A 10-year impact assessment of the Efficacy and Mechanism Evaluation (EME) programme: an independent mixed-method evaluation study

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Scientific summary

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Scientific summary

Background

The Efficacy and Mechanism Evaluation (EME) programme funds (1) trials that evaluate the efficacy of interventions with potential to promote health and (2) mechanistic studies that improve our understanding of the mechanisms of underlying diseases, treatments, potential adverse effects and the differences in response to treatments between individual patients. It was set up in 2008 as a partnership between the UK Medical Research Council (MRC) and the National Institute for Health Research (NIHR). The EME programme's remit covers new and repurposed interventions across health and technology areas. Applications are submitted to either researcher-led 'open' calls or commissioned calls. The latter target specific health or technology areas to address current health-care needs and support areas of 'market failure'.

Objectives

The NIHR Evaluation, Trials and Studies Coordinating Centre commissioned Technopolis Group (Brighton, UK) in partnership with Ipsos MORI (London, UK) to conduct an independent evaluation of the impact of the EME programme in relation to its aims, guided by a set of 15 evaluation questions.

Methods

The evaluation employed a mixed-methods approach, involving qualitative and quantitative methodology and drawing on primary and secondary sources of data. This included the following:

- Development of a programme logic model and evaluation framework.
- Secondary data analysis, including:
  - internal programme management files
  - publications reporting the main findings of 54 EME projects
  - data from the 2020 chief investigator (CI) submissions to the Researchfish® system (Interfolio UK Ltd, Cambridge, UK).
- Primary data collection and analysis of:
  - online surveys of CIs of EME projects with 'active' or 'discontinued' status (46/91; 50.5% response rate) and of CIs whose applications reached stage 2 but were not funded (28/93; 30.1% response rate) (note that discontinued projects are projects for which funding was withdrawn early because of insurmountable delivery issues)
  - semistructured interviews with CIs of completed EME awards and active projects that had published their main findings (i.e. findings that answer the primary research question) (23/45; 51.1% response rate)
  - consultation with key opinion leaders and members of the advisory committee to the evaluation ($n = 10$), including representatives from academia, research funders, industry and patient and public involvement (PPI).
- Development of five case studies that illustrate a variety of outputs, outcomes and impacts achieved.

During analysis, evidence gathered from multiple sources and perspectives was triangulated, and additional desk research was conducted to verify findings related to key outcomes. Based on the evidence, seven recommendations to enhance the programme's potential for impact and facilitate research project implementation were developed.

Results

By September 2018, 145 EME awards had been approved for a total of £175.7M. By September 2020, 53 EME projects had completed and/or published their main findings (i.e. findings relating to the primary research question) and 43 of these projects used clinical trial methodology.

Position and role of the EME programme in the research funding landscape

The EME programme bridges the gap between early proof-of-concept and effectiveness studies in the funding landscape. It is unique in its support for mechanistic studies alongside efficacy trials, which add value by lending confidence to trial findings, providing insights into the underlying biology. However, a need for more funding for proof-of-concept studies to bridge the gap between discovery research and the EME scheme was highlighted.

The programme mainly supports efficacy studies of limited or no commercial interest. Just under half (49%) of EME projects investigated repurposing of existing interventions, and 17% generated evidence to test current practice. Of the one-third (34%) of projects that supported the development or uptake of new therapies and approaches, many did not target commercialisation. Stakeholders recognised the EME programme as important in funding research that industry is unlikely to invest in. Research targeting repurposing or providing evidence to inform use of existing interventions is also likely to provide good value for money, compared with the costly and high-risk development of new interventions, and can lead to improved efficiencies in the health-care system.

Within the funding landscape, the EME programme sits among other MRC and NIHR schemes and grants provided by charities. Preceding the EME award, most interventions received funding from UK public funders (58% of projects) and charity/non-profit organisations (46% of projects), with a smaller share supported by industry (17% of projects). The percentages were similar for projects that had secured follow-on funding. A total of £355M in follow-on funding was reported, including £155M from the NIHR, £40M from the MRC and £19M from the Wellcome Trust (London, UK). CIs considered overlap with other funding sources to be limited. However, at least some projects can access alternative funding schemes; for example, one-quarter of CIs whose application to the EME programme was unsuccessful went on to conduct the proposed efficacy trial.

The most frequent co-funding source was the pharmaceutical industry (31/62, 50%), followed by 'other industry' (23/62, 37%), primarily medical technology companies and small and medium-sized enterprises (SMEs). The potential to support collaborative research with industry, particularly with SMEs, was a driver for the Department of Health and Social Care to invest in the programme as part of the nation's 'growth agenda'. However, the level of 'true' collaboration with industry is fairly low, and none of the projects is led by a SME. This is also reflected in the limited commercial opportunities presented by EME projects.

Charities/non-profit organisations co-funded 12 projects (i.e. 19% of all co-funded projects). Charities were frequently engaged to support PPI, and project management by the charities includes an advisory function. Three co-funded studies that have led to outcomes were mechanistic substudies of trials fully or partially funded by charities.

Health needs addressed by EME projects

Efficacy and Mechanism Evaluation projects were funded across nine of the top 10 causes of disability-adjusted life-years (DALYs) in the UK (based on 2017 figures) and address a range of UK health needs and government priority areas.

The portfolio does not fully align with the level of UK health needs (expressed in DALYs). For example, four of the 10 most frequent causes of DALYs are targeted by only one EME project or none at all, and the health areas 'injuries and accidents' and 'musculoskeletal' are under-represented in the EME portfolio compared with their share of UK DALYs. The largest share of projects conducted research in the category 'evaluation of treatments and therapeutic interventions', investigating pharmaceutical interventions. Projects exploring the aetiology, prevention and management of diseases were largely absent from the EME portfolio.

Commissioned calls have helped to steer research towards specific health areas. However, 44% (37/84) of commissioned calls did not lead to any funded projects. A better understanding of why the number of awards in certain areas or through certain commissioned calls is small could identify existing barriers to research and additional support measures.

Barriers to and enablers of EME research

The main challenges encountered by CIs in implementing EME projects were 'complex and slow contracting processes' (35/46, 76%), 'setting up of study sites' (30/46, 65%) and patient recruitment (28/46, 61%). Coverage of excess treatment costs and low prioritisation of research and/or lack of capacity of staff were recurring difficulties encountered when working in the NHS. Around 20% of CIs reported delays due to regulatory processes. In particular, CIs with little experience of leading clinical trials and CIs of trials that required setting up of new research structures struggled with the associated administrative burden.

External infrastructure is important for (at least some) EME projects to succeed. Enablers were Clinical Research Networks for recruitment (34/46, 74%) and Biomedical Research Centres for infrastructure and supporting research staff (17/46, 37%). In interviews, five CIs also emphasised the crucial role a funded clinical research fellow (CRF) position played for their trial.

Nearly all CIs consulted had engaged in PPI at some project stage. PPI representatives were often members of Trial Steering Committees or Trial Management Groups and contributed to the development of patient-facing information and research approaches, and the design of recruitment or retention strategies.

EME project findings and outputs

In the case of completed trials, 14% (6/43) demonstrated that the intervention tested had a positive effect, whereas 74% (32/43) demonstrated that the intervention did not have an effect on the primary outcome of the trials. The latter group of completed trials avoid further research costs and provide important evidence to inform use of interventions (e.g. seven projects showed that current clinical practice is either ineffective or potentially harmful). Four trials tested new treatment approaches that are being developed further.

Most projects (121/145, 83%) included a mechanistic study or were fully mechanistic (8/145, 6%). Mechanistic data have provided further scientific insight and lent confidence to trial findings. Five mechanistic studies have changed assumptions about the mechanisms of action of the intervention and underlying disease and have identified markers of genotypes associated with the disease under investigation.

The main findings of projects, where reported, were mostly published in the EME journal (45/53, 85%) and other peer-reviewed journals (38/53, 72%). After the EME journal, the journals accounting for publication of the largest number of studies were *The Lancet* ($n = 8$) and *The Lancet Psychiatry* ($n = 4$).

In Researchfish, the majority of projects (104/141, 74%) reported at least one publication, resulting in a total of 671 publications (predominantly journal articles). Further publications and outputs from currently active awards are expected, with 36% (16/44) of CIs of active projects indicating that the research had already led to findings, as yet unpublished.

Other outputs include sample collections, research tools (e.g. imaging techniques for assessment of disease symptoms and new outcomes-associated markers) and patient stratification approaches. A small number ($n = 4$) of projects resulted in new intellectual property (IP).

Scientific outcomes

Findings of EME projects are underpinning further research. The majority of CIs continue to pursue research on the intervention tested in the EME trial. Outputs such as sample and image collections continue to be used, supporting progress towards outcomes and impacts. More than one-third (38%) of EME projects have secured further funding. Closed trials showing 'no effect' of the intervention tested led 19% (4/21) of CIs to terminate the line of investigation and switch to other approaches, avoiding research waste. EME projects have also formed new and strengthened existing collaborations. Other outcomes include the formation of research networks and the setting up of a disease-specific registry.

Most CIs (69%, 31/45 surveyed) reported that the EME project had contributed to training and capacity building among project team members and at 'research-naive' trial sites. In particular, early-career CIs and CRFs were highlighted as having benefited from the experience. More broadly, CIs ($n = 11$) emphasised that EME projects had built or strengthened trial capacity and networks across a range of research areas.

Health outcomes and impacts

Efficacy and Mechanism Evaluation programme-funded research is generating important evidence to inform health-care decisions. Of the completed EME projects employing trial methodology, seven (16%) have informed clinical guidelines and eight (18%) have potential to do so in the future based on the nature of their findings.

In addition, three clinical trials supported by EME substudies led to changes in clinical guidelines or practice. One technology developed by an EME project was taken up into clinical guidelines and is now routinely offered in the NHS, and one (active) study has informed Public Health England testing practice.

At the time of review, only around one-third (53/145, 37%) of EME projects had completed and/or published their main findings, with more than one-quarter of research papers published in 2019 and 2020. Further outcomes and impacts from the EME programme will depend on take-up of new findings across UK health systems.

Project factors supporting health outcomes and impacts

At this stage of the EME programme, 12 projects have informed health-care guidelines or changed clinical practice:

- Three projects were substudies of trials funded by other funders, and probably benefited from the scale and patient access of the overall research projects, indicating that substudies represent good value for money.
- Nine projects span health areas and study types. Therefore, at this stage of the EME programme, no specific areas or study types emerge as more successful in achieving impact than others.
- CIs associated with institutions located in the London–Oxford–Cambridge cluster led to 42% of completed/published studies, but account for 83% (10/12) of studies that have informed guidelines or changed clinical practice. Although numbers are small, this suggests that the context of well-funded research-intensive universities may favour success in achieving impact.
- The EME programme is firmly rooted in clinical research, with nearly three-quarters of CIs reporting that the original idea for their research topic was informed by clinical researchers. Compared with successful CI applicants, a larger share of unsuccessful applicants referred to ideas stemming from patient groups. This observation merits further investigation, as research that addresses needs identified by patient groups could increase the EME programme's impact on health.

At this stage of the EME programme, the performance of projects funded through the different EME workstreams cannot be robustly compared, as only eight projects from commissioned calls have published their main research findings.

Socioeconomic impacts

To date, few projects have generated commercial revenue [i.e. only one (active) project reported that it had contributed to the formation of a spin-out company, which secured £35M in series A financing]. Four projects reported IP in Researchfish, with one project 'in the process of being licensed to a commercial entity' (not independently verified).

To achieve greater economic impact through commercial routes, project selection needs to take account of whether or not research can lead to commercial outcomes. At the same time, the EME programme funds research in areas where industry is unlikely to invest and, therefore, plays an important role in the funding landscape. This needs to be considered in setting the EME programme strategy.

Efficacy and Mechanism Evaluation projects have resulted in efficiency gains (e.g. for the NHS) either by demonstrating that a new, more expensive treatment approach does not lead to better outcomes than current practice or by showing that treatments currently offered in routine practice do not result in any benefit. With few health economic analyses available, these cost savings have not been quantified at the programme level.

Programme-level impact: influence on strategies of other funders

Although no evidence of direct influence of EME funding and research on the strategies of other funders was uncovered, the scheme may have served as a model for supporting clinical trials alongside mechanistic studies, such as Cancer Research UK's (London, UK) Experimental Medicine Awards.

Key opinion leaders interviewed felt that co-ordination with other funders could support portfolio selection by improving alignment of funding decisions, creating synergies and avoiding duplication, and, therefore, enhancing the potential for health and/or economic impact, as well as influence on wider research funding agendas.

The NIHR's focus on increasing PPI in research was described as contributing to a culture change in medical research. The EME programme was described as advanced with respect to PPI. However, PPI is still uneven across the research community.

Conclusions

Based on the evidence gathered, a set of seven recommendations was developed to enhance the EME programme's impact or address challenges:

1. Assess whether or not the level of commercial outcomes and economic impact meets the funders' expectations for the EME programme. If a stronger performance is intended, steer funding towards projects with clear commercial potential.
2. Identify areas of research addressing important health needs currently under-represented in the EME portfolio. Identify the reasons for low representation and implement support measures where appropriate.
3. Clarify the role of mechanistic studies in the EME programme, potentially 'optionalising' this component – the 'M' in the programme's name.
4. Analyse EME applications data and review scores to understand current funding gaps for proof-of-concept studies and tailor additional funding offers.
5. Improve engagement and co-ordination with other funders and explore options for partnership.

6. Ensure that project implementation plans undergo critical assessment at the proposal review stage. Take further action to support researchers in addressing common challenges.
7. Examine if EME programme implementation can be optimised in terms of:

    i. faster turnaround of application and contracting processes
    ii. coverage across disciplines by EME Funding Committee member expertise, especially in key areas of health need and non-traditional medical fields
    iii. ensuring that feedback on applications is clearly understood by applicants and consistent across review stages 1 and 2.

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EME programme

The Efficacy and Mechanism Evaluation (EME) programme funds ambitious studies evaluating interventions that have the potential to make a step-change in the promotion of health, treatment of disease and improvement of rehabilitation or long-term care. Within these studies, EME supports research to improve the understanding of the mechanisms of both diseases and treatments.

The programme supports translational research into a wide range of new or repurposed interventions. These may include diagnostic or prognostic tests and decision-making tools, therapeutics or psychological treatments, medical devices, and public health initiatives delivered in the NHS.

The EME programme supports clinical trials and studies with other robust designs, which test the efficacy of interventions, and which may use clinical or well-validated surrogate outcomes. It only supports studies in man and where there is adequate proof of concept. The programme encourages hypothesis-driven mechanistic studies, integrated within the efficacy study, that explore the mechanisms of action of the intervention or the disease, the cause of differing responses, or improve the understanding of adverse effects. It funds similar mechanistic studies linked to studies funded by any NIHR programme.

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This report

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