The next step in immorality: charging to create and cure disease

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Surrogate markers are seductive. In clinical trials and regulatory decisions, why not reach for something quick, convenient, and relatively cheap? Why stop patients receiving a treatment of plausible and potential benefit? That is the logic behind “accelerated pathways” for drug approval, such as the one used by the US Food and Drug Administration since the 1990s. But the FDA’s experience is worrying, a story of claims unproven and obligations avoided (doi:10.1136/bmj.n2059). Surrogate markers rank with subgroup analyses, composite outcomes, and secondary outcomes as great deceivers in clinical trial design and reporting. Their overuse is a triumph of commercial hype, playing on the hope of a treatment that anybody with an illness will, understandably, cling to.

The promise of drugs approved on the basis of surrogate outcomes is mostly unsupported by trials and meta-analyses that use hard clinical outcomes, such as death and disease, even when the surrogate outcome is validated (doi:10.1136/bmj.n2191). Too often, in the regulatory setting, confirmatory trials with hard outcomes are not done or done too late, and patients continue to take drugs that are ineffective or harmful (https://blogs.bmj.com/bmj/2021/09/15/surrogate-endpoints-need-complementary-patient-reported-outcomes). Germany’s Institute for Quality and Efficiency in Healthcare, IQWiG, is rare in using strict criteria to limit recommendations that are based on surrogate outcomes, although the UK’s National Institute for Health and Care Excellence is now seeking to tighten up its approval process (doi:10.1136/bmj.n2191).

As with subgroup analyses, trials that rely on surrogate markers are generally best seen as hypothesis generating. An industry that reaps billions in profits argues that such trials make drug development affordable. But the industry’s savings are picked up as costs by health services, possibly many times over, since prescribing ineffective and harmful drugs is expensive.

Such corporate manoeuvres affect the frontline of care, where overwhelming demand is being met by depleted resources. The new investment agreed for England’s NHS will not tackle chronic workforce pressures, nor boost morale of beleaguered staff in primary care (doi:10.1136/bmj.n2226; doi:10.1136/bmj.n2224), nor deliver a better future for social care (doi:10.1136/bmj.n2224; doi:10.1136/bmj.n2227). Primary care will be stretched further by decisions to offer covid vaccinations to children aged 12-15 years (doi:10.1136/bmj.n2254; https://blogs.bmj.com/bmj/2021/09/03/a-game-of-phone-tag-getting-children-of-clinically-vulnerable-parents-vaccinated-has-been-disgracefully-chaotic).

10 The “new normal” is already delivering more work, prompting media attacks on regulatory decisions, why not reach for something quick, convenient, and relatively cheap? Why stop patients receiving a treatment of plausible and potential benefit? That is the logic behind “accelerated pathways” for drug approval, such as the one used by the US Food and Drug Administration since the 1990s. But the FDA’s experience is worrying, a story of claims unproven and obligations avoided (doi:10.1136/bmj.n2059). Surrogate markers rank with subgroup analyses, composite outcomes, and secondary outcomes as great deceivers in clinical trial design and reporting. Their overuse is a triumph of commercial hype, playing on the hope of a treatment that anybody with an illness will, understandably, cling to.

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