Biomanufacturing has the potential to reduce demand for petrochemicals and mitigate climate change. Recent studies have also suggested that some of these products can be net carbon negative, effectively removing CO2 from the atmosphere and locking it up in products. This review explores the magnitude of carbon removal achievable through biomanufacturing and discusses the likely fate of carbon in a range of target molecules. Solvents, cleaning agents, or food and pharmaceutical additives will likely re-release their carbon as CO2 at the end of their functional lives, while carbon incorporated into non-compostable polymers can result in long-term sequestration. Future research can maximize its impact by focusing on reducing emissions, achieving performance advantages, and enabling a more circular carbon economy.

Importance of biomanufacturing to climate change mitigation
Rising oil prices and the climate crisis are motivating many countries to once again evaluate their reliance on petroleum-derived liquid fuels and petrochemicals [1,2]. While electrification is likely to reduce demand for gasoline and potentially diesel fuel, petrochemical production has fewer low- or zero-emission alternatives [3]. Biomanufacturing (see Glossary) offers the promise of replacing these fossil-derived chemicals and materials with renewable drop-in or performance-advantaged alternatives, while also locking atmospheric carbon up in stable forms such as building materials and plastics (many of which are ultimately landfilled after use). A number of recent papers have presented new biomanufacturing processes accompanied by a claim that they are (or can be) net carbon negative [4–7]. This raises a few questions. First, are these processes truly carbon negative? Second, is the potential magnitude of carbon removal in biomanufacturing meaningful relative to what is required to stabilize the climate? Third, how can synthetic biology and metabolic engineering research be most effectively leveraged as part of broader efforts to make manufacturing more sustainable? To answer these questions, it is useful to discuss some target molecules that can be made biologically, what applications they are used for, and how carbon flows through feedstocks, microbial production systems, and products in typical biomanufacturing systems.

State of biomanufacturing and potential to reduce petrochemical consumption
Biomanufacturing is defined as manufacturing that uses biological systems, including microbes, plant cells, and enzymes, to produce commercially relevant molecules [9]. Biomanufacturing already plays an important role in the production of pharmaceuticals, flavors and fragrances, and cosmetic additives [9]. However, these are small-volume applications. Achieving meaningful net-negative emissions requires an entirely different scale of production than what is achievable in specialty chemical and pharmaceutical markets. As such, this review will focus primarily on commodity chemicals/products.

There are so far only a small number of microbially produced commodity chemicals, including 1,3-propanediol, 1,4-butanediol, isobutanol, farnesene, lactic acid, and succinic acid [10].

Highlights
Future biomanufacturing studies must recognize the important distinction between greenhouse gas mitigation relative to the status quo and processes that result in true carbon dioxide removal.

The potential for biomanufacturing to serve as a carbon dioxide removal strategy is limited because many target products are re-oxidized to CO2 at the end of their useful life, yet this is not accounted for in recent studies.

Many precursors to commodity polymers can be made biologically and polymers offer the largest opportunity to achieve carbon dioxide removal through biomanufacturing.

Bio-based materials do reduce reliance on petroleum and may offer performance advantages relative to conventional petrochemical alternatives.

Instead of focusing on net carbon negativity, future research should focus on using biotechnology to enable a more circular and sustainable carbon economy.

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However, there has been progress in the development and optimization of new biomanufacturing routes; significant strides have been made in gas fermentation processes that utilize gases that are either low-value or waste products, such as untreated biogas, gasified crop or forest residues, and steel mill waste gas [6,11,12]. Some commodity chemicals/polymers, such as polyhydroxybutyrate (PHB), muconic acid, catechol, limonene, and latex, can also be accumulated in plants and extracted as part of a biomanufacturing system [13,14].

The question of whether most bio-based commodity chemicals and materials can reduce reliance on oil and gas has a clear answer: yes. The majority of commonly used polymers and industrial solvents are produced from petroleum and/or natural gas and, while aerobic microbial production processes can be electricity intensive, their life-cycle consumption of oil and gas is generally lower than the conventional petrochemical alternative. A study from the Argonne National Laboratory reported that reductions in total fossil energy consumption between fossil and bio-based propylene glycol, 1,3-propanediol, acrylic acid, polyethylene, succinic acid, isobutanol, and 1,4-butanediol ranged from 24% to 76% [15]. The question of whether biomanufacturing can and should be claimed as carbon negative is more complex and requires knowledge of how carbon flows through these systems into the use phase and end of life of the final products.

Emissions mitigation versus carbon-negative products

There is consensus among energy systems modelers and climate modelers that, in order to slow and ultimately stop anthropogenic climate change, most sectors must reach net-zero greenhouse gas (GHG) emissions, through a combination of renewable electricity generation, energy storage, electric transmission infrastructure investments, hydrogen production and use, and production of renewable liquid fuels [3]. This outcome is sometimes referred to as decarbonization, although it does not literally mean that all carbon is eliminated from the systems. Carbon-based fuels from renewable feedstocks can be part of a decarbonization strategy. These measures are all a form of emissions mitigation. In other words, they can replace high(er) emitting technologies that we rely on today through technological advancements and infrastructure investments, thus reducing or in some cases eliminating emissions while maintaining similar levels of service (e.g., mobility, lighting, and thermal comfort in buildings). In the context of biomanufacturing, studies have repeatedly indicated that bio-based chemicals can reduce life-cycle GHG emissions when compared against conventional petrochemicals [7,15–18].

In contrast to mitigation, a carbon-negative technology will continue to achieve net CO₂ removal from the atmosphere regardless of how much emissions mitigation has occurred in the broader economy [19]. In the near term, there is no inherent benefit to removing CO₂ relative to avoiding a comparable mass of emissions. The impact on atmospheric CO₂ concentrations and climate is identical. Policy makers and industry decision-makers are best served by devoting available resources to the most cost-effective options for avoiding or removing CO₂. However, net carbon removal is deemed necessary to reach long-term climate stabilization by compensating for sectors whose emissions are too difficult and/or costly to decarbonize [20]. To compensate for those residual emissions, and halt or reverse anthropogenic climate change, humans must make long-term investments in processes that remove CO₂ or other GHGs from the atmosphere and sequester them in a stable form. This is why carbon-negative technologies are of specific interest to the research community.

Carbon uptake routes in biomanufacturing

There are two primary mechanisms for removing CO₂ from the atmosphere: direct air capture (DAC) and uptake of CO₂ by plants. Other options do exist, such as enhanced weathering [21],
although these are earlier in their development. DAC offers a straightforward value proposition: removal of CO₂ for a price (and an energy footprint). It also requires geologic CO₂ storage or some path to CO₂ utilization that does not re-emit carbon to the atmosphere, such as biological conversion by algae or gas fermentation. As long as the cost of DAC exceeds the cost of CO₂ emissions mitigation strategies on a per-tonne basis, emissions mitigation should be prioritized over DAC. However, making early investments in research, development, and demonstration is important to ensure that future scale-up of CO₂ removal can occur. In contrast to DAC, CO₂ uptake by plants and the use of these feedstocks in biomanufacturing offer greater economic co-benefits in the form of saleable products, but less certainty as to the scalability and long-term stability of carbon storage. Plants will fix carbon in the form of cellulose, hemicellulose, lignin, starch, sugars, proteins, pectins, and other compounds. These forms of carbon are not stable and, in the absence of intervention, will decompose to CO₂. Deep-rooted plants may also sequester carbon to soils for some finite period of time [22], although soil carbon sequestration is outside the primary focus of this review.

Plant biomass, once harvested, can serve as the input to biomanufacturing processes. In many biomanufacturing processes, sugars serve as the feedstock, and these sugars are consumed by microbes capable of producing the products of interest or intermediates that can be chemically upgraded to final products. Lignin-derived compounds or an intermediate produced from plant material, such as biogas from anaerobic digestion or syngas from gasification, may also be used as a feedstock [7,23]. Biogenic (meaning nonfossil) carbon entering the facility in the form of sugars or other bioavailable compounds will be incorporated into the product, some will be emitted as CO₂ during bioconversion, additional carbon will be incorporated into cell mass, and some residual carbon will remain in wastewater for further treatment. The two primary opportunities for sequestration lie in the CO₂ waste stream from bioconversion (and potentially wastewater treatment), if captured, and the final product itself.

When exploring the potential for capturing the waste CO₂ stream from bioconversion, there is a crucial distinction between processes that operate anaerobically, those that operate aerobically by sparging with pure oxygen, and those that operate aerobically by sparging with air. Anaerobic processes and those sparged with pure oxygen produce a nearly pure CO₂ stream that can be captured and sequestered without the use of amine scrubbers, membrane separation, or other processes required to separate CO₂ from N₂ and other gases in combustion flue gases [24]. Cell-based meat production, for example, may sparge bioreactors with O₂-enriched air and, as a result, can offer an opportunity for (comparatively) low-cost carbon capture and sequestration [25]. Aerobic processes, which are more common for the production of many advanced bioproducts, produce a more dilute CO₂ waste stream that will require scrubbers or some other separation as described previously. In either case, once this CO₂ is captured, it must be pumped to underground storage or converted into some other stable form. Recent research has explored biological conversion of CO₂ to products provided an energy source is available (e.g., H₂ or CH₄) [23]. While this does not guarantee net carbon negativity, it does offer the possibility of GHG emissions reductions and another useful life for carbon that would likely otherwise be emitted.

Once the feedstock, whether it is plant material or a gaseous input, is converted to a product, the ultimate use and disposal (or recycling) of that product is the key to whether it will sequester carbon or simply release CO₂ back to the atmosphere. This is the distinction between achieving a more circular carbon economy and achieving net carbon negativity. Bio-based materials whose carbon is re-oxidized to CO₂ at their end of life still mitigate climate change; that carbon will be taken up through re-growth of feedstocks. However, the only way to permanently (or semi-
permanently) remove carbon from the atmosphere is to sequester it underground or in some other stable form. Table 1 summarizes some key chemicals that can be produced biologically for use in materials, with a focus on products that currently rely on petrochemicals. It also lists the likely fate of different products once they reach the end of their useful life. Some products and precursors cannot yet be directly biologically produced. If its production requires one or more chemical upgrading steps, it is not included in Table 2. For example, terephthalic acid can only be produced through chemical or hybrid biological–chemical approaches [26], although some have suggested that there may be novel biological routes developed in the future [27].

Table 1. Biomanufactured chemicals, global demand, carbon content, likely fate of carbon by application type, and recent studies on biomanufacturing processes

| Biomanufactured chemical | Approximate annual global demand (million tonnes/year) | Carbon content (mass %) | Market applications | Typical fate(s) of carbon at end of life | Refs a |
|--------------------------|--------------------------------------------------------|-------------------------|---------------------|----------------------------------------|-------|
| Ethylene                 | 165 (in 2017)                                          | 86%                     | Polymers, precursor to many industrial chemicals, hormone for plant ripening/flowering | Polymers: landfilled, incinerated, leaked to environment | [28–31] |
| Ethanol                  | 98 (in 2021)                                           | 52%                     | Fuel, solvent, food, pharmaceuticals | Compostable polymers: landfilled, incinerated, leaked to environment, oxidized to CO₂ during composting | [32,33] |
| Styrene                  | 28 (2019)                                              | 92%                     | Polymers | Solvents: primarily oxidized to CO₂ upon disposal through incineration or other destructive treatment | [34–37] |
| Monoethylene glycol (MEG) | 25 (in 2020)                                          | 39%                     | Polymers, engine coolants, antifreeze | Lubricants: primarily oxidized to CO₂ (after recycling), some automotive lubricants incorporated into asphalt after disposal | [38–40] |
| Propylene glycol         | 2.7 (in 2020)                                          | 47%                     | Polymers, food, pharmaceuticals, e-cigarettes | Lubricants: primarily oxidized to CO₂ (after recycling), some automotive lubricants incorporated into asphalt after disposal | [41,42] |
| Acetone                  | 6.85 (2021)                                            | 62%                     | Industrial solvent, precursor to acrylic glass and bisphenol A | Resins/coatings: landfilled, incinerated | [6,43] |
| Isobutanol               | 6.7 (in 2021)                                          | 66%                     | Resins and coatings, solvent, plasticizers, fuel | Pharmaceuticals, food, personal care, clearing agents: oxidized to CO₂ (a fraction of landfilled food waste will be emitted as CH₄ from landfills) | [44–48] |
| Acrylic acid             | 6.3 (2020)                                             | 50%                     | Polymers | Fuels: oxidized to CO₂ | [49,50] |
| Adipic acid              | 3.9 (2018)                                             | 49%                     | Polymers, food and pharmaceutical additive | | |
| 1,4-butanediol           | 2.79 (2020)                                            | 53%                     | Solvent, polymers | | [55–57] |
| IPA                     | 2.15 (2020)                                            | 60%                     | Pharmaceuticals, cosmetics and personal care products, solvent and cleaning agent | | [6,58] |
| Lactic acid              | 1.39 (2021)                                            | 40%                     | Polymers, pharmaceuticals, cleaning products | | [59–61] |
| Sebacic acid             | 0.2 (production capacity, 2020)                        | 59%                     | Polymers, lubricants | | [62,63] |
| 1,3-propanediol          | 0.146 (2014)                                           | 47%                     | Polymers, solvent | | [57,64–68] |
| Suconic acid             | 0.016–0.03 (in 2016)                                   | 41%                     | Polymers, food, pharmaceuticals, solvent production | | [69–71] |
| Farnesene                | 0.00815 (2015)                                         | 88%                     | Lubricants, cosmetics, fragrances, fuel | | [72,73] |
| Diamines                 | Varies by compound                                     | ~50% (varies)           | Polymers, pharmaceuticals, many others | | [74] |

aRecent studies on biomanufacturing processes.
Bio-based products as carbon sinks

For a biomanufacturing process to be carbon negative, it must sequester more carbon than it emits over the entire lifetime of the process. Usually, this means biogenic carbon is incorporated into the product that remains sequestered in some stable form through its end of life (Figure 1, Key figure). This narrows the range of products that can reasonably be deemed carbon negative. Solvents, for example, (Table 1) are commonly combusted at their end of life or discharged to a wastewater treatment plant where their carbon will ultimately be oxidized to CO₂ and released into the atmosphere. Two recent studies are notable for having claimed net carbon-negative production. Liew and colleagues [6] published net-negative carbon footprints for acetone and isopropanol (IPA), which are primarily used as solvents but can be used in other applications. Wang and colleagues [4] also claimed a negative carbon footprint for production of a benzene, toluene, ethylbenzene, and xylene (BTEX) product mixture. In both cases, the studies used a system boundary (scope) known as cradle-to-gate (as opposed to cradle-to-grave) (see the description by Scown and Keasling [10]). In other words, they did not include the final fate of carbon in those products once they leave the production facility. If the results are used to compare a bio-based route to a fossil-based production route, the choice of system boundary is immaterial, as both products will be treated identically in their use and disposal. However, in an absolute sense, the choice of system boundaries affects the conclusions. These negative emissions values should not necessarily be interpreted as an indication that such processes will achieve net carbon removal from the atmosphere.

Table 2. Global demand and approximate carbon storage potential of commodity polymers

| Polymer resin types | Global demand 2022 (million tonnes/year)² | Projected 2030 demand (million tonnes/year)² | Approximate carbon content (mass %)³ | 2030 annual carbon sink potential: 90% landfilled (million tonnes CO₂/year)³ | 2030 annual carbon sink potential: 50% landfilled (million tonnes CO₂/year)³ | Key chemical precursors |
|---------------------|-------------------------------------------|---------------------------------------------|------------------------------------|---------------------------------------------------------------------------------|---------------------------------------------------------------------------------|------------------------|
| PET                 | 27                                        | 28                                          | 63%                                | 58                                                                              | 32                                                                              | Monoethylene glycol (MEG); terephthalic acid                                    |
| HDPE                | 61                                        | 63                                          | 86%                                | 180                                                                             | 99                                                                              | Ethylene                                                            |
| PVC                 | 56                                        | 58                                          | 38%                                | 73                                                                              | 40                                                                              | Chlorine, ethylene                                                     |
| LDPE/LLDPE          | 59                                        | 61                                          | 86%                                | 170                                                                             | 96                                                                              | Ethylene                                                            |
| PP                  | 80                                        | 82                                          | 86%                                | 230                                                                             | 130                                                                             | Propylene                                                             |
| PS                  | 23                                        | 24                                          | 92%                                | 73                                                                              | 40                                                                              | Styrene                                                              |
| PUR                 | 20                                        | 20                                          | 41%                                | 27                                                                              | 15                                                                              | Disocyanates, polyols (including 1,4-butanediol, MEG)                      |
| Fibers              | 66                                        | 68                                          | 70%³                               | 160                                                                             | 87                                                                              | MEG, terephthalic acid, acrylic acid, sebacic acid, adipic acid, caprolactam succinic acid, cellulose, 1,3-propanediol, diamines, many others |
| Other               | 110                                       | 110                                         | 66%                                | 240                                                                             | 133                                                                             | Many others                                                          |
| Total               | 502                                       | 514                                         | N/A                                | 1212                                                                            | 673                                                                             | N/A                                                                  |

Abbreviations: HDPE, high-density polyethylene; LDPE, low-density polyethylene; LLDE, linear low-density polyethylene; PET, polyethylene terephthalate; PP, polypropylene; PS, polystyrene; PUR, polyurethane; PVC, polyvinyl chloride.
²Extrapolated from 2019 global demand based on an assumed 3% annual growth rate.
³Carbon contents based on US Environmental Protection Agency data [81], except where noted.
⁴Calculated by multiplying 2030 projected demand by resin-specific fractional carbon content, fraction of resin type landfilled, and (44/12) to convert carbon mass to CO₂ mass.
⁵Calculated based on the average (mean) carbon contents of PET, nylon 6, and acrylic.

Bio-based products as carbon sinks

For a biomanufacturing process to be carbon negative, it must sequester more carbon than it emits over the entire lifetime of the process. Usually, this means biogenic carbon is incorporated into the product that remains sequestered in some stable form through its end of life (Figure 1, Key figure). This narrows the range of products that can reasonably be deemed carbon negative. Solvents, for example, (Table 1) are commonly combusted at their end of life or discharged to a wastewater treatment plant where their carbon will ultimately be oxidized to CO₂ and released into the atmosphere. Two recent studies are notable for having claimed net carbon-negative production. Liew and colleagues [6] published net-negative carbon footprints for acetone and isopropanol (IPA), which are primarily used as solvents but can be used in other applications. Wang and colleagues [4] also claimed a negative carbon footprint for production of a benzene, toluene, ethylbenzene, and xylene (BTEX) product mixture. In both cases, the studies used a system boundary (scope) known as cradle-to-gate (as opposed to cradle-to-grave) (see the description by Scown and Keasling [10]). In other words, they did not include the final fate of carbon in those products once they leave the production facility. If the results are used to compare a bio-based route to a fossil-based production route, the choice of system boundary is immaterial, as both products will be treated identically in their use and disposal. However, in an absolute sense, the choice of system boundaries affects the conclusions. These negative emissions values should not necessarily be interpreted as an indication that such processes will achieve net carbon removal from the atmosphere.
Some bioproducts do have greater potential to lock carbon away in a stable form. Automotive lubricants may be recycled, with some portion diverted for use as a low-value fuel, and an additional fraction incorporated into asphalt. In the case of lubricants, it makes sense to partially credit this carbon going to asphalt as being sequestered, with practices likely varying by region [75]. The fate of bio-based precursors to polymers, such as polyethylene terephthalate (PET), high-density polyethylene (HDPE), low and linear low-density polyethylene (LDPE and LLDPE, respectively), polypropylene (PP), and nylon will depend on where the materials are ultimately used. In Germany, for example, 61% of plastics were incinerated as of 2016, 39% were recycled, and <1% were landfilled [76]. By contrast, >90% of plastics in the USA are landfilled. This can make a generalized carbon accounting for bio-based plastics challenging. The same material may be carbon negative in one country and not in another. Compostable polymers, if successfully
broken down in commercial composting facilities, will also release their carbon back into the atmosphere. However, evidence suggests that many do not; polylactic acid (PLA) does not break down sufficiently in commercial composting operations and must be screened out and landfilled [77]. If landfilled, the majority of carbon in PLA will remain sequestered.

Polymers likely represent one of the largest opportunities for biomanufacturing to sequester carbon in stable forms, assuming the majority of material is not incinerated or fully broken down through composting. Table 2 shows the most common commodity polymers, the carbon contained in total global production for each type, and the primary chemical precursors. Future demand is estimated based on the simplifying assumption of 3% annual demand growth each year across all polymer types. Only a subset of these materials can currently be replaced with bio-based alternatives. However, estimating the total carbon storage potential is useful for gauging the relative significance of bio-based polymers in broader climate change mitigation efforts. For perspective, 2021 global energy-related CO2 emissions were estimated to be 34.9 Gt [78]. The simple calculations in Table 2 suggest that, even if all polymer products (plastics, rubbers, fibers, and so forth) were produced from bio-based materials and then 90% of those products were landfilled, this strategy would sequester approximately 1.2 Gt CO2 annually, or 3.4% of current annual emissions. If recycle rates for these polymers increase, there will be a proportional decrease in the potential for carbon sequestration, effectively creating a circular carbon economy rather than net carbon removal. Achieving a 50% recycle rate for polymers would reduce the sequestration potential to around 0.67 Gt CO2/year or 1.9% of global energy-related CO2 emissions (Table 2). It is worth noting that treating plastics as a carbon sink rather than focusing on improving recycle rates has other serious implications. This point is echoed in a recent article by Meys and colleagues [79], which focuses on the goal of achieving net carbon-neutral plastics through increased circularity rather than attempting to treat plastics as a carbon sink. Accumulation of waste in landfills limits the future use of that land for other beneficial purposes, while improper disposal of plastic waste causes the accumulation of microplastics in the environment, the health implications of which are still not fully understood [80].

Building materials are another potentially interesting carbon sink, although the role for biomanufacturing is still evolving. The largest opportunities for carbon sequestration are in the bulk materials that can include bio-based materials: timber and concrete. Bio-aggregates such as hemp or wood can be incorporated into concrete. Much like polymers, there are potential tradeoffs between treating building materials as carbon sinks versus designing buildings for increased recyclability and waste reduction. The dual (and sometimes competing) priorities of increased recyclability, carbon sequestration, and improved use-phase performance are reflected in recent selections for the US Advanced Research Projects Agency–Energy (ARPA-E) Harnessing Emissions into Structures Taking Inputs from the Atmosphere (HESTIA) program[80], which includes projects that aim to develop everything from cellulose-mycelium composites to bio-based adhesives for oriented strand board and bio-based concrete additives/aggregates. Increasing sequestration of biogenic carbon in buildings by using timber in large commercial or multi-family residential buildings, in contrast to some of the materials discussed previously, is occurring and is likely to continue. A recent analysis explored the magnitude of carbon that might be sequestered annually if timber use were increased in construction in the form of glue-laminated (glulam) beams or cross-laminated timber (CLT) panels [82]. In a business-as-usual scenario, only 0.037 Gt CO2/year would be sequestered and if timber use were dramatically increased in urban structures, as much as 2.5 Gt CO2/year could be sequestered [82]. These values do not account for any wood that is combusted or otherwise oxidized in construction and demolition waste each year. There
are additional efforts to develop materials with higher carbon contents; for example, biochar can be incorporated into building materials to increase the total carbon content to around 90% [82]. The field of biomanufacturing carbon-negative building materials is rapidly developing and, given recent research investments, some leading strategies may emerge in the next 5 years.

**Concluding remarks and future perspectives**

Based on the market sizes and target molecules, biomanufacturing seems poised to play a non-negligible, but limited, role in capturing and sequestering carbon from the atmosphere. This role may expand if CO₂ capture is integrated with new biomanufacturing facilities on a large scale (see **Outstanding questions**) or if biomanufactured materials gain substantial uptake in markets for building materials. Readers should be wary of claims of net carbon-negative production if the final product is not a stable material that will be sequestered in a long-lived application or stored underground, as these values are often the result of incomplete system boundaries in life-cycle assessments rather than true net carbon removal. Solvents, for example, will not offer long-term, stable carbon storage. In terms of final product options, polymers present the largest near-term carbon sequestration opportunity, although this will require continued landfilling of large quantities of waste in exchange for modest climate benefits.

Rather than focusing on the narrow goal of achieving net carbon negativity, scientists, industry leaders, and policy makers should think more broadly about how biotechnology can enable a more circular and sustainable carbon economy. In the near term, GHG mitigation strategies are equally impactful when compared with net-negative options. Additionally, the benefits of reducing reliance on petrochemicals extend well beyond the climate to ecological, human health, and geopolitical impacts. Refocusing biomanufacturing on achieving emissions reductions, creating a circular carbon economy, and providing a wide array of performance-advantaged products will ensure that biotechnology has a leading role to play in a more sustainable future.

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**Declaration of interests**

None are declared.

**Resources**

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