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Incidence and outcomes of acute mesenteric ischaemia: a systematic review and meta-analysis

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ABSTRACT

Objective To estimate the incidence of acute mesenteric ischaemia (AMI), proportions of its different forms and short-term and long-term mortality.

Design Systematic review and meta-analysis.

Data sources MEDLINE (Ovid), Web of Science, Scopus and Cochrane Library were searched until 26 July 2022.

Eligibility criteria Studies reporting data on the incidence and outcomes of AMI in adult populations.

Data extraction and synthesis Data extraction and quality assessment with modified Newcastle-Ottawa scale were performed using predeveloped standard forms. The outcomes were the incidence of AMI and its different forms in the general population and in patients admitted to hospital, and the mortality of AMI in its different forms.

Results From 3064 records, 335 full texts were reviewed and 163 included in the quantitative analysis. The mean incidence of AMI was 6.2 (95% CI 1.9 to 12.9) per 100 000 person years. On average 5.0 (95% CI 3.3 to 7.1) of 10 000 hospital admissions were due to AMI. Occlusive arterial AMI was the most common form constituting 68.6% (95% CI 63.7 to 73.2) of all AMI cases, with similar proportions of embolism and thrombosis.

Overall short-term mortality (in-hospital or within 30 days) of AMI was 59.6% (95% CI 55.5 to 63.6), being 68.7% (95% CI 60.8 to 74.9) in patients treated before the year 2000 and 55.0% (95% CI 45.5 to 64.1) in patients treated from 2000 onwards ($p<0.05$). The mid/long-term mortality of AMI was 68.2% (95% CI 60.7 to 74.9). Mortality due to mesenteric venous thrombosis was 24.6% (95% CI 17.0 to 32.9) and of non-occlusive mesenteric ischaemia 58.4% (95% CI 48.6 to 67.7). The short-term mortality of revascularised occlusive arterial AMI was 33.9% (95% CI 30.7 to 37.4).

Conclusions In adult patients, AMI is a rarely diagnosed condition with high mortality, although with improvement of treatment results over the last decades. Two thirds of AMI cases are of occlusive arterial origin with potential for better survival if revascularised.

PROSPERO registration number CRD42021247148.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This systematic review used a comprehensive search for articles on the incidence and outcomes of acute mesenteric ischaemia.
⇒ A considerable number of studies was identified and included for mortality outcome.
⇒ Included studies were mainly retrospective single-centre studies including patients recruited over a long time period.
⇒ Meta-analyses on mortality according to age group or gender, and assessment of other outcomes were not possible.

INTRODUCTION

Acute mesenteric ischaemia (AMI) is a potentially fatal vascular catastrophe.[1] Inadequate blood flow to the intestine may result from mesenteric arterial embolism or thrombosis or by acute mesenteric venous thrombosis (MVT).[2] Insufficient perfusion may also occur without an acute thrombo-embolic high-grade stenosis or occlusion of large mesenteric arteries—non-occlusive mesenteric ischaemia (NOMI).[2] AMI is said to be a rare condition, yet the incidence is poorly documented. Few studies have addressed it among the general population or hospitalised patients, and recent guidelines have, therefore, relied on estimated levels.[2] No systematic analysis on incidence of AMI is available. The most accurate report on the proportion of different forms of AMI comes from a population with an 87% autopsy rate studied between 1970 and 1982.[3]

In contrast to the lack of data on incidence, the poor outcome of AMI has been well demonstrated. The systematic analysis of 45 studies published before 2002 demonstrates an overall mortality of 74% or 64% depending on whether only supportive or unlimited care was applied.[4] A review of 54 studies from 1956 to 2012 found in-hospital mortality of approximately 60% in the studies published from 2002 to 2012, and suggested a slight reduction in mortality over time.[5] Data from the past decade suggest that some improvement may have taken place as a result of a multidisciplinary approach and

developments in many medical fields (eg, better diagnostics, endovascular procedures, management of short bowel syndrome, home parenteral nutrition).[6–8] Whether this has truly resulted in improved outcomes from AMI is unknown.

The aim of this study was to clarify the incidence of AMI and its different forms among adults in the general population, and in those admitted to hospital and presenting to hospital emergency departments, and to determine the outcomes of AMI and its different forms stratified as to whether treatment was before or after the year 2000.

MATERIALS AND METHODS

A study protocol, following the items presented in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines[9] was developed. Details of the protocol were registered on PROSPERO and can be accessed at https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=247148.

Inclusion criteria for studies

Studies meeting the following criteria were included in the review:

1. Conducted in:
   - General adult (≥ 18 years old) population (whole country, sub-national area, administrative area, area served by hospital) in any of the 218 countries of the world,[10]
   - Adult patients admitted to hospital and/or
   - Adult patients presenting to hospital emergency departments.
2. Presenting data on:
   - AMI incidence or containing data for the numerator and denominator of the estimation fraction, with the diagnosis of AMI based on clinical data, imaging, laparotomy and/or autopsy report. The incidence of AMI in this review was defined as the number of patients newly diagnosed with AMI in the population of interest over 12 months. The incidence of the subtypes of AMI—occlusive AMI (occlusive arterial AMI), NOMI, and MVT, was also explored and/or
   - AMI outcomes: all-cause mortality (in-hospital, 30-day and the longest reported); intensive care unit length of stay, hospital length of stay and need for home parenteral nutrition.

Literature search

Biomedical literature databases MEDLINE (Ovid), Web of Science and Scopus were searched on 23 March 2021 (since inception) and the Cochrane Library on 24 March 2021 (since inception). An initial search strategy was developed for MEDLINE, which was then adapted for other databases. An additional search with the same strategy was performed on 26 July 2022. No publication status or language restrictions were set, but only articles in languages understood by at least one member of the study team were reviewed. Reading knowledge of the study team members involved in abstract and full-text assessment is as follows: KT—English, Russian and Ukrainian, ARB—English, Russian and German, JK—English and Russian, AF—English, French and Italian, OK—English, Russian and Ukrainian, JS—English and Russian. Although the initial search strategy was unlimited, letters, commentaries, editorials, case studies, case-series with<10 cases and reviews were subsequently excluded.

The electronic search strategy is presented in online supplemental file 1.

Systematic reviews, set aside in the full-text review phase, served as a source of potentially eligible original studies. In addition, the references of publications included in reviews were screened for additional reports of the same study and other relevant studies.

Definitions and study groups

We included studies where the diagnosis of AMI was based on clinical data, imaging (CT or angiography), and laparotomy and/or autopsy report as reported in the original study. During the review process, the studies were categorised as to whether they included patients with all forms of AMI, or patients only with occlusive arterial AMI, MVT or NOMI.

Subgroups

Further, the studies were classified according to patient selection as follows:

- Independent of management—studies including all patients independent of applied treatments, including no treatment.
- Operated patients—studies including only patients who underwent surgery for AMI (with or without revascularisation, including explorative laparotomy/laparoscopy).
- Revascularised patients—studies including only patients with revascularisation (endovascular, open or combined).

Selection of studies and assessment of the risk of bias

Records retrieved from the predefined electronic databases were merged and duplicates removed. The publications were first screened by title and abstract. Full texts of all potentially eligible publications were retrieved and read. Studies were included in the review when all the predefined inclusion criteria were met. Study characteristics were extracted, and their methodological quality assessed according to the Newcastle-Ottawa Scale (NOS).[11] We modified the scale as follows: first, under the Selection category the representativeness of the study population was evaluated instead of 'exposed cohort', while the selection of the non-exposed cohort and ascertainment of exposure were omitted. Thus, for this category, instead of four stars a study could receive a maximum of two stars. Second, when evaluating the Outcome category, we looked at the adequacy of follow-up of the study population instead of cohorts. Thus, the maximum total number

of stars available was seven. Studies were considered at low risk of bias when receiving four or more stars.

For review, data extraction and quality assessment, standard forms were developed and used. All abstracts were reviewed by two independent researchers, whereas full-text articles were reviewed by one researcher and checked by the second reviewer when creating evidence tables for different outcomes. In the case of uncertainty or discrepancy at any step, consensus of the two researchers had to be reached, after consulting a third researcher if necessary.

Data synthesis

Random-effects meta-analyses were used to combine the estimates of AMI incidence, mortality and proportions in subgroups. Random-effects meta-analysis was preferred due to assumption that observed estimates of treatment effect vary across studies because of real differences in treatment effect in each study as well as sampling variability. By default, generic inverse variance was used for pooling the studies. If subgroup analyses were needed, the generalised linear mixed models method was used instead.

For incidence meta-analysis incidence per 100 000 person years was used. For outcomes of AMI and its different forms, proportion (in %) of all events was used.

The results are presented using forest plots along with I^2 statistic, τ^2 and Cochran's Q-test to describe the heterogeneity. To compare two meta-analysis estimates, random-effects meta-regression was used.

If 95% CIs on incidence estimates were lacking for N<15, the exact method was used.[12]

Analyses were performed using R software (V.4.1.0, R Foundation for Statistical Computing, Vienna, Austria).

Detailed description of data synthesis is presented in online supplemental file 2.

Patient and public involvement

Patients and the general public were not involved in the design or planning of the study.

RESULTS

Literature search and quality assessment

After removal of duplicates, 2591 records were obtained from the initial search, and an additional 178 records were identified through other sources, making 3064 potentially eligible articles (figure 1). On screening the titles and abstracts, 2729 records were excluded, leaving 335 studies for full-text assessment. Review of these articles excluded 172 of them for various reasons (figure 1). Twelve articles were systematic reviews; thus 163 were considered eligible for quantitative synthesis (meta-analysis): 152 retrospective and 11 prospective studies.

All studies included in meta-analyses received more than four points on the modified NOS, indicating low risk of bias (see online supplemental table 1). This is accounted for by the robustness of the outcomes we studied (AMI and mortality) and on the assumption that most patients with AMI were detected.

Four articles in Chinese were excluded as no member of the study team has command of this language.

Incidence of AMI and proportions of its different forms

General population

We found five studies (one of them a series of studies)[13–16] that addressed the incidence of AMI in the general

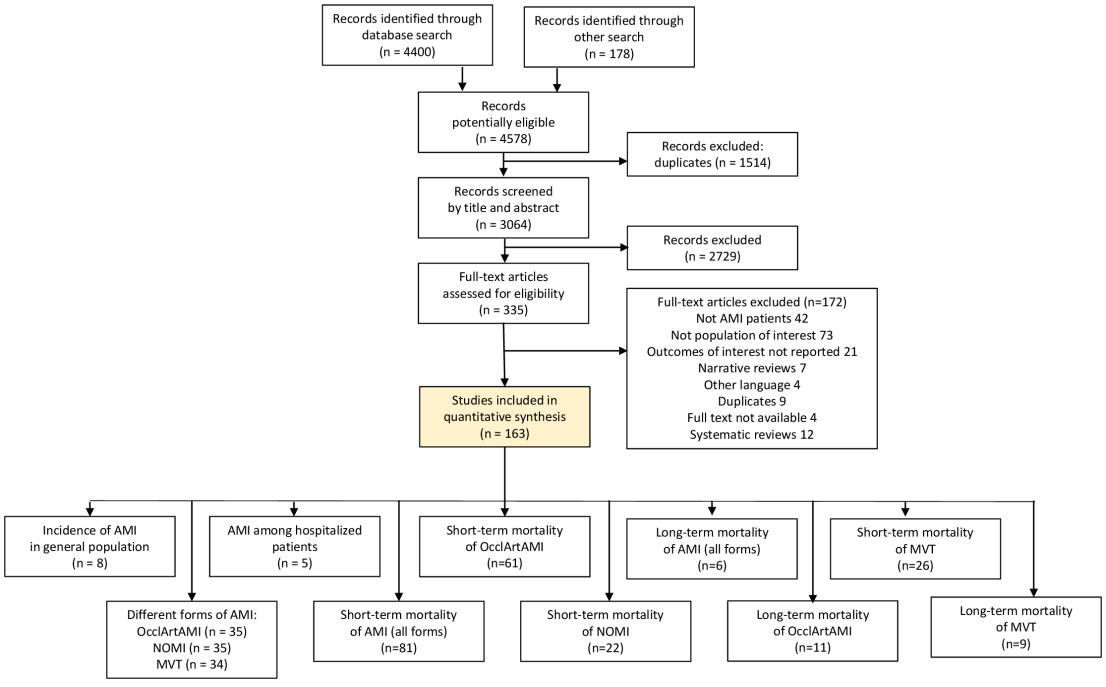

Figure 1 Flow diagram showing the selection of studies included in the review. AMI, acute mesenteric ischaemia; MVT, mesenteric vein thrombosis; OcclArtAMI, occlusive arterial AMI.

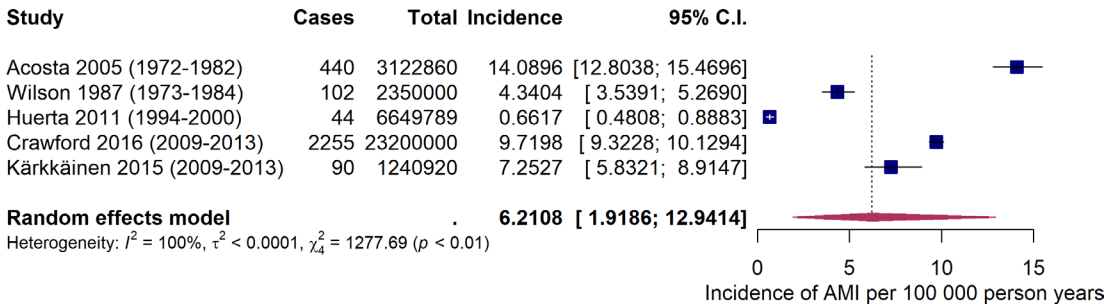

Figure 2 Incidence of acute mesenteric ischaemia in general population, cases per 100 000 person years.

population (figure 2).[13–20] Among them, only one study reported a population-wide autopsy rate (87%).[13–16]

On average 6.2 (95% CI 1.9 to 12.9), new cases of AMI were diagnosed annually per 100 000 inhabitants. These studies cover 1970–2013 and are exclusively from high income countries.

It was not possible to perform quantitative synthesis on the incidence of different forms of AMI in general populations. This was, however, reported in the investigation of the population of Malmö, Sweden, in the years 1970–1982, and in a study from Finland, investigating the population of Kuopio in the years 2009–2013. They report 8.6 (95% CI 7.6 to 9.7) and 4.5 (95% CI 2.5 to 8.1) cases of occlusive arterial AMI, 2.0 (95% CI 1.5 to 2.5) and 2.0 (95% CI 0.8 to 4.8) cases of NOMI, and 1.8 (95% CI 1.3 to 2.2) and 0.5 (95% CI 0.21.1) cases of MVT per 100 000 person years, respectively.[14–16 20]

Thirty-eight studies reported the proportions of different forms of AMI in their cohorts.[14 17 21–56] Quantitative analysis demonstrates that the most common form is occlusive arterial, constituting 68.6% (95% CI 63.7 to 73.2) of all AMI cases (online supplemental figure 1). NOMI accounts for 15.1% (95% CI 11.8 to 18.7) and MVT for 11.5% (95% CI 9.1 to 14.2) of cases. Arterial occlusion was roughly equally thrombotic and embolic (30.0% (95% CI 24.4 to 36.3) and 33.3% (95% CI 27.3 to 39.9) of all AMI cases, respectively), some studies simply reporting occlusive arterial AMI without distinguishing between the two.

Retrieved data were insufficient for quantitative synthesis of the incidence in different age groups. Single studies indicate that the occurrence of AMI increases with age. Acosta *et al* showed that in Swedish population occlusive arterial AMI increases dramatically with age in both men and women, reaching 85.8 (95% CI 61.5 to 110.0) per 100 000 person years at age 80–84 years, and 189.5 (95% CI 145.1 to 233.9) in those over 85 years, respectively.[15] Similar exponential growth of all forms of AMI is demonstrated in the Finnish population, reaching 60 cases per 100 000 person years at ages over 80 years.[20] The studies included in our analysis of the incidence in the general population, indicate a significantly higher proportion of women, at 58.3% (95% CI 56.5 to 60.2) .[13–20]

Hospitalised patients

Five studies reported the proportion of patients with AMI among hospitalised patients and were included in the meta-analysis (figure 3).[19 42 57–59] On average, 5.0 (95% CI 3.3 to 7.1) of 10 000 hospital admissions are due to AMI.

Emergency department patients

A meta-analysis was not possible. A single study demonstrated that 1.4% of patients admitted to an emergency department with abdominal pain suffered from AMI.[60] Another study reported that 3.6% of patients≥65 years who present to hospital for emergency surgery have intestinal ischaemia.[61]

Outcomes of AMI and its different forms

Short-term mortality

In total, 81 studies were included in meta-analysis of short-term mortality of AMI, defined as either in-hospital or within 30-days.[17 19 22 24–28 32–37 39–43 45 47–52 56–58 60 62–112] The overall mortality was 59.6% (95% CI 55.5 to 63.6) and was only slightly lower in sub-analysis of the 33 studies, which included patients who had been operated on (figure 4).[19 24 27 33 35 36 40 41 43 47 51 58 92–111] Short-term mortality was 51.7% (95% CI 37.5 to 65.5) in prospective

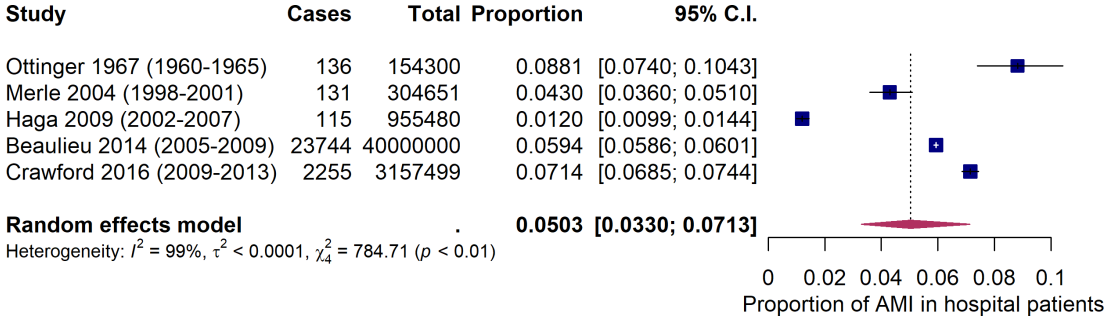

Figure 3 Proportion of patients with acute mesenteric ischaemia (AMI) among hospitalised patients.

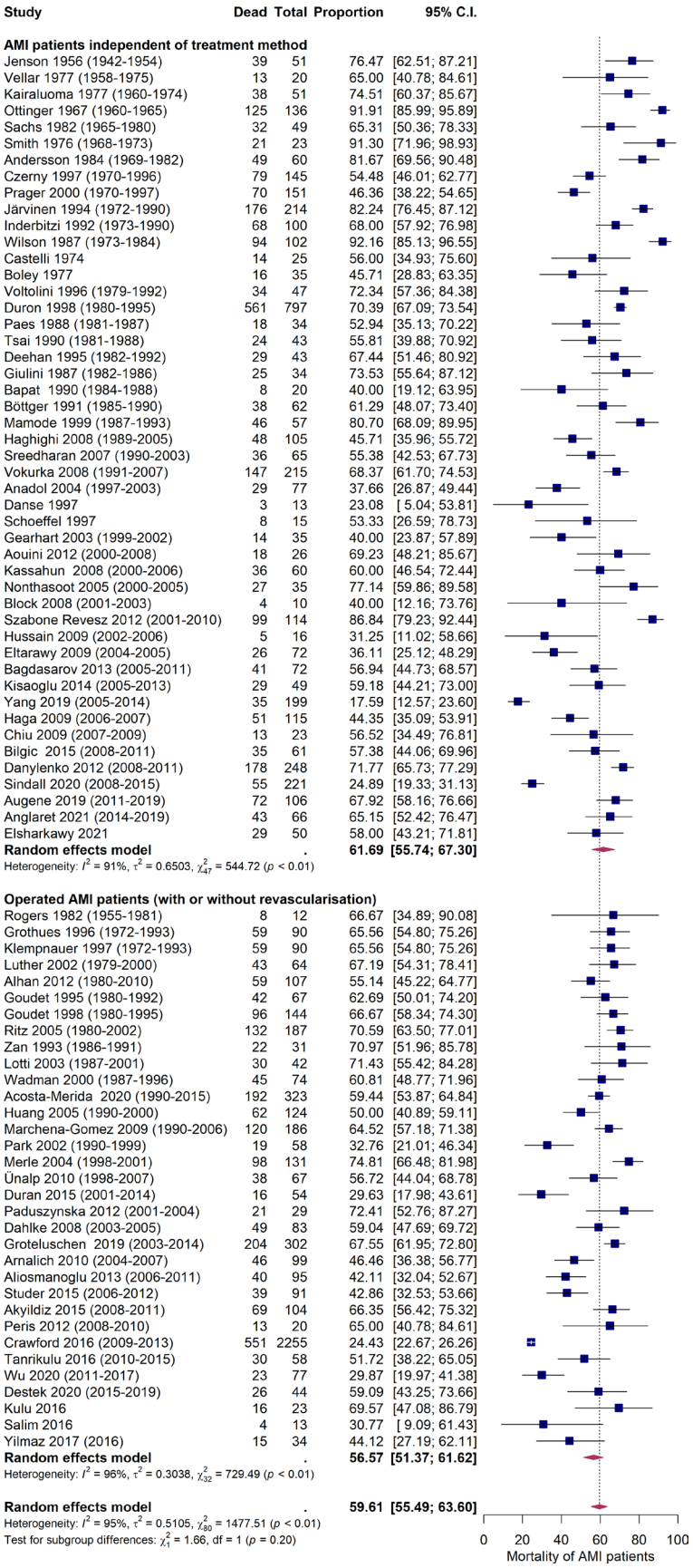

Figure 4 Short-term (hospital or 30 days) mortality of acute mesenteric ischaemia (all forms). Subgroup analyses of studies including all patients independent of treatment method (upper panel) and of studies including only operated patients (lower panel) are presented. In brackets, the period of patient inclusion is indicated. AMI, acute mesenteric ischaemia.

(n=9)[32 39 49 60 78 82 87 89 112] and 62.9% (95% CI 56.5 to 68.8) in retrospective (n=37)[17 25 26 28 37 42 45 48 50 57 62–77 79–81 83–86 88 90 91] studies (p=0.15). Table 1 illustrates the evolution of mortality over time. The pooled mortality in the 25 studies from before 2000 including patients independent of treatment method was 68.7% (95% CI 60.8 to 74.9) compared with 55.0% (95% CI 45.5 to 64.1) in the 18 studies where recruitment commenced later (p=0.027) (table 1). Five studies with patients included from both before and after 2000 were excluded from this analysis because the published data did not permit allocation of individuals to one or other era.[48 75–78] Sensitivity analysis stratifying the studies only according to the date the first patient was enrolled, and thereby including all available studies, showed a difference in mortality from 65.5% to 52.5% (p=0.025).

Sixty-one studies addressed the short-term mortality of occlusive arterial AMI.[6 22 25 27 31–35 38 39 42 48 49 59 62 66 93 113–153] Meta-analysis showed an overall mortality of 51.8% (95% CI 46.3 to 57.3) (online supplemental figure 2). The sub-analysis of 24 studies on patients who underwent revascularisation demonstrated a mortality of 33.9% (95% CI 30.7 to 37.4).[6 59 131–148 150–153]

Short-term mortality of patients with NOMI was reported in 22 studies, and 7 of these analyse the outcome of surgery (online supplemental figure 3).[22 25 27 31–33 35 38 39 42 48 49 93 154–162] The overall mortality of NOMI independent of treatment was 58.4% (95% CI 48.6 to 67.7) and was similar in the studies including operated patients.

Twenty-seven studies reported the short-term outcome of MVT with a pooled mortality rate of 24.6% (17.0–32.9) (online supplemental figure 4).[22 25 27 31–34 38 39 42 48 49 54 55 62 66 93 116 118 163–170]

Mid-term and long-term mortality

Few studies reported longer outcomes, the follow-up period ranging from 6 months to 5 years. Analysis of six such studies showed 68.2% (95% CI 60.7 to 74.9) overall mortality at a minimum of 6 months (figure 5).[24 31 41 98 100 171] Eleven studies addressed only occlusive arterial patients with AMI, and meta-analysis demonstrated an overall mid-term/long-term mortality of 59.0% (95% CI 44.9 to 71.7) in this subgroup (figure 6).[6 121 127 129 131 137 140 144 146 151 172] MVT had better mid/long-term outcome, analysis of nine studies showing a mortality of 28.9% (95% CI 15.2 to 44.8) (figure 7).[54 163–165 167 169 170 173 174]

DISCUSSION

This systematic review and meta-analysis showed that AMI occurred in 6/100 000 person-years and in 0.05% of hospital admissions. There were considerable differences in the incidences of AMI found in different studies, which might be explained by study methods, evolving of diagnostics over time and autopsy rate. There is likely to be a bias towards underestimation of incidence due to incomplete retrieval of cases detected at autopsy and low overall autopsy rates in the studied populations.[3] In a population-based study conducted between 1970 and 1982 with an autopsy rate of 87%, 79% of patients with occlusive arterial AMI were diagnosed at autopsy.[15] The current proportion of patients not diagnosed in life is very uncertain due to low autopsy rates. In the present review, AMI was more common in women, but the great majority of studies did not control for the longer life expectancy among women in most, if not all, of the studied countries. The different forms of AMI have variable incidence and mortality, with occlusive arterial AMI constituting two thirds of all AMI cases. Revascularised occlusive arterial AMI and MVT carry the best prognosis for survival, but the overall mortality of AMI remains very high, exceeding 50%. The real mortality rate is likely higher, since a substantial number of AMI cases are diagnosed only at autopsy,[15 17] and the autopsy rate in most studied countries is generally very low, and almost non-existent among the oldest age groups.[175 176]

Incidence of AMI

The incidence of AMI in the general population and its proportion of hospital admissions have not been assessed in systematic reviews before. The results of this study illustrate the very low incidence of AMI when compared with other cardiovascular diseases such as stroke (up to 265/100 000 person-years)[177] or myocardial infarction (up to 1170/100 000 person-years).[178] Similarly, many other conditions requiring emergency surgery are more common (eg, acute appendicitis: 100/100 000,[179] gastrointestinal bleeding: 19–57/100 000, or perforated peptic ulcer: 4–14/100 000).[180] However, AMI was more common than ruptured abdominal aortic aneurysm, and the age-specific incidence of AMI was higher than the incidence of acute appendicitis in patients over 75 presenting with an acute abdomen.[20] The studies included in the present meta-analysis were all retrospective and mostly single-centre studies originating from a wide time span, introducing risks of information bias. There are additional confounding factors, such as changes in demography and diagnostic methods and activity. Accordingly, it is not possible to draw any firm conclusions regarding changes in incidence of AMI over time.

Proportion of different forms of AMI

The great majority of the studies included for analyses of the proportions of different forms of AMI were also retrospective single-centre studies. Additionally, somewhat different definitions of AMI were used, with some studies excluding specific forms such as aortic dissection where others included all cases of AMI independent of mechanism. In our analysis, the forms other than occlusive arterial AMI, MVT and NOMI accounted for <5% of all reported cases of AMI and were not further addressed in detail. However, considering that not all studies considered these 'other' forms at all, the real proportion of 'other' is most probably higher than shown by our analysis. Also, in the literature, there is no uniform consensus

Table 1 Hospital-day or 30-day mortality of acute mesenteric ischaemia in studies including patients treated before or after year 2000

Group	Study	Study years	Died	Number of patients	Mortality (%)
Patients treated before 2000	Jenson and Smith[62]	1942–1954	39	51	76.47
	Vellar and Doyle[63]	1958–1975	13	20	72.83
	Kairaluoma *et al*[64]	1960–1974	38	51	74.51
	Ottinger and Austen[57]	1960–1965	125	136	91.91
	Sachs *et al*[22]	1965–1980	32	49	65.31
	Patterson[65]	1968–1973	21	23	91.30
	Andersson *et al*[66]	1969–1982	49	60	81.67
	Czerny *et al*[25]	1970–1996	79	145	54.48
	Prager *et al*[26]	1970–1997	70	151	46.36
	Järvinen *et al*[67]	1972–1990	176	214	82.24
	Inderbitzi *et al*[28]	1973–1990	68	100	68.00
	Wilson *et al*[17]	1973–1984	94	102	92.16
	Castelli *et al*[68]	n/a	14	25	56.00
	Boley *et al*[32]	n/a	16	35	45.71
	Voltolini *et al*[34]	1979–1992	34	47	72.34
	Duron *et al*[69]	1980–1995	561	797	70.39
	Paes *et al*[37]	1981–1987	18	34	52.94
	Tsai *et al*[70]	1981–1988	24	43	55.81
	Deehan *et al*[71]	1982–1992	29	43	67.44
	Giulini *et al*[72]	1982–1986	25	34	73.53
	Bapat *et al*[73]	1984–1988	8	20	40.00
	Böttger *et al*[39]	1985–1990	38	62	61.29
	Mamode *et al*[74]	1987–1993	46	57	80.70
	Danse *et al*[60]	n/a	3	13	23.08
	Schoeffel *et al*[49]	n/a	8	15	53.33
	Subtotal		**1628**	**2276**	
	Mortality (95% CI)			**68.67 (60.78 to 74.91)**	
Patients treated after 2000	Aouini *et al*[79]	2000–2008	18	26	69.23
	Kassahun *et al*[80]	2000–2006	36	60	60.00
	Nonthasoot *et al*[81]	2000–2005	27	35	77.14
	Block *et al*[82]	2001–2003	4	10	40.00
	Szabone Revesz[50]	2001–2010	99	114	86.84
	Hussain *et al*[83]	2002–2006	5	16	31.25
	Eltarawy *et al*[84]	2004–2005	26	72	36.11
	Bagdasarov *et al*[45]	2005–2011	41	72	56.94
	Kisaoglu *et al*[85]	2005–2013	29	49	59.18
	Yang *et al*[86]	2005–2014	35	199	17.59
	Haga *et al*[42]	2006–2007	51	115	44.35
	Chiu *et al*[87]	2007–2009	13	23	56.52
	Bilgic *et al*[88]	2008–2011	35	61	57.38
	Danylenko *et al*[89]	2008–2011	178	248	51.90
	Sindall *et al*[90]	2008–2015	55	221	24.89
	Augene *et al*[91]	2011–2019	72	106	67.92
	Anglaret *et al*[56]	2014–2019	43	66	65.15

Continued

Table 1 Continued

Group	Study	Study years	Died	Number of patients	Mortality (%)
	Elsharkawy *et al*[112]		29	50	58.00
	Subtotal		**796**	**1543**	
	Mortality (95% CI)			**54.97 (45.53 to 64.06)**	
				p=0.0266	

about the forms of mesenteric ischaemia that should be included in the definition of AMI. For example, the World Society of Emergency Surgery guidelines suggest considering only interruption of the blood supply to the small bowel in their definition of AMI, which is unfortunate since the superior mesenteric artery typically supplies not only the distal part of the duodenum and small bowel but also the large bowel up to the mid transverse colon, and NOMI may affect any part of the intestine as well as being responsible for extra-intestinal organ ischaemia.[14 181] At the same time, the European Society of Vascular Surgery guidelines include acute colonic ischaemia, pointing out that acute colonic ischaemia is often erroneously labelled as ischaemic colitis.[2] In present study, colonic ischaemia and/or ischaemic colitis were not included as specific key words in the literature search. Retrieved papers reporting acute inferior mesenteric artery ischaemia among all other forms of AMI were, however, included in the analysis.

Outcomes of AMI

Whereas outcomes of other vascular catastrophes such as acute coronary syndrome and stroke have improved substantially during the past few decades, the mortality after AMI remains high, although with some improvement observed. However, it remains possible that selection bias due to less consistent reporting of cases diagnosed post-mortem in more recent decades plays a role in this finding. The mortality data in the present review are, however, in accordance with two earlier systematic reviews. Inclusion of 78 studies from 1956 to 2020 in the present analysis leads to a pooled mortality of 59%, while Schoots *et al*[4] calculated a pooled in-hospital mortality of 73% from 47 studies published from 1967 to 2002, and Adaba *et al*.[5] 63% from 52 articles published from 1956 to 2012. We were not able to analyse if AMI mortality has changed over the last decade as most of the studies included patients over long periods of time (10 years and more) and only three had cases between years 2012 and 2022.

Different forms of AMI at their different stages are encountered by different specialists and are often studied as separate entities. Thereby, progress in management of specific forms of AMI has been achieved, concerning mainly the endovascular and hybrid therapy of occlusive arterial AMI.[6 123] In this review, intestinal revascularisation was seen to be associated with an almost halved mortality compared with the overall mortality in patients with occlusive arterial AMI. Considering that occlusive arterial AMI is the most common form of AMI, a larger effect on the reduction of overall mortality could have been expected with the development of endovascular therapy since the turn of the millennium; similarly to Adaba *et*

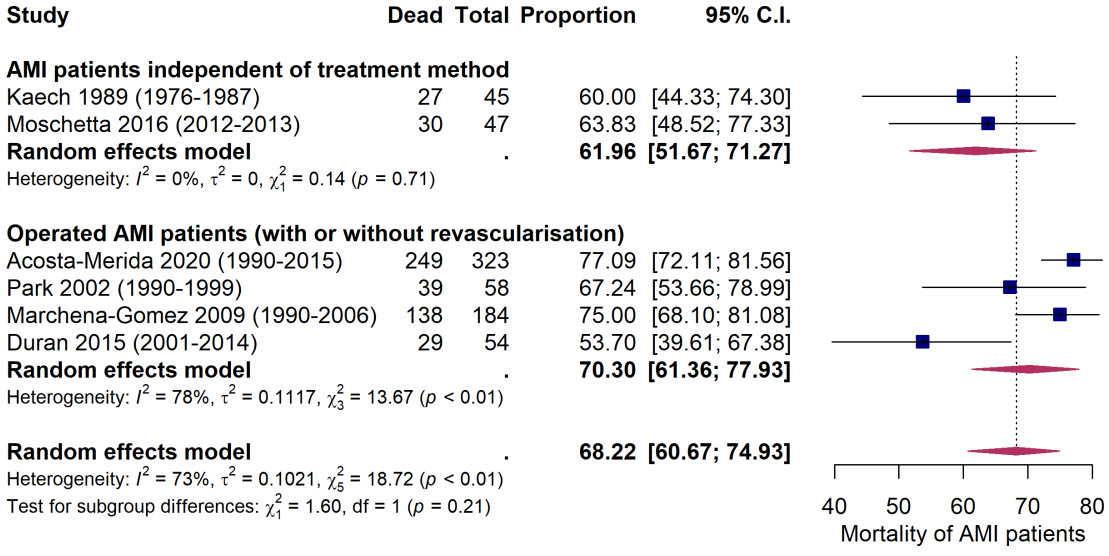

Figure 5 Long-term (6 months to 5 years) mortality of acute mesenteric ischaemia, all forms. Subgroup analyses of studies including patients independent of treatment method (upper panel) and of studies including only operated patients (lower panel) are presented. In brackets, the period of patient inclusion is indicated. AMI, acute mesenteric ischaemia.

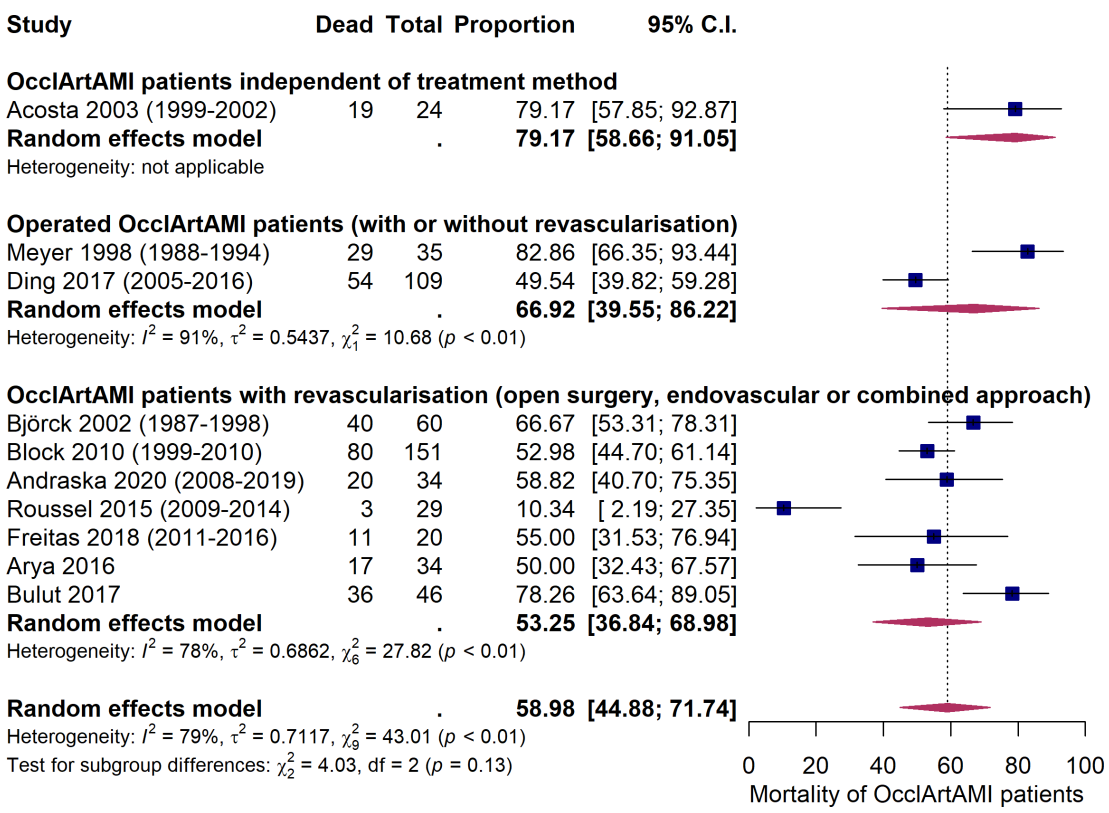

Figure 6 Long-term (6 months to 5 years) mortality of occlusive arterial acute mesenteric ischaemia (OcclArtAMI). Subgroup analyses of studies including patients independent of treatment method (upper panel), of studies including only operated patients (middle panel), and of studies including only patients with revascularisation (lower panel) are presented. In brackets, the period of patient inclusion is indicated.

al,[5] we showed only a modest reduction. Late diagnosis despite round-the-clock availability of contrast-enhanced computed tomography (at least in high-income countries) contributes to the continued low rate of intestinal revascularisation and high mortality in patients with occlusive arterial AMI. This explanation is supported by two studies using data from a large nationwide database, reporting attempted revascularisation rates of only 2.9–4.2%.[59 136] As clinical signs of AMI are non-specific and reliable specific biomarkers are lacking, the diagnosis is often delayed resulting in progression of intestinal ischaemia to transmural intestinal necrosis and peritonitis before the diagnosis is made.[84 121]

In this systematic review, we only focused on survival outcome, as data on other patient-relevant outcomes (presence of stoma, need of parenteral nutrition, quality of life) are scarce, justifying future prospective studies. We also omitted analysis of hospital length of stay, although this was initially planned, because it was greatly influenced by early and very high mortality, as well as lack of data. These outcomes are important, however, and should be considered when comparing different treatment methods.

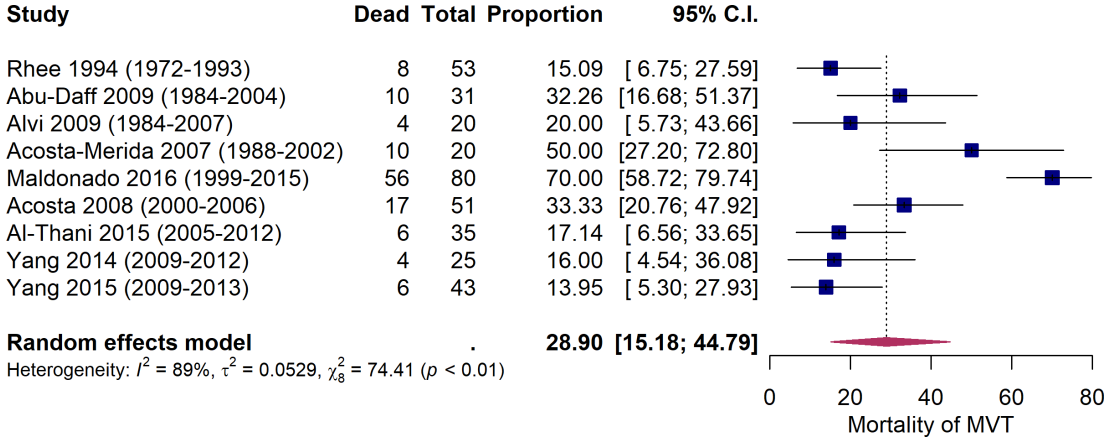

Figure 7 Long-term (2 months to 5 years) mortality of mesenteric vein thrombosis (MVT). In brackets, the period of patient inclusion is indicated.

Mid-term to long-term mortality was only slightly higher than short-term mortality in our analysis, suggesting that a high proportion of the patients surviving initial hospitalisation for AMI, actually have a favourable prognosis.

Strengths and limitations

This study has supplied data to assist in the planning of a prospective multicentre study (ClinTrials number NCT05218863).[182] The aim of this planned study is to identify the incidence and outcome of AMI in hospitalised patients, describe clinical and laboratory variables of different forms of AMI at baseline and map the patterns of diagnosis and management. This international research programme should contribute to development of an algorithm for diagnosis and management of AMI. We believe that obtaining an overall picture of AMI rather than focusing on each form of AMI separately is needed to increase knowledge and awareness among physicians and ultimately to improve outcome. The main strength of the present study is provision of a broad overview of the existing literature on AMI. Among the limitations are: (1) by not including the term 'colonic ischaemia' or the misnomer 'ischaemic colitis' in the search strategy we might have missed some studies on AMI. However, reporting in articles is almost exclusively based on the forms of AMI differentiated based on pathophysiological mechanism, while both the small and large bowel are often affected in occlusive arterial AMI and NOMI; (2) the long study periods and single-centre retrospective nature of most of the studies, where the evidence can only be improved by future studies; (3) the pooling of studies with somewhat different definitions and management algorithms, where we created categories to minimise these differences; (4) the inherent risk of bias, both publication bias of the studies, and possible bias in the assessment of the studies, although no efforts were spared to avoid this.

In summary, the present systematic analysis estimated the incidence of AMI in the general population and hospitalised patients, forming basis for planning of future prospective studies. Two thirds of AMI cases are of occlusive arterial origin with the potential for better survival, if diagnosed promptly and revascularised in time. AMI due to MVT carries the best spontaneous prognosis. Despite some progress in revascularisation techniques, and improved survival since the millennium, emergency revascularisation rates remain low and mortality remains very high. There is great potential for future improvement.

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Global incidence and outcomes of acute mesenteric ischaemia: a systematic review and meta-analysis.

Supplement 1. Search strategy

Search dates – MEDLINE (Ovid), Web of Science and Scopus on March 23, 2021, Cochrane Library on March 24th, 2021; Updated July, 26, 2022

Ovid MEDLINE(R) and Epub Ahead of Print, In-Process, In-Data-Review & Other Non-Indexed Citations and Daily

Ovid MEDLINE(R)

1	Ischemia/
2	(ischemia or ischaemia or ishemia or ishaemia).ab,ti.
3	1 or 2
4	exp Mesentery/
5	exp Mesenteric Vascular Occlusion/
6	mesentery.ab,ti.
7	mesenteric.ab,ti.
8	4 or 5 or 6 or 7
9	3 and 8
10	exp Mesenteric Ischemia/
11	acute mesenteric ischemia.ab,ti.
12	acute mesenteric ischaemia.ab,ti.
13	acute mesentery artery ischaemia.ab,ti.
14	acute mesenteric artery ischaemia.ab,ti.
15	acute mesentery artery ischemia.ab,ti.
16	acute mesenteric artery ischemia.ab,ti.
17	acute mesenteric thrombosis.ab,ti.
18	acute mesenteric embolism.ab,ti.
19	bowel infarction.ab,ti.
20	acute mesenteric arterial thrombosis.ab,ti.
21	acute mesenteric arterial embolism.ab,ti.
22	acute mesenteric venous thrombosis.ab,ti.
23	nonocclusive mesenteric ischemia.ab,ti.
24	intestinal ischemia.ab,ti.
25	mesenteric infarction.ab,ti.
26	splanchnic ischemia.ab,ti.
27	bowel ischemia.ab,ti.
28	gut ischemia.ab,ti.
29	vascular insufficiency of intestine.ab,ti.
30	mesenteric thromboembolism.ab,ti.
31	10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30
32	9 or 31
33	exp Prevalence/
34	prevalence.ab,ti.
35	population-based.ab,ti.
36	population based.ab,ti.

37	general population.ab,ti.
38	exp Incidence/
39	Incidence.ab,ti.
40	Epidemiology/
41	ep.fs.
42	mo.fs.
43	33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42
44	32 and 43
45	exp Humans/
46	exp Animals/
47	45 and 46
48	46 not 47
49	44 not 48
50	exp Infant, Newborn/
51	(infant or newborn or neonate or baby).mp.
52	50 or 51
53	49 not 52

Scopus

Set	Query
7	(((TITLE-ABS-KEY(ischemia OR ischaemia OR ishemia OR ishaemia)) AND (TITLE-ABS-KEY("Mesenteric Vascular Occlusion" OR mesentery OR mesenteric))) OR (TITLE-ABS-KEY("acute mesenteric ischemia" OR "acute mesenteric ischemia" OR " acute mesenteric ischaemia" OR "acute mesentery artery ischaemia" OR "acute mesenteric artery ischaemia" OR "acute mesentery artery ischemia" OR "acute mesenteric artery ischemia" OR "acute mesenteric thrombosis" OR "acute mesenteric embolism" OR "bowel infarction" OR "acute mesenteric arterial thrombosis" OR "acute mesenteric arterial embolism" OR "acute mesenteric venous thrombosis" OR "nonocclusive mesenteric ischemia" OR "intestinal ischemia" OR "mesenteric infarction" OR "splanchnic ischemia" OR "bowel ischemia" OR "gut ischemia" OR "vascular insufficiency of intestine"))) AND (TITLE-ABS-KEY(prevalence OR incidence OR "population based" OR "population-based" OR "general population"))
6	TITLE-ABS-KEY(prevalence OR incidence OR "population based" OR "population-based" OR "general population")
5	((TITLE-ABS-KEY(ischemia OR ischaemia OR ishemia OR ishaemia)) AND (TITLE-ABS-KEY("Mesenteric Vascular Occlusion" OR mesentery OR mesenteric))) OR (TITLE-ABS-KEY("acute mesenteric ischemia" OR "acute mesenteric ischemia" OR " acute mesenteric ischaemia" OR "acute mesentery artery ischaemia" OR "acute mesenteric artery ischaemia" OR "acute mesentery artery ischemia" OR "acute mesenteric artery ischemia" OR "acute mesenteric thrombosis" OR "acute mesenteric embolism" OR "bowel infarction" OR "acute mesenteric arterial thrombosis" OR "acute mesenteric arterial embolism" OR "acute mesenteric venous thrombosis" OR "nonocclusive mesenteric ischemia" OR "intestinal ischemia" OR "mesenteric infarction" OR "splanchnic ischemia" OR "bowel ischemia" OR "gut ischemia" OR "vascular insufficiency of intestine"))
4	TITLE-ABS-KEY("acute mesenteric ischemia" OR "acute mesenteric ischemia" OR " acute mesenteric ischaemia" OR "acute mesentery artery ischaemia" OR "acute mesenteric artery ischaemia" OR "acute mesentery artery ischemia" OR "acute mesenteric artery ischemia" OR "acute mesenteric thrombosis" OR "acute mesenteric embolism" OR "bowel infarction" OR "acute mesenteric arterial thrombosis" OR "acute mesenteric arterial embolism" OR "acute mesenteric venous thrombosis" OR "nonocclusive mesenteric ischemia" OR "intestinal ischemia" OR "mesenteric infarction" OR "splanchnic ischemia" OR "bowel ischemia" OR "gut ischemia" OR "vascular insufficiency of intestine")
3	(TITLE-ABS-KEY(ischemia OR ischaemia OR ishemia OR ishaemia)) AND (TITLE-ABS-KEY("Mesenteric Vascular Occlusion" OR mesentery OR mesenteric))
2	TITLE-ABS-KEY("Mesenteric Vascular Occlusion" OR mesentery OR mesenteric)
1	TITLE-ABS-KEY(ischemia OR ischaemia OR ishemia OR ishaemia)

Cochrane Library

ID	Search
#1	MeSH descriptor: [Mesenteric Ischemia] explode all trees
#2	("acute mesenteric ischemia" OR "acute mesenteric ischemia" OR "acute mesenteric ischaemia" OR "acute mesentery artery ischaemia" OR "acute mesenteric artery ischaemia" OR "acute mesentery artery ischemia" OR "acute mesenteric artery ischemia" OR "acute mesenteric thrombosis" OR "acute mesenteric embolism" OR "bowel infarction" OR "acute mesenteric arterial thrombosis" OR "acute mesenteric arterial embolism" OR "acute mesenteric venous thrombosis" OR "nonocclusive mesenteric ischemia" OR "intestinal ischemia" OR "mesenteric infarction" OR "splanchnic ischemia" OR "bowel ischemia" OR "gut ischemia" OR "vascular insufficiency of intestine"):ti,ab,kw (Word variations have been searched)
#3	#1 OR #2

Web of Science Core Collection 1980–2021, all languages and document types

TS=title, abstract, author keywords

Set	Results	Query
# 7	1,073	#6 AND #5 Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI Timespan=All years
# 6	1,690,501	TS=prevalence OR TI=prevalence OR TS= incidence OR TI=incidence OR TI= population based OR TI= population-based OR TI=general population Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI Timespan=All years
# 5	16,500	#4 OR #3 Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI Timespan=All years
# 4	14,666	TS=(acute mesenteric ischemia OR acute mesenteric ischemia OR acute mesenteric ischaemia OR acute mesentery artery ischaemia OR acute mesenteric artery ischaemia OR acute mesentery artery ischemia OR acute mesenteric artery ischemia OR acute mesenteric thrombosis OR acute mesenteric embolism OR bowel infarction OR acute mesenteric arterial thrombosis OR acute mesenteric arterial embolism OR acute mesenteric venous thrombosis OR nonocclusive mesenteric ischemia OR intestinal ischemia OR mesenteric infarction OR splanchnic ischemia OR bowel ischemia OR gut ischemia OR vascular insufficiency of intestine) Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI Timespan=All years
# 3	7,099	#2 AND #1 Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI Timespan=All years
# 2	52,671	TS=(Mesenteric Vascular Occlusion OR mesentery OR mesenteric) Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI Timespan=All years
# 1	280,395	TS=(ischemia OR ischaemia OR ishemia OR ishaemia) Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI Timespan=All years

Global incidence and outcomes of acute mesenteric ischaemia: a systematic review and meta-analysis.

Supplement 2. Statistical methods

In the context of random-effects meta-analysis we assume that the true effect sizes differ between studies. For example the true effect size θ_i for each study can be higher or lower in studies where participants are older, more educated, healthier etc. If we were to perform infinite number of studies, then the true effect sizes would be distributed normally around mean μ with variance τ^2, *ie* $\theta_i \sim N(\mu, \tau^2)$. In random-effects meta-analysis it is assumed that the studies we have access to represent a random sample from this distribution.

In the random-effects model we assume that the observed mean Y for any study *i* is represented as

$$Y_i = \mu + \xi_i + \varepsilon_i,$$

where μ is the grand mean, ξ_i is the difference, between the grand mean (μ) and the true mean for study *i* (θ_i) and ε_i is the difference, between the true mean of *i*-th study and the observed mean, ie $\xi_i = \theta_i - \mu$ and $\varepsilon_i = Y_i - \theta_i$. Here it is assumed that $Y_i \sim N(\theta_i, V_i)$.

The inverse variance weights method assigns every study *i* some weight. As we have two sources of variance (from ξ_i and ε_i), we have two components to the overall study error variance. We will denote the within-study variance V_i and the between-study variance τ^2. The weight assigned to each study can be then calculated by

$$W_i = \frac{1}{V_i + T^2},$$

where T^2 is the sample estimate for τ^2.

The combined effect or weighted mean M across *k* studies is then calculated as

$$M = \frac{\sum_{i=1}^{k} W_i Y_i}{\sum_{i=1}^{k} W_i}.$$

The meta-analysis error variance V_M of the combined effect *M* is then represented as

$$V_M = \frac{1}{\sum_{i=1}^{k} W_i}.$$

(Borenstein M, Hedges LV, Higgins JP, Rothstein HR (2010): A basic introduction to fixed-effect and random-effects models for meta-analysis. *Research Synthesis Methods*, **1**, 97—111)

Now let the Y_i denote the number of patients with outcome in study *i* and N_i the total number of patients in study *i.* Denote variable of interest as proportion π, its log odds for *i*-th study as $\theta_i = logit(\pi_i)$. The standard approach would be to estimate the effect parameter θ_i by $\log(\frac{Y_i}{N_i - Y_i})$ with standard error $\sqrt{V_i} = \frac{1}{Y_i} + \frac{1}{N_i - Y_i}$. Instead the generalized linear mixed models approach works as follows.

Now the true distribution of Y_i is known to be

$$Y_i \sim \text{Binomial}\left(\mathrm{N_i}, \frac{\exp(\theta_i)}{1+\exp(\theta_i)}\right).$$

As θ_i is assumed to be distributed normally around the grand mean μ, then the model alltogether is called binomial-normal model and it is a random intercept logistic regression model. Therefore a generalized linear mixed model can be fitted in order to estimate the grand mean μ.

In context of subgroup analysis this approach considers subgroup to be a covariate and takes into account that some studies are more similar (belong to the same subgroup) and allows us to estimate the grand mean as well as subgroup mean ($\mu + \beta_{subgroup_j}$).

(Stijnen T, Hamza TH, Ozdemir P (2010): Random effects meta-analysis of event outcome in the framework of the generalized linear mixed model with applications in sparse data. *Statistics in Medicine*, **29**, 3046—67)

Global incidence and outcomes of acute mesenteric ischaemia: a systematic review and meta-analysis

Supplement 3. Quality assessment of individual studies

In total, 163 studies were included in systematic analysis.

Supplementary Table 1. Quality assessment of individual studies included in quantitative synthesis. Maximum score of seven stars indicates a good quality, while studies receiving less than four stars are considered of weak quality.

Study	Selection rating (number of stars)	Comparability rating (number of stars)	Outcome rating (number of stars)	Study quality (total number of stars)
Abu-Daff 2009	2	2	3	7
Acosta 2003	2	2	3	7
Acosta 2004	2	2	3	7
Acosta 2005	2	2	3	7
Acosta 2006	2	2	3	7
Acosta 2006	2	2	3	7
Acosta 2008	2	2	3	7
Acosta 2010	2	2	3	7
Acosta 2012	2	2	3	7
Acosta-Merida 2020	2	2	3	7
Acosta-Merida 2007	2	2	3	7
Akyildiz 2015	2	2	2	6
Alhan 2012	2	2	3	7
Aliosmanoglu 2013	2	2	2	6
Al-Thani 2015	2	2	3	7
Alvi 2009	2	2	3	7
Amitrano 2007	2	2	3	7
Anadol 2004	2	2	3	7
Andersson 1984	2	2	3	7
Andraska 2020	2	2	3	7
Andraska 2022	2	2	3	7
Anglaret 2021	1	2	3	6
Aouini 2012	2	2	1	5
Arnalich 2010	2	2	3	7
Arthurs 2011	2	2	3	7
Arya 2016	2	2	3	7
Augene 2019	2	2	3	7
Baeshko 2004	1	2	3	6
Bagdasarov 2013	2	2	2	6
Bapat 1990	2	2	2	6
Beaulieu 2014	2	2	3	7
Bergan 1975	2	2	3	7
Beyaz 2022	1	2	3	6
Bilgic 2015	2	2	3	7
Björck 2002	2	2	3	7
Block 2008	2	2	3	7
Block 2010	2	2	3	7
Boley 1977	2	2	3	7
Boos 1992	2	2	3	7
Böttger 1991	2	2	3	7
Branco 2015	2	2	3	7

Brunaud 2001	2	2	3	7
Bryant 1997	2	2	3	7
Bulut 2017	2	2	3	7
Calame 2020	2	2	3	7
Castelli 1974	2	2	3	7
Char 2003	2	2	3	7
Chiu 2009	2	2	3	7
Chou 2021	1	2	3	6
Clark 1984	2	2	3	7
Clavien 1988	2	2	3	7
Crawford 2016	2	2	3	7
Czerny 1997	1	2	3	6
Dahlke 2008	1	2	3	6
Danse 1997	2	2	3	7
Danylenko 2012	2	2	3	7
Deehan 1995	2	2	3	7
Destek 2020	2	2	3	7
Dinc 2015	2	2	3	7
Ding 2017	2	2	3	7
Duran 2015	2	2	2	6
Duron 1998.	2	2	3	7
Edwards 2003	2	2	3	7
Elsharkawy 2021	1	2	3	6
Eltarawy 2009	2	2	3	7
Endean 2001	2	2	3	7
Endo 2021	2	2	3	7
Erben 2018	2	2	3	7
Freeman 2005	2	2	3	7
Freitas 2018	2	2	3	7
Gawenda 1997	2	2	3	7
Gearhart 2003	2	2	3	7
Girault 2021	1	2	3	6
Giulini 1987	2	2	3	7
Goudet 1995	2	2	3	7
Goudet 1998	2	2	3	7
Groteluschen 2019	2	2	3	7
Grothues 1996	2	2	3	7
Guttman 2021	2	2	3	7
Haga 2009	2	2	3	7
Haghighi 2008	2	2	3	7
Hagmüller 1988	2	2	3	7
Hansen 1976	2	2	3	7
Howard 1996	2	2	3	7
Huang 2005	2	2	3	7
Huerta 2011	2	2	3	7
Hussain 2009	2	2	2	6
Inderbitzi 1992	2	2	3	7
Järvinen 1994	2	2	3	7
Jenson 1956	2	2	3	7
Kaech 1989	2	2	3	7
Kairaluoma 1977	2	2	3	7
Kärkkäinen 2015	2	2	3	7
Kärkkäinen 2015	2	2	3	7
Kaser 2015	2	2	3	7
Kassahun 2008	2	2	3	7
Kisaoglu 2014	2	2	3	7
Klempnauer 1997	2	2	2	6
Krausz 1978	2	2	3	7

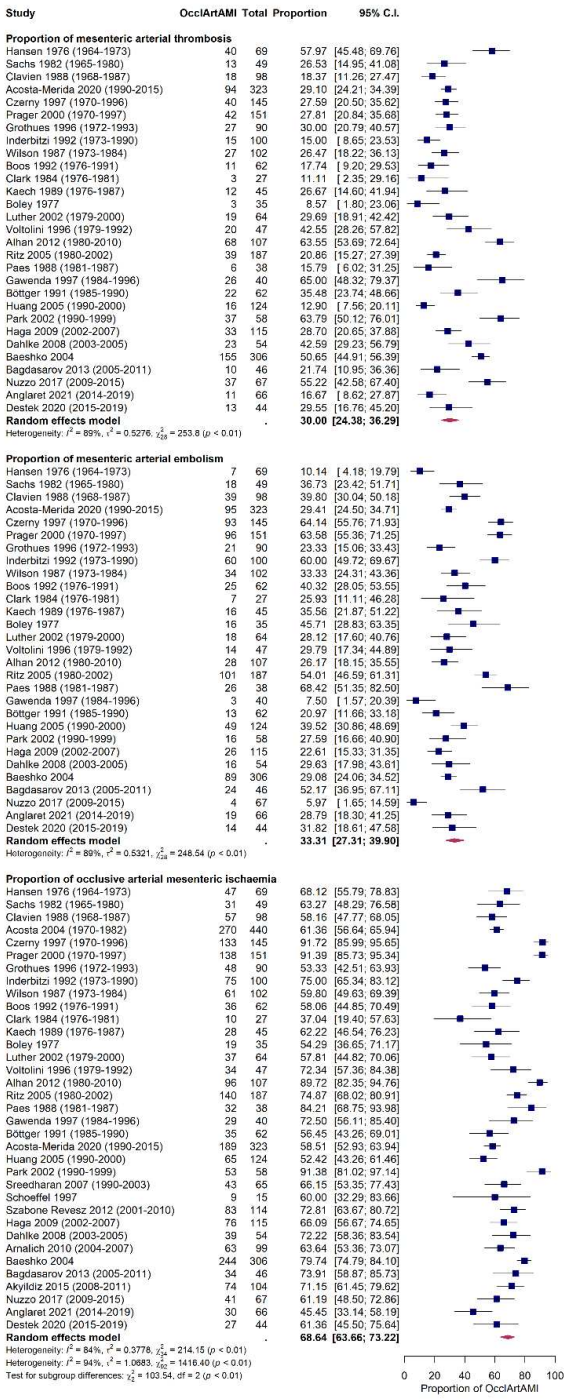
Kulu 2016	2	2	3	7
Lotti 2003	1	2	3	6
Luther 2002	2	2	3	7
Maldonado 2016	2	2	3	7
Mamode 1999	2	2	2	6
Marchena-Gomez 2009	2	2	2	6
Merle 2004	2	2	3	7
Meyer 1998	2	2	3	7
Moschetta 2016	2	2	3	7
Naazar 2021	1	2	2	6
Newton 2011	2	2	3	7
Nonthasoot 2005	2	2	3	7
Nuzzo 2017	2	2	3	7
Ottinger 1967	2	2	3	7
Ottinger 1978	2	2	3	7
Paduszynska 2012	2	2	3	7
Paes 1988	2	2	3	7
Park 2002	2	2	3	7
Peris 2012	2	2	3	7
Prager 2000	2	2	3	7
Puippe 2015	2	2	3	7
Raupach 2016	2	2	3	7
Reissfelder 2011	2	2	3	7
Rhee 1994	2	2	3	7
Riemenschneider 1987	2	2	3	7
Ritz 2005	2	2	3	7
Rogers 1982	2	2	3	7
Roussel 2015	2	2	3	7
Ryer 2012	2	2	3	7
Sachs 1982	2	2	3	7
Safioleas 2006	2	2	3	7
Salim 2016	2	1	3	6
Salim 2018	2	2	3	7
Schermerhorn 2009	2	2	3	7
Schoeffel 1997	2	2	3	7
Sindall 2020	2	2	3	7
Singh 1996	2	2	3	7
Smith J 1976	2	2	3	7
Sreedharan 2007	2	2	3	7
Stahl 2020	2	2	3	7
Stockmann 2000	2	2	3	7
Studer 2015	2	2	3	7
Swerdlow 2019	2	2	3	7
Szabone Revesz 2012	2	2	3	7
Takiguchi 2020	2	2	3	7
Tang 2020	1	2	3	6
Tanrikulu 2016	2	2	3	7
Tsai 1990	1	2	3	6
Ünalp 2010	2	2	1	5
Vellar 1977	1	2	3	6
Vokurka 2008	2	2	2	6
Voltolini 1996	2	2	3	7
Wadman 2000	2	2	3	7
Wadman 2010	2	2	2	6
Wilson 1987	2	2	3	7
Wu 2020	2	2	2	6
Yang 2014	2	2	2	6
Yang 2015	2	2	3	7

Yang 2019	2	2	3	7
Yasuhara 2005	2	2	3	7
Yilmaz 2017	2	2	3	7
Zan 1993	2	2	3	7
Zettervall 2017	2	2	3	7
Zhang 2017	2	2	3	7

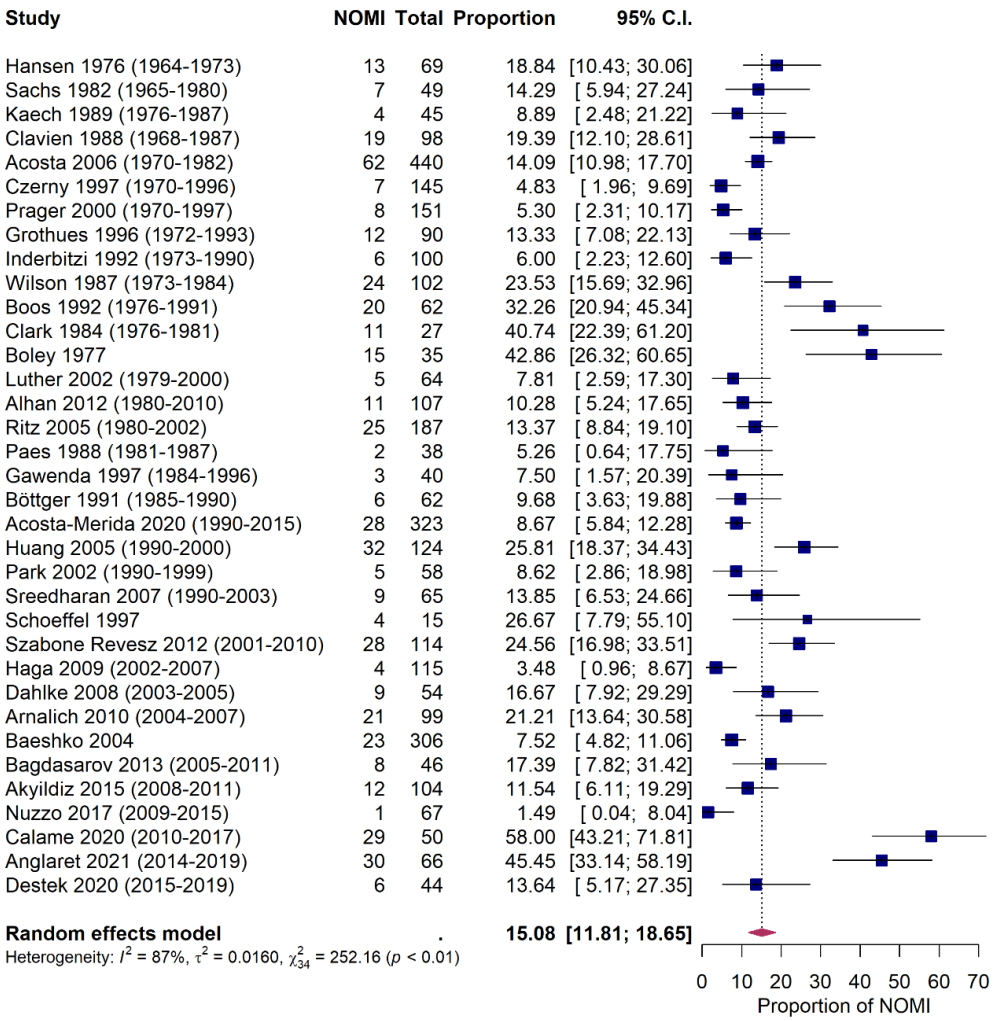
Supplementary Figures.

Supplementary Figure 1. Proportions of different forms of acute mesenteric ischaemia.

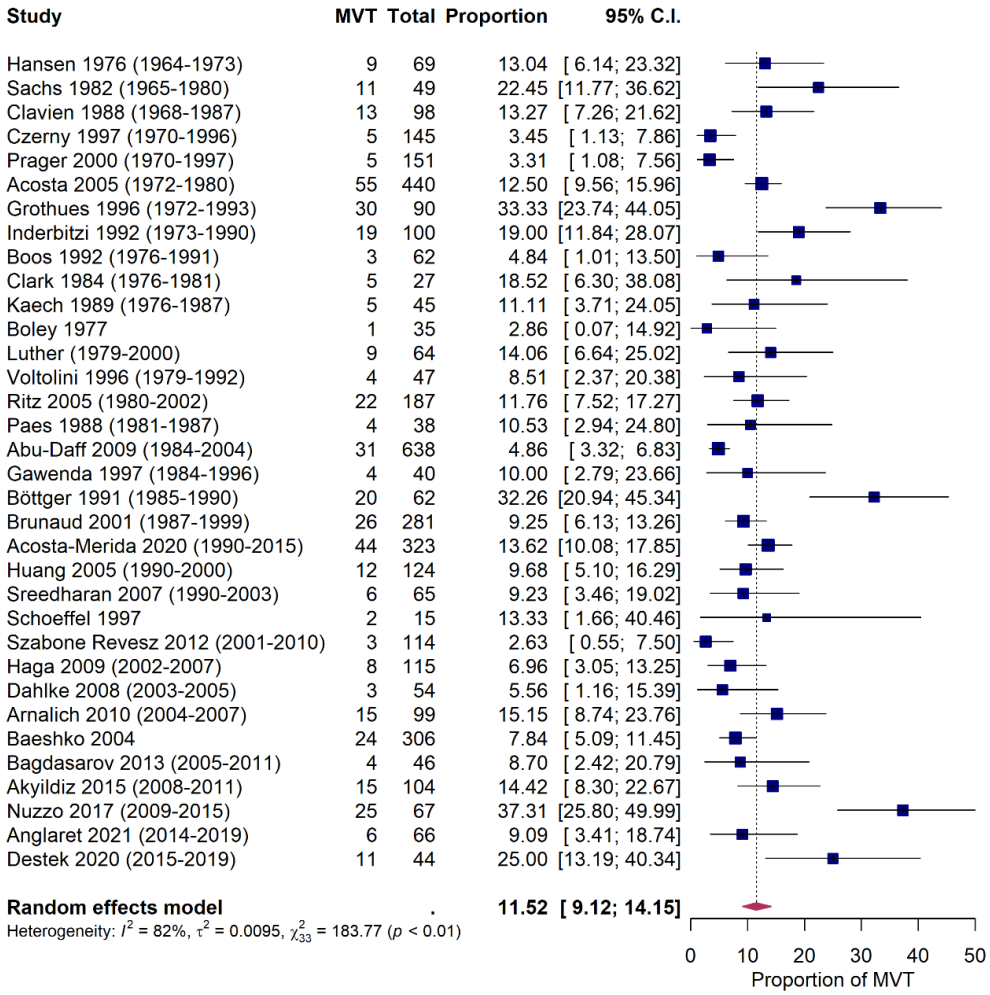
a. Proportion (%) of occlusive arterial mesenteric ischaemia (OcclArtAMI)



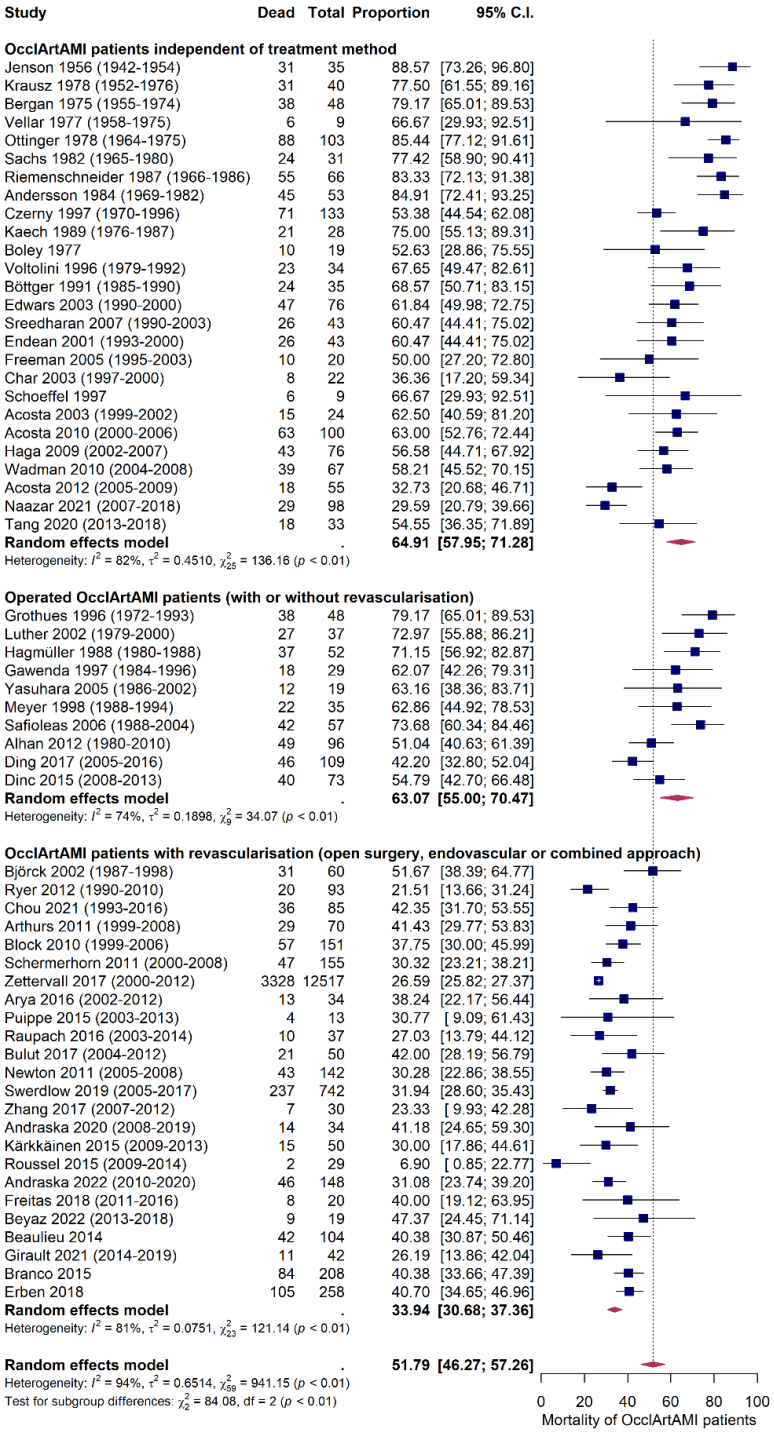
b. Proportion (%) of non-occlusive mesenteric ischaemia (NOMI)



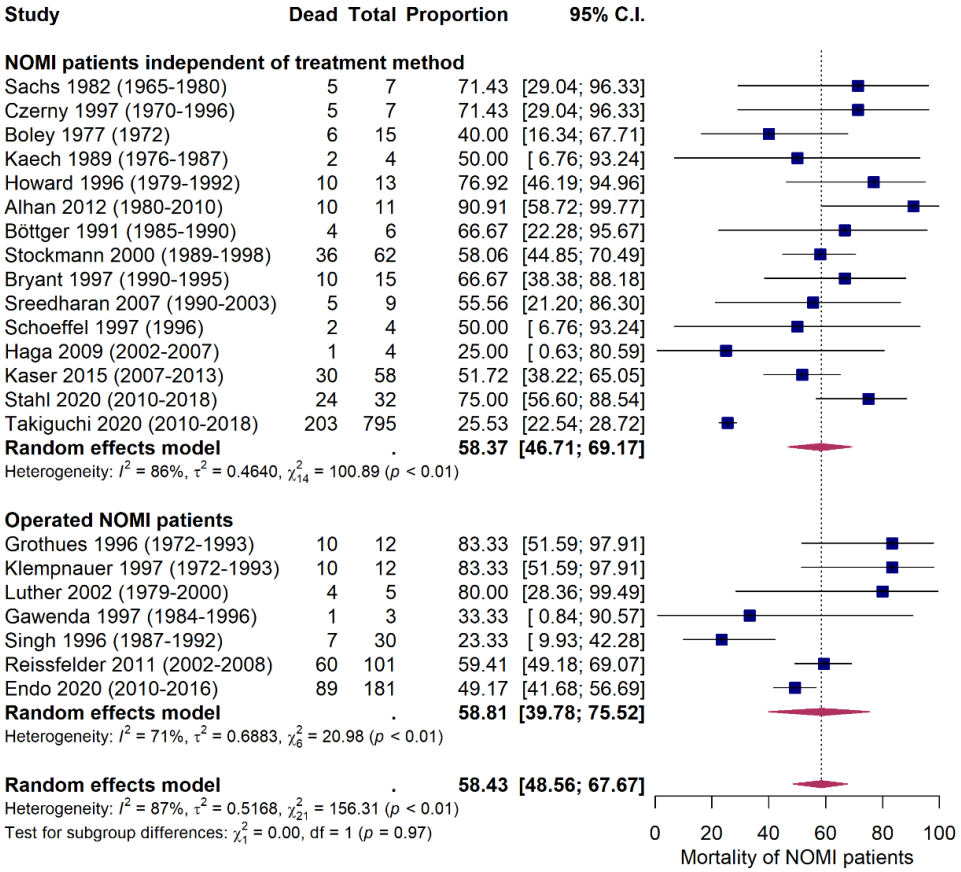
c. Proportion (%) of venous mesenteric thrombosis (MVT)



Supplementary Figure 2. Short-term (hospital or 30-days) mortality of occlusive arterial form of acute mesenteric ischaemia (OcclArtAMI). Selection of the studies is specified in the headings of the panels. In brackets, the period of patient inclusion is indicated.



Supplementary Figure 3. Short-term (hospital or 30-days) mortality of non-occlusive mesenteric ischaemia (NOMI). Subgroup analyses of studies including patients independent of treatment method (upper panel), and of studies including only operated patients (lower panel) are presented. In brackets, the period of patient inclusion is indicated.



Supplementary Figure 4. Short-term (hospital or 30-days) mortality of mesenteric vein thrombosis (MVT). In brackets, the period of patient inclusion is indicated.