
Re AK [2001] 1 FLR 129.
Rothstein M, Alcalde M, Elster R et al. (2003) Quarantine and isolation: lessons learned from SARS. Unpublished report to the Centers for Disease Control and Prevention, November 2003. (available at http://www.louisville.edu/medschool/ibhpl/../../../fig/pdf/SARS REPORT.pdf, last visited
World Health Organization (2007) *Ethical Considerations in Developing a Public Health Response to Pandemic Influenza*. Geneva: World Health Organization.

Armed conflict

Bruderlein C and Leaning J (1999) New challenges for humanitarian protection. *BMJ* **319**: 430–5.
Coghlan B, Ngoy P, Mulumba F et al. (2007) *Mortality in the Democratic Republic of Congo: An Ongoing Crisis*. New York/Melbourne: International Rescue Committee/Burnett Institute.
Human Security Centre (2005) *Human Security Report 2005: War and Peace in the 21st Century*. Vancouver: University of British Columbia.
IASC (2009) *Health Cluster Guide: A Practical Guide for Country-level Implementation of the Health Cluster*. Geneva: Inter Agency Standing Committee/World Health Organization.
Miller KE and Rasmussen A (2010) War exposure, daily stressors, and mental health in conflict and post-conflict settings: bridging the divide between trauma-focused and psychosocial frameworks. *Soc Sci Med* **70**: 7–16.
Murray CJ, King G, Lopez AD et al. (2002) Armed conflict as a public health problem. *BMJ* **324**: 346–9.
Prudhorn C and Spiegel PB (2007) A review of methodology and analysis of nutrition and mortality surveys conducted in humanitarian emergencies from October 1993 to April 2004. *Emerg Themes Epidemiol* **4**: 10.
Roberts L and Hofmann CA (2004) Assessing the impact of humanitarian assistance in the health sector. *Emerg Themes Epidemiol* **1**: 3.
Spiegel PB, Checchi F, Colombo S and Paik E (2010) Health-care needs of people affected by conflict: future trends and changing frameworks. *Lancet* **375**: 341–5.
Stewart F (2002) Root causes of violent conflict in developing countries. *BMJ* **324**: 342–5.
United Nations (2005) *Humanitarian Response Review*. Geneva: United Nations.
Working Group for Mortality Estimation in Emergencies (2007) Wanted: studies on mortality estimation methods for humanitarian emergencies, suggestions for future research. *Emerg Themes Epidemiol* **4**: 9.

Genetics

Rose G, Khaw K-T and Marmot M (2008) *Rose's Strategy of Preventive Medicine*. Oxford: Oxford University Press.

Further reading

Checchi F and Roberts L (2005) *Interpreting and Using Mortality Data in Humanitarian Emergencies: a Primer for Non-epidemiologists*. London: Overseas Development Institute.

Checchi F, Gayer, M, Freeman Grais R and Mills E (2007) *Public Health in Crisis-affected Populations: A Practical Guide for Decision-makers*. London: Overseas Development Institute.

European Convention on Human Rights [1950, as updated 2010] Convention for the Protection of Human Rights and Fundamental Freedoms (accessed at www.echr.coe.int/NR/rdonlyres/D5CC24A7-DC13-4318-B457-5C9014916D7A/0/ENG_CONV.pdf)

Hingorani A and Humphries S (2005) Nature's randomised trials. *Lancet* **3;366** (9501): 1906–8.

Hingorani AD, Shah T, Kumari M, Sofat R and Smeeth L. (2010) Translating genomics into improved healthcare. *BMJ* **341**: c5945.

Holmes MV, Shah T, Vickery C et al. (2009) Fulfilling the promise of personalized medicine? Systematic review and field synopsis of pharmacogenetic studies. *PLoS One* **4**(12): e7960.

Human Security Centre (2005) *Human Security Report 2005: War and Peace in the 21st Century*. Vancouver: University of British Columbia.

Leaning J, Briggs S and Chen L (eds). (1999) *Humanitarian Crises: The Medical and Public Health Response*. Cambridge, MA: Harvard University Press.

McCarthy MI, Abecasis GR, Cardon LR et al. (2008) Genome-wide association studies for complex traits: consensus, uncertainty and challenges. *Nature reviews* **9**(5): 356–69.

Online Resource: The use of epidemiological tools in conflict-affected populations: open-access educational resources for policy-makers (http://conflict.lshtm.ac.uk/page_02.htm).

Pearson TA and Manolio TA (2008) How to interpret at Genome-wide Association Study. *JAMA* **299**(11): 1335–44.

Rose G (1985) Sick individuals and sick populations. *International Journal of Epidemiology* **14**(1): 32–8.

SMART (2006) Measuring Mortality, Nutritional Status, and Food Security in Crisis Situations: SMART Methodology (Version 1). Standardised Monitoring and Assessment of Relief and Transitions Programme (SMART) (available at www.smartindicators.org).