Reuse of polyp traps, a way to approach sustainability: A multicentric non-inferiority study.

Protocol identifying number: POLYPTRAP

Confidentiality Statement

This document contains confidential information that must not be disclosed to anyone other than the Sponsor, the Investigator Team, regulatory authorities, and members of the Ethics Committee.

Sponsor: Institut de Recerca de l'Hospital de la Santa Creu i Sant Pau –

IIB Sant Pau

Investigator Coordinator: Dr. Carlos Guarner Argente

TABLE OF CONTENTS

1. INTRODUCTION

1.1 BACKGROUND INFORMATION

Climate change is the phenomenon of increase of the global temperature because of greenhouse gas (GHG) emissions (1) which is one of the main concerns of humanity and it has a huge impact on human health. This impact is not only direct due to the effect of heat waves or to the consequences of extreme weather events, but also indirect due to the modifications that generates in ecosystems, economies and social structures (2).

The four major GHGs are: carbon dioxide, methane, nitrous oxide and industrial gases as fluorinated gases. Considering that not all GHGs affect equally to global warming, a standardised unit, the carbon dioxide equivalents (CO_2e), is used to quantify GHG emissions allowing to measure the equivalent global warming impact (3). Higher temperatures produced by GHG emissions increase the transmission of infectious diseases (4), puts in risk food and water security leading to malnutrition and famine, and prompts the loss of biodiversity (1), among others.

The Paris Agreement set in 2016 was a landmark in the multilateral climate change process as it was the first time a binding agreement brought all nations aligned to fight climate change (5). Its primary goal was to limit the temperature increase to 2^{o}C above pre-industrial levels by 2025 at the latest, and to achieve a 43% reduction by 2030 (5).

Climate change has a huge impact on human health but, paradoxically, the healthcare provision contributes to global warming and therefore to human health (1,6). Healthcare climate footprint is equivalent to 4.4% of the global net emissions worldwide (6–9). These emissions can be classified in 3 scopes: scope 1) direct emissions caused by healthcare facilities and healthcare vehicles, which suppose the 17% of the sector's worldwide footprint; scope 2) emissions related to purchased energy sources, which make up the 12%; and scope 3) indirect emissions caused by packaging, transport and production of food products, goods, services, and consumables , which constitute the remaining 71% (7,9,10). Europe is the third contributor to the healthcare climate footprint, behind China and the United States (9). In Spain, the healthcare sector contributes 4.5% to the total national footprint (9). Healthcare must respond to the growing climate emergency, not only by treating the health consequences, but also by radically reducing its own emissions (9).

Endoscopy Units are considered the third highest contributors to the healthcare carbon footprint and generation of waste (1,11), due to the large volume of procedures performed and to the high amount of garbage generated (3). This fact should not be underestimated as 18 million endoscopy procedures are performed each year in the USA (3).

A single endoscopy generates about 1.5 kg of plastic waste (3) and 28.4 kg of CO_2e (11). The daily material of the endoscopic unit, included in scope 3, mainly consists of consumables, which are plastic-predominant and not recycled (3). Each patient may require multiple one-use products, such as: privacy gowns, plastic bags for personal belongings, intravenous cannulas with dressing, soakers, syringes with medication and gauzes. For the endoscopy procedure, specific devices such as biopsy forceps, snares, diathermy pads, histology pots and many others may also be needed. Many of these

devices used to be reusable, but they have become single-use in recent decades without solid scientific data supporting the change (12). The main reasons for this change are the fear of patient cross-contamination and the manufacturer's pressure. However, for most devices, this risk has not been demonstrated or could be clinically insignificant. In fact, the use of single use material has been controversial, especially for devices that penetrate the epithelial barrier (3,13), but several studies suggest that the risk of cross contamination attributable to the reuse of this material should be reconsidered when adequately reprocessed and disinfected (13,14). Hence, we should reconsider using single-use devices taking into account its higher financial costs and environmental impact (12).

The European Society of Gastrointestinal Endoscopy (ESGE) and the European Society of Gastroenterology and Endoscopy Nurses and Associates (ESGENA) have published a position statement with a specific section for single use material suggesting that there is an urgent need to reassess and reduce the environmental and economic impact of single-use endoscopic devices (13). The ESGE-ESGENA recommends conducting research to quantify and minimise the environmental impact of GI endoscopy and include in future clinical guidelines and regulations aspects like the reprocessing and disinfection of single use devices (13). This is undoubtedly impossible to achieve without the support of the manufacturers.

The polyp trap is a device used to collect polyps removed from intestinal mucosa. Made of plastic, it comprises multiple wells where different samples can be collected. The polyp trap is connected on one side to the endoscope extraction exit and to the suction tube on the other side. According to the manufacturers, it is a single-use device and must be replaced between patients. However, the polyp trap has a low probability of cross-contamination with the patient after washing, as fluids circulate unidirectionally from the endoscope to the suction device and are never in direct contact with the patient. Before its introduction, polyps were collected with simpler alternatives, such as the use of gauzes. However, they are increasingly being used in endoscopy units. At the Hospital de Sant Pau we used approximately 3800 polyp traps the last year. This represents a cost of 5700€ and an increase in CO_2e. Nevertheless, many endoscopy units already reuse polyp traps in their clinical practice. Therefore, we aim to analyse the risks, costs and CO_2e of using single-use polyp traps or reusing them.

1.2 RATIONALE OR JUSTIFICATION

Our study falls within the sustainable endoscopy ("Green Endoscopy") and responds to the call of the ESGE and the Spanish Society of Digestive Endoscopy (SEED) to carry out research that helps to design future clinical guidelines considering reprocessing and disinfection of single-use material (13). Hopefully, our results may push manufacturers to rethink and facilitate the production of reusable devices. That could have a positive impact on the endoscopy footprint as it could reduce scope 3 emissions.

This measure, designed to reduce the environmental impact of the unit, has been prioritised following the 2x2 decision matrix on the relative cost (effort) and benefits of reducing carbon emissions proposed by Hernandez LV et al (1). Its implementation would require very little effort for the entire team, it would fit in with the already established endoscopy unit dynamics and does not imply an additional economic expense, but rather a reduction on the number of devices used. In relation to the reduction of CO_2 emissions, every action counts, and reducing is more effective than reusing, which is

more effective than recycling (1). Establishing actions that have high adherence by the team is paramount to success.

The aim of this study is to observe and evaluate whether there is any difference between the incidence of post-endoscopy infection, pathology results, costs, and CO_2e in those centres in which the polyp trap was discarded or reused, to evaluate the security and possible benefits of reusing polyp traps.

2. OBJECTIVES AND PURPOSE

2.1 PRINCIPAL OBJECTIVE

To evaluate whether the rate of infection is similar after colonoscopies using a reused or a disposed polyp trap.

2.2 SECONDARY OBJECTIVES

1. To evaluate the risk of postprocedural fever after colonoscopy with a reused or a disposed polyp trap.
2. To evaluate the risk of error in the anatomopathological study, due to persistence of biological material in a reused polyp trap.
3. To estimate the carbon footprint of discarding and reusing polyp traps.
4. To calculate the cost of discarding and reusing polyp traps.
5. To assess other complications of the procedure (bleeding, perforation).

3. SOURCE OF INFORMATION AND DATABASE

Data about patients and endoscopy will be collected immediately before and after the endoscopy. Follow-up will consist in a centralised telephonic interview 7 days later. When considered necessary, a review of the medical records will be performed by each participant centre investigators. Data will be collected in the platform RedCap.

4. TRIAL DESIGN

4.1 SUMMARY OF TRIAL DESIGN

This is a non-commercial, prospective, observational, non-inferiority study to evaluate whether reusing or discarding polyp traps after colonoscopy has a similar infection rate. Participant hospitals will be separated into two groups, according to their standard clinical practice: A) reuse or B) dispose polyp traps after a colonoscopy with polypectomy. Centres will participate with their current method

of using polyp traps. Work dynamics will not change as patients will be recruited from centres that routinely reuse or dispose polyp traps.

All colonoscopies in which a polyp trap has been used will be included. Patient and Endoscopy information will be recorded at the moment of the colonoscopy, except for the evaluation of the pathology report, which will be performed 10-15 days after the procedure. This information will be sent daily to the IP institution through the electronic report. At the IP institution there will be an investigator in charge of the phone contact follow-up for all the patients. Patient, endoscopy and follow up information will be recorded according to the CRF included in the Attachment A. In case of adverse events requiring hospitalisation, medical records will be reviewed by the endoscopist at each institution.

The duration of the participation for each patient in the clinical trial is 7 days or, in case of complication, until it is solved. The day of the procedure the patient will obtain the protocol information, and the informed consent will be obtained.

4.2 PRIMARY AND SECONDARY ENDPOINTS/OUTCOME MEASURES

Primary endpoint:

- **To evaluate whether the rate of infection is similar after colonoscopies using a reused or a disposed polyp trap**: to calculate the rate of infection, all clinical suspicions of infection will be recorded. The infection can be defined as “confirmed” if there is a positive culture or if there is suspicion by clinical, laboratory, and image techniques (CT, MRI), and a positive blood culture is obtained. It will be defined as “suspected” when clinical and/or image is suggestive of infection (i.e. fever), but microbial confirmation is not obtained. This will be measured during patient’s follow up and recorded at the CRF. All confirmed or suspected infections will be evaluated by the study panel, to determine whether it can be associated to the polyp trap, to other endoscopy complications (such as perforation or bronchoaspiration), or non-related to the colonoscopy, and weather the infection was clinically relevant. The panel evaluating the case will not be informed about the proceeding centre of the patient, so they will be blinded to the reuse or not of the polyp trap. If resolution of the complication is longer than the study follow-up period, it will be extended until it is solved. Additionally, to determine the relation of the infection with the polyp trap, in the reused polyp trap group, each trap will be traced to detect related infections.

Secondary endpoints:

- **To evaluate the risk of error in the anatomopathological study, due to persistence of biological material in a reused polyp trap:** all anatomopathological reports will be reviewed. Results suspicious of cross-sampling (i.e. adenocarcinoma for a normal appearing polyp) will be recorded and analysed using the polyp trap traceability.

- **To estimate the carbon footprint of disposable versus reusable polyp traps using life cycle assessment methodology.**

- **To calculate the cost of disposable versus reusable polyp traps:** the type, unit cost and number of polyp traps used at each institution will be recorded, to determine total costs at each group.

- **To assess other complications of the procedure (bleeding, perforation):** The other secondary outcomes pretend to assess other complications related to colonoscopy with trap use (such as bleeding or perforation). The diagnosis of bleeding or perforation after the procedure will be confirmed according to the protocol at each institution. The evaluation of these secondary outcomes will be performed during the procedure and all the follow up period and will be managed according to protocol for each event at each institution. All of them will be recorded at the CRF. If resolution of the complication is longer than the study period, follow up will be extended until it is solved.

  Procedure outcomes will be graded as "mild" if the patient is discharged in the initial 24 hours, without need of further interventions. They will be graded as "severe" if they require hospitalisation longer than 24 hours, radiological or endoscopic drainage, blood transfusion, or resuscitation manoeuvres. A "fatal" complication will be described if a related death occurs.

5. STUDY POPULATION

5.1 INCLUSION CRITERIA

- All patients who undergo an elective colonoscopy will be recruited for the study.
- Written informed consent to participate in the study and willingness to be contacted by telephone for follow-up.

5.2 EXCLUSION CRITERIA

- Patients who complete the colonoscopy without a polypectomy.
- Patients who complete the colonoscopy without the use of a polyp trap.

6. STUDY PROCEDURES

6.1 INFORMED CONSENT

Patients' informed consent will be obtained immediately before the colonoscopy. The participant must personally sign and date the latest approved version of the informed consent form before any study specific procedures are performed.

Written and verbal versions of the Participant Information Sheet and Informed Consent (Attachment B) will be presented to the participants detailing no less than: the exact nature of the study; the implications and constraints of the protocol; the known side effects and any risks involved in taking part. It will be clearly stated that the participant is free to withdraw from the study at any time for any reason without prejudice to future care, and with no obligation to give the reason for withdrawal.

The participant will be allowed as much time as wished to consider the information, and the opportunity to question the Investigator, their GP or other independent parties to decide whether they will participate in the study. Written Informed Consent will then be obtained by means of participant dated signature and dated signature of the person who presented and obtained the informed consent. The person who obtained the consent must be suitably qualified and experienced and will have been authorised to do so by the Principal Investigator. A copy of the signed Informed Consent will be given to the participants. The original signed form will be retained at the study site.

7. STATISTICAL METHODS AND SAMPLE SIZE

7.1 STATISTICAL ANALYSIS

Patient demographic data (sex, age) will be used to assess baseline comparability of the study groups. This will be reported as means, standard deviations, or proportions and will be analysed using the $\chi 2$ and Fisher exact test for qualitative variables and t test for quantitative parameters.

One time use of single-use polyp traps is the standard of care, as it is the actual manufacturers' recommendation. A comparable risk of infection when reusing traps would be acceptable. For this reason, for the analysis of the primary outcome, a non-inferiority study will be performed. The risk of infection will be reported as a proportion. The 95% confidence intervals for proportions will be analysed with the Wilson method.

The secondary outcomes of carbon footprint, costs, and other endoscopy complications will be reported as total emissions (CO2 Kg equivalents) and total costs per group and will be analysed with t test.

The secondary outcomes of other endoscopy adverse events will be reported as proportions and will be analysed with the $\chi 2$ and Fisher exact test.

The statistical analysis will be performed at the end of the study period by a statistician of the sponsor institution, with the SPSS (v).

7.2 SAMPLE SIZE CALCULATION

The present study was planned to evaluate the non-inferiority of reusing polyp traps versus discarding polyp traps in terms of post-procedure rate of infection (the primary endpoint of the study). Evidence about the rate of infection after an endoscopic procedure is scarce. It was previously estimated to be 1 in 1.8 million endoscopic procedures but recent studies have suggested this could be a significant underestimation (15). According to the Ofstead et al (16) described rates of postendoscopy complications ranging from 0.5% to 3.4%, including fever, diarrhoea, abdominal pain, and other signs and symptoms that may indicate infection. We expect a very low infection rate of 0.2% in both groups, considering that the triplication of this risk to 0.6% would not be acceptable, then assuming a non-inferiority margin (δ) of 0,4%, a unilateral α-error of 0.05, and a power (β-error) of 20%, and a low rate of losses (5%), a total of 3238 patients will be required to complete the analysis of the primary outcome. The samples size was calculated with Sample Power (v 3.0.1).

7.3 INTERIM ANALYSES AND STOPPING RULES

An interim analysis is not planned. If there is an incidence of serious infections (those including need for surgery, endoscopic drainage, ICU management, prolonged admission to the hospital greater than 7 days, or death) superior to 5%, the study will be temporarily stopped. Results will be compared among study groups, and the study will be terminated if significance or clinically relevant differences are observed.

8. DIRECT ACCESS TO SOURCE DATA/DOCUMENTS

Direct access will be granted to authorised representatives from the sponsor, host institution and the regulatory authorities to permit audits and inspections.

9. ETHIC, DEONTOLOGICAL AND REGULATORY CONSIDERATIONS

The Investigator will ensure that this study is conducted in accordance with the principles of the Declaration of Helsinki (17), ICH Guidelines for Good Clinical Practice and in full conformity with relevant regulations.

The protocol, CRF and any applicable documents will be submitted to an appropriate Ethics Committee (EC) and Regulatory Authority for written approval.

All substantial amendments to the original approved documents will be also sent to an appropriate Ethics Committee (EC) and Regulatory Authority for written approval.

The study staff will ensure that the participants' anonymity is maintained. The participants will be identified only by a participant ID number on the CRF and any electronic database. All documents will be stored securely and only accessible by trial staff and authorised personnel. The study will comply with the Data Protection Legislation which requires data to be anonymized as soon as it is mandatory to do so.

10. DATA HANDLING AND RECORD KEEPING

Data will be recorded in the platform RedCap according to the attached form (attachment A). The person introducing the data will be identified and the date will be recorded. For any further annotation, the name of the investigator and the date will also be recorded. The paper data will be stored under key protection.

Once each case is completed, the data will be transferred and stored to an SPSS data sheet. The SPSS datasheet will also be stored under password protection.

All data collected in paper and SPSS will be associated only to an anonymous research number. Patient identifiers will be stored in a separate data sheet along with the anonymous number key, also secured

under password protection. Patient identifiers will not be disclosed to anyone except for the researchers who are authorised to be involved in the project. The number key will be discarded after the data for an individual patient have been collected.

Records will be stored at the GI department of PI investigator for 5 years after the end of the study.

The PI and a researcher at the PI institution will be responsible for the data collection, recording and quality.

11. REFERENCES

1. Hernandez L V., Agrawal D, Skole KS, Crockett SD, Shimpi RA, von Renteln D, et al. Meeting the environmental challenges of endoscopy: a pathway from strategy to implementation. Gastrointest Endosc [Internet]. 2023;98(6):881-888.e1. Available from: https://doi.org/10.1016/j.gie.2023.07.031
2. Watts N, Adger WN, Agnolucci P. Health and climate change: Policy responses to protect public health. Environnement, Risques et Sante. 2015;14(6):466–8.
3. Siau K, Hayee B, Gayam S. Endoscopy's Current Carbon Footprint. Tech Innov Gastrointest Endosc. 2021;344–52.
4. Romanello M, McGushin A, Di Napoli C, Drummond P, Hughes N, Jamart L, et al. The 2021 report of the Lancet Countdown on health and climate change: code red for a healthy future. Lancet. 2021;398(10311):1619–62.
5. UNFCCC. The Paris Agreement [Internet]. [cited 2024 Feb 5]. Available from: https://unfccc.int/process-and-meetings/the-paris-agreement
6. Lenzen M, Malik A, Li M, Fry J, Weisz H, Pichler PP, et al. The environmental footprint of health care: a global assessment. Lancet Planet Heal [Internet]. 2020;4(7):e271–9. Available from: http://dx.doi.org/10.1016/S2542-5196(20)30121-2
7. Henniger D, Lux T, Windsheimer M, Brand M, Weich A, Kudlich T, et al. Reducing scope 3 carbon emissions in gastrointestinal endoscopy: Results of the prospective study of the "Green Endoscopy Project Würzburg." Gut. 2023;(scope 3):1–6.
8. Tennison I, Roschnik S, Ashby B, Boyd R, Hamilton I, Oreszczyn T, et al. Health care's response to climate change: a carbon footprint assessment of the NHS in England. Lancet Planet Heal [Internet]. 2021;5(2):e84–92. Available from: http://dx.doi.org/10.1016/S2542-5196(20)30271-0
9. Karliner J, Slotterback S, Boyd R, Ashby B, Steele K. Health Care's Climate Footprint How the Health Sector Contributes. Arup [Internet]. 2019;(September):48. Available from: https://www.arup.com/perspectives/publications/research/section/healthcares-climate-footprint
10. Eckelman MJ, Huang K, Lagasse R, Senay E, Dubrow R, Sherman JD. Health care pollution and public health damage in the united states: An update. Health Aff. 2020;39(12):2071–9.
11. Lacroute J, Marcantoni J, Petitot S, Weber J, Levy P, Dirrenberger B, et al. The carbon footprint of ambulatory gastrointestinal endoscopy. Endoscopy. 2022;55(10):918–26.
12. Cunha Neves JA, Rodriguez De Santiago E, Pohl H, Lorenzo-Zúniga V, Cunha MF, Voiosu AM,

et al. Perspectives and awareness of endoscopy healthcare professionals on sustainable practices in gastrointestinal endoscopy: Results of the LEAFGREEN survey. Endoscopy. 2023;

13. Rodríguez De Santiago E, Dinis-Ribeiro M, Pohl H, Agrawal D, Arvanitakis M, Baddeley R, et al. Reducing the environmental footprint of gastrointestinal endoscopy: European Society of Gastrointestinal Endoscopy (ESGE) and European Society of Gastroenterology and Endoscopy Nurses and Associates (ESGENA) Position Statement. Endoscopy. 2022;54(8):797–826.

14. Nabi Z, Tang RSY, Sundaram S, Lakhtakia S, Reddy DN. Single-use accessories and endoscopes in the era of sustainability and climate change—A balancing act. J Gastroenterol Hepatol. 2023;1–11.

15. McCafferty CE, Aghajani MJ, Abi-Hanna D, Gosbell IB, Jensen SO. An update on gastrointestinal endoscopy-associated infections and their contributing factors. Ann Clin Microbiol Antimicrob [Internet]. 2018;17(1):1–6. Available from: https://doi.org/10.1186/s12941-018-0289-2

16. Ofstead CL, Dirlam Langlay AM, Mueller NJ, Tosh PK, Wetzler HP. Re-evaluating endoscopy-associated infection risk estimates and their implications. Am J Infect Control [Internet]. 2013;41(8):734–6. Available from: http://dx.doi.org/10.1016/j.ajic.2012.10.008

17. Association WM. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. JAMA. 2013;310(20):2191–4.

Attachment A: Data form

POLYPTRAP Data Form

EXCLUSION CRITERIA: Any polyp trap used during the procedure? Yes / No

DEMOGRAPHICS
Patient ID: **Gender:** M / F **Institution:**
Age:

MEDICAL HISTORY
Active infectious process (at the moment of endoscopy): Yes / No
Observations:

ENDOSCOPY **Date:** **Time:**

Endoscopic :

- ◯ Bleeding
- ◯ Perforation
- ◯ Bronchoaspiration
- ◯ Other: Comments:
- ◯ None

For institutions reusing polyp traps: Polyp trap ID:

ANATOMOPATHOLOGICAL RESULT Consistent with findings in the endoscopy / Inconsistent (if inconsistent, add comment)

FOLLOW-UP

A) Any symptoms suggesting infection

- ◯ Fever
- ◯ Bacteraemia
- ◯ Bronchoaspiration / Pneumonia
- ◯ Other: Comments:
- ◯ None

Event related to endoscopy: Yes / Probably / Doubtfully / No
Event related to polyp trap: Yes / Probably / Doubtfully / No

B) Other adverse events: Yes / No **Type:** Bleeding / Perforation / Others
Comment:

C) Need of hospitalisation
Yes / No

D) Need of admission in intensive care unit
Yes / No

E) Fatal outcome
Yes / No
Comments: