mutations that spread throughout normal tissues might even protect against cancer[9,10].

Li *et al.* report that a notable fraction of tissue samples across different sites, such as the oesophagus and the rectum, contained three or more mutations thought to drive cancer – although it is not clear whether these driver mutations were present together in the same cell. This is consistent with previous work demonstrating the presence of up to three driver mutations in normal airway cells from people who smoke[11]. Three driver mutations is uncomfortably close to the average four or five that are found in cancers[12], particularly given the limited sampling of normal tissue so far. Indeed, if cells with three driver mutations can easily be found in a small tissue sample, cells with four or five drivers probably exist in that tissue as well – without necessarily giving rise to cancer.

These new insights invite us to reconsider how we genetically define cancer. If having multiple driver mutations does not make a cancer, what does? Is a particular, tissue-specific combination of mutations required? Or is the presence of such mutations required in addition to permissive environmental conditions? Chromosomal abnormalities have often been cited as being specific to cancer cells, but both Li *et al.* and Park *et al.* report that normal cells in some tissues contain chromosomal changes as well.

It is likely that full clarification will be possible only with the generation of a 'normal-tissue genome atlas', in which the mutational composition of different tissues is carefully mapped across many individuals as a function of age, medical history and lifestyle. Only then can we hope to answer the foundational question about the genetic definition of cancer with some rigour.

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1. Park, S. *et al. Nature* **597**, 393–397 (2021).
2. Coorens, T H. H. *et al. Nature* **597**, 387–392 (2021).
3. Li, R. *et al. Nature* **397**, 398–403 (2021).
4. Moore, L. *et al. Nature* **597**, 381–386 (2021).
5. Bizzotto, S. *et al. Science* **371**, 1249–1253 (2021).
6. Ju, Y. S. *et al. Nature* **543**, 714–718 (2017).
7. Spencer Chapman, M. *et al. Nature* **595**, 85–90 (2021).
8. Martincorena, I. *et al. Science* **348**, 880–886 (2015).
9. Zhu, M., Lu, T., Yopp, A. C., Wang, T. & Zhu, H. *Cell* **177**, 608–621 (2019).
10. Colom, B. *et al.* Preprint at bioRxiv https://doi.org/10.1101/2021.06.25.449880 (2021).
11. Yoshida, K. *et al. Nature* **578**, 266–272 (2020).
12. Campbell, P. J. *et al. Nature* **578**, 82–93 (2020).

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Human behaviour

Text-message nudges encourage vaccination

Mitesh S. Patel

A field trial shows that text-message 'nudges' encourage people to get vaccinated against COVID-19. To be effective, nudge approaches such as this must combine three aspects: they must prompt, enable and motivate behaviour. **See p.404**

Nudges are subtle changes to the way in which choices are offered or information is framed that can have an outsize impact on behaviour. As the supply of COVID-19 vaccines increases around the world, many nations are faced with the challenge of how best to encourage people to get vaccinated. Although various campaigns to do this have been implemented, little is known about which types of approach work and which do not. On page 404, Dai *et al.*[1] present findings from a large field experiment that reveal new insights into the three key elements that must be combined in strategies aimed at increasing the likelihood that people will get their vaccination against COVID-19.

Dai and colleagues set out to determine whether a single text message from a person's health-care provider could change COVID-19 vaccination rates. In addition, they tested whether vaccination rates differed when recipients were told the vaccine was already theirs – that is, when they had psychological ownership of the vaccine. These text messages included phrases such as the vaccine has "just been made available to you", and encouraged recipients to "claim your dose". Such an approach has been used successfully to nudge influenza vaccination[2], but has not previously been tested for vaccination against COVID-19.

In the main clinical trial, more than 93,000 individuals in a large health-care system who had not organized an appointment by the first weekday after an initial invitation were randomly placed in a control group or a test group and then followed for 4 weeks. These individuals were among the first wave of people eligible for vaccinations (owing to age or pre-existing medical conditions). Of the control-group individuals who did not receive any text-message reminders, 13.9% got

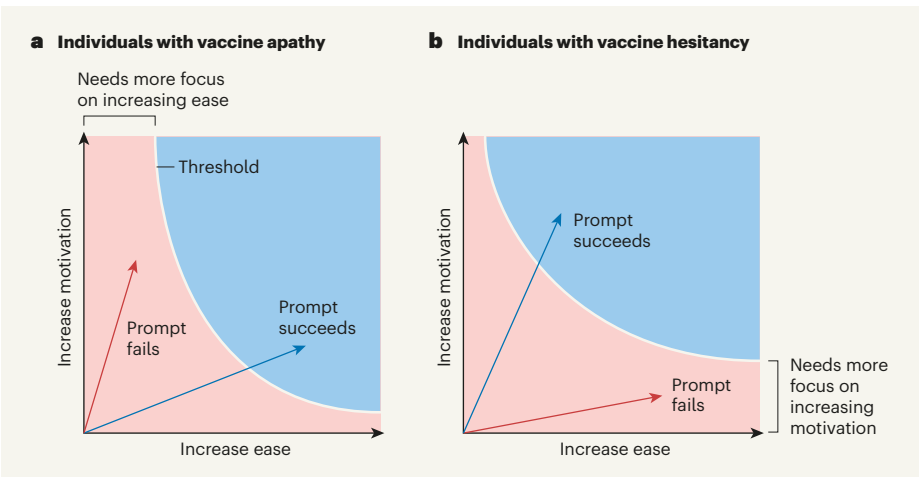

Figure 1 | Nudges to encourage vaccination uptake will depend on individuals' attitudes. Nudges are ways in which information is presented or choices offered that drive behavioural change. Dai *et al.*[1] report the effects of sending individuals text-message reminders to encourage them to book an appointment to receive their vaccine against COVID-19. According to the Fogg Behavior Model, nudges should combine three aspects for success: they should prompt an action, increase motivation and make action easier. But nudges need to be tailored to individuals with different attitudes. **a**, If individuals are apathetic about getting a vaccine, prompting nudges will need to focus more on making it easier to arrange an appointment. Dai *et al.* achieved this by including a link to the booking website in the text messages. **b**, If individuals are more hesitant about getting vaccinated, such nudges will need to focus on increasing motivation.

vaccinated. Among individuals who received a simple text-message reminder with a link to a website where they could schedule a COVID-19 vaccine appointment, the vaccination rate increased to 17.1%. Adding language to induce psychological ownership further increased vaccination rates to 18.2%.

Before this clinical trial, the investigators conducted an online experiment with individuals participating as hypothetical patients. They found that asking individuals to watch a two-minute educational video on the vaccine led to slightly higher stated intentions to get vaccinated than were seen for individuals who had not watched the video. However, unexpectedly, when the authors added a link to this video in the text-messaging experiment, it led to slightly lower vaccination rates than did sending text messages alone.

These conflicting results might be explained by some key differences between the two studies. For example, the online group of hypothetical patients had a mean age of 37 years, and 100% were required to watch the video, whereas individuals in the clinical trial had a mean age of 73 years and only 21% watched the video. Although the precise reasons for the inconsistent effect of the video are unclear, these findings demonstrate the value of conducting rigorous testing of approaches in real-world groups of individuals, rather than hypothetical ones[3].

So, how can we apply these findings to future vaccination efforts? According to the Fogg Behavior Model (see behaviormodel.org), three key aspects need to be combined to successfully nudge behaviour: ability to act, motivation and a prompt. Moreover, the best nudging approaches to use will vary depending on individuals' attitudes towards the COVID-19 vaccine (Fig. 1). For example, individuals who are hesitant about the vaccination often have a strong emotional response to the risks and benefits of the vaccine, whereas those who are apathetic about it have weakly held attitudes and often have not invested much effort in considering vaccination[4]. Appropriately tailoring interventions to the population of interest is likely to lead to higher success than is a one-size-fits-all approach.

First, interventions should aim to make the intended behaviour easier. In this case, the text messages provided a link to schedule an appointment. This made setting up vaccination quick and convenient. This aspect of the intervention boosted vaccination rates the most and probably addressed barriers among people with vaccine apathy who were unlikely to go out of their way to look up scheduling information (Fig. 1a).

Second, interventions should focus on increasing an individual's motivation for the intended behaviour. The text-message reminders that invoked psychological ownership probably boosted vaccination by increasing motivation. However, compared with the simple text-with-link intervention, the increase in vaccine uptake following this intervention was relatively small (about 1 percentage point). The investigators also tried sending a second text-message reminder after another eight days to those who had still not scheduled an appointment. Individuals in this group were probably more hesitant than were those who had already set up their vaccine appointment, and that second reminder did not change overall vaccination rates compared with the control group. Individuals with vaccine hesitancy thus might often require further approaches to increase motivation (Fig. 1b), either through other types of nudge or different approaches, such as incentives[5,6].

Third, interventions should prompt action. Sending a text message to consider vaccination forces a person to think about the decision 'now', rather than relying on them to remember to think about it on their own. The best channel for sending the notification will probably vary for different groups of people. For example, someone who is not tech-savvy might respond better to a phone call.

Although even the best text-messaging approach in the clinical trial increased vaccination by only a few percentage points, one must keep in mind that these approaches were very low cost and, if applied on a broader scale, could lead to millions of extra vaccinations that might otherwise have been delayed or not occurred at all. Nudges can be an effective tool for changing an individual's behaviour, but they must be carefully designed. As health systems, public-health agencies and other stakeholders look for methods to increase COVID-19 vaccination rates, they should consider ways to implement nudges that make getting a vaccine easier, that increase motivation and that prompt action.

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1. Dai, H. *et al. Nature* **597**, 404–409 (2021).
2. Milkman, K. L. *et al. Proc. Natl Acad. Sci. USA* **118**, e2101165118 (2021).
3. Patel, M. *Nature* **590**, 185 (2021).
4. Wood, S. & Schulman, K. *JAMA* **325**, 2435–2436 (2021).
5. Patel, M. S. *Nature Hum. Behav.* **2**, 720–721 (2018).
6. Volpp, K. G. & Cannuscio, C. C. *N. Engl. J. Med.* **385**, e1 (2021).

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From the archive

A look at psychology in industrial workplaces, and a mystery surrounding fish in a Swiss lake.

100 years ago

An Introduction to the Psychological Problems of Industry. By F. Watts — The fact that our industrial system has a human, as well as a material, side has been brought prominently into view in recent times, and it is beginning to be recognised clearly that no perfect or satisfactory industrial system can be attained along the road of purely material progress. Hence industrialists all over the world who have hitherto had their eyes turned wholly on physical science as the main source from which contributions to industrial progress were to be expected are now turning their eyes towards the sister science of psychology so long neglected and misunderstood ... Mr Watts has made a serious and, on the whole, very successful attempt to apply the newer psychology of human tendencies and emotions — the psychology of ... Trotter, Freud, and Jung — to the conditions and problems of industrial life ... The use made of the Freudian psychology to interpret the phenomena of social unrest is particularly noticeable.

From *Nature* 15 September 1921

150 years ago

A sensational story has been reprinted in the English papers from the *Swiss Times*, with respect to the disappearance of several persons while bathing during the present season in the Lake of Wallenstadt, a circumstance attributed to fishes of enormous size in the lake. Dr. Frank Buckland, while not placing implicit faith in the story, suggests that the obnoxious fish may perhaps be specimens of *Siluris glanis* which have strayed from their accustomed habitat in the Lower Danube, or descendants of the monstrous Kaiserlautern pike mentioned by Conrad Gesner, or perhaps huge carps or mythical creatures existing only in the brains of enthusiastic tourists. More explicit information would be very desirable.

From *Nature* 14 September 1871