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## A perspective of precision medicine in the management of COVID-19

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#### Abstract



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The idea of precision medication is turning out progressively to be famous. The utilization of enormous information, genomics and other "omics" like metabolomics; proteomics and transcriptomics; could soon cause the fantasy of personalized medication to turn into a reality. The most recent advancements in precision medication permit the adjustment of helpful approaches in various pathologies based on the particular molecular interpretation of the patient. Precision medication (PM) represents a new way of thinking about infection detection; prevention and treatment. The use of PM grounds in an emerging COVID virulent disease is becoming more prominent. Various discoveries revealed that severe acute respiratory disorder COVID-2 (SARS CoV-2) is accountable for the Coronavirus disease -2019 (COVID-19), which caused slew of procedures to restrict viral spread, affecting people's habits and lifestyles. According to the viral genomic sequencing, the SARS-CoV-2 spike protein uses angiotensin-converting enzyme 2 (ACE2), which is established on the ciliated epithelial cells of the human lungs as its particular receptor. In this specific situation; precision medication is an integrative helpful methodology that thinks about conventional elements (i.e. age, sex, clinical aggregate), just as arising hereditary qualities and connections with natural components, to individualize prevention; diagnosis, treatments and prognosis. The aim of this review was to summarize how precision medicine is impactful in the management of COVID-19.

Keywords: Metabolomics, Proteomics, ACE2, Transcriptomics

#### 1. Introduction

Coronaviruses (CoVs) have emerged as one of the most common microorganisms in the recent outbreaks of respiratory sickness; indicating a serious global health issue (de Wit et al., 2016). People are infected with four different Coronaviruses, all of which cause common colds. Severe acute respiratory syndrome (SARS) outbreaks were caused by two species, one in China in 2002-2003 by Severe acute respiratory syndrome coronavirus (SARS CoV), and the other by the Middle east respiratory syndrome coronavirus (MERS CoV); both of which emerged in 2012 and demonstrated limited human-to-human transmission but a high case fatality rate (CFR), as highlighted by de Wit et al., (2016). SARS-CoV-2; is a coronavirus that causes severe acute respiratory symptoms; emerged in China around the end of 2019 and spread quickly over the world, producing the Coronavirus disease 2019 (COVID-19) epidemic (Crisci et al., 2020). Following an initial pause, COVID-19 cases took a stunning turn and spread over the world; affecting nearly 1.8 million people in 185 countries on 12th April, 2020 (Crisci et al., 2020). PM (personalized medicine) is a novel disease management paradigm that is rapidly gaining acceptance (Sagner et al., 2017). PM applies ongoing development in omic sciences; molecular sciences and bioinformatics for the diagnosis and dealing of mental health problems. A previous study conducted by Hamburg and Collins, (2010) revealed that this innovative methodology focuses on four essential concepts in addition to drug sensitivity to pain and disease. The importance of a precision strategy in the final selection of medication for clinical treatment of COVID-19 including; infection prevention, control measures and supportive care is highlighted in this study, which is likely critical in the management of the COVID-19 pandemic.

Prediction which is the part of precision medicine is the process of anticipating the occurrence of diseases by looking at risk factors, lifestyle factors and societal variables. Prevention refers to proposing activities that can delay the progression of the pathology before the primary symptoms appear, as well as completing auxiliary anticipation once the illness has been subsided. Personalization involves investigating the hereditary, sub-atomic and specific components of every person and microorganism; prescribing the best restorative methodology adjusted to their situation (Sagner et al., 2017). The biomedical research; academic institutions, wellness experts, and most importantly the patient must all engage. In light of information on the pathophysiological components and varieties of clinical aggregates of a disease, PM seeks to categorize the finest administration techniques that allow for a precise conclusion. This encourages a preventative, proactive and restorative methodology tailored to the patient's characteristics and needs; thus advancing the patient's health (Andryukov et al., 2021). The three stages of PM include the following: (1) Pathophysiology; recognizable proof of molecular components of the disease and its variations; (2) Prediction/findings; recognition of biomarkers and explicit indicative apparatuses, and (3) the executives; obstructing/meddle those systems for anticipation or for potential treatment (Merad and Martin, 2020). The World Health Organization (WHO) classified COVID-19 as a pandemic on March 11<sup>th</sup>, 2020. According to Ye et al, (2020), the pathophysiological processes of CoV; particularly SARS CoV and SARS CoV-2, were linked to increased immune response in the host as a result of viral contamination. Ramos-Lopez et al., (2020) added that sometimes this response is unreasonable leading to inflammatory cytokine storm, causing broad tissue harm and body brokenness or dysfunction. According to Rodriguez-Morales et al., (2020), the conveyance example of other respiratory tract COVID-19 relies upon various boundaries; such as their fundamental reproductive number (R0), nature of the virus, exchange or travel in ecological conditions within the influenced nation, nature of society and population size. Asthenia, cough, fever and mild respiratory illness are some of the clinical

signs of this viral infection (Atri et al., 2020). Furthermore, acute respiratory distress syndrome, pneumonia and respiratory failure are more serious respiratory injuries that have incendiary effects on adipokines and on the other mediators (Atri et al., 2020). Recently, Chen et al., (2020a) added that late exams have revealed the presence of hepatic, neurological, renal and cardiovascular problems in some patients. Gathering of patients that are asymptomatic or with gentle indications throughout the disease have a moderately short recuperation time (Watanabe et al., 2020). The existence of related metabolic disorders including; diabetes, obesity, hypertension, as well as age of more than 60 years, have all been recognized as risk factors for the chronicity and seriousness of COVID-19 disease (Conti et al., 2020: Gralinski and Menachery, 2020). Between 1<sup>st</sup> of January, 2020 and the 21<sup>th</sup> February. 2020; Rodriguez-Morales et al., (2020) distributed 19 investigations; the vast majority of them were from China. The patients had on average 52 years old, and men accounted for 56 % of the total. Comorbidities were present in 37 % of cases, with cardiovascular disease; hypertension, and diabetes being the most frequent, in addition to persistent liver infection, chronic obstructive pulmonary disease (COPD) and malignancies. According to Lechien et al., (2020), the most common clinical signs were; cough, fever and dyspnea. Other clear indications included myalgia, sore throat, cerebral pain, looseness of the bowels and exhaustion. One of the components had been identified as the loss of smell and taste.

#### 2. Laboratory conclusions

The most common laboratory findings of COVID-19 include; C-reactive protein, high albumin, lactate dehydrogenase (LDH), erythrocyte sedimentation rate (ESR) and compact lymphocyte count (Crisci *et al.*, 2020). Creatinine, ferritin levels and liver profile were all adjusted in the same way. <u>Huang *et al.*</u>, (2020) found that the severity of COVID-19 illness was connected to the increased D-dimer levels. Generally, 96.8 % of viral RNA was detected in blood, and the same was true in the nasopharyngeal aspirates (NPA),

as revealed by Crisci et al., (2020). On confirmation, many pneumonia patients have normal serum procalcitonin levels; however, these levels are almost always elevated in those who require intensive care unit (ICU) care (Wang et al., 2020a; Chen et al., 2020b). The numbers and percentages of lymphocytes, white blood cells and neutrophils differed dramatically between positive and negative reverse transcriptionpolymerase chain reaction (RT-PCR) cases for COVID-19/or SARS-CoV-2 patients, as recorded by Mardani et al., (2020). C-reactive protein (CRP), alanine aminotransferase (ALT), lactate dehydrogenase (LDH), urea and neutrophils (NEU) have excellent precisions in predicting cases with positive RT-PCR for COVID-19 (Goudouris, 2021).

#### 3. Virulence of SARS-COV-2

In late December 2019, experts from the Chinese Ministry of Health confirmed the death of a patient in Wuhan city who had been suffering from viral pneumonia of unknown origin. Finally, another COVID was identified as the source of COVID-19 after a brief period of late human-human transmission was hypothesized (Cruz *et al.*, 2021). The Coronaviridae family includes the tale infection, which has a large (30-kb) single-stranded positive-sense RNA genome (Crisci et al., 2020). The remaining genome encodes for core structural proteins as well as auxiliary genes, which help the virus to generate virions and change the host's reaction. According to the preliminary investigations, Li et al., (2020b); Liu et al., (2020) reported that SARS-CoV-2 is identical to its namesake virus in that the spike protein uses angiotensin-converting enzyme 2 (ACE2) as its cell surface receptor. In the human lungs, the ACE2 receptor is located on the surface of the ciliated epithelial cells, and its activation influences the infection's tropism. SARS-CoV-2 uses the host cell trans-membrane carboxy-peptidase ACE2 as a receptor to enter the cells (Sarver and Wong, 2021). By activating the S protein; Trans membrane serine protease 2 (TMPRSS2), which is a type 2 TM serine protease found on the host cell membrane; promotes viral entrance into the cell (Fig. 1). It is assumed that viral contamination requires the articulation of both ACE2 and TMPRSS2 in objective cells (Huang *et al.*, 2020). The viral load (VL) of SARS-CoV maximized 10 days after onset of symptoms; in contrast, a new study conducted by Argyropoulos *et al.*, (2020) that included 94 individuals from China's Guangzhou Eighth Individuals' Hospital recorded that SARS CoV-2 viral load peaked 0.7 days before onset of side effects; implying that transmission occurred from the start of the disease (Peiris *et al.*, 2003; Riley *et al.*, 2003). Recently, Argyropoulos *et al.*, (2020)

discovered that the analytic viral load is higher in the non-hospitalized patients, and has a significant inverse relationship with the term of indications. They added that higher viral load is observed in mild illness as opposed to severe illness; as they mirrored the time from the start of contamination. Detection of the viral genetic-material by RT-PCR in various samples; with greater sensitivity in the nasopharyngeal swab and the bronchoalveolar lavage, is the standard method for diagnosing SARS-CoV-2 infection (Goudouris, 2021).

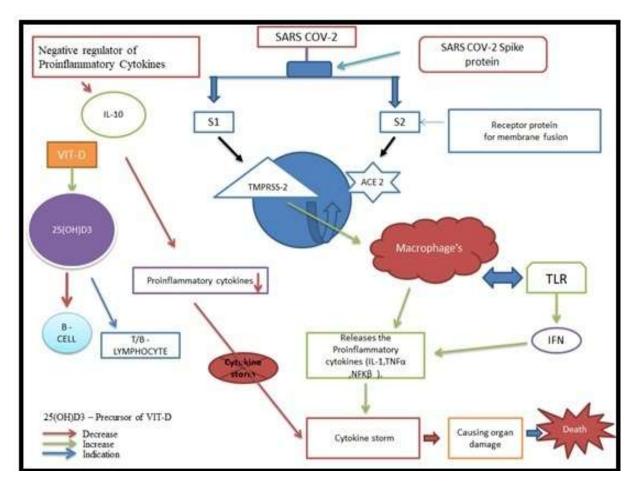


Fig. 1: Signaling pathways in response to COVID 19

Where; ACE, Angiotensin converting enzyme; TMPRSS-2, trans-membrane serine protease 2; IFN, interferon; IL-1, interleukin- 1; TLR, toll like receptor

Obesity alters the articulation of ACE2 and TMPRSS2 in the lower respiratory tract, and these changes may lead to the development of COVID-19 (Sarver and Wong, 2021). A previous study conducted by Zhou *et al.*, (2020a) also reported that TMPRSS2 is profoundly communicated in the corneal epithelium and the conjunctiva, recommending that visual surface cells could be the passage of SARS-CoV-2; just as a store for individual to-individual transmission.

As a polymorphic gene, the gene coding for the Interlukin-1 receptor antagonist (IL-1RA) has gotten a lot of interest. This gene is located on chromosome 2 near the genes that code for IL-1 $\dot{\alpha}$  and L-1<sub> $\beta$ </sub> (Conti and Younes, 2020). The inflammatory immunological responses are triggered by IL-1 $\dot{\alpha}$  and IL- $_{\beta}$ . They bind to an IL-1 receptor found on the surface of a variety of cells; triggering a cytokine cascade that results in the recruitment and activation of macrophage and neutrophil, fever and vascular dilation, in addition to a powerful pro-inflammatory immune response (Papa et al., 2020). The major purpose of the IL-1 framework is to protect the body from a wide range of dangers, including sickness, microbial colonization and malignant transformation. The IL-1 and IL-6 might engage in recreation of a crucial function in severe lung inflammation, which can lead to acute respiratory distress syndrome (ARDS); causing death of the patient (Peiris et al., 2003; Riley et al., 2003). IL-6 is regarded as a central middle person that produces an alert sign under unfavorable circumstances. When this warning signal is triggered by a contamination; it spreads throughout the body, triggering macrophage and monocyte cells, and triggering specialized pathogen recognition receptors (PRRs). In addition, IL-6 also serves as a warning signal to the body when tissue damage occurs (Atri et al., 2020).

### 4. Biomarkers in COVID-19 infection

According to Zhang *et al.*, (2020), the term cytokine storm (CS) refers to a stream of proinflammatory cytokines that is overwhelming and uncontrollable. In infectious diseases, CS usually begins in a single contaminated area and then spreads through the bloodstream. In total of 41 inpatients, <u>Huang *et al.* (2020)</u> calculated the cytokine levels and reported that the granulocyte colony stimulating factor; fibroblast growth factor and the Interferon's (IFNs), IL-1B, IL1ra, IL-7, IL-8, IL-9 and IL-10 levels were higher in 13 ICU patients than in 28 non-ICU patients. Several chemokines such as; CCL2, CCL3, CCL5, have also been found to be elevated in severe COVID-19 cases (<u>Wang *et al.*</u>, 2020a; Li *et al.*, 2020a; Chen *et al.*, 2020a).

#### 5. Immunity and immune response

Serologic testing is a valuable tool for determining population invulnerability and identifying those people who are less likely to be re-infected. Lymphocytopenia is one of the most apparent COVID-19 symptoms (Li et al., 2020b). Both the T cells and the natural killer T- cells are reduced in the COVID-19 patients, and this reduction is linked to the severity of the illness; similar to the memory helper T cells. The T cells that regulate the immune system are also known as the regulatory T cells (Zhang et al., 2020). Shrinkage of spleen; large cell degeneration, regional hemorrhagic necrosis, macrophage phagocytosis and macrophage proliferation were among the autopsy findings (Crisci et al., 2020). As a result of spleen shrinkage, the number of lymph nodes decreases, resulting in atrophy and putrefaction. According to Zhang et al., (2020), immunohistochemistry revealed that the CD4+ T cells and CD8+ T cells are reduced in the spleen and lymph nodes. A recent study conducted by Yao et al., (2020) revealed that monocytes and macrophages are the most common invading cells in the lung; with lymphocytes being uncommon. Moreover, the lung displays a unique two-sided diffuse alveolar damage with cell fibromyxoid exudates. These findings don't appear to be identified with a hyper cytokine discharge that is activated by the actuated T cells in the late phase of viral contamination. They're also hyper-activating signals

of alveolar macrophages; in reaction to the viral infection, the epithelial and endothelial cells released a storm of cytokines and chemokine (Shimabukuro-Vornhagen *et al.*, 2018: Conti *et al.*, 2020). Recently, Zhang *et al.*, (2020) proposed two possible explanations for the loss of resistance framework in the COVID-19 patients: lymphocytes were directly assailed by infection or lymphocytes might be indirectly damaged by the CS. According to Xu *et al.*, (2020), as the SARS-CoV-2 was contaminating the intention cells via ACE2, but the lymphocytes lack ACE2 articulation; it is suggested that the lymphocytes were annihilated by the CS.

# 6. Management of COVID-19 pandemic using precision medicine

The main objective of this study was to show how we can manage COVID-19 disease by precision medication. Precision medicine is an integrative therapeutic methodology that considers traditional elements such as; age, clinical aggregates and sexual orientation, as well as arising hereditary qualities and their associations with environmental variables; in order to personalize diagnosis, prevention, prognosis and treatments (Ramos-Lopez et al., 2020). Following the precision medication standards, the COVID-19 pandemic administration should foresee the presence of illnesses through monitoring the lifestyles, risk factors and social determinants; and provide interventions that can slow the progression of the disease before it manifests itself (Crisci et al., 2020). To carry out the concerned prevention; investigating the molecular, hereditary and the specific elements of each person and microbe, in addition to prescribing the most helpful methodology tailored to the patient's condition; most importantly require the collaboration of biomedical examination, health experts and scholarly organizations (Crisci et al., 2020).

#### 7. Preventive measures

According to the WHO, basic preventive activities should be coordinated to setting up and planning clean systems, observing and evaluating the developing pandemic and its impact. This is in addition to implementing relief measures, which include total correspondence activities and endeavors to slow the spread of the disease; plan, scale up and ensure progression of medical services arrangements (Wang et al., 2020b). During the conflict stage; wide range of activities with varying degrees of severities and immovability's should be carried out to prevent local area spread. Examples of these include; screening at airports, travel limitations, line terminations, approaching traveler restrictions, screening railway stations and transit stations, cancellation of religious, sporting and cultural events. If supported local area transmission took place; the health authorities must guarantee that the crisis is managed efficiently and that sufficient well-being and calculated assets are available (Crisci et al., 2020).

Arrival of the post-genomic era and creation of new logical methods signified the beginning of the 21<sup>th</sup> century. According to Andryukov et al., (2021), monomarker diagnostics have been replaced by a unique system for collecting and assessing comprehensive profiles of all molecular determinants of biological structures. Referring to the simultaneous advancement of new perceptive stages and biostatistics; it become feasible to generate progressive omix-advances covering the whole area of molecular cell research, including genomics; proteomics, ipidomics, metabolomics and transcriptomics (Al-Mozaini and Mansour, 2016; Zhou et al., 2020b). Every one of these breakthroughs considers a different group of chemicals, each using its own equipment to investigate certain profiles in explicit systems, tissues or cells, and therapeutically uses a rational technique that does not dependent on hypotheses (Andryukov et al., 2021). Recently, rising numbers of omix-advances have become available for clinical indicative research. where they are used for prediction; diagnosis, dynamics and assessment of the pathophysiological reasons of a disease (Zhou et al., 2020b; Florindo et al., 2020; Andryukov et al., 2021). When it's impossible to isolate the single biomarker involved in the illness; new molecular and metabolic profiling

methods and genomic screening are currently being used in the diagnosis of pathology in patients with ambiguous medical indications (Zhou *et al.*, 2020a; Florindo *et al.*, 2020; Andryukov *et al.*, 2021).

According to the previous studies conducted by Al-Mozaini and Mansour, (2016); Andryukov et al., (2021), personalized laboratory research medication is cutting-edge consequence of sophisticated a progressive omics-technologies, which unlike combined lab medication; does not rely on a single diagnostic marker, but rather on a change in the profile of a number of markers. Battagello et al., (2020) reported that using "-omics" (proteomics, genomics and metabolomics) to estimate and search for new biomarkers helps the fast recognition of cell stress chemicals that are indicative of pathology. The study of molecular stress signals such as viral instigation; is a potential area for finding novel biomarkers (Florindo et al., 2020; Andryukov et al., 2021). Recently, Battagello et al., (2020) compiled information on the importance of cell stress signals throughout the SARS-CoV-2 illness; penetration and replication in cells, and suggested that the presence of clinical manifestations in individual patients was due to the infection's transcendent injury and attack on cells (Chen et al., 2020b). Increased mobility of serine protease 2 (TMPRSS 2) and modulation of the function of the renin-angiotensin framework, both of which are strongly linked to ACE2; have been identified as molecular indicators of entry of SARS-CoV-2 into the host cells (Lukassen et al., 2020; Luo et al., 2020). In infectious disease clinical practice, physicians are regularly presented with variety of concerns about individual susceptibility among individuals who have the same sickness caused by an indistinguishable culprit. This variety is based on the combination of different individual characteristics such as age; sex, genetic polymorphism and the existence of comorbidities. This distinctive arrangement of biological factors decides singular reaction to contaminate and underlies the idea of personalized medication, as proposed by Sagner et al., (2017); Andryukov et al., (2021).

# 8. Modern omix-technologies in COVID-19 infection

One of the current omix-advancements' goals is to build molecular profiles of the bio-substrates in this manner; such as the protein profile of pathological urine or the metabolic profile of the selected physiological fluids. Recent studies of Florindo et al., (2020); Wendt et al., (2020); Andryukov et al., (2021) highlighted that dysregulation of lipid digestion and transport in COVID-19 patients was discovered, which backs up prior studies that revealed that altered cholesterol homeostasis has a negative impact on COVID-19 prognosis and on the viability of the antiviral treatment/therapies. Based on these data, the scientists suggested that evaluation of the urine proteomic profile might be utilized to separate and forecast the course of COVID-19. Moreover, representation of the protein range can also help with the pathophysiology of the unique COVID disease (Wu et al., 2020).

Liu *et al.* (2020) described a novel study that looked at the symptomatic function of urine proteome analysis in identifying COVID-19 illness progression from mild to severe clinical structures, as well as recovery using mass spectrometry. The quantity of proteins linked to complement initiation and hypoxia was considerably raised in patients with a severe course of contamination, whereas the content of proteins related to platelet degranulation, glucose and fat digestion was significantly reduced (Liu *et al.*, 2020).

## 9. Personalized aspect associated with immunesenescence

Dysfunction of the mitochondria plays a role in an immuno-senescence from another perspective. Despite the various intracellular capacities; the mitochondria is a self-governing subcellular organelle that directs building of the innate antiviral immunity in a straightforward manner (Singh *et al.*, 2020; Maggi *et al.*, 2020). As an outcome, a personalized evaluation of

the risk of SARS-CoV-2 contamination and separation of complexities in COVID-19 patients can determine the patients' unique vulnerability to disease. Moreover, markers used to notice the mitochondrial dysfunction such as layer depolarization and mitochondrial enzyme activity, showed efficacy for personalizing evaluation of the danger of SARS-CoV-2 contamination and separation of complexities (Hoffmann et al., 2020; Andryukov et al., 2021). A portion of the unanswered inquiries concerning the pathogenic parts of COVID-19 might be settled by singular evaluation of the invulnerable reaction of the patients to the infection; specifically the asymptomatic clinical types of contamination, and the contrasts recorded in the harshness of illness relying on sex and age, as reported by recent studies of Sungnak et al., (2020); Sarver and Wong, (2021). The scientists appear to be on the verge of reaching a COVID-19 multi-marker research centerbased conclusion, which will increase treatment viability and also improve cost adequacy.

Few victories in the control of COVID-19 pandemic have been achieved; owing widely to the proved critical lab diagnostic instruments based on molecular/ hereditary and immunoassay techniques. Recently, Zhou et al., (2020b) reported that these techniques need a very long time to be enhanced; although currently they present a vital aspect for distinguishing and controlling the expansion of COVID-19. During the COVID-19 pandemic, the expertise gained at the end of the SARS and MERS epidemics was used to build a research center process for detecting the SARS-CoV-2 infection and antibodies against it. Information about SARS-CoV-2 is developing dramatically, and surprising disclosures will additionally be conceivable later on. For example; a modification in the fundamental determinant protein S is described by the recently discovered strain SARS-CoV2 Spike D614G (Ogawa et al., 2020). Controlling the COVID-19 pandemic will involve the deployment of a variety of analytic testing procedures developed at the research facilities; where the affectability and specificity will improve as SARS-CoV-2 is further investigated. Wang et al. (2020b) set out to develop a precision pharmaceutical technique for single-patient diagnosis during the clinic preventative control, in addition to therapy; in order to lower the rate of contamination and prevent the nosocomial diseases. Finally, the author underlines the necessity of personalized medication to combat the COVID-19 pandemic in terms of exploring the reasons of the individual weakness of SARS CoV-2; as well as boosting the productivity and cost-effectiveness of patient's treatment in the last section.

#### Conclusion

The COVID-19 pandemic caused widespread concern around the world as the etiologic agent is a rare microorganism, which lacks a specific treatment and has put the world's health systems in grave jeopardy. Personalized medicine is the collection of varieties of localized and individual data including clinical, hereditary, lifestyle and other biomarkers data. This type of medicine focuses on identifying the changeable aspects in patients, which can be treated more effectively with better phenotypic recognition or with better knowledge of the core causative mechanisms. Controlling the COVID-19 pandemic needs the deployment of varieties of research facilitybased analytic testing procedures, which will become more effective and explicit as SARS-CoV-2 is better investigated. Development of additional logical stages for lab-based rapid detection of COVID-19 remain critical and of pressing medical concern. The author underlines the significance of using tailored medicine to battle the COVID-19 pandemic, and investigate the causes of individual vulnerability to SARS-CoV-2; in order to increase the competence and costeffectiveness of patient's treatment in the near future.

### **Conflict of interest**

The authors declare no conflict of interests.

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## Ethical approval

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