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ORIGINAL ARTICLE

# Does it matter where you get your surgery for colorectal cancer?

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## Abstract

**Background** The influence of hospital-related factors on outcomes following colorectal surgery is not well-established. The aim of our study was to evaluate the relationship between hospital factors on outcomes in surgically managed colorectal cancer patients.

**Methods** We performed a 2-year (2014–2015) analysis of the NIS database. Adult (> 18 years) patients who underwent open or laparoscopic colorectal resection were identified using ICD-9 codes. Patients were stratified based on hospital: volume (low vs. high), teaching status, and location (urban vs. rural). Outcome measures were complications and mortality. Multivariate logistic regression was performed.

**Results** A total of 153,453 patients with CRC were identified of which 35.3% underwent surgical management. Mean age was 69 ± 13 years, 51.6% were female, and 67% were white. Twenty-seven percent of the patients were managed at a high-volume center, 48% at intermediate-volume center while 25% at a low-volume center. Complications and mortality rates were lower in patients who were managed at high-volume centers and urban hospitals, while no difference was noticed based on teaching status. On regression analysis, patients managed at high-volume centers (OR 0.76 [0.56–0.89]) and urban hospitals (OR 0.83 [0.64–0.91]) have lower odds of complications; similarly, high-volume centers (OR 0.79 [0.65–0.90]) and urban facility (OR 0.87 [0.70–0.92]) were associated with lower odds of mortality. However, there was no association between teaching status and outcomes.

**Conclusion** Hospital factors significantly influence outcomes in patients with CRC managed surgically. High-volume centers and urban facilities have relatively better outcomes. Regionalization of care along with the appropriate availability of resources may improve outcomes in patients with CRC.

**Level of evidence** Level III, Retrospective Observational Study

**Keywords** Colorectal cancer · Hospital volume · Urban · Rural · Teaching hospital

## Introduction

Colorectal cancer (CRC) is considered as one of the leading causes of morbidity and cancer-related deaths nationally and worldwide. It ranks third in terms of overall incidence and cause of death in the USA [1]. In 2018, it is estimated that more than 1.8 million incident cases were diagnosed and approximately 861,000 deaths due to CRC [2]. This makes CRC

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a major burden on the population and the healthcare system. Fortunately, the overall incidence of CRC has been declining in the last several decades [3]. This is attributed to the implementation of effective screening guidelines and the early detection of precursor lesions [4]. The current trends in mortality are also encouraging [5]. It is generally difficult to interpret changes in mortality as it is influenced by a wide spectrum of different variables. However, we can postulate that new and advanced treatment options has led to decreased mortality from CRC.

CRC mortality is primarily dependent on the stage of the disease, and the 5-year survival typically ranges from a 90% for localized cancers to 70% in the setting of regional spread to 10% for patients with metastatic disease [6]. There are also multiple variables related to the patient's risk factors, intraoperative events, and in-hospital course. Recently, there is a growing interest in the influence of hospital-related factors on outcomes following CRC resection [7]. When looking at cancer patients, large sample sized studies have demonstrated that hospital volume in terms of operations performed per year can have a substantial effect on outcomes following procedures associated with high rate of mortality such as pancreatic resections [8]. Some prior studies have suggested that a volume outcome relationship may also exist for CRC surgery which is performed more frequently but with less substantial morbidity and mortality rates. Other than hospital volume which is an easily measured proxy measure for experience, the teaching status of the hospital and its location in an urban or rural setting are also plausible predictors of post-operative outcomes. However, these characteristics have not been properly investigated. All these hospital characteristics play a role in the patient's decision-making process regarding the optimal site of care and help identify areas of improvement in care [9]. To better explore the effect of these hospital-related variables on outcomes, we sought to evaluate and quantify the relationship between hospital factors on outcomes in surgically managed colorectal cancer patients using a nationally representative sample. We hypothesized that patients managed at higher volume centers have better in-patient outcomes compared to those managed at a lower volume centers.

## Materials and methods

### Dataset

We performed a 2-year (2014–2015) analysis of the Nationwide Inpatient Sample (NIS) database. The NIS is one of the largest all-payer national databases in the USA that is developed and maintained as a part of the Health Care Cost and Utilization Project (HCUP). It includes patients from community and general hospitals and teaching medical centers; however, it does not include data from long-term facilities. Every year, the NIS contains information for nearly 7 million unweighted discharges nationally. In our study, the use of NIS database was according to the regulations of the data-use agreement from the HCUP. NIS promotes comparative studies of health care services and supports health care policy research on multiple subjects including but not limited to national and regional analyses, admissions for rare conditions, patient safety and quality of care metrics, variation in medical practice, and access to care. Institutional Review Board Approval was waived for this study because the NIS database contains only deidentified data.

### Patient population and stratification

Adult patients (age ≥ 18) with colorectal cancer undergoing surgical management (open and laparoscopic) were included in the analysis using the Ninth Revision of the International Classification of Disease Diagnosis (ICD-9 codes) codes for colon and rectal cancer. We excluded patients who were managed non-operatively. Patients were stratified based on hospital volume into three categories (low, intermediate, and high volume). We then identified centers with low (< 45 cases/year), intermediate (45 ≤ volume ≤ 135 cases per year), and high volume (> 135 cases/year) according to the terciles of annual case volume. For volume identification, we ran frequency distribution by facility in order to obtain the number of patients admitted for each facility during the study period.

### Variables analyzed and outcome measures

The following data were analyzed: patient demographics (age, gender, race), hospital location (urban area vs. rural area), teaching status (teaching hospital vs. non-teaching hospital), Charlson comorbidity index (calculated from the number of comorbidities provided by the NIS dataset), surgical setting (emergency vs. elective), insurance (Medicare, Medicaid, private/self-pay, other), and income (lowest quartile vs. highest quartile). Our outcome measures were complications and mortality. Complications analyzed included pneumonia, myocardial infarction, urinary tract infection, deep venous thrombosis/pulmonary embolism, surgical site infection, and sepsis. A sub analyses were performed based on hospital location and teaching status.

### Statistical analysis

We reported descriptive statistics. Data with normal distribution are reported as mean ± standard deviation (SD) for continuous variables, as median (interquartile range (IQR)) for continuous variables without normal distribution, and as proportions (% percentage) for the categorical variables. To analyze the differences between the two patient groups on the univariate level, we used a chi-square test for categorical

variables, the Mann-Whitney *U* test for continuous non-parametric data, and the independent Student's *t* test for continuous parametric data.

In order to ascertain the effect of hospital volume on outcomes while adjusting for measurable confounding factors, we performed a hierarchical mixed-effects logistic regression model with a random effect for the hospital identifier. This approach takes into account the hierarchical structure of the data among patients from the same center. For the following covariates: patient's demographics, comorbidities, Charslon comorbidity index, and type of surgery, we evaluated the association between each covariate and the binary outcomes, on a univariate level. Variables detected to have a $p$ value < 0.2 after performing the univariate analysis were selected for inclusion in the multivariable logistic regression model. Hosmer-Lemeshow goodness of fit test was used to assess the model fitness. The Hosmer-Lemeshow test exceeded 0.05 and the tolerance was greater than 0.1 for all independent variables with a variance inflation factor of less than 10.0. In our study, alpha was set at 5% and a value of $p < 0.05$ was considered statistically significant. All statistical analyses in our study were performed using the Statistical Package for Social Sciences (SPSS, version 24; SPSS, Inc.).

### Missing data analysis

Missing data were treated as missing completely at random (MCAR). Multiple imputations using a missing value analysis technique to account for the missing values was performed. Multiple imputation is a statistical technique that aims to allow for the uncertainty about the missing data by creating several plausible imputed data sets and appropriately combining results obtained from each of them. For multiple imputation, the original dataset was analyzed for random missing data points using Little's MCAR test. Then the Markov Chain Monte Carlo method was utilized for multiple imputations. This method refers to a collection of methods for simulating random draws from non-standard distributions.

## Results

A total of 153,453 patients with CRC were identified of which 35.3% ($n = 54,220$) underwent surgical management and were included in the study. Upon stratification of the sample by hospital volume: 13,555 were admitted to low-volume centers, 26,026 were admitted to intermediate-volume centers, and 14,639 were admitted to high-volume centers (Fig. 1). Low-volume center is defined as < 45 cases/year, intermediate-volume center as 45 ≤ volume ≤ 135 cases per year, and high-volume center as > 135 cases/year. Overall, the mean age was 67 ± 13 years, 51% were male. Majority of patients included in our study (71%) were white. More than a third (37%) of the patient sample were admitted to teaching hospitals, which were more likely to be located in an urban setting (82%). The patient sample was not free from comorbidities the median Charlson Comorbidity Index was 5 [3–8]. Most patients underwent their procedure electively (65%) and were insured by Medicare (57%) (Table 1).

Patients in the high-volume group were more likely to be younger ($p < 0.01$) and are more likely to be admitted to teaching hospitals ($p < 0.01$). In addition, these patients were more likely to undergo an elective procedure and were less likely to be insured by Medicare ($p < 0.01$). In terms of their socioeconomic status these patients were more likely to belong to the highest income quartile ($p < 0.01$) relative to the intermediate- and low-volume groups. Patients admitted to the intermediate-volume centers were more likely to be black in race ($p < 0.01$) and were more likely to be insured by Medicare ($p < 0.01$). Patients admitted to low-volume centers were the least likely to be admitted to a teaching hospital ($p < 0.01$) and belonged mostly to the lowest income quartile ($p < 0.01$).

On univariate analysis, patients in the high-volume group were the least likely to develop in-hospital complications (21.3%), followed by the intermediate-volume group (28.1%), and the low-volume group (33.9%) ($p < 0.01$). The most common complication observed was pneumonia, followed by UTI, and DVT/PE. A similar trend was observed when examining the rates of mortality among the three groups. Patients admitted to high-volume centers had the least mortality rates (2.2%), followed by the intermediate-volume group (3.1%), and the low-volume group (4.5%) ($p = 0.02$) (Table 2).

A sub-analysis was performed restratifying the sample based on the urban versus rural location of the center. A total of 8,133 patients were admitted to rural centers while 46,087 were admitted to urban centers. Examining the study's primary outcomes, it is evident that urban centers were associated with lower rates of overall complications (27% vs. 39%; $p < 0.01$) and mortality (3.2% vs. 6.5%; $p < 0.01$) when we stratified the sample based on the teaching status of the center. A total of 24,339 patients were admitted to teaching hospitals while 29,821 were admitted to urban centers. Apparently, there was no association between the teaching status of the hospital and the rates of overall complications ($p = 0.43$) and mortality ($p = 0.67$) (Table 3).

On multivariable logistic regression analysis, we adjusted for measurable baseline imbalances between the three volume groups. High-volume centers were associated with reduced odds of in-hospital complications (OR 0.76 [0.56–0.89]; $p < 0.01$) (OR [95% CI], $p$ value) as well as urban hospitals (OR 0.83 [0.64–0.91]; $p < 0.01$). When evaluating mortality on a multivariable level, high-volume centers were associated with reduced odds of mortality (OR 0.79 [0.65–0.90]; $p < 0.01$) as well as urban hospitals (OR 0.87 [0.70–0.92]; $p < 0.01$) (Table 4).

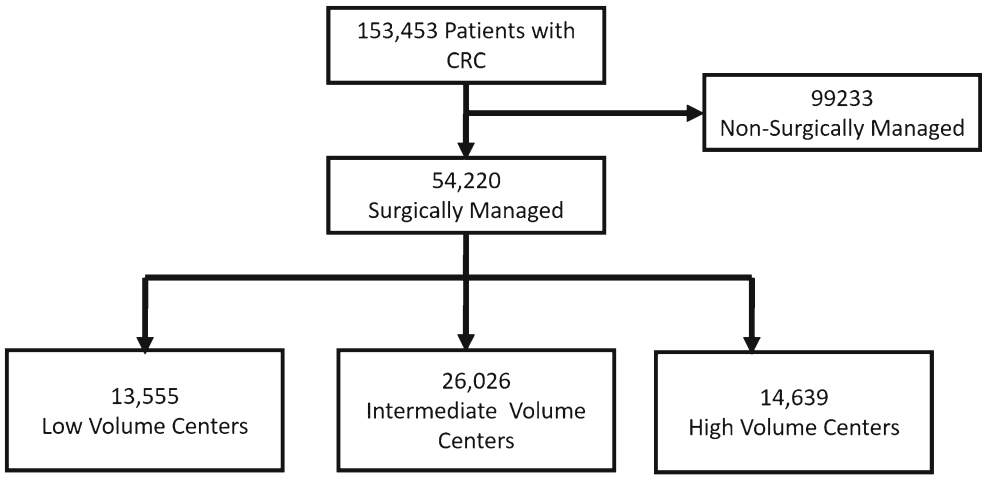


**Fig. 1** Patient flow diagram

## Discussion

The results of our study demonstrate that in patients with surgically managed CRC, admission to higher volume centers is associated with reduced rates of in-hospital complications, and mortality. In addition, we also showed that the center location in terms of urban versus rural settings also has a bearing on outcomes and that urban center are associated with superior post-operative outcomes relative to rural centers. The teaching status of the hospital apparently had no effect on the studied outcomes.

Beyond patient-related factors, there is considerable variation in surgical mortality between institutions attributed to the quality of care [10, 11]. The results signify that hospital characteristics play an important role in determining eventual surgical outcomes and these factors need to be taken into consideration by patients especially those who are at higher risk of complications, and will have a prolonged length of stay. A clear trend was observed toward reduction in the rate of complications and mortality upon increasing the center CRC surgery volume even in a technically straightforward procedure such as colectomy [12]. Additionally, Diers et al. on their

**Table 1** Patient characteristics

| Variable | Low-volume ($n$ = 13,555) | Intermediate-volume ($n$ = 26,026) | High-volume ($n$ = 14,639) | $p$ value |
|---|---|---|---|---|
| Age, mean (SD) | 67.9 (13.7) | 67.9 (13.1) | 65.5 (13.5) | < 0.01* |
| Gender, female, $n$ (%) | 50.4% | 51.5% | 51.6% | 0.20 |
| Race, $n$ (%) | | | | |
| White | 72.6% | 70.1% | 70.9% | < 0.01* |
| Black | 8.4% | 11.0% | 10.3% | < 0.01* |
| Teaching hospital, $n$ (%) | 35.4% | 36.5% | 40.3% | < 0.01* |
| Location, $n$ (%) | | | | |
| Urban area | 85.6% | 82.6% | 79.2% | < 0.01* |
| Rural area | 14.4% | 17.4% | 20.8% | < 0.01* |
| Charlson comorbidity index > 3, median [IQR] | 5 [4–8] | 5 [3–8] | 5 [3–8] | < 0.01* |
| Elective surgery, $n$ (%) | 62.0% | 63.1% | 73.3% | < 0.01* |
| Insurance, $n$ (%) | | | | |
| Medicare | 59.0% | 59.4% | 51.7% | < 0.01* |
| Medicaid | 7.4% | 9.2% | 7.6% | < 0.01* |
| Private/self-pay | 31.2% | 29.2% | 38.5% | < 0.01* |
| Other | 2.4% | 2.2% | 2.2% | < 0.01* |
| Income quartile, $n$ (%) | | | | |
| Lowest | 31.8% | 27.1% | 23.4% | < 0.01* |
| Highest | 10.3% | 17.9% | 24.7% | < 0.01* |

*Statistically significant $p$ value < 0.05

**Table 2** Outcomes based on volume

| Outcome | Low-volume ($n$ = 13,555) | Intermediate-volume ($n$ = 26,026) | High-volume ($n$ = 14,639) | $p$ value |
|---|---|---|---|---|
| Overall complications, $n$ (%) | 33.9% | 28.1% | 21.3% | < 0.01* |
| Pneumonia, $n$ (%) | 5.0% | 4.5% | 2.7% | < 0.01* |
| MI, $n$ (%) | 1.4% | 1.1% | 0.9% | < 0.01* |
| UTI, $n$ (%) | 5.2% | 5.9% | 4.7% | < 0.01* |
| DVT/PE, $n$ (%) | 2.0% | 2.3% | 2.1% | 0.21* |
| SSI, $n$ (%) | 3.6% | 3.6% | 3.3% | 0.20 |
| Sepsis, $n$ (%) | 4.5% | 4.3% | 3.3% | < 0.01* |
| pRBCs transfusion, $n$ (%) | 6.2% | 6.1% | 6.3% | 0.72 |
| Mortality, $n$ (%) | 4.5% | 3.1% | 2.2% | 0.02* |

*Statistically significant $p$ value < 0.05

nationwide 4-year review in Germany, they have found that patients who underwent colonic resection at high volume hospitals have improved outcomes compared to those managed at a low volume hospitals (13). This volume outcome relationship has been demonstrated consistently in patients undergoing major cancer surgery and the literature has shed light on this association several times. Morch et al. conducted a systematic review to summarize and present recent evidence on this relationship. After reviewing 32 studies reporting on 15 different surgical procedures, most reviews supported the presence of a volume-outcome relationship. This is association was most prevalent in colorectal cancer, breast cancer, and bariatric surgery [12]. There are also numerous other reports on reduced mortality after cancer surgery done in high-volume specialty centers as compared with low- and medium-volume units [13, 14] along with studies including a similar cohort of CRC patients [15, 16]. The results reported are in line with the findings of our study. Despite these consistent observations, our understanding as to why higher volume leads to more favorable surgical outcomes is not yet established. One potential explanation for this finding is that hospital volume is a surrogate measure of hospital experience and potentially surgeon experience. Accumulating experience allows healthcare systems to minimize errors in management [15]. In addition, high-volume surgeons and hospitals may be more experienced in creating a safer clinical environment for the management of CRC patients implementing standardized protocols and clinical pathways that increase the safety of the surgery [12–14]. At the same time, high-volume hospitals tend to have a wider spectrum of clinical services offered such as critical care medicine and sophisticated diagnostic and treatment services. These centers may also be better equipped in the timely recognition, and the handing post-operative complications and are more efficient at recognizing and rescuing patients from these complications. Studies have demonstrated that a superior hospital-based technological sophistication in many surgical services is associated with lower mortality and failure to rescue rates [17]. In recent years, volume has been used increasingly as a proxy for quality of care and this could be a strategy to improve the quality of care especially when it comes to stimulated efforts to regionalize certain high-risk patients. However, the overall impact of regionalization of care has become a subject of interest recently, and it has not been completely elucidated. Regionalization is implicated in discontinuing CRC surgery in many centers leading to patient relocation and referral in case a volume threshold has been adopted [18]. Whether the magnitude benefits of regionalization of CRC surgery outweigh the associated disadvantages is a matter of public policy debate.

When we examined the effect of the center location (urban versus rural) on effects, we also detected an interesting association. Urban centers are associated with significantly lower in-hospital complications and eventual mortality. This association apparently is not confounded by hospital volume-outcome relationship as the data reveals that urban centers were most likely to be low-volume CRC surgery centers yet still have superior outcomes. In addition when we adjusted for differences in volume on a multivariable level in the regression model, the urban status of the hospital had an independent effect on lowering the rates of complications and mortality. This is an important healthcare disparity to highlight from a public health perspective. Many studies have demonstrated that patients with rural circumstances with colon cancer tend to have worse outcomes and survival [19]. Rural populations make up approximately 15% of the US population and face unique challenges relative to patients living in metropolitan regions [20, 21]. This could be potentially explained by the complex relationship between disease characteristics, delayed diagnoses, stage at the time of diagnosis, treatment, health literacy, socioeconomic status, and other factors involving access to care [21]. Unger et al. studied a clinical trial database consists of 36,995 patients to better understand and assess cancer disparities based on the geographical distribution [22]. Surprisingly, they demonstrated that rural status was not a

**Table 3** Sub-analysis based on hospital location and teaching status

| Hospital location | Rural ($n$ = 8,133) | Urban ($n$ = 46,087) | $p$ value |
|---|---|---|---|
| Overall complications, $n$ (%) | 39% | 27% | < 0.01* |
| Mortality, $n$ (%) | 6.5% | 3.2% | < 0.01* |
| Teaching status | Non-teaching ($n$ = 29,821) | Teaching ($n$ = 24,399) | $p$ value |
| Overall complications, $n$ (%) | 28.6% | 28.2% | 0.43 |
| Mortality, $n$ (%) | 3.7% | 3.6% | 0.67 |

*Statistically significant $p$ value < 0.05

reliable predictor of adverse outcomes. But because the study design was a randomized clinical trial, treatment was received in the form of a guideline and protocol driven cancer care. In their study, the authors elaborate that rural and urban patients with cancer can actually have similar outcomes when receiving treatment in a controlled setting (i.e., randomized clinical trials). This approach aids in minimization of the observed survival disparities between rural and urban patients. The results of our study contradict the findings by Unger et al.; this could be explained by the difference in the study design as we utilized a nationally representative database and there might be unmeasurable disparities in care across rural and urban centers which are responsible for the inferior outcomes eventually observed. There can also be unmeasurable differences in the patient population admitted to rural areas. In the logistic regression model, we adjusted for all imbalances within the scope of the used database to minimize these biases and we still detected an independent protective effect of urban status of the hospital.

Hospital teaching status was surprisingly independent of the outcomes examined. The literature regarding this relationship is inconclusive [23, 24] as there can be multiple differences and variability in the healthcare system, approach to management, and definition of teaching status and this makes the study of this relationship more difficult. Resident involvement may also have unpredictable effects on eventual outcomes [25], operative time, and post-operative surveillance. To note, the percentage of emergency cases was not significantly different among low and medium-volume centers. However, it was significantly lower in high-volume centers relative to both medium- and low-volume centers. This could be related to the difficulties associated with transferring such patients to higher volume centers upon presentation to a low- or medium-volume center. Patients with emergency surgery have higher disease acuity and are predisposed to higher rates of mortality. This is a pertinent confounding factor that could partially explain the higher rate of mortality in medium- and low-volume centers observed on univariate analysis. However, upon adjustment for operative acuity in the regression model, the volume outcome relationship persisted. At the same time, the percentage of emergency cases was significantly higher in rural centers relative to urban centers and the association between urban centers and improved outcomes persisted after adjusting for operative acuity in the regression model. We have modified the manuscript to include this information.

Our study is not without limitations. First, there are limitations attributed to the retrospective nature of the analysis, erroneous database entries, and the effect of unmeasurable confounding factors which cannot be captured. The utilized database would benefit from additional granularity regarding disease-related parameters, intra-operative events, and center-related characteristics. The availability of such variables would reduce unmeasurable confounding bias and would further strengthen the conclusions of the study. We are uncertain whether there are undetected imbalances in such unmeasured confounding factors and this highlights the need for more data to further investigate the study's hypothesis. There are also limitations attributed to the lack of longer term follow-up. The Nationwide Inpatient Sample database captures only in-hospital adverse events and mortality. Furthermore, information regarding the disease process (stage, grade, distant metastasis) which has an important contribution to predicting outcomes is unavailable in the database and cannot be ascertained. Intraoperative variables such as adverse events, complications, resident involvement [25], and estimated blood loss also are not reported in the database and these could potentially affect the findings. Despite these limitations, our study analyzes a large nationally representative sample of CRC patients and demonstrates a robust volume outcome relationship and outlines the contribution of other hospital characteristics in dictating outcomes. This can potentially identify areas of improvement in surgical quality and can guide quality improvement programs. In terms of external validity, our study shares similar conclusion with the study by Diers et al. (13). They performed a 4-year

**Table 4** Multivariate logistic regression for outcomes

| | OR | 95 % CI | $p$ value |
|---|---|---|---|
| Complications | | | |
| High-volume center | 0.76 | [0.56–0.89] | < 0.01* |
| Urban hospital | 0.83 | [0.64–0.91] | < 0.01* |
| Mortality | | | |
| High-volume center | 0.79 | [0.65–0.90] | < 0.01* |
| Urban hospital | 0.87 | [0.70–0.92] | < 0.01* |

*Statistically significant p value < 0.05

**Controlling for patient's demographics (age, gender, ethnicity, race), comorbidities (Charslon comorbidity index), and type and approach of surgery

analysis of a nationwide German database including patients with colonic cancer resection and found that patients managed at high level centers have improved outcomes compared to those who were managed at low-volume centers. Our study also paves the way for future investigations on the subject in further identifying the reasons behind the observed differences.

## Conclusion

Hospital factors significantly influence outcomes in patients with colorectal cancer managed surgically. Patients managed at high-volume centers and urban facilities have relatively better outcomes compared to those who managed at a low-volume center and rural facilities, respectively. Therefore, regionalization of care along with the appropriate availability of resources may lead to improve outcomes in patients with colorectal cancer.

**Author contributions** Study design and conception: VN, MH, KH, AE, BJ, VP
Data acquisition: AC, VN, KH, MH, PO
Statistical analysis: PO, VN, KH, MH
Manuscript writing: AE, MH, KH, VN, VP
Critical revision: AC, VN, KH, MH, PO, VP, BJ

### Compliance with ethical standards

**Conflict of interest** The authors declare that they have no conflict of interest.

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