Supplementary Appendix

Squeeze Study

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List of collaborators

Local investigators and national coordinators (National coordinators in red). Listed in alphabetical order by country and then by center.

First name and middle initial(s)	Last Name	Institution	City	Country
Meriem	Abodun	CHU Saadna Mohamed Abdenour	Sétif	Algeria
Souad	Bouaoud	CHU Saadna Mohamed Abdenour	Sétif	Algeria
Kamel	Bouchenak	CHU Saadna Mohamed Abdenour	Sétif	Algeria
Hind	Saada	CHU Saadna Mohamed Abdenour	Sétif	Algeria
Amine	Naili	EPH Sidi Ghiles	Sidi Ghiles	Algeria
Shruti	Chitnis	Fiona Stanley Hospital	Murdoch	Australia
Marlena	Bartmanska	Fiona Stanley Hospital	Murdoch	Australia
Lip-Yong	Choo	Fiona Stanley Hospital	Murdoch	Australia
Jolene	Lim	Fiona Stanley Hospital	Murdoch	Australia
Estelle	Meirau	Fiona Stanley Hospital	Murdoch	Australia
Rhys	Powell	Fiona Stanley Hospital	Murdoch	Australia
Erica	Remedios	Fiona Stanley Hospital	Murdoch	Australia
Jam	Sadullah	Fiona Stanley Hospital	Murdoch	Australia
Alex	Shivarev	Fiona Stanley Hospital	Murdoch	Australia
Archana	Shrivathsa	Fiona Stanley Hospital	Murdoch	Australia
Marissa	Woodburn	Logan Hospital – Metro South Health Queensland Australia	Meadowbrook	Australia
Andrew	Hughes	Logan Hospital – Metro South Health Queensland Australia	Meadowbrook	Australia
Benjamin	King-Koi	Logan Hospital – Metro South Health Queensland Australia	Meadowbrook	Australia
Anil	Mall	Logan Hospital – Metro South Health Queensland Australia	Meadowbrook	Australia
Tharindu	Vithanage	Logan Hospital – Metro South Health Queensland Australia	Meadowbrook	Australia
Baraniselvan	Ramalingam	Nepean Hospital, NSW, Australia	Kingswood,NSW	Australia
Malcolm Ronald James	Bannerman	Nepean Hospital, NSW, Australia	Kingswood,NSW	Australia
Clare Margaret	Shiner	Nepean Hospital, NSW, Australia	Kingswood,NSW	Australia
Trylon Matthew	Tsang	Nepean Hospital, NSW, Australia	Kingswood,NSW	Australia
David	Highton	Princess Alexandra Hospital, Brisbane Australia	Woolloongabba	Australia
Steven	Ayotte	Princess Alexandra Hospital, Brisbane Australia	Woolloongabba	Australia
Allison	Kearney	Princess Alexandra Hospital, Brisbane Australia	Woolloongabba	Australia
Edward	Thornely	Princess Alexandra Hospital, Brisbane Australia	Woolloongabba	Australia
Susanna	Van Haeringen	Princess Alexandra Hospital, Brisbane Australia	Woolloongabba	Australia
Amos	Moody	Queen Elizabeth II Jubilee Hospital	Brisbane	Australia
Daniel	Kim	Queen Elizabeth II Jubilee Hospital	Brisbane	Australia

Claire	Rose	Queen Elizabeth II Jubilee Hospital	Brisbane	Australia
Mahmoud	Ugool	Queen Elizabeth II Jubilee Hospital	Brisbane	Australia
Will	Zore	Queen Elizabeth II Jubilee Hospital	Brisbane	Australia
Andrew	Toner	Royal Perth Hospital, Australia	Perth	Australia
Patricia	Anagnostides	Royal Perth Hospital, Australia	Perth	Australia
Jodie	Jamieson	Royal Perth Hospital, Australia	Perth	Australia
Hilary	Leeson	Royal Perth Hospital, Australia	Perth	Australia
Susan	March	Royal Perth Hospital, Australia	Perth	Australia
Ronithung	Ovung	Royal Perth Hospital, Australia	Perth	Australia
Alessandra	Parini	Royal Perth Hospital, Australia	Perth	Australia
Toby	Shipway	Royal Perth Hospital, Australia	Perth	Australia
Wai Phen Arthur	Teo	Royal Perth Hospital, Australia	Perth	Australia
Huw	Wilkins	Royal Perth Hospital, Australia	Perth	Australia
Kahina	Wotton-Hamrioui	Royal Perth Hospital, Australia	Perth	Australia
Jodie	Jamieson	Sir Charles Gairdner Hospital	Perth	Australia
Sarah	Liew	Sir Charles Gairdner Hospital	Perth	Australia
Ashleigh	Cargill	Sir Charles Gairdner Hospital	Perth	Australia
Dale	Currigan	Sir Charles Gairdner Hospital	Perth	Australia
Edward	Gomm	Sir Charles Gairdner Hospital	Perth	Australia
Calvin	Lo	Sir Charles Gairdner Hospital	Perth	Australia
Peri	Mickle	Sir Charles Gairdner Hospital	Perth	Australia
Marli	Smit	Sir Charles Gairdner Hospital	Perth	Australia
Simon	Bradbeer	St Vincent's Hospital Melbourne	Melbourne	Australia
Paul	Köglberger	Klinikum Wels-Grieskirchen Gmbh	Wels	Austria
Thomas	Geitmann	Klinikum Wels-Grieskirchen Gmbh	Wels	Austria
Laurenz	Hell	Klinikum Wels-Grieskirchen Gmbh	Wels	Austria
Johann	Knotzer	Klinikum Wels-Grieskirchen Gmbh	Wels	Austria
Dimitar	Tonev	University Hospital "Tsaritsa Yoanna - ISUL"	Sofia	Bulgaria
Tanislav	Ilchev	University Hospital "Tsaritsa Yoanna - ISUL"	Sofia	Bulgaria
Dimitrinka	Todorova	University Hospital "Tsaritsa Yoanna - ISUL"	Sofia	Bulgaria
Karim	Ladha	Saint Michael's Hospital	Toronto	Canada
Ciara	Hanley	Saint Michael's Hospital	Toronto	Canada
Gabriella	Mattina	Saint Michael's Hospital	Toronto	Canada
Janneth	Pazmino-Canizares	Saint Michael's Hospital	Toronto	Canada
Bijan	Teja	Saint Michael's Hospital	Toronto	Canada
Matteo	Parotto	Toronto General Hospital	Toronto	Canada
Samareh	Ajami	Toronto General Hospital	Toronto	Canada
Humara	Poonawala	Toronto General Hospital	Toronto	Canada
Carlos Jose	Perez Rivera	Fundacion Cardioinfantil	Bogota	Colombia
Laura	Ramirez	Fundacion Cardioinfantil	Bogota	Colombia
Juan P.	Garcia-Mendez	Fundacion Cardioinfantil	Bogota	Colombia
Sharon	Idarraga	Fundacion Cardioinfantil	Bogota	Colombia
Ileana	Lulic	Clinical Hospital Merkur	Zagreg	Croatia
Gorana	Fingler	Clinical Hospital Merkur	Zagreg	Croatia
Jadranka	Pavicic Saric	Clinical Hospital Merkur	Zagreg	Croatia
Jakov	Jozić	University Hospital Sveti Duh	Zagreg	Croatia
Višnja	Nesek Adam	University Hospital Sveti Duh	Zagreg	Croatia
Tatjana	Goranović	University Hospital Sveti Duh	Zagreg	Croatia

Marija	Josipović	University Hospital Sveti Duh	Zagreg	Croatia
Ida	Kožul	University Hospital Sveti Duh	Zagreg	Croatia
Tina	Tomić Mahečić	University Hospital Centre Zagreb	Zagreg	Croatia
Leonora	Bračun	University Hospital Centre Zagreb	Zagreg	Croatia
Josip	Kovačević	University Hospital Centre Zagreb	Zagreg	Croatia
Katarina	Lojna	University Hospital Centre Zagreb	Zagreg	Croatia
Anton	Šarčević	University Hospital Centre Zagreb	Zagreg	Croatia
Marko	Tripković	University Hospital Centre Zagreb	Zagreg	Croatia
Karlo	Uroda	University Hospital Centre Zagreb	Zagreg	Croatia
Olav Lilleholt	Schjørring	Aalborg University Hospital	Aalborg	Denmark
Steen Kåre	Fagerberg	Aalborg University Hospital	Aalborg	Denmark
Birgitte	Brandsborg	Aarhus University Hospital	Aarhus N	Denmark
Zidryne	Karaliunaite	Aarhus University Hospital	Aarhus N	Denmark
Jens Aage	Kølsen-Petersen	Aarhus University Hospital	Aarhus N	Denmark
Christian	Melchior Olesen	Aarhus University Hospital	Aarhus N	Denmark
Mikkel Andreas	Strømgaard Andersen	Aarhus University Hospital	Aarhus N	Denmark
Henrik	Wolsted	Bispebjerg Og Frederiksberg Hospital	Copenhagen	Denmark
Aleksander	Fjeld Haugstvedt	Bispebjerg Og Frederiksberg Hospital	Copenhagen	Denmark
Stefan	Gärtner	Bispebjerg Og Frederiksberg Hospital	Copenhagen	Denmark
Christine	Hangaard Hansen	Bispebjerg Og Frederiksberg Hospital	Copenhagen	Denmark
Mirjana	Cihoric	Copenhagen University Hospital Hvidovre	Copenhagen	Denmark
Nicolai Bang	Foss	Copenhagen University Hospital Hvidovre	Copenhagen	Denmark
Amalie	Rosendahl	Copenhagen University Hospital Herlev	Copenhagen	Denmark
Laurits S.	Kromberg	Copenhagen University Hospital Herlev	Copenhagen	Denmark
Marina A.	Nielsen	Copenhagen University Hospital Herlev	Copenhagen	Denmark
Bjarne O.	Nielsen	Copenhagen University Hospital Herlev	Copenhagen	Denmark
Morten	Vester-Andersen	Copenhagen University Hospital Herlev	Copenhagen	Denmark
Rasmus Philip	Nielsen	Gødstrup Hospital	Herning	Denmark
Katrine Maul	Andersen	Gødstrup Hospital	Herning	Denmark
Mark	Billmann	Gødstrup Hospital	Herning	Denmark
Lars H	Lundstrøm	Nordsjællands Hospital	Hillerød	Denmark
Gine	Glargaard	Nordsjællands Hospital	Hillerød	Denmark
Christine N	Svendsen	Nordsjællands Hospital	Hillerød	Denmark
Michael	Bøndergaard	Regional Hospital Randers	Randers	Denmark
Jacob	Steinmetz	Rigshospitalet	Copenhagen	Denmark
Felicia	Dinesen	Rigshospitalet	Copenhagen	Denmark
Liva Thoft	Jensen	Rigshospitalet	Copenhagen	Denmark
Lars Simon	Rasmussen	Rigshospitalet	Copenhagen	Denmark
L. Andreas H.	Burén	The Regional Hospital In Horsens, Dept. Of Anaesthesia	Horsen	Denmark

Yomna E.	Dean	Alexandria Main University Hospital	Alexandria	Egypt
Elsakka	Abdelrahman	Alexandria Main University Hospital	Alexandria	Egypt
S. Rozan	Samah	Alexandria Main University Hospital	Alexandria	Egypt
Rozza	Hebatullah	Alexandria Main University Hospital	Alexandria	Egypt
Sabry	Ahmed	Alexandria Main University Hospital	Alexandria	Egypt
Shehata	Sameh	Alexandria Main University Hospital	Alexandria	Egypt
Shehata	Mostafa	Alexandria Main University Hospital	Alexandria	Egypt
Talat	Nesreen	Alexandria Main University Hospital	Alexandria	Egypt
Dina	Ramadan	Alexandria Main University Hospital	Alexandria	Egypt
Mohamed	Shemies	Alexandria Main University Hospital	Alexandria	Egypt
Yousef	Tanas	Alexandria Main University Hospital	Alexandria	Egypt
Ahmed	Abbas	Assiut University Hospital	Assiut	Egypt
Mostafa	Abbas	Assiut University Hospital	Assiut	Egypt
Gena	Elassall	Assiut University Hospital	Assiut	Egypt
Saied	Elsawy	Assiut University Hospital	Assiut	Egypt
Ramy	Hassan	Assiut University Hospital	Assiut	Egypt
Magdy	Mahdy	Assiut University Hospital	Assiut	Egypt
Fatma	Monib	Assiut University Hospital	Assiut	Egypt
Abdelrahman	Ramdan	Assiut University Hospital	Assiut	Egypt
Mahmoud	Saad	Assiut University Hospital	Assiut	Egypt
Khaled	Abdelwahab	Mansoura Oncology Center - Mansoura Universty	Mansoura	Egypt
Ahmed	Eid	Mansoura Oncology Center - Mansoura Universty	Mansoura	Egypt
Omar	Hamdy	Mansoura Oncology Center - Mansoura Universty	Mansoura	Egypt
Eman	Mansour	Mansoura Oncology Center - Mansoura Universty	Mansoura	Egypt
Moataz Maher	Emara	Mansoura University Gastrointestinal Surgery Center – Mansoura University Faculty Of Medicine	Mansoura	Egypt
Mohamed	Bonna	Mansoura University Gastrointestinal Surgery Center – Mansoura University Faculty Of Medicine	Mansoura	Egypt
Maiseloon	Mogahed	Mansoura University Gastrointestinal Surgery Center – Mansoura University Faculty Of Medicine	Mansoura	Egypt
Hamza	Asmaa	Menoufia University Hospital	Shebin Elkom	Egypt
Salma	Elnoamany	Menoufia University Hospital	Shebin Elkom	Egypt
Zeinab	Ismail	Menoufia University Hospital	Shebin Elkom	Egypt
Mohamed	Sameh	Menoufia University Hospital	Shebin Elkom	Egypt
Eman Ibrahim	El-Desoki Mahmoud	National Hepatology & Tropical Medicine Research Institute	Cairo	Egypt
Ahmed	Hegazi	National Hepatology & Tropical Medicine Research Institute	Cairo	Egypt

Ahmed	Samy	National Hepatology & Tropical Medicine Research Institute	Cairo	Egypt
Aiman	Al-Touny	Anesthesia And Intensive Care Department, Faculty Of Medicine, Suez Canal University	Ismaïlia	Egypt
Shimaa	Al-Touny	Anesthesia And Intensive Care Department, Faculty Of Medicine, Suez Canal University	Ismaïlia	Egypt
Eman	Teema	Anesthesia And Intensive Care Department, Faculty Of Medicine, Suez Canal University	Ismaïlia	Egypt
Edmundo	Pereira De Souza Neto	Centre Hospitalier De Montauban	Montauban	France
Kevin	Arandel	Centre Hospitalier De Montauban	Montauban	France
Remi	Bouquerel	Centre Hospitalier De Montauban	Montauban	France
Benjamin	Le Gaillard	Centre Hospitalier De Montauban	Montauban	France
Christophe	Pelletier	Centre Hospitalier De Montauban	Montauban	France
Antoine	Strzelecki	Centre Hospitalier De Montauban	Montauban	France
Emmanuel	Boselli	Centre Hospitalier Pierre Oudot	Bourgoin-Jallieu	France
Nicolas	Chardon	Centre Hospitalier Pierre Oudot	Bourgoin-Jallieu	France
Pierre	Rodriguez	Centre Hospitalier Pierre Oudot	Bourgoin-Jallieu	France
Guillaume	Besch	Centre Hospitalier Universitaire De Besancon	Besancon	France
Julien	Villeneuve	Centre Hospitalier Universitaire De Besancon	Besancon	France
Grégoire	Wallon	Centre Léon Bérard	Lyon	France
Mathilde	Lefevre	Centre Léon Bérard	Lyon	France
Pierre-Grégoire	Guinot	CHU Dijon	Dijon	France
Belaid	Bouhemad	CHU Dijon	Dijon	France
Maxime	Nguyen	CHU Dijon	Dijon	France
Guillaume	Raveau	CHU Dijon	Dijon	France
Gilles	Lebuffe	CHU Lille	Lille	France
Hélène	Beloeil	CHU Rennes	Rennes	France
Ludovic	Meuret	CHU Rennes	Rennes	France
Bounes	Fanny	CHU Toulouse Rangueil	Toulouse	France
Nicolas	Ducrocq	Clinique Du Millénaire - Montpellier - France	Montpellier	France
Philippe	Guerci	Institut Lorrain Du Cœur Et Des Vaisseaux - University Hospital Of Nancy	Nancy	France
Fanny	Crouton	Institut Lorrain Du Cœur Et Des Vaisseaux - University Hospital Of Nancy	Nancy	France
Stephanie	Chevalier	La Sagesse, Rennes	Rennes	France
Marc	Anger	La Sagesse, Rennes	Rennes	France
Marc	Danguy Des Deserts	Military Hospital Clermont-Tonnerre	Brest	France
Philippe	Aries	Military Hospital Clermont-Tonnerre	Brest	France
Nicolas	Herzog	Military Hospital Clermont-Tonnerre	Brest	France
Johan	Schmitt	Military Hospital Clermont-Tonnerre	Brest	France

Xavier	Tete	Military Hospital Clermont-Tonnerre	Brest	France
Sascha	Treskatsch	Charité - Universitätsmedizin Berlin	Berlin	Germany
Golschan	Asgarpur	Charité - Universitätsmedizin Berlin	Berlin	Germany
Tobias	Schäzl	Charité - Universitätsmedizin Berlin	Berlin	Germany
Theodor	Kempe	Charité - Universitätsmedizin Berlin	Berlin	Germany
Philipp	Brandhorst	Charité - Universitätsmedizin Berlin	Berlin	Germany
Henriette	Hegermann	Charité - Universitätsmedizin Berlin	Berlin	Germany
Oliver	Hölsken	Charité - Universitätsmedizin Berlin	Berlin	Germany
Bernadette	Kleikamp	Charité - Universitätsmedizin Berlin	Berlin	Germany
Sophie	Reimers	Charité - Universitätsmedizin Berlin	Berlin	Germany
Lars	Bergmann	Universitätsklinikum Knappschaftskrankenhaus Bochum	Bochum	Germany
Andreas	Mania	Universitätsklinikum Knappschaftskrankenhaus Bochum	Bochum	Germany
Christoph	Sponholz	Jena University Hospital	Jena	Germany
Amir	Ali Akbari	Justus-Liebig-University Giessen	Gießen	Germany
Moritz	Herzberg	Justus-Liebig-University Giessen	Gießen	Germany
Ann-Catrin	Paul	Justus-Liebig-University Giessen	Gießen	Germany
Götz	Schmidt	Justus-Liebig-University Giessen	Gießen	Germany
Emmanuel	Schneck	Justus-Liebig-University Giessen	Gießen	Germany
Christian	Koch	Justus-Liebig-University Giessen	Gießen	Germany
Marit	Habicher	Justus-Liebig-University Giessen	Gießen	Germany
Michael	Sander	Justus-Liebig-University Giessen	Gießen	Germany
Heinrich	Klingler	Klinikum Oldenburg AÖR	Oldenburg	Germany
Mareike	Diekmann	Klinikum Oldenburg AÖR	Oldenburg	Germany
Sebastian	Schmid	Universitätsklinikum Ulm	Ulm	Germany
Raimund	Huf	Universitätsklinikum Ulm	Ulm	Germany
Benedikt	Schick	Universitätsklinikum Ulm	Ulm	Germany
Julia	Wallqvist	University Hospital RWTH Aachen	Aachen	Germany
Kowark	Ana	University Hospital RWTH Aachen	Aachen	Germany
Linda	Grüßer	University Hospital RWTH Aachen	Aachen	Germany
Rolf	Rossaint	University Hospital RWTH Aachen	Aachen	Germany
Hanna	Schröder	University Hospital RWTH Aachen	Aachen	Germany
Sebastian	Ziemann	University Hospital RWTH Aachen	Aachen	Germany
Daniel	Reuter	University Medicine Rostock	Rostock	Germany
Annika	Haas	University Medicine Rostock	Rostock	Germany
Bernd	Saugel	University Medical Center Hamburg-Eppendorf	Hamburg	Germany
Tom	Daubenfeld	University Medical Center Hamburg-Eppendorf	Hamburg	Germany

Moritz	Flick	University Medical Center Hamburg-Eppendorf	Hamburg	Germany
Alina	Kröker	University Medical Center Hamburg-Eppendorf	Hamburg	Germany
Lorenz	Rosenau	University Medical Center Hamburg-Eppendorf	Hamburg	Germany
Christina	Vokuhl	University Medical Center Hamburg-Eppendorf	Hamburg	Germany
Mirja	Wegge	University Medical Center Hamburg-Eppendorf	Hamburg	Germany
Luisa	Weskamm	University Medical Center Hamburg-Eppendorf	Hamburg	Germany
Kassiani	Theodoraki	Arataieion University Hospital, Athens, Greece	Athens	Greece
Sofia	Apostolidou	Arataieion University Hospital, Athens, Greece	Athens	Greece
George	Gkiokas	Arataieion University Hospital, Athens, Greece	Athens	Greece
Konstantinos	Stamatis	Arataieion University Hospital, Athens, Greece	Athens	Greece
Chrysoula	Stachtari	General Hospital Of Thessaloniki Georgios Papanikolaou.	Thessaloniki	Greece
Meltem	Perente	General Hospital Of Thessaloniki Georgios Papanikolaou.	Thessaloniki	Greece
Georgios	Pistiolas	General Hospital Of Thessaloniki Georgios Papanikolaou.	Thessaloniki	Greece
Charalampos	Martinos	Naval And Veterans Hopistal Of Athens	Athens	Greece
Theodoros	Aslanidis	Agios Pavlos General Hospital Of Thessaloniki	Thessaloniki	Greece
Eirini	Sidiropoulou	Agios Pavlos General Hospital Of Thessaloniki	Thessaloniki	Greece
Anna	Efthymiou	Saint Savvas Hospital	Athens	Greece
Ghrysanthi	Sklavou	Saint Savvas Hospital	Athens	Greece
Nikolaos	Barbetakis	Theagenio Cancer Hospital	Thessaloniki	Greece
Apostolos	Gogakos	Theagenio Cancer Hospital	Thessaloniki	Greece
Achilleas	Lazopoulos	Theagenio Cancer Hospital	Thessaloniki	Greece
Eleni	Mavroudi	Theagenio Cancer Hospital	Thessaloniki	Greece
Dimitrios	Paliouras	Theagenio Cancer Hospital	Thessaloniki	Greece
Thomas	Rallis	Theagenio Cancer Hospital	Thessaloniki	Greece
Evangelia	Samara	Tzaneio General Hospital Piraeus	Piraeus	Greece
Ioanna	Iatrelli	Tzaneio General Hospital Piraeus	Piraeus	Greece
Eleni	Panagiotou	Tzaneio General Hospital Piraeus	Piraeus	Greece
Eumorfia	Kondili	University Hospital Of Heraklion Crete	Heraklion	Greece
Anthoula	Ntakoula	University Hospital Of Heraklion Crete	Heraklion	Greece
Eleftherios	Papadakis	University Hospital Of Heraklion Crete	Heraklion	Greece
Konstantinos	Sorokos	University Hospital Of Heraklion Crete	Heraklion	Greece
Martin I	Sigurdsson	Landspitali University Hospital	Reykjavik	Iceland
Helgi	Egilsson	Landspitali University Hospital	Reykjavik	Iceland

Piyush	Ranjan	All India Institute Of Medical Sciences, New Delhi, India	New Delhi	India
Puneet	Khanna	All India Institute Of Medical Sciences, New Delhi, India	New Delhi	India
Arun	Kumar	All India Institute Of Medical Sciences, New Delhi, India	New Delhi	India
Ashu Sara	Mathai	Believers Church Medical College Hospital	Thiruvalla	India
Gincy Ann	Lukachan	Believers Church Medical College Hospital	Thiruvalla	India
Radhika	Nair	Believers Church Medical College Hospital	Thiruvalla	India
Kalpana	Balakrishnan	Cancer Institute (Women's India Association)	Chennai	India
Punitha	Chockalingam	Cancer Institute (Women's India Association)	Chennai	India
Shah	Bhagyesh	Cims hospital	Ahmedabad	India
Edward Johnson	Joseph	Kanyakumari Govt Medical College, Tamil Nadu	Nagercoil	India
Veena	Gopal	Nanjappa Multispeciality Hospital	Shimoga,karnataka	India
Arjun	Bhagavath K R	Nanjappa Multispeciality Hospital	Shimoga,karnataka	India
Shivakumar	Channabasappa	Subbaiah Institute Of Medical Sciences	Shivamogga	India
Pooja	Shah	Subbaiah Institute Of Medical Sciences	Shivamogga	India
Najah	Hadi	Al-Sadr Medical City Teaching Hospital In Najaf	Najaf	Iraq
Ali Najeh	Al-Awwady	Al-Sadr Medical City Teaching Hospital In Najaf	Najaf	Iraq
Maytham Aqeel	Al-Juaifari	Al-Sadr Medical City Teaching Hospital In Najaf	Najaf	Iraq
Angelo	Giacomucci	Azienda Ospedaliera Di Perugia	Perugia	Italy
Francesco	Brunelli	Azienda Ospedaliera Di Perugia	Perugia	Italy
Elisa	Scarpone	Azienda Ospedaliera Di Perugia	Perugia	Italy
Elena Giovanna	Bignami	Azienda Ospedaliero-Universitaria Di Parma - University Of Parma	Parma	Italy
Valentina	Bellini	Azienda Ospedaliero-Universitaria Di Parma - University Of Parma	Parma	Italy
Andrea	Bonetti	Azienda Ospedaliero-Universitaria Di Parma - University Of Parma	Parma	Italy
Jessica	Colla	Azienda Ospedaliero-Universitaria Di Parma - University Of Parma	Parma	Italy
Savino	Spadaro	Azienda Ospedaliera Universitaria Di Ferrara	Ferrara	Italy
Giacomo	Baldisserotto	Azienda Ospedaliera Universitaria Di Ferrara	Ferrara	Italy
Paolo	Priani	Azienda Ospedaliera Universitaria Di Ferrara	Ferrara	Italy
Margherita	Sella	Azienda Ospedaliera Universitaria Di Ferrara	Ferrara	Italy
Andrea	Russo	Fondazione Policlinico A. Gemelli IRCSS	Rome	Italy

Laura	Cascarano	Fondazione Policlinico A. Gemelli IRCSS	Rome	Italy
Bruno	Romanò	Fondazione Policlinico A. Gemelli IRCSS	Rome	Italy
Giulia	Torregiani	IFO Regina Elena	Rome	Italy
Maurizio	Cecconi	IRCCS Humanitas Research Hospital	Milan	Italy
Massimiliano	Greco	IRCCS Humanitas Research Hospital	Milan	Italy
Nicolò	Martinetti	IRCCS Humanitas Research Hospital	Milan	Italy
Sergio	Palma	IRCCS Humanitas Research Hospital	Milan	Italy
Andrea	Pradella	IRCCS Humanitas Research Hospital	Milan	Italy
Rosella	Nicoletti	Ospedale Madonna Delle Grazie	Matera	Italy
Barbara	Bacer	Ospedale Maggiore Carlo Alberto Pizzardi	Bologna	Italy
Martina	Guarnera	Ospedale Maggiore Carlo Alberto Pizzardi	Bologna	Italy
Michela	Lotierzo	Ospedale Maggiore Carlo Alberto Pizzardi	Bologna	Italy
Sara	Miori	Ospedale Santa Chiara	Trento	Italy
Sergio	Lassola	Ospedale Santa Chiara	Trento	Italy
Andrea	Sanna	Ospedale Santa Chiara	Trento	Italy
Iacopo	Cappellini	Ospedale Santo Stefano	Prato	Italy
Filippo	Becherucci	Ospedale Santo Stefano	Prato	Italy
Lucia	Zamidei	Ospedale Santo Stefano	Prato	Italy
Guglielmo	Consales	Ospedale Santo Stefano	Prato	Italy
Lorenzo	Tutino	Ospedale Santo Stefano	Prato	Italy
Luigi	Vetrugno	Ospedale Universitario “Santa Maria Della Misericordia” Di Udine	Udine	Italy
Gloria	Marson	Ospedale Universitario “Santa Maria Della Misericordia” Di Udine	Udine	Italy
Gianluca	Zani	Santa Maria Delle Croci Hospital, Ravenna	Ravenna	Italy
Giulia	Felloni	Santa Maria Delle Croci Hospital, Ravenna	Ravenna	Italy
Maurizio	Fusari	Santa Maria Delle Croci Hospital, Ravenna	Ravenna	Italy
Claudio	Gecele	Santa Maria Delle Croci Hospital, Ravenna	Ravenna	Italy
Massimo	Terenzoni	Santa Maria Delle Croci Hospital, Ravenna	Ravenna	Italy
Andrea	Cortegiani	University Hospital Policlinico P. Giaccone	Palermo	Italy
Giulia	Catalisano	University Hospital Policlinico P. Giaccone	Palermo	Italy
Tatiana	Catania Cucchiara	University Hospital Policlinico P. Giaccone	Palermo	Italy
Dario Calogero	Fricano	University Hospital Policlinico P. Giaccone	Palermo	Italy
Giulia	Ingoglia	University Hospital Policlinico P. Giaccone	Palermo	Italy
Mariachiara	Ippolito	University Hospital Policlinico P. Giaccone	Palermo	Italy

Claudia	Marino	University Hospital Policlinico P. Giaccone	Palermo	Italy
Gabriele	Presti	University Hospital Policlinico P. Giaccone	Palermo	Italy
Lucia	Mirabella	University Of Foggia	Foggia	Italy
Antonio	De Candia	University Of Foggia	Foggia	Italy
Nicole	Pepe	University Of Foggia	Foggia	Italy
Kiyoyasu	Kurahashi	International University of Health and Welfare (IUHW), School of Medicine	Narita	Japan
Munehito	Uchiyama	International University Of Health And Welfare Narita Hospital	Narita	Japan
Hiroshi	Morimatsu	Okayama University Hospital	Okayama	Japan
Kosuke	Kuroda	Okayama University Hospital	Okayama	Japan
Kaori	Yamashita	Okayama University Hospital	Okayama	Japan
Tatsuya	Kida	Yokosuka Kyosai Hospital	Yokosuka	Japan
Tomohide	Takei	Yokosuka Kyosai Hospital	Yokosuka	Japan
Sohaib	Al-Omary	Princess Basma Teaching Hospital	Irbid	Jordan
Lara	Alnajjar Lara	Princess Basma Teaching Hospital	Irbid	Jordan
Majjd	Alnajjar Lara	Princess Basma Teaching Hospital	Irbid	Jordan
Amro	Abuleil	Royal medical services, Amman	Amman	Jordan
Antigona	Hasani	American Hospital Kosovo & Faculty Of Medicine, University Of Prishtina	Pristina	Kosovo
Marin	Almahroush	Abu-Salim Trauma Hospital	Tripoli	Libya
Marya	Bensalem	Abu-Salim Trauma Hospital	Tripoli	Libya
Mawadaa	Alttir	Abu-Salim Trauma Hospital	Tripoli	Libya
Muhammed	Elhadi	Faculty Medicine University of Tripoli	Tripoli	Libya
Akram	Alkseek	Gharyan Central Hospital	Gharyan	Libya
Hibah Bileid	Bakeer	Gharyan Central Hospital	Gharyan	Libya
Eman	Abdulwahed	Tripoli Central Hospital	Tripoli	Libya
Entisar	Alshareea	Tripoli Central Hospital	Tripoli	Libya
Reem	Ghmagh	Tripoli Central Hospital	Tripoli	Libya
Doaa	Gidiem	Tripoli Central Hospital	Tripoli	Libya
Enas	Soula	Tripoli Central Hospital	Tripoli	Libya
Mohd Zulfakar	Mazlan	Universiti Sains Malaysia	Kota Bharu	Malaysia
Sanihah	Che Omar	Universiti Sains Malaysia	Kota Bharu	Malaysia
Mohamad Hasyizan	Hassan	Universiti Sains Malaysia	Kota Bharu	Malaysia
Shamsul Kamalrujan	Hassan	Universiti Sains Malaysia	Kota Bharu	Malaysia
Huda	Zainal Abidin	Universiti Sains Malaysia	Kota Bharu	Malaysia
Ion	Chesov	Chisinau City Hospital No.1	Chisinau	Moldova
Mihai	Tiple	Chisinau City Hospital No.1	Chisinau	Moldova
Natalia	Zadiraca	Chisinau City Hospital No.1	Chisinau	Moldova
Diana	Boleac	Institute Of Emergency Medicine	Chisinau	Moldova
Doina	Oglinda	Institute Of Emergency Medicine	Chisinau	Moldova
Abdelghafour	El Koundi	Military Teaching Hospital Mohammed V	Rabat	Morocco
Hicham	Balkhi	Military Teaching Hospital Mohammed V	Rabat	Morocco
Mustapha	Bensghir	Military Teaching Hospital Mohammed V	Rabat	Morocco

Noureddine	Kartite	Military Teaching Hospital Mohammed V	Rabat	Morocco
Abdelilah	Ghannam	National Institute Of Oncology Of Rabat" - "Mohammed V University In Rabat - National Institute Of Oncology Of Rabat	Rabat	Morocco
Othman	Belarabi	National Institute Of Oncology Of Rabat" - "Mohammed V University In Rabat - National Institute Of Oncology Of Rabat	Rabat	Morocco
Zakaria	Belkhadir	National Institute Of Oncology Of Rabat" - "Mohammed V University In Rabat - National Institute Of Oncology Of Rabat	Rabat	Morocco
Brahim	El Ahmadi	National Institute Of Oncology Of Rabat" - "Mohammed V University In Rabat - National Institute Of Oncology Of Rabat	Rabat	Morocco
Elisavet	Karkala	Akershus Universitetssykehus	Nordbyhagen	Norway
Maria Christina	Ravn	Akershus Universitetssykehus	Nordbyhagen	Norway
Oda Uhlin	Husebekk	Alesund Sjukehus	Alesund	Norway
Renate	Johnsen	Alesund Sjukehus	Alesund	Norway
Ib	Jammer	Haukeland University Hospital, Bergen	Bergen	Norway
Vegard	Lundevall	Haukeland University Hospital, Bergen	Bergen	Norway
Wiszt	Radovan	Innlandet Hospital Trust	Elverum	Norway
Andreas	Haugerud	Innlandet Hospital Trust	Elverum	Norway
Ine Karoline	Stenersen	Innlandet Hospital Trust	Elverum	Norway
Agnete	Prydz	Østfold Hospital Kalnes	Grålum	Norway
David Frederic	Knutsen	Østfold Hospital Kalnes	Grålum	Norway
Heidi Marthea	Ohnstad	Østfold Hospital Kalnes	Grålum	Norway
Roy B.	Olsen	Sorlandet Hospital Arendal, Norway	Arendal	Norway
Elise Runde	Krogstad	Sorlandet Hospital Arendal, Norway	Arendal	Norway
Anna	Sigurdardottir	Sorlandet Hospital Arendal, Norway	Arendal	Norway
Krzych	Łukasz	Central Clinical Centre, Medical University Of Silesia	Katowice	Poland
Michal	Szewczyk	Central Clinical Centre, Medical University Of Silesia	Katowice	Poland
Cristina	Granja	Centro Hospitalar do Algarve, Faro	Faro	Portugal
Catarina	Dourado	Centro Hospitalar E Universitário De Coimbra (CHUC)	Coimbra	Portugal
Nidia	Gonçalves	Centro Hospitalar E Universitário De Coimbra (CHUC)	Coimbra	Portugal
Francisco	Matias	Centro Hospitalar E Universitário De Coimbra (CHUC)	Coimbra	Portugal
Ana	Raimundo	Centro Hospitalar E Universitário De Coimbra (CHUC)	Coimbra	Portugal
Rui Pedro	Cunha	Centro Hospitalar Lisboa Ocidental, Lisbon	Lisbon	Portugal

Miguel	Tavares	Centro Hospitalar Universitário Do Porto - Hospital Santo António	Porto	Portugal
Alexandre	Pinto	Centro Hospitalar Universitário Do Porto - Hospital Santo António	Porto	Portugal
Cristina	Torrão	Centro Hospitalar Universitário Do Porto - Hospital Santo António	Porto	Portugal
Lnês	Amaral	Centro Hospitalar Universitário Do Porto - Hospital Santo António	Porto	Portugal
Ana Rita	Costa	Centro Hospitalar Universitário Do Porto - Hospital Santo António	Porto	Portugal
Ricardo	Marinho	Centro Hospitalar Universitário Do Porto - Hospital Santo António	Porto	Portugal
Miguel	Ricardo	Centro Hospitalar Universitário Do Porto - Hospital Santo António	Porto	Portugal
César	Vidal	Centro Hospitalar Universitário Do Porto - Hospital Santo António	Porto	Portugal
Alice	Santos	Centro Hospitalar Universitario Sao Joao	Porto	Portugal
Julia	Mendonça	Centro Hospitalar Universitario Sao Joao	Porto	Portugal
Daniela	Xara	Centro Hospitalar Universitario Sao Joao	Porto	Portugal
Raul	Neto	Centro Hospitalar Vila Nova Gaia/ Espinho	Vila Nova de Gaia	Portugal
João Tiago	Rodrigues	Centro Hospitalar Vila Nova Gaia/ Espinho	Vila Nova de Gaia	Portugal
Ricardo	Amaral	Unidade Local De Saúde De Trás-Os-Montes E Alto Douro, Portugal.	Vila Real	Portugal
Diogo	Oliveira	Unidade Local De Saúde De Trás-Os-Montes E Alto Douro, Portugal.	Vila Real	Portugal
José	Sampaio	Unidade Local De Saúde De Trás-Os-Montes E Alto Douro, Portugal.	Vila Real	Portugal
Francisca	Cardoso	Hospital Santa Luzia, ULSAM – Viana Do Castelo	Viana do castelo	Portugal
José	Caldeiro	Hospital Santa Luzia, ULSAM – Viana Do Castelo	Viana do castelo	Portugal
Rogério	Corga	Hospital Santa Luzia, ULSAM – Viana Do Castelo	Viana do castelo	Portugal
Edite	Mendes	Hospital Santa Luzia, ULSAM – Viana Do Castelo	Viana do castelo	Portugal
Pedro	Moura	Hospital Santa Luzia, ULSAM – Viana Do Castelo	Viana do castelo	Portugal
Rita	Passos	Hospital Santa Luzia, ULSAM – Viana Do Castelo	Viana do castelo	Portugal
Francisco	Silva	Hospital Santa Luzia, ULSAM – Viana Do Castelo	Viana do castelo	Portugal
Sofia	Trovisco	Instituto Português De Oncologia Do Porto	Porto	Portugal

Inês	Fonseca	Instituto Português De Oncologia Do Porto	Porto	Portugal
Décio	Pereira	Instituto Português De Oncologia Do Porto	Porto	Portugal
Lina	Miranda	Instituto Português De Oncologia Do Porto	Porto	Portugal
Muhammad Shakeel	Riaz	Hamad Medical Corporation	Doha	Qatar
Hamed	Elgendy	Hamad Medical Corporation	Doha	Qatar
Hashaam	Ghafoor	Hamad Medical Corporation	Doha	Qatar
Mohammed	Haji	Hamad Medical Corporation	Doha	Qatar
Vipin	Kumari	Hamad Medical Corporation	Doha	Qatar
Lakshmi	Ramanathan	Hamad Medical Corporation	Doha	Qatar
Jassim	Rauf	Hamad Medical Corporation	Doha	Qatar
Nissar	Shaikh	Hamad Medical Corporation	Doha	Qatar
Abdul Gafoor	Tharayil	Hamad Medical Corporation	Doha	Qatar
Marija	Toleska	University Clinical Center "Mother Teresa" Skopje; University "Ss. Cyril And Methodius" Skopje, Macedonia	Skopje	Republic Of North Macedonia
Aleksandar	Dimitrovski	University Clinical Center "Mother Teresa" Skopje; University "Ss. Cyril And Methodius" Skopje, Macedonia	Skopje	Republic Of North Macedonia
Filip	Naumovski	University Clinical Center "Mother Teresa" Skopje; University "Ss. Cyril And Methodius" Skopje, Macedonia	Skopje	Republic Of North Macedonia
Angela	Trposka	University Clinical Center "Mother Teresa" Skopje; University "Ss. Cyril And Methodius" Skopje, Macedonia	Skopje	Republic Of North Macedonia
Ioana Marina	Grintescu	Clinical Emergency Hospital Of Bucharest	Bucharest	Romania
Cristian	Cobilinschi	Clinical Emergency Hospital Of Bucharest	Bucharest	Romania
Ana-Maria	Cotae	Clinical Emergency Hospital Of Bucharest	Bucharest	Romania
Liliana	Mirea	Clinical Emergency Hospital Of Bucharest	Bucharest	Romania
Raluca	Ungureanu	Clinical Emergency Hospital Of Bucharest	Bucharest	Romania
Liana	Valeanu	Emergency Institute For Cardiovascular Diseases CC Iliescu	Bucharest	Romania
Bianca	Morosanu	Emergency Institute For Cardiovascular Diseases CC Iliescu	Bucharest	Romania
Serban	Bubenek-Turtoni	Emergency Institute For Cardiovascular Diseases CC Iliescu	Bucharest	Romania
Cornel	Robu	Emergency Institute For Cardiovascular Diseases CC Iliescu	Bucharest	Romania
Alida	Moise	Prof. Dr. Gerota Hospital	Bucharest	Romania
Carmen	Balescu	Prof. Dr. Gerota Hospital	Bucharest	Romania
Catalin Traian	Guran	Prof. Dr. Gerota Hospital	Bucharest	Romania
Madalina	Herman	Prof. Dr. Gerota Hospital	Bucharest	Romania

Alexander	Kulikov	Burdenko National Medical Research Centre Of Neurosurgery, Moscow	Moscow	Russia
Igor	Zabolotskikh	Kuban State Medical University With Clinical Facility "Territorial Hospital #2"	Krasnodar	Russia
Dmitriy	Fedunets	Kuban State Medical University With Clinical Facility "Territorial Hospital #2"	Krasnodar	Russia
Nikita	Trembach	Kuban State Medical University With Clinical Facility "Territorial Hospital #2"	Krasnodar	Russia
Valerii	Subbotin	Moscow Clinical Scientific Center Na Loginov	Moscow	Russia
Ilyas	Izmailov	Moscow Clinical Scientific Center Na Loginov	Moscow	Russia
Maria	Miroshnichenko	Moscow Clinical Scientific Center Na Loginov	Moscow	Russia
Ekaterina	Orlova	Moscow Clinical Scientific Center Na Loginov	Moscow	Russia
Elizaveta	Serdobintseva	Moscow Clinical Scientific Center Na Loginov	Moscow	Russia
Mikhail	Kirov	Northern State Medical University	Arkhangelsk	Russia
Aleksey	Avidzba	Northern State Medical University	Arkhangelsk	Russia
Vsevolod	Kuzkov	Northern State Medical University	Arkhangelsk	Russia
Anton	Nikonov	Northern State Medical University	Arkhangelsk	Russia
Sergey	Astrakov	Novosibirsk State University With Clinical Facility City Clinical Hospital #25	Novosibirsk	Russia
Elena	Neporada	Novosibirsk State University With Clinical Facility City Clinical Hospital #25	Novosibirsk	Russia
Victoria	Khoronenko	P.A. Herzen Moscow Cancer Research Institute	Moscow	Russia
Vladislav	Karpeikin	P.A. Herzen Moscow Cancer Research Institute	Moscow	Russia
Anna	Malanova	P.A. Herzen Moscow Cancer Research Institute	Moscow	Russia
Pavel	Suvorin	P.A. Herzen Moscow Cancer Research Institute	Moscow	Russia
July	Zaharenkova	P.A. Herzen Moscow Cancer Research Institute	Moscow	Russia
Sergey	Efremov	Saint Petersburg State University Hospital	Saint-Petersburg	Russia
Oleg	Kuleshov	Saint Petersburg State University Hospital	Saint-Petersburg	Russia
Alexey	Kulikov	Saint Petersburg State University Hospital	Saint-Petersburg	Russia
Elizaveta	Leonova	Saint Petersburg State University Hospital	Saint-Petersburg	Russia
Olivera	Marinkovic	CHC Bezaniska Kosa	Belgrade	Serbia
Ana	Sekulic	CHC Bezaniska Kosa	Belgrade	Serbia
Ivan	Palibrk	Clinic For Digestive Surgery-The First Surgical Clinic, University Clinical Center Serbia	Belgrade	Serbia

Marija	Djukanovic	Clinic For Digestive Surgery-The First Surgical Clinic, University Clinical Center Serbia	Belgrade	Serbia
Svetlana	Sreckovic	Clinic For Orthopedics Surgery And Traumatology, University Clinical Center Of Serbia	Belgrade	Serbia
Radmila	Klacar	Clinic For Orthopedics Surgery And Traumatology, University Clinical Center Of Serbia	Belgrade	Serbia
Dragana	Vracevic	Clinic For Orthopedics Surgery And Traumatology, University Clinical Center Of Serbia	Belgrade	Serbia
Miodrag	Milenovic	Emergency Center, University Clinical Center Of Serbia; Faculty Of Medicine, University Of Belgrade	Belgrade	Serbia
Aleksandra	Nikolic	Emergency Center, University Clinical Center Of Serbia; Faculty Of Medicine, University Of Belgrade	Belgrade	Serbia
Marija	Rajkovic	Emergency Center, University Clinical Center Of Serbia; Faculty Of Medicine, University Of Belgrade	Belgrade	Serbia
Dragana	Lončar Stojiljković	Institute For Cardiovascular Diseases Belgrade	Belgrade	Serbia
Nikola	Djukanović	Institute For Cardiovascular Diseases Belgrade	Belgrade	Serbia
Biljana	Novaković	Institute For Cardiovascular Diseases Belgrade	Belgrade	Serbia
Maja	Stojanovic	University Clinical Center "Zvezdara"	Belgrade	Serbia
Milan	Markovic	University Clinical Center "Zvezdara"	Belgrade	Serbia
Slobodan	Popovic	University Clinical Center "Zvezdara"	Belgrade	Serbia
Janez	Dolinar	General Hospital Novo Mesto	Novo Mesto	Slovenia
Sandra	Blagojević Štembergar	General Hospital Novo Mesto	Novo Mesto	Slovenia
Goran	Kurnik	General Hospital Novo Mesto	Novo Mesto	Slovenia
Peter	Poredos	University Medical Centre Ljubljana	Ljubljana	Slovenia
Vanja	Oven	University Medical Centre Ljubljana	Ljubljana	Slovenia
Andreja	Möller Petrun	University Medical Centre Maribor	Maribor	Slovenia
Bojana	Drobnjak	University Medical Centre Maribor	Maribor	Slovenia
Maša	Furman	University Medical Centre Maribor	Maribor	Slovenia
Marko	Lokar	University Medical Centre Maribor	Maribor	Slovenia
Jernej	Novak	University Medical Centre Maribor	Maribor	Slovenia
Katarina Katja	Primožič	University Medical Centre Maribor	Maribor	Slovenia
Palesa	Motshabi Chakane	Charlotte Maxeke Johannesburg Academic Hospital (CMJAH)	Parktown, Johannesburg	South Africa

Sithandiwe	Dingezweni	Charlotte Maxeke Johannesburg Academic Hospital (CMJAH)	Parktown, Johannesburg	South Africa
Leballo	Gontse	Charlotte Maxeke Johannesburg Academic Hospital (CMJAH)	Parktown, Johannesburg	South Africa
Zainub	Jooma	Charlotte Maxeke Johannesburg Academic Hospital (CMJAH)	Parktown, Johannesburg	South Africa
Hlamatsi	Moutlana	Charlotte Maxeke Johannesburg Academic Hospital (CMJAH)	Parktown, Johannesburg	South Africa
LUNGANGA TOMS	LUSHIKU	Chris Hani Baragwanath Academic Hospital	Soweto, Johannesburg	South Africa
GRACE	MANJOORAN	Chris Hani Baragwanath Academic Hospital	Soweto, Johannesburg	South Africa
PALESA	MOGANE	Chris Hani Baragwanath Academic Hospital	Soweto, Johannesburg	South Africa
MATHABE	SEHLAPELO	Chris Hani Baragwanath Academic Hospital	Soweto, Johannesburg	South Africa
Sean	Chetty	Stellenbosch University, Cape Town	Cape Town	South Africa
Stephen	Venter	Tygerberg Hospital	Cape Town	South Africa
Triesie	Lotz	Tygerberg Hospital	Cape Town	South Africa
Pablo	Monedero	Clínica Universidad De Navarra	Pamplona	Spain
Carmen	Cara-Gilabert	Clínica Universidad De Navarra	Pamplona	Spain
Angela	Escribano-Arranz	Clínica Universidad De Navarra	Pamplona	Spain
Marta	Luque-Peláez	Clínica Universidad De Navarra	Pamplona	Spain
Pablo	Montero-López	Clínica Universidad De Navarra	Pamplona	Spain
Inigo	Iñigo Rubio-Baines	Clínica Universidad De Navarra	Pamplona	Spain
Carmen	Sala-Trull	Clínica Universidad De Navarra	Pamplona	Spain
Ana María	García Sánchez	Complejo Asistencial De Zamora	Zamora	Spain
Cristina	Blanco Dorado	Complejo Asistencial De Zamora	Zamora	Spain
Angela	Casquero Murciego	Complejo Asistencial De Zamora	Zamora	Spain
Francisco	García Lázaro	Complejo Asistencial De Zamora	Zamora	Spain
Yaiza	Molero Diez	Complejo Asistencial De Zamora	Zamora	Spain
F Javier	García-Miguel	Complejo Hospitalario Segovia	Segovia	Spain
Estefania	Chamorro Garci	Complejo Hospitalario Segovia	Segovia	Spain
Rosalia	Navarro-Perez	Hospital Clinico San Carlos	Madrid	Spain
Luis	Santé	Hospital Clinico San Carlos	Madrid	Spain
Andrea	Gutiérrez	Hospital Clínico Universitario Valencia	Valencia	Spain
Marta	Luzón	Hospital Clínico Universitario Valencia	Valencia	Spain
Rosalba	Martinez	Hospital Clínico Universitario Valencia	Valencia	Spain
Eduardo	Passariello	Hospital Clínico Universitario Valencia	Valencia	Spain
Ana	Ruiz	Hospital Clínico Universitario Valencia	Valencia	Spain
Ferran	Serralta	Hospital Clínico Universitario Valencia	Valencia	Spain
Jaume	Valero	Hospital Clínico Universitario Valencia	Valencia	Spain
Susana	Altaba Tena	Hospital General Universitario De Castellón	Castellón de la Plana	Spain
Maria Lidon	Mateu Campos	Hospital General Universitario De Castellón	Castellón de la Plana	Spain
Luisa	Cueva Castro	Hospital Sant Pau	Barcelona	Spain
Albert	Bainac Albadalejo	Hospital Sant Pau	Barcelona	Spain
Astrid	Batalla Gonzalez	Hospital Sant Pau	Barcelona	Spain

Cecilia	Diez García	Hospital Sant Pau	Barcelona	Spain
Marta	Giné Servén	Hospital Sant Pau	Barcelona	Spain
Laura	Pardo Pinzón	Hospital Sant Pau	Barcelona	Spain
Hector	Villanueva Sanchez	Hospital Sant Pau	Barcelona	Spain
Ángel	Becerra-Bolaños	Hospital Universitario De Gran Canaria Doctor Negrin	Las Palmas de Gran Canaria	Spain
Antonio	Arencibia-Almeida	Hospital Universitario De Gran Canaria Doctor Negrin	Las Palmas de Gran Canaria	Spain
Gema	Hernanz-Rodríguez	Hospital Universitario De Gran Canaria Doctor Negrin	Las Palmas de Gran Canaria	Spain
Virginia	Muiño-Palomar	Hospital Universitario De Gran Canaria Doctor Negrin	Las Palmas de Gran Canaria	Spain
Nazario	Ojeda-Betancor	Hospital Universitario De Gran Canaria Doctor Negrin	Las Palmas de Gran Canaria	Spain
Aurelio	Rodríguez-Pérez	Hospital Universitario De Gran Canaria Doctor Negrin	Las Palmas de Gran Canaria	Spain
José Ignacio	García-Sánchez	Hospital Universitario Fundación Alcorcón	Alcorcon	Spain
Tamara	Brunete	Hospital Universitario Fundación Alcorcón	Alcorcon	Spain
David	Delgado	Hospital Universitario Fundación Alcorcón	Alcorcon	Spain
Pablo	Redondo	Hospital Universitario Fundación Alcorcón	Alcorcon	Spain
Viviana	Varón	Hospital Universitario Fundación Alcorcón	Alcorcon	Spain
Diana	Zamudio	Hospital Universitario Fundación Alcorcón	Alcorcon	Spain
Javi	Ripolles	Infanta Leonor Univesrity Hospital - Madrid	Madrid	Spain
Susana	González-Suárez	Vall D´Hebron University Hospital	Barcelona	Spain
Elena Regla	Gómez-González	Vall D´Hebron University Hospital	Barcelona	Spain
María Del Carmen	Iribarren Mateos	Vall D´Hebron University Hospital	Barcelona	Spain
Hytham K. S.	Hamid	East Nile Hospital	Khartoum	Sudan
Alaa	Musa	East Nile Hospital	Khartoum	Sudan
Elfayadh	Saidahmed	East Nile Hospital	Khartoum	Sudan
Ahmed	Mohamed Ibrahim Mohamed	Gadarif Teaching Hospital	Gadarif	Sudan
Muntasir	Abdelsakhi	Ibn-Sina Specialized Teaching Hospital	Khartoum	Sudan
Abdelrouf Ibrahim	Walaa	Ibn-Sina Specialized Teaching Hospital	Khartoum	Sudan
Abdulrhman	Khaity	Ibn-Sina Specialized Teaching Hospital	Khartoum	Sudan
Michelle	Chew	Department Of Anaesthesiology And Intensive Care Medicine, University Hospital, Linköping	Linköping	Sweden
Helen	Didriksson	Department Of Anaesthesiology And Intensive Care Medicine, University Hospital, Linköping	Linköping	Sweden
Carina	Jonsson	Department Of Anaesthesiology And Intensive Care Medicine, University Hospital, Linköping	Linköping	Sweden
Thorir S.	Sigmundsson	Karolinska University Hospital - Solna	Stockholm	Sweden

Anna	Granström	Karolinska University Hospital - Solna	Stockholm	Sweden
Malin	Jonsson Fagerlund	Karolinska Institutet and Karolinska University Hospital - Solna	Stockholm	Sweden
Anna	Schening	Karolinska University Hospital - Solna	Stockholm	Sweden
Arman	Valadkhani	Karolinska University Hospital - Solna	Stockholm	Sweden
Christina	Blixt	Karolinska University Hospital Huddinge	Stockholm	Sweden
Malin	Hansson	Karolinska University Hospital Huddinge	Stockholm	Sweden
Kristina	Kilsand	Karolinska University Hospital Huddinge	Stockholm	Sweden
Åke	Norberg	Karolinska University Hospital Huddinge	Stockholm	Sweden
Eva	Strandberg	Karolinska University Hospital Huddinge	Stockholm	Sweden
Egidijus	Semenas	Uppsala University Hospital	Uppsala	Sweden
Lina	Jonikaite	Uppsala University Hospital	Uppsala	Sweden
Alexander	Dullenkopf	Spital Thurgau Frauenfeld	Frauenfeld	Switzerland
Ivan	Chau	Spital Thurgau Frauenfeld	Frauenfeld	Switzerland
Lina	Petersen	Spital Thurgau Frauenfeld	Frauenfeld	Switzerland
Benedikt	Preckel	Amsterdam UMC, Location AMC	Amsterdam	The Netherlands
Ali	Kaplan	Amsterdam UMC, Location AMC	Amsterdam	The Netherlands
Jimmy	Schenk	Amsterdam UMC, Location AMC	Amsterdam	The Netherlands
Denise Petra	Veelo	Amsterdam UMC, Location AMC	Amsterdam	The Netherlands
Felix	Van Lier	Erasmus MC	Rotterdam	The Netherlands
Rene	Van Bruchem	Erasmus MC	Rotterdam	The Netherlands
Seppe SHA	Koopman	Maasstad Hospital	Rotterdam	The Netherlands
Toine	Van Den Ende	Maasstad Hospital	Rotterdam	The Netherlands
Hans D.	De Boer	Martini Hospital Groningen	Groningen	The Netherlands
Henriëtte	Smid-Nanninga	Martini Hospital Groningen	Groningen	The Netherlands
Paul A.	Van Beest	Medical Center Leeuwarden	Leeuwarden	The Netherlands
Eric E.C.	De Waal	University Medical Center Utrecht	Utrecht	The Netherlands
Thomas W.L.	Scheeren	University Medical Centre Groningen	Groningen	The Netherlands
Ilonka N.	De Keijzer	University Medical Centre Groningen	Groningen	The Netherlands
Constanze	Brucker	Wilhelmina Hospital Assen	Assen	The Netherlands
Sandra	Brookman	Wilhelmina Hospital Assen	Assen	The Netherlands
Inge J.E.	Paas	Wilhelmina Hospital Assen	Assen	The Netherlands
Lerzan	Dogan	Acibadem Altunizade Hospital	Istanbul	Turkey
Hazal	Yazgec	Acibadem Altunizade Hospital	Istanbul	Turkey
Cigdem	Yildirim Guclu	Ankara University Faculty Of Medicine	Ankara	Turkey
Sanem	Cakar Turhan	Ankara University Faculty Of Medicine	Ankara	Turkey
Basak Ceyda	Meco	Ankara University Faculty Of Medicine	Ankara	Turkey
Ali	Alagoz	University Of Health Sciences, Ankara Atatürk Sanatorium Training And Research Hospital	Ankara	Turkey

Hilal	Sazak	University Of Health Sciences, Ankara Atatürk Sanatorium Training And Research Hospital	Ankara	Turkey
Arzu	Yıldırım Ar	Fatih Sultan Mehmet Health Application Research Center, University Of Health Sciences	Istanbul	Turkey
Öznur	Demiroluk	Fatih Sultan Mehmet Health Application Research Center, University Of Health Sciences	Istanbul	Turkey
Yıldız	Yiğit	Fatih Sultan Mehmet Health Application Research Center, University Of Health Sciences	Istanbul	Turkey
Osman	Ekinci	Haydarpasa Numune Training And Research Hospital	Istanbul	Turkey
Serap	Adana Kavlak	Haydarpasa Numune Training And Research Hospital	Istanbul	Turkey
Seymanur	Altintas Filizoglu	Haydarpasa Numune Training And Research Hospital	Istanbul	Turkey
Günseli	Orhun	Istanbul Faculty Of Medicine, Istanbul University	Istanbul	Turkey
Mert	Canbaz	Istanbul Faculty Of Medicine, Istanbul University	Istanbul	Turkey
Kemal Tolga	Saracoglu	Kartal Dr Lutfi Kirdar Training And Research Hospital	Istanbul	Turkey
Elif	Akova Deniz	Kartal Dr Lutfi Kirdar Training And Research Hospital	Istanbul	Turkey
Banu	Eler Cevik	Kartal Dr Lutfi Kirdar Training And Research Hospital	Istanbul	Turkey
Ayca Sultan	Sahin	University Of Health Sciences, Kanuni Sultan Suleyman Education And Training Hospital'	Istanbul	Turkey
Ebru	Kaya	University Of Health Sciences, Kanuni Sultan Suleyman Education And Training Hospital"	Istanbul	Turkey
Hande	Gurbuz	University Of Health Sciences, Bursa Yuksek Ihtisas Training And Research Hospital	Bursa	Turkey
Derya	Karasu	University Of Health Sciences, Bursa Yuksek Ihtisas Training And Research Hospital	Bursa	Turkey
Seyda Efsun	Ozgunay	University Of Health Sciences, Bursa Yuksek Ihtisas Training And Research Hospital	Bursa	Turkey
Eren Fatma	Akcil	University Of Istanbul - Cerrahpasa	Istanbul	Turkey
Ozlem	Korkmaz Dilmen	University Of Istanbul - Cerrahpasa	Istanbul	Turkey
Yusuf	Tunali	University Of Istanbul - Cerrahpasa	Istanbul	Turkey
Kerem	Erkalp	Bagcilar Training And Educational Hospital	Istanbul	Turkiye
Ali	Ozalp	Bagcilar Training And Educational Hospital	Istanbul	Turkiye
Mehmet Salih	Sevdi	Bagcilar Training And Educational Hospital	Istanbul	Turkiye
Maryna	Freigofer	Dnipro Regional Cancer Center	Dnipro	Ukraine

Olena	Khomenko	O.O. Shalimov National Scientific Center Of Surgery And Transplantation	Kyiv	Ukraine
Pavlo	Hurin	O.O. Shalimov National Scientific Center Of Surgery And Transplantation	Kyiv	Ukraine
Dmytro	Dmytriiev	Vinnitsa National Medical University And Vinnitsa Regional Endocrinology Center	Vinnitsa	Ukraine
Eugenii	Lysak	Vinnitsa National Medical University And Vinnitsa Regional Endocrinology Center	Vinnitsa	Ukraine
Tamsin	Gregory	Airedale NHS Foundation Trust	Keighley	United Kingdom
Shaw	Alison	Airedale NHS Foundation Trust	Keighley	United Kingdom
Ratcliffe	Anita	Airedale NHS Foundation Trust	Keighley	United Kingdom
Hairsine	Brigid	Airedale NHS Foundation Trust	Keighley	United Kingdom
Adam	Farrar	Airedale NHS Foundation Trust	Keighley	United Kingdom
Samson A.	Williams	Airedale NHS Foundation Trust	Keighley	United Kingdom
Joyce	Yeung	Birmingham Heartlands Hospital	Birmingham	United Kingdom
Syed	Abid	Birmingham Heartlands Hospital	Birmingham	United Kingdom
Adetoro	Akintunde	Birmingham Heartlands Hospital	Birmingham	United Kingdom
Roshni	Bahri	Birmingham Heartlands Hospital	Birmingham	United Kingdom
Marta	Burak	Birmingham Heartlands Hospital	Birmingham	United Kingdom
Libby	Dias	Birmingham Heartlands Hospital	Birmingham	United Kingdom
Yash	Dinesh	Birmingham Heartlands Hospital	Birmingham	United Kingdom
Iman	Farah	Birmingham Heartlands Hospital	Birmingham	United Kingdom
Ciara	Gibson	Birmingham Heartlands Hospital	Birmingham	United Kingdom
Joanne	Gresty	Birmingham Heartlands Hospital	Birmingham	United Kingdom
Fiona	Harris	Birmingham Heartlands Hospital	Birmingham	United Kingdom
Alex	Jones	Birmingham Heartlands Hospital	Birmingham	United Kingdom
Chuck	Lam	Birmingham Heartlands Hospital	Birmingham	United Kingdom
William	Mciver	Birmingham Heartlands Hospital	Birmingham	United Kingdom
Teresa	Melody	Birmingham Heartlands Hospital	Birmingham	United Kingdom
Ninoshka	Merchant	Birmingham Heartlands Hospital	Birmingham	United Kingdom
Safwaan	Patel	Birmingham Heartlands Hospital	Birmingham	United Kingdom
Gursharan	Virdee	Birmingham Heartlands Hospital	Birmingham	United Kingdom
Bryan	Wong	Birmingham Heartlands Hospital	Birmingham	United Kingdom
Jessica	Davis	Bolton Hospital NHS Foundation Trust	Farnworth	United Kingdom
Jordan	Alfonso	Bolton Hospital NHS Foundation Trust	Farnworth	United Kingdom
Mohamed	Elbahnasy	Bolton Hospital NHS Foundation Trust	Farnworth	United Kingdom
Monica	Trivedi	Cambridge University Hospitals Trust	Cambridge	United Kingdom
Efthymia Maria	Kapasouri	Cambridge University Hospitals Trust	Cambridge	United Kingdom
Galina	Maneva	Cambridge University Hospitals Trust	Cambridge	United Kingdom
Peta	Masters	Cambridge University Hospitals Trust	Cambridge	United Kingdom
Malgorzata	Opalinska	Cambridge University Hospitals Trust	Cambridge	United Kingdom
Luke	Winslow	Countess Of Chester NHS Foundation Trust	Chester	United Kingdom
Bamford	Peter	Countess Of Chester NHS Foundation Trust	Chester	United Kingdom
Prince	Judith	Countess Of Chester NHS Foundation Trust	Chester	United Kingdom

Faulkner	Maria	Countess Of Chester NHS Foundation Trust	Chester	United Kingdom
Ivison	Alison	Countess Of Chester NHS Foundation Trust	Chester	United Kingdom
Barham	Elin	Countess Of Chester NHS Foundation Trust	Chester	United Kingdom
Barton	Matthew	Countess Of Chester NHS Foundation Trust	Chester	United Kingdom
Hadlett	Max	Countess Of Chester NHS Foundation Trust	Chester	United Kingdom
Russell	Nicki	Countess Of Chester NHS Foundation Trust	Chester	United Kingdom
Verghese	Prashant	Countess Of Chester NHS Foundation Trust	Chester	United Kingdom
Karunaratne	Nicholas	Countess Of Chester NHS Foundation Trust	Chester	United Kingdom
Murphy	Thomas	Countess Of Chester NHS Foundation Trust	Chester	United Kingdom
Sundar	Ashok	Croydon University Hospital	Thornton Heath	United Kingdom
Christopher	Black	Croydon University Hospital	Thornton Heath	United Kingdom
Zakaulla	Belagodu	Dartford And Gravesham NHS Trust	Dartford	United Kingdom
Ryan	Coe	Dartford And Gravesham NHS Trust	Dartford	United Kingdom
Katy	Collins	Dartford And Gravesham NHS Trust	Dartford	United Kingdom
Tracy	Edmunds	Dartford And Gravesham NHS Trust	Dartford	United Kingdom
Charlotte	Kamundi	Dartford And Gravesham NHS Trust	Dartford	United Kingdom
Prasanna	Patlola	Dartford And Gravesham NHS Trust	Dartford	United Kingdom
Laura	Johnson	Dartford And Gravesham NHS Trust	Dartford	United Kingdom
Naomi	Oakley	Dartford And Gravesham NHS Trust	Dartford	United Kingdom
Olumide	Olufuwa	Dartford And Gravesham NHS Trust	Dartford	United Kingdom
Luciana	Rusu	Dartford And Gravesham NHS Trust	Dartford	United Kingdom
Juleen	Fasham	Derriford Hospital	Plymouth	United Kingdom
Amit	Das	Derriford Hospital	Plymouth	United Kingdom
Anna	Ratcliffe	Derriford Hospital	Plymouth	United Kingdom
Ben	Parish	Derriford Hospital	Plymouth	United Kingdom
Freeman	Lizzie	Derriford Hospital	Plymouth	United Kingdom
Gary	Minto	Derriford Hospital	Plymouth	United Kingdom
Gunarathna	Perumbadage	Derriford Hospital	Plymouth	United Kingdom
Jessica	Sinclair	Derriford Hospital	Plymouth	United Kingdom
Lucy	Guile	Derriford Hospital	Plymouth	United Kingdom
Matthew	Baldwin	Derriford Hospital	Plymouth	United Kingdom
Stephanie	Pauling	Derriford Hospital	Plymouth	United Kingdom
Wael	Alhalabi	Derriford Hospital	Plymouth	United Kingdom
Moustafa	Shebl Zahra	East Kent Hospitals University NHS Foundation Trust (EKHUFT) Margate Kent	Canterbury	United Kingdom
Eva	Beranova	East Kent Hospitals University NHS Foundation Trust (EKHUFT) Margate Kent	Canterbury	United Kingdom

Tracy	Hazelton	East Kent Hospitals University NHS Foundation Trust (EKHUFT) Margate Kent	Canterbury	United Kingdom
Alicia	Knight	East Kent Hospitals University NHS Foundation Trust (EKHUFT) Margate Kent	Canterbury	United Kingdom
Trudy	Parfrey	East Kent Hospitals University NHS Foundation Trust (EKHUFT) Margate Kent	Canterbury	United Kingdom
Jhanielle	Quindoyos	East Kent Hospitals University NHS Foundation Trust (EKHUFT) Margate Kent	Canterbury	United Kingdom
Hazel	Ramos	East Kent Hospitals University NHS Foundation Trust (EKHUFT) Margate Kent	Canterbury	United Kingdom
Gabriella	Tutt	East Kent Hospitals University NHS Foundation Trust (EKHUFT) Margate Kent	Canterbury	United Kingdom
Joanne	Deery	East Kent Hospitals University NHS Foundation Trust (EKHUFT) Margate Kent	Canterbury	United Kingdom
Himanshu	Arora	East Kent Hospitals University NHS Foundation Trust (EKHUFT) Margate Kent	Canterbury	United Kingdom
David	Freeman	East Lancashire Hospitals NHS Trust	Blackburn	United Kingdom
Qasim Tayyib	Ahmed	East Lancashire Hospitals NHS Trust	Blackburn	United Kingdom
Alexander	Gurnee	East Lancashire Hospitals NHS Trust	Blackburn	United Kingdom
Rachel	Harding	East Lancashire Hospitals NHS Trust	Blackburn	United Kingdom
Tom	Mckernan	East Lancashire Hospitals NHS Trust	Blackburn	United Kingdom
Aayesha	Kazi	East Lancashire Hospitals NHS Trust	Blackburn	United Kingdom
Nicholas	Truman	East Lancashire Hospitals NHS Trust	Blackburn	United Kingdom
Stephen	Lewis	Frimley Park Hospital	Frimley	United Kingdom
Eid	Ahmed	Frimley Park Hospital	Frimley	United Kingdom
Baiju	Barath	Frimley Park Hospital	Frimley	United Kingdom
Bernardo	Solomon	Frimley Park Hospital	Frimley	United Kingdom
Hau Lam Clara	Fong	Frimley Park Hospital	Frimley	United Kingdom
Stevenson	Joe	Frimley Park Hospital	Frimley	United Kingdom
Katarzyna Anna	Marasinska	Frimley Park Hospital	Frimley	United Kingdom
Abelarde	Kaye	Frimley Park Hospital	Frimley	United Kingdom
Essuman	Lorinda	Frimley Park Hospital	Frimley	United Kingdom
Whitmarsh	Thomas	Frimley Park Hospital	Frimley	United Kingdom
Jack	Tooze	Frimley Park Hospital	Frimley	United Kingdom
Bland	Yvonne	Frimley Park Hospital	Frimley	United Kingdom
Andrew	Lowes	Gateshead Health NHS Foundation Trust (Queen Elizabeth Hospital)	Queen	United Kingdom
Mohamed	Abdelsalam	Gateshead Health NHS Foundation Trust (Queen Elizabeth Hospital)	Queen	United Kingdom
Jon	Braviner	Gateshead Health NHS Foundation Trust (Queen Elizabeth Hospital)	Queen	United Kingdom

Rachael	Lucas	Gateshead Health NHS Foundation Trust (Queen Elizabeth Hospital)	Queen	United Kingdom
Jenny	Ritzema	Gateshead Health NHS Foundation Trust (Queen Elizabeth Hospital)	Queen	United Kingdom
Nicolas	Simmers	Gateshead Health NHS Foundation Trust (Queen Elizabeth Hospital)	Queen	United Kingdom
Manushi	Vyas	Gateshead Health NHS Foundation Trust (Queen Elizabeth Hospital)	Queen	United Kingdom
Venkat	Sundaram	Glan Clwyd Hospital	Bodelwyddan	United Kingdom
Anette	Bolger	Glan Clwyd Hospital	Bodelwyddan	United Kingdom
Jennifer	Davies	Glan Clwyd Hospital	Bodelwyddan	United Kingdom
Esther	Garrod	Glan Clwyd Hospital	Bodelwyddan	United Kingdom
Victoria	Garvey	Glan Clwyd Hospital	Bodelwyddan	United Kingdom
Rachel	Manley	Glan Clwyd Hospital	Bodelwyddan	United Kingdom
Zuzana	Probier	Glan Clwyd Hospital	Bodelwyddan	United Kingdom
Angela	Pye	Glan Clwyd Hospital	Bodelwyddan	United Kingdom
Zoka	Milan	King's College Hospital	London	United Kingdom
Gudrun	Kunst	King's College Hospital	London	United Kingdom
Daveena	Meeks	King's College Hospital	London	United Kingdom
Anna	Broderick	King's College Hospital	London	United Kingdom
Kevin	O'Reilly	King's College Hospital	London	United Kingdom
Juliana	Pereira	King's College Hospital	London	United Kingdom
Bernd Oliver	Rose	Lewisham & Greenwich NHS Trust - Queen Elizabeth Hospital	London	United Kingdom
Leanne	Howard	Lewisham & Greenwich NHS Trust - Queen Elizabeth Hospital	London	United Kingdom
Estefania	Treus	Lewisham & Greenwich NHS Trust - Queen Elizabeth Hospital	London	United Kingdom
Teodora	Orasanu	Lincoln County Hospital	Lincoln	United Kingdom
Russell	Conyers	Lincoln County Hospital	Lincoln	United Kingdom
Katie	Dorr	Lincoln County Hospital	Lincoln	United Kingdom
Ellie	Farcas	Lincoln County Hospital	Lincoln	United Kingdom
Olesya	Francis	Lincoln County Hospital	Lincoln	United Kingdom
Kelly	Hubbard	Lincoln County Hospital	Lincoln	United Kingdom
Rachel	Newton	Lincoln County Hospital	Lincoln	United Kingdom
Sarah	Shephardson	Lincoln County Hospital	Lincoln	United Kingdom
Catherine	Wyatt	Lincoln County Hospital	Lincoln	United Kingdom
David	Golden	Maidstone Hospital	Maidstone	United Kingdom
Amy	Ackerley	Maidstone Hospital	Maidstone	United Kingdom
Laura	Adams	Maidstone Hospital	Maidstone	United Kingdom
Jennifer	Assimakopoulos	Maidstone Hospital	Maidstone	United Kingdom
Miriam	Davey	Maidstone Hospital	Maidstone	United Kingdom
Maddie	Lawrence	Maidstone Hospital	Maidstone	United Kingdom
Rebecca	Seaman	Maidstone Hospital	Maidstone	United Kingdom
Michala	Shah	Maidstone Hospital	Maidstone	United Kingdom
Heather	Callaghan	Maidstone Hospital	Maidstone	United Kingdom
Kailash	Bhatia	Manchester Royal Infirmary	Manchester	United Kingdom
Mohamed	Abdelmotieleb	Manchester Royal Infirmary	Manchester	United Kingdom
Victor	Bill	Manchester Royal Infirmary	Manchester	United Kingdom
Ayman	Edarous	Manchester Royal Infirmary	Manchester	United Kingdom
Samuel	Ikenga	Manchester Royal Infirmary	Manchester	United Kingdom
Rose	Jama	Manchester Royal Infirmary	Manchester	United Kingdom
Kezia	Philipose	Manchester Royal Infirmary	Manchester	United Kingdom
Manu	Sudevan	Manchester Royal Infirmary	Manchester	United Kingdom

Brendan	Sloan	Mid Yorkshire NHS Trust	Wakefield	United Kingdom
Sarah	Buckley	Mid Yorkshire NHS Trust	Wakefield	United Kingdom
Anna	Littlejohns	Mid Yorkshire NHS Trust	Wakefield	United Kingdom
Amy	Major	Mid Yorkshire NHS Trust	Wakefield	United Kingdom
Lauren	Tye	Mid Yorkshire NHS Trust	Wakefield	United Kingdom
Manoj	Wickramasinghe	Mid Yorkshire NHS Trust	Wakefield	United Kingdom
Katie	Wilson	Mid Yorkshire NHS Trust	Wakefield	United Kingdom
Richard	Stewart	Milton Keynes University Hospital	Milton Keynes	United Kingdom
Teena	Babu	Milton Keynes University Hospital	Milton Keynes	United Kingdom
Louise	Mew	Milton Keynes University Hospital	Milton Keynes	United Kingdom
Alistair	Sawyerr	North Manchester General Hospital	Manchester	United Kingdom
Sharon	Baxter-Dore	North Manchester General Hospital	Manchester	United Kingdom
Nowfal	Rahman	North Manchester General Hospital	Manchester	United Kingdom
Joanne	Rothwell	North Manchester General Hospital	Manchester	United Kingdom
Helen	T-Michael	North Manchester General Hospital	Manchester	United Kingdom
Shiny	Sivanandan	North West Anglia NHS Foundation Trust	Peterborough	United Kingdom
Kirsty	Allen	North West Anglia NHS Foundation Trust	Peterborough	United Kingdom
Daniele	Arcoria	North West Anglia NHS Foundation Trust	Peterborough	United Kingdom
Roberta	De Pretto	North West Anglia NHS Foundation Trust	Peterborough	United Kingdom
Gbemisola	Jenfa	North West Anglia NHS Foundation Trust	Peterborough	United Kingdom
Zoey	Horne	North West Anglia NHS Foundation Trust	Peterborough	United Kingdom
Zainab	Mavani	North West Anglia NHS Foundation Trust	Peterborough	United Kingdom
Graeme	Mclintock	North West Anglia NHS Foundation Trust	Peterborough	United Kingdom
Emmah	Nelly	North West Anglia NHS Foundation Trust	Peterborough	United Kingdom
Ionela	Sinanovic	North West Anglia NHS Foundation Trust	Peterborough	United Kingdom
Natalie	Temple	North West Anglia NHS Foundation Trust	Peterborough	United Kingdom
Josephine	Williams	North West Anglia NHS Foundation Trust	Peterborough	United Kingdom
Anand	Jayaraman	Northumbria Healthcare NHS Foundation Trust	Newcastle	United Kingdom
Joshua	Craig	Northumbria Healthcare NHS Foundation Trust	Newcastle	United Kingdom
Hayley	Mckie	Northumbria Healthcare NHS Foundation Trust	Newcastle	United Kingdom
Tracy	Smith	Northumbria Healthcare NHS Foundation Trust	Newcastle	United Kingdom
Gail	Waddell	Northumbria Healthcare NHS Foundation Trust	Newcastle	United Kingdom
Trish	Tsuro	Pilgrim Hospital	Boston	United Kingdom
Khaled	Ahmed	Pilgrim Hospital	Boston	United Kingdom

Alya	Amin	Pilgrim Hospital	Boston	United Kingdom
Kimberley	Netherton	Pilgrim Hospital	Boston	United Kingdom
Izuchukwu	Nwalusi	Pilgrim Hospital	Boston	United Kingdom
Bryony	Saint	Pilgrim Hospital	Boston	United Kingdom
Kinga	Szymiczek	Pilgrim Hospital	Boston	United Kingdom
Reschreiter	Henrik	Poole Hospital (University Hospitals Dorset)	Poole	United Kingdom
Leanne	Bartlett	Poole Hospital (University Hospitals Dorset)	Poole	United Kingdom
Yasmin	De'Ath	Poole Hospital (University Hospitals Dorset)	Poole	United Kingdom
Charlotte	Humphrey	Poole Hospital (University Hospitals Dorset)	Poole	United Kingdom
Emma	Langridge	Poole Hospital (University Hospitals Dorset)	Poole	United Kingdom
Rebecca	Miln	Poole Hospital (University Hospitals Dorset)	Poole	United Kingdom
Tomasz	Torlinski	QEHB University Hospitals Birmingham NHS FT	Birmingham	United Kingdom
Tony	Whitehouse	QEHB University Hospitals Birmingham NHS FT	Birmingham	United Kingdom
Ian	Ewington	Queen Elizabeth Hospital Birmingham	Birmingham	United Kingdom
Phillip	Howells	Queen Elizabeth Hospital Birmingham	Birmingham	United Kingdom
Randeep	Mullhi	Queen Elizabeth Hospital Birmingham	Birmingham	United Kingdom
Amit	Sharma	Queen Elizabeth Hospital Birmingham	Birmingham	United Kingdom
Hazel	Smith	Queen Elizabeth Hospital Birmingham	Birmingham	United Kingdom
Carla	Speziale	Queen Elizabeth Hospital Birmingham	Birmingham	United Kingdom
Julian	Giles	Queen Victoria Hospital NHS Foundation Trust	E Grinstead	United Kingdom
Joel	Lockwood	Queen Victoria Hospital NHS Foundation Trust	E Grinstead	United Kingdom
Henrik	Reschreiter	Royal Bournemouth Hospital (University Hospitals Dorset)	Bournemouth	United Kingdom
Chloe	Bascombe	Royal Bournemouth Hospital (University Hospitals Dorset)	Bournemouth	United Kingdom
Claire	Osey	Royal Bournemouth Hospital (University Hospitals Dorset)	Bournemouth	United Kingdom
Debbie	Branney	Royal Bournemouth Hospital (University Hospitals Dorset)	Bournemouth	United Kingdom
Tiller	Heather	Royal Bournemouth Hospital (University Hospitals Dorset)	Bournemouth	United Kingdom
Javen	Ramsami	Royal Bournemouth Hospital (University Hospitals Dorset)	Bournemouth	United Kingdom
Sally	Pitts	Royal Bournemouth Hospital (University Hospitals Dorset)	Bournemouth	United Kingdom
Annamaria	Wilce	Royal Bournemouth Hospital (University Hospitals Dorset)	Bournemouth	United Kingdom
Natalie	Agius	Royal Bournemouth Hospital (University Hospitals Dorset)	Bournemouth	United Kingdom
Lindsay	Rogers	Royal Bournemouth Hospital (University Hospitals Dorset)	Bournemouth	United Kingdom
Cheryl	Lindsay	Royal Bournemouth Hospital (University Hospitals Dorset)	Bournemouth	United Kingdom

Claire	Preedy	Royal Cornwall Hospital NHS Trust	Truro	United Kingdom
Luke	Hayward	Royal Cornwall Hospital NHS Trust	Truro	United Kingdom
Thomas	Clark	Royal Devon & Exeter Hospital	Exeter	United Kingdom
Kevin	Windsor	Royal Devon & Exeter Hospital	Exeter	United Kingdom
Kizzy	Baines	Royal Devon & Exeter Hospital	Exeter	United Kingdom
Ben	Dingle	Royal Devon & Exeter Hospital	Exeter	United Kingdom
Rebecca	Wilcock	Royal Devon & Exeter Hospital	Exeter	United Kingdom
Hemal	Bosamia	Royal Devon & Exeter Hospital	Exeter	United Kingdom
Toby	Lewis	Royal Devon & Exeter Hospital	Exeter	United Kingdom
Ingeborg	Welters	University of Liverpool	Liverpool	United Kingdom
Richard	Ramsaran	Royal Liverpool And Broadgreen University Hospital Trusts	Liverpool	United Kingdom
Aleem	Morenikeji	Royal Liverpool And Broadgreen University Hospital Trusts	Liverpool	United Kingdom
Annie	Smith	Royal Liverpool And Broadgreen University Hospital Trusts	Liverpool	United Kingdom
Maria Arra Carlota	Canada	Royal Liverpool And Broadgreen University Hospital Trusts	Liverpool	United Kingdom
Claire	Davies	Royal Liverpool And Broadgreen University Hospital Trusts	Liverpool	United Kingdom
Dan	Watkin	Royal Liverpool And Broadgreen University Hospital Trusts	Liverpool	United Kingdom
Jon	Machin	Royal Liverpool And Broadgreen University Hospital Trusts	Liverpool	United Kingdom
Katherine	Hodson	Royal Liverpool And Broadgreen University Hospital Trusts	Liverpool	United Kingdom
Maria	Lopez	Royal Liverpool And Broadgreen University Hospital Trusts	Liverpool	United Kingdom
Luke	Shearer	Royal Liverpool And Broadgreen University Hospital Trusts	Liverpool	United Kingdom
Nick	Sinanan	Royal Liverpool And Broadgreen University Hospital Trusts	Liverpool	United Kingdom
Maria	Norris	Royal Liverpool And Broadgreen University Hospital Trusts	Liverpool	United Kingdom
Rebecca	Vickers	Royal Liverpool And Broadgreen University Hospital Trusts	Liverpool	United Kingdom
David	Shaw	Royal Liverpool And Broadgreen University Hospital Trusts	Liverpool	United Kingdom
Victoria	Waugh	Royal Liverpool And Broadgreen University Hospital Trusts	Liverpool	United Kingdom

Karen	Williams	Royal Liverpool And Broadgreen University Hospital Trusts	Liverpool	United Kingdom
Hayaka	Amada	Royal Liverpool And Broadgreen University Hospital Trusts	Liverpool	United Kingdom
Alexander	Sell	Royal National Orthopedic Hospital	Stanmore	United Kingdom
Tuyen	Anthony	Royal National Orthopedic Hospital	Stanmore	United Kingdom
Anamaria	Gerea	Royal National Orthopedic Hospital	Stanmore	United Kingdom
Shamil	Tanna	Royal National Orthopedic Hospital	Stanmore	United Kingdom
Angus	Tulloch	Royal National Orthopedic Hospital	Stanmore	United Kingdom
Panagiota	Alexopoulou	Royal Surrey County Hospital NHS Foundation Trust	Guildford	United Kingdom
Naomi	Boyer	Royal Surrey County Hospital NHS Foundation Trust	Guildford	United Kingdom
Paula	Carvelli	Royal Surrey County Hospital NHS Foundation Trust	Guildford	United Kingdom
Benedikt	Creagh-Brown	Royal Surrey County Hospital NHS Foundation Trust	Guildford	United Kingdom
Olivia	Dow	Royal Surrey County Hospital NHS Foundation Trust	Guildford	United Kingdom
Fouad	El-Hibri	Royal Surrey County Hospital NHS Foundation Trust	Guildford	United Kingdom
Syeda	Haider	Royal Surrey County Hospital NHS Foundation Trust	Guildford	United Kingdom
James	Hilton	Royal Surrey County Hospital NHS Foundation Trust	Guildford	United Kingdom
Hannah	Mackay	Royal Surrey County Hospital NHS Foundation Trust	Guildford	United Kingdom
Wisdom	Mbama	Royal Surrey County Hospital NHS Foundation Trust	Guildford	United Kingdom
Natalia	Michalak	Royal Surrey County Hospital NHS Foundation Trust	Guildford	United Kingdom
Maskell	Nick	Royal Surrey County Hospital NHS Foundation Trust	Guildford	United Kingdom
Kanji	Rafiq	Royal Surrey County Hospital NHS Foundation Trust	Guildford	United Kingdom
Donna-May	Sanga	Royal Surrey County Hospital NHS Foundation Trust	Guildford	United Kingdom
Nasser	Syed	Royal Surrey County Hospital NHS Foundation Trust	Guildford	United Kingdom
Jerik	Verula	Royal Surrey County Hospital NHS Foundation Trust	Guildford	United Kingdom
Waldtraud	Wutte	Royal Surrey County Hospital NHS Foundation Trust	Guildford	United Kingdom
Pierson	Richard	Russells Hall Hospital	Dudley	United Kingdom
Butler	Jack	Russells Hall Hospital	Dudley	United Kingdom
Elena	Anastasescu	Russells Hall Hospital	Dudley	United Kingdom
Tania	Mellor	Russells Hall Hospital	Dudley	United Kingdom
Wallbridge	Thomas	Russells Hall Hospital	Dudley	United Kingdom
Emma	Ingall	The William Harvey Hospital	Ashford	United Kingdom
Kim	Jemmett	The William Harvey Hospital	Ashford	United Kingdom
Vicki	Priestly	The William Harvey Hospital	Ashford	United Kingdom
James	Rand	The William Harvey Hospital	Ashford	United Kingdom

Maxime	Rigaudy	The William Harvey Hospital	Ashford	United Kingdom
Reanne	Solly	The William Harvey Hospital	Ashford	United Kingdom
Sarah	Stirrup	The William Harvey Hospital	Ashford	United Kingdom
Heather	Weston	The William Harvey Hospital	Ashford	United Kingdom
Wayne	Evans	The Robert Jones And Agnes Hunt NHS Foundation Trust	Oswestry, Shropshire	United Kingdom
Chloe	Perry	The Robert Jones And Agnes Hunt NHS Foundation Trust	Oswestry, Shropshire	United Kingdom
Karen	Pilson	The Robert Jones And Agnes Hunt NHS Foundation Trust	Oswestry, Shropshire	United Kingdom
Peringathara	Biju	The Royal Orthopaedic Hospital Birmingham	Birmingham	United Kingdom
Jones	Claudette	The Royal Orthopaedic Hospital Birmingham	Birmingham	United Kingdom
Keeling	Ellie	The Royal Orthopaedic Hospital Birmingham	Birmingham	United Kingdom
Jones	James	The Royal Orthopaedic Hospital Birmingham	Birmingham	United Kingdom
Brodie	Teresa	The Royal Orthopaedic Hospital Birmingham	Birmingham	United Kingdom
Magaya	Valarie	The Royal Orthopaedic Hospital Birmingham	Birmingham	United Kingdom
Andrew	Woodgate	Torbay And South Devon NHS Foundation Trust	Torquay	United Kingdom
Kylie	Ashby	Torbay And South Devon NHS Foundation Trust	Torquay	United Kingdom
Pauline	Aspa	Torbay And South Devon NHS Foundation Trust	Torquay	United Kingdom
Kelly	Barrett	Torbay And South Devon NHS Foundation Trust	Torquay	United Kingdom
Lauren	Blunt	Torbay And South Devon NHS Foundation Trust	Torquay	United Kingdom
Sean	Caunter	Torbay And South Devon NHS Foundation Trust	Torquay	United Kingdom
Emily	Flavell	Torbay And South Devon NHS Foundation Trust	Torquay	United Kingdom
Peter	Fletcher	Torbay And South Devon NHS Foundation Trust	Torquay	United Kingdom
Angie	Foulds	Torbay And South Devon NHS Foundation Trust	Torquay	United Kingdom
Ashleigh	Fynn	Torbay And South Devon NHS Foundation Trust	Torquay	United Kingdom
Beth	Mcelroy	Torbay And South Devon NHS Foundation Trust	Torquay	United Kingdom
Bryony	Reed	Torbay And South Devon NHS Foundation Trust	Torquay	United Kingdom
Fleur	Rogers	Torbay And South Devon NHS Foundation Trust	Torquay	United Kingdom
Andrea	Ford	Torbay And South Devon NHS Foundation Trust	Torquay	United Kingdom
Emma	Bartlett	Torbay And South Devon NHS Foundation Trust	Torquay	United Kingdom
David	Golden	Tunbridge Wells Hospital	Tunbridge Wells	United Kingdom
Amy	Ackerley	Tunbridge Wells Hospital	Tunbridge Wells	United Kingdom
Laura	Adams	Tunbridge Wells Hospital	Tunbridge Wells	United Kingdom
Jennifer	Assimakopoulos	Tunbridge Wells Hospital	Tunbridge Wells	United Kingdom
Miriam	Davey	Tunbridge Wells Hospital	Tunbridge Wells	United Kingdom
Madeleine	Lawrence	Tunbridge Wells Hospital	Tunbridge Wells	United Kingdom
Rebecca	Seaman	Tunbridge Wells Hospital	Tunbridge Wells	United Kingdom

Michala	Shah	Tunbridge Wells Hospital	Tunbridge Wells	United Kingdom
Heather	Callaghan	Tunbridge Wells Hospital	Tunbridge Wells	United Kingdom
Bernd Oliver	Rose	University Hospital Lewisham	London	United Kingdom
Jacob	Burr	University Hospital Lewisham	London	United Kingdom
Rosie	Reece-Anthony	University Hospital Lewisham	London	United Kingdom
Georgia	Richmond	University Hospital Lewisham	London	United Kingdom
Kay	Spikes	University Hospital Lewisham	London	United Kingdom
Eleanor	Stranger	University Hospital Lewisham	London	United Kingdom
Danaja	Zolger	University Hospital Lewisham	London	United Kingdom
Vera	Gotz	University Hospitals Of Morecambe Bay NHS Foundation Trust,	Lancaster	United Kingdom
Ben	Wooldridge	Warwick Hospital	Warwick	United Kingdom
Bridget	Campbell	Warwick Hospital	Warwick	United Kingdom
Penny	Parsons	Warwick Hospital	Warwick	United Kingdom
Camilla	Stagg	Warwick Hospital	Warwick	United Kingdom
Dominika	Dabrowska	West Middlesex University Hospital	London	United Kingdom
Omnia	Askar	West Middlesex University Hospital	London	United Kingdom
Priyakam	Chowdhury	West Middlesex University Hospital	London	United Kingdom
Jamie	Gonzales	West Middlesex University Hospital	London	United Kingdom
Swarna	Jeyabraba	West Middlesex University Hospital	London	United Kingdom
Angelyn	Sangalang	West Middlesex University Hospital	London	United Kingdom
Amrinder	Sayan	West Middlesex University Hospital	London	United Kingdom
Surendini	Thayaparan	West Middlesex University Hospital	London	United Kingdom
Kaushik	Bhowmick	West Suffolk NHS Foundation Trust	Bury St Edmunds	United Kingdom
Sally	Humphreys	West Suffolk NHS Foundation Trust	Bury St Edmunds	United Kingdom
Nimal	Mani	West Suffolk NHS Foundation Trust	Bury St Edmunds	United Kingdom
Sarah	Pearcey	West Suffolk NHS Foundation Trust	Bury St Edmunds	United Kingdom
Shivacharan Patel	Rudrappa	West Suffolk NHS Foundation Trust	Bury St Edmunds	United Kingdom
Zi Yi	Tew	West Suffolk NHS Foundation Trust	Bury St Edmunds	United Kingdom
Lisa	Jobes	Wrexham Maelor Hospital (BCUHB)	Wrexham	United Kingdom
John	Harris	Wrexham Maelor Hospital (BCUHB)	Wrexham	United Kingdom
Rachel	Hughes	Wrexham Maelor Hospital (BCUHB)	Wrexham	United Kingdom
Emma	Mcivor	Wrexham Maelor Hospital (BCUHB)	Wrexham	United Kingdom
Rebecca	Pope	Wrexham Maelor Hospital (BCUHB)	Wrexham	United Kingdom
Mary	Roberts	Wrexham Maelor Hospital (BCUHB)	Wrexham	United Kingdom
Victoria	Whitehead	Wrexham Maelor Hospital (BCUHB)	Wrexham	United Kingdom
Peter	Alexander	Wythenshawe Hospital	Manchester	United Kingdom

Sheetal	Crasta	Wythenshawe Hospital	Manchester	United Kingdom
Sofia	Fiouni	Wythenshawe Hospital	Manchester	United Kingdom
Jane	Shaw	Wythenshawe Hospital	Manchester	United Kingdom
Luke	Ward	Wythenshawe Hospital	Manchester	United Kingdom
Simon	Davies	York And Scarborough Teaching Hospitial NHS Foundation Trust	Scarborough	United Kingdom
Harriet	Carter	York And Scarborough Teaching Hospitial NHS Foundation Trust	Scarborough	United Kingdom
Zoe	Scott	York And Scarborough Teaching Hospitial NHS Foundation Trust	Scarborough	United Kingdom
Anisha Rahmath	Varodan	Buffalo General Medical Center	Buffalo	United States Of America
Liudmila	Asaul	Buffalo General Medical Center	Buffalo	United States Of America
Konstantin	Balonov	Tufts Medical Center	Boston	United States Of America
Ana	Arias	University Of California Davis	Davis	United States Of America
Leidy	Rivas	University Of California Davis	Davis	United States Of America
Julio	Pineda	University Of California Davis	Davis	United States Of America
Neal	Fleming	University Of California Davis	Davis	United States Of America
Brittney	Saverimuttu	University Of California Davis	Davis	United States Of America
Aubrey	Yao	University Of California Davis	Davis	United States Of America
Meredith	Miller	VA Boston Health Care System	Boston	United States Of America
Anuradha	Borle	Washington University In St Louis	Washington	United States Of America
Omokhaye	Higo	Washington University In St Louis	Washington	Washington
Muthuraj	Kanakaraj	Washington University In St Louis	Washington	Washington
Additional participating institution:				
		Complejo Hospitalario Universitario Insular Materno Infantil Las Palmas de Gran Canaria	Las Palmas de Gran Canaria	Spain
		University of Campania "L.Vanvitelli"	Naples	Italy
		Sunshine Coast University Hospital	Birtinya	Australia
		Al Bashir Hospital	Amman	Jordan
ESAIC Management Team				
Sylvia	Daamen	European Society of Anaesthesiology and Intensive Care	Brussels	Belgium
Sophie	Debouche	European Society of Anaesthesiology and Intensive Care	Brussels	Belgium
Slama	Farsi	European Society of Anaesthesiology and Intensive Care	Brussels	Belgium
Pierre	Harlet	European Society of Anaesthesiology and Intensive Care	Brussels	Belgium

Flavia	Pirovano	European Society of Anaesthesiology and Intensive Care	Brussels	Belgium

Endorsements of Specialist and National Anesthesia Associations

Australian and New Zealand College of Anaesthetists (ANZCA)

Association of Anesthesiologists and Intensivists of Serbia

Association of Anaesthesiologists of Malta

Association of Anaesthesiologists-Reanimatologists of Latvia

Belgian Society of Anesthesia and Resuscitation (BSAR)

Brazilian Society of Anesthesiology (SBA)

Czech Society of Anaesthesiology and Intensive Care Medicine (CSARIM)

Dutch Society of Anaesthesiology (NVA)

European Society of Anaesthesiology and Intensive Care (ESAIC)(Sponsor)

European Society of Intensive Care Medicine (ESICM)

French Society of anesthesia, critical care and perioperative medicine (SFAR)

German Society of Anaesthesiology and Intensive Care Medicine (DGAI)

Italian Society of Anaesthesia, Analgesia, Resuscitation and Intensive Care (SIAARTI)

Portuguese Society of Anaesthesiology (SPA)

Russian Federation National Society of Anesthesiologists and Reanimatologists (FAR)

Slovenian Society of Anaesthesiology and Intensive Care (SSAICM)

Slovak Society of Anesthesiology and Intensive Medicine

Spanish Society of Anaesthesia, Reanimation and Pain Management (SEDAR)

Society of Anaesthesia and Reanimatology of the Republic of Moldova

Ukrainian Society of Anaesthesiologists

Support:

American Society of Anaesthesiologists (ASA)

Methods

Method S1: In- and exclusion criteria

We recruited two cohorts of patients.

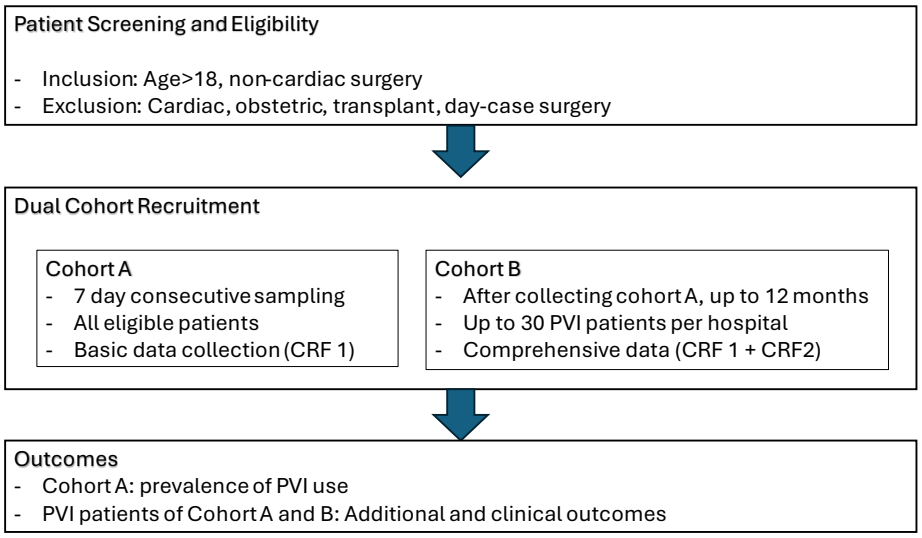
Cohort A include all patients admitted to participating hospitals during seven consecutive days with the following inclusion and exclusion criteria:

Inclusion criteria	Exclusion criteria
1. Undergoing surgery (may be planned or unplanned) 2. No plans for return home on the day of surgery. (No day case surgery) 3. Age ≥ 18 on day of surgery	1. Cardiac surgery 2. Obstetric surgery 3. Transplant surgery 4. Preoperatively long-term infusions of vasoactive drugs, such as epoprostenol (prostacyclin) 5. Mechanical circulatory support: ventricular assist device, intra-aortic balloon pump, artificial heart or similar 6. Already been enrolled in SQUEEZE

Cohort B include 30 sequential patients with **a single additional inclusion** criterion:

Inclusion criteria	Exclusion criteria
1. Postoperative Vasopressor Infusion (PVI) – as defined below.	1. Already been enrolled in SQUEEZE

Method S2: Flow chart for patient recruitment



Method S3: Definition of Postoperative Vasopressor Infusion (PVI)

Postoperative Vasopressor Infusion (PVI) is defined, for the purposes of this study, as the continuous intravenous infusion of a drug with a predominant vasoconstrictor effect (vasopressor). Therefore, repeated dosing of intravenous boluses is excluded, and infusion of a drug that is predominantly a positive inotrope (without concurrent vasopressor) is excluded. Additionally, we are not interested in vasopressor infusions that are used intra-operatively to counter the effect of general anaesthesia (or regional anaesthesia) and because this effect can take time to resolve, any infusion of vasopressor in the first hour following surgery is excluded – unless it continues after one hour following surgery. Infusions of vasopressor that are started more than 24 hours after the end of surgery is also excluded from this definition. Infusions of vasopressor that start before surgery will only be included if they also meet the above criteria.

Classification of vasoactive drugs, grouped according to predominant action. We accept that many drugs have mixed actions.

Vasopressor	Not predominantly vasopressor
• Dopamine • Epinephrine (Adrenaline) • Metaraminol • Norepinephrine (Noradrenaline) • Phenylephrine • Vasopressin or Terlipressin • Akrinor® • Angiotensin II	• Atropine • Dobutamine • Ephedrine • Etilefrine • Glycopyrronnium • Nitrates • Milrinone

Method S4: Case Report form

CRF 1					
0. Informed consent					
Is consent applicable in your centre ? *Mandatory unless the centre has an explicit and written exemption from IRB*	○ No ○ Yes		If yes date of consent:	DD-MMM-YY	
1. Patient Information					
1.1. Year of Birth *		1.2. Weight *		1.3. Height *	
1.4. Clinical Frailty Scale *	1 Very fit	○	6 Moderately Frail	○	
	2 Well	○	7 Severely Frail	○	
	3 Managing well	○	8 Very severely Frail	○	
	4 Vulnerabl :	○	9 Terminally	○	
	5 Mildly Fra il	○	10 Don't know	○	

Previous medical history *			
1.5. Coronary Artery Disease	○ No	○ Yes	
1.6. Cerebrovascular Disease	○ No	○ Yes	
1.7. Peripheral vascular Disease	○ No	○ Yes	
1.8. Atrial fibrillation	○ No	○ Yes	
1.9. Heart failure	○ No	○ Yes	
1.10. Hypertension	○ No	○ Yes	
1.11. Diabetes	○ No	○ Insulin dependent	○ Non-insulin dependent
1.12. Chronic liver disease	○ No	○ Yes	
1.13. Chronic respiratory disease	○ No	○ COPD	○ Other
1.14. Long-term steroid use	○ No	○ Yes	

1.15. Regular medications (tick all that apply, leave blank if not a regular medication)				
ACE inhibitor	If □ yes →	○ took day of surgery	○ omitted day of surgery	○ unknown
Alpha blocker	If □ yes →	○ took day of surgery	○ omitted day of surgery	○ unknown
Angiotensin receptor blocker	If □ yes →	○ took day of surgery	○ omitted day of surgery	○ unknown
Beta blocker	If □ yes →	○ took day of surgery	○ omitted day of surgery	○ unknown
Calcium channel blocker	If □ yes →	○ took day of surgery	○ omitted day of surgery	○ unknown
Diuretic	If □ yes →	○ took day of surgery	○ omitted day of surgery	○ unknown

	Fracture	○
	Bleeding	○
	Other	○

Regular NSAIDs	If □ yes →	○ took day of surgery	○ omitted day of surgery	○ unknown

Haemodynamics. Leave blank if not available		
Measurements in the past 6 months or at least 12h prior to the operating room, at rest.		
1.16. Systolic:	1.17 Diastolic:	1.18 Heart rate:
Reading immediately prior to induction of anaesthesia:		
1.19. Systolic:	1.20 Diastolic:	1.21 Heart rate:
Laboratory. Leave blank if not available, indicate which unit		
1.22. Creatinine:		mg/dl or µmol/L
1.23. Albumin		g/dL, g/L or µmol/L
1.24. Haemoglobin		g/dL, g/L or mmol/L

2. **Surgery**				
2.1 Reason for surgery *	Infection	○		
	Cancer	○		
2.2 Surgical procedure * (select single most appropriate)	Breast	○	Orthopaedic	○
	Gynaecological	○	Plastics / Cutaneous	○
	Head and neck	○	Upper gastro-intestinal	○
	Hepato-biliary	○	Neurological/spinal	○
	Kidney / urological	○	Vascular	○
	Lower gastro-intestinal	○	Other	○
2.3 Severity *	Minor	○		
	Intermediate	○		
	Major	○		

2.4. ASA-PS: *	ASA 1: Healthy person	○
	ASA 2: Mild systemic disease.	○
	ASA 3: Severe systemic disease	○
	ASA 4 Severe systemic disease that is a constant threat to life.	○
	ASA 5 A moribund person who is not expected to survive without the operation.	○
2.5. Urgency *	Urgent (includes emergency, expedited, urgent and immediate)	○
	Not urgent (includes planned/elective)	○

3. Operative	
3.1. Date of anaesthesia induction *	**DD-MMM-YY**
3.2. Time of anaesthesia induction *	**HH:MM**
3.3. Date of end of surgery *	**DD-MMM-YY**
3.4. Time of end of surgery *	**HH:MM**

3.5. Estimated blood loss (mL) *	<250 ○	251-1000 ○	1001-3000 ○	>3000 ○
3.6 /3.7 Lowest intraoperative blood pressure (paired) *	Systolic:		Diastolic:	
3.8. Anaesthesia: * (Tick all that apply)	Volatile			☐
	TIVA			☐
	Sedation without securing airway			☐
	Regional			☐
	Spinal			☐
	Epidural			☐
3.9. Airway *	Endotracheal tube			○
	Supraglottic airway			○
	O2 facemask or nasal cannula			○
3.10. Arterial line *	○ No		○ Yes	
3.11. Central venous line *	○ No		○ Yes	
3.12. Which Intra-operative vasoactive drugs [Tick all that apply]	Atropine			☐
	Akrinor ® (Cafedrin/Theodrenalin)			☐
	Dobutamine			☐
	Dopamine			☐
	Ephedrine			☐
	Epinephrine (Adrenaline)			☐
	Glycopyrronium			☐
	Metaraminol			☐
	Milrinone			☐
	Nitrates			☐
	Norepinephrine (Noradrenaline)			☐
	Phenylephrine			☐
	Vasopressin or Terlipressin			☐
3.13. Was the patient receiving a vasopressor infusion prior to anaesthesia? *			○ No	○ Yes
3.14. Fluids and blood products received during surgery:	Crystalloid			(mL)
	Colloid (starch-gelofusine-albumin)			(mL)
	Packed red blood cells			(mL)
	Fresh frozen plasma			(mL)

	Platelets	(mL)
	Whole blood or autotransfusion	(mL)

4. Post-operative
Following the end of surgery (within 24h):

4.1. Did the patient receive enteral vasopressors? (i.e. MIDODRINE) *	○ No	○ Yes
4.2. Did the patient receive **boluses** of vasopressors? *	○ No	○ Yes
4.3. Did the patient receive an **infusion** of vasopressors? *	○ No (Stop here)	○ Yes (Continue with 4.3.1 and 4.3.2)
4.3.1. **If yes**, did the infusion continue or start after 1 hour from the end of surgery?	○ No	○ **Yes**
4.3.2. **If Yes**, Did this infusion start within 24 hours from the end of surgery?	○ No	○ **Yes**

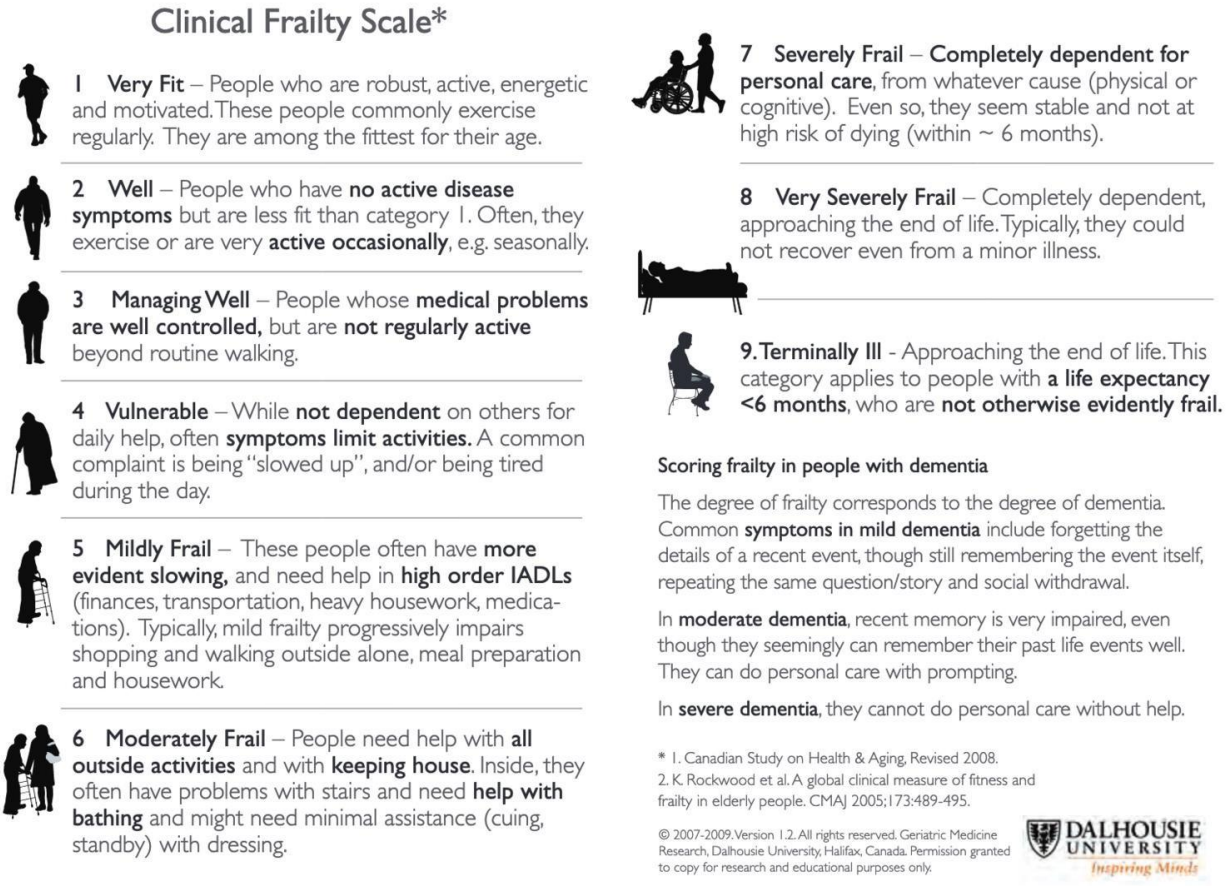
If "yes" on 4.3.1 and .4.3.2, complete CRF2

5. Outcomes

5.1. Ventilation: *	○ No	○ Invasive mechanical ventilation (IMV)	○ Non Invasive Ventilation (NIV)
5.2. Acute Myocardial Infarction *		○ No	○ Yes
5.3. New onset atrial fibrillation *		○ No	○ Yes
5.4. New onset other dysrhythmia *		○ No	○ Yes
5.5. Renal: Highest creatinine (within the first week) postoperatively			mg/dl or µmol/L indicate which unit
5.6. Renal replacement therapy *		○ No	○ Yes
5.7. Parenteral nutrition *		○ No	○ Yes

5.8. Antibiotics for a newly diagnosed infection *	○ No	○ Yes (complete □)	○ Unknown
	○ Skin or soft tissue ○ Respiratory ○ Urinary	○ Abdominal ○ Lines ○ Other	
5.9. Accordion classification of surgical complication *	○ None		
	○ Mild complication		
	○ Moderate complication		
	○ Severe complication		
	○ Death		

5.10. Date of hospital discharge **or** date of intrahospital death: *		DD-MMM-YY
5.11. Stayed an inpatient for more than 30 days? *	○ No	○ Yes



2.3. Severity of surgery:

Minor: Procedure < 30 minutes. Examples: arthroscopy without intervention, removal of cutaneous tumour, proctology procedures, biopsy or excision biopsy of small lesions, etc

Intermediate: Procedure performed in a dedicated operating room that may pose the risk of significant complications or tissue injury. Examples: laparoscopic cholecystectomy, arthroscopy with intervention, bilateral varicose vein removal, tonsillectomy, inguinal hernia repair, breast lump resection, haemorrhoidectomy, appendicectomy, partial thyroidectomy, cataract surgery, uvuloplasty, minimally invasive repair of vaginal prolapse, vaginal hysterectomy, fixation of mandibular fracture, etc

Major: Performed in a dedicated operating room and is expected to last more than 90 minutes. Examples: major gut resection, major joint replacement, mastectomy, extensive head and neck tumour resection, abdominal aortic aneurysm repair, major vascular bypass procedure, procedures involving free flap to repair tissue defect, amputation, total thyroidectomy, cystectomy, trans-urethral resection of prostate, resection of liver tumour, carotid endarterectomy, nephrectomy, total abdominal hysterectomy, spinal discectomy, etc

At one hour after the completion of surgery, is the patient:		
6.2. Receiving continuous infusion of neuraxial anaesthesia/analgesia i.e. epidural infusion *	○ No	○ Yes

CRF 2		
Postoperative vasopressor infusion		
6.1. Did this patient have an **infusion** of vasopressors that was either started or continued at least 1 hour after surgery: *	○ No (If 'No' then please do not complete any further)	○ Yes
6.3. Still receiving a sedative infusion *	○ No	○ Yes
6.4. Still has an airway in place (endotracheal tube, tracheostomy or supraglottic airway) *	○ No	○ Yes

6.5. How was it assessed that this patient should receive a vasopressor infusion? *	
○ Already receiving a vasopressor infusion and attempts to lower the infusion rate produced unacceptable hypotension, OR	
○ It was decided that the patient would no longer benefit from further attempts to increase the cardiac output through administration of IV fluids and the blood pressure was unacceptably low. This was on the basis of:	
	○ A. Clinical assessment alone (vital signs-examination-lab results)
	○ B. Clinical assessment AND a measurement of preload responsiveness using cardiac output monitoring (or some direct surrogate of)
	○ C. Clinical assessment AND a measurement of preload responsiveness using echocardiography
	○ D. Clinical assessment AND a previously established maximum for IV fluid administration has been met i.e. 2L or 20ml/kg etc...
	○ E. other:

7.1. SOFA score within 24 hours after surgery * [0-24]		(Use FAQ as required) To calculate SOFA score: https://clincalc.com/IcuMortality/SOFA.aspx

7.2 - 7.8 MAP target (complete only if MAP is specified)							
	Day 0	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6
MAP							

7.10 – 7.16 **HIGHEST** blood pressure for each day (paired) On Postoperative unit/ICU only. Leave blank if not available.							
	Day 0	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6
Systolic							
Diastolic							

7.18 – 7.24 **LOWEST** blood pressure during the day (paired)
On Postoperative unit/ICU only. Leave blank if not available.

	Day 0	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6
Systolic							
Diastolic							

7.26 – 7.32 **Vasoactive drug infusion, tick if applicable**

	Day 0	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6
Noradrenaline	□	□	□	□	□	□	□
Angiotensin II	□	□	□	□	□	□	□
Dobutamine	□	□	□	□	□	□	□
Dopamine	□	□	□	□	□	□	□
Epinephrine (Adrenaline)	□	□	□	□	□	□	□
Metaraminol	□	□	□	□	□	□	□
Milrinone	□	□	□	□	□	□	□
Phenylephrine	□	□	□	□	□	□	□
Terlipressin	□	□	□	□	□	□	□
Vasopressin	□	□	□	□	□	□	□

Total number of days: *	
7.33. receipt of ventilation (invasive or NIV)	
7.34. receipt of vasopressor infusion	
7.35. receipt of parenteral nutrition	
7.36. receipt of renal replacement therapy	
7.37. duration of stay in ICU/postoperative unit	

COVID

7.38. Did the patient have any testing for SARS-CoV2? *	○ No	○ Yes **If yes, answer below**	○ Unknown

7.38.1. **If Yes -** did the patient test positive in the perioperative period?	○ No	○ Yes

Method S5: Definitions of variables and instructions to investigators

1.1. Year of birth (mandatory)

It is not necessary for us to know a date of birth, just the year of birth.

1.2./1.3. Weight and Height (mandatory)

Estimated if necessary.

1.4. Clinical Frailty Scale

This is easiest to do after reading clinical notes and having a brief chat with the patient about their lives. It does not need to be done by a specialist like a geriatrician or occupational therapist. If it is impossible to find out this information then there is an option for "don't know".

1.5.-1.15. Previous medical history (mandatory)

A series of nine Yes/No questions about co-morbid conditions. We are not providing definitions these can be previously confirmed diagnoses or concluded from available data.

Chronic liver disease should include conditions characterised by impairment of liver function, or a significant predisposition to failure of liver function. Cirrhosis of any extent would be a 'Yes'. A single hepatic metastasis would be 'No', whereas a large number of metastases without significant remaining liver would be a 'Yes'.

COPD is Chronic Obstructive Pulmonary Disease and includes emphysema and chronic bronchitis.

Eight questions about chronic medication use, for seven of them if they are selected then a further question is asked to determine if the medication was taken on the day of surgery or not.

The medication questions are about drug classes. If you're unsure of the class of the medications the patient is taking, then please google it! A low dose aspirin (75mg, for example) does not count as an NSAID. Inhaled corticosteroids do not count as long-term steroid use.

Ideally we'd like to know if the medication was taken on the day of surgery but if it's impossible to know this then it can be indicated.

1.16.-1.21. Haemodynamics

1.16-1.18. Recent blood pressure and heart rate, if available. If not available, leave blank.

1.19.-1.21. Blood pressure and heart rate immediately before anaesthesia, should be present in most cases.

1.22.-1.24. Laboratory

Creatinine, Albumin and Haemoglobin concentration, if available. Use values closest to time of anaesthesia.

2.1.-2.2 Reason for surgery and category of surgical procedure.

Please choose the one that fits best.

We will analyse the data using the reason for surgery and the type of surgery. Please do not avoid selecting a reason or category in order to enter text into a free text box or discrepancy note. It makes a lot of work for the team and as we won't be using the entered data it's a waste of your time!

For example, for laparoscopic cholecystectomy being done for episodes of cholecystitis – please select "infection" and "upper GI surgery". Do not select "other" and "other" in order to tell us that it was a laparoscopic cholecystectomy.

2.3. Severity of surgery (minor/intermediate/major).

Please choose the one that fits best and use common sense.

- Minor: Procedure of less than 30 minutes duration performed in a dedicated operating room which would often involve extremities or body surface or brief diagnostic and therapeutic procedures. Examples include: arthroscopy without intervention, removal of small cutaneous tumour, diagnostic proctology procedures, biopsy or excision biopsy of small lesions, etc
- Intermediate: More prolonged or complex procedure performed in a dedicated operating room that may pose the risk of significant complications or tissue injury. Examples include: laparoscopic cholecystectomy, arthroscopy with intervention, bilateral varicose vein removal, tonsillectomy, inguinal hernia repair, breast lump resection, haemorrhoidectomy, appendicectomy, partial thyroidectomy, cataract surgery, uvuloplasty, minimally invasive repair of vaginal prolapse, vaginal hysterectomy, tendon repair of hand, fixation of mandibular fracture, etc
- Major: Any surgical procedure that requires anaesthesia, performed in a dedicated operating room and is expected to last more than 90 minutes. Examples include: major gut resection, major joint replacement, mastectomy, extensive head and neck tumour resection, abdominal aortic aneurysm repair, major vascular bypass procedure, procedures involving free flap to repair tissue defect, amputation, total thyroidectomy, cystectomy, trans-urethral resection of prostate, resection of liver tumour, carotid endarterectomy, nephrectomy, total abdominal hysterectomy, spinal discectomy, etc

2.4. ASA-PS

'American Society of Anaesthesiology Physical status' use the value attributed by the anaesthetist.
We do not include ASA VI in our list since organ donors are not included in SQUEEZE.

ASA grade	
I	Normal healthy patient
II	Patient with mild systemic disease
III	Patient with severe systemic disease
IV	Patient with severe systemic disease that is constant threat to life
V	Moribund patient who is not expected to survive without the operation
VI	Declared brain-dead patient whose organs are being removed for donor purposes

2.5. Urgency

Urgent (includes emergency, expedited, urgent and immediate)
Non-urgent (also known as planned or elective)

3.1.-3.2. Date and time of anaesthesia induction (mandatory)

3.3.-3.4. Date and time of end of the surgery (mandatory)

Different hospitals use different definitions for start and finish of anaesthesia and surgery and we will not force you to use one single definition – please use whatever your hospital uses. The date is necessary for the unusual occurrences of surgeries that span one day to the next.

3.5. Estimated blood loss (mandatory)

3.6. Lowest systolic and lowest diastolic (mandatory)

Values taken at the same time, selected based on the systolic. For example:

	09:05	09:10	09:15	09:20	09:25
Systolic (SBP)	120	100	90	85	92
Diastolic (DBP)	80	70	60	65	70

The lowest SBP is 85, at this time the diastolic is 65 – so these are the values we want.

We do not want SBP 85 and DBP of 60 as these values were not taken at the same time.

3.8. Anaesthesia

More than one type can be selected. TIVA refers to total intravenous anaesthesia but this is not restricted to use of specific pumps or dosing systems.

We are specifically interested in maintenance of anaesthesia not induction. For example, if the induction of anaesthesia is volatile and then TIVA is used for maintenance – please just select TIVA. If induction is with IV and then volatile is used for maintenance – please just select volatile.

Details about the epidural including level of insertion, the height of the block and the drugs given are not required. Equally, details about any spinal are not required.

3.9. Airway

Please check the most appropriate one. More than one can be selected.

3.10. Arterial line

Is there a cannula / catheter in a peripheral artery for the purposes of monitoring?

3.11. Central Venous Line

Is there a cannula / catheter in a central vein? It may be newly sited or already present for monitoring or therapy.

Please exclude peripherally inserted central cannulae (PICC), midlines or long term central venous lines for dialysis, parenteral nutrition or chemotherapy unless they are being used perioperatively for vasopressors.

3.12. Intra-operative drugs via infusion or bolus

This is a list of vasoactive medications that the patient receives during surgery. The dosing is not recorded. Please check all that applies.

Please note that this only relates to drugs given INTRA-operatively.

3.13. Was the patient receiving a vasopressor infusion prior to anaesthesia?

3.14. Fluids and blood products received during surgery

For each of six types of fluids, please enter the volume in millilitres. If the records only indicate how many units of a product, please estimate the volumes based on your local experience.

4. Five questions about post-operative vasopressors:

4.1 Yes/No question about post-operative receipt of enteral vasopressors.

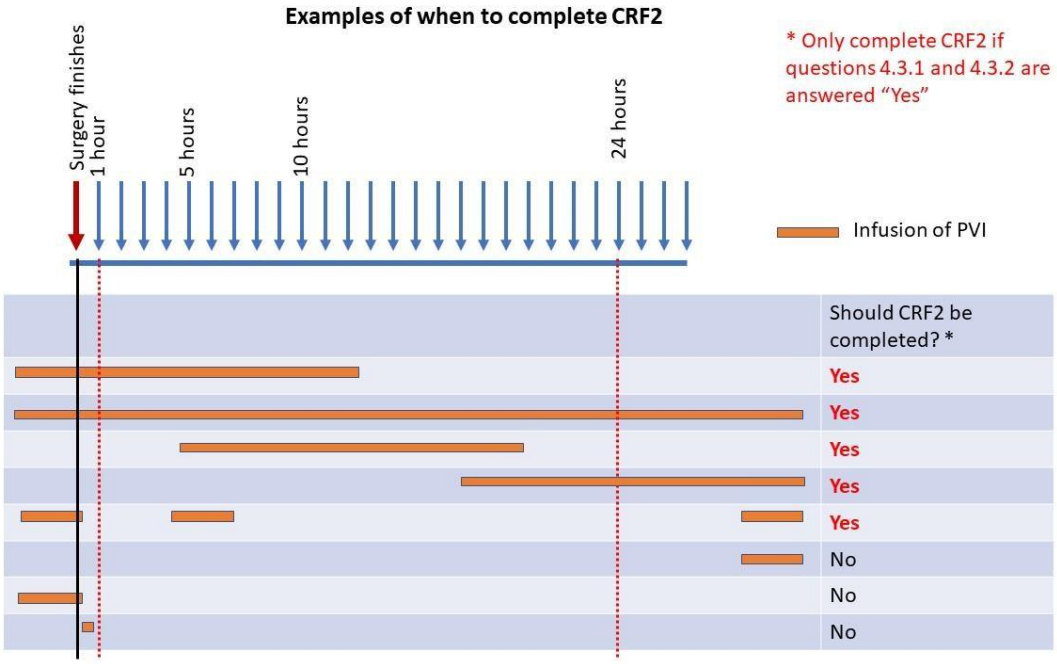
4.1 Yes/No question about **post-operative** receipt of **boluses** of vasopressors (different to earlier question about intra-operative).

4.3 Yes/No question about **post-operative** receipt of **infusions** of vasopressors (different to earlier question about intra-operative).

4.1.1 Yes/No question about if a post-operative infusion of vasopressors continued for more than 1 hour after the end of surgery.

4.1.2 Yes/No question about if a post-operative infusion of vasopressors started within 24 hours of the end of surgery.

These questions are to determine if the patient in question fulfils the criteria for PVI, which would mean that additional questions (CRF2) need to be completed.



From the protocol:

Definition: Postoperative Vasopressor Infusion (PVI) is defined, for the purposes of this study, as the continuous intravenous infusion of a drug with a predominant vasoconstrictor effect (vasopressor). Therefore, repeated dosing of intravenous boluses is excluded, and infusion of a drug that is predominantly a positive inotrope (without concurrent vasopressor) is excluded. Additionally, we are not interested in vasopressor infusions that are used intra-operatively to counter the effect of general anaesthesia (or regional anaesthesia) and because this effect can take time to resolve, any infusion of vasopressor in the first hour following surgery is excluded – unless it continues after one hour following surgery. Infusions of vasopressor that are started more than 24 hours after the end of surgery is also excluded from this definition. Infusions of vasopressor that start before surgery will only be included if they also meet the above criteria.

5.1 . Intrahospital, post-operative complications

<u>During the patient's 30 days following the date of surgery:</u>

- Ventilation: No, NIV, IMV.

If the patient received invasive mechanical ventilation (IMV, via endotracheal tube or tracheostomy) that started after the end of surgery, then please select this. If the patient *continued to receive* invasive mechanical ventilation that *started prior* to surgery, then please do NOT select this.

On the day of surgery there will often have been invasive mechanical ventilation and if that is completed (i.e. the patient was extubated) within 4 hours of the end of surgery then this would not count as a day of IMV. If IMV continues for more than 4 hours after the end of surgery then this should count as a day of postoperative IMV.

If the patient received non-invasive ventilation (NIV, including BiPAP and CPAP) via a facemask (any duration) then please select this. For the purposes of this study high flow oxygen delivered via nasal cannulae is not considered NIV.

If neither IMV nor NIV are provided then please select No.

5.2 Acute Myocardial Infarction: No/ Yes

If the clinicians believe that the patient has an acute Myocardial Infarction then please select Yes. If you're not sure (is it just a troponin rise?) then please ask your principal investigator to adjudicate.

5.3 New onset Atrial Fibrillation: No/ Yes

If the clinicians believe that the patient has atrial fibrillation that was not present prior to the operation (i.e. no history of chronic or paroxysmal AF) and is more than briefly present, then please select yes.

5.4. New onset of other dysrhythmia: No/ Yes

If the clinicians believe that patient has any new dysrhythmia (includes SVT, VF and VT) that was not present prior to the operation and is more than briefly present, then please select yes.

5.5. Highest creatinine within the first week.

This will allow us to determine if the patient met criteria for acute kidney injury (AKI). Leave blank if you do not have measured creatinine postoperatively.

5.6 . Renal replacement therapy: No/Yes.

If the patient received at least one episode of renal replacement therapy (including haemodialysis, haemofiltration, haemodiafiltration, peritoneal dialysis) and this isn't a usual occurrence for them (i.e. they don't usually require any form of renal replacement therapy, RRT) then please select Yes. It is not important if they received the RRT intermittently or continuously.

If they have chronic RRT or did not receive any RRT then please select No.

5.7 . Parenteral nutrition: No/Yes.

If the patient received at least one bag of parenteral nutrition (PN) and this isn't a usual occurrence for them (i.e. they don't have chronic intestinal failure) then please select Yes. If they have chronic intestinal failure or did not receive any PN then please select No.

Parenteral nutrition does not include simple dextrose infusions.

5.8. Antibiotics for a newly diagnosed infection:

If the clinicians believe that patient has an infection and they have started some antibiotics then please select yes. A further selection will appear and please select the most appropriate of: skin (or soft tissue), respiratory, urinary, abdominal, lines, other. During their postoperative recovery they may have multiple infections – please select all that apply.

5.9. Severity of surgical complication

This is the Accordion classification of surgical complication. Choose one of the following:

1. None
2. Mild complication: Requires only minor invasive procedures that can be done at the bedside such as insertion of intravenous lines, urinary catheters, and nasogastric tubes, and drainage of wound infections. Physiotherapy and the following drugs are allowed-antiemetics, antipyretics, analgesics, diuretics, electrolytes, and physiotherapy.
3. Moderate complication: Requires pharmacologic treatment with drugs other than such allowed for minor complications, for instance antibiotics. Blood transfusions and total parenteral nutrition are also included.
4. Severe complication: All complications requiring endoscopic or interventional radiologic procedures or re-operation as well as complications resulting in failure of one or more organ systems.
5. Death

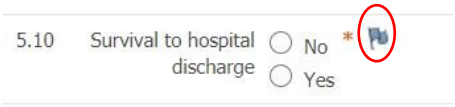
5.10. Survival to hospital discharge: Yes or No (mandatory)

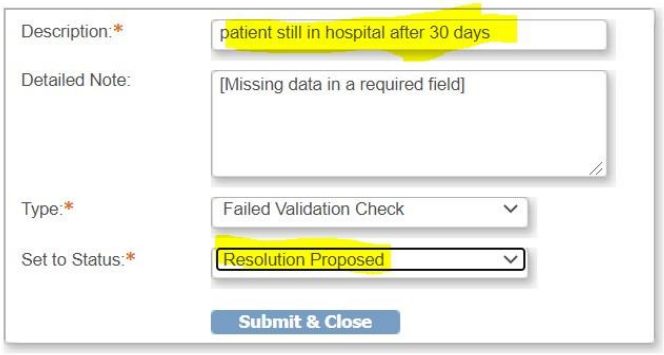
All patients are to be followed up either until discharge or for a maximum of 30 days if they stay in hospital. For the item 5.10. Survival to hospital discharge:

- If the answer is Yes the date of discharge is shown
- If the answer is No the date of death is shown

If the patient is still in the hospital you do not have additional option to indicate this status. In this case, please use the flag to enter a note and ignore question 5.10, and complete item 5.11 and save.

How to use the flag on item 5.10 :





Please monitor the patient's status until day 30 or hospital discharge. If they are alive at day 30 but die on day 31 (or later) then, for the purposes of this CRF and study, their 30-day mortality status is alive.

6.1.-6.5. The first question aims to double-check that this form is being completed only in appropriate patients. (mandatory)

Then there are three questions that aim to further characterise the patient with PVI: (mandatory)

- Are they receiving a continuous infusion of neuraxial anaesthesia/analgesia i.e. epidural infusion: Yes/No.
- Are they receiving a continuous infusion of sedative drug i.e. propofol or midazolam or similar: Yes/No.
- Does the patient have an airway in place (endotracheal tube, tracheostomy or supraglottic airway): Yes/No.

6.6. HOW was it determined that the patient should be receiving PVI. (Mandatory)
The investigator needs to determine how the clinical team decided to use a PVI. There is a choice of two options:

Either "Already receiving a vasopressor infusion and attempts to lower the infusion rate produced unacceptable hypotension"

Or "It was decided that the patient would no longer benefit from further attempts to increase the cardiac output through administration of IV fluids and the blood pressure was unacceptably low."

If the second choice is selected that the investigator must choose an option that helps us understand why this was decided, one of the following options must be chosen:

- Clinical assessment alone (vital signs-examination-lab results)
- Clinical assessment AND a measurement of preload responsiveness using cardiac output monitoring (or some direct surrogate of)
- Clinical assessment AND a measurement of preload responsiveness using echocardiography

- Clinical assessment AND a previously established maximum for IV fluid administration has been met i.e. 2L or 20ml/kg etc...
- other
- unknown

It may be difficult to determine this solely from the documentation and we would like to avoid too many patients where “other” or “unknown” is selected as it’s not useful information. Please talk to your clinicians and politely enquire which of the options is most suitable.

7.1 SOFA score

This is the sequential organ failure score. It is widely used in critical care and can simply be determined. There is a link to an online calculator.

We are interested in the *highest* score in the first 24 hours after surgery.

Calculating the SOFA score

Healthy person scores 0

Maximally sick person scores 24

Respiratory

If an Arterial Blood Gas is available then please use the values taken at the same time for PaO2 (partial pressure of oxygen in arterial blood) and FiO2 (fraction of inspired oxygen 0.21 = 21% = air)

PaO_2/FiO_2 (kPa)	SOFA score
≥ 53.3	0
< 53.3	+1
< 40	+2
< 26.7 **and** mechanically ventilated	+3
< 13.3 **and** mechanically ventilated	+4

If Arterial Blood gases have NOT been done in the 6 hours prior to enrolment, then use the values taken at the same time for SpO2 (Saturations of oxygen in arterial blood, from pulse oximetry) and FiO2 (fraction of inspired oxygen 0.21 = 21% = air)

SpO_2/FiO_2	SOFA score
≥ 512	0
< 512	+1
< 357	+2
< 214	+3
< 89	+4

Reference: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3776410/

Nervous system

Glasgow coma scale	SOFA score
15	0
13–14 (delirium)	+1

10–12 (obtunded)	+2
6–9 (semi-comatose)	+3
< 6 (comatose)	+4

Cardiovascular

If MAP hasn't been recorded or charted by Systolic and Diastolic have been, then calculate the MAP using this formula: MAP = 1/3 (SBP – DBP) + DBP norepinephrine = noradrenaline

Mean arterial pressure OR administration of vasopressors required	SOFA score
MAP ≥ 70 mmHg	0
MAP < 70 mmHg	+1
dopamine ≤ 5 µg/kg/min or dobutamine (any dose)	+2
dopamine > 5 µg/kg/min OR epinephrine ≤ 0.1 µg/kg/min OR norepinephrine ≤ 0.1 µg/kg/min	+3
dopamine > 15 µg/kg/min OR epinephrine > 0.1 µg/kg/min OR norepinephrine > 0.1 µg/kg/min	+4

NB For converting different vasopressors into norepinephrine equivalents (all in mcg/kg/min, except vasopressin in units/min): NE = norepinephrine + epinephrine + phenylephrine/10 + dopamine/100 + metaraminol/8 + vasopressin*2.5 + angiotensin II*10 (REF https://doi.org/10.1016/j.jcrc.2020.11.002)

Liver

Bilirubin µmol/L	SOFA score
< 20, or not measured	0
20-32	+1
33-101	+2
102-204	+3
> 204	+4

Coagulation

Platelets $\times 10^3/\mu l$	SOFA score
≥ 150, or not measured	0
< 150	+1
< 100	+2
< 50	+3
< 20	+4

Renal

Creatinine µmol/L (or urine output)	SOFA score
< 110	0
110-170	+1

171-299	+2
300-440 or < 500 ml/d	+3
> 440 or < 200 ml/d	+4

7.2 -7.8 MAP target

Typically, in patients receiving PVI there is a target blood pressure and most commonly it is a target for the mean arterial pressure (MAP).

We are interested in the MAP target for each of day 0, 1, 2, 3, 4, 5 and 6.

If the MAP target is documented as a range, i.e. 65-70mmHg then please use the lower number (65mmHg in this case).

If it is unknown then this can be indicated.

7.9-7.24 Blood pressure

For each day we would you to identify the highest and the lowest paired BP (systolic and diastolic) during that calendar day. Please leave blank if you have no available data.

7.25-7.32 Vasoactive drug infusions = vasopressors and/or inotropes

For each day we would you to indicate if the patient is receiving any amount of each of the vasoactive drugs as an infusion.

7.33-7.37 Outcomes

In the first 30 days following surgery, how many days (in total, not necessarily serially) was there:

1. Receipt of ventilation (IMV or NIV)
2. Vasopressor infusion
3. Parenteral nutrition
4. Renal replacement therapy
5. Time spent on the ICU/HDU/PACU.

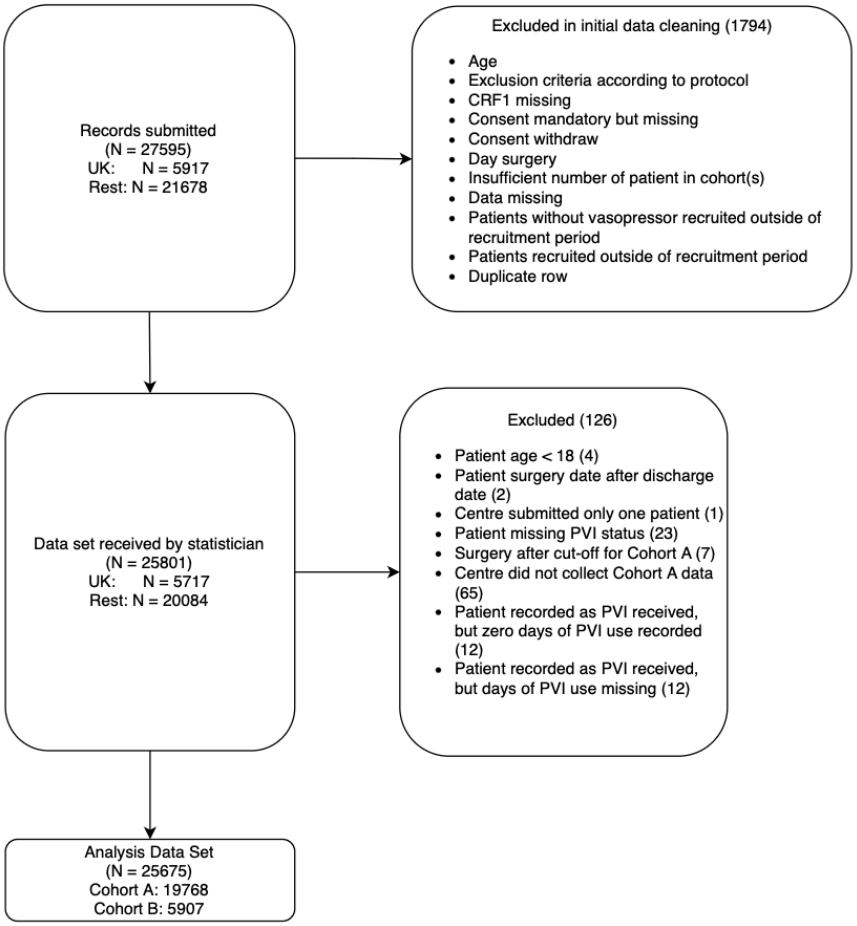
The definitions for these are unchanged from earlier.

7.38 COVID questions

Testing for the presence of virus, **not** antibodies to the virus.

The perioperative period is considered to be one week before surgery and anytime during the hospital stay after.

Method S6: Squeeze analysis data set selection



Flow diagram of the data set selection.

Method S7: Statistical data analysis: methodology

A statistical analysis plan (SAP) was published alongside the study protocol prior to completion of data collection. The analysis that was carried out deviates from the SAP in some respects. These deviations are listed, summarized and justified in detail in the Table below. There were two broad reasons for these deviations:

1. Initial exploratory analysis of the data revealed considerable variation in rates of PVI use between countries and between hospitals in the same country. The modelling of this variation became a more important aim of the analysis than had been envisaged during the planning of the study. In particular, it was important to establish whether patient characteristics could explain some or all of the variation in PVI use rates between countries and hospitals. Thus it was decided, contrary to the SAP, to use only Cohort A in analyses relating characteristics of the patient and surgical procedure to PVI use as an outcome. Inclusion of Cohort B in this analysis would have made it impossible to derive estimates of between-country or between-hospital variation, as all patients in Cohort B were in receipt of PVI by definition.
2. We encountered considerable sparsity in the data: 67 out of 228 hospitals reported no patient with PVI use in Cohort A. This made complex three-level models (patients clustered within hospitals, clustered within countries) impossible to estimate using restricted maximum likelihood or similar methods. We instead adopted a Bayesian modelling strategy, using weakly informative priors to aid convergence. This meant that some complex procedures anticipated in the SAP could not feasibly be carried out, including adapted lasso methods and fractional polynomials. We also chose to model ordinal outcomes as binary to aid interpretation of relatively complex results.

The text that follows explains the statistical methods used in more detail than the manuscript.

Table: Deviations from the Statistical Analysis Plan (SAP)

Section in the SAP	Deviation	Reason
Aim 2	Only Cohort A was used for this analysis.	Analysis under Aim 1 revealed considerable between-country variation and resulted in all countries being used for analysis. This led to a shift in focus on estimating between-country variation and examining variables that may account for it. This analysis would have been biased if Cohort B had been included, since countries differed considerably in the number of patients they submitted for Cohort B.
Aim 2	Lasso shrinkage was not used	The decision to model between-country variation necessitated a three-level model (patients within hospitals within countries) deployed for Aim 2, which was made more complicated by the presence of zeroes (hospitals and countries with no PVI use), and hence necessitated Bayesian estimation for model convergence, as well as multiple imputation of missing values. The model complexity was thus already high, and a decision was made not to add to it by additionally employing lasso shrinkage.
Aim 2	Stratification by type of anaesthesia not done.	Planned at a later stage.
Aim 2	Fractional polynomials not used.	Age was the only predictor modelled as a continuous variable. There is no standard routine for using fractional polynomials in combination with Bayesian models. Exploration suggested that a simple linear + square transformation modelled the relationship well.
Aim 2	Changes in the list of predictors (Appendix A in the SAP)	Some intraoperative covariates were mistakenly listed under "pre-operative predictors". Some covariates were added after consideration (e.g. intraoperative MAP). The preoperative covariates that were used can be seen in Table S5. The intraoperative covariates used can be seen in Table S6.
Aim 3	Ordered outcomes were modelled as binary instead.	Since models were relatively complex analytically, and the analyses are essentially exploratory, a simpler approach was preferred.
Aim 4	Information on vasopressor dosage was only collected in the UK and thus not analysed for this manuscript.	Half of national coordinators said this would be too onerous to collect.
Aim 6	Adaptive lasso was not used.	The model complexity (Bayesian three-level models) was high, and a decision was made not to add to it by additionally employing lasso shrinkage.

Modelling PVI use

Models of our primary outcome, PVI use, were estimated on Cohort A only. To model the variation of PVI use across hospitals and countries in the presence of sparsity (no observed PVI use in some hospitals and some countries), we used Bayesian mixed effects logistic regression with random intercepts for hospitals and countries. We used a weakly informative prior centred on our prior estimate of 2 % for the fixed intercept [Normal(-3.89, 100)] and non-informative priors [Cauchy(0, 10)] for the random effect standard deviations. These priors are so weak as to have essentially no effect on the point estimates or credible intervals, but they aid convergence. We call this Model 1. Estimates of the random effect variances were transformed into median odds ratios. To account for regression to the mean, country- and hospital-specific estimates of PVI use were derived using best linear unbiased estimators.

As outlined in the SAP, the distribution of country-level PVI use was visualized graphically (see Figure 1 in the manuscript, and Figures S1, S2, and S3 in the appendix) and discussed within the team, with respect to the decision whether to analyse data from high-income countries separately. There was some association of country income level and PVI use, whereby higher income in a country was associated with higher rates of PVI use. However, there was no clear-cut division of PVI use rates by country income. We thus decided to analyse data from all countries in all subsequent analyses.

To explore whether characteristics of the patient and surgical procedure could explain some of the between-country and between-hospital variation, we extended Model 1 by using a prespecified set of pre-operative variables as predictors, and estimating their fixed effects (using weakly informative default priors; Model 2). Finally, in Model 3, we added a set of prespecified intraoperative variables to Model 2. Models 2 and 3 also had the further purpose to explore associations of patient and procedure characteristics with PVI use. In both Models 2 and 3, we used the same priors for the intercept and random effect standard deviations as in Model 1. We used flat priors for the coefficients of all covariates.

Some covariates used in Models 2 & 3 had missing observations. The percentages of cases with at least one missing value were 27 % and 28 % for Models 2 and 3, respectively. We used multiple imputation for missing values to impute 30 data sets. The imputation model was the same for both Model 2 and Model 3, and contained all pre-operative variables, all intraoperative variables, and (as auxiliary variables) all outcomes. Models were estimated on all 30 data sets, with four Monte Carlo chains per data set. Point estimates of parameters were derived as the means of the posterior distribution, while the 2.5th and 97.5th percentiles were taken as the limits of 95 % credible intervals.

Exploring patient outcomes

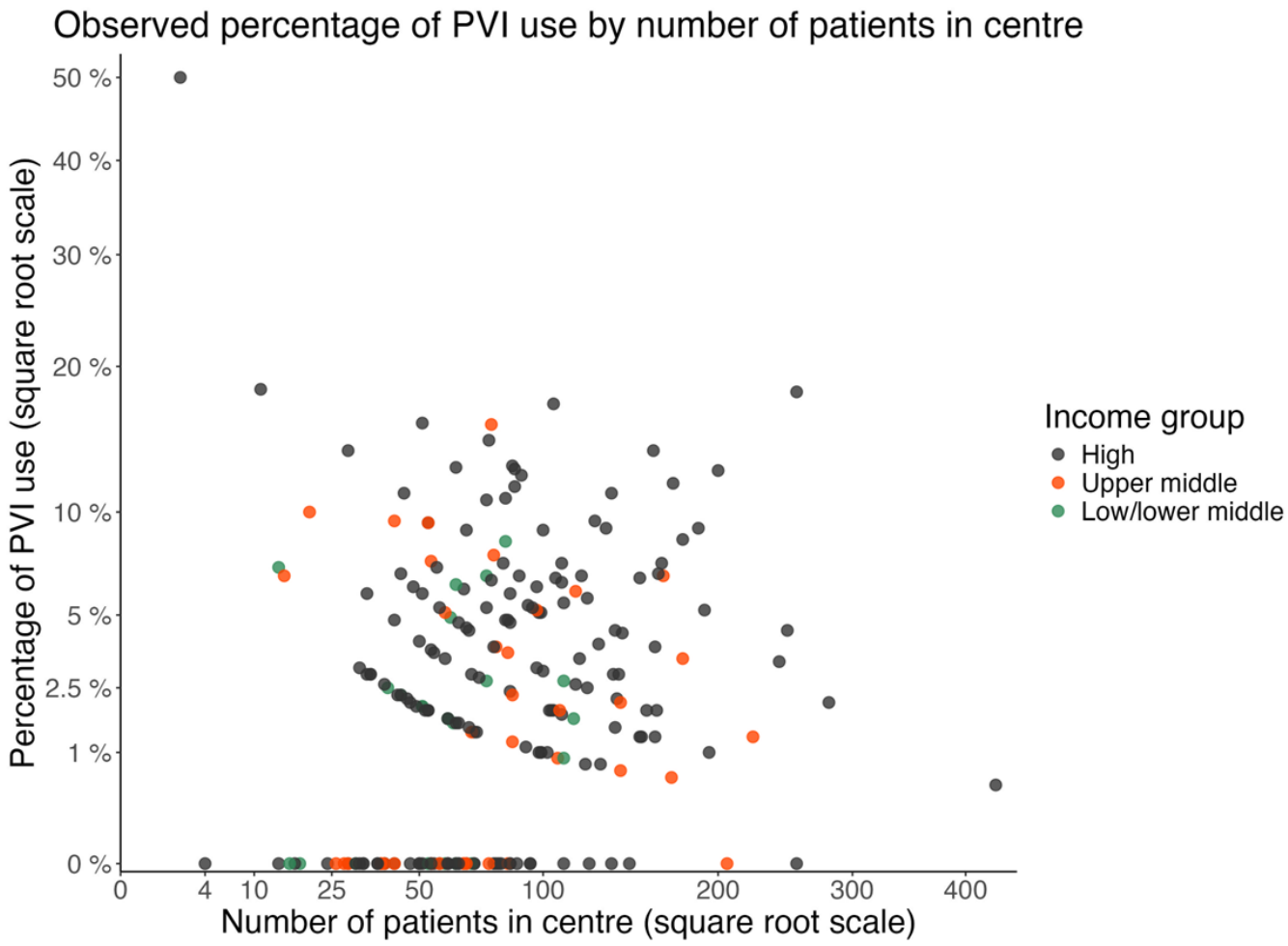
To explore patient outcomes associated with PVI use, we combined data from cohorts A and B. We conducted a comparison of Cohort B with PVI recipients in Cohort A to gauge the extent of potential selection bias. This analysis is presented in supplementary table S1. In summary, compared to PVI recipients in Cohort A, Cohort B were more likely to come from the UK, to have urgent surgery, to have major surgery, to have an intraoperative MAP < 90 mmHg, and to have an adverse outcome (Ventilation, Renal replacement therapy, Acute kidney injury, Parenteral nutrition, Atrial fibrillation, Antibiotics, Mortality). Cohort B also had longer median length of stay than PVI recipients in Cohort A.

We modelled associations between PVI use and outcomes using Bayesian multilevel logistic regression, with random intercepts for centre and country and adjusting for pre-operative variables. Bayesian multilevel quantile regression was used to model length of stay. A binary indicator for Cohort (A or B) was added to these models to adjust for residual selection bias. We used flat priors for all covariates, including for PVI use.

To explore the relationship between exposure to vasopressors (both intra- and postoperatively), we grouped patients from both cohorts into five groups: no vasopressors, intraoperative vasopressors only, boluses and enteral vasopressors (but not PVI), short-term PVI (1-2 days post-operatively) and prolonged PVI (3 days or more). We descriptively compared percentages of adverse outcomes, as well as the distribution of length of stay, across these five groups.

Figures

Figure S1: Observed percentage of PVI by number of patients per hospital.

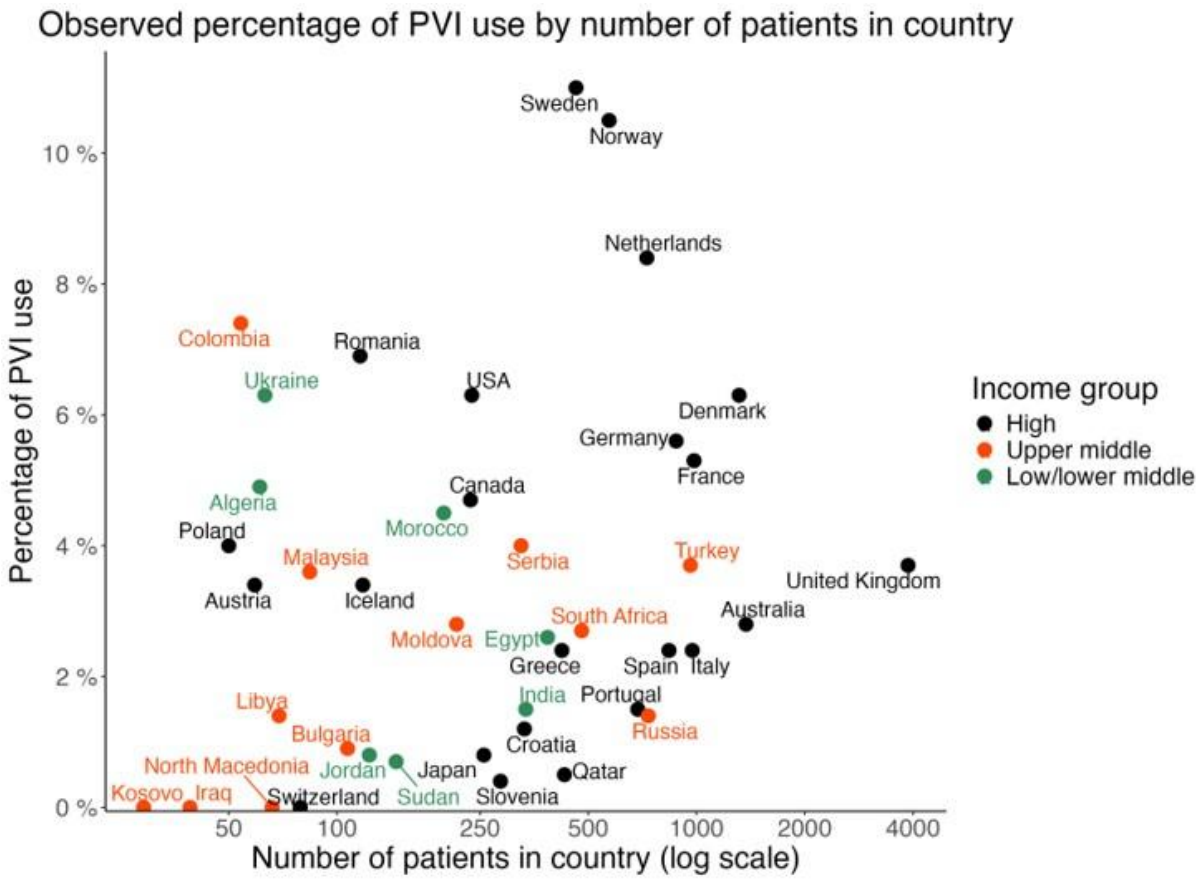


Observed percentage of Postoperative Vasopressor Infusion (PVI) by number of patients in hospital.

The scatter plot demonstrates the relationship between hospital size (x-axis) and the percentage of PVI use (y-axis), both variables presented on square root scales. Income groups defined by the 2023 World Bank Classification System.

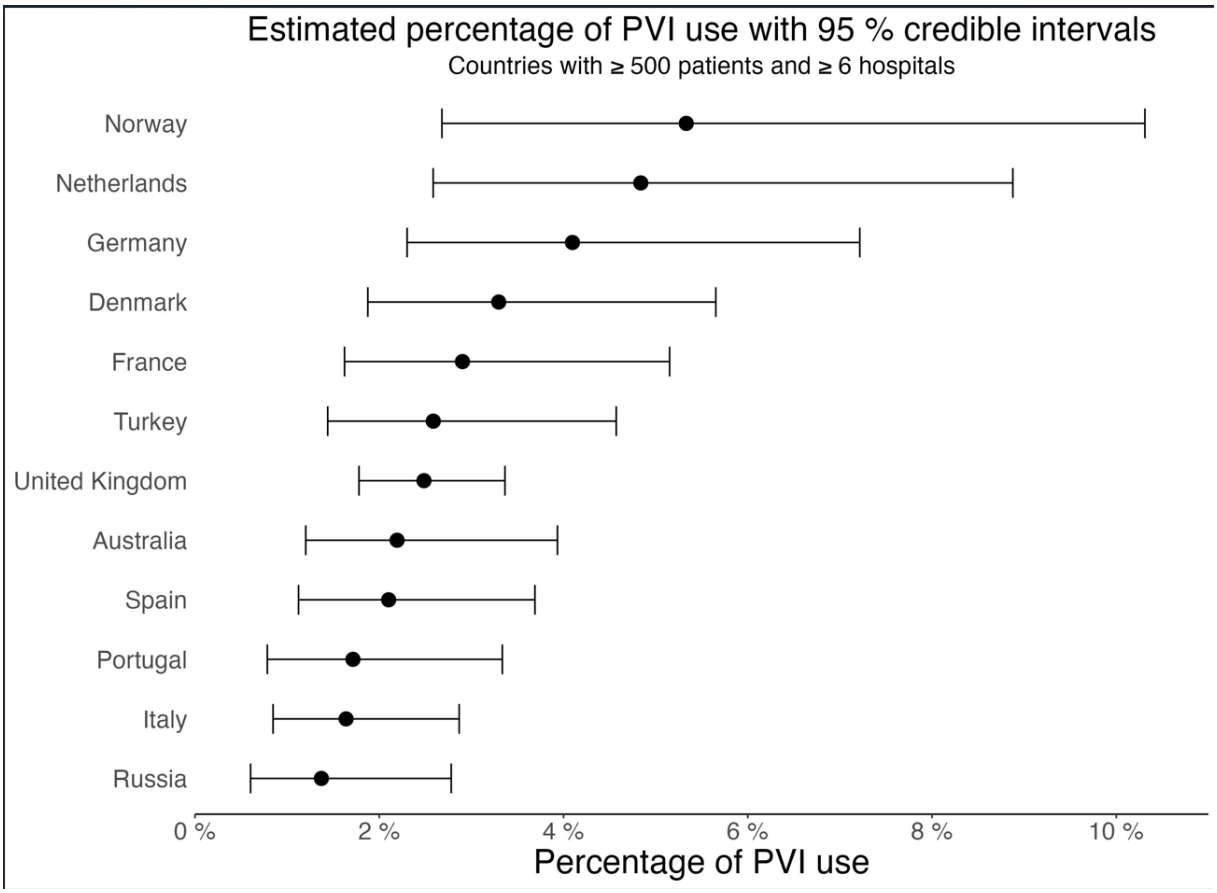
The curvilinear patterns observed in the data distribution reflect the nature of the percentage calculations in smaller hospitals, where the possible values for PVI use are constrained by the denominator. For instance, in a center with 50 patients, PVI use can only occur in 2% increments (0%, 2%, 4%, etc.), as fractional patients are not possible.

Figure S2: Observed percentage of PVI use by number of patients in country



Observed percentage of PVI use by number of patients in country in Cohort A (n = 19,768). Income groups were defined using the 2023 World Bank Classification System.

Figure S3: Estimated percentage of PVI use in countries with ≥500 patients and ≥6 participating hospitals.



Estimated percentage of PVI use in Cohort A with 95% credible intervals (best linear unbiased estimates) from Bayesian multilevel logistic regression with random effects for country and centre, but without casemix variables. To discourage over-interpretation of estimates from countries with small sample sizes, we included in this graph only countries that contributed ≥500 patients and ≥6 hospitals.

Tables

Table S1: Full Baseline description of the sample including data of missingness

Table S1a: Preoperative patient characteristics

Characteristic	Category	Cohort A: Total (N=19,768) Number	(%)	Coh A: No PVI (N=18,998) Number	(%)	Coh A: PVI (N=770) Number	(%)	Cohort B (N=5,907) Number	(%)
Age group	<50	6281	(31.8)	6175	(32.5)	106	(13.8)	861	(14.6)
	50-69	7455	(37.7)	7131	(37.5)	324	(42.1)	2286	(38.7)
	>=70	6032	(30.5)	5692	(30.0)	340	(44.2)	2760	(46.7)
	Missing	0		0		0		0	
Sex	Female	9730	(49.4)	9428	(49.8)	302	(39.3)	2461	(41.9)
	Male	9975	(50.6)	9508	(50.2)	467	(60.7)	3406	(58.1)
	Missing	63		62		1		40	
ASA Grade	ASA 1	3720	(18.9)	3692	(19.5)	28	(3.6)	262	(4.4)
	ASA 2	9064	(45.9)	8852	(46.7)	212	(27.6)	1424	(24.1)
	ASA 3	5994	(30.4)	5632	(29.7)	362	(47.1)	2632	(44.6)
	ASA 4	900	(4.6)	757	(4.0)	143	(18.6)	1393	(23.6)
	ASA 5	53	(0.3)	30	(0.2)	23	(3.0)	190	(3.2)
	Missing	37		35		2		6	
Clinical Frailty Scale	1	2495	(13.3)	2451	(13.6)	44	(6.0)	215	(3.8)
	2	6191	(32.9)	6028	(33.4)	163	(22.1)	1136	(20.1)
	3	5367	(28.6)	5156	(28.5)	211	(28.7)	1739	(30.8)
	4	2409	(12.8)	2270	(12.6)	139	(18.9)	1164	(20.6)
	5	937	(5.0)	873	(4.8)	64	(8.7)	499	(8.8)
	6	731	(3.9)	691	(3.8)	40	(5.4)	421	(7.5)
	7	505	(2.7)	461	(2.6)	44	(6.0)	336	(6.0)
	8	134	(0.7)	109	(0.6)	25	(3.4)	102	(1.8)
	9	27	(0.1)	21	(0.1)	6	(0.8)	33	(0.6)
	Missing	972		938		34		262	
Mean arterial pressure (12 hours before surgery)	<90 mmHg	4854	(30.5)	4614	(30.1)	240	(39.2)	1759	(40.3)
	90-95.99 mgHg	3203	(20.1)	3093	(20.2)	110	(18.0)	801	(18.4)
	>=96 mmHg	7866	(49.4)	7604	(49.7)	262	(42.8)	1805	(41.4)
	Missing	3845		3687		158		1542	
Mean arterial pressure (immediately prior to surgery)	<90 mmHg	5001	(27.7)	4688	(27.0)	313	(44.1)	2554	(49.9)
	90-95.99 mgHg	2935	(16.2)	2849	(16.4)	86	(12.1)	652	(12.7)
	>=96 mmHg	10130	(56.1)	9820	(56.6)	310	(43.7)	1909	(37.3)
	Missing	1702		1641		61		792	

Table S1b: Medical history

Medical history	Category	Cohort A: Total (N=19,768) Number	(%)	Coh A: No PVI (N=18,998) Number	(%)	Coh A: PVI (N=770) Number	(%)	Cohort B (N=5,907) Number	(%)
Coronary artery disease	No	17890	(90.5)	17271	(90.9)	619	(80.4)	4866	(82.4)
	Yes	1878	(9.5)	1727	(9.1)	151	(19.6)	1037	(17.6)
	Missing	0		0		0		4	
Cerebrovascular disease	No	18433	(93.2)	17773	(93.6)	660	(85.7)	5312	(90.0)
	Yes	1335	(6.8)	1225	(6.4)	110	(14.3)	592	(10.0)
	Missing	0		0		0		3	
Peripheral vascular disease	No	18443	(93.3)	17775	(93.6)	668	(86.8)	5166	(87.5)
	Yes	1325	(6.7)	1223	(6.4)	102	(13.2)	738	(12.5)
	Missing	0		0		0		3	
Arterial fibrillation	No	18381	(93.0)	17728	(93.3)	653	(84.8)	5037	(85.3)
	Yes	1387	(7.0)	1270	(6.7)	117	(15.2)	867	(14.7)
	Missing	0		0		0		3	
Heart failure	No	18698	(94.6)	18011	(94.8)	687	(89.2)	5196	(88.0)
	Yes	1069	(5.4)	986	(5.2)	83	(10.8)	707	(12.0)
	Missing	1		1		0		4	
Hypertension	No	11886	(60.1)	11529	(60.7)	357	(46.4)	2806	(47.5)
	Yes	7881	(39.9)	7468	(39.3)	413	(53.6)	3097	(52.5)
	Missing	1		1		0		4	
Diabetes	No	16624	(84.1)	16028	(84.4)	596	(77.4)	4492	(76.1)
	Insulin-dependent	990	(5.0)	934	(4.9)	56	(7.3)	503	(8.5)
	Non-insulin dependent	2152	(10.9)	2034	(10.7)	118	(15.3)	909	(15.4)
	Missing	2		2		0		3	
Chronic liver disease	No	19247	(97.4)	18522	(97.5)	725	(94.2)	5577	(94.5)
	Yes	520	(2.6)	475	(2.5)	45	(5.8)	325	(5.5)
	Missing	1		1		0		5	
Chronic respiratory disease	No	17153	(86.8)	16533	(87.0)	620	(80.5)	4726	(80.1)
	COPD	1243	(6.3)	1152	(6.1)	91	(11.8)	745	(12.6)
	Other	1371	(6.9)	1312	(6.9)	59	(7.7)	432	(7.3)
	Missing	1		1		0		4	
Steroid use	No	19073	(96.5)	18338	(96.5)	735	(95.5)	5628	(95.4)
	Yes	692	(3.5)	657	(3.5)	35	(4.5)	273	(4.6)
	Missing	3		3		0		6	

Table S1c: Regular mediations

Medication	Category	Cohort A: Total (N=19,768) Number	(%)	Coh A: No PVI (N=18,998) Number	(%)	Coh A: PVI (N=770) Number	(%)	Cohort B (N=5,907) Number	(%)
Alpha Blocker	no	19250	(97.4)	18505	(97.4)	745	(96.8)	5731	(97.0)
	yes: took day of surgery	189	(1.0)	180	(0.9)	9	(1.2)	51	(0.9)
	yes: omitted day of surgery	212	(1.1)	198	(1.0)	14	(1.8)	69	(1.2)
	yes: unknown	117	(0.6)	115	(0.6)	2	(0.3)	56	(0.9)
Angio-receptor blocker	no	17691	(89.5)	17027	(89.6)	664	(86.2)	5140	(87.0)
	yes: took day of surgery	689	(3.5)	663	(3.5)	26	(3.4)	187	(3.2)
	yes: omitted day of surgery	1091	(5.5)	1025	(5.4)	66	(8.6)	396	(6.7)
	yes: unknown	297	(1.5)	283	(1.5)	14	(1.8)	184	(3.1)
Beta blocker	no	16667	(84.3)	16135	(84.9)	532	(69.1)	4282	(72.5)
	yes: took day of surgery	2020	(10.2)	1890	(9.9)	130	(16.9)	851	(14.4)
	yes: omitted day of surgery	645	(3.3)	581	(3.1)	64	(8.3)	377	(6.4)
	yes: unknown	436	(2.2)	392	(2.1)	44	(5.7)	397	(6.7)
Calcium blocker	no	17319	(87.6)	16681	(87.8)	638	(82.9)	4966	(84.1)
	yes: took day of surgery	1160	(5.9)	1113	(5.9)	47	(6.1)	335	(5.7)
	yes: omitted day of surgery	842	(4.3)	779	(4.1)	63	(8.2)	309	(5.2)
	yes: unknown	447	(2.3)	425	(2.2)	22	(2.9)	297	(5.0)
Diuretic	no	17604	(89.1)	16980	(89.4)	624	(81.0)	4912	(83.2)
	yes: took day of surgery	779	(3.9)	740	(3.9)	39	(5.1)	294	(5.0)
	yes: omitted day of surgery	1024	(5.2)	949	(5.0)	75	(9.7)	421	(7.1)
	yes: unknown	361	(1.8)	329	(1.7)	32	(4.2)	280	(4.7)
Any antihypertensive	No	12215	(61.8)	11867	(62.5)	348	(45.2)	2780	(47.1)
	Yes	7553	(38.2)	7131	(37.5)	422	(54.8)	3127	(52.9)
NSAID	no	19000	(96.1)	18256	(96.1)	744	(96.6)	5712	(96.7)
	yes: took day of surgery	233	(1.2)	226	(1.2)	7	(0.9)	48	(0.8)
	yes: omitted day of surgery	372	(1.9)	361	(1.9)	11	(1.4)	69	(1.2)
	yes: unknown	163	(0.8)	155	(0.8)	8	(1.0)	78	(1.3)

Note: no missing values recorded for regular medications.

Table S1d: Procedure characteristics

Characteristic	Category	Cohort A: Total (N=19,768) Number	(%)	Coh A: No PVI (N=18,998) Number	(%)	Coh A: PVI (N=770) Number	(%)	Cohort B (N=5,907) Number	(%)
Reason for surgery	Infection	2841	(14.4)	2711	(14.3)	130	(16.9)	1218	(20.6)
	Fracture	4739	(24.0)	4463	(23.5)	276	(35.8)	1866	(31.6)
	Cancer	2862	(14.5)	2794	(14.7)	68	(8.8)	433	(7.3)
	Bleeding	760	(3.8)	689	(3.6)	71	(9.2)	604	(10.2)
	Other	8566	(43.3)	8341	(43.9)	225	(29.2)	1785	(30.2)
	Missing	0		0		0		1	
Surgical procedure	Breast	598	(3.0)	594	(3.1)	4	(0.5)	21	(0.4)
	Gynaecological	1383	(7.0)	1354	(7.1)	29	(3.8)	196	(3.3)
	Head and neck	1920	(9.7)	1870	(9.8)	50	(6.5)	246	(4.2)
	Hepato-biliary	979	(5.0)	920	(4.8)	59	(7.7)	457	(7.7)
	Kidney/urological	2194	(11.1)	2129	(11.2)	65	(8.4)	436	(7.4)
	Lower gastro-intestinal	2781	(14.1)	2610	(13.7)	171	(22.2)	1853	(31.4)
	Orthopaedic	4953	(25.1)	4853	(25.5)	100	(13.0)	711	(12.0)
	Plastics / Cutaneous	902	(4.6)	886	(4.7)	16	(2.1)	120	(2.0)
	Upper gastro-intestinal	1271	(6.4)	1172	(6.2)	99	(12.9)	729	(12.3)
	Neurological/spinal	1154	(5.8)	1093	(5.8)	61	(7.9)	281	(4.8)
	Vascular	920	(4.7)	830	(4.4)	90	(11.7)	592	(10.0)
	Other	711	(3.6)	685	(3.6)	26	(3.4)	264	(4.5)
	Missing	2		2		0		1	
Severity	Minor	2553	(12.9)	2536	(13.4)	17	(2.2)	102	(1.7)
	Intermediate	9857	(49.9)	9678	(51.0)	179	(23.2)	938	(15.9)
	Major	7354	(37.2)	6780	(35.7)	574	(74.5)	4866	(82.4)
	Missing	4		4		0		1	
Urgency	Urgent	6449	(32.6)	6069	(32.0)	380	(49.4)	3524	(59.7)
	Not urgent	13306	(67.4)	12917	(68.0)	389	(50.6)	2380	(40.3)
	Missing	13		12		1		3	

Table S1e: Intraoperative variables

Variable	Category	Cohort A: Total (N=19,768) Number	(%)	Coh A: No PVI (N=18,998) Number	(%)	Coh A: PVI (N=770) Number	(%)	Cohort B (N=5,907) Number	(%)
Airway	Endotracheal tube	12980	(65.9)	12273	(64.8)	707	(91.9)	5415	(91.9)
	Supraglottic	2566	(13.0)	2553	(13.5)	13	(1.7)	94	(1.6)
	O2 facemask or nasal canula	4156	(21.1)	4107	(21.7)	49	(6.4)	386	(6.5)
	Missing	66		65		1		12	
Blood loss	<250 ml	15794	(80.6)	15434	(81.9)	360	(47.4)	2749	(47.2)
	251-1000 ml	3359	(17.1)	3092	(16.4)	267	(35.2)	2024	(34.7)
	1001-3000 ml	402	(2.1)	294	(1.6)	108	(14.2)	828	(14.2)
	>3000 ml	43	(0.2)	19	(0.1)	24	(3.2)	224	(3.8)
	Missing	170		159		11		82	
Duration of operation	<120 mins	6955	(35.3)	6869	(36.3)	86	(11.2)	628	(10.7)
	120 - 239 mins	7985	(40.6)	7786	(41.1)	199	(26.0)	1706	(29.1)
	>=240 mins	4748	(24.1)	4268	(22.6)	480	(62.7)	3522	(60.1)
	Missing	80		75		5		51	
Mean arterial pressure (intra-operative)	<90 mmHg	18286	(93.2)	17540	(93.0)	746	(98.2)	5807	(98.9)
	90-95.99 mgHg	700	(3.6)	693	(3.7)	7	(0.9)	36	(0.6)
	>=96 mmHg	640	(3.3)	633	(3.4)	7	(0.9)	31	(0.5)
	Missing	142		132		10		33	

Table S1f: Type of anaesthesia

Type of anaesthesia	Category	Cohort A: Total (N=19,768) Number	(%)	Coh A: No PVI (N=18,998) Number	(%)	Coh A: PVI (N=770) Number	(%)	Cohort B (N=5,907) Number	(%)
Volatile	No	9188	(46.5)	8901	(46.9)	287	(37.3)	1924	(32.6)
	Yes	10564	(53.5)	10082	(53.1)	482	(62.7)	3981	(67.4)
	Missing	16		15		1		2	
TIVA	No	14333	(72.6)	13810	(72.7)	523	(68.0)	4336	(73.4)
	Yes	5419	(27.4)	5173	(27.3)	246	(32.0)	1569	(26.6)
	Missing	16		15		1		2	
Sedation	No	18303	(92.7)	17557	(92.5)	746	(97.0)	5775	(97.8)
	Yes	1449	(7.3)	1426	(7.5)	23	(3.0)	130	(2.2)
	Missing	16		15		1		2	
Regional	No	17987	(91.1)	17264	(90.9)	723	(94.0)	5690	(96.4)
	Yes	1765	(8.9)	1719	(9.1)	46	(6.0)	215	(3.6)
	Missing	16		15		1		2	
Spinal	No	16543	(83.8)	15823	(83.4)	720	(93.6)	5391	(91.3)
	Yes	3209	(16.2)	3160	(16.6)	49	(6.4)	514	(8.7)
	Missing	16		15		1		2	
Epidural	No	18934	(95.9)	18323	(96.5)	611	(79.5)	4933	(83.5)
	Yes	818	(4.1)	660	(3.5)	158	(20.5)	972	(16.5)
	Missing	16		15		1		2	

Table S1g: Peri-operative vasopressors

Vasopressors	Category	Cohort A: Total (N=19,768) Number	(%)	Coh A: No PVI (N=18,998) Number	(%)	Coh A: PVI (N=770) Number	(%)	Cohort B (N=5,907) Number	(%)
Preoperative vasopressors	No	19517	(98.7)	18845	(99.2)	672	(87.3)	5255	(89.0)
	Yes	248	(1.3)	150	(0.8)	98	(12.7)	647	(11.0)
	Missing	3		3		0		5	
Any intraoperative vasopressor	0	13295	(67.3)	13214	(69.6)	81	(10.5)	574	(9.7)
	1	6473	(32.7)	5784	(30.4)	689	(89.5)	5333	(90.3)
	Missing	0		0		0		0	
Enteral vasopressors	No	19684	(99.6)	18947	(99.7)	737	(95.7)	5578	(94.4)
	Yes	84	(0.4)	51	(0.3)	33	(4.3)	329	(5.6)
	Missing	0		0		0		0	
Vasopressor bolus	No	19103	(96.6)	18469	(97.2)	634	(82.3)	4629	(78.4)
	Yes	665	(3.4)	529	(2.8)	136	(17.7)	1278	(21.6)
	Missing	0		0		0		0	

Table S1h: Outcomes

Outcome	Category	Cohort A: Total (N=19,768) Number	(%)	Coh A: No PVI (N=18,998) Number	(%)	Coh A: PVI (N=770) Number	(%)	Cohort B (N=5,907) Number	(%)
Ventilation	No	18871	(95.8)	18396	(97.2)	475	(61.7)	2872	(48.6)
	Yes	822	(4.2)	527	(2.8)	295	(38.3)	3032	(51.4)
	Missing	75		75		0		3	
Myocardial infarction	No	19629	(99.7)	18872	(99.7)	757	(98.3)	5738	(97.2)
	Yes	63	(0.3)	50	(0.3)	13	(1.7)	165	(2.8)
	Missing	76		76		0		4	
Atrial fibrillation	No	19535	(99.2)	18802	(99.4)	733	(95.2)	5489	(93.0)
	Yes	156	(0.8)	119	(0.6)	37	(4.8)	414	(7.0)
	Missing	77		77		0		4	
Other dysrhythmia	No	19483	(98.9)	18766	(99.2)	717	(93.1)	5523	(93.6)
	Yes	207	(1.1)	154	(0.8)	53	(6.9)	380	(6.4)
	Missing	78		78		0		4	
RRT	No	19484	(98.9)	18759	(99.1)	725	(94.2)	5360	(90.8)
	Yes	208	(1.1)	163	(0.9)	45	(5.8)	546	(9.2)
	Missing	76		76		0		1	
Parenteral nutrition	No	19072	(96.9)	18476	(97.6)	596	(77.4)	4351	(73.7)
	Yes	619	(3.1)	445	(2.4)	174	(22.6)	1554	(26.3)
	Missing	77		77		0		2	
Antibiotics	No	17357	(88.5)	16891	(89.6)	466	(61.6)	3206	(54.8)
	Yes	2245	(11.5)	1954	(10.4)	291	(38.4)	2649	(45.2)
	Missing	166		153		13		52	
Any complications	No	14439	(73.4)	14219	(75.2)	220	(28.6)	1572	(26.7)
	Yes	5245	(26.6)	4695	(24.8)	550	(71.4)	4320	(73.3)
	Missing	84		84		0		15	
Acute Kidney Injury	No	7722	(88.7)	7290	(89.9)	432	(71.4)	3255	(66.4)
	Yes	988	(11.3)	815	(10.1)	173	(28.6)	1650	(33.6)
	Missing	11058		10893		165		1002	
30-day mortality	No	19250	(97.9)	18580	(98.3)	670	(87.5)	4932	(84.1)
	Yes	410	(2.1)	314	(1.7)	96	(12.5)	929	(15.9)
	Missing	108		104		4		46	
Length of Stay (days)	Median (IQR)	3	(1, 6)	3	(1, 6)	10	(6, 20)	12	(7, 23)
	Missing	617		496		121		1133	

Table S2: Hospital characteristics

Data describing recruiting centres showing the variety in size and distribution of specialties. N=214 out of 228 hospitals (6% have missing data). “number of hospitals beds” has n=211, all other n=214.

Variable	**Median**	**(Min, P25, P75, Max)**
Number of operating rooms	12	(2, 8, 19, 60)
Number of critical care beds	21	(0, 12, 40, 270)
Number of hospital beds	**Number**	**(%)**
<250	41	(19)
>1000	30	(14)
250-500	65	(31)
501-750	45	(21)
751-1000	30	(14)
Specialty	**Number**	**(%)**
Neurosurgery	116	(54)
ENT + Head & Neck	172	(80)
Thoracic	110	(51)
Transplant	64	(30)
Gastro_abdominal	202	(94)
Hepato_biliary_Pancreas	157	(73)
Urological_Kidney	181	(85)
Gynaecological	173	(81)
Orthopaedic	188	(88)
Trauma	161	(75)
Vascular	140	(65)

Table S3: Overview of Squeeze data

Overview of Squeeze data in Cohort A and Cohort B.

	Cohort A	**Cohort B**	**Combined data**
Number of hospitals	228	199	228
Number of countries	42	40	42
Number of patients	19,768	5,907	25,675
Number of patients receiving PVI	770	5,907	6,677
Percentage of patients receiving PVI	3.9 %	100 %	

Table S4: Estimated median odds ratios in variation of PVI use

Estimated median odds ratios (MOR) with 95 % credible intervals adjusted for pre- and for pre- and postoperative predictor variables. The higher the MOR, the higher the variation. Interpretation of MORs is as follows:

Centre: The MOR comparing two patients with the same characteristics in different centres within the same country.

Country: The MOR comparing two patients with the same characteristics in different countries, each patient being treated at a centre with typical levels of PVI use in their respective country.

Model	No covariates	Adjusting for pre-operative predictor variables only	Adjusting for pre- and intra-operative predictors
Hospital	2.30 (1.96, 2.73)	2.47 (2.10, 2.98)	2.30 (1.91, 2.85)
Country	1.78 (1.37, 2.44)	2.02 (1.55, 2.79)	1.95 (1.43, 2.84)

Table S5: Pre-operative predictors of PVI: full model results

Estimated odds ratios and random intercept standard deviations from a Bayesian mixed effects logistic regression of postoperative vasopressor infusion use in 19,768 patients (Squeeze Cohort A): Pre-operative predictors only. N = 19768, number of centres: 228; number of countries: 42 Number of events (PVI use): 770 (3.9 %). Missing values were imputed using multiple imputation with chained equations (mice) with 30 imputations. Bayesian posterior draws were combined to obtain a pooled posterior distribution. The estimates shown are the mean, 2.5th percentile and 97.5th percentile of the posterior distribution.

	Odds Ratio	95 % credible interval	
Intercept (baseline odds)	0.00011	0.00004	0.00027
Age (centred, in years)	1.00870	1.00161	1.01587
Age(centred)^2	0.99951	0.99921	0.99980
Frailty (ref: CFS score 1)			
CFS 2	1.04	0.71	1.53
CFS 3	0.87	0.59	1.31
CFS 4	0.92	0.60	1.43
CFS 5	0.88	0.53	1.44
CFS 6	0.76	0.44	1.32
CFS 7	0.95	0.55	1.65
CFS 8	2.15	1.03	4.40
CFS 9	0.90	0.25	3.00
MAP 12 hrs pre-surgery (ref: ≥ 96mgHG)			
<90mmHg	1.33	1.07	1.65
90-95.99mgHg	1.12	0.87	1.46
MAP immediately pre-surgery (ref: ≥ 96mgHG)			
<90mmHg	2.35	1.91	2.89
90-95.99mgHg	1.07	0.81	1.41
Reason for Surgery (ref: Other)			
Infection	1.67	1.25	2.22
Fracture	1.62	1.27	2.06
Cancer	1.01	0.66	1.54
Bleeding	1.73	1.19	2.51
Surgical Procedure (ref: Orthopaedic)			
Breast	0.39	0.11	1.10
Gynaecological	1.77	1.03	3.00
Head and neck	2.19	1.37	3.47
Hepato-biliary	3.31	2.06	5.30
Kidney/urological	1.84	1.18	2.88
Lower gastro-intestinal	2.76	1.89	4.07
Plastics/Cutaneous	1.60	0.82	3.03
Upper gastro-intestinal	4.30	2.83	6.58
Neurological/spinal	1.57	1.00	2.46
Vascular	3.42	2.17	5.41
Other	2.03	1.14	3.54
Severity (ref: Minor)			
Intermediate	4.59	2.75	8.05
Major	24.06	14.35	42.33

ASA Grade (ref: ASA 1)			
ASA2	2.72	1.76	4.30
ASA3	4.93	3.11	7.99
ASA4	14.29	8.47	24.53
ASA5	42.41	17.71	102.18
Urgency (ref: Not urgent)			
Urgent	1.82	1.46	2.27
Medical history			
Arterial fibrillation	1.21	0.92	1.59
Cerebrovascular	1.28	0.98	1.66
Coronary Artery	1.20	0.93	1.53
Diabetes: insulin dependent	0.82	0.58	1.15
Diabetes: non-insulin dependent	1.05	0.82	1.35
Heart failure	0.89	0.64	1.22
Hypertension	1.06	0.84	1.33
Peripheral-vascular	0.83	0.60	1.15
Chronic liver	1.38	0.92	2.04
COPD	0.96	0.72	1.27
Other chronic respiratory	0.83	0.60	1.14
Steroid use	0.78	0.51	1.16
Regular medication (ref: no)			
Ace inhibitor: took on day	0.90	0.58	1.38
omitted on day	1.08	0.80	1.46
not known if took on day	0.90	0.51	1.51
Alpha blocker: took on day	0.94	0.40	2.00
omitted on day	0.88	0.43	1.70
not known if took on day	0.16	0.02	0.74
Angio receptor: took on day	0.91	0.55	1.46
omitted on day	1.03	0.73	1.45
not known if took on day	0.83	0.40	1.61
Beta-blocker: took on day	1.16	0.89	1.51
omitted on day	1.73	1.20	2.46
not known if took on day	2.33	1.44	3.72
Calcium blocker: took on day	0.74	0.51	1.07
omitted on day	1.33	0.94	1.87
not known if took on day	0.72	0.40	1.26
Diuretic: took on day	0.78	0.51	1.17
omitted on day	0.91	0.65	1.25
not known if took on day	1.42	0.82	2.40
NSAID: took on day	0.76	0.31	1.69
omitted on day	0.86	0.42	1.66
not known if took on day	0.81	0.31	1.90
Random intercept: standard deviations			
Country	0.74	0.46	1.08
Centre	0.95	0.78	1.14

Table S6: Pre- and intra-operative predictors of PVI use (full model results)

Estimated odds ratios and random intercept standard deviations from a Bayesian mixed effects logistic regression of postoperative vasopressor infusion use in 19,768 patients (Squeeze Cohort A): Pre- and intra-operative predictors. N = 19768, number of centres: 228; number of countries: 42 Number of events (PVI use): 770 (3.9 %).

Missing values were imputed using multiple imputation with chained equations (mice) with 30 imputations. Bayesian posterior draws were combined to obtain a pooled posterior distribution. The estimates shown are the mean, 2.5th percentile and 97.5th percentile of the posterior distribution.

	Odds Ratio	95 % credible interval	
Intercept (baseline odds)	0.00015	0.00003	0.00061
PRE-OPERATIVE VARIABLES			
Age (centred, in years)	1.00875	1.00071	1.01687
Age(centred)^2	0.99975	0.99942	1.00007
Frailty (ref: CFS score 1)			
CFS 2	0.98	0.64	1.53
CFS 3	0.76	0.49	1.20
CFS 4	0.83	0.52	1.37
CFS 5	0.77	0.44	1.36
CFS 6	0.79	0.43	1.47
CFS 7	0.85	0.46	1.60
CFS 8	2.02	0.86	4.66
CFS 9	1.95	0.45	7.55
MAP 12 hrs pre-surgery (ref: ≥ 96mgHG)			
<90mmHg	1.19	0.93	1.53
90-95.99mmHg	1.28	0.95	1.73
MAP immediately pre-surgery (ref: ≥ 96mgHG)			
<90mmHg	1.92	1.51	2.45
90-95.99mmHg	0.99	0.72	1.34
Reason for Surgery (ref: Other)			
Infection	1.78	1.28	2.47
Fracture	1.13	0.86	1.50
Cancer	0.84	0.53	1.34
Bleeding	1.05	0.67	1.63
Surgical Procedure (ref: Orthopaedic)			
Breast	0.49	0.12	1.64
Gynaecological	1.56	0.83	2.90
Head and neck	2.34	1.38	3.99
Hepato-biliary	1.70	0.98	2.95
Kidney/urological	1.81	1.09	3.00
Lower gastro-intestinal	1.73	1.11	2.71
Plastics/Cutaneous	1.54	0.73	3.14
Upper gastro-intestinal	2.65	1.62	4.34
Neurological/spinal	1.73	1.04	2.88
Vascular	2.24	1.33	3.77

Other	1.96	1.03	3.69
Severity (ref: Minor)			
Intermediate	2.06	1.14	3.89
Major	3.37	1.81	6.52
ASA Grade (ref: ASA 1)			
ASA2	2.41	1.45	4.07
ASA3	3.54	2.09	6.13
ASA4	9.37	5.13	17.39
ASA5	19.65	6.86	56.66
Urgency (ref: Not urgent)			
Urgent	1.84	1.43	2.38
Medical history			
Arterial fibrillation	1.19	0.87	1.62
Cerebrovascular	1.41	1.04	1.90
Coronary Artery	1.13	0.85	1.49
Diabetes: insulin dependent	0.80	0.53	1.19
Diabetes: non-insulin dependent	1.06	0.80	1.40
Heart failure	1.11	0.77	1.60
Hypertension	0.97	0.75	1.27
Peripheral-vascular	0.80	0.55	1.16
Chronic liver	1.42	0.90	2.22
COPD	1.00	0.72	1.37
Other chronic respiratory	0.77	0.53	1.11
Steroid use	0.94	0.59	1.46
Regular medication (ref: no)			
Ace inhibitor: took on day	0.90	0.55	1.45
omitted on day	1.11	0.78	1.56
not known if took on day	0.92	0.50	1.67
Alpha blocker: took on day	0.88	0.35	2.06
omitted on day	0.82	0.36	1.77
not known if took on day	0.28	0.04	1.32
Angio receptor: took on day	0.86	0.49	1.46
omitted on day	0.92	0.62	1.35
not known if took on day	0.82	0.35	1.79
Beta-blocker: took on day	1.23	0.91	1.67
omitted on day	1.80	1.19	2.70
not known if took on day	1.91	1.11	3.25
Calcium blocker: took on day	0.71	0.46	1.08
omitted on day	1.11	0.74	1.65
not known if took on day	0.56	0.29	1.07
Diuretic: took on day	0.90	0.56	1.43
omitted on day	1.03	0.71	1.48
not known if took on day	2.20	1.20	3.97
NSAID: took on day	0.63	0.23	1.55
omitted on day	0.98	0.45	1.98
not known if took on day	0.58	0.18	1.66

INTRA-OPERATIVE VARIABLES			
Duration of operation (ref: < 120 mins)			
120-239 mins	1.03	0.73	1.47
≥ 240mins	1.62	1.10	2.39
Blood loss (ref: 0 – 250 ml)			
251-1000ml	1.44	1.13	1.85
1001-3000ml	2.39	1.56	3.66
>3000ml	4.17	1.66	10.57
Intraoperative MAP (ref: ≥ 96mgHG)			
<90mmHg	0.45	0.20	1.13
90-95.99mmHg	0.64	0.19	2.15
Type of anaesthesia (not mutually exclusive)			
Volatile	0.76	0.37	1.53
TIVA	0.73	0.36	1.45
Sedation	1.38	0.71	2.65
Regional	1.16	0.78	1.72
Spinal	0.67	0.41	1.08
Epidural	3.06	2.26	4.13
Airway (ref: O2 facemask or nasal canula)			
Endotracheal tube	1.58	0.71	3.61
Supraglottic	0.63	0.23	1.67
Vasoactive drugs (not mutually exclusive)			
Preoperative vasopressors	5.74	3.80	8.65
Any intraoperative vasopressors	7.22	5.35	9.85
Enteral vasopressors	6.98	3.53	13.82
Bolus	3.57	2.59	4.90
Crystalloid (ref: None)			
≤500ml	0.84	0.43	1.69
501-1500ml	1.01	0.54	1.95
>1500ml	2.44	1.30	4.73
Colloid (ref: None)			
≤500ml	2.24	1.65	3.04
>500ml	2.16	1.35	3.45
Blood products (ref: None)			
≤500ml	1.57	1.08	2.26
>500ml	1.94	1.33	2.82
Random intercept: standard deviations			
Country	0.70	0.37	1.09
Centre	0.87	0.68	1.10

Table S7: Distributions of outcome measures by Cohort (A or B) and PVI use

		Cohort A (N = 19768)						Cohort B (N = 5907)	
Outcome measure	**Category**	**Total**	**(%)**	**No PVI**	**(%)**	**PVI**	**(%)**	**Total**	**(%)**
Ventilation	No	18871	(95.8)	18396	(97.2)	475	(61.7)	2872	(48.6)
	Yes	822	(4.2)	527	(2.8)	295	(38.3)	3032	(51.4)
Myocardial infarction	No	19629	(99.7)	18872	(99.7)	757	(98.3)	5738	(97.2)
	Yes	63	(0.3)	50	(0.3)	13	(1.7)	165	(2.8)
Atrial fibrillation	No	19535	(99.2)	18802	(99.4)	733	(95.2)	5489	(93.0)
	Yes	156	(0.8)	119	(0.6)	37	(4.8)	414	(7.0)
Other dysrhythmia	No	19483	(98.9)	18766	(99.2)	717	(93.1)	5523	(93.6)
	Yes	207	(1.1)	154	(0.8)	53	(6.9)	380	(6.4)
RRT	No	19484	(98.9)	18759	(99.1)	725	(94.2)	5360	(90.8)
	Yes	208	(1.1)	163	(0.9)	45	(5.8)	546	(9.2)
Parenteral nutrition	No	19072	(96.9)	18476	(97.6)	596	(77.4)	4351	(73.7)
	Yes	619	(3.1)	445	(2.4)	174	(22.6)	1554	(26.3)
Antibiotics	No	17357	(88.5)	16891	(89.6)	466	(61.6)	3206	(54.8)
	Yes	2245	(11.5)	1954	(10.4)	291	(38.4)	2649	(45.2)
Complications	No	14439	(73.4)	14219	(75.2)	220	(28.6)	1572	(26.7)
	Yes	5245	(26.6)	4695	(24.8)	550	(71.4)	4320	(73.3)
AKI	No	7722	(88.7)	7290	(89.9)	432	(71.4)	3255	(66.4)
	Yes	988	(11.3)	815	(10.1)	173	(28.6)	1650	(33.6)
30-day mortality	No	19250	(97.9)	18580	(98.3)	670	(87.5)	4932	(84.1)
	Yes	410	(2.1)	314	(1.7)	96	(12.5)	929	(15.9)
Length of Stay	Median (IQR)	3	(1, 6)	3	(1, 6)	10	(6, 20)	12	(7, 23)

Table S8: Full results of outcome models

Table S8a: Ventilation. Estimates from a Bayesian mixed effects logistic regression of ventilation on PVI and pre-operative predictors of PVI. Complete cases (n = 18257, using Cohorts A and B)

	OR	95 % Credible Interval
Intercept	0.002	(0.001, 0.003)
PVI	24.418	(18.383, 32.491)
CohortB (bias adjustment)	1.087	(0.839, 1.411)
Age (centred at 60)	0.989	(0.984, 0.994)
Age (centred at 60) squared	1.000	(1.000, 1.000)
Frailty: CFS 2 (ref: CFS1)	0.990	(0.723, 1.366)
CFS 3	1.175	(0.848, 1.636)
CFS 4	1.243	(0.882, 1.767)
CFS 5	1.327	(0.889, 1.984)
CFS 6	1.348	(0.893, 2.036)
CFS 7	1.450	(0.948, 2.221)
CFS 8	2.514	(1.364, 4.568)
CFS 9	1.263	(0.456, 3.501)
MAP 12hrs prior: <90mmHg (ref: ≥96mmHg)	0.828	(0.711, 0.965)
90-95.99mgHg	0.828	(0.692, 0.987)
MAP immed. prior: <90mmHg (ref: ≥96mmHg)	1.269	(1.093, 1.477)
90-95.99mgHg	1.175	(0.968, 1.428)
Reason for surgery: Infection (ref: Other)	1.220	(1.001, 1.492)
Fracture	1.004	(0.832, 1.216)
Cancer	0.698	(0.487, 1.004)
Bleeding	1.759	(1.328, 2.315)
Surgical procedure: Breast (ref: Orthopaedic)	1.948	(0.923, 3.892)
Gynaecological	1.185	(0.739, 1.865)
Head and neck	6.154	(4.265, 8.819)
Hepato-biliary	2.739	(1.888, 3.967)
Kidney/urological	1.617	(1.120, 2.335)
Lower gastro-intestinal	2.519	(1.843, 3.448)
Plastics/Cutaneous	2.073	(1.235, 3.411)
Upper gastro-intestinal	3.925	(2.783, 5.546)
Neurological/spinal	3.679	(2.493, 5.463)
Vascular	1.349	(0.919, 1.962)
Other	3.043	(1.971, 4.622)
Operative severity: Intermediate (ref: Minor)	1.558	(1.093, 2.256)
Major	2.949	(2.054, 4.286)
ASA Grade 2 (ref: ASA 1)	1.185	(0.885, 1.605)
ASA 3	1.627	(1.193, 2.238)
ASA 4	4.011	(2.833, 5.679)
ASA 5	8.059	(4.123, 16.083)
Urgency: Urgent (ref: not urgent)	2.631	(2.212, 3.125)
Random effect SDs	**SD**	
Country	0.762	(0.471, 1.116)
Centre	1.109	(0.964, 1.274)

Table S8b: Myocardial infarction. Estimates from a Bayesian mixed effects logistic regression of myocardial infarction on PVI and pre-operative predictors of PVI. Complete cases (n = 18256, using Cohorts A and B)

	OR	95 % Credible Interval
Intercept	0.001	(0, 0.003)
PVI	3.924	(1.680, 8.634)
CohortB (bias adjustment)	1.602	(0.783, 3.571)
Age (centred at 60)	1.016	(1.002, 1.032)
Age (centred at 60) squared	1.000	(0.999, 1.001)
Frailty: CFS 2 (ref: CFS1)	0.747	(0.275, 2.372)
CFS 3	0.975	(0.361, 3.131)
CFS 4	0.842	(0.297, 2.789)
CFS 5	1.224	(0.403, 4.296)
CFS 6	1.281	(0.412, 4.670)
CFS 7	1.423	(0.439, 5.130)
CFS 8	1.279	(0.288, 5.721)
CFS 9	0.989	(0.036, 10.757)
MAP 12hrs prior: <90mmHg (ref: ≥96mmHg)	1.019	(0.665, 1.550)
90-95.99mgHg	1.078	(0.663, 1.714)
MAP immed. prior: <90mmHg (ref: ≥96mmHg)	1.009	(0.670, 1.52)
90-95.99mgHg	0.870	(0.479, 1.533)
Reason for surgery: Infection (ref: Other)	0.881	(0.512, 1.499)
Fracture	0.926	(0.548, 1.58)
Cancer	0.502	(0.178, 1.359)
Bleeding	1.560	(0.812, 2.925)
Surgical procedure: Breast (ref: Orthopaedic)	0.517	(0.022, 4.197)
Gynaecological	0.478	(0.099, 1.864)
Head and neck	1.025	(0.344, 2.82)
Hepato-biliary	1.047	(0.395, 2.791)
Kidney/urological	1.422	(0.606, 3.391)
Lower gastro-intestinal	0.734	(0.334, 1.676)
Plastics/Cutaneous	0.201	(0.009, 1.595)
Upper gastro-intestinal	0.847	(0.350, 2.105)
Neurological/spinal	0.240	(0.034, 1.093)
Vascular	2.019	(0.893, 4.691)
Other	1.120	(0.340, 3.474)
Operative severity: Intermediate (ref: Minor)	1.544	(0.607, 4.562)
Major	1.575	(0.614, 4.782)
ASA Grade 2 (ref: ASA 1)	1.573	(0.526, 5.795)
ASA 3	2.885	(0.944, 10.988)
ASA 4	3.676	(1.131, 14.295)
ASA 5	6.182	(1.436, 29.522)
Urgency: Urgent (ref: not urgent)	1.155	(0.716, 1.867)
Random effect SDs	**SD**	
Country	0.460	(0.029, 1.019)
Centre	1.025	(0.726, 1.361)

Table S8c: Atrial fibrillation. Estimates from a Bayesian mixed effects logistic regression of atrial fibrillation on PVI and pre-operative predictors of PVI. Complete cases (n = 18255, using Cohorts A and B)

	OR	95 % Credible Interval
Intercept	0.001	(0.000, 0.002)
PVI	3.910	(2.319, 6.431)
CohortB (bias adjustment)	1.440	(0.912, 2.340)
Age (centred at 60)	1.052	(1.039, 1.065)
Age (centred at 60) squared	1.000	(0.999, 1.000)
Frailty: CFS 2 (ref: CFS1)	0.879	(0.455, 1.785)
CFS 3	0.817	(0.423, 1.685)
CFS 4	0.942	(0.479, 1.935)
CFS 5	0.634	(0.300, 1.392)
CFS 6	0.712	(0.328, 1.582)
CFS 7	0.870	(0.398, 1.976)
CFS 8	0.837	(0.288, 2.322)
CFS 9	3.010	(0.764, 10.937)
MAP 12hrs prior: <90mmHg (ref: ≥96mmHg)	1.215	(0.944, 1.572)
90-95.99mgHg	1.108	(0.816, 1.503)
MAP immed. prior: <90mmHg (ref: ≥96mmHg)	0.744	(0.573, 0.968)
90-95.99mgHg	0.994	(0.710, 1.382)
Reason for surgery: Infection (ref: Other)	0.819	(0.588, 1.142)
Fracture	0.884	(0.643, 1.223)
Cancer	1.023	(0.533, 1.940)
Bleeding	0.585	(0.344, 0.960)
Procedure: Gynaecological (ref: Orthopaedic)	0.923	(0.260, 2.797)
Head and neck	2.724	(1.278, 5.658)
Hepato-biliary	1.949	(0.950, 4.054)
Kidney/urological	1.990	(1.001, 3.957)
Lower gastro-intestinal	3.077	(1.737, 5.610)
Plastics/Cutaneous	1.294	(0.533, 2.996)
Upper gastro-intestinal	3.553	(1.680, 7.396)
Neurological/spinal	0.553	(0.081, 2.361)
Vascular	4.230	(2.302, 7.965)
Other (incl Breast)*	2.103	(1.099, 4.085)
Operative severity: Intermediate (ref: Minor)	1.684	(0.828, 3.728)
Major	2.360	(1.166, 5.211)
ASA Grade 2 (ref: ASA 1)	1.332	(0.661, 2.980)
ASA 3	1.679	(0.820, 3.784)
ASA 4	2.023	(0.955, 4.698)
ASA 5	2.334	(0.868, 6.589)
Urgency: Urgent (ref: not urgent)	1.866	(1.382, 2.524)
Random effect SDs	**SD**	
Country	0.226	(0.013, 0.519)
Centre	0.719	(0.535, 0.920)

*Note: *There was no case of atrial fibrillation observed among patients receiving breast surgery, so breast surgery patients were combined with the category "other surgical procedure" in this analysis*.

Table S8d: Other dysrhythmia. Estimates from a Bayesian mixed effects logistic regression of Other dysrhythmia on PVI and pre-operative predictors of PVI. Complete cases (n = 18255, using Cohorts A and B)

	OR	95 % Credible Interval
Intercept	0.001	(0.000, 0.003)
PVI	4.869	(3.174, 7.435)
CohortB (bias adjustment)	0.728	(0.498, 1.083)
Age (centred at 60)	1.008	(0.999, 1.017)
Age (centred at 60) squared	1.000	(1.000, 1.000)
Frailty: CFS 2 (ref: CFS1)	1.747	(0.853, 3.869)
CFS 3	1.986	(0.947, 4.537)
CFS 4	1.975	(0.911, 4.574)
CFS 5	2.375	(1.068, 5.617)
CFS 6	2.114	(0.929, 5.050)
CFS 7	2.857	(1.240, 6.829)
CFS 8	2.453	(0.937, 6.690)
CFS 9	1.852	(0.361, 7.859)
MAP 12hrs prior: <90mmHg (ref: ≥96mmHg)	0.831	(0.638, 1.076)
90-95.99mgHg	0.914	(0.672, 1.230)
MAP immed. prior: <90mmHg (ref: ≥96mmHg)	1.069	(0.822, 1.399)
90-95.99mgHg	0.984	(0.685, 1.394)
Reason for surgery: Infection (ref: Other)	1.528	(1.100, 2.160)
Fracture	1.542	(1.101, 2.154)
Cancer	0.957	(0.545, 1.676)
Bleeding	1.349	(0.856, 2.086)
Surgical procedure: Breast (ref: Orthopaedic)	0.154	(0.007, 1.055)
Gynaecological	0.815	(0.372, 1.706)
Head and neck	1.452	(0.801, 2.623)
Hepato-biliary	1.069	(0.594, 1.934)
Kidney/urological	0.789	(0.439, 1.398)
Lower gastro-intestinal	0.946	(0.597, 1.519)
Plastics/Cutaneous	0.307	(0.070, 0.989)
Upper gastro-intestinal	1.294	(0.771, 2.184)
Neurological/spinal	0.973	(0.501, 1.822)
Vascular	1.150	(0.654, 2.009)
Other	1.017	(0.467, 2.088)
Operative severity: Intermediate (ref: Minor)	1.597	(0.873, 3.132)
Major	2.175	(1.174, 4.268)
ASA Grade 2 (ref: ASA 1)	1.153	(0.625, 2.255)
ASA 3	2.027	(1.082, 4.017)
ASA 4	3.186	(1.603, 6.524)
ASA 5	4.458	(1.815, 10.779)
Urgency: Urgent (ref: not urgent)	1.493	(1.112, 2.019)
Random effect SDs	**SD**	
Country	0.256	(0.011, 0.632)
Centre	0.912	(0.722, 1.122)

Table S8e: Renal replacement therapy. Estimates from a Bayesian mixed effects logistic regression of renal replacement therapy on PVI and pre-operative predictors of PVI. Complete cases (n = 18256, using Cohorts A and B)

	OR	95 % Credible Interval
Intercept	0.001	(0.000, 0.002)
PVI	3.101	(1.892, 4.965)
CohortB (bias adjustment)	1.525	(0.985, 2.441)
Age (centred at 60)	0.984	(0.977, 0.992)
Age (centred at 60) squared	1.000	(0.999, 1.000)
Frailty: CFS 2 (ref: CFS1)	1.755	(0.923, 3.526)
CFS 3	1.765	(0.914, 3.637)
CFS 4	2.046	(1.044, 4.233)
CFS 5	2.189	(1.074, 4.700)
CFS 6	2.806	(1.368, 5.980)
CFS 7	1.690	(0.786, 3.791)
CFS 8	2.565	(1.102, 6.341)
CFS 9	3.778	(1.029, 13.046)
MAP 12hrs prior: <90mmHg (ref: ≥96mmHg)	0.752	(0.590, 0.950)
90-95.99mgHg	0.710	(0.526, 0.950)
MAP immed. prior: <90mmHg (ref: ≥96mmHg)	1.594	(1.254, 2.034)
90-95.99mgHg	0.934	(0.655, 1.312)
Reason for surgery: Infection (ref: Other)	1.131	(0.868, 1.471)
Fracture	0.687	(0.499, 0.934)
Cancer	0.449	(0.226, 0.865)
Bleeding	0.977	(0.671, 1.411)
Surgical procedure: Breast (ref: Orthopaedic)	1.422	(0.381, 4.301)
Gynaecological	0.787	(0.304, 1.840)
Head and neck	1.350	(0.711, 2.569)
Hepato-biliary	1.412	(0.761, 2.628)
Kidney/urological	3.162	(1.875, 5.327)
Lower gastro-intestinal	1.399	(0.865, 2.306)
Plastics/Cutaneous	2.136	(1.081, 4.139)
Upper gastro-intestinal	1.750	(1.025, 3.030)
Neurological/spinal	0.559	(0.249, 1.194)
Vascular	2.351	(1.394, 4.043)
Other	1.880	(0.939, 3.729)
Operative severity: Intermediate (ref: Minor)	1.055	(0.684, 1.644)
Major	1.007	(0.646, 1.609)
ASA Grade 2 (ref: ASA 1)	2.117	(1.103, 4.298)
ASA 3	4.961	(2.564, 10.000)
ASA 4	10.695	(5.405, 22.089)
ASA 5	7.968	(3.239, 19.978)
Urgency: Urgent (ref: not urgent)	1.601	(1.217, 2.110)
Random effect SDs	**SD**	
Country	0.275	(0.014, 0.703)
Centre	0.921	(0.725, 1.127)

Table S8f: Parenteral nutrition. Estimates from a Bayesian mixed effects logistic regression of parenteral nutrition on PVI and pre-operative predictors of PVI. Complete cases (n = 18255, using Cohorts A and B)

	OR	95 % Credible Interval
Intercept	0.001	(0.000, 0.002)
PVI	5.423	(4.068, 7.210)
CohortB (bias adjustment)	1.071	(0.822, 1.402)
Age (centred at 60)	0.994	(0.989, 0.999)
Age (centred at 60) squared	1.000	(0.999, 1.000)
Frailty: CFS 2 (ref: CFS1)	1.380	(0.949, 2.025)
CFS 3	1.625	(1.108, 2.403)
CFS 4	1.701	(1.134, 2.554)
CFS 5	1.667	(1.065, 2.627)
CFS 6	1.806	(1.131, 2.891)
CFS 7	2.172	(1.326, 3.511)
CFS 8	4.890	(2.673, 8.924)
CFS 9	3.622	(1.465, 8.937)
MAP 12hrs prior: <90mmHg (ref: ≥96mmHg)	1.079	(0.919, 1.267)
90-95.99mgHg	0.952	(0.791, 1.143)
MAP immed. prior: <90mmHg (ref: ≥96mmHg)	1.238	(1.049, 1.453)
90-95.99mgHg	1.104	(0.900, 1.360)
Reason for surgery: Infection (ref: Other)	1.023	(0.826, 1.268)
Fracture	1.518	(1.244, 1.851)
Cancer	1.076	(0.649, 1.780)
Bleeding	0.963	(0.715, 1.293)
Surgical procedure: Breast (ref: Orthopaedic)	0.353	(0.054, 1.418)
Gynaecological	1.712	(0.932, 3.102)
Head and neck	2.708	(1.608, 4.576)
Hepato-biliary	7.058	(4.411, 11.498)
Kidney/urological	2.077	(1.277, 3.435)
Lower gastro-intestinal	9.474	(6.175, 14.841)
Plastics/Cutaneous	1.715	(0.828, 3.435)
Upper gastro-intestinal	11.715	(7.519, 18.702)
Neurological/spinal	1.413	(0.800, 2.515)
Vascular	1.702	(1.033, 2.866)
Other	1.821	(0.992, 3.290)
Operative severity: Intermediate (ref: Minor)	1.171	(0.800, 1.748)
Major	2.175	(1.489, 3.230)
ASA Grade 2 (ref: ASA 1)	1.402	(0.969, 2.049)
ASA 3	2.307	(1.575, 3.423)
ASA 4	3.037	(2.007, 4.651)
ASA 5	3.033	(1.645, 5.631)
Urgency: Urgent (ref: not urgent)	1.869	(1.532, 2.274)
Random effect SDs	**SD**	
Country	0.564	(0.304, 0.884)
Centre	0.913	(0.770, 1.074)

Table S8g: Antibiotics. Estimates from a Bayesian mixed effects logistic regression of antibiotics on PVI and pre-operative predictors of PVI. Complete cases (n = 18173, using Cohorts A and B)

	OR	95 % Credible Interval
Intercept	0.017	(0.012, 0.024)
PVI	3.396	(2.739, 4.197)
CohortB (bias adjustment)	1.078	(0.874, 1.335)
Age (centred at 60)	0.998	(0.995, 1.002)
Age (centred at 60) squared	1.000	(1.000, 1.000)
Frailty: CFS 2 (ref: CFS1)	1.388	(1.134, 1.703)
CFS 3	1.646	(1.318, 2.05)0
CFS 4	1.758	(1.391, 2.225)
CFS 5	1.826	(1.393, 2.397)
CFS 6	2.477	(1.877, 3.263)
CFS 7	1.929	(1.440, 2.592)
CFS 8	2.839	(1.848, 4.400)
CFS 9	1.720	(0.785, 3.736)
MAP 12hrs prior: <90mmHg (ref: ≥96mmHg)	1.169	(1.052, 1.299)
90-95.99mgHg	0.979	(0.865, 1.110)
MAP immed. prior: <90mmHg (ref: ≥96mmHg)	1.145	(1.024, 1.277)
90-95.99mgHg	1.016	(0.887, 1.162)
Reason for surgery: Infection (ref: Other)	2.539	(2.215, 2.909)
Fracture	1.295	(1.131, 1.487)
Cancer	1.192	(0.969, 1.468)
Bleeding	1.292	(1.042, 1.600)
Surgical procedure: Breast (ref: Orthopaedic)	0.377	(0.205, 0.650)
Gynaecological	0.660	(0.493, 0.885)
Head and neck	0.937	(0.730, 1.200)
Hepato-biliary	1.298	(1.021, 1.653)
Kidney/urological	1.326	(1.071, 1.651)
Lower gastro-intestinal	1.724	(1.433, 2.073)
Plastics/Cutaneous	1.141	(0.849, 1.528)
Upper gastro-intestinal	1.497	(1.203, 1.873)
Neurological/spinal	0.873	(0.671, 1.147)
Vascular	0.854	(0.667, 1.089)
Other	1.485	(1.124, 1.967)
Operative severity: Intermediate (ref: Minor)	1.106	(0.926, 1.323)
Major	1.511	(1.252, 1.828)
ASA Grade 2 (ref: ASA 1)	1.234	(1.020, 1.486)
ASA 3	1.484	(1.207, 1.824)
ASA 4	2.051	(1.606, 2.616)
ASA 5	1.919	(1.186, 3.097)
Urgency: Urgent (ref: not urgent)	2.164	(1.916, 2.439)
Random effect SDs	**SD**	
Country	0.300	(0.097, 0.576)
Centre	0.700	(0.600, 0.808)

Table S8h: Postoperative complications. Estimates from a Bayesian mixed effects logistic regression of postoperative complications on PVI and pre-operative predictors of PVI. Complete cases (n = 18244, using Cohorts A and B)

	OR	95 % Credible Interval
Intercept	0.037	(0.026, 0.053)
PVI	5.233	(4.214, 6.528)
CohortB (bias adjustment)	0.936	(0.745, 1.171)
Age (centred at 60)	1.002	(0.999, 1.006)
Age (centred at 60) squared	1.000	(1.000, 1.000)
Frailty: CFS 2 (ref: CFS1)	1.218	(1.035, 1.434)
CFS 3	1.398	(1.172, 1.664)
CFS 4	1.602	(1.318, 1.939)
CFS 5	1.829	(1.459, 2.302)
CFS 6	2.080	(1.629, 2.658)
CFS 7	1.693	(1.289, 2.206)
CFS 8	1.819	(1.180, 2.838)
CFS 9	2.290	(1.002, 5.364)
MAP 12hrs prior: <90mmHg (ref: ≥96mmHg)	1.050	(0.953, 1.154)
90-95.99mgHg	0.989	(0.888, 1.099)
MAP immed. prior: <90mmHg (ref: ≥96mmHg)	1.199	(1.087, 1.323)
90-95.99mgHg	1.111	(0.990, 1.247)
Reason for surgery: Infection (ref: Other)	1.503	(1.321, 1.711)
Fracture	1.285	(1.147, 1.445)
Cancer	1.059	(0.894, 1.251)
Bleeding	1.476	(1.202, 1.811)
Surgical procedure: Breast (ref: Orthopaedic)	0.624	(0.448, 0.862)
Gynaecological	0.730	(0.586, 0.908)
Head and neck	0.727	(0.598, 0.887)
Hepato-biliary	1.052	(0.848, 1.297)
Kidney/urological	0.906	(0.756, 1.085)
Lower gastro-intestinal	1.306	(1.110, 1.533)
Plastics/Cutaneous	1.038	(0.806, 1.331)
Upper gastro-intestinal	1.261	(1.045, 1.524)
Neurological/spinal	0.759	(0.614, 0.937)
Vascular	0.949	(0.772, 1.161)
Other	1.146	(0.893, 1.471)
Operative severity: Intermediate (ref: Minor)	1.772	(1.517, 2.072)
Major	3.363	(2.850, 3.988)
ASA Grade 2 (ref: ASA 1)	1.437	(1.238, 1.665)
ASA 3	1.892	(1.592, 2.245)
ASA 4	2.745	(2.203, 3.431)
ASA 5	3.338	(1.888, 6.072)
Urgency: Urgent (ref: not urgent)	1.698	(1.524, 1.888)
Random effect SDs	**SD**	
Country	0.363	(0.021, 0.802)
Centre	1.290	(1.142, 1.451)

Table S8i: Acute Kidney Injury. Estimates from a Bayesian mixed effects logistic regression of Acute Kidney Injury on PVI and pre-operative predictors of PVI. Complete cases (n = 10247, using Cohorts A and B)

	OR	95 % Credible Interval
Intercept	0.036	(0.014, 0.084)
PVI	2.784	(2.159, 3.574)
CohortB (bias adjustment)	1.023	(0.800, 1.315)
Age (centred at 60)	1.005	(1.001, 1.010)
Age (centred at 60) squared	1.000	(1.000, 1.000)
Frailty: CFS 2 (ref: CFS1)	1.221	(0.904, 1.668)
CFS 3	1.321	(0.969, 1.819)
CFS 4	1.355	(0.978, 1.889)
CFS 5	1.382	(0.958, 1.988)
CFS 6	1.521	(1.059, 2.186)
CFS 7	1.503	(1.019, 2.220)
CFS 8	1.411	(0.840, 2.367)
CFS 9	1.548	(0.657, 3.573)
MAP 12hrs prior: <90mmHg (ref: ≥96mmHg)	1.078	(0.915, 1.265)
90-95.99mgHg	1.158	(1.016, 1.322)
MAP immed. prior: <90mmHg (ref: ≥96mmHg)	0.985	(0.826, 1.175)
90-95.99mgHg	0.908	(0.793, 1.040)
Reason for surgery: Infection (ref: Other)	0.848	(0.690, 1.037)
Fracture	1.042	(0.769, 1.396)
Cancer	1.279	(0.994, 1.639)
Bleeding	0.853	(0.715, 1.015)
Surgical procedure: Breast (ref: Orthopaedic)	0.754	(0.334, 1.831)
Gynaecological	0.810	(0.374, 1.888)
Head and neck	1.769	(0.841, 4.062)
Hepato-biliary	3.551	(1.707, 8.056)
Kidney/urological	1.631	(0.793, 3.659)
Lower gastro-intestinal	1.031	(0.488, 2.35)
Plastics/Cutaneous	1.527	(0.681, 3.682)
Upper gastro-intestinal	1.372	(0.657, 3.108)
Neurological/spinal	0.626	(0.281, 1.518)
Vascular	1.930	(0.922, 4.449)
Other	1.515	(0.699, 3.543)
Operative severity: Intermediate (ref: Minor)	1.077	(0.817, 1.423)
Major	1.426	(1.079, 1.898)
ASA Grade 2 (ref: ASA 1)	1.392	(1.034, 1.878)
ASA 3	2.076	(1.520, 2.853)
ASA 4	3.069	(2.175, 4.359)
ASA 5	2.215	(1.261, 3.878)
Urgency: Urgent (ref: not urgent)	0.736	(0.633, 0.857)
Random effect SDs	**SD**	
Country	0.254	(0.027, 0.512)
Centre	0.573	(0.464, 0.688)

Table S8j: 30-day in-hospital mortality. Estimates from a Bayesian mixed effects logistic regression of 30-day mortality on PVI and pre-operative predictors of PVI. Complete cases (n = 18197, using Cohorts A and B)

	OR	95 % Credible Interval
Intercept	0.005	(0.003, 0.011)
PVI	3.819	(2.681, 5.425)
CohortB (bias adjustment)	1.024	(0.733, 1.431)
Age (centred at 60)	1.013	(1.007, 1.019)
Age (centred at 60) squared	1.000	(1.000, 1.001)
Frailty: CFS 2 (ref: CFS1)	1.324	(0.851, 2.110)
CFS 3	1.411	(0.885, 2.322)
CFS 4	1.832	(1.129, 3.019)
CFS 5	2.147	(1.282, 3.682)
CFS 6	1.784	(1.047, 3.078)
CFS 7	2.583	(1.529, 4.468)
CFS 8	3.065	(1.638, 5.837)
CFS 9	10.590	(4.366, 25.726)
MAP 12hrs prior: <90mmHg (ref: ≥96mmHg)	1.194	(0.988, 1.443)
90-95.99mgHg	1.104	(0.882, 1.378)
MAP immed. prior: <90mmHg (ref: ≥96mmHg)	1.312	(1.081, 1.590)
90-95.99mgHg	0.953	(0.727, 1.243)
Reason for surgery: Infection (ref: Other)	1.199	(0.958, 1.501)
Fracture	1.004	(0.780, 1.293)
Cancer	0.718	(0.475, 1.083)
Bleeding	1.432	(1.065, 1.915)
Surgical procedure: Breast (ref: Orthopaedic)	0.979	(0.360, 2.366)
Gynaecological	0.935	(0.516, 1.643)
Head and neck	1.069	(0.661, 1.713)
Hepato-biliary	1.248	(0.802, 1.950)
Kidney/urological	0.791	(0.509, 1.228)
Lower gastro-intestinal	1.263	(0.894, 1.802)
Plastics/Cutaneous	1.326	(0.764, 2.269)
Upper gastro-intestinal	1.496	(1.022, 2.212)
Neurological/spinal	0.607	(0.350, 1.026)
Vascular	1.021	(0.670, 1.563)
Other	0.784	(0.424, 1.423)
Operative severity: Intermediate (ref: Minor)	0.871	(0.617, 1.236)
Major	0.887	(0.622, 1.277)
ASA Grade 2 (ref: ASA 1)	0.806	(0.544, 1.207)
ASA 3	1.054	(0.702, 1.616)
ASA 4	2.586	(1.681, 4.035)
ASA 5	4.811	(2.679, 8.702)
Urgency: Urgent (ref: not urgent)	2.576	(2.049, 3.224)
Random effect SDs	**SD**	
Country	0.692	(0.476, 0.967)
Centre	0.403	(0.251, 0.554)

Table S8k: Length of stay. Estimates from a Bayesian mixed effects quantile regression of median Length of Stay on PVI and pre-operative predictors of PVI. Complete cases (n = 17169, using Cohorts A and B)

	b	95 % Credible Interval
Intercept	0.918	(0.363, 1.497)
PVI	4.453	(3.829, 5.090)
CohortB (bias adjustment)	1.965	(1.277, 2.633)
Age (centred at 60)	0.006	(0.001, 0.012)
Age (centred at 60) squared	0.000	(0.000, 0.000)
Frailty: CFS 2 (ref: CFS1)	0.169	(-0.049, 0.383)
CFS 3	0.378	(0.125, 0.633)
CFS 4	0.695	(0.375, 1.015)
CFS 5	1.398	(0.944, 1.863)
CFS 6	1.639	(1.124, 2.176)
CFS 7	1.750	(1.108, 2.383)
CFS 8	2.609	(1.341, 4.046)
CFS 9	3.549	(0.176, 7.025)
MAP 12hrs prior: <90mmHg (ref: ≥96mmHg)	0.260	(0.093, 0.425)
90-95.99mgHg	0.091	(-0.083, 0.263)
MAP immed. prior: <90mmHg (ref: ≥96mmHg)	0.236	(0.071, 0.405)
90-95.99mgHg	0.067	(-0.115, 0.249)
Reason for surgery: Infection (ref: Other)	0.762	(0.517, 1.009)
Fracture	0.536	(0.341, 0.728)
Cancer	0.451	(0.183, 0.722)
Bleeding	0.625	(0.211, 1.056)
Surgical procedure: Breast (ref: Orthopaedic)	-1.349	(-1.762, -0.938)
Gynaecological	-0.541	(-0.847, -0.241)
Head and neck	-0.501	(-0.773, -0.224)
Hepato-biliary	-0.084	(-0.426, 0.275)
Kidney/urological	-0.685	(-0.952, -0.421)
Lower gastro-intestinal	0.349	(0.073, 0.621)
Plastics/Cutaneous	0.116	(-0.245, 0.482)
Upper gastro-intestinal	0.251	(-0.090, 0.600)
Neurological/spinal	0.045	(-0.298, 0.394)
Vascular	-0.921	(-1.313, -0.525)
Other	-0.262	(-0.688, 0.176)
Operative severity: Intermediate (ref: Minor)	0.819	(0.622, 1.021)
Major	2.498	(2.262, 2.731)
ASA Grade 2 (ref: ASA 1)	0.188	(-0.003, 0.380)
ASA 3	0.855	(0.599, 1.116)
ASA 4	3.297	(2.717, 3.870)
ASA 5	5.948	(3.682, 8.788)
Urgency: Urgent (ref: not urgent)	1.088	(0.895, 1.282)
Random effect SDs	**SD**	
Country	1.305	(0.954, 1.744)
Centre	0.849	(0.705, 1.009)

Table S9: Outcomes by length of vasopressor use (full data for Figure 2)

Table S9a: Definitions of the five groups of vasopressor use displayed in Figure 2

	Vasopressors received			
Group	Intra-operative vasopressors	Bolus and/or enteral vasopressors	PVI 1-2 days	PVI 3+days
None	No	No	No	No
Intra-operative vasopressors only	Yes	No	No	No
Boluses/enteral vasopressors	(either)	Yes	No	No
PVI 1-2 days	(either)	(either)	Yes	No
Prolonged PVI	(either)	(either)	No	Yes

Table S9b: Numbers and percentages of the five categories of vasopressor use

	Number	Percent
None	9570	37.3 %
Intra-operative vasopressors only	8867	34.5 %
Intraoperative & postoperative boluses/enteral vasopressors	561	2.2 %
PVI 1-2 days	3992	15.5 %
Prolonged PVI	2685	10.5 %
Total	25675	100.0 %

Note: These percentages do not constitute estimates of population proportions, since they come from a combined data set using Cohort A and Cohort B.

Table S9c: Outcomes of surgery by category of vasopressor use (Cohort A + B combined, n = 25675)

Variable	Vasopressor use	None	(%)	Intra-operative only	(%)	Post-op bolus or enteral	(%)	PVI 1-2 days	(%)	Prolonged PVI	(%)
Ventilation	**No**	9302	(97.5)	8598	(97.4)	496	(89.5)	2510	(62.9)	837	(31.2)
	Yes	237	(2.5)	232	(2.6)	58	(10.5)	1481	(37.1)	1846	(68.8)
Myocardial infarction	**No**	9524	(99.9)	8801	(99.7)	547	(98.7)	3915	(98.1)	2580	(96.2)
	Yes	14	(0.1)	29	(0.3)	7	(1.3)	75	(1.9)	103	(3.8)
Arterial fibrillation	**No**	9510	(99.7)	8744	(99.0)	548	(98.9)	3808	(95.4)	2414	(90.0)
	Yes	28	(0.3)	85	(1.0)	6	(1.1)	182	(4.6)	269	(10.0)
Dysrhythmia	**No**	9494	(99.5)	8733	(98.9)	539	(97.3)	3801	(95.3)	2439	(90.9)
	Yes	44	(0.5)	95	(1.1)	15	(2.7)	189	(4.7)	244	(9.1)
RRT	**No**	9464	(99.2)	8755	(99.2)	540	(97.5)	3829	(95.9)	2256	(84.0)
	Yes	75	(0.8)	74	(0.8)	14	(2.5)	162	(4.1)	429	(16.0)
Parenteral nutrition	**No**	9392	(98.5)	8557	(96.9)	527	(95.1)	3276	(82.1)	1671	(62.3)
	Yes	147	(1.5)	271	(3.1)	27	(4.9)	715	(17.9)	1013	(37.7)
Antibiotics	**No**	8642	(91.0)	7779	(88.4)	470	(85.3)	2583	(65.3)	1089	(41.0)
	Yes	857	(9.0)	1016	(11.6)	81	(14.7)	1371	(34.7)	1569	(59.0)
Any complications	**No**	7556	(79.2)	6334	(71.8)	329	(59.4)	1375	(34.5)	417	(15.6)
	Yes	1979	(20.8)	2491	(28.2)	225	(40.6)	2609	(65.5)	2261	(84.4)
AKI	**No**	3280	(92.4)	3785	(88.3)	225	(83.0)	2449	(74.1)	1238	(56.1)
	Yes	268	(7.6)	501	(11.7)	46	(17.0)	855	(25.9)	968	(43.9)
Mortality (30 day)*	**No**	9394	(99.5)	8649	(99.1)	537	(98.9)	3567	(96.9)	2035	(85.1)
	Yes	43	(0.5)	75	(0.9)	6	(1.1)	114	(3.1)	355	(14.9)
Length of Stay[$]	**Median (IQR)**	11	(8, 18)	11	(8, 19)	11	(8, 18)	13	(9, 22)	20	(12, 34)

Notes: this descriptive analysis uses all patients (Cohorts A +B, receiving PVI or not, n = 25,675). Sample sizes for some outcomes differ due to missing values in the outcome variables.

**Mortality (30-day): the sample is those who survived beyond the period during which PVI use was assessed (at least 7 days), N = 24775.*

[$]Length of stay: the sample consists of patients who stayed in hospital beyond the period during which PVI use was assessed (at least 7 days), N = 8353.

Table S10 Type of vasoactive infusion given by day post-surgery (full data for Figure 3)

Infusion	Day$	Number	Percent	Infusion	Day$	Number	Percent
Noradrenaline	0	5292	79.3%	Phenylephrine	0	329	4.9%
	1	4034	60.4%		1	106	1.6%
	2	2251	33.7%		2	29	0.4%
	3	1299	19.5%		3	12	0.2%
	4	840	12.6%		4	7	0.1%
	5	616	9.2%		5	7	0.1%
	6	479	7.2%		6	7	0.1%
Angiotensin	0	6	0.1%	Terlipressin	0	21	0.3%
	1	7	0.1%		1	21	0.3%
	2	8	0.1%		2	11	0.2%
	3	5	0.1%		3	8	0.1%
	4	6	0.1%		4	6	0.1%
	5	5	0.1%		5	2	0.0%
	6	3	0.0%		6	0	0.0%
Dopamine	0	144	2.2%	Vasopressin	0	300	4.5%
	1	100	1.5%		1	297	4.4%
	2	70	1.0%		2	170	2.5%
	3	59	0.9%		3	89	1.3%
	4	55	0.8%		4	53	0.8%
	5	29	0.4%		5	38	0.6%
	6	23	0.3%		6	23	0.3%
Ephinephrine	0	258	3.9%	Dobutamine*	0	148	2.2%
	1	195	2.9%		1	165	2.5%
	2	104	1.6%		2	122	1.8%
	3	63	0.9%		3	92	1.4%
	4	49	0.7%		4	45	0.7%
	5	34	0.5%		5	33	0.5%
	6	25	0.4%		6	23	0.3%
Metaraminol	0	859	12.9%	Milrinone*	0	5	0.1%
	1	580	8.7%		1	8	0.1%
	2	259	3.9%		2	5	0.1%
	3	91	1.4%		3	5	0.1%
	4	34	0.5%		4	4	0.1%
	5	17	0.3%		5	4	0.1%
	6	7	0.1%		6	4	0.1%

Notes: Percentages are calculated relative to the total number of patients in the sample who received postoperative vasopressor infusions (n = 6,677). *The iodilators dobutamine and milrinone were not counted as vasopressors. They are included here to document their frequency of use among patients who also received post-operative infusions with vasopressors (PVI). Patients who did not receive PVI may have received iodilators, but are not included in this table.. $Day: Calendar day after surgery (0 = day of surgery)

Table S11: Assessment of postoperative vasopressor infusion need

Question 6.5 in CRF 2 asked the question: "How was it assessed that this patient should receive a vasopressor infusion?" This question was only asked about patients who did receive postoperative vasopressor infusions (according to the Squeeze definition). The responses in all Squeeze data are summarized in the table below (Cohort A + Cohort B)

Assessment of PVI need	Count	Percentage (%)
Already receiving	4313	64.6
Fluids not working: Cardiac output monitoring	413	6.2
Fluids not working: Clinical assessment alone	1227	18.4
Fluids not working: Echocardiography	129	1.9
Fluids not working: Other	40	0.6
Fluids not working: Unknown	52	0.8
Fluids not working: maximum fluids met	500	7.5
Missing	3	0.0
Total	6677	100.0

Table S12: PVI use by MAP target

	No MAP target recorded		All MAP targets ≤ 65		At least one MAP target > 65		Total	
1-2 days PVI use	1548	(64.3)	1444	(60.5)	1000	(53.1)	3992	(59.8)
3 or more days PVI use	858	(35.7)	944	(39.5)	883	(46.9)	2685	(40.2)
Total	2406	(100.0)	2388	(100.0)	1883	(100.0)	6677	(100.0)

Prolonged PVI use by MAP targets (Squeeze recipients of PVI only). Number (percentages in brackets)