compromise the acceptability, fidelity, effectiveness, and sustainability of the HOPE 4 intervention strategies when scaled up in the real world.

Although a precedent exists for scaling up donor-supported free care for a chronic communicable condition (eg, HIV infection through the US President’s Emergency Plan for AIDS Relief programme), there is no clear equivalent on the horizon for individuals with hypertension without HIV infection. A comprehensive cost-effectiveness analysis of the HOPE 4 trial is needed. Concerted efforts are required to make antihypertensive medications and statins equitably accessible in low-income and middle-income countries. A 30% reduction in premature cardiovascular mortality by the year 2030, relative to 2015, is targeted by Sustainable Development Goal 3.4. HOPE 4 and similar highly important studies should prompt the scientific and legislative communities to rethink the scale-up of large, evidence-based approaches to dramatically reduce the burden of uncontrolled hypertension and lower cardiovascular risk. Such bold strategies cannot be ignored.

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Superiority of biodegradable polymer sirolimus-eluting stents in STEMI

After the introduction of coronary drug-eluting stents in 2002, these efficacious devices were rapidly adopted in clinical practice. Nevertheless, controversy remained about the safety of drug-eluting stents in acute ST-segment elevation myocardial infarction (STEMI). Later, although in daily practice drug-eluting stents were used in all clinical scenarios and several randomised trials with few exclusion criteria evaluated drug-eluting stents in study populations that included patients with STEMI, many studies that assessed newer drug-eluting stents still excluded patients with STEMI. In 2014, based on new study results, European guidelines first recommended the use of new-generation drug-eluting stents rather than...
bare-metal stents in STEMI. Up to 30% of participants in recent allcomer trials assessing the new-generation biodegradable polymer sirolimus-eluting stent (Orsiro) were treated for STEMI. Within STEMI subgroups, only the BIOSCIENCE trial found a significant between-stent difference favouring biodegradable polymer sirolimus-eluting stents.

In *The Lancet*, Juan Iglesias and colleagues report the 1-year outcomes of the BIOSTEMI trial, which is, to our knowledge, the first dedicated randomised trial to compare biodegradable polymer sirolimus-eluting stents with durable polymer everolimus-eluting stents (Xience) in patients with STEMI. The authors should be commended for their large-scale randomised trial in a population that must have been difficult to enrol as it includes individuals in cardiogenic shock and unconscious patients, in whom a consent-by-proxy procedure was applied. Bayesian methods were used to incorporate data from 407 patients with STEMI from the BIOSCIENCE trials as historical priors, showing 1-year superiority of biodegradable polymer sirolimus-eluting stents (4%) compared with durable polymer everolimus-eluting stents (6%) for the composite endpoint of target lesion failure. In 1300 newly enrolled patients in BIOSTEMI (76% men and 24% women), biodegradable polymer sirolimus-eluting stents and durable polymer everolimus-eluting stents showed similar proportions for the safety endpoints of cardiac death and target vessel myocardial infarction, although there was a numerical difference in favour of biodegradable polymer sirolimus-eluting stents in the efficacy endpoint clinically-indicated target lesion revascularisation (1% in the biodegradable polymer sirolimus-eluting stent group vs 3% in the durable polymer everolimus-eluting stent group). Furthermore, both types of drug-eluting stent showed low and similar stent thrombosis rates. The BIOSTEMI trial will have a 2-year follow-up, which is of interest in light of the findings of the BIO-RESORT trial, which showed an advantage for biodegradable polymer sirolimus-eluting stents compared with durable polymer zotarolimus-eluting stents in target lesion revascularisation between 1-year and 2-year follow-up.

Yet which clinical endpoint is the driver of superiority? In the 1300 patients in BIOSTEMI, the individual component of target lesion failure that differed numerically between the two types of stent was target lesion revascularisation. In the subgroup of BIOSCIENCE participants with STEMI—the source of priors for the Bayesian approach—adverse event rates did not mirror these findings but showed low and similar clinically indicated target lesion revascularisation proportions for both types of stent (2% for both). In the BIOSCIENCE trial, the significantly lower target lesion failure rate in biodegradable polymer sirolimus-eluting stents (3% vs 9% in the durable polymer everolimus-eluting stent group) was mainly driven by numerical differences in the safety endpoints of cardiac death (2% in the biodegradable polymer sirolimus-eluting stent group vs 5% in the durable polymer everolimus-eluting stent group) and target vessel myocardial infarction (1% in the biodegradable polymer sirolimus-eluting stent group vs 3% in the...
durable polymer everolimus-eluting stent group). From a pathophysiological point of view, it makes sense to expect a lower target lesion revascularisation risk in culprit vessels of STEMI, as allcomer studies suggest. Myocardial scarring reduces the subtended myocardial volume. Therefore, the same degree of (recurrent) lumen narrowing that leads to angina in patients without previous STEMI might remain unnoticed after STEMI because of the smaller amount of viable myocardium. Consequently, showing superiority of biodegradable polymer sirolimus-eluting stents in reducing target lesion revascularisation is more difficult in a population with STEMI. In the BIOFLOW V trial, which excluded patients with STEMI, biodegradable polymer sirolimus-eluting stents were superior (6%) to durable polymer everolimus-eluting stents (10%) regarding target lesion failure, driven by fewer repeat myocardial infarctions (5% in the biodegradable polymer sirolimus-eluting stent group vs 8% in the durable polymer everolimus-eluting stent group). Thus, both the BIOSTEMI trial and the subgroup analysis of the BIOSCIENCE trial in patients with STEMI showed lower proportions of target lesion failure after treatment with biodegradable polymer sirolimus-eluting stents. However, the individual clinical endpoints in favour of biodegradable polymer sirolimus-eluting stents appear to be different (ie, target lesion revascularisation rather than cardiac death or target vessel myocardial infarction). Future research needs to clarify which individual clinical endpoint drives superiority.

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Sex-based differences in medications for heart failure

Men and women have noteworthy physiological differences. Beyond the traditionally accepted trends in bodyweight and physical stature, women are documented to have slower gastrointestinal motility, less intestinal enzymatic activity, and slower glomerular filtration rate than men. These translate into sex-dependent differences in medication absorption, distribution, metabolism, and excretion that can affect health outcomes.

Some physiological differences affect medication pharmacokinetics but ultimately do not translate into clinically meaningful distinctions. Others can substantially affect pharmacodynamic properties.