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COVID Surg Collaborative (2021) Impact of Bacillus Calmette-Guérin (BCG) vaccination on postoperative mortality in patients with perioperative SARS-CoV-2 infection. *BJS Open*, 5 (6). zrab131. ISSN 2474-9842

<https://doi.org/10.1093/bjsopen/zrab131>

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Impact of Bacillus Calmette-Guérin (BCG) vaccination on postoperative mortality in patients with perioperative SARS-CoV-2 infection

COVIDSurg Collaborative

Correspondence to: Mr Aneel Bhangu, Academic Department of Surgery, University of Birmingham, Birmingham, UK (e-mail: a.a.bhangu@bham.ac.uk); Professor Stephen Tabiri, Department of Surgery, University for Development Studies, Tamale, Ghana (e-mail: stabiri@uds.edu.gh)

Members of the COVIDSurg Collaborative are co-authors of this study and are listed under the heading Collaborators. For details of role see Appendix S1.

Dear Editor

During the COVID-19 pandemic, multiple theories were proposed based on the observation that countries with an ongoing national Bacillus Calmette-Guérin (BCG) immunization programme had lower SARS-CoV-2 case rates and COVID-19 mortality than countries that had stopped BCG vaccine administration. There was, however, no evidence supporting or disputing this theory^{1,2}. Owing to the uncertainty on the role of BCG vaccine on the outcomes of patients with perioperative SARS-CoV-2 infection, this international study aimed to determine whether previous BCG vaccination was associated with reduced postoperative pulmonary complications (PPC) and 30-day mortality in patients undergoing surgery who developed SARS-CoV-2 infection.

This COVIDSurg study³⁻⁵ was an international prospective cohort study that included patients who had surgery between 1 February and 31 July 2020 and were diagnosed with SARS-CoV-2 within 7 days before or 30 days after surgery. The primary outcome was the rate of 30-day PPC and the secondary outcome was 30-day postoperative mortality rate. These were compared in patients with and without BCG vaccination. A logistic regression model was used to find the odds of association. The full methodology is available in the Appendix S2.

This study included 2391 patients from 428 hospitals across 64 countries from February 2020 to July 2020. Overall, 1165 (48.9 per

cent) patients were male and 524 (21.9 per cent) were aged 70 years or older (Table S1). The BCG vaccine had been administered to 1649 (69.0 per cent) patients, of whom 1518 (63.5 per cent) had received it at least 15 years before surgery. Patients who had received a BCG vaccination were younger than patients who had not been vaccinated (70 years of age or older: 16 versus 35 per cent ($P < 0.001$)), had lower ASA (grades III–V: 30 versus 51 per cent ($P < 0.001$)), and were more likely to have surgery for benign conditions (71 versus 60 per cent; $P < 0.001$). There were no significant differences in the rates of emergency surgery, major surgery, or timing of SARS-CoV-2 infection between the groups. Of the 2391 patients, 759 (31.7 per cent) developed PPC. The 30-day mortality was 11.1 per cent ($n = 265$). Although rates of PPC were significantly lower in patients who had previously been vaccinated against BCG than those who did not (29 versus 38 per cent; $P < 0.001$) (Table 1), this did not persist on adjusted analysis (odds ratio (OR) 0.98, 95 per cent c.i. 0.79–1.22; $P = 0.3$) (Table 1). There were no significant differences in 30-day mortality rates in previously BCG-vaccinated patients versus unvaccinated patients (10 versus 13 per cent; $P = 0.062$), which remained on adjusted analysis (OR 1.25, 95 per cent c.i. 0.92–1.69; $P = 0.156$) (Table 1). Full models are presented in Tables S2 and S3.

Stratified analysis performed by timing of vaccination demonstrated that patients who were vaccinated 15 years previously or longer were less likely than patients vaccinated less than 15 years

Table 1 Impact of BCG vaccination on postoperative pulmonary complications and 30-day mortality in patients with SARS-CoV-2 infection undergoing surgery

	No. of patients (%)	Unadjusted OR (95% c.i.)	P	Adjusted OR (95% c.i.)	P
Pulmonary complications					
No BCG	278 (37.5)	REF		REF	
BCG	481 (29.2)	0.69 (0.57–0.83)	0.001	0.98 (0.79–1.22)	0.878
30-day mortality					
No BCG	96 (12.9)	REF		REF	
BCG	169 (10.2)	0.77 (0.59–1.01)	0.053	1.25 (0.92–1.69)	0.156

OR, odds ratio; BCG, Bacillus Calmette-Guérin; REF, referent.

Received: August 26, 2021. Accepted: November 15, 2021

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ago to be ASA grades III–V (30 versus 41 per cent; $P=0.033$) and were more likely to have surgery for benign disease (72 versus 57 per cent; $P<0.001$) (Table S4). There were no significant differences in rates of postoperative pulmonary complications (29 versus 34 per cent; $P=0.208$) or 30-day mortality (10 versus 14 per cent; $P=0.221$), on adjusted analysis (Tables S5 and S6).

There were important limitations to the present study. There was a broad inclusion of patients from low-, middle-, and high-income countries with varying pre- and postoperative procedures and availability of resources such as a well-equipped ICU for the management of the patient. Mortality and morbidity could have been greatly impacted by this difference. Some countries had a much higher prevalence and severity of disease, which could have also influenced outcomes.

According to these findings, prior BCG vaccination does not appear to protect SARS-CoV-2-infected patients against PPCs and 30-day mortality.

Collaborators

Stephen Tabiri, Sivesh K Kamarajah, Dmitri Nepogodiev, Elizabeth Li, Joana Simoes, Sanskrithi Sravanam, Sheila Agyeiwaa Owusu, Haruna Mahama, Yaa Nyarko Agyeman, Joshua Arthur, Sheba Mary Kunfah, Frank Enoch Gyamfi, Emmanuel Abem Owusu, Markus W. Loffler, Paul Wandoh, Aneel Bhangu, Kwabena Siaw-Acheampong, Leah Argus, Daoud Chaudhry, Brett E Dawson, James C Glasbey, Rohan R Gujjuri, Conor S Jones, Sivesh K Kamarajah, Chetan Khatri, James M Keatley, Samuel Lawday, Elizabeth Li, Harvinder Mann, Ella J Marson, Kenneth A Mclean, Maria Picciochi, Elliott H Taylor, Abhinav Tiwari, Joana FF Simoes, Isobel M Trout, Mary L Venn, Richard JW Wilkin, Aneel Bhangu, Dmitri Nepogodiev, Irida Dajti (Albania), Arben Gjata (Albania), Luis Boccalatte (Argentina), Maria Marta Modolo (Argentina), Daniel Cox (Australia), Peter Pockney (Australia), Philip Townend (Australia), Felix Aigner (Austria), Irmgard Kronberger (Austria), Kamral Hossain (Bangladesh), Gabrielle VanRamshorst (Belgium), Ismail Lawani (Benin), Gustavo Ataide (Brazil), Glauco Baiocchi (Brazil), Igor Buarque (Brazil), Muhammad Gohar (Bulgaria), Mihail Slavchev (Bulgaria), Arnav Agarwal (Canada), Amanpreet Brar (Canada), Janet Martin (Canada), Maria Marta Modolo (Chile), Maricarmen Olivos (Chile), Jose Calvache (Colombia), Carlos Jose Perez Rivera (Colombia), Ana Danic Hadzibegovic (Croatia), Tomislav Kopjar (Croatia), Jakov Mihanovic (Croatia), Jaroslav Klat (Czech Republic), René Novysedlak (Czech Republic), Peter Christensen (Denmark), Alaa El-Hussuna (Denmark), Sylvia Batista (Dominican Republic), Eddy Lincango (Ecuador), Sameh H Emile (Egypt), Mengistu Gebreyohanes Mengesha (Ethiopia), Dr. Samuel Hailu (Ethiopia), Hailu Tamiru (Ethiopia), Joonas Kauppila (Finland), Alexis Arnaud (France), Markus Albertsmeiers (Germany), Hans Lederhuber (Germany), Markus Loffler (Germany), Stephen Tabiri (Ghana), Symeon Metallidis (Greece), Georgios Tsoulfas (Greece), Maria Aguilera Lorena (Guatemala), Gustavo Grecinos (Guatemala), Tamas Mersich (Hungary), Daniel Wettstein (Hungary), Dhruv Ghosh (India), Gabriele Kembuan (Indonesia), Peiman Brouk (Iran), Mohammad Khosravi (Iran), Masoud Mozafari (Iran), Ahmed Adil (Iraq), Helen M Mohan (Ireland), Oded Zmora (Israel), Marco Fiore (Italy), Gaetano Gallo (Italy), Francesco Pata (Italy), Gianluca Pellino (Italy), Sohei Satoi (Japan), Faris Ayasra (Jordan), Mohammad Chaar (Jordan), Ildar R Fakhradiyev (Kazakhstan), Mohammad Jamal (Kuwait), Muhammed Elhadi (Libya), Aiste Gulla (Lithuania), April Roslani (Malaysia), Laura Martinez (Mexico), Antonio Ramos De La

Medina (Mexico), Oumaima Outani (Morocco), Pascal Jonker (Netherlands), Schelto Kruijff (Netherlands), Milou Noltes (Netherlands), Pieter Steinkamp (Netherlands), Willemijn van der Plas (Netherlands), Adesoji Ademuyiwa (Nigeria), Babatunde Osinaike (Nigeria), Justina Seyi-olajide (Nigeria), Emmanuel Williams (Nigeria), Sofija Pejкова (North Macedonia), Knut Magne Augestad (Norway), Kjetil Soreide (Norway), Zainab Al Balushi (Oman), Ahmad Qureshi (Pakistan), Raza Sayyed (Pakistan), Mustafa Abu Mohsen Daraghme (Palestine), Sadi Abukhalaf (Palestine), Moises Cukier (Panama), Hugo Gomez (Paraguay), Sebastian Shu (Peru), Ximena Vasquez (Peru), Marie Dione Parreno-Sacdalan (Philippines), Piotr Major (Poland), José Azevedo (Portugal), Miguel Cunha (Portugal), Irene Santos (Portugal), Ahmad Zarour (Qatar), Eduard-Alexandru Bonci (Romania), Ionut Nego (Romania), Sergey Efetov (Russia), Andrey Litvin (Russia), Faustin Ntirenganya (Rwanda), Ehab AlAmeer (Saudi Arabia), Dejan Radenkovic (Serbia), Frederick Koh Hong Xiang (Singapore), Chew Min Hoe (Singapore), James Ngu Chi Yong (Singapore), Rachel Moore (South Africa), Ncamsile Nhlathathi (South Africa), Ruth Blanco Colino (Spain), Ana Minaya Bravo (Spain), Ana Minaya-Bravo (Spain), Umesh Jayarajah (Sri Lanka), Dakshitha Wickramasinghe (Sri Lanka), Mohammed Elmujtaba (Sudan), William Jebril (Sweden), Martin Rutegård (Sweden), Malin Sund (Sweden), Arda Isik (Turkey), Sezai Leventoglu (Turkey), Tom EF Abbott (UK), Ruth Benson (UK), Ed Caruna (UK), Sohini Chakrabortee (UK), Andreas Demetriades (UK), Anant Desai (UK), Thomas D Drake (UK), John G Edwards (UK), Jonathan P Evans (UK), Samuel Ford (UK), Christina Fotopoulou (UK), Ewen Griffiths (UK), Peter Hutchinson (UK), Michael D Jenkinson (UK), Tabassum Khan (UK), Stephen Knight (UK), Angelos Koliass (UK), Elaine Leung (UK), Siobhan McKay (UK), Lisa Norman (UK), Riinu Ots (UK), Vidya Raghavan (UK), Keith Roberts (UK), Andrew Schache (UK), Richard Shaw (UK), Katie Shaw (UK), Neil Smart (UK), Grant Stewart (UK), Sudha Sundar (UK), Dale Vimalchandran (UK), Naomi Wright (UK), Sattar Alshryda (United Arab Emirates), Osaid Alser (United States), Kerry Breen (United States), Ian Ganly (United States), Haytham Kaafarani (United States), Brittany Kendall (United States), Hassan Mashbari (United States), Hamza Al Naggari (Yemen), Dennis Mazingi (Zimbabwe), EuroSurg, European Society of Coloproctology (ESCP), GlobalSurg, GlobalPaedSurg, ItsURG, PTSurg, SpainSurg, Italian Society of Colorectal Surgery (SICCR), Association of Surgeons in Training (ASiT), Irish Surgical Research Collaborative (ISRC), Joana FF Simoes (Chair), Dajti I (University Hospital Center Nene Tereza, Albania); Valenzuela JI (Hospital Velez Sarsfield, Argentina); Boccalatte LA, Gemelli NA, Smith DE (Hospital Italiano De Buenos Aires, Argentina); Dudi-Venkata NN, Kroon HM, Sammour T (Royal Adelaide Hospital, Australia); Roberts M, Mitchell D, Lah K, Pearce A, Morton A (Royal Brisbane and Women's Hospital, Australia); Dawson AC, Drane A (Gosford Hospital, Australia); Sharpin C, Nataraja RM, Pacilli M (Monash Childrens Hospital, Australia); Cox DRA, Muralidharan V, Riddiough GE, Clarke EM, Jamel W, Qin KR (Austin Hospital, Australia); Pockney P, Cope D, Egoroff N, Lott N (John Hunter Hospital, Australia); Putnis S, De Robles S, Ang Z (Wollongong Public Hospital, Wollongong, Australia); Mitteregger M, Uranitsch S, Stiegler M, Seitinger G, Aigner F (Krankenhaus der Barmherzigen Brüder Graz, Austria); Lumenta DB, Nischwitz SP, Richtig E, Pau M, Srekl-Filzmaier P, Eibinger N, Michelitsch B, Fediuk M, Papinutti A, Seidel G, Kahn J, Cohnert TU (Medical University of Graz, Austria); Messner F, Öfner D (Medical University of Innsbruck, Austria); Presl J, Varga M, Weitzendorfer M, Emmanuel K (Paracelsus Medical University, Salzburg,

Austria); Binder AD (Universitätsklinikum Tulln, Tulln, Austria); Zimmermann M, Holawe S, Nkenke E, Grimm C, Kranawetter M (Medical University of Vienna, Vienna, Austria); Rahman Mitul A, Islam N, Karim S (Dhaka Shishu (Children) Hospital, Bangladesh); Komen N, Putnis S, De Robles S, Ang E (University Hospital Antwerp (UZA), Edegem, Belgium); De Praetere H, Tollens T, Schols G, Smets C, Haenen L (Imelda Hospital, Bonheiden, Belgium); Quintens J, Van Belle K (Europe Hospitals, Belgium); Van Ramshorst GH, Pattyn P, Desender L, Martens T, Van de putte D (Ghent University Hospital, Belgium); Lerut P, Grimonprez A, Janssen M, De Smul G, Wallaert P (AZ Groeninge, Belgium); Van den Eynde J, Oosterlinck W, Van den Eynde R, Sermon A, Boeckxstaens A, Cordonnier A, De Coster J, Jaekers J, Politis C, Miserez M (UZ Leuven, Belgium); Duchateau N, De Gheldere C (Heilig Hart Ziekenhuis Lier, Belgium); Flamey N, Pattyn P (AZ Delta, Belgium); Cristiano A, Guidi B, Minussi AL, Castro S, Okoba W, Maldonado FHR, Oliveira P, Baldasso T, Santos L (Fundação Centro Médico De Campinas, Brazil); Gomes GMA, Buarque IL, Pol-Fachin L, Bezerra TS, Barros AV, da Silva AMR, Leite ALS, Silvestre DWA, Ferro CC (Hospital Santa Casa De Misericórdia De Maceió, Brazil); Araujo MS, Lopes LM, Damasceno PD, Araujo DHS (Hospital Universitário Antonio Pedro, Brazil); Laporte G, Salem MC (Irmandade Da Santa Casa De Misericórdia De Porto Alegre, Brazil); Guimaraes-Filho, MAC (Pedro Ernesto University Hospital, Brazil); Nacif L (Hospital Nove De Julho, Brazil); Flumignan RLG, Nakano LCU, Kuramoto DAB, Aidar ALS, Pereda MR, Correia RM, Santos BC, Carvalho AA, Amorim JE, Guedes Neto HJ, Areias LL, Sousa AF, Flumignan CDQ, Lustre WG, Moreno DH, Barros-Jr N, Baptista-Silva JCC (Hospital São Paulo, Brazil); Matos LL, Kowaski LP, Kulcsar MAV, Nunes KS, Teixeira MF (Instituto do Câncer do Estado de São Paulo, São Paulo, Brazil); Nunes RL, Ijichi TR, Kim NJ, Marreiro A, Muller B, Barakat Awada J (Notre Dame Intermédica - Hospital Salvalus, Brazil); Baiocchi G, Kowalski LP, Vartanian JG, Makdissi FB, Aguiar Jr S, Marques N, Carvalho GB, Marques TMDM, Abdallah EA, Zurstrassen CE, Gross JL, Zequi SC, Gonçalves BT, Santos SS, Duprat JP, Coimbra FJF (A.C. Camargo Cancer Center, Brazil); Cicco R (Instituto de Câncer Dr Arnaldo Vieira de Carvalho, São Paulo, Brazil); Takeda F, Cecconello I, Ribeiro Junior U (Instituto Do Câncer De Estado De São Paulo, Brazil); Gatti A, Oliva R, Nardi C (Hospital Geral De Pirajussara, Brazil); Slavchev M, Atanasov B, Belev N (University Hospital Eurohospital, Plovdiv, Bulgaria); Dell A, Bigam D, Dajani K, Al Riyami S (University of Alberta Hospital, Canada); Martin J, Cheng D, Yang H, Fayad A (London Health Sciences Centre and St Josephs Health Care London, Canada); Carrier FM, Amzallag E, Desroches J, Ruel M (Centre hospitalier de l'Université de Montréal, Canada); Caminsky NG, Boutros M, Moon J, Wong EG, Vanounou T, Pelletier J, Wong S, Girsowicz E, Bayne J, Obrand D, Gill H, Steinmetz O, MacKenzie K, Lukaszewski M, Jamjoum G (Jewish General Hospital, Canada); Richebé P, Verdonck O, Discepola S, Godin N, Idrissi M (Hôpital Maisonneuve-Rosemont, Canada); Briatico D, Sharma S, Talwar G, Bailey K (McMaster Children's Hospital, Hamilton, Ontario, Canada); 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Ko M, Brar A (St. Joseph's Health Centre, Canada); Mayson K (Vancouver General Hospital, Canada); Kidane B, Srinathan S (Health Sciences Centre, Canada); Escudero MI, Reyes JT (Hospital Clinico Universidad De Chile/Hospital San Jose, Chile); Modolo MM, Ramirez Nieto P, Sepulveda R, Bolbarán A, Molero A, Ruiz I (Barros Luco Trudeau, Chile); Reyes GP, Salas R, Suazo C (Hospital del Salvador, Chile); Muñoz R, Grasset E, Inzunza M, Besser N, Irarrázaval MJ, Jarry C, Bellolio F, Romero Manqui CA, Ruiz Esquide M (Hospital Clínico Universidad Católica, Chile); Fuentes T, Campos J (Hospital Sotero Del Rio, Chile); Perez Rivera CJ, Cabrera PA (Fundacion Cardioinfantil-Instituto de Cardiología, Colombia); Pinilla RE, Guevara O, Jimenez Ramirez LJ, Velasquez Cuasquen BG, Herrera Mora DR, Bonilla A, Diaz S, Manrique E, Facundo H, Velez Bernal JL, Ángel J, García M, Guzmán L, Lehmann C, Cervera S, Trujillo Sanchez LM (Instituto Nacional De Cancerologia, Colombia); Guevara R, Valbuena D, Suarez L, Jimenez G, Velandia A, Vargas J, Espinosa J, Rey S (Clínica Universitaria Colombia, Bogotá., Colombia); 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Shahine M, Yousof EA, Youssef A (Assiut University Hospital, Assiut, Egypt); Esmail E, Khalaf M (Kafr Elzyat Hospital, Egypt); Eldaly A (El-Menshaway Hospital, Egypt); Ghoneim A, Hawila A, Badr H, Elhalaby I, Abdel-bari M, Elbahnasawy M, Hamada MK, Morsy MS, Hammad M, Hammad M, Essa M, Fayed MT, Elzoghby M, Rady M, Hamad O, Salman S, Sarsik S, Abd-elsalam S, Gamal Badr S, El-Masry Y (Tanta University Hospital, Egypt); Moahmmed MMH (Zagazig University Hospitals, Zagazig, Egypt); Hailu S, Wolde A, Mengesha M, Nida S, Workneh M, Y Ahmed M, Fisseha T, Kassa D, Zeleke H, Admasu A, Laeke T, Tirsit A, Gessesse M, Addissie A (Tikur Anbessa (Black Lion) Hospital-Addis Ababa University, Ethiopia); Bekele K (Maddawalabu University Goba Referral Hospital, Ethiopia); Kauppila JH, Sarjanoja E (Länsi-Pohja Central Hospital, Finland); Testelin S, Dakpé S, Devauchelle B, Bettoni J, Lavagen N (CHU Amiens, France); Schmitt F, Lemée JM, Boucher S, Breheret R, Kün-Darbois JD, Kahn A, Gueutier A, Bigot P (CHU Angers, France); Borraccino B (Centre Hospitalier Auxerre, Auxerre, France); Lakkis Z, Doussot A, Heyd B, Manfredelli S, Mathieu P, Paquette B, Turco C, Barrabe A, Louvrier A (CHU Besançon, France); Moszkowicz D, Giovinazzo D, Bretagnol F (Hôpital Louis-Mourier - Ap-Hp, France); Police A, Charre L, Volpin E, Braham H, El Arbi N, Villefranque V, Bendjemar L (Hôpital Simone Veil, France); Girard E, Abba J, Trilling B (CHU Grenoble-Alpes, Hôpital Michallon, France); Chebaro A, Lecolle K, Truant S, El Amrani M, Zerbib P, Pruvot FR, Mathieu D, Surmei E, Mattei L, Marin H (CHU Lille, France); Christou N, Ballouhey Q, Ferrero P, Coste Mazeau P, Tricard J, Barrat B, Taibi A, Usseglio J, Laloze J, Salle H, Fourcade L (Chu Limoges, France); Duchalais E, Regenet N, Rigaud J, Waast D, Denis W, Malard O, Buffenoir K, Espitalier F, Ferron C, Varenne Y, Crenn V, De Vergie S, Cristini J, Samarut E (Nantes University Hospital, France); Tzedakis S, Bouche PA, Gaujoux S (Hôpital Cochin - Aphp, France); Kantor E (AP-HP Hopital Bichat Claude Bernard, Paris, France); 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Seeliger B, Mutter D, Philouze G, Pessaux P (IHU-Strasbourg / Strasbourg University Hospitals, France); Germain A, Chanty H, Ayav A (CHRU Nancy, France); Kassir R, Von theobald P, Sauvat F (CHU Reunion, France); O'Connor J, Mayombo Idiata M, O'Connor Z, Tchoba S (Bongolo Hospital, Gabon); Modabber A, Winnand P, Hölzle F (University Hospital Aachen, Germany); Sommer B, Shiban E, Wolf S, Anthuber M, Sommer F (University Hospital Augsburg, Germany); Kaemmerer D, Schreiber T (Zentralklinik Bad Berka, Germany); Kamphues C, Lauscher JC, Schineis C, Loch FN, Beyer K (Charité University Medicine, Campus Benjamin Franklin, Germany); Nasser S, Sehoul J (Charité Comprehensive Cancer Center, Germany); Höhn P, Braumann C, Reinkemeier F, Uhl W (St Josef-Hospital, Bochum, Germany); Weitz J, Bork U, Welsch T, Praetorius C, Korn S, Distler M (University Hospital Carl Gustav Carus, Technical University Dresden, Germany); Fluegen G, Knoefel WT, Vay C (University Hospital Duesseldorf, Germany); Golcher H, Grützmann R, Binder J (Universitätsklinikum Erlangen, Germany); Meister P, Gallinat A, Paul A (University Hospital Essen, Essen, Germany); Schnitzbauer AA, Thoenissen P, El Youzouri H, Schreckenbach T, Nguyen TA (Frankfurt University Hospital, Goethe University, Frankfurt, Germany); Eberbach H, Bayer J, Erdle B, Sandkamp R (Medical Center – Albert-Ludwigs-University of Freiburg, Faculty of Medicine, Germany); Nitschke C, Izbicki J, Uzunoglu FG, Koenig D, Gosau M, Böttcher A, Heuer A, Klatter TO, Priemel M, Betz CS, Burg S, Möckelmann N, Busch CJ, Bewarder J, Zeller N, Smeets R, Thole S, Vollkommer T, Speth U, Stangenberg M (University Medical Center Hamburg-Eppendorf, Germany); Hakami I, Boeker C, Mall J (KRH Nordstadt-Siloah Hospitals, Hannover, Germany); Schardey HM, von Ahnen T, von Ahnen M, Brunner U (Agatharied Hospital, Hausham, Germany); Tapking C, Kneser U, Hirche C, Jung M, Kowalewski KF (BG Trauma Center Ludwigshafen, Germany); Kienle P (Theresienkrankenhaus, Mannheim, Germany); Reissfelder C, Seyfried S, Herrle F, Hardt J, Galata C, Birgin E, Rahbari N, Vassos N (Mannheim University Medical Center (Universitätsmedizin Mannheim), Germany); Stoleriu MG, Hatz R (Asklepios Pulmonary Hospital, Munich Gauting, Germany); Albertsmeier M, Börner N, Lampert C, Werner J (Department of General, Visceral and Transplantation Surgery, Ludwig-Maximilians-Universität Munich, Munich, Germany); Kuehlmann B, Prantl L (University Hospital Regensburg, Regensburg, Germany); Brunner SM, Schlitt HJ, Brennfleck F, Pfister K, Oikonomou K (University Medical Center Regensburg, Department of Surgery, Germany); Reinhard T, Nowak K (RoMed Klinikum Rosenheim, Germany); Ronellenfitsch U, Kleeff J, Delank KS, Michalski CW, Szabo G (University Hospital Halle (Saale), Germany); Widyaningsih R, Stavrou GA (Klinikum Saarbrücken, Germany); Bschorer R, Mielke J, Peschel T (Helios Kliniken Schwerin, Germany); Königgrainer A, Quante M, Löffler MW, Yurttas C (University Hospital Tübingen, Department of General, Visceral and Transplant Surgery, Germany); Doerner J, Seiberth R (Helios Universitätsklinikum Wuppertal (Universität Witten/Herdecke), Germany); Bouchagier K, Klimopoulos S, Paspaliari D, Stylianidis G (Evangelismos General Hospital, Greece); Syllaios A, Baili E, Schizas D, Liakakos T, Charalabopoulos A, Zografos C, Spartalis E (Laiko University Hospital, Greece); Manatakis DK, Tasis N, Antonopoulou MI (Athens Naval and Veterans Hospital, Greece); Xenaki S, Xynos E, Chrysos E, Athanasakis E, Tsiaousis J (University Hospital of Heraklion Crete and Interclinic Hospital of Crete, Greece); Litoridis E, Tourountzi P (Kavala General Hospital, Greece); Tzovaras G, Tepetes K, Zacharoulis D, Baloyiannis I, Perivoliotis K, Hajioannou J, Korais C, Gkrinia E, Skoulakis CE, Saratziotis A, Koukoura O, Symeonidis D, Diamantis A (General University Hospital of Larissa, Greece); Tsoulfas G, Christou CD, Tooulias A, Papadopoulos V, Anthoulakis C, Grimbizis G, Zouzoulas D, Tsolakidis D (Papageorgiou General Hospital, Greece); Tatsis D, Christidis P, Loutzidou L, Ioannidis O, Astreidis I, Antoniou A, Antoniadis K, Vachtsevanos K, Paraskevopoulos K, Kalaitzidou I, Alexoudi V, Stavroglou A, Mantevras A, Michailidou D, Grivas T, Deligiannidis D, Politis S, (George Papanikolaou General Hospital of Thessaloniki, Greece); 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Echeverría-Dávila G (Hospital General San Juan De Dios, Guatemala City, Guatemala); Marín C, Icaza de Marín GC (Hospital Regional De Zacapa, Guatemala); Kok SY, Joeng HKM, Chan LL, Lim D (United Christian Hospital, Hong Kong); Novak Z, Echim T (National Institute of Oncology, Hungary); Suszták N, Banky B (Szent Borbála Kórház, Hungary); Kembuan G, Pajan H, Islam AA (Rsud Wahidin Sudirohusodo, Indonesia); Rahim F (Baghaei Hospital, Iran); Safari H (Golestan Hospital & Ahvaz Jundishapur University of Medical Sciences, Iran); Mozafari M, Brouki Milan P, Tizmaghz A, Rezaei Tavirani M (Firoozabadi Hospital, Iran); Ahmed A (Baghdad Medical City, Iraq); Hussein R (Zafaraniyah General Hospital, Iraq); Fleming C, O'Brien S, Kayyal MY, Daly A, Killeen S, Corrigan M (Cork University Hospital, Ireland); De Marchi J, Hill A, Farrell T, Davis NF, Kearney D, Nelson T (Beaumont Hospital, Ireland); Maguire PJ, Barry C, Farrell R, Smith LA, Mohan HM, Mehigan BJ, McCormick P, Larkin JO, Fahey BA, Rogers A, Donlon N, O'Sullivan H, Nugent T, Reynolds JV, Donohue C, Shokuhi P, Ravi N, Fitzgerald C, Lennon P, Timon C, Kinsella J, Smith J, Boyle T, Alazawi D, Connolly E, Butt W, Croghan SM, Manecksha RP (St. James's Hospital, Ireland); 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Tufo A, Marra E, Maida P, Marte G, Tammaro P (Ospedale

Del Mare, Italy); Bianco F, Incollingo P (Ospedale S. Leonardo - Asl Napoli 3 Sud, Castellammare Di Stabia, Italy); Izzo F, Belli A, Patrone R, Albino V, Leongito M, Granata V, Piccirillo M, Palaia R (Istituto Nazionale Tumori Fondazione, G. 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Sassari, Italy); Tuminello F, Galleano R, Franceschi A, Langone A (San Paolo, Italy); Fleres F, Spolini A, Bordoni P, Franzini M, Clarizia G, Grechi A, Longhini A (Ospedale Di Sondrio (Asst Valtellina E Alto Lario), Italy); Guaitoli E, Manca G (Perrino Hospital Brindisi, Italy); Grossi U, Novello S, Zanus G, Romano M, Rossi S (Ca' Foncello Treviso - DISCOG, Università di Padova, Italy); Ferrara F (San Carlo Borromeo Hospital, ASST Santi Paolo e Carlo, Italy); La Torre M (Fabia Mater Hospital, Rome, Italy); Pirozzolo G, Recordare A (Dell'Angelo Hospital, ULSS3 Serenissima, Venezia, Italy); Paiella S, Turri G, Rattizzato S, Campagnaro T, Guglielmi A, Pedrazzani C, Ruzzenente A, Poletto E, Conci S, Casetti L, Fontana M, Salvia R, Malleo G, Esposito A, Landoni L, De Pastena M, Bassi C, Tuveri M, Nobile S, Marchegiani G, Bortolasi L (Azienda Ospedaliera Universitaria Integrata Di Verona, Italy); Sambugaro E, Malavolta M, Moretto G, Impellizzeri H, Inama M (Ospedale Pederzoli, Italy); Barugola G, Ascari F, Ruffo G (IRCCS Ospedale Sacro Cuore Don Calabria, Negrar di Valpolicella (Verona), Italy); Granieri S, Cotsoglou C (Asst Vimercate, Italy); Berselli M, Desio M, Marchionini V, Coccozza E (ASST Settelaghi, Varese, Italy); Di Saverio S, Ietto G, Iovino D, Carcano G (University of Insubria, Ospedale di Circolo e Fondazione Macchi (Varese), Varese Lombardy, Italy); Ayasra F, Qasem A, Ayasra Y (Al-Basheer Hospital, Jordan); Al-Masri M, Abou Chaar MK, Al-Najjar H, Ghandour K, Alawneh F, Abdel Jalil R, Abdel Al S, Elayyan M, Ghanem R, Lataifeh I, Alsarairoh O (King Hussein Cancer Center, Jordan); Abu Za'nouneh FJ, Fahmawee T, Ibrahim A, Obeidat K (King Abdullah University Hospital, Jordan); Lee KJ (Keimyung University School of Medicine, Daegu, Korea); Shin SJ, Chung H (Keimyung University, Daegu, Korea); Albader I, Alabbad J, Albader MAS (Mubarak Al-Kabeer Hospital, Jabriya, Kuwait); Bouhuwaish A, Taher AS, Omar MSM (Tobruk Medical Center, Libya); Abdulwahed E, Biala M, Morgom M (Tripoli Central Hospital, Libya); Elhadi A, Alarabi A, Msherghi A, Elhajdawe F, Alsoufi A (Tripoli University Hospital, Libya); Salamah A, Salama H, Bulugma M, Almabrouk H (Zawia Teaching Hospital, Libya); Venskutonis D, Dainius E, Kubiliute E, Bradulskis S, Parseliunas A, Kutkevicius J, Subocius A (Lithuanian University of Health Sciences Kaunas Clinical Hospital, Lithuania); Cheong YJ, Masood MS (Hospital Raja Permaisuri Bainun, Ipoh, Malaysia); Ngo CW, Saravanan R, Abdul Maei N (Hospital Enche' Besar Hajjah Khalsom, Malaysia); Hayati F, Amin Sahid N (Queen Elizabeth Hospital & Universiti Malaysia Sabah, Kota Kinabalu, Sabah, Malaysia); Yanowsky Reyes G, Orozco Perez J, Damian R, Santana Ortiz R, Colunga Tinajero CA (Antiguo Hospital Civil De Guadalajara, Mexico); Cordera F, Gómez-Pedraza A, Maffuz-Aziz A, Posada JA, De la Rosa Abaroa MA, Alvarez MR, Arrangoiz R, Hernández R (ABC Medical Center, Mexico); Bozada Gutierrez K, Trejo-Avila M, Valenzuela-Salazar C, Herrera-Esquivel J, Moreno-Portillo M (Hospital General Dr. Manuel Gea González, Mexico); Pinto-Angulo VM, Sosa-Duran EE, Ziad-Aboharp H, Jimenez Villanueva X (Hospital Juárez de México, Ciudad de México, Mexico); Soulé Martínez CE, Lupián-Angulo AI (Hospital Central Norte Pemex, Mexico); Martínez Zarate J Jacobo, Reyes Rodriguez E, Montalvo Dominguez G (Hospital Médica Sur, Ciudad de México, Mexico); Becerra García FC (Hospital San Ángel Inn Chapultepec, Mexico); Melchor-Ruan J, Vilar-Compte D, Romero-Bañuelos E, Herrera-Gomez A, Meneses-Garcia A, Isla-Ortiz D, Salcedo-Hernández RA, Hernández-Nava JM, Morales-Castelan JE (Instituto Nacional De Cancerologia, Mexico); Sarre C, Posadas-Trujillo OE, Buerba GA, Alfaro-Goldaracena A, Pena Gomez-Portugal E, Lopez-Pena G; Hinojosa CA, Mercado MA (Universidad Nacional Autonoma de Mexico, Instituto Nacional de Ciencias Medicas y Nutricion Salvador Zubiran, Mexico City, Mexico); Ramos-De la Medina A, Martinez L, Duran I, Gonzalez DS, Martinez MJ, Nayen Sainz de la Fuente A (Hospital Español Veracruz, Mexico); Miguelena L, Hernández Miguelena L (Hospital Regional Veracruz, Mexico); Louraoui SM, El Azhari A, Rghioui M (Cheikh Khalifa International University Hospital, Morocco); Khya E (Moulay Youssef, Morocco); Ghannam A, Souadka A, El Ahmedi B, Belkhadir ZH, Majbar MA, Benkabbou A, Mohsine R (Institut National D'oncologie, Morocco); Oudrhiri MY, Bechri H, Arkha Y, El Ouahabi A (Centre Hospitalier Universitaire Ibn Sina Rabat, Morocco); Frima H, Bachiri S, Groen LC (Noordwest Ziekenhuisgroep, Alkmaar, Netherlands); Verhagen T, ter Brugge FM (Ziekenhuisgroep Twente, Almelo, Netherlands); Scheijmans

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Reyes Memorial Medical Center, Manila, Philippines); Sadian H, Gumarao A, Barraquio A, Cruz EM, Gonzales AD (Pasig City General Hospital, Philippines); Reyes JAS, Salud JA, Tancinco EG,

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Funding

National Institute for Health Research (NIHR) Global Health Research Unit grant (NIHR 16.136.79) using UK aid from the UK government to support global health research, Association of Coloproctology of Great Britain and Ireland, Bowel & Cancer Research, Bowel Disease Research Foundation, Association of Upper Gastrointestinal Surgeons, British Association of Surgical Oncology, British Gynaecological Cancer Society, European Society of Coloproctology, NIHR Academy, Sarcoma UK, The Urology Foundation, Vascular Society for Great Britain and

Ireland, and Yorkshire Cancer Research. The views expressed are those of the authors and not necessarily those of the National Health Service, NIHR, or UK Department of Health and Social Care.

Disclosure. The authors declare no conflict of interest.

Supplementary material

Supplementary material is available at *BJS Open* online.

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