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REVIEW

Cumulative Incidence of Venous Thromboembolic Events In-Hospital, and at 1, 3, 6, and 12 Months After Metabolic and Bariatric Surgery: Systematic Review of 87 Studies and Meta-analysis of 2,731,797 Patients

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Abstract
Systematic review/meta-analysis of cumulative incidences of venous thromboembolic events (VTE) after metabolic and bariatric surgery (MBS). Electronic databases were searched for original studies. Proportional meta-analysis assessed cumulative VTE incidences. (PROSPERO ID:CRD42020184529). A total of 3066 records, and 87 studies were included (N patients = 4,991,683). Pooled in-hospital VTE of mainly laparoscopic studies = 0.15% (95% CI = 0.13–0.18%); pooled cumulative incidence increased to 0.50% (95% CI = 0.33–0.70%); 0.51% (95% CI = 0.38–0.65%); 0.72% (95% CI = 0.13–1.52%); 0.78% (95% CI = 0–3.49%) at 30 days and 3, 6, and 12 months, respectively. Studies using predominantly open approach exhibited higher incidence than laparoscopic studies. Within the first month, 60% of VTE occurred after discharge. North American and earlier studies had higher incidence than non-North American and more recent studies. This study is the first to generate detailed estimates of the incidence and patterns of VTE after MBS over time. The incidence of VTE after MBS is low. Improved estimates and time variations of VTE require longer-term designs, non-aggregated reporting of characteristics, and must consider many factors and the use of data registries. Extended surveillance of VTE after MBS is required.

Keywords Systematic review · Meta-analysis · Morbid obesity · Bariatric surgery · Venous thromboembolism · Incidence · Laparoscopic procedure · Open surgery

Key Points

- Evidence before this study: Global estimates of venous thromboembolic events (VTE) at different timepoints after metabolic and bariatric surgery (MBS) remain uncertain.
- Added value: Meta-analysis of 2,731,797 MBS patients generated high-quality VTE incidence estimates for in-hospital and at 30 days and 3, 6, and 12 months respectively, and valuable insights into VTE patterns over time.
- Implications: VTE after MBS is low, mostly in the first month, some up to our last timepoint; variations across time must consider many interrelated factors, and vigilant surveillance after discharge and for extended periods is required.

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Introduction

Metabolic and bariatric surgery (MBS) is an effective approach for achieving weight loss and resolution of obesity-associated medical problems among patients with obesity [1, 2]. As with any surgical procedure, there is the risk of post-operative venous thromboembolic events (VTE) after MBS, which is exacerbated by the underlying obesity [3]. With the increasing global frequency of MBS [4], VTE presents a particularly serious complication with significant effects on readmission rates and mortality [3, 5, 6].

The literature has shown wide variations in the incidence of VTE after MBS [7, 8]. For instance, previous studies have reported 30-day incidences ranging from 0 to 5.66% [9, 10]. Although the number of meta-analyses on many MBS topics continues to increase [11–13], there are no systematic reviews/meta-analyses of the incidence of VTE after MBS. This is despite the available literature that could be meta-analyzed to generate high-quality estimates [5, 7, 10, 14–17]. To date, global estimates of VTE at different timepoints after MBS remain uncertain, despite the calls for more accurate estimates [7]. The current study is the first to bridge this knowledge gap.

Aim of the Study

The present study aimed to review and synthesize the evidence on the incidence of VTE after MBS. The objectives were to (1) compute global cumulative incidence of VTE at five timepoints after surgery (in-hospital, at 30 days and 3, 6, and 12 months) for studies that utilized mainly laparoscopic approach and those that used predominantly open surgical approach and (2) for the first 30 days investigate the proportions of VTE that occurred in-hospital vs post-discharge. In addition, we subgrouped the studies at each timepoint by two variables, namely, *geographic origin* and *study age* (final year of data acquisition) to explore potential sources of heterogeneity, and appraise whether such factors influenced the incidence of VTE. Evaluation of procedure- or patient-related risk factors or prophylaxis and their associations with VTE were not within the scope of this review.

Materials and Methods

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement was used to conduct and report this systematic review with meta-analysis [18]. The study protocol was registered a priori (PROSPERO ID: CRD42020184529).

Search Strategy

A systematic search for relevant studies was conducted on 27 April 2022 using PubMed, MEDLINE, and Scopus. The full search strategy, including search terms and medical subject headings (MeSH), is detailed in Supplementary File 1. The reference lists of related reviews were checked for eligible studies that were not captured in the search.

Study Selection

The inclusion criteria were original English language studies of any design, sample size, MBS procedure, or surgical approach that provided cumulative incidence of VTE or sufficient detail to calculate it for the total patient sample. Exclusion criteria included commentaries, letters, practice guidelines, reviews, and conference proceedings; studies that did not include VTE; studies that applied specific limitations to the patient populations they examined, e.g., specific age, weight or BMI cutoffs, obesity associated medical problems, or ethnicity; or questionnaire-based studies reporting subjective recall of VTE from clinicians. Studies were included if they accounted for all VTE including both deep vein thrombosis and pulmonary embolism. Studies that accounted only for specific sub-types of VTE were excluded.

Screening and Data Extraction

Duplicate titles were removed and then all references were independently screened by two authors (WEA, ML) using Covidence (Veritas Health Innovation, Australia). The first stage was title and abstract screening, and studies were excluded if both authors rejected them. In the second stage, full-text articles were screened for eligibility, and studies approved by both authors were included. Conflicts were resolved through discussion between the two authors. Data extraction was undertaken and tabulated by WEA and KE-A and verified by ML and included study identifiers, country, sample size and characteristics, data sources, duration of data acquisition, surgical procedure, approach (laparoscopic, open, robotic), and the reported incidence and timing of VTE. Missing data were calculated where possible or extracted from figures using WebplotDigitizer 4.5 (Ankit Rohatgi, USA).

Outcomes

The outcomes were cumulative incidence of VTE at five timepoints (in-hospital, 30 days, and 3, 6, 12 months) and for the first 30 days, the proportions of VTE that occurred in-hospital vs post-discharge.

Risk of Bias Assessment

Potential risk of bias was assessed using the tool by Loney et al. [19], which was developed specifically for studies of prevalence/incidence. The tool was selected for its comprehensiveness and applicability to the study objectives. It comprises eight equally weighted items yielding a maximum score of eight, with higher scores indicating lower risk of bias. Included studies were scored by ML, and then 10% was randomly selected and scored by WEA. Mean percentage agreement across the eight individual items was reported.

Data Synthesis and Statistical Analysis

All studies were cross-checked for duplicated use of data by verifying their data sources (hospital or national/regional registries), sampling timeframe, and included procedures. Where duplicate use of patient data was suspected, only the studies that minimized any overlap were included in the meta-analyses. As many of the included studies were undertaken using large administrative datasets such as NSQIP, MBSAQIP, or NIS, multiple studies included in the same year/s of data from the same registry were meticulously securitized for their procedures, patient samples, and recruitment years, in order to check, confirm, and exclude any potential duplicate use of the data of the same patients. If there was any remaining doubt, the research team undertook the extra step of contacting the authors of such papers for more verification.

Random effects proportional meta-analyses of VTE at the five timepoints were conducted using MetaXL (EpiGear, international Pty Ltd., Queensland, Australia) for Microsoft Excel. Data were transformed using the double arcsine method. This allows inclusion of zero-case studies, stabilizes variance, and has demonstrated advantages [20]. Additionally, categorical meta-analysis assessed pre- versus post-discharge 30-day incidence and was expressed as a proportion of the total number of cases.

Results were presented by surgical approach as pooling both (laparoscopic and open) approaches was deemed inappropriate because most procedures are currently undertaken laparoscopically. Most studies reported a mix of laparoscopic and open approaches; hence, cut-offs were required. As approximately half of the studies that used a majority open approach reported it for 50–80% of their procedures, and almost all studies that used a majority laparoscopic approach reported it for > 80% of their procedures, we subgrouped studies into "> 80% laparoscopic approach" vs "> 50% open approach." Furthermore, subgroup analyses were conducted on cumulative incidences at each timepoint to identify any influence of the subgroups on the pooled estimates, and to assess sources of heterogeneity. In terms of study age, we categorized studies into those with data collected up to the end of 2010 vs after 2010, as an earlier cut-off was not feasible due to a lack of relevant studies. Geographically, it was only feasible to subgroup studies into North America vs "other" countries, as roughly 70% of studies were from North America. This latter comparison was limited to studies with > 80% laparoscopic approach to minimize possible confounding due to surgical approach. Since small samples have potentially lower sensitivity to capture VTE, sensitivity analysis was undertaken excluding the small studies ($n < 2000$ patients) to assess its influence on pooled incidence of the geographical subgroups.

Heterogeneity

Heterogeneity was measured using Higgin's I^2, Cochrane's Q, and Chi^2. Given the nature of incidence data, high heterogeneity was expected due to large sample sizes and low variance. Therefore, thresholds for heterogeneity [21] were interpreted conservatively in line with recommendations regarding proportional meta-analysis [22].

Publication Bias

We used funnel plots based on sample size (rather than standard error) as they have been shown to be a valid alternative for assessing publication bias in proportional meta-analysis [23], since traditional funnel plots may indicate asymmetry when no publication bias is present [22, 23]. In addition, recent guidelines recommend qualitative methods to appraise publication bias of incidence data [22]. Hence, we assessed publication bias using a combination of both.

Results

Search Results

The PRISMA diagram (Fig. 1) shows that of 3066 retrieved articles, 87 were included in the review [5, 6, 9, 10, 14–17, 24–102], of which 68 were meta-analyzed. The studies excluded at full text and their reasons, as well as the included studies, and their subgroupings are available in Supplementary File 2.

Study Characteristics

Table 1 outlines the studies included in the review (N = 4,991,683 patients). A total of 2,259,886 patients were subsequently excluded from meta-analyses due to data overlap or aggregated data. Data of the remaining 2,731,797 patients were meta-analyzed. The largest study included 540,959 patients [31] and the smallest comprised 39 patients [60].

Geographically, 62 included studies (71.3%) were based on North American data, whereas 25 (28.7%) reported data from other countries. Surgical approach was > 80% laparoscopic in 60 studies (69.0%); > 50% open in 10 (11.5%); did not fulfill the above cut-offs for surgical approach in three (3.44%) [24, 55, 80]; and was not explicitly reported in 14 studies (16.1%). Thirty-two studies (36.8%) included data collected up to the end of 2010, 52 (59.8%) included data collected after 2010, and three studies (3.4%) did not report their data timeframe [16, 53, 99].

Thirty-six studies (41.4%) reported ≥ 3 MBS procedures, 15 (17.2%) undertook only RYGB, 14 (16.1%) included both RYGB and SG, seven (8.0%) undertook strictly SG, four

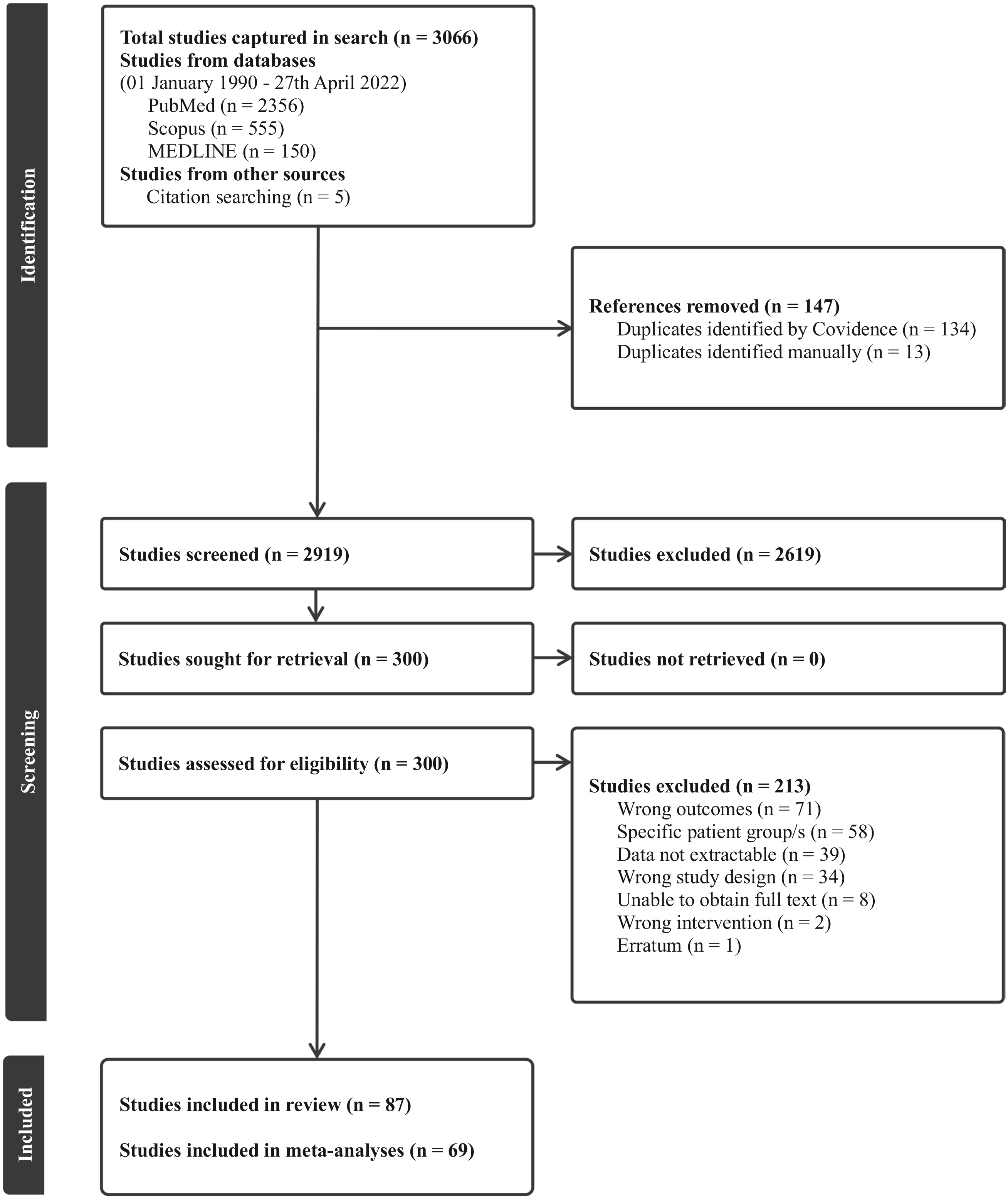


Fig. 1 PRISMA flowchart of search and screening results

Table 1 Characteristics of the 87 original studies included in the current review (4,991,683 patients)

Study	N	Country	Surgical procedure/s	Approach	Female (%)	Mean age y (range)	Mean BMI kg/m^2	Study period
Almarshad 2020 [25]	374	Saudi Arabia	M	L 98.12% + O	72.99	36.07	—	2014–2018
Al-Mazrou 2021 [24]	7235	USA	BPD-DS	L 79.1% + R	73.17	43.79	51.0 ± 18.4	2015–2018
Arterburn 2014 [26]	7457	USA	RYGB, AGB	L	83.07	46 (45.8–46.3)	44.17	2005–2009
Bellen 2013 [10]	53	Brazil	—	O 73.6% + L	—	—	—	2007–2009
Biertho 2014 [26]	800	Canada	SG, BPD-DS	L	74	43.78	48 ± 7.57	2008–2011
Blackstone 2010 [27]	2416	USA	RYGB, AGB	L	77.28	45.4	47.5 ± 8.4	2001–2008
Celik 2014 [29]	2064	Netherlands	M	L > 95%	75	44.9	44.4 ± 6.2	2008–2011
Chan 2013 [14]	500	UK	M	L	75.4	44.7 (19–77)	49.2	2007–2010
Chung 2019 [30]	230,468	USA	M	L 90%	78.46	43.33	—	2000–2015
Clapp 2022 [31]	540,959	USA	RYGB, SG	L	80	44.4 (18–80)	5.2 ± 7.7	2017–2019
Clements 2009 [32]	956	USA	RYGB	L	82.76	41	49.1 ± 0.2	2000–2008
Cottam 2018 [33]	798	USA	RYGB, SIPS	—	73.06	45.65	48.98 ± 9.21	2010–2016
Cotter 2005 [34]	107	USA	RYGB	O 94.4% + L	78.5	40 (23–69)	51.3	2000–2001
Daigle 2018 [5]	135,413	USA	M	—	78.7	44.5 ± 12	45.7 ± 8.3	2015
Dang 2019 [6]	274,221	USA	RYGB, SG	L	79.2	44.6	45.51 ± 8.01	2015–2016
Doyon 2016 [35]	43,477	USA	RYGB	L	—	44.9	46.96 ± 8.21	2005–2012
ElChaar 2019 [36]	101,599	USA	RYGB, SG	L	—	—	—	2015
Eriksson 1997 [37]	328	Sweden	M	—[a]	77.13	38 (18–67)	44	1977–1993
Fanous 2012 [38]	711	USA	RYGB	L	80.17	45.15	51.67 ± 8.6	2007–2009
Fennern 2021 [39]	43,493	USA	RYGB, SG	L 94% + O	78	Md 45	—	2007–2015
Finks 2012 [40]	27,818	USA	M	L 95% + O	78	46	48	2006–2011
Flores 2022 [41]	788	Mexico	RYGB, SG	—	80.7	38.8	43.9 ± 7.8	2012/2018
Flum 2009 [42]	4610	USA	M	L 87.2% + O	78.9	44.5	—	2005–2007
Froehling 2013 [43]	396	USA	M	O ≥ 58% + L	81.6	43.8 (18–76)	Md 46.5	1987–2005
Gambhir 2020 [44]	369,032	USA	RYGB, SG	L	79.85	—	—	2015–2017
Gonzalez 2006 [45]	660	USA	RYGB	O 52.58% + L	—	—	—	1998–2004
Gorosabel Calzada 2022 [9]	675	Spain	M	L	67.26	43	45	2010–2015; 2019–2019
Greenstein 2012 [46]	5882	USA	M	L 91.43% + O	85.4	Md 47	Md 44	2005–2009
Guerrier 2018 [47]	114,362	USA	RYGB, SG	L (% —) + O	78.96	44.5	44.5	2010–2014
Hamad 2005 [48]	668	USA	M	O 84.9% + L	86	41.7	49.6 ± 8.4	2002–2002
Haskins 2015 [49]	102,869	USA	M	L 93.4% + O	78.925	45.11	46.08 ± 8.32	2005/2012
Haskins 2019 [50]	286,704	USA	RYGB, SG	L	79.66	44.93	45.26 ± 8.06	2015–2016

Table 1 (continued)

Study	*N*	Country	Surgical procedure/s	Approach	Female (%)	Mean age *y* (range)	Mean BMI kg/m^2	Study period
Hasley 2022 [51]	638	USA	SG	L	81.7	41.3	44.4	2010–2018
Helm 2017 [52]	59,424	USA	M	—	79.1	44.79	45.93 ± 8.16	2012–2014
Hess 1998 [53]	440	USA	BPD-DS	O	78.41	39	50	1988–[b]
Hu 2018 [54]	69,365	USA	M	L 90.04% + O	65.59	Md 45	—	2011–2014
Hussain 2020 [55]	212	Australia	M	L ≥ 52.83% + O	81.13	—	—	2013–2017
Imberti 2014 [56]	250	Italy	M	L ≥ 82.5% + O	79	40.9	44.4 ± 5.4	2004–2012
Inabnet 2010 [57]	3802	USA	M	L (% —) + O	—	44.22	48.51	2005–2007
Jamal 2015 [15]	4293	USA	M	L 99.615 + O	68.5	46.14 ± 9.81	48.45 ± 12.7	2005–2013
James 2021 [58]	153	USA	SG	L	81	—	47.9 ± 5.7	2017–2019
Kakarla 2011 [59]	28,634	USA	RYGB, GBn	L	—	—	—	2005–2008
Khoursheed 2013 [60]	39	Kuwait	RYGB	L	79.49	32.4	44.5 ± 6.1	2008–2010
Krell 2014 [61]	17,057	USA	RYGB	L	79	45.8	47.6 ± 7.89	2006–2012
Kruger 2014 [62]	3460	USA	M	L 99.83% + O	83.4	44 (18–74)	46.69 ± 6.58	2004–2013
Lech 2022 [63]	291	Poland	SG	L	79	40.3	45.3 ± 8.25	2016–2017
Leeman 2020 [64]	3319	Netherlands	RYGB, SG	—	82.46	40.41	43.27 ± 4.83	2014–2018
Li 2012 [65]	97,128	USA	RYGB, AGB	L 95% + O	78.87	46	45.5 ± 6.60	2007–2010
Lins 2015 [66]	209	Brazil	RYGB	L	—	40.2	41.5	2008–2013
Mabeza 2022 [67]	537,522	USA	RYGB, SG	L 97.3% + O	79.94	44.94	—	2016–2018
Magee 2010 [68]	735	UK	M	L	79.05	Md 42 (18–72)	Md 47.9	1997–2008
Masoomi 2011 [69]	304,515	USA	M	L 86% + O	79.9	44.1	—	2006–2008
McCullough 2006 [70]	109	USA	RYGB	L	75.2	46 (10.4)	48.7 ± 7.2	2001–2003
Miller 2004 [71]	255	USA	RYGB	L	82	43.2 (18–62)	50	2000–2003
Minhem 2018 [72]	21,131	USA	SG	L	78.21	44.35	46.07 ± 8.11	2010–2013
Modasi 2019 [73]	430,936	Canada	RYGB, SG	L	79.4	49.3	46.3 ± 7.94	2015–2017
Moussa 2021 [16]	4073	UK	—	—	79.6	Md 50 (IQR: 42–58)	Md 40.2	—
Nielsen 2018 [74]	59,041	USA	M	—	79	44.8 ± 11.8	45.9 ± 8.1	2012–2014
Nimeri 2013 [75]	29,990	USA/UAE	M	L 94.41% + O	69.8	36	47.4 ± 11	2009–2012
Nimeri 2018 [17]	66,845	USA/UAE	RYGB, SG	L	79.72	44.36 ± 11.91	47 ± 9.5	2010–2016
Nudel 2021 [76]	436,807	USA	RYGB, SG	L	79.3	44.7	45.4	2015–2017
Obeid 2007 [77]	2099	USA	RYGB, AGB	O 91.9% + L	84.85	44.65	54.4	2000–2006
Poulose 2005 [78]	69,072	USA	M	L (% —) + O	85	41.6 (41.2–42.0)	—	2002
Prasad 2012 [79]	108	India	SG	L	77.78	39.3 (15–62)	44.5 ± 6.8	2008–2011
Prystowsky 2005 [80]	106	USA	RYGB	L 75% + O	74	43 (26–67)	51	2004–2005

Table 1 (continued)

Study	*N*	Country	Surgical procedure/s	Approach	Female (%)	Mean age *y* (range)	Mean BMI kg/m^2	Study period
Quebbemann 2005 [81]	822	USA	M	L	—	43 (15–74)	45.2 ± 7.1	2000–2005
Raftopoulos 2008 [82]	308	USA	M	L 96.4% + O	82.79	43.35 (18–73)	46.95	2003–2007
Ramly 2017 [83]	66,078	USA	RYGB, RYGB/ GBn removal	L	79.47	45.07 (16–90)	46.44 ± 8.28	2008–2014
Reames 2015 [84]	16,344	USA	RYGB	L	79	45.82	47.63 ± 7.83	2006–2012
Rezvani 2014 [85]	362	USA	BPD-DS	L	—	44.8	50 ± 7.1	2006–2012
Rezvani 2014 [86]	226	USA	BPD-DS	L	75.22	44.9	50.2	2009–2011
Rodríguez 2020 [87]	421	Chile	SG	L	65.56	35.35	35.94 ± 3.0791	2009–2019
Scholten 2002 [88]	481	USA	M	O 97.5% + L	83.16	44	51.05	1997–2000
Shah 2012 [89]	56	USA	AGB	L	—	38	50.9	2002–2007
Sharma 2020 [90]	737	USA	SG	L	56.31	45.3	43.9 ± 7.34	2012–2017
Singh 2012 [91]	170	USA	RYGB	—	46.47	43	47.8 ± 6.9	2004–2007
Spaniolas 2016 [92]	71,694	USA	M	L ≥ 89% + O	—	Md 45	Md 44.8	2006–2011
Steele 2011 [93]	17,434	USA	M	O 65.7% + L	82.01	43	—	2002–2005
Stroh 2012 [94]	11,835	Germany	M	—	72.5	42.2 (11–79)	48.8	2005–2010
Stroh 2016 [95]	29,561	Germany	M	L 98% + O	72.05	—	—	2005–2013
Surve 2022 [96]	5,017	USA	M	—	—	43.2 ± 12.1	44.6 ± 8.5	2016–2021
Thereaux 2018 [97]	110,824	France	M	L 95% + O	80.85	39.93 ± 11.6	—	2012–2014
Thereaux 2014 [98]	1008	France	RYGB	L	78.7	42.6 ± 11.6	47.6 ± 7.6	2004–2013
Westling 2002 [99]	116	Sweden	RYGB	O 74.1% + L	—	Md 35 (19–59)	Md 42	—[b]
Winegar 2011 [100]	73,921	USA	M	L 92.7% + O	79	45.8 ± 11.74	46 ± 7.85	2007–2009
Woo 2013 [101]	200	Korea	M	L	—	35 (14–63)	39	2009–2011
Young 2015 [102]	24,117	USA	RYGB, SG	L	78.09	44.8	46 ± 8.22	2010–2011

Due to space limitations, only the first author is cited

BPD biliopancreatic diversion, *D* duration, *DS* duodenal switch, *GB* gastric bypass, *GBn* gastric banding, *L* laparoscopic, *BMS* bariatric/metabolic surgery, *N* number of patients, *O* open approach, *RYGB* Roux-en-Y GB, *SG* sleeve gastrectomy, *y* years, *M* multiple, *Md* median, *R* robotic, *SIPS* Stomach Intestinal Pylorus-Sparing Surgery, — not explicitly reported/ cannot be computed

[a]Surgical approach not explicitly reported, assumed to be mostly open due to the sampling time frame being 1977–1993

[b]Time frame not explicitly reported, assumed to be before 2010 as publication date was before 2010

Table 2 Timeframe of incidence provided by each included study

Study	Time period assessed				
	In-hospital	30 days	3 months	6 months	12 months
Almarshad 2020[25]	■	■	■		
Al-Mazrou 2021[24]		■ †			
Arterburn 2014[26]		■ *			
Bellen 2013[10]		■			
Biertho 2014[26]		■			
Blackstone 2010[27]			■		
Celik 2014[29]	■	■	■	■	
Chan 2013[14]			■		
Chung 2019[30]		■		■	■
Clapp 2022[31]		■			
Clements 2009[32]		■			
Cottam 2018[33]		■ †			
Cotter 2005[34]	■	■			
Daigle 2018[5]		■ *			
Dang 2019[6]		■ *			
Doyon 2016[35]		■ *			
ElChaar 2019[36]		■ *			
Eriksson 1997[37]		■			
Fanous 2012[38]		■			
Fennern 2021[39]			■		
Finks 2012[40]		■			
Flores 2022[41]		■ †			
Flum 2009[42]		■			
Froehling 2013[43]	■	■	■	■	
Gambhir 2020[44]		■ *			
Gonzalez 2006[45]		■			
Gorosabel Calzada 2022[9]		■			■
Greenstein 2012[46]		■ *			
Guerrier 2018[47]		■ *			
Hamad 2005[48]	■	■			
Haskins 2015[49]		■ *			
Haskins 2019[50]		■			
Hasley 2022[51]	■	■ *	■	■	
Helm 2017[52]	■ †	■ †			
Hess 1998[53]		■			
Hu 2018[54]		■			
Hussain 2020[55]			■ †		
Imberti 2014[56]		■	■		
Inabnet 2010[57]		■ †			
Jamal 2015[15]	■			■	
James 2021[58]		■			
Kakarla 2011[59]		■ †			
Khoursheed 2013[60]		■			
Krell 2014[61]		■ *			
Kruger 2014[62]		■			
Lech 2022[63]	■	■	■	■	
Leeman 2020[64]			■ †		
Li 2012[65]			■		

Table 2 (continued)

Lins 2015[66]					
Mabeza 2022[67]					
Magee 2010[68]					
Masoomi 2011[69]					
McCullough 2006[70]					
Miller 2004[71]					
Minhem 2018[72]		*			
Modasi 2019[73]		*			
Moussa 2021[16]		†		†	†
Nielsen 2018[74]		*			
Nimeri 2013[75]		*			
Nimeri 2018[17]		†			
Nudel 2021[76]		*			
Obeid 2007[77]					
Poulose 2005[78]	†				
Prasad 2012[79]					
Prystowsky 2005[80]		†			
Quebbemann 2005[81]					
Raftopoulos 2008[82]					
Ramly 2017[83]		*			
Reames 2015[84]		*			
Rezvani 2014[86]					
Rezvani 2014[85]					
Rodríguez 2020[87]					
Scholten 2002[88]					
Shah 2012[89]	‡				
Sharma 2020[90]					§
Singh 2012[91]	†	†	†	†	†
Spaniolas 2016[92]		†			
Steele 2011[93]					
Stroh 2012[94]			†		
Stroh 2016[95]					
Surve 2022[96]		†			
Thereaux 2018[97]					
Thereaux 2014[98]					
Westling 2002[99]					
Winegar 2011[100]			*		
Woo 2013[101]					
Young 2015[102]		*			

Due to space limitations, only the first author is cited; m: months; d: days; Grey shaded boxes indicate that data was explicitly provided or was able to be calculated; * Study was excluded from all meta-analyses of this time point due to significant overlap in data with other studies; † Study excluded from at least one meta-analysis for this timepoint due to overlap or insufficient information about surgical approach or sampling timeframe, but included in others; ‡ Patients were scanned 2 to 3 days post-surgery, data was included as in-hospital; § Timeframe for incidence data was 15-months, but was included in the 12-month analysis

(4.6%) conducted only BPD-DS, six (6.9%) included RYGB and adjustable gastric banding or removal, three (3.4%) reported other combinations [27, 33, 89], and two studies (2.3%) did not report their included procedures [10, 16].

Seventy-three studies (83.9%) reported the sex distribution of their sample, with females comprising a mean of 77.6%. Fourteen (16.1%) did not report sex distribution. Seventy-two studies (82.8%) reported the mean age of

Table 3 Summary of findings

Timing of VTE		Studies	Total sample	Cases	Incidence	Heterogeneity		
		N	*N*	*N*	% of patients (95% CI)	I^2 (%)	*Q*	Chi², *p*
In-hospital								
Surgical approach	> 80% laparoscopic	14	1,064,822	1613	0.15 (0.13; 0.18)	72.00	47.23	0.00
	> 50% open	5	19,086	157	0.43 (0.05; 0.94)	75.00	16.03	0.00
Country	North America	8	921,508	1353	0.14 (0.11; 0.18)	80.00	34.31	0.00
	Other countries	6	143,404	260	0.18 (0.16; 0.20)	0.00	3.02	0.70
Year of study	Up to 2010 *	12	467,383	984	0.32 (0.18; 0.49)	96.00	301.16	0.00
	After 2010	10	745,191	1085	0.15 (0.12; 0.18)	61.00	22.93	0.00
30 Days								
Surgical approach	> 80%laparoscopic	30	1,380,293	7371	0.50 (0.33; 0.70)	99.00	4056.37	0.00
	> 50% open	10	22,295	466	2.02 (1.51; 2.57)	60.00	22.29	0.01
Country	North America	18	1,262,051	6960	0.58 (0.34; 0.87)	100.00	3985.54	0.00
	Other countries	12	117,090	402	0.34 (0.17; 0.55)	59.00	26.72	0.01
Year of study	Up to 2010 *	22	34,918	536	1.29 (0.81; 1.83)	91.00	228.18	0.00
	After 2010	25	1,421,225	7606	0.43 (0.27; 0.63)	99.00	4027.98	0.00
3 months								
Surgical approach	> 80%laparoscopic	14	796,797	4042	0.51 (0.38; 0.65)	95.00	242.97	0.00
	> 50% open	1	396	8	2.14 (0.83; 3.68)	N/A	N/A	N/A
Country	North America	6	681,559	3458	0.61 (0.40; 0.86)	98.00	230.26	0.00
	Other countries	7	113,174	574	0.37 (0.14; 0.65)	52.00	12.61	0.05
Year of study	Up to 2010 *	7	113,180	286	0.39 (0.19; 0.63)	87.00	44.47	0.00
	After 2010	11	697,485	3775	0.48 (0.39; 0.58)	82.00	54.81	0.00
6 months								
Surgical approach	> 80%laparoscopic	7	238,062	6177	0.72 (0.13; 1.52)	96.00	151.07	0.00
	> 50% open	3	18,311	537	2.36 (1.44; 3.41)	64.00	5.54	0.06
Country	North America	3	235,399	6165	1.45 (0.56; 2.69)	96.00	53.82	0.00
	Other countries	4	2663	12	0.31 (0.10; 0.74)	16.00	3.58	0.31
Year of study	Up to 2010 *	4	18,481	537	1.67 (0.57; 3.03)	83.00	17.64	0.00
	After 2010	7	238,062	6177	0.72 (0.13; 1.52)	96.00	151.07	0.00
12 months								
Surgical approach	> 80%laparoscopic	3	231,880	7559	0.78 (0.00; 3.49)	98.00	108.89	0.00
	> 50% open	1	16,929	579	3.38 (3.15; 3.70)	N/A	N/A	N/A
Country	North America	2	231,205	7559	1.60 (0.00; 5.00)	97.00	37.77	0.00
	Other countries	1	675	0	0.04 (0.00; 0.25)	N/A	N/A	N/A
Year of study	Up to 2010*	2	17,099	579	1.32 (0.00; 5.79)	93.00	14.75	0.00
	After 2010	3	231,880	7559	0.78 (0.00; 3.49)	98.00	108.89	0.00

*Includes 2010; *N/A* Not Applicable

their sample, with an average of 42.9 ± 3.02 years, while seven (8%) provided the median age for the sample, and eight studies (9.2%) did not report age. Sixty-four studies (73.6%) reported mean BMI (46.1 ± 6.0 kg/m^2 across all studies), six (6.9%) provided their median BMIs, while 17 studies (19.5%) did not report BMI.

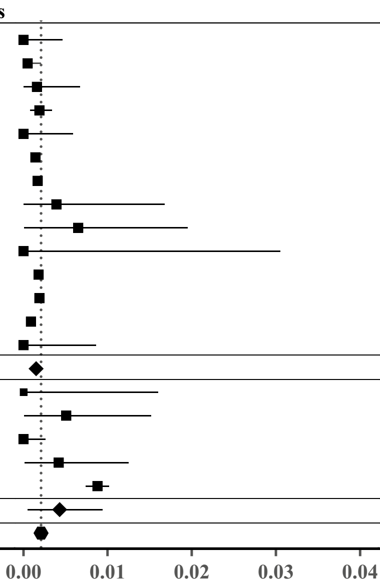
Table 2 shows the time point/s of incidence provided by each included study (i.e., the specific meta-analysis/es that each study contributed to, as well as the studies that were excluded from primary (not sub-grouped) meta-analysis of any given time point due to significant overlap in data with other studies. Data sources of each included study are outlined in Supplementary File 3.

Risk of Bias Appraisal

The mean risk of bias score was 5.82 ± 1.43, with a range of 3–8 (Supplementary File 4). Fifty studies (57.5%) scored six or higher, indicating a low risk of bias. The 20 studies with lower scores of 3–4 were mainly due to small sample

A

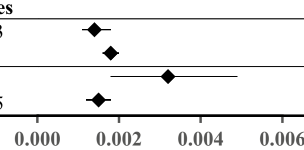
All studies	Total sample	Cases	Incidence	LCI 95%	HCI 95%	Weight (%)
Almarshad 2020[25]	374	0	0.0000	0.0000	0.0046	1.45
Celik 2014[29]	2064	1	0.0005	0.0000	0.0021	5.28
Hasley 2022[51]	638	1	0.0016	0.0000	0.0067	2.29
Jamal 2015[15]	4293	8	0.0019	0.0008	0.0034	7.60
Lech 2022[63]	291	0	0.0000	0.0000	0.0059	1.16
Mabeza 2022[67]	537522	753	0.0014	0.0013	0.0015	12.73
Masoomi 2011[69]	304515	518	0.0017	0.0016	0.0019	12.68
Miller 2004[71]	255	1	0.0039	0.0000	0.0168	1.02
Raftopoulos 2008[82]	308	2	0.0065	0.0001	0.0195	1.22
Shah 2012[89]	56	0	0.0000	0.0000	0.0305	0.24
Stroh 2016[95]	29561	52	0.0018	0.0013	0.0023	11.64
Thereaux 2018[97]	110824	207	0.0019	0.0016	0.0021	12.47
Winegar 2011[100]	73921	70	0.0009	0.0007	0.0012	12.31
Woo 2013[101]	200	0	0.0000	0.0000	0.0086	0.82
>80% laparoscopic approach	**1064822**	**1613**	**0.0015**	**0.0013**	**0.0018**	**82.90**
Cotter 2005[34]	107	0	0.0000	0.0000	0.0160	0.45
Froehling 2013[43]	396	2	0.0051	0.0001	0.0152	1.52
Hamad 2005[48]	668	0	0.0000	0.0000	0.0026	2.37
Scholten 2002[88]	481	2	0.0042	0.0001	0.0125	1.80
Steele 2011[93]	17434	153	0.0088	0.0074	0.0102	10.95
>50% open approach	**19086**	**157**	**0.0043**	**0.0005**	**0.0094**	**17.10**
Pooled	**1083908**	**1770**	**0.0021**	**0.0016**	**0.0028**	**100.00**



Heterogeneity	I^2 (%)	Q	Chi², p
>80% laparoscopic	72.00	47.23	0.00
>50% open	75.00	16.03	0.00
Pooled	93.11	261.18	0.00

B

Subgroups		Studies	Total sample	Cases	Incidence	LCI 95%	HCI 95%	Weight (%)
Country	North America	8	921508	1353	0.0014	0.0011	0.0018	64.97
	Other countries	6	143404	260	0.0018	0.0016	0.0020	35.03
Year	Up to 2010 (inclusive)	12	467383	984	0.0032	0.0018	0.0049	45.97
	After 2010	10	745191	1085	0.0015	0.0012	0.0018	54.03



Subgroups	Heterogeneity	I^2 (%)	Q	Chi², p
Country	North America	80.00	34.31	0.00
	Other countries	0.00	3.02	0.70
Year	Up to 2010 (inclusive)	96.00	301.16	0.00
	After 2010	61.00	22.93	0.00

Fig. 2 In-hospital incidence of venous thromboembolic events. Forest plot showing: **A** > 80% laparoscopic and > 50% open; **B** pooled results by two subgroupings—country (North America vs other countries, limited to studies comprising > 80% laparoscopic surgical approach to minimize confounding from surgical approach) and year (last year of data inclusion before and including 2010 vs after 2010, not limited by surgical approach). Square data points: incidence from individual studies; diamond-shaped data points: pooled values from subgroups; hexagonal data points: pooled values from all studies that reported relevant data

sizes, potentially biased sampling frames, or poor reporting. Items 2 and 4 had the lowest number of studies receiving a score for them (50.57% and 42.53%, respectively). Average inter-rater agreement for the 10% of the studies randomly selected was 79.17% ± 17.25 across the nine items.

Meta-analysis

The summary of findings of the meta-analyses at the different time points and their subgroupings is depicted in Table 3. Below, we detail the findings at each time point individually.

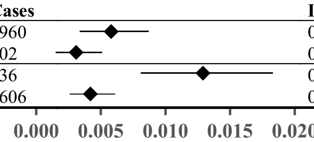
A

All studies	Total sample	Cases	Incidence	LCI 95%	HCI 95%	Weight (%)
Almarshad 2020[25]	374	1	0.0027	0.0000	0.0115	2.20
Biertho 2014[27]	800	2	0.0025	0.0000	0.0075	2.77
Celik 2014[29]	2064	4	0.0019	0.0004	0.0044	3.22
Chung 2019[30]	230468	3754	0.0163	0.0158	0.0168	3.59
Clapp 2022[31]	540959	1689	0.0031	0.0030	0.0033	3.59
Clements 2009[32]	956	4	0.0042	0.0009	0.0095	2.88
Fanous 2012[38]	711	8	0.0113	0.0046	0.0205	2.69
Finks 2012[40]	27818	93	0.0033	0.0027	0.0041	3.56
Flum 2009[42]	4610	20	0.0043	0.0026	0.0065	3.41
Gorosabel Calzada 2022[9]	675	0	0.0000	0.0000	0.0025	2.66
Haskins 2019[50]	286704	844	0.0029	0.0027	0.0031	3.59
Hu 2018[54]	69365	180	0.0026	0.0022	0.0030	3.58
Imberti 2014[56]	250	3	0.0120	0.0015	0.0302	1.84
James 2021[58]	153	2	0.0131	0.0002	0.0390	1.41
Kakarla 2011[59]	28634	111	0.0039	0.0032	0.0046	3.56
Khoursheed 2013[60]	39	0	0.0000	0.0000	0.0438	0.51
Kruger 2014[62]	3460	14	0.0040	0.0022	0.0065	3.36
Lech 2022[63]	291	0	0.0000	0.0000	0.0059	1.98
Lins 2015[66]	209	1	0.0048	0.0000	0.0204	1.68
Magee 2010[68]	735	0	0.0000	0.0000	0.0023	2.71
McCullough 2006[70]	109	2	0.0183	0.0003	0.0545	1.13
Miller 2004[71]	255	3	0.0118	0.0015	0.0296	1.86
Nimeri 2018[17]	66845	234	0.0035	0.0031	0.0040	3.58
Quebbemann 2005[81]	822	1	0.0012	0.0000	0.0052	2.79
Raftopoulos 2008[82]	308	6	0.0195	0.0065	0.0385	2.03
Rezvani 2014[86]	226	2	0.0088	0.0001	0.0265	1.75
Rodríguez 2020[87]	421	4	0.0095	0.0020	0.0215	2.30
Thereaux 2014[98]	1008	10	0.0099	0.0046	0.0171	2.91
Thereaux 2018[97]	110824	379	0.0034	0.0031	0.0038	3.58
Woo 2013[101]	200	0	0.0000	0.0000	0.0086	1.64
>80% laparoscopic approach	**1380293**	**7371**	**0.0050**	**0.0033**	**0.0070**	**78.36**
Bellen 2013[10]	53	3	0.0566	0.0074	0.1386	0.66
Cotter 2005[34]	101	1	0.0099	0.0000	0.0421	1.08
Eriksson 1997[37]	328	8	0.0244	0.0100	0.0443	2.08
Froehling 2013[43]	396	7	0.0177	0.0066	0.0334	2.25
Gonzalez 2006[45]	660	23	0.0348	0.0221	0.0503	2.64
Hamad 2005[48]	668	7	0.0105	0.0039	0.0199	2.65
Hess 1998[53]	440	6	0.0136	0.0045	0.0270	2.33
Obeid 2007[77]	2099	28	0.0133	0.0088	0.0187	3.23
Steele 2011[93]	17434	379	0.0217	0.0196	0.0240	3.54
Westling 2002[99]	116	4	0.0345	0.0075	0.0771	1.18
>50% open approach	**22295**	**466**	**0.0202**	**0.0151**	**0.0257**	**21.64**
Pooled	**1402588**	**7837**	**0.0075**	**0.0056**	**0.0098**	**100.00**

Heterogeneity	I^2 (%)	Q	Chi^2, p
>80% laparoscopic	99.00	4056.37	0.00
>50% open	60.00	22.29	0.01
Pooled	99.15	4597.93	0.00

B

Subgroups		Studies	Total sample	Cases	Incidence	LCI 95%	HCI 95%	Weight (%)
Country	North America	18	1262051	6960	0.0058	0.0034	0.0087	65.57
	Other countries	12	117090	402	0.0034	0.0017	0.0055	34.43
Year	Up to 2010 (inclusive)	22	34918	536	0.0129	0.0081	0.0183	40.05
	After 2010	25	1421225	7606	0.0043	0.0027	0.0063	59.95



Subgroups	Heterogeneity	I^2 (%)	Q	Chi^2, p
Country	North America	100.00	3985.54	0.00
	Other countries	59.00	26.72	0.01
Year	Up to 2010 (inclusive)	91.00	228.18	0.00
	After 2010	99.00	4027.98	0.00

◂**Fig. 3** Thirty-day cumulative incidence of venous thromboembolic events. Forest plot showing: **A** > 80% laparoscopic and > 50% open; **B** pooled results by two subgroupings—country (North America vs other countries, limited to studies comprising > 80% laparoscopic surgical approach to minimize confounding from surgical approach) and year (last year of data inclusion before and including 2010 vs after 2010, not limited by surgical approach). Square data points: incidence from individual studies; diamond-shaped data points: pooled values from subgroups; hexagonal data points: pooled values from all studies that reported relevant data

In-Hospital Incidence of VTE

Meta-analysis of in-hospital incidence of VTE included 19 studies (1,083,908 patients, Fig. 2A), reporting a wide range of incidences (0–0.88%). Studies with > 80% laparoscopic approach exhibited lower pooled incidence of VTE (0.15%; I^2 = 72%) compared to those with > 50% open approach (0.43%; I^2 = 75%). Figure 2 B shows the subgroup analysis: North American studies had slightly lower incidence (0.14%, I^2 = 80%) compared to other countries (0.18%; I^2 = 0%), and studies using data collected up to the end of 2010 displayed higher incidence (0.32%; I^2 = 96%) compared to those after 2010 (0.15%; I^2 = 61%).

Thirty-Day Cumulative Incidence of VTE

Meta-analysis of 30-day cumulative incidence of VTE included 40 studies (1,402,588 patients, Fig. 3A), reporting a wide range of incidences (0–5.66%). Studies with > 80% laparoscopic approach exhibited lower incidence (0.50%; I^2 = 99%) compared to those with > 50% open approach (2.02%; I^2 = 60%). Figure 3 B shows the subgroup analysis: North American studies had higher incidence (0.58%; I^2 = 100%) compared to other countries (0.34%; I^2 = 59%), and studies with data collected up to the end of 2010 demonstrated higher incidence (1.29%, I^2 = 91%) compared to those after 2010 (0.43%; I^2 = 99%).

Three-Month Cumulative Incidence of VTE

Meta-analysis of the 3-month cumulative incidence of VTE included 15 studies (797,193 patients, Fig. 4A), reporting a wide range of incidences (0%-3.31%). Studies with > 80% laparoscopic approach exhibited lower incidence (0.51%; I^2 = 95%) compared to those with > 50% open approach (2.14%; I^2 not applicable); Fig. 4B shows the subgroup analysis: North American studies had higher incidence (0.61%; I^2 = 98%) compared to other countries (0.37%; I^2 = 52%); and studies using data up to the end of 2010 had lower incidence (0.39%; I^2 = 87%) compared to those after 2010 (0.48%; I^2 = 82%).

Six-Month Cumulative Incidence of VTE

Meta-analysis of the 6-month cumulative incidence of VTE included 10 studies (256,373 patients, Fig. 5A), reporting a wide range of incidences (0–2.99%). Studies with > 80% laparoscopic approach exhibited lower incidence (0.72%; I^2 = 96%) compared to those with > 50% open approach (2.36%; I^2 = 64%). Figure 5 B shows the subgroup analysis: North American studies had higher incidence (1.45%; I^2 = 96%) compared to other countries (0.31%; I^2 = 16%), and studies using data up to the end of 2010 displayed higher incidence (1.67%; I^2 = 83%) in comparison with those after 2010 (0.72%; I^2 = 96%).

Twelve-Month Cumulative Incidence of VTE

Meta-analysis of the 12-month cumulative incidence of VTE included six studies (248,809 patients, Fig. 6A). Included studies reported a wide range (0–3.42%) of incidences. Studies with > 80% laparoscopic approach exhibited lower incidence (0.78%; I^2 = 98%) compared to those with > 50% open approach (3.38%; I^2 not applicable). Figure 6 B shows the subgroup analysis: North American studies had higher incidence (1.60%; I^2 = 97%) compared to other countries (0.04%; I^2 not applicable), and studies using data up to the end of 2010 displayed higher incidence (1.32%; I^2 = 93%) in comparison with those after 2010 (0.78%; I^2 = 98%).

Incidence of VTE Within 30 Days: In-hospital vs Post-Discharge

Meta-analysis of 11 studies that reported both in-hospital and 30-day incidence (Supplementary File 5) showed that 60% (95% CI 57–63%; I^2 = 88.16%) of the 30-day VTE occurred after discharge, based on 1073 events.

VTE Over Time

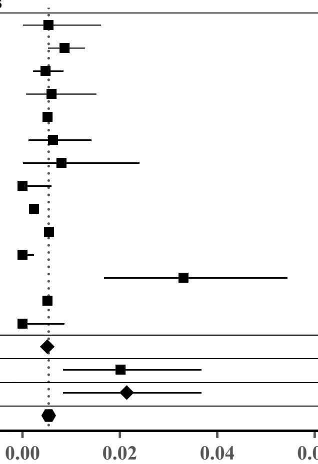
Cumulative incidence of VTE over time is depicted in Fig. 7. Incidence generally increased up to the last timepoint examined (12 months post-MBS). Incidence for > 80% laparoscopic approach was consistently lower compared to the > 50% open approach (Fig. 7A). Subgroup analyses displayed variations across time; incidence from North American studies was higher for most timepoints (based on > 80% laparoscopic procedures only) (Fig. 7C). Sensitivity analysis removing studies with sample sizes < 2000 patients increased the incidence for both subgroups and largely accounted for differences at 30 days (North America 0.43% vs other 0.31%) and 3 months (North America 0.49% vs other 0.51%), but not at 6 months (North America 1.83% vs other 0.48%). Sensitivity analysis was not possible for 12-month data.

Publication Bias

Figure 8 depicts the funnel plots of cumulative incidence of VTE. At some timepoints, more studies reported lower incidence (Fig. 8A–C), and there was a relative paucity of

A

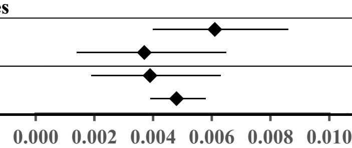
All studies	Total sample	Cases	Incidence	LCI 95%	HCI 95%	Weight (%)
Almarshad 2020[25]	374	2	0.0053	0.0001	0.0161	2.66
Blackstone 2010[28]	2416	21	0.0087	0.0053	0.0128	8.64
Celik 2014[29]	2064	10	0.0048	0.0022	0.0084	8.08
Chan 2013[14]	500	3	0.0060	0.0007	0.0152	3.35
Fennern 2021[39]	43493	224	0.0052	0.0045	0.0058	14.18
Hasley 2022[51]	638	4	0.0063	0.0013	0.0142	4.02
Imberti 2014[56]	250	2	0.0080	0.0001	0.0240	1.89
Lech 2022[63]	291	0	0.0000	0.0000	0.0059	2.15
Li 2012[65]	97128	236	0.0024	0.0021	0.0027	14.48
Mabeza 2022[67]	537522	2961	0.0055	0.0053	0.0057	14.68
Magee 2010[68]	735	0	0.0000	0.0000	0.0023	4.45
Rezvani 2014[85]	362	12	0.0331	0.0168	0.0544	2.59
Thereaux 2018[97]	110824	567	0.0051	0.0047	0.0055	14.51
Woo 2013[101]	200	0	0.0000	0.0000	0.0086	1.55
>80% laparoscopic approach	**796797**	**4042**	**0.0051**	**0.0038**	**0.0065**	**97.22**
Froehling 2013[43]	396	8	0.0202	0.0083	0.0368	2.78
>50% open approach	**396**	**8**	**0.0214**	**0.0083**	**0.0368**	**2.78**
Pooled	**797193**	**4050**	**0.0054**	**0.0041**	**0.0068**	**100.00**



Heterogeneity	I^2 (%)	Q	Chi², p
>80% laparoscopic	95.00	242.97	0.00
>50% open	N/A	N/A	N/A
Pooled	94.45	252.12	0.00

B

Subgroups		Studies	Total sample	Cases	Incidence	LCI 95%	HCI 95%	Weight (%)
Country	North America	6	681559	3458	0.0061	0.0040	0.0086	65.85
	Other countries	7	113174	574	0.0037	0.0014	0.0065	34.15
Year	Up to 2010 (inclusive)	7	113180	286	0.0039	0.0019	0.0063	40.99
	After 2010	11	697485	3775	0.0048	0.0039	0.0058	59.01



Subgroups	Heterogeneity	I^2 (%)	Q	Chi², p
Country	North America	98.00	230.26	0.00
	Other countries	52.00	12.61	0.05
Year	Up to 2010 (inclusive)	87.00	44.47	0.00
	After 2010	82.00	54.81	0.00

Fig. 4 Three-month cumulative incidence of venous thromboembolic events. Forest plot showing: **A** > 80% laparoscopic and > 50% open; **B** pooled results by two subgroupings—country (North America vs other countries, limited to studies comprising > 80% laparoscopic surgical approach to minimize confounding from surgical approach) and year (last year of data inclusion before and including 2010 vs after 2010, not limited by surgical approach). Square data points: incidence from individual studies; diamond-shaped data points: pooled values from subgroups; hexagonal data points: pooled values from all studies that reported relevant data

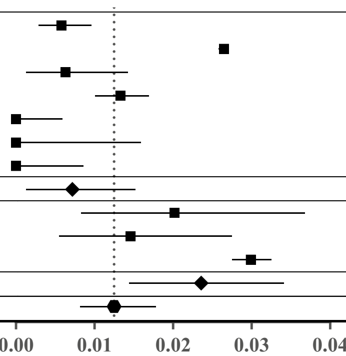
studies of moderate sample sizes; hence, studies clustered at the upper (larger sample sizes) and lower (smaller sample sizes) ends of the *Y* axis (Figs. 8C–E). Qualitatively, countries outside of North America were underrepresented. Roughly three quarters of the studies reported North American data, with many using data registries. For instance, 28 (40.58%) of 69 studies reporting 30-day incidence used North American registry data, introducing considerable overlap of patient data across studies. Figure 8 B shows an unusual 'stacking' pattern of very similar incidences of VTE suggesting the duplicate use of patient data by different studies.

Discussion

Patients with obesity are at risk of VTE in the post-MBS period [8, 100], and those who develop VTE have an increased risk of mortality [5, 6]. Despite this, no previous

A

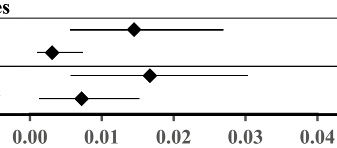
All studies	Total sample	Cases	Incidence	LCI 95%	HCI 95%	Weight (%)
Celik 2014[29]	2064	12	0.0058	0.0029	0.0096	12.85
Chung 2019[30]	230468	6104	0.0265	0.0258	0.0271	14.75
Hasley 2022[51]	638	4	0.0063	0.0013	0.0142	9.96
Jamal 2015[15]	4293	57	0.0133	0.0101	0.0169	13.78
Lech 2022[63]	291	0	0.0000	0.0000	0.0059	7.18
Prasad 2012[79]	108	0	0.0000	0.0000	0.0159	3.85
Woo 2013[101]	200	0	0.0000	0.0000	0.0086	5.82
>80% laparoscopic approach	**238062**	**6177**	**0.0072**	**0.0013**	**0.0152**	**68.18**
Froehling 2013[43]	396	8	0.0202	0.0083	0.0368	8.31
Scholten 2002[88]	481	7	0.0146	0.0055	0.0275	9.00
Steele 2011[93]	17434	522	0.0299	0.0275	0.0325	14.51
>50% open approach	**18311**	**537**	**0.0236**	**0.0144**	**0.0341**	**31.82**
Pooled	**256373**	**6714**	**0.0125**	**0.0082**	**0.0178**	**100.00**



Heterogeneity	I^2 (%)	Q	Chi^2, p
>80% laparoscopic	96.00	151.07	0.00
>50% open	64.00	5.54	0.06
Pooled	94.53	164.50	0.00

B

Subgroups		Studies	Total sample	Cases	Incidence	LCI 95%	HCI 95%	Weight (%)
Country	North America	3	235399	6165	0.0145	0.0056	0.0269	49.73
	Other countries	4	2663	12	0.0031	0.0010	0.0074	50.27
Year	Up to 2010 (inclusive)	4	18481	537	0.0167	0.0057	0.0303	35.30
	After 2010	7	238062	6177	0.0072	0.0013	0.0152	64.70



Subgroups	Heterogeneity	I^2 (%)	Q	Chi^2, p
Country	North America	96.00	53.82	0.00
	Other countries	16.00	3.58	0.31
Year	Up to 2010 (inclusive)	83.00	17.64	0.00
	After 2010	96.00	151.07	0.00

Fig. 5 Six-month cumulative incidence of venous thromboembolic events. Forest plot showing: **A** > 80% laparoscopic and > 50% open; **B** pooled results by two subgroupings—country (North America vs other countries, limited to studies comprising > 80% laparoscopic surgical approach to minimize confounding from surgical approach) and year (last year of data inclusion before and including 2010 vs after 2010, not limited by surgical approach). Square data points: incidence from individual studies; diamond-shaped data points: pooled values from subgroups; hexagonal data points: pooled values from all studies that reported relevant data

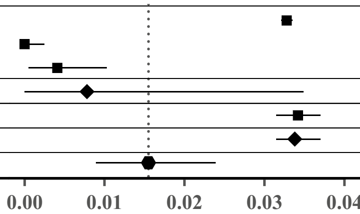
study has meta-analyzed the incidence of VTE after MBS. The present systematic review and meta-analysis presented high-quality cumulative incidences of VTE pooled from nearly 5 million patients worldwide. The in-hospital, 30-day, and 3-, 6- and 12-month incidences provide clinically relevant and meaningful information regarding the timing and patterns of VTE, to guide the follow-up, detection, and prevention of this life-threatening complication. The review also explored the influence of surgical approach, geographical origin, and study age on incidence of VTE. To our knowledge, this is the first study to undertake such a task.

In terms of the incidence of VTE at the five timepoints under examination, our observed cumulative incidence of VTE exhibited an increasing trend in-hospital, and at 30 days and 3, 6 and 12 months, for the > 80% laparoscopic approach (0.15%, 0.50%, 0.51%, 0.72%, and 0.78% respectively) and for the > 50% open approach (0.43%, 2.02%, 2.14%, 2.36%, and 3.38% respectively). Such increasing pattern is consistent with two studies that reported incidences of VTE after MBS of $0.88\%_{\text{in-hospital}}$, $2.17\%_{1\ \text{month}}$, and $2.99\%_{6\ \text{month}}$ [93] and $0.3\%_{7\ \text{days}}$, $1.9\%_{30\ \text{days}}$, $2.1\%_{3\ \text{months}}$, and $2.1\%_{6\ \text{months}}$ [43]. Therefore, MBS patients require clinical vigilance to continue for an extended period, in order to identify VTE and reduce the risk of morbidity and mortality.

Individual studies reported a wide range of incidences at each timepoint. Such variations could be due to patient features such as age, BMI, or comorbidity [103]; surgical

A

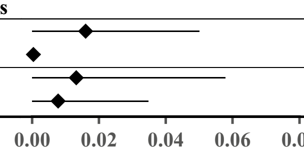
All studies	Total sample	Cases	Incidence	LCI 95%	HCI 95%	Weight (%)
Chung 2019[30]	230468	7556	0.0328	0.0321	0.0335	29.73
Gorosabel Calzada 2022[9]	675	0	0.0000	0.0000	0.0025	20.24
Sharma 2020[90]	737	3	0.0041	0.0005	0.0103	20.80
>80% laparoscopic approach	**231880**	**7559**	**0.0078**	**0.0000**	**0.0349**	**70.77**
Steele 2011[93]	16929	579	0.0342	0.0315	0.0370	29.23
>50% open approach	**16929**	**579**	**0.0338**	**0.0315**	**0.0370**	**29.23**
Pooled	**248809**	**8138**	**0.0155**	**0.0089**	**0.0239**	**100.00**



Heterogeneity	I^2 (%)	Q	Chi², p
>80% laparoscopic	98.00	108.89	0.00
>50% open	N/A	N/A	N/A
Pooled	97.28	110.37	0.00

B

Subgroups		Studies	Total sample	Cases	Incidence	LCI 95%	HCI 95%	Weight (%)
Country	North America	2	231205	7559	0.0160	0.0000	0.0500	67.13
	Other countries	1	675	0	0.0004	0.0000	0.0025	32.87
Year	Up to 2010 (inclusive)	2	17099	579	0.0132	0.0000	0.0579	35.91
	After 2010	3	231880	7559	0.0078	0.0000	0.0349	64.09



Subgroups	Heterogeneity	I^2 (%)	Q	Chi², p
Country	North America	97.00	37.77	0.00
	Other countries	N/A	N/A	N/A
Year	Up to 2010 (inclusive)	93.00	14.75	0.00
	After 2010	98.00	108.89	0.00

Fig. 6 Twelve-month cumulative incidence of venous thromboembolic events. Forest plot showing: **A** > 80% laparoscopic and > 50% open; **B** pooled results by two subgroupings—country (North America vs other countries, limited to studies comprising > 80% laparoscopic surgical approach to minimize confounding from surgical approach) and year (last year of data inclusion before and including 2010 vs after 2010, not limited by surgical approach). Square data points: incidence from individual studies; diamond-shaped data points: pooled values from subgroups; hexagonal data points: pooled values from all studies that reported relevant data

characteristics, such as operative time [103], MBS procedure, or surgical approach [100, 104, 105]; or study characteristics, such as study design, years of data acquisition, and sample size.

Across studies that reported both in-hospital and 30-day VTE, 60% of events occurred after discharge, concurring with previous reports where up to 80% of VTE occurred after discharge [52, 93, 100]. Higher post-discharge incidence of VTE might be partly attributed to short in-hospital stays of only a few days [106, 107], compared to longer post-discharge periods. Similarly, we found that most VTE occurred within the first 30 days, consistent with observations from some of the included studies [43, 52]. This further highlights the importance of vigilance during this period.

The present study noted that cumulative incidence across the > 80% laparoscopic studies was consistently lower than the > 50% open approach for all timepoints, consistent with previous findings at 30 days [105], 90 days [100], and 5 years [104]. Notwithstanding, some literature has demonstrated no differences in VTE outcomes between laparoscopic vs open approaches [108–110].

As for the subgroup analyses, we explored the effects of study age and geographical origin.

Studies using data up to the end of 2010 demonstrated higher incidences at most timepoints, compared to more recent studies, likely due to the larger proportion of > 50% open approach studies in the former subgroup. Factors that have contributed to the reduction in VTE since the turn of the century include the shift from open to laparoscopic approaches, MBS technical advancements, pre-/post-surgery thromboprophylaxis, and enhanced recovery regimens [68, 111–115].

To explore geographical differences, we compared North American studies to other countries. Despite limiting this to > 80% laparoscopic studies to minimize confounding from surgical approach, incidence from North American studies

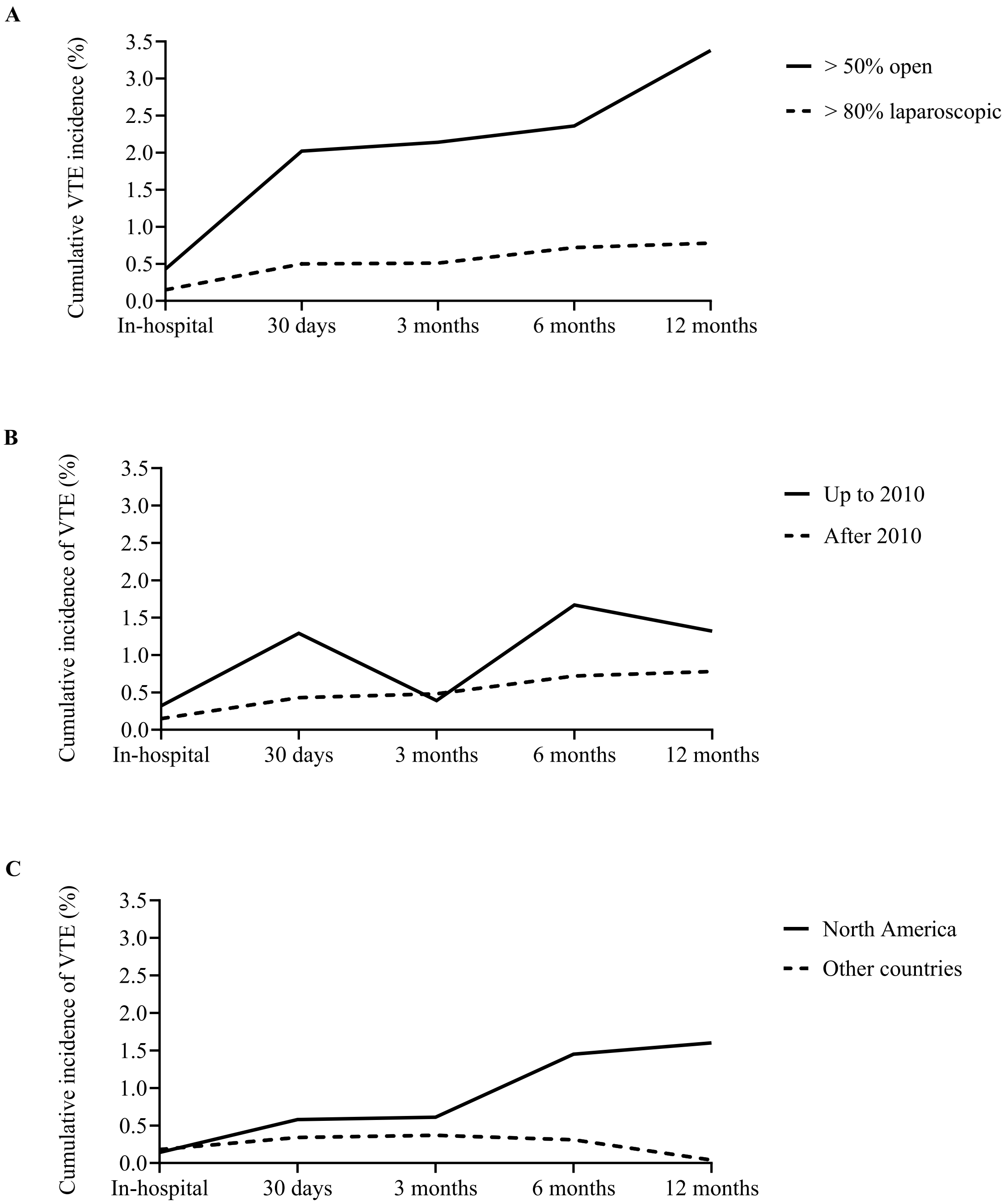


Fig. 7 Total and sub-grouped cumulative incidence of VTE after metabolic and bariatric surgery across time: **A** by surgical approach (> 50% open vs > 80% laparoscopic), **B** by study age (up to and including 2010 vs after 2010), **C** by geographical origin (North America vs other countries). VTE, venous thromboembolic events

was higher for most timepoints. Sensitivity analysis removing studies with less than 2000 patients increased the incidence of the other countries group closer to that of North American studies at 30 days and 3 months, the timepoints where both subgroups used large samples from registry data, indicating the influence of sample size.

The current review identified only one study that assessed outcomes beyond the first few years after MBS [16]. This study found that over a median of 10.7 years post-surgery, MBS patients exhibited significantly less VTE compared to non-MBS patients matched for sex, age, and baseline BMI [16]. This suggests that despite our observed shorter-term incidence of VTE, MBS appears to offer "protection" (e.g., decreases in BMI),

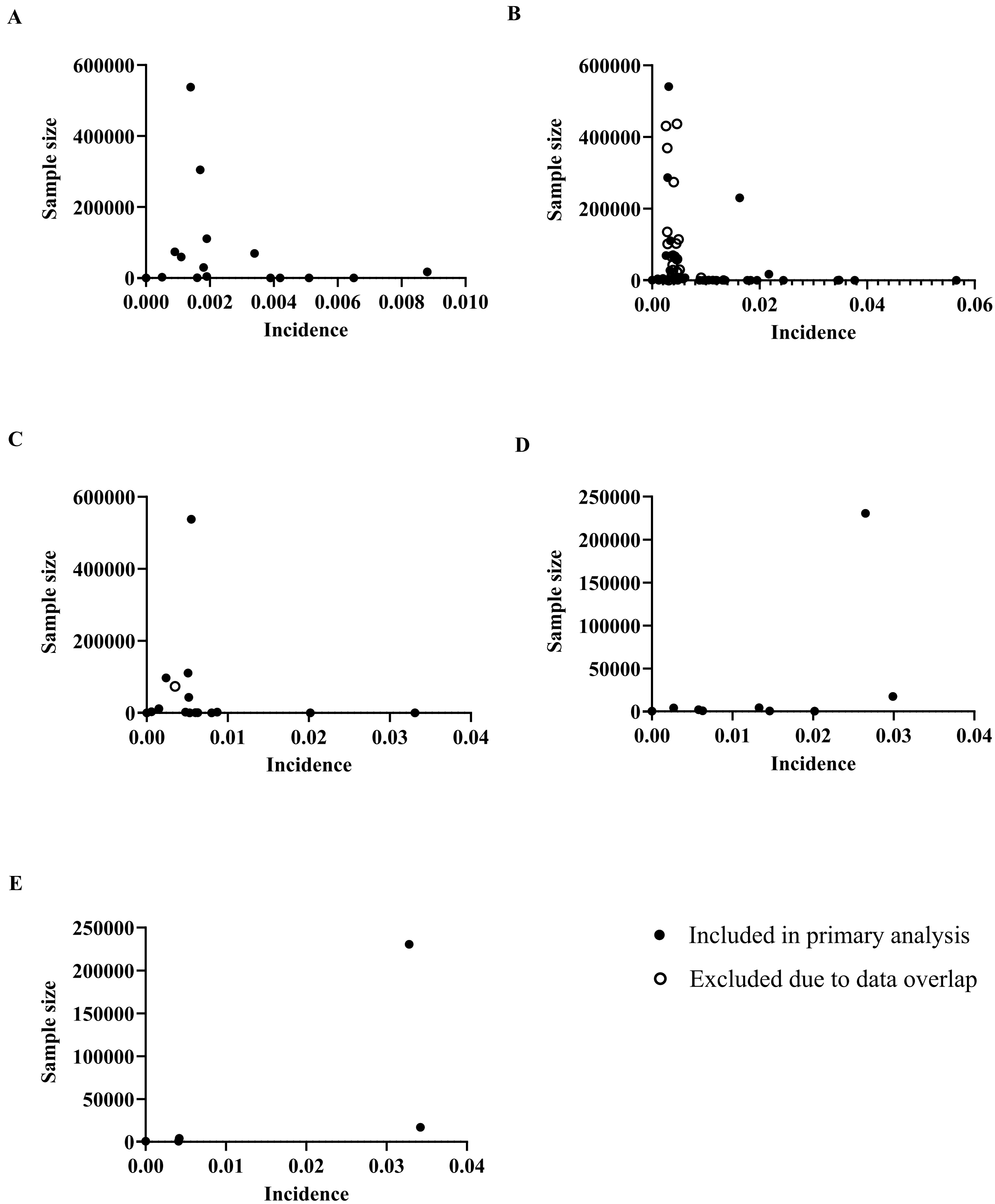


Fig. 8 Panel of Funnel plots of all included studies presenting data for cumulative incidence of venous thromboembolic events: **A** in-hospital, **B** 30-day, **C** 3-month, **D** 6-month, and **E** 12-month. Solid black dots indicate studies included in the primary meta-analysis; open circles indicate studies excluded from the primary meta-analysis due to significant overlap of included patient data

resulting in lower long-term risk of VTE [7]. Future research should include longer-term assessment of VTE after MBS.

Collectively, the above suggests that a deeper understanding of the variations in VTE across time must consider the interrelationships between surgical approach (and hence study age) and sample size (and hence the use of data registries and geographical origin), amongst other factors.

In terms of the quality of estimates, risk of bias within and across studies and heterogeneity, slightly more than half of the included studies exhibited low risk of bias. Some of the studies displaying higher risk of bias were due to small sample sizes, potentially biased sampling frames, or poor reporting. North American studies were over-represented, with many utilizing large national/regional registries. This led to considerable overlap of patient data, which increased our efforts to identify and exclude overlapping data to ensure the validity of the meta-analysis. Heterogeneity in the overall meta-analyses was high at all timepoints. Subgrouping reduced some heterogeneity; however, it remained high for the > 80% laparoscopic approach and the North American subgroups, both of which included the studies with the largest sample sizes and lowest variance. This is consistent with others who noted that measures of heterogeneity such as Higgin's I^2 may indicate high heterogeneity in proportional meta-analysis, even when data are consistent [22].

This review has some limitations. Many studies reported 30-day incidence, while others reported inconsistent timepoints, rendering interpretations of incidence across individual studies difficult. However, this variation enabled us to assess cumulative incidence and its patterns over time. Additionally, as most studies were retrospective, based on patient charts/records, pooled incidences are likely to reflect *symptomatic* VTE. As it was only possible to use the > 80% laparoscopic and > 50% open subgroups, this would have resulted in some contamination within the subgroups, suggesting that our observed VTE differences between surgical approaches could be underestimated. It would have been beneficial to include elements of the prophylaxis undertaken as well as operative time in the analysis. However, the extent of non-reporting, aggregated or undetailed reporting of these items, and in the case of prophylaxis, the numerous and wide variations in the chemo/mechanical prophylaxis protocols used singly or in combination at different times and durations of administration, with or without inferior vena cava filters, transfusions, or stoppage of chemical thromboprophylaxis where required would result in countless combinations thereof, which mitigated against a meaningful analysis. Notwithstanding, some of the included studies reported that duration of surgery for patients who experienced VTE after MBS was longer than that of matched control patients [29], and that operative time was significantly longer in patients who experienced a post-operative VTE [52] and a significant predictor of or associated with of post-operative VTE [40, 44].

Future studies would benefit from prospective designs, better (non-aggregated) reporting of sample/procedure characteristics and timeframes, assessment of longer-term VTE, and greater representation from outside of North America. Future meta-analyses should be aware of studies utilizing large national/regional registries that could lead to considerable overlap of patient data. Future researchers should be mindful of the differences across data registries when conducting research to ensure that significant proportions of events are not missed. The current study clearly demonstrated that the time course of VTE post-surgery is dynamic. As such, researchers presenting primary research on such complications need to clearly relate reported incidences to a given timeframe post-surgery, and those synthesizing such studies should be careful not to aggregate incidences related to different timeframes, since this would render any reported values meaningless.

This study has many strengths. We assessed the pooled incidence of VTE after MBS at five timepoints. Subgroup analysis included surgical approach, geographical origin of the studies, and study age. We meticulously identified potential overlap of patient data, including that from large registries, and excluded such studies from the meta-analysis, enhancing the internal validity [116]. The extremely large number of patients worldwide enhances the external validity and generalizability of the findings. To our knowledge, this is the most extensive and comprehensive systematic review/meta-analysis of VTE after MBS over several timepoints that has been undertaken, and probably the largest systematic review/meta-analysis conducted to date in the field of surgery/health in general in terms of the number of patients.

Conclusion

We pooled a large number of studies and patients worldwide to provide high-quality estimates of VTE and valuable insights into its patterns over time. For studies that utilized a mainly laparoscopic approach, in-hospital incidence of VTE and cumulative incidence at 30 days and 3, 6 and 12 months were 0.15%, 0.50%, 0.51%, 0.72%, and 0.78% respectively. Most VTE occurred in the first 30 days, of which 60% was after discharge, although we observed some VTE up to our last timepoint. Incidence was consistently lower for laparoscopic compared to open MBS. Lower incidences from studies outside of North America were largely due to smaller sample sizes. Deeper understanding of the variations in VTE across time must consider the interrelationships between surgical approach, geographical origin, study age, and sample size, amongst other factors. Post-operative surveillance needs to be particularly vigilant after discharge and continue thereafter for an extended period to detect VTE and reduce the risk of associated morbidity and mortality. These findings provide clinically relevant estimates of VTE to inform policy, clinical practice, and research.

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Author Contribution WEA and ML were responsible for the study conception and design. WEA, KE-A, and ML performed the data collection and acquisition of datasets. ML and WEA provided the data analysis. WEA, ML, and KE-A were responsible for writing and revising the manuscript. AE-M and AAA edited the manuscript. The authors also critically reviewed and approved the final version of this paper.

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Declarations

Ethical Approval For this type of study formal consent is not required.

Informed Consent Informed consent does not apply.

Conflict of Interest The authors declare no competing interests.

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