SOCIAL SCIENCE

The mathematics of murder

A mathematical model of gun ownership has been developed that clarifies the debate on gun control and tentatively suggests that firearms restrictions may reduce the homicide rate.

ADELINE LO & JAMES H. FOWLER

The mass killing of 20 children and 6 adults on 14 December 2012 at Sandy Hook Elementary School in Newtown, Connecticut (Fig. 1), has revived an enduring controversy about gun control in the United States. Gun-control advocates believe that widespread gun ownership increases the rate of gun-related crime and homicide, whereas critics argue that gun availability actually decreases gun violence because potential assailants are less likely to commit such crimes if they believe citizens are armed. But who is right? In an article published in *PLoS ONE*, Wodarz and Komarova[1] describe an elegant and highly parsimonious mathematical model designed to answer exactly this question. And, in an extremely cautious way, they suggest that more guns make things worse.

DAMIAN DOVARGANES/AP/PRESS ASSOCIATION IMAGES

Figure 1 | A prayer vigil for the victims of the Sandy Hook shooting.

The scientific literature suggests that gun homicides are influenced by various interwoven factors, including the rate of legal and illegal gun possession, the national prevalence of armed and unarmed attacks, the likelihood of fatalities in such attacks, and the quality and quantity of general law enforcement[2–5]. Gun-control policy is clearly only one key variable in a complex social system. But work on the issue is typically conducted by scholars who collect data on types of gun-control policy and numbers of gun homicides, and look for correlations while controlling for certain important variables — such as whether the locations of the homicides are rural or urban, or whether it is easy to obtain arms illegally.

The problem is that many of these correlations are difficult to interpret. If gun deaths are higher in states with stricter gun-control laws, is this because gun restrictions cause higher crime or because politicians react to higher crime by enacting more restrictions? It is with this difficulty in mind that Wodarz and Komarova have created their formal model of gun ownership.

The modelling of complex social phenomena is not new. As early as 1974, the economist Gary Becker took a supply-and-demand approach to the 'production' of crime and punishment, using his model to show how crime might be minimized with various public and private policies that make criminal behaviours 'costly'[6]. But Becker's analysis did not explicitly tackle the thorny problem of gun control, and the scholars who followed also tended to focus more on abstract models.

By contrast, Wodarz and Komarova's model is explicitly designed to address gun-control policies and their effects. At the core of the model is the rate of gun ownership. Strict laws might lower the rate and permissive laws might increase it, but the mechanism itself does not matter — the goal of the model is to clarify what assumptions are necessary to measure the effect of overall gun ownership on the rate of firearms-related homicides.

Wodarz and Komarova assume that there is a positive relationship between the number of gun owners and the number of potential gun-related attackers. This is reasonable: if there are no guns, there will be no attacks with guns. But the authors also assume that there is a negative relationship between the rate of gun ownership and the likelihood that a gun-wielding attacker actually uses his or her weapon. This is because non-criminals may own guns, too. If a potential victim possesses a gun, a potential attacker might think twice about attacking.

A few other factors are also included in the model, such as the risk of dying in a gun attack, and the availability and take-up of illegal arms in the face of varying levels of gun control. But the key insight is that there are essentially two perfect worlds, one in which no one owns a gun (meaning no one is able to attack) and one in which everyone owns a gun (meaning no one is willing to attack). In between, we get the worst of both worlds because some criminals have guns and they choose to use them. This means that the effect of gun availability is crucially dependent on where we sit between these two worlds.

This is social science at its very best. Rather than crafting yet another highly abstract formal model, Wodarz and Komarova create a model that is directly relevant to an extremely important societal issue. And rather than overly emphasizing the results of their model, they conduct an exercise in caution, highlighting the importance of grounding models in sound and accurate assumptions — because a model is only as good as the assumptions from which it proceeds.

Using their best guess about values estimated or implied from the existing literature, Wodarz and Komarova show that their model implies that stricter laws are the best way to reduce gun deaths. But they are quick to point out that there are some assumptions that are vital to the model for which we have no reliable measurement. So although the model does lend support to arguments in favour of gun

control, it is fair to say that the jury is still out.

The most obvious contribution Wodarz and Komarova make towards the study of gun-control policies is in highlighting key parameters that require further empirical investigation. Collaborative efforts between sociologists, political scientists and other scholars can now move forward in an objective way to advance our understanding of gun-control policies by focusing on the assumed values that are currently less well measured. Armed with these, the model might help us to resolve — perhaps once and for all — the debate on gun ownership. ■

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BIOLOGICAL TECHNIQUES

An embryonic view of tumour development

A genome-wide screen of developing mouse embryos, performed using RNA-interference techniques, finds new suspects in skin cancer. But some factors seem to have opposing roles in cancer and normal-tissue maintenance. SEE ARTICLE P.185

PAWEL J. SCHWEIGER & KIM B. JENSEN

Gene function has traditionally been studied using organisms in which individual genes have been either eliminated or artificially expressed in excess. The discovery in the 1990s of RNA interference (RNAi) — the process by which small RNA molecules specifically inhibit gene expression by binding to and destroying messenger RNAs — established a new framework for investigating gene function. Until now, however, genome-wide screens using RNAi techniques have been limited mainly to cultured cells, and so cannot take into account the complex cellular interactions that govern normal tissue behaviour or that lead to the development of diseases such as cancer. On page 185 of this issue, Beronja *et al.*[1] describe the first *in vivo* genome-wide RNAi screen, which was performed in mouse embryos with the aim of identifying genes involved in the development of non-melanoma skin cancer*.

Non-melanoma skin cancer — one of the most prevalent tumour types — occurs in the epidermal cells that make up the outer layer of the skin. In the developing embryo, the epidermis forms during mid-gestation from the surface ectoderm and gradually matures into an impermeable barrier with associated structures, such as hair follicles. Early studies of non-melanoma skin cancer identified members of the *Ras* gene family as potent drivers of the disease[2], but a lack of techniques for studying gene activity at the single-cell level[3] has meant that little is known about other genes involved in the maintenance of these, and other, tumours.

The team presenting the current paper previously described an approach[4] for achieving RNAi in the developing epidermis. In this technique, cells in the surface ectoderm of mouse embryos are transduced by means of lentiviral vectors carrying short hairpin RNAs (shRNAs), which are cleaved to RNAi sequences once the shRNAs are expressed in a cell. The researchers have now extended this approach to screen the entire genome of the epidermal cells, using a library of shRNA molecules designed to interfere with every mRNA in mouse cells. Because cells in the developing epidermis divide in an extremely reproducible manner, any RNAi sequence that alters the normal rate of proliferation can be identified as either enriched or depleted in a pool of RNAi sequences. Thus, by comparing the relative abundance of shRNA sequences in the embryos' genomic DNA at the time of RNAi induction (embryonic day 9.5) and nine days later, the authors were able to identify genes that, when inhibited, cause proliferative advantages or disadvantages.

Beronja and colleagues conducted two such screens: one to assess genes involved in normal epidermal development and the other to assess genes implicated in the development of tumours induced by enhanced expression of *Hras1*. The top candidate gene to emerge in both screens, but with an opposite effect on proliferation, was that encoding the β-catenin protein. This finding is in line with previous reports[5,6] showing that β-catenin is required for the development of non-melanoma skin cancer and that loss of this protein specifically in the epidermis causes hyperproliferation.

β-Catenin is an integral component of adherens junctions — protein complexes that form between cells in epithelial and endothelial tissues — and is therefore key to

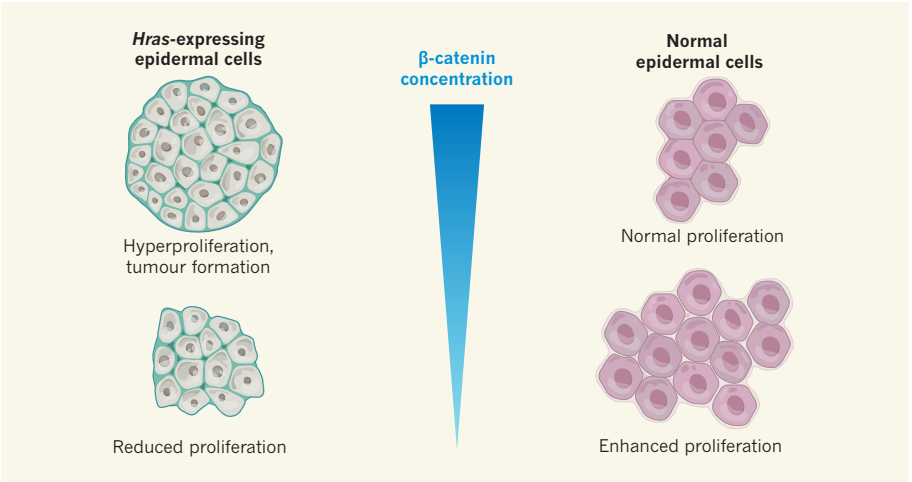

Figure 1 | Role of β-catenin in normal and cancer-prone skin cells. Beronja and colleagues' *in vivo* whole-genome RNA interference (RNAi) screen[1] of epidermal cells expressing the oncogene *Hras* identified β-catenin as essential for maintaining cellular hyperproliferation in this model of cancer; inhibiting expression of the protein led to decreased proliferation. The authors infer that this effect is mediated through β-catenin's involvement in the Wnt signalling pathway. By contrast, the same screen in normal epidermal cells revealed that RNAi-induced inhibition of β-catenin led to enhanced proliferation in such cells. Follow-up experiments suggest that this effect results from β-catenin's role in maintaining the adherens-junction protein complexes between epidermal cells; disruption of these junctions impairs the contact-inhibition processes that keep cell proliferation in check.

*This article and the paper under discussion[1] were published online on 14 August 2013.