Chapter 10
Particularisation to an Individual

Abstract In Sect. 7.1, we discussed extrapolation from a study population to a target population. In this chapter, we treat particularisation from a study population to one of its members. In both cases, evidence of similarity of mechanisms plays a crucial role.

Inference from an effectiveness claim involving a whole population to effectiveness in one of its members is of central importance in medical diagnosis, prognosis, and treatment. This mode of inference is often called *direct inference* (Kyburg et al. 2001; Wallmann 2017; Wallmann and Williamson 2017).

The case we discuss here is very simple. Evidence of effectiveness in only one population to which the individual belongs is available. The case in which such evidence for several such populations is available is much more complicated and we will not deal with it here. If one has established effectiveness in a population, then one has also established that there is a mechanism operating that connects the putative cause and effect. Now, the population may not be entirely homogeneous with respect to this mechanism: some individuals will exemplify the mechanism while others may not. One way to establish that mechanisms in the population are applicable to a particular individual is by assessing how homogeneous the population is with respect to the mechanism of action. Inference from a homogeneous population to individuals is more likely to succeed, because most individuals will exhibit the mechanism responsible for causation in the population.

V.-P. Parkkinen et al., *Evaluating Evidence of Mechanisms in Medicine*,
SpringerBriefs in Philosophy, https://doi.org/10.1007/978-3-319-94610-8_10

However, in most cases there will be subpopulations for which effectiveness does not hold. There may be several reasons for this kind of *exceptionality*. Firstly, in some such subpopulations the mechanism responsible for effectiveness in the whole population simply does not operate. For instance, while drinking considerable amounts of milk is normally safe, subpopulations with lactase deficiency should drink only small amounts of milk. Considering whether crucial features of the mechanism responsible for effectiveness are present in the particular individual can therefore increase certainty about whether the causal claim is applicable to the individual. Secondly, counteracting mechanisms may operate in some subpopulations. For instance, exercising is normally beneficial for preventing stroke by lowering blood cholesterol, but smoking may counteract these beneficial effects by raising blood cholesterol. With this in mind, the following questions can assist the evaluation of evidence of mechanisms for direct inference:

Particularisation to an individual

What is the status of the claim that the mechanism of action in the population is responsible for effectiveness in the individual? Consider the following questions; can both be answered in the affirmative?

Exemplification. Are the crucial features of the mechanism of action in the population preserved in the individual?

Masking. Are there further mechanisms operating in the individual that counteract the mechanism operating in the population?

When ruling out masking, one needs to pay attention to co-morbidities, social mechanisms, genetic susceptibility and many more. For instance, when assessing whether a certain patient with breast cancer will benefit from a treatment by trastuzumab, one needs to test for HER2. HER2 if overexpressed, increases cell growth over its normal limits. Trastuzumab blocks the effects of overexpression of HER2. If the patient does not overexpress HER2, the drug will not work for her (Bange et al. 2001). Note that if exemplification has been established and masking ruled out, it is possible to particularise a population-level causal claim to an individual without the need for the population to be homogeneous with respect to the mechanism of action. On the other hand, a high degree of homogeneity provides *prima facie* evidence for exemplification and against masking, and thereby supports particularisation.

Example. Lactose intolerance

The world population is not very homogeneous with the reaction to milk intake. About 65% of people are lactose intolerant at some point in their lives. However, in different populations there are differing frequencies of lactose intolerant members. Only 5% of Northern Europeans and more than 90% in some populations in East Asia are lactose intolerant, for instance (NIH 2017). This is because in East Asia lactase deficiency is quite common, while it is quite unusual in Northern Europe. Now, establishing that the patient has no lactase deficiency may be sufficient to establish that she may safely drink milk at high doses. However, even if ruling out lactase deficiency is not possible, establishing homogeneity in a relevant subpopulation may provide grounds for provisionally establishing causality in its members. If, for instance, a patient is North European, this may make it quite plausible that she can drink milk safely. If, on the other hand, a patient is East Asian, this may make it quite plausible that she cannot drink milk safely.

Example. The Shonubi case

Nigerian drug-mule Shonubi was caught on his eighth trip from Nigeria on the JFK airport carrying heroin in his digestive tract (Colyvan et al. 2001). For sentencing purposes, it was assessed whether the total amount of drugs smuggled on his seven prior trips was greater than a specific amount M. There was statistical data available for the amount of drugs carried by balloon-swallowing heroin smugglers from Nigeria. Moreover, there is a social mechanism involving these smugglers that helps to explain the amount of drugs they smuggle: the local drug organisation trains the mules in balloon-swallowing for several weeks and threatens people who refuse with violence (Izenman 2000).

It seems best to estimate the amount of drugs smuggled by Shonubi on his seven prior trips by the average amount smuggled by balloon-swallowing heroin smugglers from Nigeria. There is high quality mechanistic evidence for application to Shonubi available. Firstly, the mechanism that connects balloon-swallowing heroin smugglers from Nigeria to the quantity of drugs smuggled does apply to Shonubi. The local organisation did indeed train Shonubi by similar methods to those applied to other drug mules, for instance. Secondly, it seems that, for all we know, there is no counteracting mechanism that makes Shonubi an exceptional drug mule. Note that the trip on which he was caught was already his eighth. Thirdly, although there is some variability with respect to the amount smuggled within balloon-swallowing heroin smugglers from Nigeria, virtually all drug mules smuggled more than M grams. Hence, the balloon-swallowing heroin smugglers from Nigeria is arguably a sufficiently homogeneous population.

Table 10.1 Determining the status of the causal claim in the individual given the status of the causal claim in the population and the status of the claim that the mechanism of action in individual and population is similar

		Similarity of mechanism in individual and population				
		Established	Provisionally established	Other cases	Provisionally ruled out	Ruled out
Causation in population	Established	Established	Provisionally established	Arguable	Speculative	Speculative
	Provisionally established	Provisionally established	Arguable	Speculative	Speculative	Speculative
	Arguable	Arguable	Speculative	Speculative	Speculative	Speculative
	Speculative	Speculative	Speculative	Speculative	Speculative	Speculative

To obtain the status of effectiveness for a particular individual, one can combine the status of the effectiveness claim in the population with the status of the mechanistic similarity claim (i.e., the claim that there is exemplification and no masking), as in Table 10.1.

A few remarks shed some light on this table.

First, observe that effectiveness in an individual can almost never be ruled out by the fact that the mechanism responsible for effectiveness in the population is not present in the individual. After all, the individual may exemplify an alternative mechanism of action. I.e., the individual may be a member of a different population, which also exhibits effectiveness but with a different mechanism of action, and this alternative mechanism is present in the individual.

Second, particularisation is a special case of extrapolation. When particularised, a causal claim is extrapolated to the subpopulation of population-members that share all the relevant properties of the individual. This target subpopulation will typically be small, but it remains a subpopulation. Suppose, for instance, we are interested in whether a 30 year old Norwegian farmer will develop an adverse reaction when drinking milk. 95% of individuals in Northern Europe show no such reaction. Here, the target population relevant to particularisation may contain only the farmer in question, while the study population is the class of all Northern Europeans.

Third, there are nevertheless some differences between the evaluation of external validity and the evaluation of particularisation to an individual. Particularisation to the individual is more likely to succeed than is extrapolation from a study population to a target population that is not a subpopulation of the study population. This is because causality established in a population is more informative about individuals in this population than about individuals in different populations. For instance, if the population is very homogeneous, then particularisation to the individual is likely to succeed while extrapolation to other populations may well fail. This fact is reflected in the above tables. Consider the case where no studies are available which involve the particular individual. If mechanistic similarity is provisionally

established and effectiveness is established in the population, the causal claim is *provisionally established* for the individual, according to the particularisation table. In the case of external validity, if mechanistic similarity between the study and target populations is provisionally established and effectiveness is established in the study population, effectiveness in the target population is only *arguable* (see Sect. 7.2). It is worth emphasizing here though that particularisation to an individual is still an extrapolation, and should still be considered fallible.

Note finally that, in contrast to the method of evaluating external validity in Sect. 7.2, in the present chapter we treat the case where there is no evidence for causation obtained by studies directly on the target population.

References

Bange, J., Zwick, E., & Ullrich, A. (2001). Molecular targets for breast cancer therapy and prevention. *Nature medicine*, *7*(5), 548–552.

Colyvan, M., Regan, H. M., & Ferson, S. (2001). Is it a crime to belong to a reference class? *Journal of Political Philosophy*, *9*(2), 168–181.

Izenman, A. J. (2000). Assessing the statistical evidence in the Shonubi case. In J. Gastwith (Ed.), *Statistical science in the courtroom* (pp. 415–443). New York: Springer.

Kyburg, H., & Teng, C. M. (2001). *The Theory of probability*. Cambridge: Cambridge University Press.

NIH (2017). Lactose intolerance: US national library of medicine, genetics home reference. https://ghr.nlm.nih.gov/condition/lactose-intolerance.

Wallmann, C., & Williamson, J. (2017). Four approaches to the reference class problem. In G. Hofer-Szabo & L. Wroński (Eds.), *Making it formally explicit: Probability, causality, and determinism*. Dordrecht: Springer.

Wallmann, C. (2017). A Bayesian solution to the conflict of narrowness and precision in direct inference. *Journal for General Philosophy of Science*, *48*, 485–500.