

## Catastrophic expenditure rates and barriers for treatment adherence in patients with colorectal cancer in India

CROCODILE study group; Kingsley, P. A.; Simoes, J.; Bodhisattva, B.; Chakrabortee, S.; Clarke, J.; Dutta, R.; Haque, P. D.; Jolly, K.; Mittal, R.; Morton, D.; Oppong, R.; Phillips, A.; Pipara, A.; Seenivasagam, R. K.; Suroy, A.; Veetil, S. K.; Bhangu, A.; Ghosh, D.

DOI:

[10.1111/codi.15674](https://doi.org/10.1111/codi.15674)

License:

Creative Commons: Attribution (CC BY)

*Document Version*

Publisher's PDF, also known as Version of record

*Citation for published version (Harvard):*

CROCODILE study group, Kingsley, PA, Simoes, J, Bodhisattva, B, Chakrabortee, S, Clarke, J, Dutta, R, Haque, PD, Jolly, K, Mittal, R, Morton, D, Oppong, R, Phillips, A, Pipara, A, Seenivasagam, RK, Suroy, A, Veetil, SK, Bhangu, A & Ghosh, D 2021, 'Catastrophic expenditure rates and barriers for treatment adherence in patients with colorectal cancer in India: the CROCODILE study protocol', *Colorectal Disease*, vol. 23, no. 8, pp. 2161-2172. <https://doi.org/10.1111/codi.15674>

[Link to publication on Research at Birmingham portal](#)

### General rights

Unless a licence is specified above, all rights (including copyright and moral rights) in this document are retained by the authors and/or the copyright holders. The express permission of the copyright holder must be obtained for any use of this material other than for purposes permitted by law.

- Users may freely distribute the URL that is used to identify this publication.
- Users may download and/or print one copy of the publication from the University of Birmingham research portal for the purpose of private study or non-commercial research.
- User may use extracts from the document in line with the concept of 'fair dealing' under the Copyright, Designs and Patents Act 1988 (?)
- Users may not further distribute the material nor use it for the purposes of commercial gain.

Where a licence is displayed above, please note the terms and conditions of the licence govern your use of this document.

When citing, please reference the published version.

### Take down policy

While the University of Birmingham exercises care and attention in making items available there are rare occasions when an item has been uploaded in error or has been deemed to be commercially or otherwise sensitive.

If you believe that this is the case for this document, please contact [UBIRA@lists.bham.ac.uk](mailto:UBIRA@lists.bham.ac.uk) providing details and we will remove access to the work immediately and investigate.



## TRIAL PROTOCOL

# Catastrophic expenditure rates and barriers for treatment adherence in patients with colorectal cancer in India: The CROCODILE study protocol

## CROCODILE study group

### \*Correspondence

Joana Simoes, NIHR Global Health Research Unit on Global Surgery, Heritage Building, University of Birmingham, Mindelson Way, Birmingham B15 2TH, UK.  
Email: jfs945@bham.ac.uk

### Funding information

This research was funded by the National Institute for Health Research (NIHR) (NIHR 16.136.79) using UK aid from the UK Government to support global health research. The views expressed in this publication are those of the author(s) and not necessarily those of the NIHR or the UK government.

### Abstract

**Aim:** Little is known about the delivery of colorectal cancer treatment in India and its associated costs. The aim of this study is to identify financial and nonfinancial barriers to adherence to colorectal cancer treatment in India.

**Method:** CROCODILE is a mixed-methods study with a quantitative and a qualitative workstream. The quantitative workstream will be a prospective cohort study to assess treatment adherence and catastrophic expenditure rates among patients with colorectal cancer in India. Consecutive newly diagnosed patients with histopathologically proven colorectal cancer from five tertiary hospitals in India will be included. Catastrophic expenditure will be defined as a treatment cost higher than 40% of nonsubsistence annual household income. Treatment costs will include medical, nonmedical and indirect expenses. Income assessment will be compared between three methods: patient-reported income, the International Wealth Index and the Gapminder tool. The qualitative workstream will explore the views and experiences of colorectal cancer patients and professionals about barriers to and facilitators for treatment adherence. Individual semi-structured interviews with three to five patients and cancer care professionals in each centre will be performed. An analytical framework will be developed to perform the analysis, through a combined approach (deductive and inductive). The results will be triangulated with the quantitative workstream for mutual knowledge enrichment.

**Conclusion:** The CROCODILE study will identify barriers to and facilitators for colorectal cancer delivery in India, influencing research and policy decisions. It will explore the feasibility of collecting data on patient-level costs and income to inform future economic evaluations in cancer and surgical care.

### KEYWORDS

colon cancer, rectal cancer, surgery, surgical oncology, medical oncology, radiation oncology, catastrophic expenditure, financial catastrophe, treatment adherence

† A complete list of the investigators is included in Appendix 1.

## INTRODUCTION

Colorectal cancer is the sixth most common cancer in India, with a recent increase among young men under 50, who are typically active and have a long life expectancy [1–3]. To support this burden, access to effective colorectal cancer care is essential to improve individual and societal health. The ratio of oncologists per cancer patient in India is 1:2000, compared with a ratio of 1:100 in Western countries [4]. There is also a major shortage of radiotherapy services, with only 545 machines existing in the country in 2019 [5]. This is not enough to meet even half of patients' needs, according to World Health Organization (WHO) guidance. Nearly 80% of cancer surgery in India is provided by general surgeons in district hospitals [6]. Although the National Cancer Control Programme in India has streamlined the delivery of oncological treatment, inefficiencies in referral systems and centralization of treatment for complex cases have resulted in fragmentation of care [6,7]. Chronic underfunding of the public sector in India has led to the general perception that the care provided in public facilities is of low quality and this has allowed the emergence of an expensive and underregulated private sector [6].

In combination, these factors have created heterogeneity in the availability and accessibility of cancer care. Little is known about the factors influencing patients' options and decisions regarding colorectal cancer treatment once a diagnosis is made. Improving cancer care and its outcomes has been prioritized in the WHO sustainable development goals (goal 3.4) and by international research networks [8,9].

The aim of this study is to identify financial and nonfinancial barriers for adherence to colorectal cancer treatment in India, using prospectively collected frontline patient-level data. Data on patients' expenditure and income is typically hard to collect, as it is time-consuming and susceptible to recall and social desirability bias. To overcome these common limitations, both now and in the future, this study will also assess the feasibility of new data collection methods for assessing patient income.

## METHODS

CROCODILE is registered on the ClinicalTrials.gov platform (NCT04517032) and the Central Trials Registry of India with the number CTRI/2020/09/027896. Indian Council of Medical Research, University of Birmingham and hospital level ethical approvals were obtained for the study.

### Study setting and design

This study will be run in five hospitals in India where cancer treatment is available and routinely delivered. This will be a prospective, multicentre, mixed-methods study with two main workstreams:

1. quantitative workstream: a prospective cohort feasibility study to determine treatment adherence and catastrophic expenditure rates;
2. qualitative workstream: to explore patient and professional views and experiences of barriers to and facilitators for adherence to colorectal cancer treatment.

Our research involves identification of barriers for treatment adherence and quantification of their impact on patients' ability to receive and pay for treatment. A mixed-methods design is therefore appropriate for CROCODILE.

## QUANTITATIVE WORKSTREAM

This protocol follows the STROBE guidelines for cohort studies [10].

### Objectives

The primary objective of this workstream is to assess treatment adherence in colorectal cancer patients in India at 6 months after treatment decision.

The secondary objectives are:

1. to determine the treatment adherence rate at 6 weeks and 3 months after treatment decision;
2. to assess the catastrophic expenditure rate at 6 weeks, 3 and 6 months after treatment decision;
3. to identify the main drivers of treatment costs in colorectal cancer treatment;
4. to assess the feasibility of data collection on treatment costs and patient income;
5. to compare patient-reported income with income assessed through the International Wealth Index and the Gapminder Foundation household pictures pool [11].

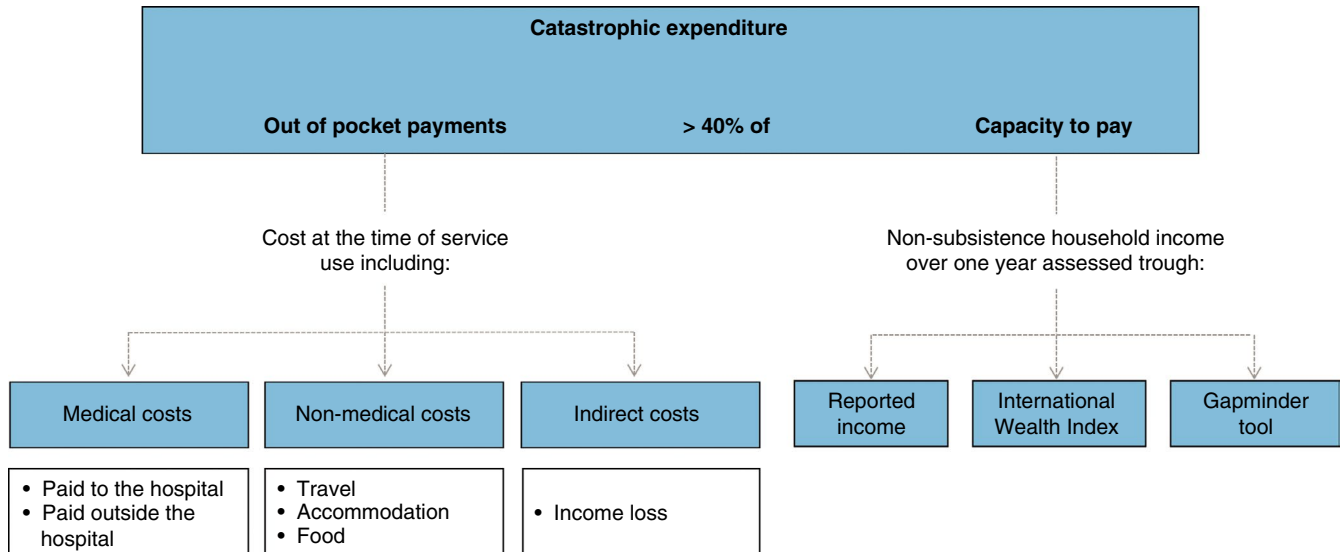
### Inclusion criteria

This study will include consecutive newly diagnosed adult patients (18 years of age or older) with a histopathologically proven malignant colorectal cancer.

### Exclusion criteria

Patients will be excluded if histopathology is unavailable or reveals a premalignant colorectal tumour (e.g. an adenoma). Patients for whom a treatment plan is made at the recruiting centre but who undergo the full course of treatment in another hospital will be excluded, as well as patients for whom telephone follow-up is not possible.





**FIGURE 1** Types of treatment cost and patient income assessment methods

This will include direct medical costs (paid to the hospital and other healthcare facilities or services), direct nonmedical costs (travel, accommodation, food expenses needed to receive treatment) and indirect costs (income loss due to absence from work while being treated). Full definitions and further details are available in Appendix 3. Expenditure data will be collected based on an individual perspective (rather than societal), so only payments which affect patients' household expenditure will be included. This will be done at three timepoints (6 weeks, 3 and 6 months after treatment decision).

Capacity to pay will be defined as nonsubsistence household income over 1 year, i.e. household income after paying for food and household expenses (including rent, loans, mortgage, water and electricity supply). Patient income data will be collected in a face-to-face assessment at the point of entry in the study through three distinct methods: reported patient income, the International Wealth Index and the Gapminder tool (see Appendix 4 for further details on methods for assessing patient income).

The main drivers of treatment cost will be the five most expensive items or services within colorectal cancer treatment, identified from the hospital bills. Categories will be predefined (e.g. theatre fees, ward fees, etc) and further cost categories will be added as data are collected. Funding schemes (e.g. Ayushman Barat, the Prime Minister Relief Fund or others), loans or donations used to support treatment cost for each patient will be recorded.

## Sample size

From the previous literature on health and cancer care-related catastrophic expenditure in low and middle income countries (LMICs), the anticipated proportion of cancer patients suffering catastrophic expenditure is around 45% [13,14]. For a prespecified

absolute precision of 10% and 5% (error margins recommended by the United Nations for household surveys), a respective sample size of 95–380 patients would be required at a confidence interval of 95% [15].

A pragmatic trade-off is needed for health economic analysis within interventional and observational studies. Longer assessments with fewer patients are likely to mitigate against recall bias and provide more reliable data, rather than performing a larger number of surveys [16]. Therefore, a final sample size of 200 patients is feasible for the CROCODILE study.

## Data analysis

Statistical analysis will be undertaken using the R v.3.6.1 (R Project for Statistical Computing). An initial analysis will describe the overall treatment adherence and catastrophic expenditure rates in our sample of 200 patients. For all outcome measures, the appropriate summary statistics will be presented with the adequate effect measures, 95% confidence intervals and two-sided test *p*-values. Data completeness rates on costs and income will be reported as a secondary outcome. Completeness rates will be described separately for medical, nonmedical and indirect costs, and for the three methods for income assessment.

## Subgroup analysis

A subgroup analysis will be performed to explore the impact on treatment adherence and expenditure of distance from home to the hospital. Catastrophic expenditure and treatment adherence rates will be compared between patients being treated at a local versus a distant hospital.

## Sensitivity analysis

A sensitivity analyses will be performed to describe catastrophic expenditure rates using two different thresholds: 20% versus 40% of nonsubsistence household income. Different thresholds have been used to define catastrophic expenditure and there is no consensus to date [17]. The correlation between catastrophic expenditure rates at these two cut-offs and patient wealth level can inform future studies on the advantages and disadvantages of both methods.

## QUALITATIVE WORKSTREAM

### Aim

The aim of the qualitative workstream will be to explore the views and experiences of colorectal cancer patients and professionals regarding barriers to and facilitators for treatment adherence.

### Participants

The participants in this workstream will be adults (18 years of age or older) who are diagnosed with colorectal cancer (histopathologically proven) or cancer care professionals who usually work with colorectal patients. The participants need to be able to provide written informed consent (signature or a fingerprint).

### Participant identification and consent

Patients and professionals will be identified from surgical oncology, medical oncology or radiation oncology departments. Patients included in the qualitative and quantitative workstreams will overlap. A participant information sheet (Appendix 5) will be given to each participant before consent is taken by a researcher trained in qualitative methods.

### Sample size and sampling method

For this workstream, three to five patients and three to five professionals will be included from each participating site. Purposive sampling will aim for diversity around patients' demographic and social features, wealth levels and types of treatment. A range of professionals will be invited to participate, enabling exploration of specialty-specific challenges that patients might face while being treated in the different oncology disciplines (medical, surgical and radiation oncology). At the time of inclusion in the quantitative workstream, demographic, economic and disease data will be collected, enabling identification of patients suitable for inclusion in the qualitative part of the study.

## Methodological approach

A generic qualitative approach will be used in this study with a main focus on participants' experience of challenges regarding treatment adherence [18]. A combination of inductive and deductive approaches will be used to build the framework for analysis. A literature search of barriers to access and receipt of cancer treatment in LMICs will be performed to preselect codes and themes to be included in the framework (deductive approach). Further codes and categories will be generated from the collected data through unrestricted coding (inductive approach). Planning of the interviews will be aligned with this, ensuring that pre-identified topics are covered with the participants but also allowing the space for new unexpected aspects to be raised during the interviews.

### Data collection and management

One-to-one interviews will be conducted with all the participants. A semistructured approach will be used, with a few prompt questions but allowing the participants to express their views (topic guide for interviews in Appendix 6 and 7). The interview will be planned to last between 30 and 60 min and will take place in the most convenient location possible for participants. Due to the travel restrictions related to COVID-19, the interviews might need to be done remotely via video call. For participants who cannot communicate fluently in English, an onsite interpreter will be used to allow translation of the questions into the local language and answers back to English. Interpreters will be trained about the need for accurate translation and confidentiality prior to undertaking interviews.

The interviews will be digitally recorded after the participants' consent and written notes will be taken. The interviews will then be transcribed clean verbatim and anonymized before analysis. NVivo v.12 will be used to assist data management. The transcript will be coded by a researcher before the categories and themes emerging from the data are identified. A second researcher will code the first set of three or four interviews, maximizing interpretation of the data and refining the labelling and coding strategy for the subsequent transcripts.

### Data analysis

From the available methodologies for qualitative data analysis, framework analysis is recognized as the most useful for health systems and policy informing research [19]. An analytical framework will be used for the transcripts to be indexed to the different codes and categories within the framework matrix. While charting the data into the framework, the researchers will keep a record of illustrative quotes to enrich the final conclusions of this workstream.

Data interpretation will be developed from the identified categories and themes, and the connections between them. The main domains of the results of the study will be the barriers to and the solutions for treatment adherence. The consolidated criteria for reporting qualitative research (COREQ) will be used to report the

results. Finally, the results of this workstream will be interpreted together with the results of the quantitative workstream, to provide a deeper understanding of patients' options and decisions.

## DISCUSSION

The CROCODILE study will identify a vulnerable group of patients in India who struggle to adhere to a treatment plan for colorectal cancer either because they cannot pay for it or due to other reasons. The Lancet Oncology Commission recommends that the scaling up of cancer services should be based on a country's cancer burden and state of cancer care, highlighting the importance of including both patients and cancer care providers in this process [20]. CROCODILE will provide real-world data on the rates of catastrophic expenditure, barriers that patients face to treatment adherence and how to overcome them.

Financial protection is one of the global health priorities defined by the WHO (sustainable development goal 3.8) and mitigating against catastrophic expenditure has also been prioritised by the Lancet Commission on Global Surgery [21]. An evaluation of 74 000 Indian household surveys showed that when family members were affected by cancer households more likely to make OOP healthcare payments and had higher rates of asset sales than households not affected by cancer [22]. CROCODILE will validate novel methods for patient-level data collection on catastrophic expenditure. The results will be used to inform health economic evaluations alongside global interventional and observational studies.

We acknowledge the exploratory nature of this study, and we will draw careful conclusions from our results. The number and type of hospitals taking part in CROCODILE (four charity hospitals and one government hospital) might influence the type of patients included in the study and their views.

The COVID-19 pandemic has had a huge impact on non-COVID research. Although the study design has not been changed as a result of the pandemic, its delivery has been affected. The research teams are being trained through online platforms. Onsite training with direct contact with patients, patient files and hospital bills has not been possible, which makes data collection more challenging. The results will be interpreted in light of the effects of the pandemic on cancer care.

## ACKNOWLEDGEMENTS

India Institute Fellowship scheme for supporting this research, under the Strategic Global Engagement programme of the University of Birmingham.

## CONFLICT OF INTEREST

There are no conflicts of interest to declare.

## ETHICAL STATEMENT

Indian Council of Medical Research, University of Birmingham and hospital level ethical approvals were obtained for the study.

## AUTHOR CONTRIBUTION

All the listed co-authors have contributed to the design and draft of this protocol, critical revision, final approval of the version to be published and agreed to be accountable for the accuracy and integrity of the produced work.

## DATA AVAILABILITY STATEMENT

Data can be requested from all the participating centres and will be made available for further analysis.

## REFERENCES

1. GLOBOCAN: Global Cancer Observatory. [https://gco.iarc.fr/today/online-analysis-table?v=2018&mode=cancer&mode\\_population=continents&population=900&populations=356&key=asr&sex=0&cancer=39&type=0&statistic=5&prevalence=0&population\\_group=0&ages\\_group%5B%5D=0&ages\\_group%5B%5D=17&group\\_cancer=1&include\\_nmssc=1&include\\_nmssc\\_other=1#collapse-group-0-3](https://gco.iarc.fr/today/online-analysis-table?v=2018&mode=cancer&mode_population=continents&population=900&populations=356&key=asr&sex=0&cancer=39&type=0&statistic=5&prevalence=0&population_group=0&ages_group%5B%5D=0&ages_group%5B%5D=17&group_cancer=1&include_nmssc=1&include_nmssc_other=1#collapse-group-0-3). Accessed 14 July 2020.
2. Mathew A, Baby B, Wang K, Sirohi B, Lei F, Chen Q, et al. Colorectal cancer incidence in younger adults in India. *Gut*. 2020;69:1899–900.
3. Haleshappa RA, Rao SA, Garg S, Kuntegowdanahalli CL, Kanakasetty GB, Dasappa L. Is colorectal cancer in young (<40 Years) different from those in the elderly (>40 years): experience from a regional care center. *Indian J Med Paediatr Oncol*. 2017;38:466–70.
4. Gulia S, Sengar M, Badwe R, Gupta S. National Cancer Control Programme in India: proposal for organization of chemotherapy and systemic therapy services. *J Glob Oncol*. 2017;3:271–4.
5. Munshi A, Ganesh T, Mohanti BK. Radiotherapy in India: history, current scenario and proposed solutions. *Indian J Cancer*. 2019;56:359–63.
6. Sullivan R, Alatiser OI, Anderson BO, Audisio R, Autier P, Aggarwal A, et al. Global cancer surgery: delivering safe, affordable, and timely cancer surgery. *Lancet Oncol*. 2015;16:1193–224.
7. Gelband HJP, Sankaranarayanan R, Horton S. *Cancer Disease Control Priorities*. 3rd ed. vol. 3. Washington, DC: World Bank; 2015.
8. NIHR Global Health Research Unit on Global Surgery. Prioritizing research for patients requiring surgery in low- and middle-income countries. *Br J Surg*. 2019;106:e113–20.
9. World Health Organisation, Global Monitoring report on Financial Protection in health 2019. <https://www.who.int/publications/i/item/global-monitoring-report-on-financial-protection-in-health-2019>. Accessed 14 July 2020.
10. Elm EAD, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP, et al. Strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. *Br Med J*. 2007;335:806.
11. Gapminder Foundation. Dollar Street 2015. <https://www.gapminder.org/dollar-street>.
12. Global Tuberculosis Programme. Protocol for survey to determine direct and indirect costs due to tuberculosis and to estimate proportion of TB-affected households experiencing catastrophic total costs due to TB. World Health Organization; 2015.
13. The ACTION Study Group. Catastrophic health expenditure and 12-month mortality associated with cancer in southeast Asia: results from a longitudinal study in eight countries. *BMC Med*. 2015;13:190.
14. Mahal A, Karan A, Engelgau M. The Economic Implications of Non-Communicable Disease for India. The International Bank for Reconstruction and Development/The World Bank; 2010.
15. Lwanga SK, Lemeshow S & World Health Organization. Sample size determination in health studies: a practical manual. World Health



- Organization; 1991. <https://appswho.int/iris/handle/10665/40062>.
16. Sweeney S, Vassall A, Foster N, Simms V, Ilboudo P, Kimaro G, et al. Methodological issues to consider when collecting data to estimate poverty impact in economic evaluations in low-income and middle-income countries. *Health Econ.* 2016;25(Suppl 1):42-52.
  17. Xu K, Evans DB, Kawabata K, Zeramdini R, Klavus J, Murray CJL. Household catastrophic health expenditure: a multicountry analysis. *Lancet.* 2003;362:111-7.
  18. Caroline Bradbury-Jones JB, Clark MT, Herber OR, Wagstaff C, Taylor J. The state of qualitative research in health and social science literature: a focused mapping review and synthesis. *Int J Soc Res Methodol.* 2017;20:627-45.
  19. Gale NK, Heath G, Cameron E, Rashid S, Redwood S. Using the framework method for the analysis of qualitative data in multi-disciplinary health research. *BMC Med Res Methodol.* 2013;13:117.
  20. Qu LG, Brand NR, Chao A, Ilbawi AM. Interventions addressing barriers to delayed cancer diagnosis in low- and middle-income countries: a systematic review. *Oncologist.* 2020;25:e1382-95.
  21. The Lancet Commission of Global Surgery. Global Surgery 2030: evidence and solutions for achieving health, welfare, and economic development. *Lancet.* 2015;386:569-624.
  22. Mahal A, Karan A, Fan VY, Engelgau M. The economic burden of cancers on Indian households. *PLoS One.* 2013;8:e71853.

**How to cite this article:** CROCODILE study group.

Catastrophic expenditure rates and barriers for treatment adherence in patients with colorectal cancer in India: The CROCODILE study protocol. *Colorectal Dis.* 2021;23:2161-2172. <https://doi.org/10.1111/codi.15674>

## APPENDIX 1

### CROCODILE study group co-authors

P. A. Kingsley† (Radiation Oncology, Christian Medical College and Hospital, Ludhiana, Punjab, India), J. Simoes† (National Institute for Health Research (NIHR) Global Health Research Unit on Global Surgery, University of Birmingham, UK; Hospital Garcia de Orta, Portugal), B. Bodhisattva (Surgical Oncology, All India Institute of Medical Sciences Rishikesh, Rishikesh, Uttarakhand, India), S. Chakrabortee (National Institute for Health Research (NIHR) Global Health Research Unit on Global Surgery, University of Birmingham, UK), J. Clarke, (Institute of Applied Health Research, University of Birmingham, UK) R. Dutta, (Institute of Applied Health Research, University of Birmingham, UK), P. D. Haque, (Institute of Applied Health Research, University of Birmingham, UK), K. Jolly (Institute of Applied Health Research, University of Birmingham, UK), R. Mittal (Colorectal Surgery, Christian Medical College and Hospital, Vellore, Tamil Nadu, India), D. Morton (National Institute for Health Research (NIHR) Global Health Research Unit on Global Surgery, University of Birmingham, UK), R. Oppong (Health Economics Unit, Institute of Applied Health Research, University of Birmingham, UK), A. Phillips (Medical Oncology, Christian Medical College and Hospital, Ludhiana, Punjab, India), A. Pipara (Colorectal Surgery, Tata Medical Center, Kolkata, West Bengal, India), R. K. Seenivasagam (Surgical Oncology, All India Institute

of Medical Sciences Rishikesh, Rishikesh, Uttarakhand, India), A. Suroy (India Hub, NIHR Global Health Research Unit on Global Surgery, Christian Medical College and Hospital, Ludhiana, India), S. K. Veetil (Surgical Oncology, Christian Medical College and Hospital, Ludhiana, Punjab, India), A. Bhangu\* (National Institute for Health Research (NIHR) Global Health Research Unit on Global Surgery, University of Birmingham, UK), D. Ghosh\* (Surgical Oncology, All India Institute of Medical Sciences Rishikesh, Rishikesh, Uttarakhand, India).

\*Joint senior authors.

†Joint first authors.

## APPENDIX 2

### Patient information sheet (CROCODILE quantitative workstream)

#### BACKGROUND

Previous studies show that colorectal cancer (CRC) patients in India present with more advanced disease compared to western patients. The main goals of this project are to explore barriers in access to cancer treatment in India, particularly affordability of care.

#### WHAT THIS STUDY ENTAILS

To do this, we need to collect data about your disease and the treatment you received, including how much it cost for you. You were enrolled in this study because you have a CRC diagnosis and you will undergo treatment. Participation in this study will have no impact on your treatment. No changes to your treatment will be made whether you decide to participate or not.

#### TIME COMMITMENT

The time commitment for you is very low (about 20 minutes). Whilst you are in hospital we will invite you to answer the survey and we will support you in any questions you have about it. At 6 weeks, 3 months and 6 months after this in-person contact, we will make a telephone call to confirm the total cost of cancer treatment with you. After this, your participation will be over and nothing further will need to be done.

#### INFORMATION TO BE COLLECTED

We will collect data about your disease and the treatment you were or will be given. Data about your treatment cost will be collected from hospital records. You will be asked to fill a survey with some details about your income and the assets you own. Besides that, you will be asked to identify 5 pictures of house goods that look like your own. The questionnaire also covers transport, food and accommodation expenses. If any questions make you uncomfortable, you do not have to answer them.

#### CONFIDENTIALITY

Information about you will be kept confidential. Your telephone contact will be used only for the study purpose and will be kept in



a locked secure place in the hospital. You will be given the choice to share your email in case you want to get feedback about the study results. If you don't wish to share it or don't hold an e-mail account, you can always ask the local research partners (NIHR Global Surgery India Hub) for this information, if you are interested. The least possible information about you that is needed for the research will be sent to the University of Birmingham which is coordinating this study. It will be stored for 05 years but will then be destroyed. We will keep the data as safely and less detailed as possible; no

records of your name e-mail or telephone will be kept in the study central files.

### CONSENT

It is up to you to decide to join the study. If you agree to take part, we will ask you to sign (or fingerprint) a consent form. You are free to leave the study, without giving a reason. If requested, we can remove your information from the study. Withdrawing from the study will not affect the care you receive.

## APPENDIX 3

### Details of cost data collection

Type of cost	Definition	Examples	Data source	Timing of collection
Direct costs	Out-of-pocket payments made directly by the patient and their household			
Direct medical	Out-of-pocket payments for colorectal cancer diagnosis and treatment, made by the patient's household			
In the hospital	Direct payments to the recruiting hospital	Surgical fees, radiotherapy fees	Hospital bills	Follow-up
Outside the hospital	Direct payments to other hospitals or healthcare facilities or providers	Drugs from the pharmacy, dressing costs	Patient	Face-to-face assessment, follow-up
Direct nonmedical	Out-of-pocket payments related to the use of cancer care health services in the recruiting hospital, made by the patient's household			
Travel	Payments made by patient's household for: daily commuting to the hospital (patient and/or companions); long-distance travelling (patient and/or household members)	Bus or taxi to the hospital, flight or train to the hospital	Patient	Follow-up
Accommodation	Payments made by the patient's household for accommodation near the hospital in order to access treatment (patient and/or companions)	Staying in a hotel near the hospital to attend multiple outpatient visits	Patient	Follow-up
Food	Payments made by the patient's household for food near the hospital in order to access treatment (patient and/or companions)	Food bought by patient's relatives while staying away from home	Patient	Follow-up
Indirect costs	Income losses related to absence from work due to colorectal cancer care, incurred by the patient or any household member (this excludes leave days when salary is not penalized)	Income not earned by the patient during hospital admission	Patient	Follow-up

## APPENDIX 4

### Details of patient income assessment

The patient income assessment will be performed by a trained researcher during the face-to-face assessment, at the point of study entry, through three different methods: reported household income and capacity to pay, the International Wealth Index (IWI) and the Gapminder assessment tool.

### REPORTED HOUSEHOLD INCOME AND CAPACITY TO PAY

This is made up of three parts:

1. Reported total household income: amount of money earned per month by all the household members who work and produce income.
2. Reported nonsubsistence household income: share of the total household income which is left after household subsistence expenses are paid for. Subsistence expenses include housing (rent, loan, mortgage, electricity and water access).
3. Capacity to pay: nonsubsistence household income over 1 year (non-subsistence household monthly income multiplied by 12 months).



## INTERNATIONAL WEALTH INDEX

The IWI (see questionnaire below) is a validated tool for wealth assessment with 12 questions about household assets that individuals

might or might not own. Each asset has a relative weight and contribution to the IWI score. The final score ranges from 0 to 100 and reflects the household wealth.

### Asset measurement for the IWI

	Do you own this item?
Consumer durables	Do you own this item?
Television	Yes/no
Refrigerator	Yes/no
Phone	Yes/no
Car	Yes/no
Bike	Yes/no
Do you have one or more of these utensils: chair, table, clock, watch, water cooker, radio, fan or mixer?	Yes/no
Do you have one or more of these utensils: washer, dryer, computer, motorbike, motorboat, air conditioner, or generator?	Yes/no
Housing characteristics	
Which is your floor material? (choose one of the options below)	<input type="checkbox"/>
Earth, dung, sand	<input type="checkbox"/>
Cement, concrete, raw wood	<input type="checkbox"/>
Finished floor with parquet, carpet, tiles, ceramic	<input type="checkbox"/>
How is your toilet facility? (choose one of the options below)	
Traditional pit latrine, hanging toilet, or no toilet facility	<input type="checkbox"/>
Public toilet, improved pit latrine	<input type="checkbox"/>
Private flush toilet	<input type="checkbox"/>
How many rooms are there in your house? (choose one of the options below)	
Zero or one	<input type="checkbox"/>
Two	<input type="checkbox"/>
Three or more	<input type="checkbox"/>
Public utilities	
Access to electricity	Yes/no
Water source: (choose one of the options below)	
Spring, surface water, unprotected well	<input type="checkbox"/>
Public tap, protected well or tanker truck	<input type="checkbox"/>
Bottled water or water piped into dwelling or premises	<input type="checkbox"/>

Previous research has found that an exponential function is the best way to describe relationship between the IWI score and household income (1):

$$\text{Income (per day, in dollars)} = 1.489056 \times \exp(0.02918 \times \text{IWI score})$$

The coefficient in the formula above was based on data from several population-level surveys, including the Indian Human Development Survey.

### GAPMINDER ASSESSMENT TOOL

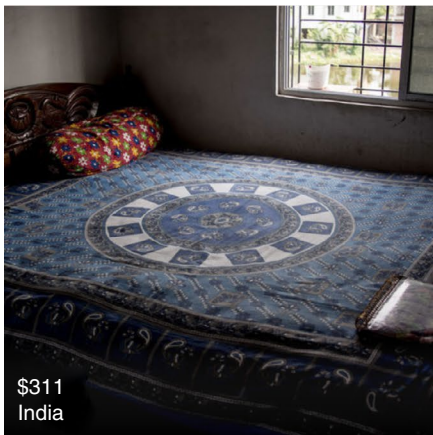
The Gapminder Foundation created the Dollar Street project, which aims to show how people live their daily lives through pictures taken from all over the world (2). Household income is collected from each

household and each picture is matched to the income of the household where it belongs.

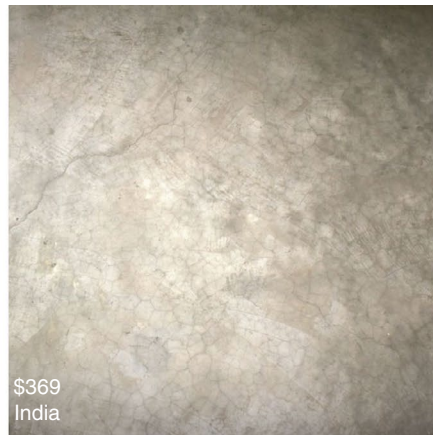
Given that each picture is matched to a specific income, this can be a user friendly way to assess patients' income, which is typically hard to collect. Patients will be asked to select the household items that look most like their own from the pool of pictures available on the Gapminder website for that particular item. By including all the pictures available in the Dollar Street project for that particular item we will ensure that a discriminatory range of matching incomes is available. Only pictures from India will be presented to patients.

Patient income will be calculated as a mean average of the incomes matched to the pictures selected by the patient. An example is given below:

Pictures chosen by the patient:



\$311  
India



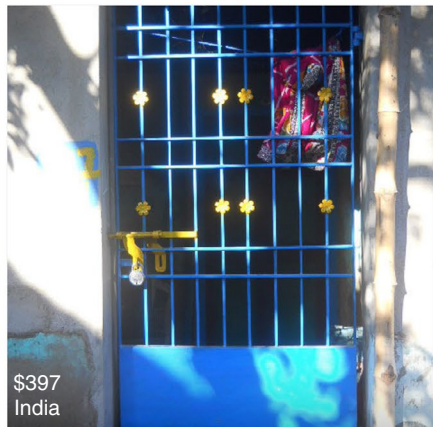
\$369  
India



\$369  
India



\$369  
India



\$397  
India

Income calculation =  $(311+369+369+369+397)/5 = 363$  US dollars. The exchange rate at the date of patient assessment will be used for conversion to Indian rupees.

## REFERENCES

- (1) Lindgren M. (2015) Gapminder Foundation. Available from: <https://drive.google.com/drive/folders/0B9jWD65HiLUnRm5ZNWIMSU5GNEU>
- (2) Gapminder Foundation (2015). Dollar Street. Available from: <https://www.gapminder.org/dollar-street>

## APPENDIX 5

### Participant information sheet (CROCODILE qualitative workstream)

## BACKGROUND

Colorectal cancer is the 4th most incident cancer in India according to World Health Organization and its incidence is increasing. Previous studies show that colorectal cancer patients in India are usually younger than in the West and have more advanced disease. This study aims to explore patient and healthcare professional's perspectives on how patients access treatment care in India.

## WHAT THIS STUDY ENTAILS

Participation in this study will have no impact on patient treatment. You were enrolled in this study because you are either a patient with a CRC diagnosis or a healthcare professional in charge of CRC patients (diagnosis or treatment). A researcher will ask you about the steps involved in receiving cancer treatment, difficulties in that process and your views on what should be done differently to facilitate access to cancer care.

## TIME COMMITMENT

The time commitment for you is about 1 h. Once this interview is completed, your participation will be over.

## INFORMATION TO BE COLLECTED

Only basic information will be collected. This will include information about you, your illness, how did you seek health care and your ideas about how to improve access to cancer care. During the interview the researcher may make some notes. The researcher will ask for permission to audio record their interview with you (this is optional). If any questions make you uncomfortable, you do not have to answer them.

## CONFIDENTIALITY

Information about you will be kept confidential. You will be given the choice to share your email in case you want to get feedback about



the study results. If you don't wish to share it or don't hold an e-mail account, you can always ask the local research partners (NIHR Global Surgery India Hub) for this information, if you are interested. The least possible information about you that is needed for the research will be sent to the University of Birmingham which is coordinating this study. This information will be stored for 05 years but will then be destroyed. We will keep the data as safely and less detailed as possible; no records of your name or e-mail will be kept in the study central files.

## CONSENT

It is up to you to decide to join the study. If you agree to take part, we will ask you to sign (or fingerprint) a consent form. You are free to leave the study, without giving a reason. If requested, we can remove your information from the study up to 30 days after your interview. Withdrawing from the study will not affect the care you receive.

## APPENDIX 6

### Interview topic guides for patients

#### INTRODUCTIONS AND THANKING FOR THE TIME

##### Before the interview:

1. Brief introduction to the study and its goals: 'The purpose of this study is to understand patients' experiences while receiving treatment for cancer and how we can improve those'.
2. Obtain and sign consent form, after answering any questions the patient might have about the study goals, participant withdrawal during or after the interview and the confidentiality of the data.
3. Remind the patient that the interview will be about their treatment pathway and challenges but that they will have time to talk about any other related issues that they might want to talk about or that were not covered.
4. Start audio recording and begin the interview.

#### QUESTIONS AND PROMPTS FOR THE INTERVIEW

##### About the patient treatment pathway

1. Tell me about how you were diagnosed with colorectal cancer.
2. What was your experience of trying to find help regarding your symptoms?
3. Have you decided to have treatment in the same hospital? How have you decided about that?

##### About barriers to receiving treatment

4. When your doctor told you that you would need treatment, what were your thoughts?
  - (a). Did you think of anything that could make it difficult for you to have treatment?
  - (b). Did you and your relatives needed to make any arrangements

for you to begin treatment?

5. While you were receiving treatment, were there any struggles?
  - (a). Did you felt like you needed to stop at any point?

##### About economic factors

6. How did you pay for your treatment?
7. Have you had access to any funding schemes to help you pay for your treatment?
  - (a). How was it applying those funds?
  - (b). Could anything be improved to make it easier for you to apply or access those funds?

##### About social and cultural factors

8. Have you experienced any disadvantage in receiving cancer treatment?

## SUMMARY AND CONCLUSIONS

9. Is there anything that you would change in your treatment pathway to make it easier for you to receive treatment?
10. Is there anything else you would like to tell me?

## APPENDIX 7

### Interview topic guide for cancer care professionals

#### INTRODUCTIONS AND THANKING FOR THE TIME

##### Before the interview:

1. Brief introduction to the study and its goals: 'The purpose of this study is to understand patients' experiences while receiving treatment for cancer and how we can improve those'.
2. Obtain and sign consent form, after answering any questions the professional might have about the study goals, participant withdrawal during or after the interview and the confidentiality of the data.
3. Remind the participant that the interview will be about treatment pathways and adherence but that they will have time to talk about any other related issues that they might want to talk about or that were not covered.
4. Start audio recording and begin the interview.

#### QUESTIONS AND PROMPTS FOR THE INTERVIEW

##### About the patient treatment pathway

1. In which setting do you usually see colorectal cancer patients?
  - a. Which types of cancer treatment are you involved in?
2. Tell me about how easy you think it is for patient to access cancer care?
  - a. What can be the main barriers and facilitators?

##### About barriers to receiving treatment

3. When you propose a cancer treatment to a patient, what are their main concerns regarding taking the treatment?
  - a). (Do you have patients for whom you have proposed a treatment but have never started it? What were the reasons?
4. After patients start their treatment with you, are there some who stop half way?
  - (a). What are the reasons for patients to do that?  
About economic factors
5. How do your patients find paying for their treatment?
6. Which funding schemes might be available for them?
  - (a). Do they have difficulties applying or accessing those funds?
  - (b). What do you think could be improved to make it easier for patients to apply?

#### About social and cultural factors

7. Do you think you are any social groups for whom it's more difficult to receive care?
  - (a). Do you think cultural habits or beliefs can prevent some people from receiving or continuing treatment?
8. Do you think it is more difficult for women or men to get cancer treatment? Is there a difference?

#### Other factors

9. From what you know, do you think there are other issues stopping patients in India from having their cancer treatment done?

#### SUMMARY AND CONCLUSIONS

10. What do you think that could be done to make it easier to patients to receive cancer care?
11. Is there anything else you would like to tell me?