Tranexamic acid after major trauma
A randomised trial set in Australia recruited 1310 adults with major trauma who had a high risk of trauma induced coagulopathy according to the seven-point COAST score. Six months after prehospital treatment with tranexamic acid or placebo, there was no difference in survival with a favourable outcome (moderate to no disability) between the two arms of the trial (53.7% v 53.5% respectively). A secondary outcome of death at 28 days found a benefit from tranexamic acid: 17.3% versus 21.8%.

The linked editorial reminds us that “disability is not a constant characteristic of a person, but the result of an interaction between the person and the environment, and both change over time” and that severe disability doesn’t necessarily mean a poor quality of life—which may make a small, short term survival benefit worthwhile.

Aspirin and anaemia: a new chapter
Oh aspirin, what a life you’ve led. From your humble, willow bark beginnings to your glittering career as a big-pharma blockbuster drug, and then your existential search to find your place in the modern world.

But time and tide wait for no drug: the 2018 ASPREE study enrolled 19 114 people aged 70 years or over in the United States and Australia and found that those randomised to receive aspirin had a higher risk of death after a median 4.7 year follow-up period than those randomised to receive placebo (12.7 v 11.1 events per 1000 person years). A post hoc analysis of the same study has now found that rates of anaemia were higher in the aspirin arm of the study and a decline of haemoglobin concentration of 4.2 g/L per five years in those taking aspirin versus 3.6 g/L per five years in the control group. I hear that aspirin has no plans to retire, but the authors of this study suggest considering periodic monitoring of haemoglobin among older people taking aspirin.

Family treatment for childhood obesity
Many consultations make a lot more sense when you know your patient’s family—whether that’s from caring for them over many years or by seeking out a fellow GP who can recite the family’s dramas as if it were an Eastenders storyline. Although we so often see that patterns of behaviour can be understood well at a family level, family based interventions seem few and far between.

Continuous or intermittent antibiotics in critically ill patients
Prolonged infusions of β-lactam antibiotics rather than standard intermittent infusion received a weak recommendation from the Surviving Sepsis Campaign in 2021. The largest trial to date of continuous infusion versus intermittent administration of meropenem in critically ill patients has just been published. It found no survival benefit from continuous infusion, or any differences in any of the study’s secondary outcomes.

However, the study recruited a high proportion of patients who had received prior antibiotics in intensive care (median five days in intensive care before enrolment), and only 10% had a confirmed bloodstream infection. We may need to wait for the much larger, and memorably titled, BLING III study to settle the question of whether continuous or intermittent antibiotics are more effective in this group of patients.

FROM THE JOURNALS
Edited highlights of weekly research reviews

A randomised trial of 453 children who were overweight or obese recruited from primary paediatric care were offered family based treatment that used “behavioural techniques to develop healthy eating, physical activity, and parenting behaviours within families.” Although children in the intervention group had better weight outcomes between six and 24 months than those who received usual care, this didn’t reach the threshold for a clinically meaningful weight change. Considering a problem through a family lens may help to understand it, but solutions tend to be harder to come by.

Cardiovascular safety of testosterone gel
This industry-funded trial, for which the sponsor codesigned the research protocol, has reassuring conclusions about the cardiovascular safety of topical testosterone therapy in men with hypogonadism. The 5204 participants had a mean age of 63 years, and over half had cardiovascular disease (the rest had increased cardiovascular risk). No difference was found between those taking testosterone and those taking placebo in a composite outcome of cardiovascular events after a mean follow-up of 33 months. There was also no difference in incidence of prostate cancer—another safety concern with testosterone treatment—although those allocated to receive testosterone did have a slightly higher increase in PSA levels.

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Ms Olsen is a 65 year old woman with hypercholesterolaemia and hypertension. Her doctor tells her that she can reduce her risk of getting a major cardiovascular event by up to 50% if she takes a statin. “That’s great,” she thinks, “50% reduction is a lot!” She feels happy and well informed and plans to take the statin.

After she comes home, she remembers her recent conversation with a car dealer (she really needed a new car). He told her a car he had in his lot was reduced in price by 15%. May be a good deal, she thought, and asked for the price of the car. Unfortunately it was far too high, even with the 15% off. She thought the dealer had not been honest since he did not tell her the price upfront, only the discount.

Risk for disease and for treatment effects is conveyed in many ways: relative or absolute, in percentages, hazards, or odds ratios. Some are more informative than others, and many of the most frequently used are hard to understand.

This article outlines how to convey benefits, harms, and burden of interventions to patients and society in an informative way, and offers pointers for communicating absolute and relative risks in consultation with patients, colleagues, and policy makers.

WHAT YOU NEED TO KNOW

- Relative effects of treatments are often described in patient encounters, scientific journals, and mass media, although used alone to guide decision making they are insufficient and potentially misleading

- Absolute treatment effects together with the absolute risk of disease one wants to prevent or treat are more informative and should be used instead

- Discussions about action thresholds for absolute disease risk and absolute treatment effects are important in patient encounters and elsewhere in the healthcare system

Risk is conveyed in many ways: relative or absolute, in percentages, hazards, or odds ratios
**Conveying risk and treatment effects**

We believe that scientific publishing must take a fair share of blame for our suboptimal patient information about disease risks and treatment effects. Relative effect estimates such as hazard ratios, relative risks, or odds ratios have been standard in reports of observational studies and clinical trials for decades. Many scientific reports highlight relative effects,¹⁴ while the underlying absolute numbers are hard to uncover, often requiring skill and time that is not at most clinicians’ disposal.

In a pivotal trial of screening for colorectal cancer with sigmoidoscopy in the UK in 2017, the main outcome was reported as “colorectal cancer incidence was reduced by 26% (hazard ratio 0.74; 95% confidence interval 0.70 to 0.80; P<0.0001).”¹⁴ The trial informed the decision to introduce population screening for colorectal cancer in the UK. While the trial reporting was not incorrect, the hazard ratio alone is insufficient as the basis of an informed decision about whether to introduce screening. In this case, the decision must take into consideration the absolute risks of colorectal cancer which the reported relative risk reduction applies to.

Media reporting on new medical interventions swiftly follows the publication of trial results, and typically conveys to the public the relative effects presented in the scientific paper. This can be appealing, as the relative effects often look more impressive than the absolute effects and attract more attention. But it does not provide unbiased information or enable appropriate decision making.

If scientific journals are obscuring the absolute risk reduction in favour of seemingly larger and more eye catching relative effects, it is understandable the media will pick this up and present this side of the narrative.

**How to communicate risk, benefit, and harm**

Appropriate decision making requires discussion of outcomes relevant to the patient, and conscious communication of four features, which we outline below using the case of Ms Olsen:

**What is the absolute risk of the disease without treatment?**

For Ms Olsen with hypertension and elevated cholesterol in which statin therapy is considered; what is her risk (eg, in the next 10 or 15 years) of having a major cardiovascular event (myocardial infarction or stroke) without statins?

**What is the benefit of the treatment in question to reduce that risk?**

It may be the absolute risk difference or a relative risk reduction.

**What is the reduction of risk for Ms Olsen in the next 10 or 15 years to develop a major cardiovascular event with statins, as compared with no statins?**

**What is the absolute risk of the disease with the treatment?**

What is the risk for Ms Olsen in the next 10 or 15 years to develop a major cardiovascular event with statins?

**What are the absolute risks of harms and what is the burden of the treatment?**

What is the absolute risk of harms and side effects (eg, diarrhoea or muscle pain) of taking a statin for Ms Olsen in the next 10 or 15 years, and what is the burden for her to take the treatment (eg, costs, check-up appointments, downstream testing, and how statin therapy may affect her quality of life through potential fear of being at risk for disease)?

If one needs to choose for brevity, absolute numbers should be used because relative effects can be calculated from them, but not the other way around.
Considering absolute risks in guidelines: colorectal cancer screening

A BMJ Rapid Recommendations guideline aimed at improving decision making on colorectal cancer screening by applying the features above. We were members of the guideline panel, which decided that the recommendations should take into account both absolute and relative risks. The panel concluded that, although a relative risk reduction by screening of about 25% as reported in the pivotal trial was statistically significant, it appears small in people with a low risk for colorectal cancer. When considering the balance of benefits and harms related to the screening procedures, the panel decided not to recommend screening for individuals with a low absolute risk of disease. In a consensus process, the panel also defined any absolute risk of colorectal cancer smaller than 3% over 15 years without screening as the lower threshold for when to act at all. The panel argued that in individuals with a risk lower than 3% over 15 years, the 26% relative risk reduction corresponds to an absolute risk reduction which may not outweigh the harms and burdens of screening. The guideline was criticised by some experts, who argued that the relative risk reduction of 25% in colorectal cancer incidence is considerable and should encourage “increasing screening uptake and access to organised screening” without mentioning absolute risks and benefits.

Patient encounter with Ms Olsen

Applying the principles above and adding numerical examples, an informative encounter for Ms Olsen would include:

- First, to estimate her absolute risk of a cardiovascular event, eg, by using a 10 year risk calculator. Over a 10 year period, her risk of having a heart attack or stroke is about 6%
- Second, to apply the expected reduction to the estimated absolute risk (6%). Let’s say that the 50% reduction as suggested by her doctor is accurate (although it may be more like 20% to 25%), reducing her risk by half would give her a risk difference of 3%
- Third, to tell her that her risk of having a major cardiovascular event is 3% if she chooses to use a statin
- Fourth, to inform her about the absolute frequency of side effects of statin therapy, eg, a 5% risk of muscle pain and 10% risk of digestive problems, such as constipation, diarrhea, or bloating.

When to act on risk?

Conveying absolute risks and risk reductions instead of less informative relative numbers requires training and conscious communication. The most difficult question, however, remains: how high should a risk for a disease or condition be to act on, given a certain reduction of that risk by a therapy or treatment? Establishing thresholds for when to act is more difficult because it is sensitive to individual and societal values and preferences.

In any discussion of what a healthcare system should offer, use of absolute numbers is crucial to ensure equitable care.

On the patient level, understanding of personal perceptions and preferences for benefits and harms of interventions to reduce a certain disease risk is important. Ms Olsen may be interested to act on a risk of 6% for a cardiovascular event, but she may not bother to take any treatment action if her risk were 3%. Other patients may see it differently and would be willing to start statins at a lower risk than Ms Olsen.

Although risk calculators for future disease are getting better and can predict individual risk quite accurately for some diseases, they still lack for many others. Collections of risk calculators and decision aids are available online for doctors and patients, such as the “Care that fits” initiative from the Mayo Clinic (carethatfits.org). However, some patients may agree or disagree to undergo a treatment or action regardless of the framing and facts of risk and effects, and base their decision on other factors, such as experiences of family members with the relevant disease, or financial constraints from prescription charges.

The strategy for individual patients (such as Ms Olsen) using the four described features can also be applied in decision making at a society level. Many healthcare systems provide reimbursed interventions, tests, and treatments. Most public healthcare systems also have priority guidelines and established menus of treatment options, which are offered to the population. Such priorities need to take into account absolute risk and risk reductions.

Some healthcare systems have also defined general action thresholds for interventions and treatment. In the UK, the National Institute for Health and Care Excellence has established a threshold of £20 000 to £30 000 and uses quality adjusted life years as the measure of threshold risks and benefits. Other countries, like the US, actively stay away from this difficult topic and do not include threshold discussions in clinical guidelines. Few healthcare systems, however, are rigorously using absolute risks and absolute benefits and harms in a transparent way using the features above. We believe that what is made available in a healthcare system needs scrutiny and transparent explanation using absolute risks and benefits and harms.

In our opinion, no situations in clinical medicine benefit from the use of relative instead of absolute differences for understanding in conversations between doctors and patients, or among doctors when discussing treatment options for a patient. In discussions of what a healthcare system should offer, use of absolute numbers is crucial to ensure equitable care. Absolute risks and absolute risk reductions should be used in communication with patients, colleagues, decision makers, and the media. Relative reductions may be used in addition to absolute reductions to illustrate or exemplify, but only in addition and not instead of absolute effects and risks.

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Towards zero carbon healthcare: asthma care

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Asthma affects over 260 million people and causes more than 460,000 premature deaths annually worldwide.1

There is variation in asthma care and its carbon footprint globally: the UK, for example, has a high hospital admission rate and mortality for asthma compared with other high-income countries,1,2 and it has a high carbon footprint from inhalers. At the centre of these two problems is an over-reliance on pressurised metered dose inhalers (pMDIs)—short acting β agonist (SABA) reliever pMDIs in particular3 but also inhaled corticosteroid preventer pMDIs.4

There is no clinical rationale for this inter-country variation, and we, therefore, use the UK as an example of a country where there are many opportunities for change. The principles that we present apply globally.

What is the problem?

Widespread use of inhalers with high carbon footprints

The National Health Service (NHS) in England is the only healthcare system in which emissions have been comprehensively calculated, and in this system 13% of the emissions under its direct control (excluding supply chain emissions) are due to inhalers used to treat asthma and other airways diseases.4 This equates to 3% of the total NHS carbon footprint.

SABA inhalers contribute 67% of England’s inhaler carbon footprint,5 and 70% of all inhalers issued in England are pMDIs, (a higher proportion than in many other countries in Europe, such as only 13% of inhalers used in Sweden being pMDIs).8 Within England, variation with the proportion of corticosteroid preventer inhalers that are pMDIs has also been demonstrated; this ranges from 37% in North Tyneside to 70% in North East Lincolnshire.9

High SABA use is also associated with poor clinical outcomes, as shown in a confidential inquiry investigating deaths from asthma or anaphylaxis in the four UK nations between February 2012 and January 2013.2 This confirms that there are two strong incentives for changing asthma care practice: to reduce morbidity and mortality and to reduce the impact of asthma care on the environment.

Following a move away from chlorofluorocarbon propellants, as part of the global commitment laid out in the 1989 Montreal Protocol on Substances that Deplete the Ozone Layer,10 pMDIs now contain hydrofluorocarbons (HFCs). These are over 1000 times more potent as greenhouse gases than carbon dioxide (CO2).8,11 Although the 2019 Kigali Amendment added HFCs to the Montreal Protocol,11 exemptions are in place for medical uses such as inhalers. Dry powder inhalers (DPIs) and soft mist inhalers (SMIs) have substantially lower carbon footprints than pMDIs as they do not contain HFCs.8,11 Although there is no standardised method for measuring the carbon footprint of inhalers, best estimates support a broad categorisation based on HFC propellant gas into low (inhalers that do not use HFC gases), moderate (inhalers that use the HFC named HFA134a), and high carbon inhalers (inhalers that use the HFC named HFA227ea) (see table).11

Overdiagnosis and underdiagnosis of asthma

Asthma is both underdiagnosed and overdiagnosed—patients are commonly given a SABA inhaler for breathlessness or wheeze without diagnostic pulmonary function tests (peak flow diary, spirometry with...
reversibility, bronchial provocation test, or exhaled nitric oxide). A study of NHS prescription data from England in 2017 found that up to 30% of patients in England with a diagnostic label of asthma did not have the disease. These and other patients may be using SABA inhalers without clinical benefit, with a high environmental cost.

Under diagnosis also exists and increases the risks of daily symptoms, exacerbations, and airway remodelling. Questionnaires and objective testing of 10,000 randomly selected people aged 14-44 years in Copenhagen identified 493 with “definite asthma”; of these, 50% had not been diagnosed previously. Survey data from 192 young adults entering US military service who had respiratory symptoms on exercise, suggested that, of those diagnosed with asthma at enrolment (using spirometry in all and bronchial provocation testing in 67%), a diagnosis of asthma had never been previously considered in 30%.

Lack of regulation and incentives that support appropriate inhaler use, reuse, and disposal

Many inhalers do not have dose counters, which means there is a risk of patients throwing away partly used inhalers prematurely. Most inhalers are disposed of in domestic waste and, because of the lack of large scale recycling schemes globally, end up in landfill where their HFCs are leaked into the atmosphere. Additionally, very few inhalers are reusable or refillable. The Respimat (tiotropium bromide) SMI has a reusable dispenser, and refills are available; however, the entire inhaler is often re-prescribed rather than the just refill cartridge on its own.

Factors such as plastic and metal pollution also contribute to environmental damage; but carbon footprint is the best described environmental impact of inhalers.

Carbon footprint by inhaler type (according to PresQIPP inhaler carbon footprint comparison tool)

<table>
<thead>
<tr>
<th>Inhaler type</th>
<th>Carbon dioxide equivalent (kg CO₂e)</th>
<th>Equivalent km driven in a mid-size petrol car</th>
</tr>
</thead>
<tbody>
<tr>
<td>All dry powder inhalers and soft mist inhalers</td>
<td>1-24</td>
<td>5-130</td>
</tr>
<tr>
<td>Pressurised metered dose inhalers (pMDIs):</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Containing HFA 134a (most pMDIs)</td>
<td>7-240</td>
<td>38-1209</td>
</tr>
<tr>
<td>Containing HFA 227ea (Flutiform and Symbicort MDI)</td>
<td>429-835</td>
<td>2323-4521</td>
</tr>
</tbody>
</table>

| *Only Symbicort MDI contains HFA227ea. Symbicort Turbohaler is a dry powder inhaler. |

Up to 30% of patients in England with a diagnostic label of asthma did not have the disease.

What are the solutions?

Look for opportunities to optimise clinical care

• Ensure diagnoses are correct (see box 1). Global Initiative for Asthma (GINA) and National Institute for Health and Care Excellence (NICE) guidelines recommend offering spirometry with reversibility, peak flow diary monitoring, and fractional exhaled nitric oxide (FeNO), where available, to both newly diagnosed patients and existing patients who are taking SABA alone. Bronchial provocation testing is recommended when there remains diagnostic doubt. However, we acknowledge that, in areas with limited healthcare infrastructure and resource, making an accurate diagnosis can be more challenging if availability of spirometry and peak flow testing are limited.

While we advocate for objective pulmonary function testing, we advise that, when clinicians are confident about a diagnosis of asthma, patients can be treated with inhaled corticosteroid or corticosteroid plus long acting β agonist (LABA) while waiting for objective pulmonary function testing; and that a peak flow diary and/or eosinophilia on full blood count can be considered as adequate confirmation if objective pulmonary function testing is not available.

• If asthma is confirmed, use shared decision making to create a self management plan, and transition to a corticosteroid or corticosteroid-LABA inhaler as the primary medication, as per guidelines from GINA.

• Identify patients who are issued more than three SABA inhalers a year and – optimise their treatment in line with GINA and...
British Thoracic Society guidelines, ensuring they are receiving the right drug, device, and dose to control disease

- optimise inhaler technique—in person ideally or via video, supported by specialist nurses or pharmacists—and increase use of maintenance and reliever treatment (MART) and anti-inflammatory reliever (AIR) regimens with the aim of eliminating SABA use in appropriate patients (see box 2)\(^{22,23}\) Additional training may be required so all professionals can reliably assess and teach inhaler technique.\(^{24,25}\)

These measures will reduce the carbon footprint of asthma care even before any changes to inhaler device are considered.

- Other opportunities to optimise treatment, as outlined above, include when patients present with exacerbations, repeat prescription requests, and during routine asthma reviews.

- Within shared decision making conversations, discuss non-pharmacological factors such as allergen and air pollution exposure, physical activity, immunisation, and psychosocial factors.

- If patients have exacerbations despite optimised treatment, consider assessment for biological therapies such as omalizumab, mepolizumab, and reslizumab where available.\(^{26}\)

Consider prescribing lower carbon inhalers

- Encourage practitioner behaviour change to favour DPIs (and SMIs) over pMDIs.\(^{19,27}\) A post hoc analysis of 2236 patients in England showed reduced asthma symptoms and greater productivity in daily activities in patients switching from pMDI to DPI.\(^{27}\)

- Assess for suitability to use DPIs. DPIs require a deep, quick inhalation and may not be suitable for all patients. Young children and frail older adults, in particular, may not have the technique or inspiratory capacity to achieve this (consider objective testing with a peak flow measuring device if there is doubt). In one UK asthma service, 93.7% of adult patients achieved necessary peak inspiratory flow for high resistance DPIs.\(^{28}\) A review of studies across Europe, Japan, Argentina, and the US that included children as young as 3 years old concluded that the evidence supports the efficacy of DPI in treating asthma and chronic obstructive pulmonary disease irrespective of patient age, even during acute exacerbations.\(^{29}\)

There is international variation in the age deemed suitable for DPI use: for example, in the UK this is age 12 years, whereas in Finland children as young as 6 years are recommended DPIs.\(^{30}\)

- When choosing inhalers, make shared decisions with patients after discussing the patient’s ability to use the device effectively, preference, their ability to maintain effective inhaler technique and the environmental impact. This is reflected in a NICE decision aid on asthma inhalers and climate change.\(^{31}\) Avoid blanket switches (where patients are not involved in the decision, merely informed of the switch), which include a change of device or active ingredient, as these can be unsafe and disempowering for patients.

- In a survey of 12 145 UK asthma patients, although 65% were unaware of the carbon footprint of pMDIs, 60% of pMDI users would consider changing device for environmental reasons and 85% thought asthma patients should be encouraged to use more environmentally friendly inhalers.\(^{32}\)

However, always discuss environmental impact collaboratively and sensitively. It is important that patients do not stop their treatment due to concerns about its environmental impact. It is the responsibility of healthcare systems, not individuals, to reduce the environmental impact of care. Be warned that concern about clinical risks from changes in practice that are not evidence based can lead to inaction and persisting poor clinical and environmental outcomes.\(^{1,33}\)

- Consider cost as part of a wider shared decision making process, as it might be a barrier to change, although many inhaler switches are at least cost-neutral. If a switch to a DPI is more expensive, consider the full cost of care\(^{34}\) because, if control is improved with increased use of inhaled corticosteroid, then any increased cost may be offset by the reduced need for multiple SABAs and by reduced exacerbations. Nevertheless, in some countries, including where patients directly purchase their medications, the cost of DPIs can be a barrier.\(^{34}\)

Consider opportunities to reduce the carbon footprint of asthma care even for those remaining on pMDIs

- Prescribe fewer puffs of a higher strength inhaler as this reduces the amount of propellant used (see box 3).

- Prescribe a SABA pMDI with a lower carbon footprint: one which uses a low volume of propellant (such as Salamol or Airomir) in place of inhalers that use a high volume of propellant (such as Ventolin).

- Avoid the highest carbon footprint inhalers (those containing propellant HFA227ae, see table) unless no alternative exists.

**Box 3** Hypothetical case where environmental impact is reduced for a patient who requires pMDI

**Clinical scenario**—An adult patient with no recent exacerbations and who is open to change in order to reduce the environmental impact of their asthma care is found to be able to use pMDI most effectively.

**Previous medication regimen**—Qvar (beclomethasone dipropionate) pMDI 50 μg 2 puffs twice a day and Ventolin (salbutamol) pMDI 100 μg 1 puff as required.

**New medication regimen**—Qvar (beclomethasone dipropionate) pMDI 100 μg 1 puff twice daily and Airomir (salbutamol) pMDI 100 μg 1 puff as required.

**Estimated carbon savings per year**—404 kg CO\(_2\)e (equivalent to ~2035 km (Oxford, UK, to Rome, Italy) driven in a petrol car).

pMDI = pressurised metered dose inhaler, CO\(_2\)e = carbon dioxide equivalent.
EDUCATION INTO PRACTICE

• What dosing regimens and lower carbon footprint options could you offer to asthma patients who continue to need pressurised metered dose inhalers?
• How do you create asthma care plans that optimally manage symptoms with a reduced need for short acting β agonist inhalers?
• What could your practice do to campaign for changes to prevent asthma?

• Prioritise non-pharmacological interventions such as allergen and air pollution avoidance, physical activity, and immunisation.
• Reduce the frequency of automatic repeat prescriptions for SABA inhalers, or change prescriptions to be available only on request.
• Encourage patients to use every dose in their inhalers (facilitated by dose counters on inhalers).

Campaign for system changes, innovation of inhaler design, and implementation of recycling schemes

• Engage national and regional leaders to drive change as international policy alone is unlikely to deliver the urgent change required.
• Implement schemes for recycling or incineration of all inhalers to ensure any remaining HFC is salvaged or destroyed. In England, community pharmacies are required to advise patients to return inhalers to pharmacies for disposal (currently, incineration is not yet linked to recycling). A pilot postal scheme in Leicestershire, England had 20,049 inhalers returned and recycled over 12 months, saving an estimated 119.3 tonnes of CO₂e.
• Actively amplify the voice of clinicians and patients—pharmaceutical companies have an opportunity to innovate device design to reduce environmental impact but are unlikely to do so without this demand. Pharma-led solutions could include: use of lower GHG HFC propellants in pMDIs, such as HFA 152a and HFO-1234ze which are in development; reducing plastic use (for all inhalers) to protect ocean health; and the adoption of circular economy principles in which waste and pollution are designed out of inhaler devices and materials can be recycled and reused.

Place a greater focus on asthma prevention

• Collaborate with patients to advocate for policies and interventions to prevent asthma by reducing indoor and outdoor air pollution, strengthening tobacco control policies, improving housing, and addressing all causes of health inequalities.
• Work to match resource allocation, particularly in terms of quality improvement project support, staff time, and research funding, with the urgency of the need for change.

GLOBAL EFFORTS TO REACH NET ZERO FOR ASTHMA CARE

• To reach net zero, low cost, low carbon inhalers will need to be made available in all countries. The WHO includes budesonide and budesonide-formoterol in the list of essential medicines for asthma. There are ongoing efforts to make such medications available in functioning health systems at all times, in appropriate dosage forms, of assured quality, and at prices individuals and health systems can afford.
• A retrospective analysis of data from hospitalisations in the Brazilian public health system of individuals with asthma aged from 1 to 49 years, showed that, since the provision of free access to beclometasone and salbutamol inhalers in 2011, there has been a reduction in hospitalisations for asthma.
• Inhaled corticosteroid is under-prescribed and underused in India, contributing to an estimated 42% of global asthma deaths. An editorial in Lung India suggests that, if corticosteroid or corticosteroid-fomoterol inhalers were to come under the Drug Price Control Order Act in India, access to them would improve.
• Both NHS England and Scotland have committed to net zero by 2040 for the emissions they control. Unfortunately, NHS England recently removed financial incentives that rewarded general practitioners for prescribing lower carbon inhalers.
• National and local prescribing guidelines are an opportunity to address climate change in clinical practice. National guidance in Finland, New Zealand, and the UK specifically recommend taking into account the carbon footprint of inhalers when prescribing for asthma. In Finland, dry powder inhalers are recommended as the primary form of administration for most school age children and adults.
The study included 130 people with painful diabetic neuropathy. They were being treated at 13 primary and secondary care centres in the UK.

People were randomly allocated to one of three treatment pathways:

- Amitriptyline with pregabalin, if needed
- Duloxetine with pregabalin, if needed
- Pregabalin with amitriptyline, if needed.

People took the first drug for six weeks; the second was added for a further 10 weeks if the pain was not controlled. They then moved on to another pathway. For each pathway, the dose of the drug was gradually increased to the level a person could tolerate (without the side effects becoming too much).

The study design intended for people to complete the pathways one after the other (in a randomised order) for approximately 50 weeks overall. Some people dropped out of the trial itself, but 84 completed at least two pathways.

What did this study do?

The researchers found that, during the final week of each pathway:

- All three treatment pathways reduced pain to a similar degree
- Treatments in combination provided additional pain relief in some people whose pain did not respond to one medication alone.

Sleep and quality of life were improved to a similar degree for all three pathways; and the costs for each of the pathways were roughly the same.

Side effects were as expected for each drug. For instance, several people experienced dizziness with pregabalin, nausea with duloxetine, and dry mouth with amitriptyline. The three pathways had similar numbers of serious side effects. Combination treatment was generally well tolerated, and few people discontinued treatment. People were most likely to continue with pregabalin supplemented by amitriptyline.

The study included people with painful diabetic neuropathy. But many others experience painful neuropathy from other causes (such as cancer or multiple sclerosis).

One of the study’s strengths is that it reflects clinical practice, the researchers say. Most patients start taking one medication and need to begin taking another after a few months if their pain is still not managed.

The study took longer to carry out than other clinical trials, which may partly explain why one in three people did not complete the planned 50 weeks.

Why is this important?

The study should reassure clinicians that any of these drugs, or drug combinations, can provide effective pain relief. Combination treatment was safe, and helped people whose pain was not adequately managed with one medication. All the trialled combinations of pregabalin, amitriptyline, and duloxetine provided similar pain relief.

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What’s next?

Clinicians could discuss the benefits and drawbacks of each medication with patients, to explore their preferences. The best treatment pathway for an individual may depend on the side effects people experience.

The study was not set up to compare single versus combination therapy. However, the findings suggest that people whose pain is not managed adequately with one medication could be treated with two, the researchers say.

This study included people with painful diabetic neuropathy. But many others experience painful neuropathy from other causes (such as cancer or multiple sclerosis).
TENS machine overuse

This is reticulated hyperpigmentation with multiple erosions and superficial ulceration on the back of a woman in her 50s. She had been using a transcutaneous electrical nerve stimulation (TENS) machine for several months to relieve back pain from multiple spinal compression fractures and regularly left the device in place overnight.

Erythema ab igne was diagnosed as well as acute thermal burns. This condition is a complication of direct and prolonged exposure to heat that can occur anywhere on the skin. Patients with longstanding erythema ab igne are at risk of developing squamous cell and Merkel cell carcinoma. During review of their pain management, patients should be counselled about the appropriate use of TENS machines.

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Patient consent obtained.

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If you would like to write a Minerva picture case, please see our author guidelines at bit.ly/29HCBAL and submit online at bit.ly/29yyGSx

β blockers in stable ischaemic heart disease

Although β blockers substantially reduce all-cause and cardiovascular mortality in people who have survived an acute myocardial infarction, their benefit is less clear in people with stable coronary artery disease. In an observational study of 30,000 patients in Ontario, Canada, all diagnosed with coronary artery disease after elective angiography, slightly fewer than half were prescribed a β blocker. Compared with people not prescribed a β blocker, their absolute risk of a composite endpoint of all-cause mortality and hospitalisation for heart failure or myocardial infarction was reduced by around 2% (JACC doi:10.1016/j.jacc.2023.04.021).

Residual insulin secretion in people with type 1 diabetes

Type 1 diabetes results from autoimmune destruction of pancreatic β cells, but the destruction is often incomplete, according to data from Finland. Although children with multiple autoantibodies and HLA risk genotypes progressed to absolute insulin deficiency rapidly, many people with type 1 diabetes had detectable serum C-peptide concentrations decades after the diagnosis. The presence of serum C-peptide was associated with lower HbA1c and cholesterol concentrations, and with fewer microvascular complications (Lancet Diabetes Endocrinol doi:10.1016/S2213-8587(23)00123-7).

Children breastfed for longer were more likely to achieve high marks

Breastfeeding and educational achievement

Children who had been breastfed tended to obtain better examination results at the age of 16 than children who hadn’t been breastfed, according to the UK’s Millennium Cohort Study. A dose-response relation was present, where children breastfed for longer were more likely to achieve high marks. The investigators adjusted for a wide range of socioeconomic variables, which included a measure of maternal cognitive ability, but the possibility of residual confounding remains (Arch Dis Child doi:10.1136/archdischild-2022-325148).

Guillain-Barré syndrome

An international collaboration that gathered data on 1,200 patients with Guillain-Barré syndrome reports that examination of cerebrospinal fluid (CSF) showed albuminocytological dissociation, defined as an increased protein level (>0.45 g/L) in the absence of elevated white cell count (<50 cells/μL), in around 70%. High CSF protein levels were associated with the demyelinating subtype of the condition and severe disease. Patients with Miller Fisher syndrome or predominantly distal muscle weakness tended to have lower CSF protein levels (Neurology doi:10.1212/WNL.0000000000007282).

Journal guidelines

Biomedical journals each have their own idiosyncratic requirements for manuscript submission. Most authors spend time and effort formatting their papers to meet their chosen journal’s guidelines because they believe, probably correctly, that this makes acceptance more likely. Of course, if the paper is rejected, as it often is, they have to spend more time reformatting it for submission to another journal. An estimate of the time spent by scientists worldwide reformatting papers sent to biomedical journals puts the cost of this largely wasted effort at more than $200m each year (BMC Med doi:10.1186/s12916-023-02882-y).

Measures to reduce traffic speed

A longitudinal study from Montreal, Canada, finds only weak evidence that traffic calming measures, such as curb extensions and speed humps, reduce fatal or serious collisions among road users. However, traffic calming interventions were predominantly implemented on local roads, where collisions are only one third as frequent as on arterial roads. An analysis restricted to intersections on local roads did show a worthwhile reduction in collisions attributable to calming measures. The next challenge is to invent effective traffic calming for arterial roads (Am J Epidemiol doi:10.1093/aje/kwad136).

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