

## PEER REVIEW HISTORY

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### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	Cervical cancer screening in rural Bhutan with the careHPV test on self-collected samples: an ongoing cross-sectional, population-based study (REACH-Bhutan)
<b>AUTHORS</b>	Baussano, Iacopo; Tshering, Sangay; Choden, Tashi; Lazzarato, Fulvio; Tenet, Vanessa; Plummer, Martyn; Franceschi, Silvia; Clifford, G; Tshomo, Ugyen

### VERSION 1 - REVIEW

<b>REVIEWER</b>	Dr Srabani Mittal Child in Need Institute India
<b>REVIEW RETURNED</b>	02-Mar-2017

<b>GENERAL COMMENTS</b>	Well carried out community based study. Minor comments in the materials and methods section: 1. Did the local health workers receive any special training on community mobilization for HPV DNA based cervical cancer screening? 2. Was the self-collection by women done in presence of the study team nurse? 3. What was the average time taken to deliver careHPV test reports to the BHUs? 4. Few lines on the recall mechanism of screen positive women to be added
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<b>REVIEWER</b>	Adhemar Longatto Faculty of Medicine São Paulo University, Brazil.
<b>REVIEW RETURNED</b>	14-Mar-2017

<b>GENERAL COMMENTS</b>	This is an important manuscript that address optional tools to make cervical screening in remote and poor regions. Despite of the well-addressed design of study, the introduction lack of the principal objective. A sentence of one or two lines clearly expressing the goal of the study can contribute to improve the comprehension of the study. Also, the authors did not discuss their results with other recent studies using careHPV with the same objective, performed in rural and remote areas of the world. This is particularly important if we consider that careHPV and other HPV tests with similar characteristics can contribute to reduce cervical high grade lesions in areas where screening programs are not adequately performed. Below the authors will find few studies that can contribute to improve this side of Discussion section. 1: Obiri-Yeboah D, Adu-Sarkodie Y, Djigma F, Akakpo K, Aniakwa-Bonsu E,
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Amoako-Sakyi D, Jacques S, Mayaud P. Options in human papillomavirus (HPV) detection for cervical cancer screening: comparison between full genotyping and a rapid qualitative HPV-DNA assay in Ghana. *Gynecol Oncol Res Pract.* 2017 Mar 3;4:5. doi: 10.1186/s40661-017-0041-1. PubMed PMID: 28270915; PubMed Central PMCID: PMC5335847.

2: Segondy M, Kelly H, Magooa MP, Djigma F, Ngou J, Gilham C, Omar T, Gombri-Lompo O, Michelow P, Doutre S, Clavero O, Chikandiwa A, Sawadogo B, Didelot MN, Costes V, Méda N, Delany-Moretlwe S, Mayaud P. Performance of careHPV for detecting high-grade cervical intraepithelial neoplasia among women living with HIV-1 in Burkina Faso and South Africa: HARP study. *Br J Cancer.* 2016 Aug 9;115(4):425-30. doi: 10.1038/bjc.2016.207. PubMed PMID: 27434037; PubMed Central PMCID: PMC4985351.

3: Tuerxun G, Yukejaier A, Lu L, Aierken K, Mijiti P, Jiang Y, Abulizi A, Zhang Y, Abuduxikuer G, Abulizi G, Li H. Evaluation of careHPV, Cervista Human Papillomavirus, and Hybrid Capture 2 Methods in Diagnosing Cervical Intraepithelial Neoplasia Grade 2+ in Xinjiang Uyghur Women. *Oncologist.* 2016 Jul;21(7):825-31. doi: 10.1634/theoncologist.2015-0447. PubMed PMID: 27317575; PubMed Central PMCID: PMC4943388.

4: Lorenzi AT, Fregnani JH, Possati-Resende JC, Antoniazzi M, Scapulatempo-Neto C, Syrjänen S, Villa LL, Longatto-Filho A. Can the careHPV test performed in mobile units replace cytology for screening in rural and remote areas? *Cancer Cytopathol.* 2016 Aug;124(8):581-8. doi: 10.1002/cncy.21718. PubMed PMID: 27070446.

5: Labani S, Asthana S. Age-specific performance of careHPV versus Papanicolaou and visual inspection of cervix with acetic acid testing in a primary cervical cancer screening. *J Epidemiol Community Health.* 2016 Jan;70(1):72-7. doi: 10.1136/jech-2015-205851. PubMed PMID: 26248549.

6: Bansil P, Lim J, Byamugisha J, Kumakech E, Nakisige C,

	Jeronimo JA. Performance of Cervical Cancer Screening Techniques in HIV-Infected Women in Uganda. J Low Genit Tract Dis. 2015 Jul;19(3):215-9. doi: 10.1097/LGT.000000000000090. PubMed PMID: 25551591.
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### VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Dr Srabani Mittal

Child in Need Institute, India

Please leave your comments for the authors below

Well carried out community based study.

Response. Thank you.

Minor comments in the materials and methods section:

1. Did the local health workers receive any special training on community mobilization for HPV DNA based cervical cancer screening?

Response. The Bhutanese principal investigator instructed local health workers from each Basic Health Units (BHUs) on community mobilization and HPV DNA based cervical cancer screening key features. Furthermore, the BHUs provide primary health care to the Bhutanese population; therefore local health workers are regularly involved in community mobilization initiatives targeted to public health prevention programs. We have amended the text of the methods section accordingly [Pg 6, Lines 107-8].

2. Was the self-collection by women done in presence of the study team nurse?

Response. The study team nurse provided guidance to the participants on how to perform the self-collection but did not attend the self-collection procedure. We have amended the text of the methods section accordingly [Pg 7, Lines 127-9].

3. What was the average time taken to deliver careHPV test reports to the BHUs?

Response. The central laboratory in Thimphu delivered careHPV results to each BHUs in a median of 11 days (inter-quartile range: 9 to 33 days). We have amended the text of the methods section [Pg 7, Lines 136-7] and the discussion section accordingly [Pg 13, Lines 255-7].

4. Few lines on the recall mechanism of screen positive women to be added

Response. We briefly describe the recall mechanism [Pg 7, Lines 137-8] Health workers invited careHPV positive, and a subset of negative women, for the follow-up visit at the BHU. However, details on the recall mechanism, clinical management of careHPV-positive women and performance of careHPV testing will be reported in future publications.

Reviewer: 2

Adhemar Longatto

Faculty of Medicine São Paulo University, Brazil.

Please leave your comments for the authors below

This is an important manuscript that address optional tools to make cervical screening in remote and poor regions.

Response. Thank you.

Despite of the well-addressed design of study, the introduction lacks of the principal objective. A sentence of one or two lines clearly expressing the goal of the study can contribute to improve the comprehension of the study.

Response. The main aim of REACH Bhutan study is to assess the feasibility, outcomes, and challenges of cervical cancer screening based on the careHPV test on self-collected samples among women 30–60 years of age in rural areas of the country.

To better address and delineate the aims of the study and the scope of the findings described in the current report, we amended the last paragraph of the introduction section [Pg 5, Line 92 to page 6, Line 96].

“In the current report we describe the study design, target population, recruitment and sample collection methods, key study participants characteristics, and the patterns of participation. Details on the performance of careHPV testing, and clinical management of careHPV-positive women will be reported in future publications.”

Also, the authors did not discuss their results with other recent studies using careHPV with the same objective, performed in rural and remote areas of the world. This is particularly important if we consider that careHPV and other HPV tests with similar characteristics can contribute to reduce cervical high grade lesions in areas where screening programs are not adequately performed.

Response. We fully agree with the reviewer that our findings about the performances of careHPV must be discussed with reference to other recent studies with the same objective, using the same test and performed in rural/remote areas of the world. To put our study in a wider context, we have therefore modified the beginning of the discussion section [Pg 11, Lines 209-11] and refer to reports about the evaluation of the implementation of Care-HPV screening in under-served populations from Asia, Africa, and Latin America.

#### VERSION 2 – REVIEW

<b>REVIEWER</b>	Dr Srabani Mittal Child in Need Institute, Kolkata India
<b>REVIEW RETURNED</b>	03-Apr-2017

<b>GENERAL COMMENTS</b>	Responses to the queries well addressed. Revisions have indeed improved the quality of the manuscript. Wishing good luck with the publication and look forward to the performance of Care HPV in the selected population in future
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<b>REVIEWER</b>	Adhemar Longatto-Filho Faculty of Medicine São Paulo University, Brazil
<b>REVIEW RETURNED</b>	01-Apr-2017

<b>GENERAL COMMENTS</b>	The authors have improved the paper with well-addressed informations.
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