

TB Practecal

Innovating MDR-TB Treatment

Application of the MSF clinical trial transparency policy: cost analysis of TB- PRACTECAL, a multicentre phase 2b–3 trial in drug-resistant tuberculosis

Dzintars Gotham¹, Manuel Martin¹, Melissa J Barber^{1,2}, Emil Kazounis³, Charlotte Batts³, Roz Scourse¹, Greg Elder¹, Bern-Thomas Nyang'wa⁴.

1. MSF Access Campaign. 2. Yale Collaboration for Regulatory Rigor, Integrity, and Transparency (CRRIT), USA.
3. MSF UK, London, UK. 4. MSF Operational Center, Netherlands.

Background on the TB-PRACTECAL trial

- Drug-resistant tuberculosis has for decades been difficult to treat and has lacked effective and easy-to-use treatment regimens
- Phase 2b-3 adaptive trial testing shorter all-oral regimens in drug-resistant TB
- 3 sub-studies on cost-effectiveness, quality of life outcomes, and pharmacokinetics/pharmacodynamics
- Testing three new regimens for DR-TB vs standard of care
- Managed and financed by MSF, with 19 partner organisations
- 2017-2022
- Trial sites in Uzbekistan, Belarus, and South Africa
- 7 clinic facilities
- 250+ staff involved
- 552 patients enrolled & 321 on sub-studies

Site	Enrolment
Belarus	
Minsk	99
South Africa	
THINK – Doris Goodwin	56
THINK – Don McKenzie	107
Wits – Helen Joseph	12
Wits – King DiniZulu	30
Uzbekistan	
Nukus/Karalpakstan	193
Tashkent	55

Headline result: new BPaLM regimen was superior to the accepted standard of care

The findings of TB-PRACTECAL were a key factor in WHO adopting this regimen as a new first-line

Why care about clinical trial costs?

- Detailed costs of a clinical trial have, to our knowledge, never previously been reported
- High costs of trials are frequently used to justify high prices for health products; lack of transparency is a barrier to policy discussions in this space
- Lack of transparency undermines clinical trial planning, budgeting and fundraising
- Presumed high costs may dissuade certain research groups/organizations
- Increased transparency in the costs of clinical trials has long been called for by MSF and others, as well as by the World Health Assembly
- MSF's Clinical Trial Transparency Policy (CTTP), adopted in 2022, commits to publishing clinical trial results and clinical trial costs

Objectives

1. To collect, analyse and publish the clinical trial costs of the MSF TB-PRACTECAL clinical trial, as a first step to implementing MSF's new CTTT.
2. Contribute more broadly to global health and political efforts to improve transparency in the R&D ecosystem, including through designing a data collection tool.

Outputs:

Abstracts at MSF Scientific Days conferences, PPRI

Journal article

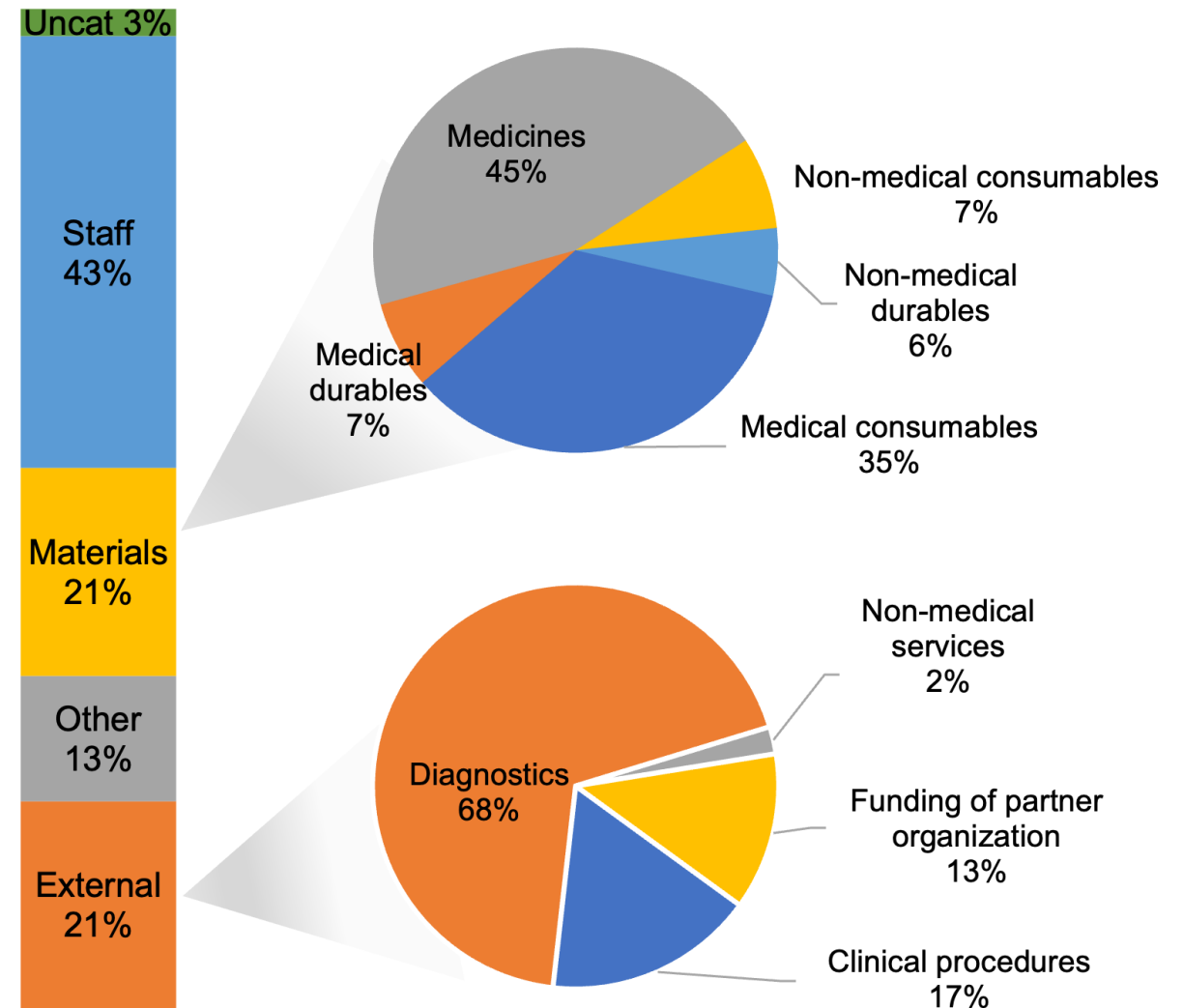
Clinical trial cost reporting tool (Transparency-CORE)

Methods

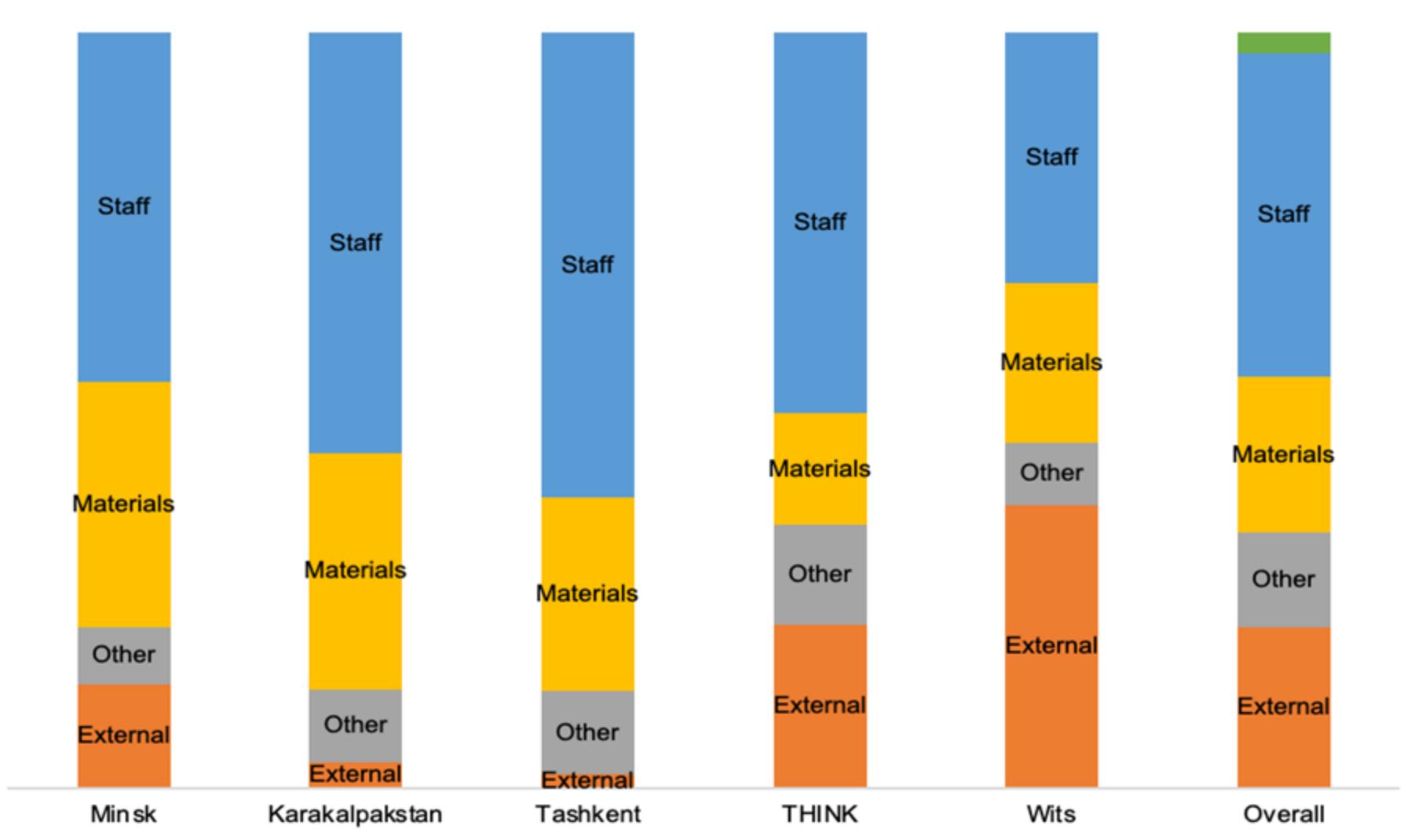
1. Analysis of TB-PRACTECAL costs using MSF accounting records, covering the period 1 January 2013 to 30 June 2023, 6 trial sites, and several implementing partners
2. A cost categorization system was developed, splitting costs into 27 categories, grouped as:
 1. Central activity costs
 2. Trial site activity costs
 1. Staff
 2. Materials
 3. External services
 4. Other
 5. Uncategorizable
3. Analysis by year, by site, and by per-patient averages
4. Analysis of medicines costs
5. To place the findings in context, we undertook a literature review on clinical trial costs and clinical trial cost estimation

Results

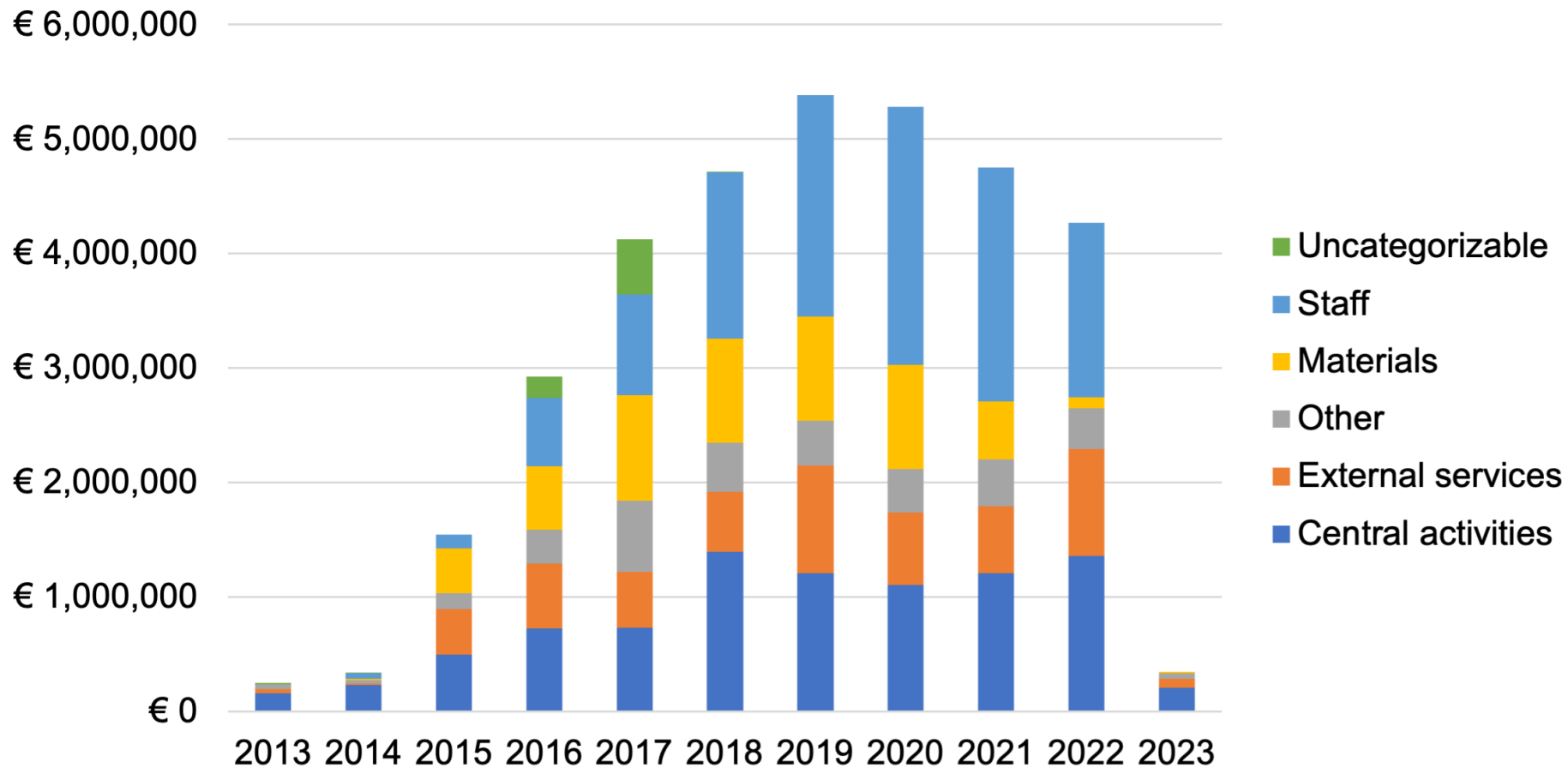
- Total costs of the TB-PRACTECAL programme (main trial + 3 sub-studies) were €33.9 million
- 26% of costs were at the ‘central’ level (e.g. trial management by MSF UK, 72% were at the ‘trial site’ level
- Trial site costs were driven by staff costs
- Mean cost per patient enrolled was €61,460 across the whole trial (including trial management overhead).
- When only site-level costs were considered, per-patient costs ranged €19,998–45,942 across the six sites.



Cost structure comparison across sites



Costs over time



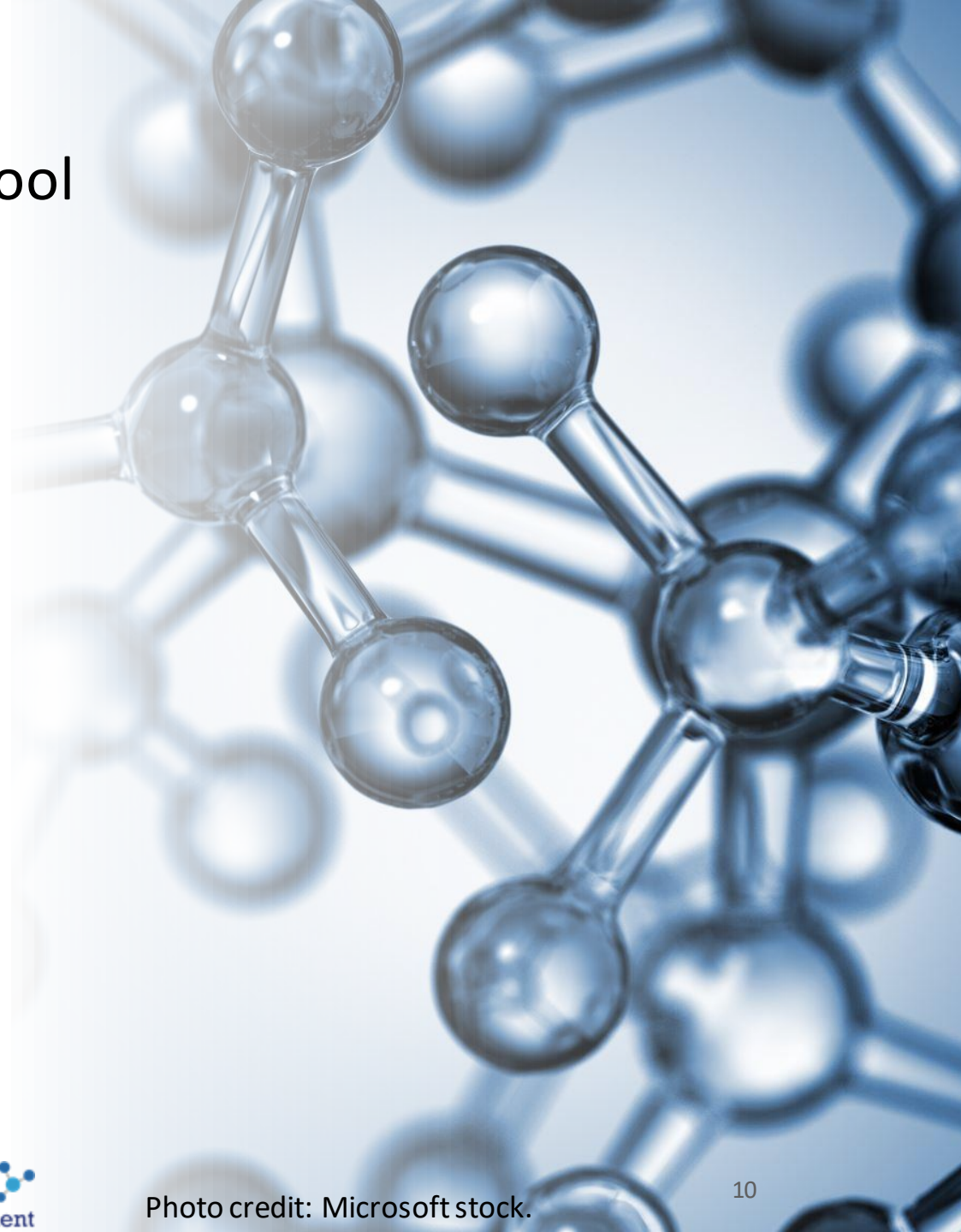
15% costs were incurred before the start of enrolment, 6% of costs after the last follow-up patient visit.

Conclusions

- When published, this will be **the first detailed report of actual expenditures in a specific clinical trial**
- Main drivers were staff costs, external diagnostic services, and medicines costs
- Overall trial costs sit within lower end of previously reported range of trial costs (US\$7-221 million per trial, for phase 2 and 3 pharmaceutical trials), despite several factors likely exerting an upward pressure on costs:
 - Phase 2b and 3 adaptive trial
 - Long trial duration
 - Inclusion of sub-studies
 - Use of high-quality clinical endpoints
 - Longer-term investments that would likely not be incurred in industry trials
 - MSF having to cover (majority of) investigational medicine costs

Clinical Trial Transparency Cost Reporting Tool (Transparency-CORE)

- List of 27 categories developed based on
 - Literature review
 - Utilizes standard MSF accounting categories as far as possible
 - Iterative process balancing ease of use with granularity
- The reporting tool includes a template Excel file that offers automatic categorization and summary tables



Policy implications

Greater clinical trial cost transparency can:

1. Support evidence-based discussions around equitable R&D models and incentives, and equitable pricing, and improve accountability
2. Provide valuable information for research organizations considering trials – particularly in LMICs
3. Inform improved economic analysis, including, for example, by identifying opportunities for increased efficiency



Future plans

- MSF calls on all research organizations to publicly disclose their clinical trial costs. The MSF Clinical Trial Transparency Cost Reporting Tool can be used as a guide to support these efforts.
- MSF is exploring the possibility of working with partners to develop standardized *STROBE* guidelines for clinical trial cost reporting, along the lines of established guidelines for the reporting of e.g. systematic reviews (PRISMA) or economic analyses (CHEERS)
- Exploring similar analysis for the endTB trial (MSF, PIH, IRD, funded by Unitaid).
- There is a need for continued advocacy to improve R&D cost transparency more broadly – including for governments to enact legislation to mandate disclosure of disaggregated R&D costs.



Thanks and acknowledgements

We thank the experts who joined workshops to inform the methods and analysis: Ava Alkon (MSF), Candice Sehoma (MSF), Francisco Vegas, Nigel Masbayi (DNDi), Hassaan Zahid (MSF), Laura McCullagh (MSF), Laurence Vielfaure (DNDi), Christopher Morten, Rachel Cohen (DNDi), Olivier Wouters (LSE), Caleb Alexander (Johns Hopkins Bloomberg School of Public Health), Christophe Perrin (MSF), Jeanne Roussel (MSF), Carole Mitnick (Harvard Medical School).

We thank Nicola James (MSF) and Marion Conijn (MSF) for assistance in data collection. We thank the participants of the TB-PRACTECAL trial.

Extra slides

COST CATEGORIES – CENTRAL ACTIVITIES	Expenditure	Percentage
Central activities	€ 8,825,285	26%
Trial monitoring	€ 3,550,957	10%
Trial management	€ 3,304,868	10%
Trial planning	€ 1,253,698	4%
Data management	€ 317,475	1%
Regulatory compliance	€ 138,615	0.4%
Pharmacovigilance (safety reporting)	€ 63,665	0.2%
Central activities - not allocable to above categories	€ 7,841	0.02%
Analysis of results, publication	€ 188,167	1%

COST CATEGORIES – TRIAL SITE ACTIVITES	Expenditure	Percentage
Trial site activities	€ 25,100,571	74%
Trial site staff costs	€ 10,849,002	32%
Trial site staff (specifically contracted)	€ 10,849,002	32%
External services supporting work at clinical trial sites	€ 5,203,371	15%
External clinical procedures	€ 417,581	1%
External diagnostics	€ 2,637,491	8%
External non-medical services	€ 1,442,418	4%
Funding of partner organization, not divisible into functions	€ 705,881	2%
Purchase of materials	€ 5,212,607	15%
Medical consumables (excl. medicines and vaccines)	€ 1,803,083	5%
Medical durables	€ 360,029	1%
Medicines	€ 2,326,620	7%
Non-medical consumables	€ 428,668	1%
Non-medical durables	€ 294,207	1%
Other	€ 3,152,342	9%
Banking and tax	€ 7,311	0.02%
Community engagement	€ 151,335	0.4%
Facility operating costs	€ 408,674	1%
Losses, theft, expiries	€ 114,966	0.3%
Miscellaneous	€ 909,290	3%
Transport and travel	€ 1,560,766	5%
Uncategorizable	€ 683,250	2%
TOTAL	€ 33,925,855	100%