Interpreting a lateral flow SARS-CoV-2 antigen test

Oliver T Mytton, Noel McCarthy, Jessica Watson, Penny Whiting

Lateral flow devices (LFDs) are being used to test asymptomatic people for covid-19 as part of the approach in the UK and elsewhere to control the spread of the disease and to enable society to reopen.1–4

The risks and benefits of using LFDs for widespread testing of asymptomatic people are the subject of ongoing uncertainty and debate.5–7 Despite concerns about accuracy, LFD tests continue to be widely used. In the week ending 19 May, 4.9 million registered tests were undertaken in England.8 People taking a test receive advice on what their result means and what they should do; however, the widespread use of these tests means doctors may increasingly be asked about them (for example, when patients with a recent result present to services).

This practice pointer considers how to interpret and communicate results from LFD tests based on our current understanding of the tests’ performance.

What is a lateral flow device?

Lateral flow devices can detect the presence of a target substance in a liquid, typically in a single use disposable device. Their use is well established for home pregnancy testing. For covid-19, these devices are detecting a SARS-CoV-2 antigen, consequently sometimes they are termed “rapid antigen tests.” A large number of SARS-CoV-2 antigen LFD tests are available internationally.9 In the UK the Innova test is approved by the Medicines and Healthcare products Regulatory Agency to identify covid-19 in people who do not have symptoms and is the only test widely used.10 The US drug and device regulator, the Food and Drug Administration, has not approved the Innova test and in June 2021 issued a safety communication warning the public not to use the test based on concerns that its performance had not been adequately established.11

Other LFDs have met minimum standards and are being field tested in the UK.12 This article focuses on interpreting the Innova LFD; the underlying principles will be similar for the interpretation of other tests.

What is the UK policy?

Currently the government is making LFDs freely available to all adults and secondary school children (age 11+) in England, with advice to test twice each week to detect cases in people without symptoms.1 In addition, visitors to care homes in England are also expected to undertake an LFD before their visit. Northern Ireland, Wales, and Scotland are also making these tests widely available, although the recommendations between countries vary.2–4 Independent of government, some employers are establishing their own testing schemes.

Anyone who has a positive LFD test result is advised to act as if they have symptoms of covid-19—ie, they and their household should isolate and arrange a confirmatory polymerase chain reaction (PCR) test within two days. If the confirmatory test is negative, they are advised that they do not need to isolate.13 If the confirmatory test is positive, then they are advised to continue to isolate for 10 days.

If people have symptoms of covid-19, they are asked to book a PCR test to rule out covid-19, rather than use an LFD. Typically, people who have had a positive result from a recent PCR test are advised not to participate in regular LFD testing for 90 days.14-15 People who have been vaccinated are still encouraged to test. The performance of these tests in people who have been vaccinated has not been directly evaluated. Concerns have been raised that people who have been vaccinated may have a lower viral load, therefore will be less likely to test positive, although

What you need to know

• The positive predictive value of a positive lateral flow device (LFD) test depends on the underlying likelihood of disease
• When the disease incidence is low, a positive result should be validated by a polymerase chain reaction (PCR) test. However, if your clinical opinion is that covid-19 is likely, then a positive test is likely to be reliable
• LFD testing is not recommended when the person has symptoms of covid-19, as a negative LFD is not sufficient to rule out covid-19
• If a symptomatic patient informs you that they have had a negative covid-19 test, check what type of test was done
• If covid-19 is clinically suspected, a PCR test is recommended, even if the patient has received a negative result from a recent LFD test
people who have been vaccinated are also less likely to transmit the virus. Given the LFD is an antigen test, vaccination will not trigger a positive test result.

Recommendations for use of LFDs are changing rapidly. Trials include “test to enable” (eg, testing before attending a large cultural or sporting event) and “test to release” (eg, daily testing of contacts of cases, with a negative test enabling a partial relaxation of the 10 day isolation requirements).\(^{5,17}\)

**How do LFD tests perform?**

Some of the concern around LFDs relates to their ability correctly to pick up cases of SARS-CoV-2 infection, particularly when deployed in home and community testing. Test accuracy is defined in terms of sensitivity and specificity.\(^{18}\) Real world performance depends on test characteristics but also the likelihood of disease in the individual and the quality of the testing.

Data on the sensitivity and specificity of the Innova LFD test are limited. A Cochrane review synthesised the current evidence for a wide variety of LFDS.\(^{19}\) However, all the studies on the Innova LFD included in the review had not been peer reviewed, and some more recent, relevant evaluations were not included as they were published after the end date of the searches (30 September 2020).\(^{20-21}\) The Cochrane review reports a range of estimates for sensitivity and specificity in different contexts of use.\(^{18}\) The sensitivity of LFDS (the proportion of people with disease who have a positive test, or the true positive rate), according to the review, ranged from 28% (when used in an outbreak investigation) to 79% (when used by laboratory scientists), and the specificity (proportion of patients without the disease who have a negative test, or the true negative rate) from 99.5% to 99.9%.\(^{19}\) Recent analysis by Public Health England, not included in the Cochrane review, suggests the specificity may exceed 99.9%.\(^{21}\)

These estimates of sensitivity and specificity are based on evaluating the LFD tests against a gold standard of PCR.\(^{4}\) However, the PCR test has limitations as the gold standard test for diagnosing SARS-CoV-2 infection. First, it is not 100% sensitive, meaning that some people will be missed when relying on PCR testing for diagnosis.\(^{18}\) Second, a PCR test can detect very low levels of virus present in a sample, meaning a positive PCR test does not necessarily equate with people being infectious.

The median time for which an individual will test positive with a PCR test is the range 22-33 days, longer than the typical infectious period.

**How sensitive are LFDs at identifying people who are infectious?**

In the UK, LFDs are being used primarily to prevent spread of SARS-CoV-2 by finding cases among people who do not have symptoms of covid-19. Key to this is the sensitivity of LFDs in identifying people who are currently infectious. In this context, LFDs’ poor ability to detect people who are not infectious (but who recently had the infection) is not a concern. The PCR test, in contrast, identifies those who are currently infectious, and those who were previously infected but are no longer infectious. We need to be mindful of this when assessing data evaluating the accuracy of LFD tests against a PCR reference standard.

Assessing the performance of LFDs in identifying people who are infectious depends on having a good measure of infectiousness. One proxy measure of infectiousness is the Ct value from a PCR test. The Ct value is the number of PCR cycles required to detect the virus, with a low Ct value indicating a large concentration of virus present in the tested sample. The measured Ct value is only likely to be a proxy for the viral load in the patient, as it will depend on the sample quality.\(^{21}\)

Evidence shows a strong correlation between Ct values and in vitro infectiousness\(^{24}\) and some evidence for increased risk of transmission from patients with higher Ct values.\(^{25}\) However, no agreed Ct threshold exists for infectiousness. Transmission is also likely to be influenced by other factors (eg, host immunity, social distancing, and mask wearing) as well as how infectious the case is.

Some of the variation in reported sensitivity is explained by variation in the Ct value.\(^{4,27}\) For example, a large evaluation of community testing in Liverpool (not included in the Cochrane review) among people without symptoms found relatively high sensitivity when testing people with a lower Ct (>80% for samples requiring fewer than 20 PCR cycles to detect the virus—ie, Ct <20), but very low sensitivity at high Ct values (6% for a Ct value of 30-35).\(^{27}\) Taking a conservative threshold for an infectious sample (a Ct value ≤25) from the Liverpool study (n=5869) was relatively large and reflected real world use, with trained lay testers, and although it was primarily an evaluation of supervised testing rather than home testing, it is more relevant than data from the Cochrane review,\(^{19}\) which comes exclusively from the early Public Health England (PHE) evaluation.\(^{26}\)
Other factors affecting test sensitivity

The Liverpool and PHE evaluations suggested that some of the reported variation in sensitivity could be explained by the quality of the testing undertaken.\(^{26,27}\) That includes taking the sample, processing it, and reading the test. For example, the PHE evaluation reported higher sensitivity (79%) when the testing was undertaken by laboratory scientists compared with non-scientists (58%).\(^{28}\) This was based on limited data, but nonetheless raises the possibility that home testing (which increasingly predominates) may be less sensitive than testing performed in supervised test centres.

What do clinicians need to know to understand a test result?

Test characteristics (sensitivity and specificity) alone are of limited value in interpreting the test result. Knowing the pre-test probability, or the underlying likelihood of an individual having covid-19, is vital for interpreting the test result.

To assess this, inquire about why the test was done, as well as other factors that might influence underlying risk of covid-19, including:

- epidemiological link (eg, contact with a known case or link to an outbreak)
- travel to or residence in an area of higher transmission
- occupational risk
- symptoms suggestive of covid-19
- vaccination status
- history of previous infection.

A good understanding of the local epidemiology (local UK data are available at https://coronavirus.data.gov.uk/) can improve interpretation. Where it is known, it may be helpful to shift the pre-test probability up or down based on age or other risk factors. For example, if assessing the result of a student, knowledge of recent outbreaks among students or high infection rates in young adults would push an estimate up. Conversely, rates of infection tend to be lower in older adults who have fewer social contacts and (in the UK) are now mostly immunised.

Pre-test probability is an important driver of the post-test probability

Also consider the quality of the testing (eg, who did the test, their familiarity with testing, and whether they used a recognised test). The sensitivity and possibly the specificity may decline if the quality of testing is weaker.

The calculator (see bmj.com) uses sensitivity, specificity, and pre-test probability to estimate the likelihood that someone with a positive test actually has the infection. It can also be used to estimate other parameters: the negative predictive value (the likelihood that someone with a negative test does not have the infection), as well as the likelihood of having a false positive or a false negative.

Interpreting a positive test result

The table shows how the post-test probability of being infectious increases as the underlying pre-test probability increases. It also shows how the post-test probability changes as the test characteristics (sensitivity and specificity) change. We have given three scenarios for test performance (boxes 1, 2)—in part to reflect ongoing debate about the accuracy of these tests, but also to reflect possible real differences in performance based on the quality of testing.

Different values of sensitivity and specificity influence the post-test probability, and the pre-test probability is an important driver of the post-test probability, which underscores the importance of estimating the underlying likelihood of that person having the disease. When disease levels are lower and the testing is restricted to people who do not have symptoms, the pre-test probability is often likely to be very low, less than 0.1%. At the lower levels of pre-test probability, the post-test probability will be lower, and false positive results become more likely (box 1). Confirmatory PCR should be undertaken to reduce the risk of false positives. For this reason, in April 2021 NHS Test and Trace recommended that confirmatory PCR testing was reinstated for all positive LFD tests.\(^{29}\)

Despite this, in some circumstances the pre-test probability may be substantially higher, even when disease levels are low. Current guidelines recommend...
In support of this approach, a recent trial found that open, share uncertainty, and avoiding oversimplifying. Communicating test results is not easy. We suggest that when sharing information about LFDs with the public it is best to be 48 hours of his positive LFD test result. 13 He and his household should recommend that a positive result from a LFD test requires PCR undertaking by a healthcare professional to ensure a good sample is taken.

LFDs should not be used to test people with symptoms of covid-19, but widespread availability means these tests are often used by people with symptoms, and some people may develop symptoms shortly after testing. These people will have an elevated risk of covid-19, which might be substantially higher than the background prevalence in the community. Close contacts will also have an elevated risk of covid-19. If the pre-test probability was 20%, the post-test probability of being infectious given a positive LFD test is likely to exceed 96%.

Interpreting a negative test

To determine the reliability of a negative LFD test, pre-test probability needs to be taken into account. For most people being tested who do not have symptoms this is likely to be low or very low. A negative LFD test result will reduce the post-test probability of having disease (table 1), but it does not eliminate fully the possibility of infectiousness. If we assume a sensitivity of 50%, a negative test result will approximately halve the post-test probability of disease.

Identify any factors that might indicate a higher pre-test probability. For example, people with symptoms or who have been a contact of a case will have an elevated risk of covid-19, potentially greater than the background prevalence in the community, and a negative LFD should therefore be treated with caution. If covid-19 is suspected clinically, arrange a PCR test. More generally, when a patient states they have had a negative covid-19 test, the clinician should check whether this was an LFD test or a PCR test and reinforce the need to isolate if symptomatic until the patient has received a PCR test result.

Communicating test results

Distilling the complexity and uncertainty surrounding test results is not easy. We suggest that when sharing information about LFDs with the public it is best to be open, share uncertainty, and avoiding oversimplifying. In support of this approach, a recent trial found that wording that incorporated uncertainty around SARS-CoV-2 PCR tests led to fewer people interpreting results as definitive, and more people taking a cautious behavioural interpretation (continued self-isolation if symptomatic with a negative test). 29

A source of concern is that people might interpret a negative result as a “green light” and stop or reduce other protective behaviours. If this attitude is widespread, the benefits of testing, in terms of identifying cases and preventing transmission, could be offset by people relaxing effective measures that stop spread. Very limited empirical evidence supports or refutes these concerns. However, almost 40% of those who used an LFD test in Liverpool reported that they may change their behaviour based on a negative test result—22% reported they would be more likely to engage in low risk activities such as outdoor exercise, and 9% said they would be more likely to visit friends and family, an activity that was actively discouraged at the time of the study because of the higher risk of transmission. 27

The terms “red light” to describe a positive result (ie, stop all activities and isolate immediately) and “orange light” to describe a negative test (ie, continue to proceed with caution) may be helpful means to guide people’s behaviour.

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HOW THIS ARTICLE WAS CREATED

This article was produced at speed. We searched Pubmed, Cochrane Covid-19 study register, Google, Google Scholar, and the WHO Global Research Covid-19 database using the terms “covid,” “SARS-CoV-2,” “sensitivity,” “specificity,” “diagnosis,” “test,” “lateral flow,” and “Innovia.” This was supplemented by discussion with colleagues and identifying relevant references cited in the identified papers.
Treating opioid use disorder in primary care

Megan Buresh, Robert Stern, Darius Rastegar

STATE OF THE ART REVIEW

Opioid use disorder (OUD) is a common problem that contributes to morbidity and mortality worldwide. An estimated 26.8 million people had OUD globally in 2016, a 47.3% increase from 1990, with the highest prevalence in high income North America, followed by North Africa and the Middle East.

Many people with OUD use needles to administer the drug, leading to infectious complications including HIV and hepatitis B and C. The covid-19 pandemic has led to an increase in deaths owing to overdose in 2020, adding urgency to the need for screening and treatment in primary care settings.

Substance use disorders (SUDs) have traditionally been treated in specialised programmes separate from other healthcare, but an increasing move towards the integration of SUD treatment into primary care is supported by evidence.

Screening for OUD

Several methods for screening for unhealthy drug use exist, one of the simplest of which is to ask the following two questions:

1. How many days in the past 12 months have you used drugs other than alcohol? (seven or more is positive)
2. How many days in the past 12 months have you used drugs more than you meant to? (two or more is positive).

In a study of more than 1200 primary care patients, these two questions were found to be more than 90% sensitive and specific for drug use disorder. A positive screen should prompt further questioning about the frequency, quantity, and impact of drug use.

Tools such as the Current Opioid Misuse Measure and the Prescription Opioid Misuse Index are also available to screen for OUD among people who received prescribed opioids.

Diagnosis of OUD

Opioid use disorder is characterised by loss of control over the use of opioids, resulting in physical, psychological, and social harms. The Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5) provides diagnostic criteria for OUD, which are the same for all substances and based on the presence of at least two of 11 criteria, which can be divided into four clusters:

- **Impaired control**—use in larger amounts or over a longer period of time than intended; persistent desire to cut down or multiple unsuccessful attempts at cutting down or stopping use; great deal of time spent using substance or recovering from its effects; and intense desire to use or craving for the substance.
- **Social impairment**—substance use resulting in failure to fulfil obligations at work, school, or home; substance use causing or exacerbating interpersonal problems; and important social, occupational, or recreational activities given up or reduced owing to substance use.
- **Risk use**—recurrent use of substance in physically hazardous situations; and continued use despite negative physical or psychological consequences.
- **Pharmacological dependence**—tolerance to the effects of the substance; and withdrawal symptoms with cessation of substance use.

An important caveat is that “symptoms of tolerance and withdrawal occurring during appropriate medical treatment with prescribed medications (eg, opioid analgesics, sedatives, stimulants) are specifically not counted when diagnosing a substance use disorder.”

Treatment

Brief interventions

The implementation of brief interventions for substance use has received much attention in recent years, often as part of screening, brief interventions, and referral to treatment. Evidence on the effectiveness of brief interventions in primary care settings is mixed, with earlier studies reporting more positive outcomes than recent ones. These interventions seem to be most effective for people with low risk use. Counselling delivered by primary care clinicians over many visits for patients with whom they have a longitudinal relationship may have a larger effect, but research is needed to demonstrate this.

Psychosocial treatment

Several psychosocial treatments can help people with OUD, including self-help groups, counselling (individual or group), and residential treatment. Although these are typically delivered outside the primary care setting, clinicians can help to facilitate linkage to these treatments for patients who are interested. The evidence supporting these interventions, either alone or in combination with pharmacotherapy, is limited and the effect is generally much lower than that observed with pharmacotherapy alone.
Buprenorphine is a long acting partial opioid agonist that is highly effective for treatment of OUD. Several buprenorphine formulations are available in the UK, some of which are co-formulated with naloxone to discourage injection or intranasal use.

Evidence supports use of a daily buprenorphine dose of 16 mg or higher for most patients. A systematic review of 31 studies including 5430 patients found that dosing of 16 mg sublingual buprenorphine daily was non-inferior to methadone. Another systematic review and clinical trial found that higher sublingual buprenorphine doses (up to 32 mg/day) were associated with better treatment outcomes. At a time when fentanyl and high potency opioids are available, many patients may need doses of buprenorphine above 16 mg and should be offered doses up to 32 mg daily. Patients who do not respond to doses up to 32 mg/day should be considered for methadone treatment.

Drug testing should be used as a therapeutic tool, in a patient centred rather than punitive way

Buprenorphine maintenance is more effective than short term taper (or medically supervised withdrawal) and is associated with long term retention in primary care settings. Buprenorphine has a high binding affinity, which contributes to its safety, but it can displace other opioids and lead to “precipitated withdrawal” if it is administered too soon after use of a full agonist. Precipitated withdrawal can be avoided by waiting to administer buprenorphine until the patient develops symptoms of opioid withdrawal (a sign of low receptor occupancy)—usually 8 to 12 hours after heroin or short acting prescription opioids—and using a low initial dose of buprenorphine. Longer periods may be needed (up to 18-24 hours) for patients using fentanyl because of its lipophilicity.

Traditionally, the standard of care includes monitoring adherence to buprenorphine with periodic drug testing, although no evidence shows that drug testing improves clinical outcomes. When used, drug testing should be used as a therapeutic tool, in a patient centred rather than punitive way. For example, a positive test for illicit opioid can prompt discussion about whether a patient needs an increase in the buprenorphine dose to suppress cravings and what triggers the patient’s drug use. In general, use of other drugs is not a reason to discontinue treatment for OUD and the three drugs approved for this indication are buprenorphine, methadone, and extended release naltrexone. The dosing and outcomes for these drugs are summarised in the table.

### Overview of pharmacotherapy for opioid use disorder (OUD)

<table>
<thead>
<tr>
<th>Medication</th>
<th>Mechanism of action</th>
<th>Formulations for OUD treatment</th>
<th>Dosing</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buprenorphine</td>
<td>Partial opioid agonist</td>
<td>Sublingual tablet/film, weekly and monthly SC injections, implant</td>
<td>Sublingual: 8-32 mg daily, SC injections: Subscide: 300 mg monthly × 2 months, followed by either 100 or 300 mg maintenance dose; Brixadi (CAM-2038, Braeburn): 8, 16, 24, and 32 mg weekly or 64, 96, and 128 mg monthly</td>
<td>Mortality Decreased Ilicit opioid use Decreased</td>
</tr>
<tr>
<td>Methadone</td>
<td>Full opioid agonist</td>
<td>Oral (tablet, liquid)</td>
<td>60-200 mg daily*</td>
<td>Mortality Decreased Ilicit opioid use Decreased</td>
</tr>
<tr>
<td>XR-naltrexone</td>
<td>Opioid antagonist</td>
<td>Intramuscular injection</td>
<td>380 mg IM once monthly</td>
<td>No significant effect Ilicit opioid use Decreased</td>
</tr>
</tbody>
</table>

IM=intramuscular, SC=subcutaneous, XR=extended release.

*Maximum allowed dose of methadone varies, and emerging evidence suggests that patients may need higher doses than previously allowed.
†Based on limited evidence; primarily observational studies with relatively small numbers receiving naltrexone.

Drug testing should be used as a therapeutic tool, in a patient centred rather than punitive way

**Pharmacotherapy**

**Medically supervised withdrawal**

Medically supervised withdrawal, or using medications to wean patients rapidly from opioids, is not recommended owing to increased risk of relapse and overdose after treatment of withdrawal. Most patients return to opioid use shortly after withdrawal treatment is complete, even when engaged in abstinence based treatment.

**Opioid agonist treatment**

Long term pharmacotherapy is the mainstay of treatment for OUD and the three drugs approved for this indication are buprenorphine, methadone, and extended release naltrexone. The dosing and outcomes for these drugs are summarised in the table.

The best evidence exists for the long acting full opioid agonist methadone and partial opioid agonist buprenorphine. Both are on the World Health Organization’s list of essential medications. Termination of pharmacotherapy is associated with high mortality rates in multiple large cohort studies, with a particularly high risk immediately after discontinuation of treatment. In the UK general practice cohort study, the risk of mortality was eight times higher in the first few weeks after discontinuation of treatment compared with the risk after four weeks or more on treatment (adjusted mortality incidence rate ratio 8.15, 5.45 to 12.91).

**Methadone**

Methadone is a highly effective treatment, with a systematic review showing its efficacy in decreasing illicit opioid use compared with no medication across six randomised controlled trials (RCTs) (risk ratio 0.66, 95% confidence interval 0.56 to 0.78). A systematic review of 221 studies including 2279 patients found that higher doses of methadone were associated with higher retention in treatment (relative risk 1.36, 95%
of reaching a dose suppressing opioid craving while patients are monitored for craving, withdrawal, risk of respiratory depression. As the dose is increased, other day). Closer medical monitoring is needed than an effective dose is achieved (for example, by 5 mg every other day). An RCT comparing extended release naltrexone with sublingual buprenorphine in 570 participants over 24 weeks found that outcomes (opioid negative urine, opioid abstinent days) with extended release naltrexone were inferior in intention to treat analysis (P<0.001); however, among patients who were successfully inducted, outcomes were similar in the extended release naltrexone and buprenorphine groups. This was owing to a significant induction hurdle for extended release naltrexone with significantly fewer patients successfully initiated on extended release naltrexone (204/283; 72%) than buprenorphine (270/287; 94%) (P<0.001).

A systematic review of 34 studies of extended release naltrexone for OUD found that the success of induction was lower in studies that included patients who needed opioid detoxification (62.6%, 95% confidence interval 54.5% to 70.0%) compared with studies that included patients already detoxified from opioids (85.0%, 78.0% to 90.1%). Only 44.2% (33.1% to 55.9%) of patients took all scheduled injections of extended release naltrexone, which were usually six or fewer. To date, studies have failed to show a significant effect of extended release naltrexone on the risk of overdose and death; this may be because observational studies have generally had small numbers of people on this treatment. More longer term studies are needed, including pragmatic studies in primary care settings.

Naloxone
The opioid antagonist naloxone is a key tool in curbing mortality owing to opioid overdose and can be easily prescribed from community settings to both patients with OUD and affected friends and family members. Prescription of naloxone with brief education is safe and effective in community settings; it should be prescribed to all patients with OUD, as well as patients likely to witness an overdose (including those living in high prevalence communities or with a family member with OUD).

When to refer for specialty treatment
Indications for referral to specialty treatment include continued use of drugs or alcohol with evidence of harm and deterioration in functioning.

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What I never consented to
Andrés J Lessing describes the worry of incidental findings and how the process of giving consent could be improved

I have a complex medical history and have experienced many tests, procedures, and surgeries. Over the years, I have consented to seemingly endless risks that came with these procedures, including adverse reactions, infection, bleeding, nerve damage, function loss, and even death. But one element was never included in consent forms or conversations—the possibility of an incidental finding. I have never consented to what I now know is common and called “incidentaloma.”

I am 41 and have neurofibromatosis type 1 (NF). I have survived NF related cancers three times and participated in multiple investigational studies along the way. These included myriad magnetic resonance imaging (MRI) and computed tomography (CT) scans and surgeries. Some of the scans showed lesions that were unexpected, and these prompted further discussion with my neurologists, surgeons, and physicians, as well as additional treatments, and extra anxiety on my part.

I cannot recall once the possibility of incidental findings on the consent forms I signed, or more importantly—in discussions with my doctors.

The worry of incidentalomas
One of my first incidentalomas was found after surgery for an NF related malignant peripheral nerve sheath tumour. I woke up without sensation from the top of my right shoulder down through my hand and fingers. An exploratory MRI scan detected a growth near the pineal gland in my brain. Questions were raised about metastasis, new malignancy, and more, even though none of this explained the sensory loss. Every six months thereafter, lying as still as possible in the loud MRI scanner, I wondered and worried about the growth in my brain. After years of biannual scans, I located a childhood MRI scan that confirmed the growth had been there all along and was likely a benign pineal cyst. Thus began my journey with incidentalomas.

Ten years after my last recurrence of the cancer was removed, I volunteered for a full-body MRI scan as part of a study. The scan identified a lesion in my right axilla near the site of my many surgeries and radiation field. My doctors ordered a follow-up MRI three months later, which showed growth of the lesion and led to a fifth surgery in this area. The lesion turned out to be skeletal muscle with atrophy, fibroadipose tissue, and fat necrosis and very fortunately was not a cancer recurrence. However, CT scans I’d had in preparation for the surgery found thyroid nodules not previously seen. Additional investigations ensued, as did doctors’ visits, further studies, and continued worry. The nodules turned out to be common and nothing of concern. With each benign finding, I was initially shocked and overwhelmed with gratitude. I thanked my team of doctors and thought of friends who did not survive my rare type of cancer. But each incidentaloma resulted in more tests, more loss of function, added worry, and hardship.

Redefining the consent process
Some will say it is not possible to address every potential outcome in consent. However, a simple reminder of the possibility (indeed, high likelihood) of incidental findings—and what we might do to address them—would have been helpful. My choices might have been the same, but I believe we would have felt better prepared for whatever was to come.

The consent process should educate patients on the benefits and risks of treatment and should include discussing the possibility of incidental findings and possible responses, including watchful waiting rather than further tests and more surgeries. I share my story because I wish my doctors had discussed with me these possibilities during the consent process.

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Competing interests: None declared.
CASE REVIEW

A lump in the hand

A man in his late 40s presented to his general practitioner with a history of skin changes and two lumps in his left hand, which had been present for several years. He thought the symptoms were from repeated trauma after carrying heavy buckets as part of his job. The nodular lumps had recently increased in size. In the months before referral, the patient began to experience a severe burning sensation in the nodules in his hand, which interrupted his sleep. Examination of the hand revealed an area of skin tethering with a palpable thickening deep to it in the palm over the hypothenar eminence (fig 1, fig 2). Two small erythematous lumps were found, one proximal to the main lesion at the wrist crease and another on the ulnar border of the hypothenar eminence. In addition, the patient had numbness over the ulnar border of the hand, little finger, and half of the ring finger, and weakness in the intrinsic muscles of the hand (palmar and dorsal interossei). He had a positive Froment’s sign (weakness of the adductor pollicis muscle, supplied by the ulnar nerve, resulting in the need for thumb flexion, using flexor pollicis longus action, to provide pinch grip). These signs of numbness and weakness followed an ulnar nerve distribution.

1 What are the differential diagnoses for a lump in the hand?

2 Is this lesion more likely to be benign or malignant?

3 What investigations are required to confirm the diagnosis?

Fig 1 | Volar surface of the hand showing skin tethering over the hypothenar eminence

Fig 2 | Lateral view of the hand showing small proximal erythematous lesion at the wrist crease, in addition to skin tethering

ENDGAMES

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LEARNING MODULE

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MINERVA

Frostbite of the mouth after partying

This is a severe frostbite injury in a man in his 20s who inhaled laughing gas (nitrous oxide) at a party while on holiday in Amsterdam. He presented to the emergency room with progressive pain and swelling of the oral cavity after placing his lips over the valve of a nitrous oxide tank and inhaling the gas. Examination revealed frostbite of the mouth with necrosis of the oral mucosa. He was admitted to the intensive care unit for pain management and for monitoring because of concerns about airway obstruction due to excessive swelling of the lips, mouth, and cheeks. Oral hygiene was advised for the mucosal necrosis and antibiotics were administered to prevent secondary infection. Recreational exposure to cryogenic agents such as laughing gas can cause cutaneous or oral mucosal injuries within minutes. Upper airway compromise is life threatening, and monitoring in the intensive care unit should be considered to ensure prompt intervention if required. Kiran C Baran (kbaran@rkz.nl), Annebeth Meij de Vries, Red Cross Hospital, Beverwijk, Netherlands

Patient consent obtained.

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The genetics of cognitive decline

Scores on the mini-mental state examination were tracked for five years in 350 twin pairs from Sweden, all aged 80 or older. Four distinct trajectories emerged: high baseline remaining stable; high baseline with slow decline; impaired at baseline followed by decline; and impaired at baseline followed by rapid decline. Most twins, whether monozygotic or dizygotic, followed a different trajectory from their co-twin. Lifestyle and environmental exposures, rather than genetics, may be the main determinants of cognitive change in later life (Age Ageing doi:10.1093/ageing/afaa239).

Sleep disturbances, diabetes, and mortality

A study from the UK Biobank finds that people who say that they sleep badly—around a quarter of participants—have worse health. Disturbed sleep was associated with a roughly 10% increased risk of mortality from all causes (J Sleep Res doi:10.1111/jsr.13392). The presence of both diabetes and frequent sleep disturbances carried a greater mortality risk than either condition alone.

Children who swallow magnets

Young children sometimes swallow magnets because they don’t know what they are. Older children swallow them accidentally when trying to mimic the appearance of a pierced tongue or cheek. Most magnets pass through the gut without causing harm, but there’s a danger of bowel loops being pinched together if more than one has been swallowed. Consider laparotomy if magnets distal to the stomach show no movement on serial imaging (Arch Dis Child 10.1136/archdischild-2021-321848).

Blood pressure treatment in patients with atrial fibrillation

A meta-analysis of 22 trials concludes that treatment to lower blood pressure is as effective in people with atrial fibrillation as it is in those in sinus rhythm. Risk reductions were proportional to blood pressure reduction. Over 4.5 years of follow-up, a reduction of 5 mm Hg in systolic pressure reduced the risk of a major cardiovascular event by around 10% in patients with and without atrial fibrillation (PLoS Med doi: 10.1371/journal.pmed.1003599).

Diet and pregnancy

A healthy diet at the time of conception reduces the risk of several common complications of pregnancy, according to a study of 2000 women in the US. Women with a high consumption of fruits, vegetables, whole grains, nuts, and legumes and a low consumption of red and processed meat had lower risks for gestational diabetes, pre-eclampsia, and preterm birth (Am J Clin Nutr doi: 10.1093/ajcn/nqab145).

NSAIDs do not cause postoperative bleeding

Non-steroidal anti-inflammatory drugs are unlikely to increase the risk of bleeding when used for analgesia after surgery. A systematic review looked at trials of NSAIDs over a range of surgical procedures. No difference was seen in rates of haematoma, frequency of return to the operating room for bleeding, or need for blood transfusion between the NSAID and non-NSAID groups (J Am Coll Surg doi: 10.1016/j.jamcollsurg.2021.01.005).

A laboratory leak would be better than zoonotic spillover

Whatever you think about the theory that SARS-CoV-2 emerged from a laboratory leak, it’s arguable that this is the best explanation we can hope for. Although it would be appalling to have to acknowledge that the pandemic was caused by human error and scientific misjudgment, it would at least inform us how to be safer in the future. If covid-19 is a zoonotic spillover from infected wildlife it will be much harder to guard against a recurrence (https://unherd.com/2021/06/why-we-should-welcome-the-lab-leak-theory/).

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