illuminate the core problems at the heart of global cancer control: from insufficient funding and governance failures through to deficits in workforces fundamental to cancer treatment, such as surgery and radiotherapy.[4,5] High-income countries spend substantial amounts on cancer control and research, yet the resources dedicated to enhancing capability and capacity in partner LMICs remain poor. Likewise, development assistance for health provides little direct help to build cancer control systems.[6] Both of these things have to change if the gap in outcomes is to be narrowed. Oncoplutocracy, in which cancer progress only benefits wealthy countries and patients, needs to stop. However, delivery of better and affordable cancer control is a two-way street. Many LMICs, particularly in the upper-middle bracket, need to properly fund their public health and cancer care systems, and to adopt rigorous governance models to improve the quality of care.[7] Regional cooperation could also pay dividends in this respect, to help to build workforce capacity and capability, particularly across continental Africa where progress is already being made by many individual countries.[8]

Delivery of affordable, equitable, and high-quality cancer care demands the alignment of policy, politics, and solutions for cancer control.[9] Planning and measurement of these policies and solutions require real data from real patients, including both epidemiological and hospital care data. Far too much policy and planning is based on modelled data, which might benefit no-one and which gives a false sense of thinking that both the research community and policy makers fully grasp what the problem is. To achieve the sort of cancer intelligence systems that countries and patients need, a new international, long-term vision must urgently be found for sustainable support of national registries and transnational studies such as CONCORD-3. National and regional governments must recognise that population-based cancer registries are key policy tools, both to monitor the impact of cancer prevention strategies and to evaluate the effectiveness of the health system for all patients diagnosed with cancer.

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Filling the gaps in COPD: the TRIBUTE study

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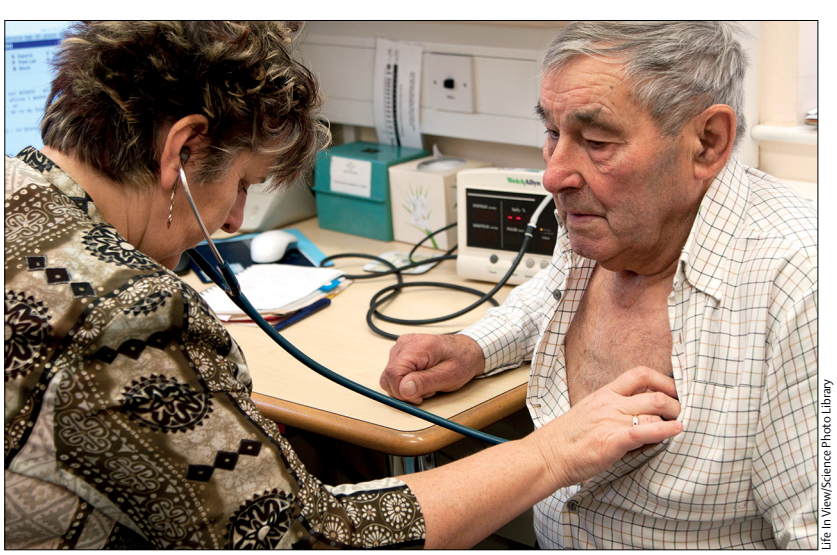
Chronic obstructive pulmonary disease (COPD) is a major public health problem because of its high prevalence (about 10% of the adult population), rising incidence (COPD is predicted to be the third global cause of death by 2020), and high associated personal, social, and economic costs.[1] Regular physical activity, appropriate vaccination, and avoiding toxic exposures (eg, tobacco smoking) are important non-pharmacological approaches for the management of patients with COPD.[1] Meanwhile, pharmacological treatment for COPD is fundamentally based on the use of inhaled drugs: long-acting bronchodilators (long-acting antimuscarinic agents, long-acting β_2 agonists, or both), with or without inhaled corticosteroids.[1] The Global Initiative for Chronic Obstructive Lung Disease (GOLD) recommends these drugs be used (alone or in combination) on the basis of the severity of symptoms present and the previous history of COPD exacerbations, a marker of the risk of future exacerbation episodes.[1] The GOLD recommendations are based on the best available scientific evidence and, where evidence is absent, on expert opinion.[1]

The prevention of disease exacerbations is a key therapeutic goal in patients with COPD.[1] In *The Lancet*, Alberto Papi and colleagues[2] present the results of a randomised, parallel-group, double-blind, double-dummy, controlled, multicentre trial (TRIBUTE)[2] designed to test the superiority of a triple combination of an inhaled corticosteroid, long-acting β_2 agonist, and long-acting antimuscarinic agent (extra-fine formoterol fumarate, glycopyrronium, and beclometasone dipropionate; in a single inhaler, two inhalations twice per day; n=764) relative to a double combination of a long-acting β_2 agonist and long-acting antimuscarinic agent (indacaterol and glycopyrronium; in a single inhaler, one inhalation per day; n=768) without inhaled corticosteroid, in terms of the prevention of COPD exacerbation episodes over 1 year of follow-up.[2] The main results show that, first, the annual rate of moderate-to-severe COPD exacerbations was 15% lower in patients receiving the triple combination than in patients receiving the double combination (0·50 per patient per year [95% CI 0·45–0·57] *vs* 0·59 per patient per year [0·53–0·67], p=0·043). Notably, however, differences were not significantly different when moderate and severe exacerbations were analysed separately or when time to first exacerbation was considered. Second, the incidence of pneumonia, a relevant side-effect of inhaled corticosteroids in patients with COPD,[1] did not differ between the groups.[2]

TRIBUTE is an important contribution to the management of COPD because it is the first study to my knowledge that addresses the important gap in understanding regarding triple therapy versus double therapy for preventing COPD exacerbations. In fact, the results of TRIBUTE support (and extend) the current GOLD recommendations.[1] However, a number of issues require careful consideration.

First, the incidence of COPD exacerbations was low in both groups of the study.[2] This could suggest that both treatments were effective in reducing the rate of COPD exacerbations, which is good news for patients. Yet this low incidence also suggests that, although triple therapy significantly reduced the annual rate of exacerbations compared with double therapy, treatment will have to be maintained for several years to prevent a single exacerbation episode. Given this relatively small effect size, it is important that TRIBUTE also showed that, at the doses used in the study (348 µg total daily dose), beclometasone dipropionate did not affect the incidence of pneumonia.[2] Second, the specific long-acting β_2 agonists differed between triple therapy and double therapy (extra-fine formoterol fumarate versus indacaterol) and the inhaler devices also differed between regimens. The latter potential confounder is likely to have been addressed by the double-dummy design of the study, but differences in bronchodilator efficacy between the two long-acting β_2 agonists could have affected the results. Third, it is important to remember that the patients enrolled in TRIBUTE were at the most severe end of the COPD spectrum since they had severe or very severe airflow limitation (forced expiratory volume in 1 s <50% of reference), were symptomatic at screening despite treatment (COPD Assessment Test score ≥10), and had experienced at least one documented moderate or severe COPD exacerbation in the previous year.[2] This means that the results of TRIBUTE only apply to this specific population of patients and cannot be generalised to other patients with milder COPD. Finally, the effects of triple therapy on the COPD exacerbation rate were particularly evident in patients with chronic bronchitis or elevated circulating eosinophils (but not in those with emphysema or low circulating eosinophils). Future studies will have to address the potential clinical usefulness of these two treatable traits[3] for the personalised management of COPD.

The results of TRIBUTE help better position triple therapy in a single inhaler within the clinical management of COPD. It will be of great interest to compare these results with those of a similar study, IMPACT (NCT02164513),[4] that is likely to be published soon.



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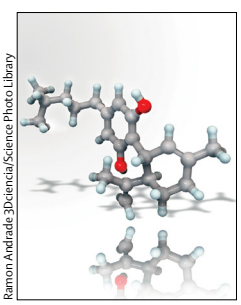
Cannabidiol for drop seizures in Lennox-Gastaut syndrome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Lennox-Gastaut syndrome is a rare epilepsy with childhood onset and is characterised by multiple seizure types, typically tonic, atonic, and atypical absences in which non-convulsive status epilepticus (atypical absence, tonic, myoclonic, or mixed) is common. Generally, the electroencephalogram shows generalised slow spike-and-wave discharges in wakefulness and sleep and paroxysmal fast rhythms in sleep. Learning and behavioural difficulties are common. Causes include structural or acquired brain lesions, metabolic disease, and genetic abnormalities. Epilepsy in Lennox-Gastaut syndrome is pharmacoresistant, and to date no single antiepileptic drug has been shown to be superior. After failure of first-line conventional antiepileptic drugs, second-line therapies include rufinamide, clobazam, felbamate, and zonisamide, and non-pharmacological treatments such as ketogenic diet, vagus nerve stimulation therapy, corpus callosotomy, and in a few cases resective surgery.[1]

In *The Lancet*, Elizabeth Thiele and colleagues[2] report a randomised, double-blind placebo-controlled phase 3 trial of add-on 20 mg/kg oral cannabidiol as a novel antiepileptic drug in 171 patients with Lennox-Gastaut syndrome. Many different pharmacoresistant epilepsy syndromes exist, and the children and adults in this study are representative of patients who are likely to be seen in clinical practice. This study identifies the benefit of cannabidiol on seizure frequency, provides early indications of expectations and treatment response profiles, describes both common and important side-effects, and the association between side-effects and concomitant sodium valproate use. The primary endpoint was percentage change from baseline in monthly frequency of drop seizures during the treatment period and the median percentage reduction from baseline was 43·9% (IQR −69·6 to −1·9) in the cannabidiol group (n=86) and 21·8% (IQR −45·7 to 1·7) in the placebo group (n=85). The estimated median difference between the treatment groups was −17·21 (95% CI −30·32 to −4·09; p=0·0135) during the 14-week treatment period. These findings and those from previous studies[3,4] indicate that cannabidiol is efficacious.

Scientific, clinical, and popular interest in cannabidiol has increased considerably in the past decade. Historical reports and in-vitro and in-vivo studies led to the consideration of cannabidiol as an antiepileptic drug, and anecdotal reports suggested that cannabidiol-enriched preparations have efficacy. Open-label expanded access programmes[3] suggested broad-range efficacy of cannabidiol in the epilepsies and were followed by randomised controlled trials in patients with rare epilepsies, in Dravet syndrome,[4] and now in *The Lancet* in Lennox-Gastaut syndrome.[2]

Excitement about cannabidiol on social media exceeded that in the clinical field. Many clinicians might have first been made aware of cannabidiol for epilepsy by patients and families. The voice of patients and parents is a powerful advocate for treatment, encouraging and supporting both professionals and the public. Although such advocacy is important, caveats do exist. Content published on social media does not necessarily undergo peer review, governance challenge, or editorial gate-keeping. Readers might attribute the same value to this content as they would to scientific study. For cannabidiol, uncontrolled availability of non-pharmaceutical preparations and oils containing cannabidiol has enabled patients and parents to self-prescribe. Furthermore, the distinction between cannabidiol and medical marijuana has not always been understood. Cannabidiol that is produced pharmacologically does not contain