Swasthya Health स्वास्थ्य

# Asthma drug budesonide shortens recovery time in non-hospitalised patients with COVID-19

PRINCIPLE is the world's largest Phase 3 platform randomised controlled trial to find clear evidence of an effective COVID-19 treatment for use in the community that can significantly shorten recovery time.

Prof Mahendra G Patel said, 'Early treatment with inhaled budesonide shortens recovery time by a median of three days in patients with COVID-19 who are at higher risk of more severe illness and are treated in the community'.

Inhaled budesonide is a safe, relatively inexpensive and readily available corticosteroid commonly used around the world in inhalers to treat asthma and chronic obstructive pulmonary disease. It was added to the PRINCIPLE trial on 28th November 2020.

Recruitment for the inhaled budesonide arm of the trial stopped on 31st March 2021 since, in the view of the Trial Steering Committee, enough patients had been enrolled to establish whether or not the drug had any meaningful benefit on time to recovery. Obtaining further data on hospital admissions or death was unlikely due to the reducing number of cases in the UK.

For the interim report, a total of 961 patients were randomly assigned to receive inhaled budesonide at home and were compared with 1819 patients randomly assigned to the usual standard of NHS care alone. Of these, 751 people in the budesonide group and 1028 in the usual care group were SARS-CoV-2 positive and included in the primary interim analysis.

Based on the interim analysis using the latest data from 25th March 2021, the results showed the estimated median time to self-reported recovery for inhaled budesonide was 3.011 days shorter compared to usual care (95% Bayesian credible interval 1.134 to 5.410 days), with a high probability (0.999) of being superior to the usual standard of care. 32% of those taking inhaled budesonide, compared to 22% in the usual care group, recovered within the first 14 days since being randomised into the trial and subsequently have remained well until 28 days (relative risk 1.46, 95% CI 1.23 - 1.74). Participants in the budesonide group also reported greater wellbeing after two weeks (mean difference in WHO-5 Wellbeing score + 3.37 ,95% CI 0.97 – 5.76, p = 0.006).

Among patients who had completed all 28 days of study follow up by 25th March 2021, 8.5% (59/692) in the budesonide group were hospitalised with COVID-19 compared with 10.3% (100/968) in the usual care group (estimated percentage benefit, 2.1% [95% BCI -0.7% – 4.8%], probability of superiority 0.928). Since fewer than expected people were admitted to hospital in the trial, and with COVID-19 cases and hospitalisations continuing to drop in the UK, it is not clear from this interim analysis whether budesonide reduces hospitalisations.

Patients with COVID-19 symptoms that started within 14 days and who are at higher risk of a poor outcome from the illness could join the trial and those with a positive SARS-CoV-2 result were included in the main analysis. Patients treated with inhaled budesonide were asked to inhale 800 micrograms twice a day for 14 days and were followed-up for 28 days. All patients were aged over 50 with an underlying health condition that put them at more risk of serious COVID-19 illness, or aged over 65.

Joint Chief Investigator, Professor Chris Butler, a South Wales GP and Professor of Primary Care from the University of Oxford's Nuffield Department of Primary Care Health Sciences, said: 'PRINCIPLE, the world's largest platform trial of community-based treatments for COVID-19, has found evidence that a relatively cheap, widely available drug with very few side effects helps people at higher risk of worse outcomes from COVID-19 recover quicker, stay better once they feel recovered, and improves their wellbeing. We therefore anticipate that medical practitioners around the world caring for people with COVID-19 in the community may wish to consider this evidence when making treatment decisions, as it should help people with COVID-19 recover quicker.

'This exciting finding about the beneficial effects of inhaled budesonide would not have been possible without the contribution of those patients who volunteered to participate: your gift of taking part will help doctors and nurses provide better evidence-based care for people with COVID-19 worldwide. It also stands as a monument to the far-sighted funders of PRINCIPLE, the UK-wide clinical research networks who have been absolutely key to the successful implementation of the trial, all the general practices and clinicians who support PRINCIPLE, NHS Digital, HDRUK, the Therapeutics Task Force and the hard work and dedication of our study team and oversight committees in the Primary Care Clinical Trials Unit.'

Joint Chief Investigator, Professor Richard Hobbs, Head of Oxford University's Nuffield Department of Primary Care Health Sciences, said: 'For the first time we have high-quality evidence of an effective treatment that can be rolled out across the community for people who are at most risk of developing more severe illness from COVID-19. Unlike other proven treatments, budesonide is effective as a treatment at home and during the early stages of the illness. This is a significant milestone for this pandemic and a major achievement for community-based research.'

Professor Mona Bafadhel, from Oxford University's Nuffield Department of Medicine, and a Consultant Respiratory Physician, led the earlier STOIC Phase 2 efficacy study of inhaled budesonide for early COVID-19 and led the development of the budesonide study arm for PRINCIPLE. She said: 'The news that the findings of the earlier-phase STOIC trial, which reported at the beginning of the year, have been replicated at scale here in the PRINCIPLE trial is outstanding. We are now sure that we have a treatment that will benefit patients with early COVID-19 worldwide Inhaled budesonide is readily available worldwide and commonly used to treat asthma and chronic obstructive pulmonary disease.'

Professor Fiona Watt, Executive Chair of the Medical Research Council, which co-funded the study, said: 'Researchers involved in the PRINCIPLE trial have overcome considerable logistical hurdles to set up a world-leading rigorous drug trial in people's homes. We are now rewarded with the first inexpensive and widely available drug that can shorten recovery times for COVID-19 patients in the community. People around the world will be helped to recover faster thanks to these exciting new results.'

As soon as all remaining patients in the trial have completed their follow-up and a full analysis has been completed, detailed results on time to recovery and hospitalisations will be published. For this preliminary report, 92.8% of people randomised to the budesonide arm had the opportunity to complete 28 days of follow-up.

PRINCIPLE launched in April 2020 with the intention that drugs shown by the trial to have a clinical benefit could be rapidly introduced into routine NHS primary care. The trial is evaluating a range of potential community treatments for COVID-19 to reduce recovery time and prevent hospital admissions and deaths. It is recruiting participants who are most at risk of serious COVID-19 illness, either due to their age, symptoms, or an underlying health condition.

PRINCIPLE has pioneered an innovative methodology for community-based research that allows for many treatments to be efficiently and rapidly assessed in a single trial, resulting in this world-first finding of an effective community-based treatment during the course of a pandemic. Typically for trials of this size in the community, patient recruitment would take place opportunistically via general practices. Yet in PRINCIPLE,

while general practice remains critical to delivery of the trial, everyone across the UK, regardless of where they are registered to receive their health care, can sign-up if they are eligible. To date, more than 4,700 patients have volunteered to join PRINCIPLE, making it the world's largest platform trial of COVID-19 treatments to take place in community settings.

In January 2021, PRINCIPLE demonstrated that the antibiotics azithromycin and doxycycline are not effective treatments for COVID-19 in the early stages of the illness, changing clinical practice in the UK and internationally. PRINCIPLE continues to investigate the effects of treatment in the community with colchicine, a commonly used anti-inflammatory, and favipiravir, an antiviral used in Japan to treat influenza.

*PRINCIPLE is led from the Primary Care Clinical Trials Unit at the University of Oxford's Nuffield Department of Primary Care Health Sciences. PRINCIPLE is supported by a large network of care homes, pharmacies, NHS 111 Hubs, hospitals, and 1,401 GP practices across England, Wales, Scotland and Northern Ireland. The trial is integrated with the Oxford RCGP Research and Surveillance Centre and works closely with the NIHR Clinical Research Network, NHS DigiTrials, Public Health England, Health and Care Research Wales, NHS Research Scotland and the Health and Social Care Board in Northern Ireland. PRINCIPLE is funded by a grant to the University of Oxford from UK Research and Innovation and the Department of Health and Social Care through the National Institute for Health Research as part of the UK Government's rapid research response fund.*

*Source: University of Oxford News Release, 12 April 2021*
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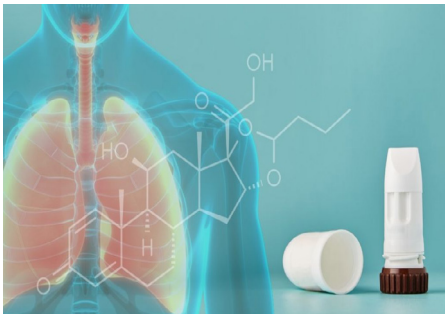



# An interview with Director of Central Institute of Psychiatry of Ranchi: Dr Basudeb Das

*Edited by Avinash Sharma, Associate Professor of Psychiatry*

Ranchi is the capital of the Indian state of Jharkhand that was separate state for the tribal regions of South Bihar, northern Orissa, western West Bengal. Prof Nandini Chokraborthy intervied the newly appointed Director of Central Institute of Psychiatry, Dr Basudeb Das.

**1. How does it feel to be the newly appointed Medical Director for Central Institute of Psychiatry, Ranchi?**

I feel a sense of immense responsibility in heading the Institute. I am keenly aware of the challenges as well as the opportunities that the Institute faces and I am hopeful of being able to do the very best job I can possibly do.

**2. Tell us a bit about your journey since Medical College and your choice of psychiatry as a specialty?**

Psychiatry typically tended to be given minimal emphasis in the under-graduate curriculum, at least when I was a medical student during 1989-94 at R G Kar Medical College, Kolkata. I must confess here that psychiatry was not my first choice though I was inquisitive about it while doing my House Officership in the Department of General Medicine there. I started the journey in the year 1998 along with my now accomplished colleague Dr Nandini Chakravorty, after getting selected at the Central Institute of Psychiatry, Ranchi. I started loving it then because of its uniqueness in many aspects and the satisfaction it gives after healing the troubled minds. The suffering mental health issues causes in our society is immense, yet under-appreciated. People suffering from mental health problems face an uphill task when it comes to employment opportunities or even integrating into their communities in a meaningful way. I felt a strong urge to work for those afflicted with mental illnesses and improve the services that are provided to them. It's like a dream come true for being appointed as the Director of the same after serving it for more than two decades in various capacities.

**3. How has the practice of psychiatry changed in the last 15 years in India?**

The most notable change, which also happens to be fairly recent, is the widespread use of tele-mental health all across the country. The ongoing COVID-19 pandemic has catalysed the introduction of both the Guidelines for Telehealth in India as well the adoption of this technology. Given the severe shortage of psychiatrists in the country, and the fact that most psychiatrists tend to be clustered in urban or metropolitan areas, tele-mental health should go a long way in enabling much needed access to residents of rural and remote parts of India.

The other major change, which too is relatively recent, is the enactment of The Mental Healthcare Act of 2017. This is an impressively progressive legislation which has introduced a whole new set of mechanisms in the care of the mentally ill, be it advanced directives, nominated representatives, setting up of mental health tribunals, mandatory use of modified electro-convulsive therapy (ECT), etc. In my opinion, in the last 15 years, there has been a slight but palpable decline in the amount of stigma associated with mental illnesses – people are less hesitant to contact mental health professionals now, especially in urban settings.

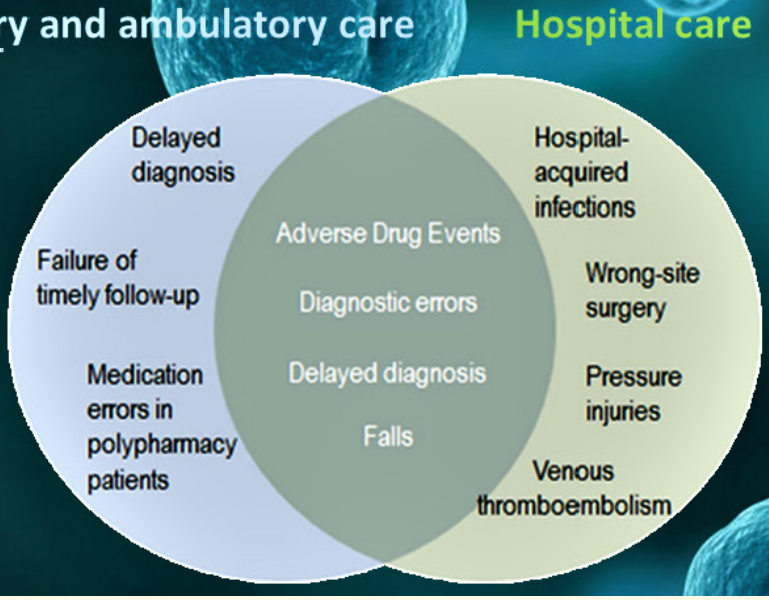
**Dr Basudeb Das.**

**4. What is your vision for the Central Institute of Psychiatry for the future?**

As your readership might be aware, this century old Institute has many firsts to its credit – be it the setting up the first postgraduate training in Psychiatry in the country in 1922, to the first Occupational Therapy department anywhere in India, the use of ECTs in the early 1940s, the use of psychotropics such as chlorpromazine and lithium soon after their introduction in the West, etc. I would very much like to carry forward this legacy of providing excellence in clinical care, with patients and caregivers having access to the latest, evidence-based care at the Institute. Providing quality training to the next generation of mental health professionals is a top priority area too. In this regard, I am attempting to expedite recruitment of faculty for any positions that are lying vacant. We have a fantastic library and have other resources to enable us to optimise research output. Attracting research grants and collaborating with top research institutions, nationally and hopefully, internationally, is another area which will receive adequate focus. ❑

# Improve patient safety by eliminating adverse events in health care settings

*It is estimated that every year more than 300,000 patients acquire a healthcare associated infection (HCAI, HAI or nosocominal infection)as a result of care with in the NHS.*

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