The costs of surgical site infection after abdominal surgery in middle income countries

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The costs of surgical site infection after abdominal surgery in middle-income countries: Key resource use In Wound Infection (KIWI) study

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SUMMARY

Background: Surgical site infection (SSI) is the most common complication of abdominal surgery, with substantial costs to patients and health systems. Heterogeneity in costing methods in existing SSI studies makes multi-country comparison challenging. The objective of the study was to assess the costs of SSI across middle-income countries.

Methods: Centres from a randomized controlled trial assessing interventions to reduce SSI (FALCON, ClinicalTrials.gov, NCT03700749NCT) were sampled from two upper-middle- (India, Mexico) and two lower-middle- (Ghana, Nigeria) income countries. The Key resource use In Wound Infection (KIWI) study collected data on postoperative resource use and costs from consecutive patients undergoing abdominal surgery with an incision >5 cm (including caesarean section) that were recruited to FALCON between April and October 2020. The overall costs faced by patients with and without SSI were compared by operative field contamination (clean-contaminated vs contaminated-dirty), country and timing (inpatient vs outpatient).

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Findings: A total of 335 patients were included in KIWI; SSI occurred in 7% of clean-contaminated cases and 27% of contaminated-dirty cases. Overall, SSI was associated with an increase in postoperative healthcare costs by 75.3% (€412 international Euros) after clean-contaminated surgery and 66.6% (€331) after contaminated-dirty surgery. The highest and lowest cost increases were in India for clean-contaminated cases (€517) and contaminated-dirty cases (€223), respectively. Overall, inpatient costs accounted for 96.4% of the total healthcare costs after clean-contaminated surgery and 92.5% after contaminated-dirty surgery.

Conclusion: SSI was associated with substantial additional postoperative costs across a range of settings. Investment in health technologies to reduce SSI may mitigate the financial burden to patients and low-resource health systems.

Introduction

Surgical site infection (SSI) is defined as a postoperative infection of the surgical wound and is a worldwide problem [1] which impacts on health outcomes and has financial consequences [2,3]. The degree of wound contamination at time of surgery (clean, clean-contaminated, contaminated, dirty) [4] is a known risk factor [5]. SSI is a particular problem in low- and middle-income countries (LMICs) due to a higher incidence rate [6,7] coupled with a greater share of patient out-of-pocket healthcare expenditure [8] compared with high-income countries (HICs). Higher antimicrobial resistance in LMIC settings [7] makes it harder to prevent and treat SSI. Patients who incur an SSI typically have a longer inpatient stay and higher post-discharge healthcare costs compared with patients without an SSI [9] and severe infections can substantially increase healthcare resource use and costs [10]. Quantifying the costs associated with an SSI is a vital component in the economic assessment of interventions to reduce these complications [11].

To date, evidence on the magnitude of the cost burden of SSI in LMICs has been limited to single-centre studies with differences in study design impeding comparability [12]. Single-centre settings are only representative of the single centre and country setting and therefore reduces generalizability. Many of the LMIC SSI studies undertook SSI detection and cost collection only up to hospital discharge [12]. Therefore, the lack of post-discharge follow-up severely limits the validity of these studies as SSI commonly occurs after discharge [13] and the additional costs associated with SSI are shown to persist beyond discharge and 30 days [14]. Consequently, a reliable estimate of the cost burden of SSI in LMICs does not currently exist. Reducing surgical site infections in low-income and middle-income countries (FALCON) was a randomized control trial undertaken in seven LMIC countries (Benin, Mexico, Rwanda, Nigeria, Ghana, India, South Africa) assessing the effectiveness of interventions to reduce SSI [15,16]. The Key resource use In Wound Infection (KIWI) study was carried out within the FALCON trial in order to estimate the cost burden associated with SSI. The specific objectives of KIWI were to (1) measure the additional within-hospital resource use for patients with SSI compared to patients without SSI and attach unit costs to this additional resource use; (2) identify and measure the resource use for patients who have SSI detected after hospital discharge; (3) explore the relative cost burden for patients with contaminated-dirty operations compared to patients with clean-contaminated surgeries; and (4) explore the healthcare needs and resource use of patients with an unresolved SSI at 30 days and beyond.

Methods

FALCON trial

The KIWI study was a study within the FALCON trial. FALCON [15,16] was a pragmatic, 2 × 2 factorial, stratified, multicentre randomized controlled trial, evaluating measures to reduce SSI rates in patients undergoing surgery with an abdominal incision. The primary clinical outcome for the FALCON trial was SSI up to 30 days after surgery. Patients were stratified by their predicted wound contamination (clean-contaminated or contaminated-dirty wounds) [4]. Patients with abdominal skin incision $\geq$5 cm were randomized between (1) 2% alcoholic chlorhexidine and non-coated suture, (2) 2% alcoholic chlorhexidine and triclosan-coated suture, (3) 10% aqueous povidone-iodine and non-coated suture, and (4) 10% aqueous povidone-iodine and triclosan-coated suture. FALCON included patients undergoing emergency or elective surgery, for any operative indication, including trauma surgery.

Setting

Participating FALCON centres in India, Ghana, Nigeria and Mexico were included in KIWI. The list and type of hospitals is shown in Supplementary Table S1. SSI was defined using the Centers for Disease Control and Prevention (CDC) criteria as per the FALCON trial [17] and was assessed at hospital discharge and at 30 days post-surgery time points for all patients.

Population

Consecutive adult patients recruited to the FALCON trial were eligible for the KIWI study. A minimum target of 100 consecutive patients per country was planned, with at least two hospitals per country invited to participate. No formal sample size calculation was used for the KIWI study. Consideration of sample size for economic endpoints in randomized control trials are rare [18], complex [19] and there is no agreed approach on the calculations [20].

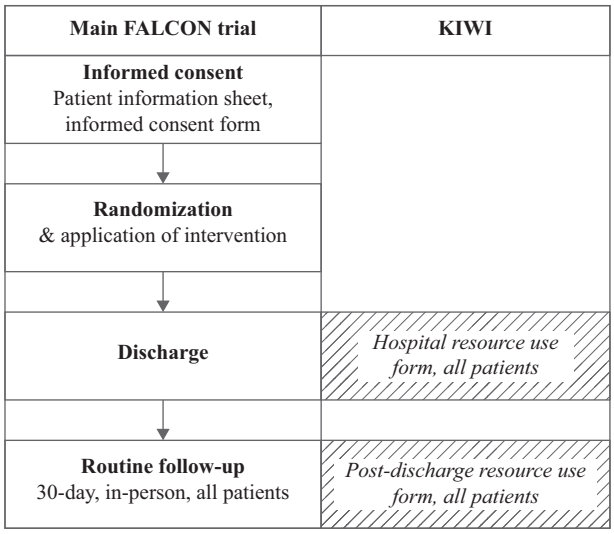

Figure 1. Resource use forms timepoints alongside the FALCON trial.

Data collection up to 30-day follow-up

Resource use for SSI and non-SSI patients was collected using additional Case Report Forms (CRFs) within the FALCON trial completed at hospital discharge (FALCON Hospital Resource Use Form) and as close to 30 days post-surgery as possible (FALCON Post-Discharge Resource Use Form, Figure 1). These forms were purposely aligned with the data collection points within the FALCON trial to minimize burden.

Inpatient resource use up to 30 days post-surgery was collected via a dedicated FALCON hospital resource use form (see Appendix S6). This was designed in partnership with international surgeons involved in the care of abdominal surgery patients and specifically aimed to collect relevant cost data on resource items that would be likely to vary between patients with and without SSI in the local contexts in which these were measured. After some iterative development, the resource use questionnaires were piloted with the first five patients in each site to ensure consistency of reporting and that no relevant costs were missed. Inpatient resources items collected were postoperative length of stay, wound dressing changes, laboratory investigations, and healthcare resource use (e.g., antibiotics, painkillers) associated with patient discharge.

The FALCON Post-Discharge Resource Use Form collected information up to 30 days post-surgery. Relevant data included any post-discharge consultation and consumable costs along with any travel costs and income loss from attending post-discharge healthcare visits. The costs associated with travel and lost income for family members who accompanied patients were also recorded where applicable.

When the prospective recruitment for KIWI commenced, the host trial had finished recruiting predicted clean-contaminated cases and was only recruiting predicted contaminated-dirty cases. To collect information on the clean-contaminated cases, retrospective data collection via telephone interview was undertaken in India and Mexico. To minimize recall bias, consecutive clean-contaminated patients who had most recently completed follow-up were contacted. Electronic patient records were used to complete the hospital resource use forms for the retrospective cases.

Data collection beyond 30-day follow-up

For patients with an unresolved SSI at 30 days post-surgery, additional telephone follow-up was completed 14 days later (as

Table I
Patient characteristics

Predicted contamination	Clean-contaminated			Contaminated-dirty				
	Overall	Mexico	India	Overall	Ghana	India	Mexico	Nigeria
	N (%)							
Sex								
Male	22 (12)	10 (12)	12 (12)	98 (64)	66 (65)	30 (65)	0 (0)	2 (50)
Female	160 (88)	74 (88)	86 (88)	55 (36)	35 (35)	16 (35)	2 (100)	2 (50)
Total	182 (100)	84 (100)	98 (100)	153 (100)	101 (100)	46 (100)	2 (100)	4 (100)
SSI								
No	170 (93)	83 (99)	87 (89)	111 (73)	81 (80)	27 (59)	1 (1)	2 (50)
Yes	12 (7)	1 (1)	11 (11)	42 (27)	20 (20)	19 (41)	1 (50)	2 (50)
Inpatient SSI	9	0	9	33	13	18	0	2
Outpatient SSI	6	1	5	15	9	5	1	0
Unresolved wound infection at postoperative day 30	3%	0%	5.1%	16%	9.9%	28.3%	0%	25%
Length of stay in days, mean (standard error)	4.98 (0.3)	2.79 (0.3)	6.85 (0.4)	8.88 (0.6)	7.90 (0.7)	10.54 (1.1)	8.5 (1.5)	14.25 (5.6)
Age in years, mean (standard error)	34.8 (0.9)	36.1 (1.3)	33.6 (1.2)	42.2 (1.3)	41.1 (1.6)	44.2 (2.5)	42 (3)	49.3 (3.2)
Timing of 1st post-discharge follow-up								
Prospective (up to 40 days follow-up)	0 (0)	0 (0)	0 (0)	122 (80)	96 (95)	24 (52)	0 (0)	4 (100)
Retrospective: 40 days to 6 months	60 (33)	2 (2)	58 (59)	12 (8)	5 (5)	7 (15)	0 (0)	0 (0)
Retrospective: 6 months—12 months	79 (43)	39 (46)	40 (41)	17 (11)	0 (0)	15 (33)	2 (100)	0 (0)
Retrospective: beyond 12 months	43 (24)	43 (51)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

SSI, surgical site infection.

close to postoperative day 45 as practical) to collect resource use information related to their ongoing wound infection. For patients with an unresolved wound infection at 45 days after surgery, a final third telephone call was completed 14 days later (as close to postoperative day 60 as practical). To maximize the sample size, the analysis on the post-discharge costs of unresolved wound infection included those with missing hospital resource forms.

Valuation of resource use data

For inpatient resource use valuation, hospital unit cost information at each participating centre was collected by the trial staff. Post-discharge costs were collected in post-discharge CRFs. Costs were expressed in Euro with a cost year of 2020. Costs were adjusted by their country's purchasing power parity (PPP) conversion factor [21]. Where a country's PPP conversion factor was unavailable, an implied conversion factor from the International Monetary Fund was used instead [22].

Perspective

The primary analysis adopted the perspective of the health service provider. Within this perspective, direct medical costs (e.g., hospital length of stay, lab investigations, reoperations and antibiotics) were included. A secondary analysis was conducted which adopted a societal perspective which included direct non-medical costs (travel costs) and indirect costs (productivity loss costs) incurred by the patient and their family.

Analysis

The postoperative mean costs faced by patients with SSI and without SSI, respectively, were presented on a per-country basis and stratified by predicted surgery type (clean-contaminated, contaminated-dirty). Mean costs were presented due to their relevance to resource allocation decisions (i.e., mean per patient cost multiplied by number of patients equals the total cost). Postoperative costs were further subdivided into inpatient and post-discharge costs. Where extended follow-up was carried out on patients with unresolved wound infection, the costs are shown at 45 days and 60 days post-surgery. The costs of patients who had suffered an inpatient SSI versus those who suffered an SSI after hospital discharge were also explored. For contaminated cases, a sensitivity analysis compared the cost differences between retrospective and prospective cases. As cost differences can be explained by factors other than the presence of an SSI, a regression analysis was undertaken to assess whether SSI was a statistically significant determinant of healthcare costs. The regression analysis used a multi-level generalized linear model with a log-link and gamma distribution and adjusted for patient characteristics (age, gender, emergency/elective, predicted contamination, SSI). A complete-case analysis was undertaken, where patients with missing CRFs were removed. The analysis was undertaken in STATA 17. No discounting of costs was undertaken as the time horizon was less than a year [23].

Ethical approval

Ethical approval for data collection up to 30 days was approved within the main FALCON protocol (ERN_180230) at

Table II
Total postoperative costs of surgical site infections (SSIs) (€)

	Clean-contaminated								Contaminated-dirty							
	Overall		Mexico		India		Overall		Ghana		India					
	No SSI	SSI	No SSI	SSI	No SSI	SSI	No SSI	SSI	No SSI	SSI	No SSI	SSI				
Sample size	170	12	83	1	87	11	111	42	81	20	27	19				
Postoperative inpatient costs, mean (standard error)	€532 (36)	€855 (151)	€619 (68)	€954 (—)	€450 (23)	€846 (165)	€461 (45)	€763 (58)	€366 (38)	€642 (98)	€756 (131)	€913 (53)				
Post-discharge healthcare costs, mean (SE)	€15 (4)	€104 (61)	€8 (5)	0 (—)	€22 (7)	€113 (66)	€36 (36)	€66 (6)	€44 (8)	€100 (27)	€8 (2)	€32 (6)				
Total postoperative healthcare costs, mean (SE)	€547 (36)	€959 (179)	€627 (67)	€954 (—)	€471 (25)	€959 (196)	€497 (66)	€828 (14)	€410 (40)	€742 (107)	€763 (132)	€945 (55)				
Travel and income loss, mean (SE)	€58 (14)	€106 (41)	€30 (17)	0 (—)	€85 (21)	€115 (44)	€181 (39)	€169 (39)	€212 (52)	€239 (70)	€79 (33)	€121 (40)				
Societal costs, mean (standard error)	€605 (38)	€1064 (203)	€656 (68)	€954 (—)	€557 (33)	€1074 (222)	€678 (55)	€997 (70)	€623 (59)	€981 (117)	€843 (139)	€1066 (82)				

SE, standard error.

the University of Birmingham and in the countries where the trial was recruiting. Data collection of patients beyond 30 days required a protocol amendment and ethical approval. Extended follow-up received university ethics (ERN_18-0230A) as well as local ethics approvals. Ethical approval for protocol amendments for extended follow up in participating countries was affected by the onset of COVID-19 and was delayed by postponement of ethics committee meetings and/or deprioritization of non-COVID research studies. Only Ghana had ethical approvals for the extended follow up of patients.

Results

Prospective recruitment for KIWI was open in India (June 2020 to October 2020), Nigeria (April 2020 to October 2020), Mexico (May 2020 to October 2020) and Ghana (May 2020 to October 2020). Due to COVID-19, no prospective study enrolment of contaminated dirty cases was possible in Mexico as the centres were closed for recruitment. To overcome this, we included contaminated dirty cases in the retrospective analysis along with the clean-contaminated cases in Mexico. The number of participating centres varied by country (India ($N = 3$), Ghana ($N = 5$), Nigeria ($N = 2$) and Mexico ($N = 3$)).

Patient characteristics

Table I and Supplementary Tables S2 and S3 show the characteristics of the patients included in the study. Clean-contaminated cases ($N = 186$) were collected retrospectively in India and Mexico. Clean-contaminated cases were mainly female (88%), and 67% of clean-contaminated cases underwent caesarean section. Most clean-contaminated cases (67%) were contacted beyond six months of their initial recruitment to the trial. For the contaminated-dirty cases, patients were mainly male, older, and had a higher proportion of SSI (27% vs 7%) compared with the clean-contaminated cases. The proportion of SSI at postoperative day 30 was also higher in contaminated-dirty cases (16%) compared with clean-contaminated cases (3%). Inpatient SSIs were more common than outpatient SSIs in both clean-contaminated cases and contaminated-dirty cases.

India had the largest sample size ($N = 144$), and Nigeria had the lowest sample size ($N = 4$). Ghana had the largest number of contaminated cases whilst India had the largest number of clean-contaminated-dirty cases. In Mexico, only one patient in each contamination arm suffered an SSI.

Clean-contaminated postoperative resource use and costs

Postoperative and post-discharge costs are shown in Supplementary Table S4 and Table II with the resource use information provided in Supplementary Table S5. Hospital investigations were the largest contributor of inpatient postoperative costs in India while it was the lowest contributor in Mexico. In India, patients with an SSI had longer postoperative lengths of stay, more investigations and wound dressing changes compared with patients without an SSI. There was a large difference in patients having post-discharge healthcare visits in Mexico (4%) compared with India (87%). Overall, an SSI increased total healthcare postoperative costs by 75.3% in the clean-contaminated arm (€959 vs €547) (Table II). Broadening the cost perspective to include travel costs and income loss from the post-discharge visits increased the additional costs associated with an SSI (€1064 vs €656).

Contaminated-dirty postoperative resource use and costs

Postoperative and post-discharge costs are shown in Supplementary Table S4 and Table II for contaminated-dirty cases with information on the postoperative and post-discharge resource use given in Supplementary Table S6. Due to low sample size, the contaminated-dirty cases of Mexico ($N = 2$) and Nigeria ($N = 4$) are presented in Supplementary Table S6 for completeness. Hospital investigations were the largest contributor of inpatient postoperative costs in Ghana and India. Most patients in India and Ghana had post-discharge healthcare visits. Post-discharge costs for patients with an SSI in both India and Ghana were at least double those of patients without an SSI. Overall, an SSI increased total healthcare postoperative costs by 66.6% in the contaminated-dirty arm (€828 vs €497) (Table II). The inclusion of travel costs and income loss associated with post-discharge visits widened the cost difference between patients with and without an SSI, respectively (€1074 vs €678).

Extended follow-up

Information on the costs by patients in Ghana with an unresolved wound infection by 30, 45 and 60 days is shown in Supplementary Table S8. For patients with an unresolved wound infection, they continued to incur additional post-discharge costs although there was 42.9% follow up at the postoperative 45-day telephone follow-up.

Table III
Costs of prospective versus retrospective patients with and without surgical site infection (SSI)

Contaminated-dirty	Prospective SSI	Retrospective SSI	Prospective no SSI	Retrospective no SSI
Sample size (*N*)	25	14	97	17
Postoperative inpatient costs, mean (SE)	€669 (59)	€888 (285)	€399 (28)	€901 (106)
Post-discharge healthcare resource use, mean (SE)	€79 (23)	€28 (6)	€38 (7)	€45 (8)
Total postoperative healthcare costs, mean (SE)	€748 (64)	€916 (284)	€437 (29)	€946 (112)
Travel and income loss, mean (SE)	€193 (59)	€160 (63)	€184 (44)	€134 (44)
Societal costs, mean (SE)	€941 (72)	€1075 (277)	€620 (47)	€1080 (136)

SE, standard error.

Sensitivity analysis

Supplementary Table S9 shows the results of the sensitivity analysis scenarios. Inpatient SSIs were more expensive compared with SSIs which developed post-discharge. Comparing prospective with retrospective cases, postoperative inpatient costs were much higher in the retrospective arm while post-discharge healthcare costs were slightly higher in the prospective arm (Table III). The multi-level model results are shown in Supplementary Table S10. Being female, the presence of an SSI, being an emergency admission, and being a contaminated-dirty case were all statistically significant variables in affecting the total postoperative healthcare costs.

Discussion

SSI is associated with additional postoperative costs in patients undergoing abdominal surgery across Ghana, Mexico, Nigeria and India. The overall mean additional postoperative costs with SSI were higher in clean-contaminated cases compared with contaminated-dirty cases. Looking at the inpatient resource use, the additional investigations and hospital length of stay for a patient with an SSI compared with a patient without an SSI was generally higher in the clean-contaminated arm compared with the contaminated-dirty arm. Collected postoperative costs considered both direct healthcare costs and indirect costs arising from post-discharge healthcare resource use. Patients with an SSI had higher costs in both postoperative inpatient costs and post-discharge costs compared with patients without an SSI. Even after controlling for different variables in a multi-level generalized linear model analysis, SSI was a statistically significant variable in determining postoperative healthcare costs.

Postoperative inpatient costs constituted most of the total healthcare costs in both clean-contaminated and contaminated-dirty cases. An exploratory investigation in Ghana showed that the costs of unresolved SSI persist beyond 30 days with the 45- and 60- postoperative day post-discharge costs in addition to the 30 postoperative day post-discharge costs. This is an important finding because 37.5% of prospective patients with an SSI were unresolved at 30 days post-surgery, potentially underestimating the true postoperative costs of SSI by limiting the data collection window.

This represents the first multi-continental study assessing the postoperative costs associated with SSI. Resource use was collected in standardized forms within a trial setting, allowing comparability of findings across the countries. This study helps address some of the literature gaps by providing cost information on surgical patients beyond discharge in low-resource settings. Participating countries had more than one centre participating to increase generalizability of the findings.

There were several study limitations. The use of retrospective data collection for clean-contaminated cases may have affected the post-discharge healthcare estimates due to recall bias [24]. Another study limitation was the absence of any low-income countries. Thus, the additional costs of SSI could not be generalized to these settings. Another limitation was the adoption of implied PPP exchange rate for the comparative cost results. This risks the possibility of measurement error bias if the implied PPP exchange rate differed from the true PPP rates. The low sample size and event rate in Nigeria and Mexico, respectively, further limits the precision and the reliability of the estimates in these countries. Lastly, the SSI cost differences between countries may be influenced by other factors including the clinical processes and the types of hospitals (charity, private, government).

Previous studies have looked at the additional cost of SSI in Mexico [25], India [26] and Ghana [27]. These were all single-centre studies with the India and Mexico studies only considering postoperative costs up to discharge. The additional cost of a patient with an SSI compared with a patient without an SSI varied considerably with it being 20.2% higher in the Ghana study [27] and 270.4% higher in the India study [26] (not reported in the Mexico study [25]). The Ghana study looked at both direct and indirect costs up to 30 days post-surgery in a teaching hospital. They found that the average additional cost of SSI was €210 in direct costs and €119 in indirect costs in a mix of clean-contaminated and contaminated-dirty patients. This compares with an average additional €332 in direct costs and €160 in indirect cost in the present study (contaminated-dirty patients only). The prospective data collection in the current study was undertaken during the COVID-19 pandemic which may have affected the generalizability of the SSI incidence, inpatient and post-discharge resource use of surgical patients compared with studies undertaken in non-pandemic times.

In conclusion, the host FALCON trial did not show any benefit of the interventions in terms of SSI prevention [16]. However, SSI represents an additional financial burden in surgical patients. Investments in developing systems of safe surgery that reduces SSI will help reduce the financial burden of patients in low-resource settings. Future research can use the present study estimates of the costs of SSI with effectiveness data to assess the cost-effectiveness of SSI prevention interventions in different country settings using decision analytic modelling to inform resource allocation decisions. Further, the joint parameter uncertainty of the decision analytic model, taken from the mean and standard error of the model input estimates, can be assessed using probabilistic sensitivity analysis [28]. To help address retrospective data collection and lack of low-income-country limitations, a planned cost study within another multi-national randomized control trial assessing interventions to reduce SSI [29] includes prospective data on clean-contaminated cases and the inclusion of Rwanda to explore the costs of SSI in this income setting. Given the additional costs beyond the postoperative 30-day period, future research should consider extending cost follow-up for patients with SSI in all countries to capture all relevant costs and consequences for these patients.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jhin.2023.03.023.

Author contributions

M.M. chaired the writing committee, contributed to the conceptualization, carried out the analysis, wrote the first draft and edited the manuscript. J.G., T.R., A.B. and D.G.M. contributed to the conceptualization, commented on and edited the manuscript. A.R. de la M., D.N.G., A.O.A. and S.T. contributed data to the study and commented on the manuscript. F.N., S.J. and T.P. commented on and edited the manuscript.

Conflict of interest statement

The authors declare no competing interests.

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