April 2024

Transparency CORE: Clinical Trial Cost Reporting Toolkit

A user manual

Background and objectives

In 2022, Médecins Sans Frontières/Doctors Without Borders (MSF) adopted a Clinical Trial Transparency Policy (CTTP), which commits to open sharing of information and costs related to clinical trials led or supported by MSF. To pilot the implementation of the policy, MSF publicly committed in late 2022 to publishing the costs of the TB-PRACTECAL clinical trial, a multi-country, randomised controlled trial to report on the efficacy and safety of a six-month, all-oral treatment regimen for people living with tuberculosis (TB).

Costs or estimates of clinical trials are rare, even in the academic literature, and an institutional commitment to sharing clinical trial costs requires a standard operating procedure. Such a standard operating procedure needs to define which cost elements are relevant to report, which are to be excluded, and how to aggregate the relevant ones.

The process of developing and executing a methodology to identify all the costs related to TB-PRACTECAL also allowed the development of the Transparency CORE toolkit to facilitate the analysis and publication of future clinical trial costs. The toolkit consists of this manual, which provides the standard operating procedures for costing a trial and different cost categories used therein, and an Excel template for cost reporting and analysis. As this toolkit is based on the experience of publishing the costs for just one MSF-led clinical trial, it may evolve based on its applicability and implementation in subsequent trials.

While MSF staff conducting and publishing clinical trials are the primary audience of this toolkit, it can be adapted and used by others who want to shed light on the underreported area of clinical trial costs.

Standard operating procedure

During clinical trial planning

1. Involvement of clinical trial partners
    a. Inform any trial partners of plans to publish the costs of the clinical trial. Should any data sharing agreements be necessary to secure the necessary financial data, they should be negotiated at this stage.
    b. Request that, as much as possible and practical, trial partners share financial data in the same or similar format to the MSF accounting codes or the Transparency CORE cost categories – see section on cost category explanation below.
2. Budgeting for the clinical trial
    a. Ensure that any budgeting tools used are easily transferable to MSF accounting codes or the Transparency CORE cost categories.
    b. Ensure that the budget for the clinical trial in question contains resources to collate financial data, conduct the necessary analysis, and publish the clinical trial cost data.

During the conduct of the clinical trial

Ensure that cost data for all cost categories is recorded throughout the clinical trial and includes, at a minimum:

1. The location of the cost incurred (i.e., a site-related cost or a central cost).
2. The expenditure amount – if in a currency other than euros, this amount should be converted to euros as close to the day of expense as possible.
3. The date of expense.

Cost data collection is greatly simplified by the use of the standard MSF bookkeeping template. However, where this is not possible, collecting additional information to aid later cost categorisation may be necessary. This may involve the review of other accounting templates used, contracts, expense ledgers, requesting individual invoices, and discussion with trial managers.

Data analysis & publication

Overview

To standardise the cost reporting output, we developed an Excel template that aids data entry and analysis. It includes a facility to allow easy adaptation for other bookkeeping expense categorisation systems.

The template contains two input sheets (highlighted in green), one cost category conversion sheet (highlighted in yellow), and 5 data analysis output sheets (highlighted in red).

Adding data

The main data input sheet ("Data input") is configured to accept any number of lines of expenses, any number of trial sites, and any date range.

The required input variables are:

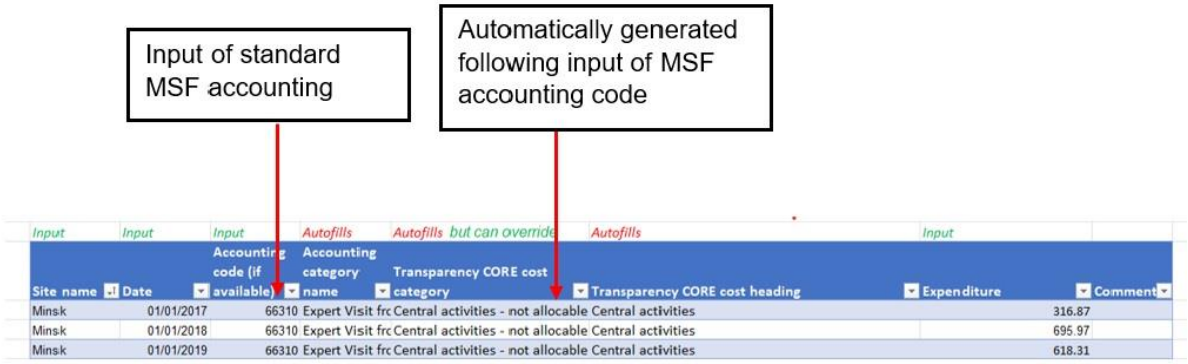
1. Site name – "central activities"[1] are considered a separate site named "central"
2. Expenditure amount (can be zero or negative)[2]
3. Date of expense
4. Transparency CORE cost category
5. Enrolment per site (input only in the "Enrolment" sheet)

Adding an MSF accounting code[3] will automatically generate a Transparency CORE cost category in line with the cross-mapping developed during the analysis of the MSF TB-PRACTECAL trial. Alternatively, the tool provides a facility (in the "Cost categories" sheet) that allows the expense codes of any other bookkeeping system to be mapped to the Transparency CORE cost categories. When this is done, the alternative bookkeeping codes can be entered into the "MSF acct code" column (see Figure) and the relevant cost category will be loaded.

[1] See explanation for "central activities" in section below

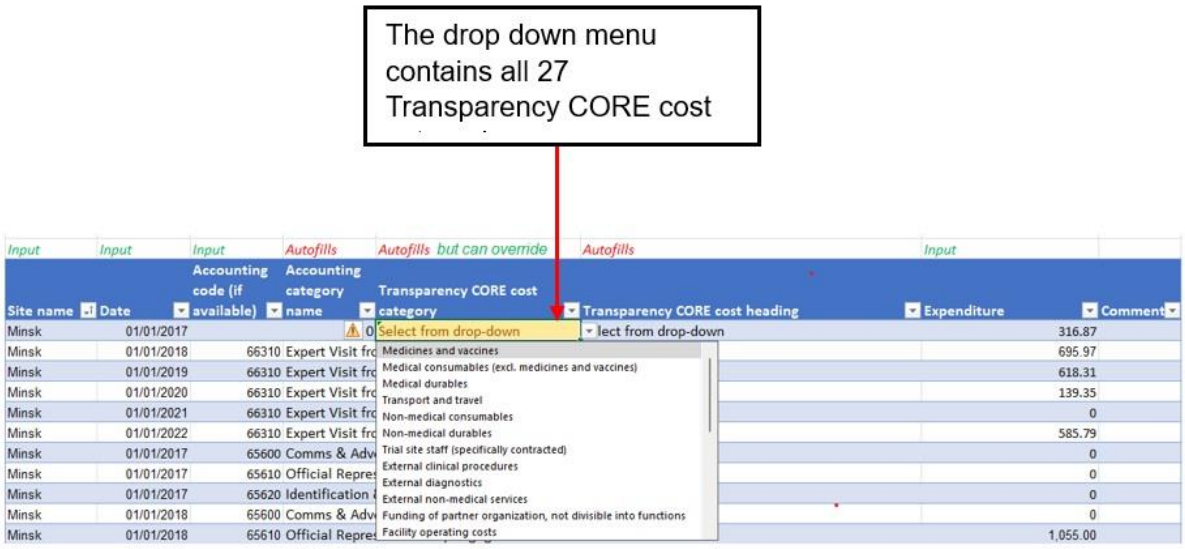
[2] Note: the data input sheet does not automatically convert currencies, so all values should only be inputted after currency conversion

[3] MSF standard accounting templates are reported at three levels of detail (e.g., "60 Purchase of medical items" as the least granular and "60000 Medicines" as the most granular accounting level). Only the most granular level of data should be used in this template. Using more than one level of aggregation will result in double counting (see also "Cost categories" sheet). For cases where expenses are reported at the highest level, but not the lowest, additional accounting codes are provided in the "cost categories" (yellow) sheet.



The "Data input" sheet in the costing template

If no standard MSF accounting code is available or the expense is deemed to belong to a different cost category, the MSF accounting code cell can be left blank and a Transparency CORE cost category can be manually selected from a drop-down menu. Note that when manually selecting a cost category, the definitions provided in the "cost category definition" section should be used as guidance to select the appropriate category.



Adding a cost category manually

When adding sites within the "enrolment" sheet, care must be taken that this is spelt the same (including spaces) as in the "data input" sheet, to ensure that both the "per patient" sheets display the correct values.

Dealing with missing cost data

In cases where it is known that expenses related to one of the cost categories were incurred, but actual data is missing, existing investigational tariff lists or indices may be used to estimate costs. Examples include the UK NIHR 2023-2024 Interactive Costing tool and the Johns Hopkins Standard Costs and Fees for Sponsored Clinical Trials 2023-2024.

Generally, these tariff lists are updated annually, and care must be taken to use a tariff list that both best represents the setting in which the clinical trial took place as well as the year of the expenditure.

Cost categorisation

By default, 27 cost categories are used, organised under 6 headings. This list of categories, as well as their definitions, was developed during analysis of the TB-PRACTECAL trial and can be found in the "cost category definition" section of this document.

A cross-mapping of standard accounting "codes" for these 27 cost categories is available in the Excel template. The Excel template will automatically assign cost categories wherever standard MSF accounting codes are available in the Data Input sheet. However, a customised cost category list and/or a customised cross-mapping to accounting codes can be used.

Additional instructions are provided in the "Cost categories" sheet.

"Central activities"

In the cost categorisation sheet mentioned above and set as the default in this template, "central" costs are separate from "trial site" costs. In the cost categorisation scheme used here, "central" costs refer to costs related to trial planning, regulatory concerns, high-level management across various sites, analysis of findings, and publishing findings. These are costs that would often be incurred by a "central" office. "Trial site" costs are those associated with clinical implementation of the trial at trial sites – costs of clinical products and services, and facility costs, among others (see "Cost categories" sheet for a full breakdown).

Data analysis output

The Excel template automatically produces several summary tables:

1. Costs aggregated by expense type (category)
2. Costs aggregated by expense type (category) by time period (e.g., year)
3. Costs aggregated by expense type (category) by trial site
4. Average cost per patient: averages when "central" (management) costs are included and excluded ("trial site attributable per-patient costs")
5. Average cost per patient by site and by expense type (category)

Any changes made to the data input requires a refresh of the pivot tables in the data analysis output sheets highlighted in red. We recommend that "Refresh all" is used.

General technical notes

- Normal best practices for work in Excel should be followed: PivotTables should be refreshed whenever used.
- Care should be taken to ensure data formats are correct (e.g., dates for dates, numbers for numbers).
- Most summary tables are configured as PivotTables. They are presented on separate sheets to avoid errors due to "spill", which could otherwise occur if many categories, sites, or years are used.
- All PivotTables refer to the named data table "Data_input", on the "Data input" sheet. This means that any added rows or columns, or any changes in names of headers, will automatically be captured as source data in the PivotTables. However, due to the need to use a GETPIVOTDATA function in the calculation of trial site attributable per-patient costs (in the sheet "per-patient global"), the names of columns "Expenditure" and "Transparency CORE cost heading" should not be changed (or, if they are changed, the GETPIVOTDATA formulae need to be adjusted accordingly).

Additional suggested cost analyses not included in the Excel template

Comparing costs of trial planning vs trial management/conduct vs closeout: Utilising the outputs of the costs by "category over time" sheet and the dates of first randomisation and last-patient-last-visit. This comparison may be helpful to compare trials with different levels of complexity (therefore requiring more planning and closeout costs).

Sub-analyses of cost categories: In some cases, sub-analyses of cost categories may be relevant to shed light on the relative contribution of individual components. For example, in the analysis of the TB-PRACTECAL trial, the "medicines and vaccines" cost category was disaggregated because it revealed the (unusually) high cost contribution of the investigational medical product.

Options for publishing clinical trial cost data

1. Publish clinical trial cost data as a separate academic publication (e.g., TB-PRACTECAL).
2. Publish clinical trial cost data as an appendix to the clinical trial publication.
3. Publish clinical trial cost data on MSF's/other institution's website.
4. Create a public repository for the costs of MSF's/other institution's clinical trial costs.

Cost category definition

Cost categories	Definition
1. Central activities	*Central activities – also sometimes referred to as "sponsor activities" – are expenditures incurred by the trial sponsors and include support to sites, as well as expenditures on services that support all sites, including trial planning, day-to-day trial management, administration, statistical analysis, adverse effect monitoring, laboratory quality assurance and control.*
1.1 Trial planning (protocol development etc.)	*All central costs which are incurred prior to the randomisation of the first patient and are not incurred by the sites themselves. These costs do not include transport/travel, purchase of materials or community engagement.*
1.2 Regulatory compliance	*Trial costs which are related to trial and/or pharmaceutical regulatory requirements.*
1.3 Trial management	*Trial management costs, including staff time required for day-to-day management and administration*.
1.4 Data management	*Costs related to storage, cleaning, dissemination and other management of subject and trial data as well as staff time allocated to this end.*
1.5 Trial monitoring [including lab and clinical source data verification (SDV)]	*Costs related to laboratory and clinical source data validation as well as staff time allocated to this end.*
1.6 Pharmacovigilance (safety reporting)	*Costs related to safety reporting of the investigational medical product in question as well as staff time allocated to this end.*
1.7 Analysis of results, publication	*Staff time allocated to the analysis of results data, manuscript preparation, publication submission processes, presentation of results at conferences, etc.*
1.8 Central activities - not allocable to below categories	*Not allocable office costs, not related to site costs.*
2. Trial site staff costs	*Staff costs incurred by sites – sometimes also referred to as "investigator costs".*
2.1 Trial site staff (specifically contracted)	*Personnel costs (including salary and benefits for all staff dedicated to clinical trial implementation at trial sites).*
2.2 HR costs of field staff supporting clinical trial	*HR costs of field staff supporting clinical trial implementation as part of their project management functions.*

implementation as part of their project management functions	
3. External services supporting work at clinical trial sites	*Costs related to outsourced/contracted activities. This may differ greatly depending on the trial and trial partners.*
3.1 External clinical procedures	*Cost of external procedures (clinical procedures including clinical examinations).*
3.2 External diagnostics	*Costs of external validation of samples.*
3.3 External non-medical services	*Outsourced non-medical services (this is the non-medical counterpart to 3.1 and 3.2).*
3.4 Funding of partner organisation, not divisible into functions	*Note: This category is only used for MSF expenditures classed as "funding of partner org", where it cannot be categorised as "external clinical procedures" or "external diagnostics" or one of the categories under "sponsor costs".*
4. Purchase of materials (medical and non-medical)	
4.1 Medicines and vaccines	*Costs of drugs and vaccines used during the clinical trial. This includes both investigational medical product and medicines or vaccines utilised in the standard medical care of patients involved in the trial.*
4.2 Medical durables	*Clinical trial materials - medical – assets**
4.3 Medical consumables (excl. medicines and vaccines)	*Clinical trial materials - medical – consumables** which do not fall under 4.1*
4.4 Non-medical durables	*Clinical trial materials - nonmedical – assets**
4.5 Non-medical consumables	*Clinical trial materials - nonmedical – consumables***
5. Other	
5.1 Share of project cost associated with trial	*If the clinical trial is embedded in an ongoing project, a cost estimation for those patients in the project involved in the trial.*
5.2 Community engagement	*Resources allocated for specific community engagement activities.*
5.3 Transport and travel	*Including transport of staff, medical and non-medical materials, assets, and consumables.*
5.4 Facility operating costs	*Costs associated with building or maintaining clinical trial infrastructure.*
5.5 Banking and tax	*Financial costs, in particular banking costs and taxes.*
5.6 Losses, theft, expiries	*Losses, theft, and expiries.*
5.7 Misc	*Miscellaneous*
6. Uncategorisable	*Expenditures where details are lacking*

* refers to any land, buildings, physical infrastructure, machinery or equipment
** refers to items which are consumed in the execution of the clinical trial. It includes, but is not restricted to, single-use items.

Frequently asked questions - FAQs

Why are the cost categories split into central vs site costs?

Various terms have been used for these concepts previously; "central" costs have sometimes been described as "sponsor" costs, with "trial site" costs described as "investigator" costs. This separation allows an apples-to-apples comparison between sites – even if one of the sites also hosts the "central activities"– and allows the assessment of the relative cost contribution of trial management, administration and support for trial sites.

Why does the cost reporting tool report "per patient" costs?

In a systematic review conducted ahead of the analysis of the TB-PRACTECAL trial, per-patient costs emerged as a common metric in clinical trial cost analyses. Although the number of clinical trial subjects is often a key determinant of clinical trial costs, substantial cost variations exist even among trials with a similar number of clinical trial subjects.

How can clinical trial costs analysed using this tool be compared to each other?

Reports and estimates of clinical trial costs use a wide variety of different methodologies and estimation methods, including or excluding different cost elements, and therefore comparisons of cost estimates come with significant limitations.

Although this tool aims to standardise the approach to calculating clinical trial costs, comparisons of costs among trials analysed using this tool should include sufficient nuance in their conclusions. This is because trial characteristics may inherently be different, certain costs may be absorbed by other actors or health systems, and inconsistencies in cost data collection can have profound effects on the final values reported. Nonetheless, as more clinical trial cost data is published, the standardised approach will give prospective trial sponsors and funders a clearer empirical basis for estimating clinical trial costs in low-resource and humanitarian settings.

What changes need to be made for this tool to be used by other institutions (i.e., not MSF) conducting clinical trials?

The organisation's bookkeeping expense codes will need to be entered in the "Cost categories" sheet. This will require decisions to be made about which standardised cost category is most applicable to each expense category used by the organisation.
