

Current Status and Prospects of Robotic Pancreatic Surgery

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Abstract

Introduction: Over the past four decades, the introduction of laparoscopic surgery to pancreatic surgery has been driven by expectations around reduced blood loss, diminished postoperative pain, accelerated recovery, and shorter hospital stays. The increase in robotic surgery has suggested further benefits by providing three-dimensional views, increased flexibility, and ergonomic advantages. Despite its potential, the adoption of robotic surgery in pancreatic surgery has been cautious due to concerns about its cost, lack of tactile feedback, and steep learning curve.

Methods: This review explores recent research findings for robotic surgery in pancreatic surgery, examining its safety, feasibility, short-term and long-term outcomes, costs, and learning curve. It evaluates studies including retrospective analyses, randomized controlled trials (RCTs), and meta-analyses, to present a comprehensive overview.

Results: Robotic surgery has been introduced into procedures including pancreaticoduodenectomy (PD) and distal pancreatectomy (DP). Studies indicate that it feasible, showing comparable or improved outcomes compared to open and laparoscopic approaches. Robotic surgery often results in shorter operative times, reduced blood loss, shorter hospital stays, and lower complication rates, particularly in PD. In DP, robotic surgery demonstrated superior spleen preservation and lower conversion rates. Long-term and oncologic outcomes are comparable to traditional methods, with some studies suggesting improved recurrence-free survival. However, robotic surgery incurs higher initial and overall costs.

Conclusion: Robotic surgery offers significant advantages in pancreatic surgery, particularly in complex procedures like PD. Despite its higher costs and extended learning curve, the benefits of enhanced precision, reduced trauma, and improved recovery make it a promising alternative to conventional methods. Further multicentre RCTs are necessary to validate these findings.

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Introduction

Minimally invasive surgery, represented by laparoscopic surgery, has been utilized in pancreatic surgery for nearly 40 years. Almost any type of pancreatic resection can be performed laparoscopically^[1]. Compared with open surgery, laparoscopic surgery offers several advantages, including reduced blood loss, diminished postoperative pain, accelerated functional recovery, and shorter hospital stays^[2, 3]. These benefits have led to its widespread adoption. Robotic surgery (RS) represents an evolution of laparoscopic techniques and was initially introduced as a remote operation system in the late 1990s^[4]. Compared with traditional laparoscopic surgery, RS provides threedimensional views, enhanced flexibility, and minimizes the impact of surgeons' hand tremors^[5]. Additionally, it offers ergonomic benefits by allowing surgeons to remain seated during procedures, thus reducing fatigue^[5]. In recent years, RS has been widely employed in urology, gynecology, gastrointestinal surgery, and other fields^[6]. With the advent of robotic technology in hepatobiliary and pancreatic surgery, the proportion of minimally invasive procedures, including both laparoscopic and robotic surgeries, has increased significantly^[7]. Robotic surgery has been applied in various simple and complex pancreatic surgeries, demonstrating initial feasibility and safety^[8, 9]. However, RS has limitations, such as the lack of tactile feedback and high equipment costs $[10, 11]$. Consensus on robotic surgery's safety, effectiveness, economic feasibility, and learning curve in the context of pancreatic diseases remains lacking^[12-16]. Further research and discussions are necessary to establish standardized protocols and guidelines.

This review examines recent research findings on RS in pancreatic procedures, summarises the current status of RS applications in pancreatic surgery, and discusses prospects for its use.

Safety and Feasibility

Pancreatic surgery is one of the most challenging clinical disciplines. Even in high-volume centers, pancreatic surgery has high perioperative mortality and complication rates[17, 18]. Previous studies have suggested limited clinical benefits of laparoscopic pancreaticoduodenectomy (LPD) compared to open pancreaticoduodenectomy (OPD) [19, 20]. In addition, minimally invasive pancreatic surgery has a longer learning curve^[21]. Therefore, surgeons are cautious about performing robotic pancreatic surgery (RPS). Melvin et al.[22] first reported robotic pancreatic resection in 2003. Over the past two decades, the number of centers performing RPS has risen gradually $[23]$, and the proportion of patients undergoing RPS has significantly $increased^{[24-27]}$.

Pancreatic resection includes pancreaticoduodenectomy (PD), distal pancreatectomy (DP), central pancreatectomy

(CP), enucleation, and total pancreatectomy. Several single-center retrospective studies have demonstrated that robotic systems can safely perform these procedures^[9, 25, 28-30]. Lai et al.^[29] retrospectively analyzed patients undergoing PD from January 2000 to February 2012. Compared with open pancreaticoduodenectomy (OPD), robotic pancreaticoduodenectomy (RPD) showed comparable overall complication rates, mortality rates, R0 resection rate, and harvested lymph node numbers[29]. A recent phase 2b randomized controlled trial study (EUROPA) also reached similar conclusions, indicating the safety and feasibility of RPD^[31]. There are no obvious contraindications to RPS in patients with vascular resection and reconstruction^[25], advanced $age^{[30, 32]}$, previous abdominal surgery^[33], and obesity^[34]. It is worth noting that a meta-analysis reported a higher incidence of postoperative venous thromboembolism (VTE) in minimally invasive pancreaticoduodenectomy (MIPD) compared to OPD, but failed to analyze further the association between RPD and VTE risk^[35].

Short-term Outcomes

Short-term Outcomes of Robotic Pancreaticoduodenectomy

Pancreaticoduodenectomy, involving complex anatomy and multiple anastomoses, is one of the technically demanding abdominal procedures.[26] The clinical benefits of LPD over OPD remain controversial, primarily due to significantly longer operating time [12, 19, 20, 36] and potential association with severe complications^[37]. A multicenter randomized controlled trial (RCT) comparing LPD and OPD was prematurely terminated due to safety concerns^[37]. RPD has significantly improved short-term outcomes compared with LPD. A multicenter retrospective cohort study in Korea showed that the operative time (377 minutes vs. 428 minutes, P<0.001) and the postoperative hospital stay (11.9 days vs. 14.2 days, P=0.001) of RPD were significantly shorter than that of LPD^[38]. Zhang et al.^[39] performed a propensity score matching (PSM) analysis of patients who underwent RPD or LPD from nine centers in China between 2015 and 2022, revealing a shorter operating time (270.0 minutes vs. 305.0 minutes, P<0.001) in the RPD group. RPD was also reported to have a lower rate of conversion to open surgery^[26, 40, 41] and a higher rate of revascularization(7.9% vs 5.6%, P=0.040)[39]. This may be attributed to the technical advantages of robotic systems, such as 3D visualization and greater flexibility, in anatomical dissection and hemorrhage control. Furthermore, RPD also showed superior postoperative outcomes to LPD, such as lower overall complication rates, severe complication rates^[26], and more textbook outcomes/optimal outcomes^[26, 38]. These results partly explain why the percentage of centers performing LPD in Europe has decreased while the number of centers

performing RPD has increased over the years [23].

OPD remains the standard surgical approach for treating pancreatic head lesions^[31]. Although a high-volume center reported that the operative time of RPD was significantly longer than that of OPD [453 (408-529) vs. 306 (247-362) minutes; P<0.001] [12], this value is much longer than the results from previous multicenter studies^[38, 39]. After the learning curve, RPD may be superior to OPD in terms of operation time and blood loss^[42]. Recently, a multicenter, open-label RCT in China compared the short-term outcomes of RPD and OPD^[43]. All operations were performed by surgeons who passed the RPD and OPD learning curves $[43]$. The results were analyzed in the modified intention-to-treat (mITT) and per-protocol (PP) populations^[43]. Secondary outcomes indicated that, after accounting for the learning curve, RPD showed shorter operative time in both mITT and PP analysis (mITT: 245.0 (220.0-330.0) vs. 298.0 (245.0- 385.0), p=0.0013; PP: 245.0 (218.0-320.0) vs. 298.5 $(245.0-390.0)$, p=0.0005)^[43]. The study also reported several exciting results, including shorter postoperative length of stay (LOS), less estimated blood loss (EBL), faster postoperative recovery, and shorter surgery-first adiuvant therapy interval^[43]. There were no significant differences in the incidence of complications such as pancreatic fistula, bile leakage, abdominal infection, postoperative pancreatectomy haemorrhage, and 90 day mortality $[43]$. In addition, RS is a protective factor for pancreatic surgical wound infection^[44], and RPD also showed a lower wound infection rate than OPD^[45, 46]. Among elderly patients, RPD also offered the advantages of shorter operative time, shorter postoperative LOS, and less EBL compared with OPD^[32].

These favorable short-term results suggest that RS fully demonstrates the advantages of minimally invasive surgery in PD. This allows patients with benign and premalignant diseases to undergo surgical treatment with minimal trauma^[47] and facilitates the early initiation of adjuvant therapy for patients with malignant diseases $[43, 6]$ 48].

Short-term Outcomes of Robotic Distal Pancreatectomy

Although DP is less complex than PD, it is still associated with a high rate of complications and mortality^[49]. Compared to open distal pancreatectomy (ODP), minimally invasive distal pancreatectomy $(MIDP)$ has been widely adopted $[49]$. MIPD reduces blood loss and shortens functional recovery while ensuring safety^[49]. A single-center retrospective study comparing patients undergoing open, laparoscopic, and robotic DP found that ODP had significantly higher intraoperative blood loss (p<0.001) and tended to have a more extended hospital stay (p=0.05) compared with

robotic distal pancreatectomy (RDP) and laparoscopic distal pancreatectomy (LDP)^[50]. Additionally, robotic approaches in DP reported less blood loss^[51] and shorter LOS^[52]compared to ODP. Notably, in radical antegrade modular pancreatosplenectomy (RAMPS), robotic surgery not only resulted in less blood loss and shorter hospital stay than open surgery but also reported shorter operative time^[53]. RDP is also superior to ODP regarding postoperative complication rates^[52, 53]. A retrospective PSM analysis showed that in patients without visceral obesity, the incidence of clinically relevant postoperative pancreatic fistula (CR-POPF) was significantly lower in RDP than in ODP (9.52% vs. 26.98%, p=0.011) [54]. Furthermore, studies have reported that RDP is more likely to preserve the spleen and splenic vessels than ODP^[51]. Spleen-preserving distal pancreatectomy (SPDP) has a lower incidence of VTE and infection than distal pancreatosplenectomy (DPS), suggesting that RDP may help reduce trauma in patients with benign and low-grade tumors of the pancreatic body and tail^[51]

Compared with LDP, RDP often reports lower conversion rates^[27, 55-57] and higher spleen preservation rates^[27, 52]. An international multicenter retrospective PSM study, excluding centers with fewer than 15 MIDP procedures annually to eliminate learning curve effects, found that RDP was still associated with improved conversion rates, spleen preservation and readmission, and splenic vessel preservation^[27]. In patients scheduled for SPDP, robotic surgery had shorter operative time, less blood loss, lower transfusion frequency, and shorter postoperative hospital stay than laparoscopic surgery^[58]. In obese patients, RDP also showed better short-term results than LDP^[34]. This suggests that RDP may have certain advantages in delicate operations and narrow spaces, thus making it more recommended for SPDP^[59]. However, among the overall patients undergoing DP, the RDP group often had a longer operative time^{[27, 52, 56, 57,} ^{60, 61]}. There was no significant difference between LDP and RDP regarding postoperative complication rates and short-term mortality^[27, 60, 62, 63]. Müller et al.^[64] identified benchmark values for RDP surgical outcomes based on data from 16 international expert centers and compared it with a laparoscopic control group from 4 high-volume centers. The study found that LDP had significantly higher conversion rates and overall complications^[64]. Further, multicenter RCT studies are needed to compare the short-term outcomes of RDP and LDP.

Short-term Outcomes of Other Robotic Pancreatectomy

For benign and low-grade pancreatic lesions, parenchymasparing pancreatectomy (central pancreatectomy, duodenum-preserving partial pancreatic head resection, enucleation, and uncinate resection) can reduce the incidence of postoperative pancreatic insufficiency^[65].

However, limited high-quality evidence compared robotic approaches with`` laparoscopic or open approaches in these procedures. Zheng et al.^[65] conducted a systematic review of the effectiveness of RS in parenchyma-sparing pancreatectomy. Compared with open parenchymasparing pancreatectomy, RS had shorter operative time, less blood loss, and shorter LOS but appeared to have a higher incidence of POPF^[65].

An RCT study compared the short-term outcomes of robotic versus open middle pancreatectomy^[66]. Robotic surgery was associated with reduced LOS, operation time, blood loss and clinical POPF rate, and accelerated postoperative recovery^[66]. Ou et al. ^[67] retrospectively analyzed 146 patients who underwent robotic or open enucleation of tumors in the proximal pancreas. The robotic group was superior to the open group in terms of shorter operative time (90.0 minutes vs. 120.0 minutes, P<0.001), decreased blood loss (20.0 ml vs. 100.0 minutes, P=0.001), and lower incidence of clinically relevant POPF (43.5% vs. 61.1%, P=0.040)^[67]. The postoperative recurrence rates and long-term functional outcomes were comparable^[67]. A case-control study by Najafi et al.[68] demonstrated that robotic pancreatectomy and laparoscopic pancreatectomy had comparable shortterm results.

As for total pancreatectomy, a PSM study reported that the median operative time was significantly decreased in patients who underwent robotic surgery compared with those who underwent open surgery [300 (250- 360) minutes vs. 360 (300-525) minutes, P=0.031][69]. In addition, the robotic cohort also reported a higher rate of en bloc resection and spleen preservation^[69]. The 30-day morbidity and 90-day mortality were similar between the two approaches^[69].

Long-term and Oncologic Outcomes

Several studies have indicated that robotic pancreatectomy has similar R0 resection and lymph node harvested compared to open and laparoscopic approaches[42, 43, 48, 63, 70, 71]. However, a systematic review of four studies reported a higher lymphadenectomy rate but a lower R0 resection rate in RPD than in open $[72]$. Nickel et al.[12] found that in patients with pancreatic ductal adenocarcinoma (PDAC), fewer lymph nodes were harvested [24 (18-27) vs. 33 (27-39); P<0.001] with RPD versus OPD, but both met the internationally accepted benchmark criteria for OPD. Daouadi et al.^[55] reported that RDP had higher rates of margin negative resection (0 vs. 36%, P<0.005) for PDAC patients and improved lymph node yield for both malignant and benign lesions [19 (17-24) vs. 9 (7-11), P<0.0001] than that of LPD. A meta-analysis of 43 studies with 6757 patients also showed that RDP was associated with a higher lymph node vield than LDP (MD=3.95, 95% CI 1.67-6.23)^[73].

However, the differences in lymph node harvested and R0 resection rates do not appear to affect long-term survival outcomes. In the PDAC population, the median diseasefree survival (DFS) and overall survival (OS) of RPD and OPD^[74]. The study by Weng et al.^[48] also demonstrated that in patients with pancreatic cancer who receive adjuvant chemotherapy, OS was comparable between the robotic pancreatectomy (RP) and open pancreatectomy (OP). Nevertheless, the RP group had a better recurrencefree survival (RFS; 17 months vs 14 months, P=0.015), with multivariate Cox analysis identifying RP as an independent predictor of improved RFS^[48]. Additionally, more patients in the RP group completed≥6 cycles of adjuvant chemotherapy^[48]. Other studies suggest that RP might be associated with improved OS in PDAC patients, particularly those undergoing RPD^[70]. This may be partly attributable to the faster postoperative recovery and shorter surgery-first adjuvant therapy interval of robotic surgery. For specific PDAC populations, early initiation of adjuvant chemotherapy improves prognosis^[75, 76].

There were also no significant differences in median RFS and OS between RPD and LPD^[39]. An international multicenter retrospective cohort study reported a comparable R0-resection rate and overall survival between RDP and LDP despite an improved lymph node yield in RDP [56]. A retrospective PSM study by Qu et al.^[63] found no significant differences in RFS and OS between PDAC patients undergoing robotic or laparoscopic DPS. Robotic pancreatectomy offered comparable long-term and oncological outcomes to laparoscopic and open pancreatectomy.

Costs

In pancreatic surgery, robotic methods have shown high procedure-related costs and overall in-hospital costs. The secondary outcomes of the German EUROPA study showed that RPD was more expensive than OPD regarding the procedure-related costs (4744±1254€ vs. 866±459€, difference in means [95%CI]: 3878 [3410; 4347], p<0.001)^[31]. Some studies have shown that RPD has advantages in LOS and postoperative complications, which may help reduce postoperative hospital stay $costs^{[77]}$ and reach comparable overall $costs^{[77, 78]}$. Kowalsky et al.[79] reported that enhanced recovery after surgery (ERAS) combined with RPD synergistically decreases hospital stay and overall cost.

Nevertheless, according to the results of EUROPA results, RPD still appeared to have significantly higher overall hospital costs (33502±22314€ vs. 21429±12427€, the difference in means [95%CI]: 12073 [2932; 21213], p=0.011)^[31]. Similar or higher costs were also reported for $RDP^{[57, 60, 80, 81]}$ and robotic enucleation^[82]. However, in a study comparing the economic impact of RDP, LDP, and ODP, the overall costs were significantly higher for ODP, particularly in hospital stay costs^[80]. This may be related

to the considerably longer LOS and higher complication rates of ODP[80].

Notably, RPS may improve patients' quality of life. A study suggests that RDP had a higher probability of being more cost-effective than LDP when a willingness to pay exceeds 4,800 Euros per Quality Adjusted Life Year (QALY)^[60]. However, this conclusion may not be universally applicable due to the vast differences in healthcare policies across various countries and regions.

The Learning Curve

Due to the complexity of pancreatic surgery, especially PD, the 2020 Miami International Evidence-based Guidelines on Minimally Invasive Pancreas Resection recommended that minimally invasive pancreatic surgery be performed in high-volume centers to reduce morbidity and mortality^[83]. RPS has demonstrated an incredibly prolonged learning curve, even in high-volume centers. Boone et al.[84] reported that statistical improvements in EBL (600 mL vs. 250 mL, P=0.002) and conversion rates (35.0% vs. 3.3%, P<0.001) of RPD occurred after 20 cases. Pancreatic fistula rates and operative time were reduced after 40 and 80 cases, respectively^[84]. Including more consecutive cases, the learning curve for RPD operative time may extend to 240-250 patients^[16,] ^{25]}. For surgeons who have passed the RPD learning curve, an additional 35 cases are required to attain proficiency in performing RPD with vascular resection^[85]. However, structured training programs and mentorship from experienced surgeons can help shorten the learning curve of RPD[86]. In centers trained in dedicated RPD training programs, significant improvements in operative time, major complication rates, and textbook outcomes were observed after 15, 62, and 84 cases, respectively $[87]$.

Compared with RPD, fewer cases are required to master RDP. The RDP operative time improved significantly after 10-31 cases[88, 89] and stabilized after 40-66 cases [89-91]. Current studies on the RPS learning curve primarily focus on operating time or blood loss. There is still a lack of identification regarding the learning curve for primary textbook outcomes in RDP and other RPS. An international multicenter retrospective study stated that the learning curve length of MIDP for textbook outcomes was considerable with 85 procedures but did not further analyze in the RDP subgroup^[92]. There was no significant difference between the learning curve for RPD versus LPD and RDP versus LDP^[93].

Robotic Pancreatic Surgery in China

The robotic surgical system was first introduced to China in 2006[94], with the initial reports of RPS emerging in 2009[95]. In recent years, the number of centers and surgeries performing robotic pancreatic surgery in China

has gradually increased. A single-center study indicated that the proportion of robotic methods in pancreatic surgery rose from 10.44% in 2012 to 72.06% in 2017^[96]. However, by the end of 2022, RPS accounted for less than 2% of all robotic surgeries across all disciplines in China[94].

Ding et al.^[97] systematically reviewed the current status of MIPD in China and found no inferior perioperative and short-term oncological outcomes were observed in MIPD of China compared with some large international meta-analyses. The median surgical time for the RPD subgroup was 387.6 minutes, with a median blood loss of 232.5 ml and a conversion rate of 18.0%^[97]. A singlecenter retrospective study in 2018 reported the short-term outcomes of 1010 cases of RPS, including 417 cases of RPD and 428 cases of RDP^[96]. The mortality and severe complication rates in the total cohort were comparable to data reported by other international centers^[96]. The median operative time for the RPD group was 300 minutes (120-720 minutes), with an R1 resection rate of 3.44%. For the RDP group, the operative time was 170 minutes (30-340 minutes), with an R1 resection rate of 2.09%[96]. In recent years, Chinese research teams have also reported several large-scale, high-quality clinical studies on RPS $[39, 43, 67]$, indicating that high-volume centers in China have attained mature experience with RPS.

While most robotic surgeries in China are performed using the Da Vinci surgical system, China's robotic laparoscopic surgical robots are emerging to compete for market share. The Micro Hand S surgical robot has passed Phase I clinical trials in general surgery, demonstrating feasibility and safety^[98]. A prospective cohort study showed that China's Kangduo surgical robot's short-term outcomes in colon cancer surgery were not inferior to the Da Vinci system^[99]. In the future, China's surgical robots are expected to achieve technological breakthroughs, injecting fresh vitality into the surgical robot market.

Limitations and Prospects

The application of robotic surgery in pancreatic surgery is gradually expanding. However, robotic systems also have certain limitations. Firstly, robotic surgery systems lack compatible surgical instruments. The Cavitron Ultrasonic Surgical Aspirator (CUSA), known for its ability to expose vascular and ductal structures finely, is commonly used in liver parenchyma transection^[100]. Studies have shown that CUSA may help reduce the occurrence of pancreatic fistula after DP^[101], but it has not yet been integrated into robotic systems. The laparoscopic CUSA in robotic procedures must be operated by a skilled assistant at the bedside, which may be impractical in clinical applications^[102]. The ultrasonic scalpel can effectively

Table 1: Key papers

cut tissue and seal small blood vessels and has been integrated into robotic systems^[103]. However, it lacks other robotic tools' full range of motion and is relatively less flexible^[103]. The integration of practical instruments and the improvement of existing tools may further improve the surgical outcomes of robotic systems.

Another limitation of robotic surgery is the lack of natural tactile feedback[104]. Robotic tactile feedback systems can only provide simple sensory signals such as vibration and pressure, which may limit the accurate identification of lesions^[104]. Intraoperative ultrasound can precisely locate lesions, assess vascular invasion, and detect liver metastases, aiding in staging and determining the extent of resection^[105, 106]. However, as mentioned above, robotic systems also lack integrated ultrasound instruments. The laparoscopic ultrasound instruments may conflict with robotic mechanical arms. In the future, it is still necessary

to explore better tactile feedback mechanisms to achieve precise surgery^[104].

In addition, as mentioned previously, high costs may also limit the application of robotic surgery. Patti et al.^[107] reported that Intuitive Surgical Inc. (ISI) occupies a major share of the surgical robotic market. The price of ISI's robots ranges from \$910,000 to \$2.5 million, with annual maintenance contracts of \$125,000^[107]. Even without considering equipment purchase and maintenance costs, the variable costs of robotic surgery are also high $[31, 108]$. Robotic surgery is expected to reduce postoperative costs by improving clinical outcomes^[109]. Competitors entering the market are also likely to reduce the price of robotic equipment and consumables in the future, thereby reducing surgical costs^[107].

RPS still has significant room for development. New concepts are constantly being proposed, such as singleport robotic systems. Single-port robots, while retaining flexible wrist joints and 3D views, can reduce the incidence of incision complications and improve cosmetic outcomes [110] with lower postoperative pain scores^[111, 112]. Liu et al.^[110] reported 23 patients who underwent singleport robotic pancreatic surgery, one of whom underwent single-port robotic pancreaticoduodenectomy. None of the patients experienced severe complications or death postoperatively, preliminarily demonstrating the feasibility of single-port robotic pancreatic surgery^[110].

It is worth noting that most of the current studies on robotic pancreatic surgery are observational studies, and multicenter RCT studies are needed to clarify the safety and effectiveness. In addition, it is necessary to establish internationally accepted benchmarks for RPS, to provide reference standards for technical learning, and to provide reliable evidence for comparing the efficacy among different populations and surgical methods.

Conclusion

Over two decades of practice have shown that experienced surgeons can safely perform various robotic pancreatic procedures (table 1). Robotic systems offer advantages such as 3D viewing, increased flexibility, and hand tremor filtering. This may result in better short-term outcomes in surgeries with narrow operating spaces or complex anatomical structures (such as pancreaticoduodenectomy). Robotic surgery has also achieved comparable long-term outcomes to open or laparoscopic approaches, demonstrating bright application prospects. However, RPS has certain limitations, including an exceptionally steep learning curve, necessitating specialized training programs to enhance safety. Multicenter RCTs are needed to clarify its safety and efficacy, and internationally recognized benchmarks are expected to be established.

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Competing interests

The authors declare no conflicts of interests in this work.

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