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## Somatostatin analogues for acute bleeding oesophageal varices (Review)

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[Intervention Review]

# Somatostatin analogues for acute bleeding oesophageal varices

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[pcg@cochrane.dk](mailto:pcg@cochrane.dk).**Editorial group:** Cochrane Hepato-Biliary Group**Publication status and date:** Stable (no update expected for reasons given in 'What's new'), published in Issue 2, 2012.**Citation:** Gøtzsche PC, Hróbjartsson A. Somatostatin analogues for acute bleeding oesophageal varices. *Cochrane Database of Systematic Reviews* 2008, Issue 3. Art. No.: CD000193. DOI: [10.1002/14651858.CD000193.pub3](https://doi.org/10.1002/14651858.CD000193.pub3).

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## ABSTRACT

### Background

Somatostatin and its derivatives are sometimes used for emergency treatment of bleeding oesophageal varices in patients with cirrhosis of the liver.

### Objectives

To study whether somatostatin or its analogues improve survival or reduce the need for blood transfusions in patients with bleeding oesophageal varices.

### Search methods

PubMed and *The Cochrane Library* were searched (1 November 2011). Reference lists of publications, contacts with authors.

### Selection criteria

All randomised trials comparing somatostatin or analogues with placebo or no treatment in patients suspected of acute or recent bleeding from oesophageal varices.

### Data collection and analysis

The outcome measures extracted were: mortality, blood transfusions, use of balloon tamponade, initial haemostasis and rebleeding. Intention-to-treat analyses including all randomised patients were conducted if possible; a random-effects analysis was preferred if there was significant heterogeneity between the trials ( $P < 0.10$ ). The trials were divided in two groups: trials with a low risk of bias, which had concealed allocation of patients and were double-blind, and other trials.

### Main results

We included 21 trials (2588 patients). The drugs did not reduce mortality significantly (relative risk 0.97, 95% confidence interval (CI) 0.75 to 1.25, for the trials with a low risk of bias, and 0.80, 95% CI 0.63 to 1.01, for the other trials). Units of blood transfused were 0.7 (0.2 to 1.1) less with drugs in the trials with a low risk of bias and 1.5 (0.9 to 2.0) less in the other trials. Number of patients failing initial haemostasis was reduced, relative risk 0.68 (0.54 to 0.87). Number of patients with rebleeding was not significantly reduced for the trials with a low risk of bias, relative risk 0.84 (0.52 to 1.37) while it was substantially reduced in the other trials, relative risk 0.36 (0.19 to 0.68). Use of balloon tamponade was rarely reported.

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**Authors' conclusions**

The need for blood transfusions corresponded to one half unit of blood saved per patient. It is doubtful whether this effect is worthwhile. The findings do not suggest a need for further placebo-controlled trials of the type reviewed here. A large placebo controlled trial enrolling thousands of patients is needed if one wishes to rule out the possibility that a worthwhile effect on mortality might have been overlooked.

**PLAIN LANGUAGE SUMMARY****Somatostatin analogues for acute bleeding oesophageal varices**

Cirrhosis of the liver is a chronic, progressing disease that is most commonly caused by excessive use of alcohol or by hepatitis C infection. The liver tissue is replaced by connective tissue, which leads to loss of liver function. People with cirrhosis of the liver may develop varicose veins (enlarged blood vessels or varices) in the gullet. Bleeding varices can be life-threatening. The hormone somatostatin, or similar drugs like octreotide and vapreotide, can be used to try to stop the bleeding. The review of 21 trials (2588 patients) found that the tested drugs did not reduce deaths. There was a small reduction in the need for blood transfusions, corresponding to one half unit of blood saved per patient. It is doubtful whether this effect is worthwhile.

## BACKGROUND

Somatostatin is an oligopeptide hormone that has reduced portal blood flow or hepatic venous pressure gradient in most experimental studies, both in animals and in man (Samnegaard 1980; Hanisch 1992; Cirera 1995; Villanueva 2001), while its effect on intraoesophageal pressure is more equivocal (Greco 1982; Kleber 1988; Hanisch 1992; Nevens 1994). Octreotide and vapreotide are derivatives of somatostatin that have a much longer half-life than the native hormone but similar properties (McCormick 1992; Albillos 1994; Lamberts 1996; Calès 2001), apart from the effect on portal pressure of octreotide which is very short-lived, at best (Møller 1997; Escorsell 2001).

Somatostatin analogues are sometimes used for emergency treatment of bleeding oesophageal varices in patients with cirrhosis of the liver. We reviewed the randomised trials that compared these drugs with placebo or no treatment. The present systematic review is an update of our previous review (Gøtzsche 2005).

## OBJECTIVES

To study whether somatostatin or its analogues improve survival or reduce the number of blood transfusions in patients with suspected or verified acute or recently bleeding oesophageal varices.

## METHODS

### Criteria for considering studies for this review

#### Types of studies

Randomised trials comparing somatostatin or its analogues with placebo or no treatment, irrespective of language, publication type, or year of publication. Trials where it is clear that the allocation was not concealed were not included.

#### Types of participants

Patients suspected of acute or recent bleeding from oesophageal varices. Stable patients in trials studying the effect on rebleeding were not included.

#### Types of interventions

Experimental: somatostatin, given intravenously, or analogues, given intravenously or subcutaneously.

Control: placebo or no treatment.

Trials that specified that all patients, in addition to the trial drugs, should undergo sclerotherapy or ligation, or other types of co-intervention, were accepted.

#### Types of outcome measures

1. Mortality.
2. Number of blood transfusions.
3. Number with balloon tamponade.
4. Number failing initial haemostasis.
5. Number with rebleeding.

### Search methods for identification of studies

PubMed from 1966 onwards and *The Cochrane Library* were searched with the terms (somatostatin OR octreotide OR

vapreotide OR lanreotide) combined with (varic\* OR bleed\* OR hemorrhag\* OR hematemesis OR melena); date of last searches November 2011. Abstracts from conference proceedings were provided by The Cochrane Hepato-Biliary Group and the group's trial register was searched in January 2008.

We accepted reports in any language, unpublished trials, and trials published only as abstracts in an attempt to minimise the impact of publication bias, although proper assessment of the trials is rarely possible in this difficult area based on summary data alone. We scanned reference lists of trial reports and contacted the authors. Decisions on inclusion of trials were made by the two authors independently; disagreements were settled by discussion.

## Data collection and analysis

### Data collection

We extracted data on type of drug, dosage and duration, number of randomised patients, the randomisation and blinding procedures, exclusions from analysis, deaths, number of blood transfusions and number of patients with balloon tamponade, initial haemostasis, and rebleeding. We contacted the authors when the information was unclear or insufficient. Data extraction was made by the two authors independently; disagreements were settled by discussion.

### Risk of bias

The trials were divided in two groups, according to risk of bias. To qualify for the low bias risk group, the allocation of patients to treatment groups had to be concealed and the trials had to be double-blind (Schulz 1995). Blinding was chosen as an additional criterion to the quality of the allocation process, since we and other trialists have observed that decisions to use balloon tamponade or to give transfusions, or whether or not to define a patient as a therapeutic failure could be influenced by knowledge of the treatment assignment (Morales 2007).

### Statistical methods

Intention-to-treat analyses were conducted if possible. A random effects analysis was preferred if there was significant heterogeneity between the trials ( $P < 0.10$ ). The  $I^2$  statistic was used to describe the degree of heterogeneity; it can be interpreted as the proportion of the observed discrepancy in the estimation of the effect, within a group of trials, which cannot be accounted for by random variation (Higgins 2003). For blood transfusions, the standard deviations were quite variable across trials and the distributions were very skewed. Therefore, we checked our calculation of the weighted mean difference by calculating a simple average of the reported number of transfusions, weighted by the sample sizes of the trials (Gøtzsche 1989). As this led to very similar results, we present below only the weighted mean differences. When the authors had reported data at several time points on bleeding control, we chose 48 h whenever possible as this interval was most often used by the authors. Criteria for failing initial haemostasis and for rebleeding were those used by the trial authors, although we and other trialists (Morales 2007) are aware that the authors' decisions on cut-offs and definitions could have been biased. For mortality, we preferred data at six weeks, if available, since it is clinically relevant and recommended by trialists in this area (Baveno II 1996).

## RESULTS

### Description of studies

We included 21 trials (average of about 100 patients per trial, range 60-383). Seven trials were funded by industry; ten trials had no information on funding; and four trials were funded by public sources or had no funding (Gøtzsche 1995; Shiha 1996; Villanueva 2001; Morales 2007). See graphs and Table: 'Characteristics of included studies' for details.

All patients had suspected or verified acute or recent bleeding from oesophageal varices. Endoscopic confirmation prior to randomisation was mentioned in 12 of the trials (Valenzuela 1989; Moretó 1994; Pauwels 1994; Besson 1995; Sung 1995; Shah 1996; Shiha 1996; Farooqi 2000; Freitas 2000; Zuberi 2000; Villanueva 2001; Morales 2007); in an additional study, this occurred for half of the patients (Burroughs 1990). In the other studies it was either not mentioned or they were of a pragmatic design, mirroring what happens in practice where a definitive diagnosis is not always possible before treatment is started. In 14 studies, most patients underwent sclerotherapy (Moretó 1994; Besson 1995; Gøtzsche 1995; Shah 1996; Shiha 1996; Signorelli 1996; Avgerinos 1997; Signorelli 1997; Farooqi 2000; Freitas 2000; Zuberi 2000; Villanueva 2001; Souza 2003; Morales 2007) in another, ligation (Sung 1995) as part of the trial protocol, and in one trial the patients either underwent sclerotherapy or ligation (Calès 2001).

The dose schedules and length of treatment were quite variable:

- somatostatin bolus 250 µg: Moretó 1994 (no subsequent infusion).
- somatostatin bolus 100 µg/h and infusion 50 µg/h: Souza 2003 (3 days).
- somatostatin infusion 250 µg/h: Gøtzsche 1995 (24 h for each bleeding episode).
- somatostatin bolus 250 µg and infusion 250 µg/h: Avgerinos 1997 (up to eight bolus injections, infusion for 5 days); Burroughs 1990 (5 days); Isaac 1994 (15 h); Pauwels 1994 (till 2 h after bleeding arrest); Valenzuela 1989 (up to 30 h); Villanueva 2001 (bolus every 12 h, infusion for 5 days).
- somatostatin infusion 3.5 µg/kg/h or octreotide 0.1 mg subcutaneously: Signorelli 1996 (5 days).
- octreotide infusion 25 µg/h: Besson 1995 (5 days); Freitas 2000 (48 h); Shiha 1996 (5 days).
- octreotide bolus 50 µg and infusion 25 µg/h: Signorelli 1997 (5 days).
- octreotide infusion 50 µg/h: Burroughs 1996 (5 days); Farooqi 2000 (48 h); Shah 1996 (36 h or 48 h, contrasting information); Zuberi 2000 (5 days).
- octreotide bolus 50 µg and infusion 50 µg/h: Sung 1995 (5 days).
- octreotide bolus 50 µg, infusion 50 µg/h for 24 h, and 25 µg/h for another 24 h (Morales 2007).
- vapreotide bolus 50 µg and infusion 50 µg/h: Calès 2001 (5 days).

### Risk of bias in included studies

The allocation was concealed and the trial was double-blind in ten trials (Burroughs 1990; Moretó 1994; Besson 1995; Gøtzsche 1995; Shiha 1996; Avgerinos 1997; Zuberi 2000; Calès 2001; Villanueva 2001; Morales 2007); in addition, blinding during data analysis was

used in four trials (Avgerinos 1997; Burroughs 1990; Gøtzsche 1995; Calès 2001).

Eight trials included all or nearly all (> 90%) of the randomised patients in the analysis (Moretó 1994; Besson 1995; Gøtzsche 1995; Sung 1995; Avgerinos 1997; Zuberi 2000; Villanueva 2001; Morales 2007). In four trials (Burroughs 1990; Pauwels 1994; Burroughs 1996; Calès 2001), some of the randomised patients were excluded because the source of bleeding was judged to be non-variceal. In the remaining trials it was not clear whether there had been additional patients that were not accounted for.

### Effects of interventions

We included 21 trials (2588 patients). The drugs did not reduce mortality significantly, relative risk (RR) 0.97, 95% confidence interval (CI) 0.75 to 1.25, for the trials with low risk of bias, and 0.80 (95% CI 0.63 to 1.01) for the other trials (see graphs). The result was similar for those trials where active drug was administered for five days, RR 0.90 (95% CI 0.74 to 1.09) for the trials with low risk of bias.

For average number of blood transfusions, the trials with low risk of bias were significantly heterogeneous ( $P = 0.06$ ,  $I^2 = 47%$ ). The heterogeneity was caused by two trials (Burroughs 1990; Gøtzsche 1995) that both reported a median difference of three transfusions but in opposite directions. The average effect for the trials with low risk of bias was 0.7 (95% CI 0.2 to 1.1) units of blood products saved with somatostatin analogues. The result was very similar if the two outliers were excluded, 0.7 units (95% CI 0.4 to 1.0), or if the analysis was restricted to the seven trials with low risk of bias where active drug was administered for five days, 0.8 units (95% CI 0.4 to 1.2). The standard deviations were quite variable across trials and the distributions were very skewed. Even so, all but two trials reported means rather than medians. As just noted, the use of medians in two trials did not have any impact on the meta-analysis, which is supported by the fact that the difference between drug and placebo in three other trials that reported both means and medians were very similar for the two measures of effect (Besson 1995; Villanueva 2001; Morales 2007). Because of the skewness, it is doubtful whether the best method to combine the trials is to use the weighted mean difference. Reassuringly, however, a simple average of the reported number of transfusions, weighted by the sample sizes of the trials, gave a similar result. In the other trials, the average number of units of blood products saved was twice as large as for the trials with low risk of bias: 1.5 units (95% CI 0.9 to 2.0).

There was significant heterogeneity for number of patients failing initial haemostasis and for rebleeding, both for trials with low risk of bias and for other trials, with  $I^2$  around 50% to 60%. The estimates for number of patients failing initial haemostasis were similar for trials with low risk of bias and for other trials, and the combined estimate showed a significant reduction, RR 0.68 (95% CI 0.54 to 0.87). For rebleeding, the estimates were very different, RR 0.84 (95% CI 0.52 to 1.37) for trials with low risk of bias and 0.36 (95% CI 0.19 to 0.68) for other trials. Use of balloon tamponade was rarely reported.

## DISCUSSION

It is complicated to perform trials in acute bleeding oesophageal varices. Unlike many other medical emergencies, for example, myocardial infarction, patients are scarce and therefore, it is difficult to obtain a consecutive flow of patients and a routine that

is strictly adhered to. Furthermore, the threshold for giving blood transfusions and using balloon tamponade, and the possibility of having acute diagnostic and therapeutic endoscopy performed, is likely to vary considerably, even within the same trial, depending on the available clinicians and their competing duties. Heterogeneity is therefore to be expected, both within and between trials. Potential sources of heterogeneity between trials are: quality of allocation concealment; blinding of clinicians, outcome assessors and data analysts; nature and dose of drugs; duration of treatment; Child's grade; type of bleeding (index versus interval bleeding); inclusion before or after end of haemorrhage; criteria for definition of successful initial haemostasis and for rebleeding episodes; presence of ulcers or gastric varices; time between randomisation and start of treatment; confirmation of diagnosis by acute endoscopy; concomitant use of sclerotherapy or ligation; and concomitant use of balloon tamponade, transfusions and drugs.

Apart from mortality, there was considerable heterogeneity between the reviewed trials. The causes for heterogeneity can be explored by sensitivity analyses, for example, by analysing subgroups of trials or by relating the effect to dose or other covariates. However, there is a narrow limit to the number of exploratory analyses one can perform in a small sample of trials, and such analyses should preferably be specified in the protocol to avoid spurious conclusions, arising from data driven *post hoc* analyses. The most acceptable subgroup analyses are those for which there is empirical evidence that the grouping criterion is related to the size of the effect. We therefore limited subgroup analysis to double-blind trials with an adequately concealed randomisation since such trials are expected to give the most unbiased effect estimates (Schulz 1995). As expected, other trials reported more positive effects than trials with low risk of bias. This was also shown in a meta-analysis that compared emergency sclerotherapy with vasoactive drugs (D'Amico 2003) where the mortality risk difference was 1% (95% CI -4% to 7%) in good-quality trials and 8% (2% to 14%) in poor-quality trials, ie, the mortality difference was statistically significant in the poor-quality trials which is misleading.

Even after this division of the trials, considerable heterogeneity remained. Unfortunately, other trial characteristics have not indicated a plausible explanation why the results of the various trials are so different. Some researchers have suggested that the trial by Valenzuela is atypical because of the high rate of bleeding control in the placebo group, 83% (Valenzuela 1989). However, this result may simply be a random high; it refers to only 36 patients and the 95% CI for the true rate is 67% to 94%. Sixty-seven per cent is not an unusually high rate and the measured rate of 83% is not significantly different from the 65% rate in the experimental group. Perhaps even more important, the recorded rate is a matter of definition. For how long should the gastric aspirate be without blood and what interval is necessary between bleeds before it should be called a bleeding arrest rather than just a temporary control of bleeding? Finally, Valenzuela's results are in good agreement with the other trials apart from number of patients with bleeding control (initial haemostasis) which agrees well, however, with the result of another trial (Götzsche 1995).

The applied doses and length of treatment varied between the trials. There are now many trials, which have used varying doses in pathophysiological experiments, measuring, for example, hepatic venous pressure gradient and variceal pressure. The results from

such trials are conflicting. In one experiment, the authors found that the effects of bolus doses of octreotide were independent of dose and transitory, and that tachyphylaxis developed quickly (Escorsell 2001). Since it is also unclear whether results from such experiments can be translated directly to the clinical setting and to clinical outcomes, and since there was no obvious relation between dose and effect in the reviewed trials, we did not pursue this possibility further. Our review cannot give reliable evidence about the relative effects of the individual somatostatin analogues as they were all compared with placebo or no treatment, and not with each other, but with this important reservation, they seemed to have similar effects.

The length of treatment is probably of minor importance since, if effective, one would expect the drugs to be superior to no treatment whether the treatment was stopped two hours after bleeding arrest or was given for five days continuously. As expected, length of treatment was unrelated to the outcome.

Seven of the trials we identified were reported as abstracts (Isaac 1994; Moretó 1994; Burroughs 1996; Shiha 1996; Signorelli 1996; Signorelli 1997; Souza 2003). We contacted the authors but received only three replies. One author sent a published paper (Shiha 1996), another an unpublished manuscript (Moretó 1994), and a third noted that the trial was submitted for publication (Burroughs 1996). An additional trial of about 150 patients, which we had wished to include in an earlier version of this review (that also comprised trials in patients with early rebleeding), appears not to have been reported at all (UCB trial 1996). When we contacted the sponsor, UCB in Belgium, we received a letter that stated that UCB is an ethical company, and that all data are proprietary solely to the UCB who has the exclusive right to make whatever it deems desirable. We find this attitude unethical as trial participants contribute altruistically to research for the benefit of future patients (Chalmers 1990).

Our results are likely exaggerated because of publication bias (Stern 1997; Hopewell 2004; Scherer 2004) and reporting bias within trials (Chan 2004). In Shah 1996, for example, there were several important discrepancies between data as published in a conference abstract and data reported in a subsequent journal article (see Table: Characteristics of included studies). Patients could also have been excluded in those trial reports that lacked a satisfactory account of all randomised patients. In two trials, mortality was given as percentages of patients which did not concord with the number randomised, no matter how many patients we assumed could have been excluded from the analysis (Signorelli 1996; Freitas 2000).

The purpose of a meta-analysis is to give a general overview of treatments, rather than paying attention to specific details such as one might wish to do in an individual trial. It is therefore sensible to include all randomised trials. In narrative review articles and editorials, somatostatin, octreotide, and other treatments are frequently recommended for emergency treatment of bleeding oesophageal varices, sometimes with claims of bleeding control in up to 80% (Sharara 2001) or even 90% to 95% of the cases (Bornman 1994; Williams 1994). Such claims are misleading, as the bleeding often stops spontaneously. Placebo may apparently 'control' bleeding in an impressive number of cases, and clinicians may feel that their preferred intervention is effective, whatever its nature. Systematic reviews of rigorously performed randomised

trials with a placebo or a no-treatment control group is the only reliable way of judging the effect of any remedy in bleeding oesophageal varices.

The most relevant outcome measures seem to be mortality and bleeding (measured as the number of blood transfusions) since other outcome measures are derived from these. It should be noted, however, that number of transfusions is a surrogate outcome that can be unreliable in trials that are not effectively blinded. In fact, we found that the number of saved transfusions in the unblinded trials was twice the number in the blinded trials. Numbers with rebleeding were also quite different for the two groups of trials, with the most optimistic estimate obtained in the unblinded trials. Criteria for blood transfusions, bleeding control, and the timing of the measurements were rarely stated in the trial reports, and if there were none in the trial protocols either, there is a substantial risk for biased assessments. We agree with the authors of a recent trial report who noted that: "For a devastating medical emergency like acute variceal bleeding, the only outcome that really matters is survival, since a better hemostasis control without a greater survival will not be translated into a better quality of life to patients who will survive from hours to a few days in the hospital" (Morales 2007).

The somatostatin analogues did not have a significant effect on mortality whereas they had a significant effect on number of blood transfusions. However, the total drug effect, combining the number of transfusions used during both the acute bleeding and during any rebleeds, corresponded to only one half unit of blood saved per patient in the trials with low risk of bias. It is doubtful whether this effect is worthwhile.

## AUTHORS' CONCLUSIONS

### Implications for practice

The effect of somatostatin analogues corresponded to one half unit of blood saved per patient. It is doubtful whether this effect is worthwhile.

### Implications for research

Our findings do not suggest a need for further placebo-controlled trials of the type reviewed here. A huge placebo controlled trial is needed if one wishes to rule out the possibility that a worthwhile effect on mortality may have been overlooked. Since the point estimate for relative risk was 0.97 for the trials with low risk of bias and the control group death rate was 19%, it would require 25,000 patients in each group to be 20% certain not to overlook such a difference in mortality. If one uses the most optimistic mortality estimate compatible with our data which is the lower limit of the confidence interval, it would require 1,000 patients per group not to overlook such a 25% reduction in mortality. It should be noted, however, that such a large effect on mortality is highly unlikely, given the data we have presented in this review. It is therefore difficult to justify further placebo-controlled trials.

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Contact Editor: Christian Gluud, Denmark.



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\* Indicates the major publication for the study

## CHARACTERISTICS OF STUDIES

### Characteristics of included studies [ordered by study ID]

#### Avgerinos 1997

Methods	<p>Generation of allocation sequence: computer, blocks of four; concealment of allocation sequence: sealed, opaque envelopes.</p> <p>Blinding: double-blind, analysis also blinded.</p> <p>Intention-to-treat: yes.</p> <p>Interim analysis: five.</p> <p>Follow-up period: 6 weeks.</p>
Participants	<p>Greece, Belgium, The Netherlands. N = 205 (no exclusions from analyses).</p> <p>Clinical suspicion of upper-gastrointestinal bleeding (endoscopy after randomisation, performed in 201/205 patients, varices found in 152).</p>

#### Somatostatin analogues for acute bleeding oesophageal varices (Review)

**Avgerinos 1997** (Continued)

Cirrhosis (mostly alcoholic) or history and examination compatible with portal hypertension.

Interventions

Experimental: somatostatin infusion 250 µg/h for 5 days plus up to eight bolus injections of 250 µg.  
Control: placebo.  
All patients with varices underwent sclerotherapy (77 versus 75).

Outcomes

Mortality after 6 weeks.  
Number of blood products.  
Failure of therapy.  
Ease of sclerotherapy.

Notes

49/205 had other source of bleeding than varices. SDs in the paper are not SDs but SEs.  
Funding: industry (UCB).

**Risk of bias**

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Low risk	A - Adequate

**Besson 1995**

Methods

Generation of allocation sequence: NS, blocks of four; concealment of allocation sequence: prepackaged and numbered by company, code kept by statistician.  
Blinding: double-blind.  
Intention-to-treat: yes.  
Interim analysis: no information.  
Follow-up period: 15 days.

Participants

France. N = 199 (no exclusions from analysis, no patients lost to follow-up).  
Endoscopically confirmed acute or recently (< 24 h) bleeding varices.  
Liver cirrhosis (mostly alcoholic).

Interventions

Experimental: octreotide infusion 25 µg/hour for 5 days.  
Control: placebo.  
All patients underwent sclerotherapy.

Outcomes

Mortality after 15 days.  
Survival without rebleeding.  
Number of blood transfusions.  
Number with initial haemostasis (24 h).  
Number with rebleeding (1 to 5 days).

Notes

Placebo patients had a worse prognosis than octreotide treated patients, eg, 47 per cent versus 26 per cent were in Child-Pugh class C.  
Funding: industry (Sandoz provided the drugs).

**Risk of bias**

**Somatostatin analogues for acute bleeding oesophageal varices (Review)**

**Besson 1995** (Continued)

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Low risk	A - Adequate

**Burroughs 1990**

Methods	<p>Generation of allocation sequence: table of random numbers; concealment of allocation sequence: sealed opaque envelopes.</p> <p>Blinding: double-blind, analysis also blinded.</p> <p>Intention-to-treat: yes.</p> <p>Interim analysis: none.</p> <p>Follow-up period: 30 days.</p>
Participants	<p>UK. N = 133 bleeding episodes (13 excluded after randomisation as endoscopy showed non-variceal bleeding).</p> <p>Clinical suspicion of bleeding varices (endoscopy before randomisation in 62/120 of the bleeding episodes).</p> <p>Half of the patients had alcoholic cirrhosis.</p>
Interventions	<p>Experimental: somatostatin infusion 250 µg bolus and 250 µg/h for 5 days.</p> <p>Control: placebo.</p> <p>Trial failures (22 versus 35) underwent sclerotherapy or staple transection.</p>
Outcomes	<p>Mortality after 30 days.</p> <p>Number of blood and plasma transfusions.</p> <p>Number with initial haemostasis (5 days).</p> <p>Number with balloon tamponade.</p> <p>Number with rebleeding (following start of infusion).</p>
Notes	<p>Only 92 patients participated in the trial but 28 were admitted twice. Transfusions given as medians.</p> <p>Funding: industry (Serono, provided drugs and contributed to the running of the trial).</p>

**Risk of bias**

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Low risk	A - Adequate

**Burroughs 1996**

Methods	<p>Generation of allocation sequence: NS; concealment of allocation sequence: NS.</p> <p>Blinding: double-blind. Intention-to-treat: NS.</p> <p>Interim analysis: NS.</p> <p>Follow-up period: 42 and 90 days.</p>
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**Somatostatin analogues for acute bleeding oesophageal varices (Review)**

### Burroughs 1996 (Continued)

Participants	Europe and USA. N=383 (260 evaluable portal hypertensive sources, 193 variceal bleeds; exclusions from analyses not clear). Clinical suspicion of bleeding varices (endoscopy after start of drug treatment).
Interventions	Experimental: octreotide infusion 50 µg/h for 5 days.  Control: placebo.  Trial failures underwent sclerotherapy.
Outcomes	Mortality after 42 and 90 days. Number with initial haemostasis (5 days).
Notes	Abstract, paper re-submitted. Funding: industry (Sandoz).

#### Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	B - Unclear

### Calès 2001

Methods	Generation of allocation sequence: NS, blocks of four; concealment of allocation sequence: prepackaged, sealed and numbered boxes by company.  Blinding: double-blind, analysis also blinded.  Intention-to-treat: yes.  Interim analysis: NS.  Follow-up period: 6 weeks.
Participants	France and Switzerland. N = 227 (31 excluded from analysis as they did not bleed from portal hypertension; 7 versus 4 were lost to follow-up). Clinical suspicion of active or recent variceal bleeding (endoscopy after randomisation). Liver cirrhosis (mostly alcoholic).
Interventions	Experimental: vapreotide infusion 50 µg bolus and 50 µg/h for 5 days.  Control: placebo.  All patients but 12 underwent sclerotherapy or band ligation.
Outcomes	Mortality after 6 weeks. Number of blood and plasma transfusions. Number with initial haemostasis (at endoscopy and after six and 48 hours). Number with rebleeding (two to five days and six to 42 days).
Notes	No data on early (two to five days) or late (six to 42 days) recurrence of bleeding (rates were low, not significantly different). Funding: industry (Debiopharm).

#### Risk of bias

### Somatostatin analogues for acute bleeding oesophageal varices (Review)

**Calès 2001** (Continued)

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Low risk	A - Adequate

**Farooqi 2000**

Methods	Generation of allocation sequence: NS; concealment of allocation sequence: NS.  Blinding: none.  Intention-to-treat: NS.  Interim analysis: NS.  Follow-up period: NS.	
Participants	Pakistan. N = 141 (in analyses, number of randomised patients and exclusions not stated). Endoscopically confirmed acute variceal bleeding. Liver cirrhosis, mainly hepatitis B and C.	
Interventions	Experimental: octreotide infusion 50 µg/hour for 48 hours.  Control: no drug.  All patients underwent sclerotherapy.	
Outcomes	Mortality. Number with initial haemostasis. Prevention of rebleeding.	
Notes	Substantial risk of bias: criteria for bleeding control not defined, open study, and length of follow-up not defined. Funding: NS.	

**Risk of bias**

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	B - Unclear

**Freitas 2000**

Methods	Generation of allocation sequence: NS; concealment of allocation sequence: NS.  Blinding: none.  Intention-to-treat: yes.  Interim analysis: NS. Follow-up period: 48 hours.	
Participants	Portugal. N = 86 (no exclusions described, but some patients seem to be lost to follow-up, see Note field). Active bleeding at endoscopy from varices.	

**Somatostatin analogues for acute bleeding oesophageal varices (Review)**



### Freitas 2000 (Continued)

	Liver cirrhosis (mostly alcoholic).
Interventions	Experimental: octreotide infusion 25 µg/h for 48 hours.  Control: no drug.  All patients underwent sclerotherapy or band ligation after 48 hours.
Outcomes	Mortality (time period not clear, but given after 30 days in results). Number of blood transfusions. Number with initial haemostasis (immediately, 48 h and seven days after bleeding arrest). Number with rebleeding.
Notes	Mortality given as percentages of patients which do not concord with the number randomised. The mortality data (27% vs 31%) are therefore unreliable and have not been used in our meta-analyses. No reply to our letter. Funding: NS.

#### Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	B - Unclear

### Gøtzsche 1995

Methods	Generation of allocation sequence: table of random numbers; concealment of allocation sequence: consecutively numbered sealed medicine packages.  Blinding: double-blind with blinding also during data analysis and writing of manuscript.  Intention-to-treat: yes.  Interim analysis: none.  Follow-up period: 6 weeks.
Participants	Denmark. N = 86 (86 in analyses). Clinical suspicion of bleeding varices (endoscopy ultimately performed in 81/86 of the patients). Verified or suspected cirrhosis (mostly alcoholic).
Interventions	Experimental: somatostatin infusion 250 µg/h for 24 hours for each bleeding episode.  Control: placebo.  Most patients (33 versus 35) underwent sclerotherapy.
Outcomes	Mortality after six weeks. Number of blood transfusions. Number with balloon tamponade. Number with initial haemostasis (24 h). Number of bleeding episodes. Number of days with bleeding.
Notes	Transfusions given as medians. Funding: none (DuraScan delivered coded drugs, somatostatin was purchased at market price).

**Gøtzsche 1995** (Continued)

**Risk of bias**

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Low risk	A - Adequate

**Isaac 1994**

Methods	Generation of allocation sequence: NS; concealment of allocation sequence: NS. Blinding: none. Intention-to-treat: NS. Interim analysis: NS. Follow-up period: NS.
Participants	Singapore. N not stated (exclusions not stated). Variceal haemorrhage.
Interventions	Experimental: somatostatin bolus infusion 250 µg and 250 µg/h for 15 h. Control: none. Drug given before sclerotherapy.
Outcomes	Number of blood transfusions. Number with initial haemostasis (15 h).
Notes	Abstract, no reply from author to our letter. Funding: NS.

**Risk of bias**

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	B - Unclear

**Morales 2007**

Methods	Generation of allocation sequence: computer, 4 to3 ratio; concealment of allocation sequence: "randomly assigned", "sealed opaque envelopes". Blinding: placebo infusion (hospital pharmacy made the placebo infusion and covered both drugs with black protections). Intention-to-treat: yes, but two patients randomised to placebo with liver carcinoma secondarily excluded. Interim analysis: NS. Follow-up period: 7 days.
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**Somatostatin analogues for acute bleeding oesophageal varices (Review)**

**Morales 2007** (Continued)

Participants	Brazil. N = 70 (68 in analyses). Variceal bleeding, acute or recent, at endoscopy. Cirrhosis diagnosed by liver biopsy or by clinical, biochemical and echocardiographic findings. Mostly caused by hepatitis.
Interventions	Experimental: octreotide bolus infusion 50 µg, 50 µg/h for 24h, and 25 µg/h for another 24h.  Control: placebo.  Drug given after sclerotherapy.
Outcomes	Mortality after one week. Number of blood transfusions. Number with initial haemostasis (2 days). Number with rebleeding.
Notes	Funding: Ministry of Education.

**Risk of bias**

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Low risk	A - Adequate

**Moret6 1994**

Methods	Generation of allocation sequence: NS; concealment of allocation sequence: opaque envelopes.  Blinding: double-blind.  Intention-to-treat: yes.  Interim analysis: trial stopped after pilot phase.  Follow-up period: till discharge from hospital.
Participants	Spain. N = 63 (63 in analyses). Bleeding varices confirmed at endoscopy. All but one had cirrhosis (mostly alcoholic).
Interventions	Experimental: somatostatin bolus infusion 250 µg.  Control: placebo.  All patients underwent sclerotherapy.
Outcomes	Mortality in hospital. Number of blood transfusions. Number with initial haemostasis (24 h). Number with rebleeding (24 h).
Notes	Abstract; unpublished manuscript provided by author. Trial addressed ease of sclerotherapy, somatostatin had an effect on this. Funding: NS.

**Risk of bias**

**Somatostatin analogues for acute bleeding oesophageal varices (Review)**

**Moretó 1994** (Continued)

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Low risk	A - Adequate

**Pauwels 1994**

Methods	Generation of allocation sequence: NS; concealment of allocation sequence: NS.  Blinding: none.  Intention-to-treat: no.  Interim analysis: no information.  Follow-up period: one month.	
Participants	France. N = 60 bleeding episodes (11 excluded as varices was not the source of bleeding, no information on losses to follow-up), 3 groups. Acutely bleeding varices (diagnosis by endoscopy or lavage). Probably cirrhosis, no details.	
Interventions	Experimental 1: somatostatin infusion 250 µg bolus and 250 µg/h till two hours after bleeding arrest.  Experimental 2: terlipressin.  Control: no treatment.	
Outcomes	Mortality after one month. Number of blood transfusions. Number with initial haemostasis (48 h). Number with balloon tamponade. Number with rebleeding (2 days).	
Notes	No information is given on the number of patients who underwent endoscopy. Funding: NS.	

**Risk of bias**

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	B - Unclear

**Shah 1996**

Methods	Generation of allocation sequence: NS; concealment of allocation sequence: "sealed envelopes".  Blinding: unclear, see Interventions.  Intention-to-treat: yes.  Interim analysis: NS. Follow-up period: NS.	
Participants	Pakistan. N = 105 (87 in some analyses in conference abstract, not stated whether there were exclusions or losses to follow-up).	

**Somatostatin analogues for acute bleeding oesophageal varices (Review)**

**Shah 1996** (Continued)

Active variceal bleeding or recent bleed.  
Type of cirrhosis mostly viral, diagnosed by biopsy or otherwise.

**Interventions**

Experimental: octreotide infusion 50 µg/h for 36 h (conference abstract) or 48 h (article).  
Control: no treatment according to conference abstract but placebo saline according to article.  
All patients underwent sclerotherapy.

**Outcomes**

Mortality.  
Number with initial haemostasis (24 h).  
Number with rebleeding (after 24 h).

**Notes**

Unreliable study; contrasting information in conference abstract and full article. For example, claimed difference in mortality in abstract is not mortality, but survival without rebleeding; denominators and treatment in control group are also inconsistent. No reply to our emails.  
Funding: NS.

**Risk of bias**

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	B - Unclear

**Shiha 1996**

**Methods**

Generation of allocation sequence: random tables; concealment of allocation sequence: sealed opaque envelopes.  
Blinding: none.  
Intention-to-treat: yes.  
Interim analysis: no information.  
Follow-up period: 7 days.

**Participants**

Egypt. N = 189 (not stated whether there were exclusions or losses to follow-up).  
Active variceal bleeding (diagnosis by endoscopy).  
Probably cirrhosis, no information; half of the patients were positive for hepatitis markers.

**Interventions**

Experimental: octreotide infusion 25 µg/hour for 5 days.  
Control: no treatment.  
All patients underwent sclerotherapy.

**Outcomes**

Mortality after 7 days.  
Number of blood transfusions.  
Number with rebleeding (after 7 days).

**Notes**

Funding: University research project, not supported by manufacturer.

**Risk of bias**

Bias	Authors' judgement	Support for judgement
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**Shiha 1996** (Continued)

Allocation concealment (selection bias)	Low risk	A - Adequate
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**Signorelli 1996**

Methods	Generation of allocation sequence: NS; concealment of allocation sequence: NS. Blinding: NS, probably open. Intention-to-treat: NS. Interim analysis: NS. Follow-up period: 5 days.
Participants	Italy. N = 94 (number in analyses not stated, not stated whether there were exclusions or losses to follow-up). Acute variceal bleeding. Type of cirrhosis not stated.
Interventions	Experimental 1: somatostatin infusion 3.5 µg/kg/h for 5 days. Experimental 2: octreotide 0.1 mg s.c. every 8 h for 5 days. Control: placebo, no details whether similar to one of the drugs. All patients underwent sclerotherapy.
Outcomes	Mortality after 5 days. Number of blood transfusions. Number with initial haemostasis (5 days).
Notes	Abstract. Results given as percentages of patients which do not concord with the number randomised, no matter how many patients might be missing in the analyses. The data are therefore unreliable and have not been used in our meta-analyses. No reply to our letters. Funding: NS.

**Risk of bias**

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	B - Unclear

**Signorelli 1997**

Methods	Generation of allocation sequence: NS; concealment of allocation sequence: NS. Blinding: none. Intention-to-treat: NS. Interim analysis: NS. Follow-up period: 5 days.
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**Somatostatin analogues for acute bleeding oesophageal varices (Review)**

**Signorelli 1997** (Continued)

Participants	Italy. N = 86 (86 in analyses, not stated whether there were exclusions or losses to follow-up). Acute variceal bleeding. Type of cirrhosis not stated.
Interventions	Experimental: octreotide bolus 50 µg and infusion 25 µg/h for 5 days.  Control: no treatment.  All patients underwent sclerotherapy.
Outcomes	Mortality after 5 days. Number of blood transfusions. Number with initial haemostasis (5 days).
Notes	Abstract. No reply to our letters. Funding: NS.

**Risk of bias**

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	B - Unclear

**Souza 2003**

Methods	Generation of allocation sequence: NS; concealment of allocation sequence: NS.  Blinding: NS.  Intention-to-treat: NS.  Interim analysis: NS.  Follow-up period: 3 days for bleeding, not stated for mortality.
Participants	Brazil. N = 143 (112 in analyses). Acute variceal bleeding. Liver cirrhosis and schistosomiasis.
Interventions	Experimental: somatostatin infusion 100 µg bolus and 50 µg/h for 3 days.  Control: placebo.  Drugs started 2 hours before endoscopy, all were to undergo sclerotherapy.
Outcomes	Mortality. Number with rebleeding (3 days).
Notes	Abstract from 2003. Funding: NS.

**Risk of bias**

Bias	Authors' judgement	Support for judgement
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**Souza 2003** (Continued)

Allocation concealment (selection bias)	Unclear risk	B - Unclear
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**Sung 1995**

Methods	Generation of allocation sequence: computer, random numbers; concealment of allocation sequence: opaque envelopes.  Blinding: none.  Intention-to-treat: no.  Interim analysis: NS.  Follow-up period: 30 days.
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Participants	Hong Kong. N = 100 (6 excluded and 4 lost to follow-up). Endoscopically confirmed acute or recently bleeding varices. Most had hepatitis as cause of portal hypertension.
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Interventions	Experimental: octreotide bolus 50 µg and infusion 50 µg/h for 5 days.  Control: no treatment.  All patients underwent endoscopic ligation.
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Outcomes	Mortality after 30 days. Number of blood transfusions. Number with initial haemostasis (24 h). Number with balloon tamponade. Number with rebleeding (within 2 days of variceal ligation).
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Notes	Transfusions given as medians, SD estimated from an exact P value. Funding: industry (Sandoz).
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**Risk of bias**

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Low risk	A - Adequate

**Valenzuela 1989**

Methods	Generation of allocation sequence: computer; concealment of allocation sequence: NS.  Blinding: double-blind.  Intention-to-treat: no.  Interim analysis: NS. Follow-up period: not defined.
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Participants	USA. N=102 (84 in analyses). Endoscopically confirmed acute or recently bleeding varices. Most had alcoholic liver disease.
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**Somatostatin analogues for acute bleeding oesophageal varices (Review)**



**Valenzuela 1989** (Continued)

Interventions Experimental: somatostatin infusion 250 µg bolus and 250 µg/h for up to 30 hours.  
Control: placebo.

Outcomes Mortality (time interval not stated).  
Total volume of blood transfusions.  
Number with initial haemostasis (30 h).  
Time to cessation of bleeding.  
Number with rebleeding (1 to 2 days).

Notes Transfusions given in litres, converted to units of blood (one unit is 300 ml).  
Funding: industry (Serono).

**Risk of bias**

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	B - Unclear

**Villanueva 2001**

Methods Generation of allocation sequence: computer; concealment of allocation sequence: sealed opaque envelopes.  
Blinding: double-blind.  
Intention-to-treat: no.  
Interim analysis: no.  
Follow-up period: 6 weeks.

Participants Spain. N = 46 (40 in analyses, 3 very likely excluded before randomisation, not clear whether the other 3 were excluded after randomisation).  
Endoscopically confirmed acute or recently bleeding varices.  
Type of cirrhosis not stated.

Interventions Experimental: somatostatin infusion 250 µg bolus every 12 h and 250 µg/h, both for 5 days.  
Control: placebo (saline).  
All patients underwent sclerotherapy.

Outcomes Mortality (4 died, not divided on treatment groups).  
Total volume of blood transfusions (units of packed red cells).  
Number with initial haemostasis (control of bleeding for first 24 h, and no rebleeding within next 4 days).

Notes Experimental study, main outcome was hepatic venous pressure gradient.  
Funding: public (hospital foundation).

**Risk of bias**

Bias	Authors' judgement	Support for judgement
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**Villanueva 2001** *(Continued)*

Allocation concealment (selection bias)	Low risk	A - Adequate
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**Zuberi 2000**

Methods	Generation of allocation sequence: table of random numbers; concealment of allocation sequence: prepackaged, sealed and numbered cartons.  Blinding: double-blind.  Intention-to-treat: yes.  Interim analysis: NS.  Follow-up period: 5 days.
Participants	Pakistan. N = 70 (not stated whether there were exclusions or losses to follow-up). First episode of active or recent variceal bleeding, endoscopically confirmed.
Interventions	Experimental: octreotide infusion 50 µg/h for five days.  Control: placebo.  All patients underwent sclerotherapy.
Outcomes	Mortality after 5 days. Number of blood and plasma transfusions during hospitalisation. Number with initial haemostasis (24 h). Number with rebleeding (5 days).
Notes	Twenty-two patients died before endoscopy and were therefore not randomised. Funding: NS.

**Risk of bias**

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Low risk	A - Adequate

NS: not stated; SD: standard deviation; SE: standard error; h: hours.

**Characteristics of excluded studies** *[ordered by study ID]*

Study	Reason for exclusion
<a href="#">Brunati 1996</a>	Abstract, N = 55, not stated it was a randomised trial. Author did not reply to our letter.
<a href="#">D'Amico 1998</a>	Prophylactic study (prevention of rebleeding after control of acute bleeding).
<a href="#">Jenkins 1997</a>	Concerns long-term prevention of rebleeding in fully stable patients; does not address the control of acute bleeding.
<a href="#">Primignani 1995</a>	No data on acute bleeding, concerns rebleeding in stable patients.

**Somatostatin analogues for acute bleeding oesophageal varices (Review)**

Study	Reason for exclusion
Ruiz del Arbol 1994	Small trial (N = 15 to 20 per group), no clinical outcomes but haemodynamic variables up to 15 minutes after drug administration.
Shields 1993	Concerns long-term prevention of rebleeding in fully stable patients; does not address the control of acute bleeding.
Silva 2004	Not fully randomised. Because of a high rate of rebleeding in the octreotide arm, only 13 patients received this drug, whereas randomisation continued in the two other arms.
UCB trial 1996	Concerns early rebleeding. Unpublished trial, about 150 patients. The sponsoring company, UCB Pharma, Belgium, has refused to give access to data, and the investigators are unable to publish as they signed a contract stating that the results belong to the company.

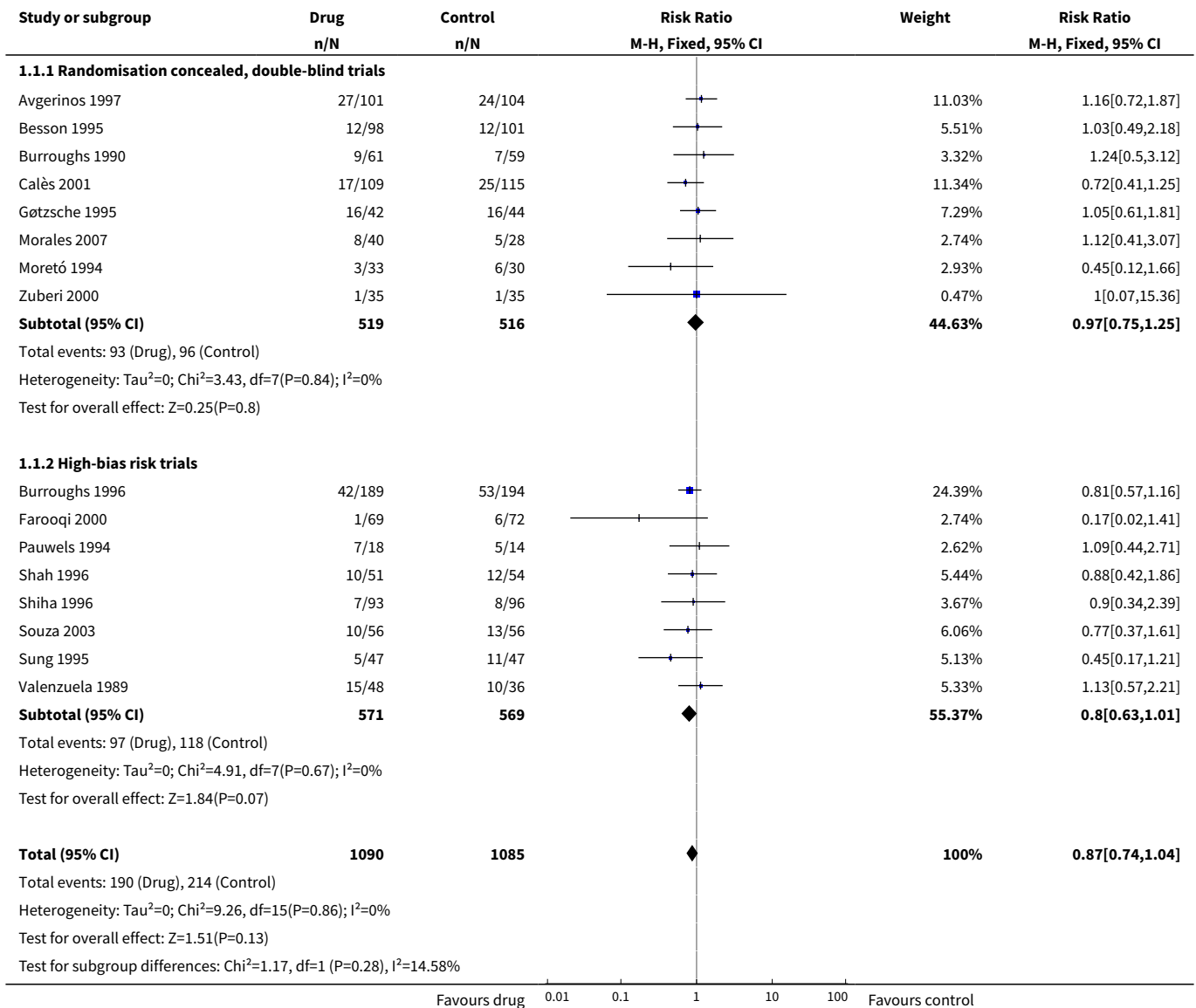
## DATA AND ANALYSES

### Comparison 1. Somatostatin analogues versus placebo or no treatment

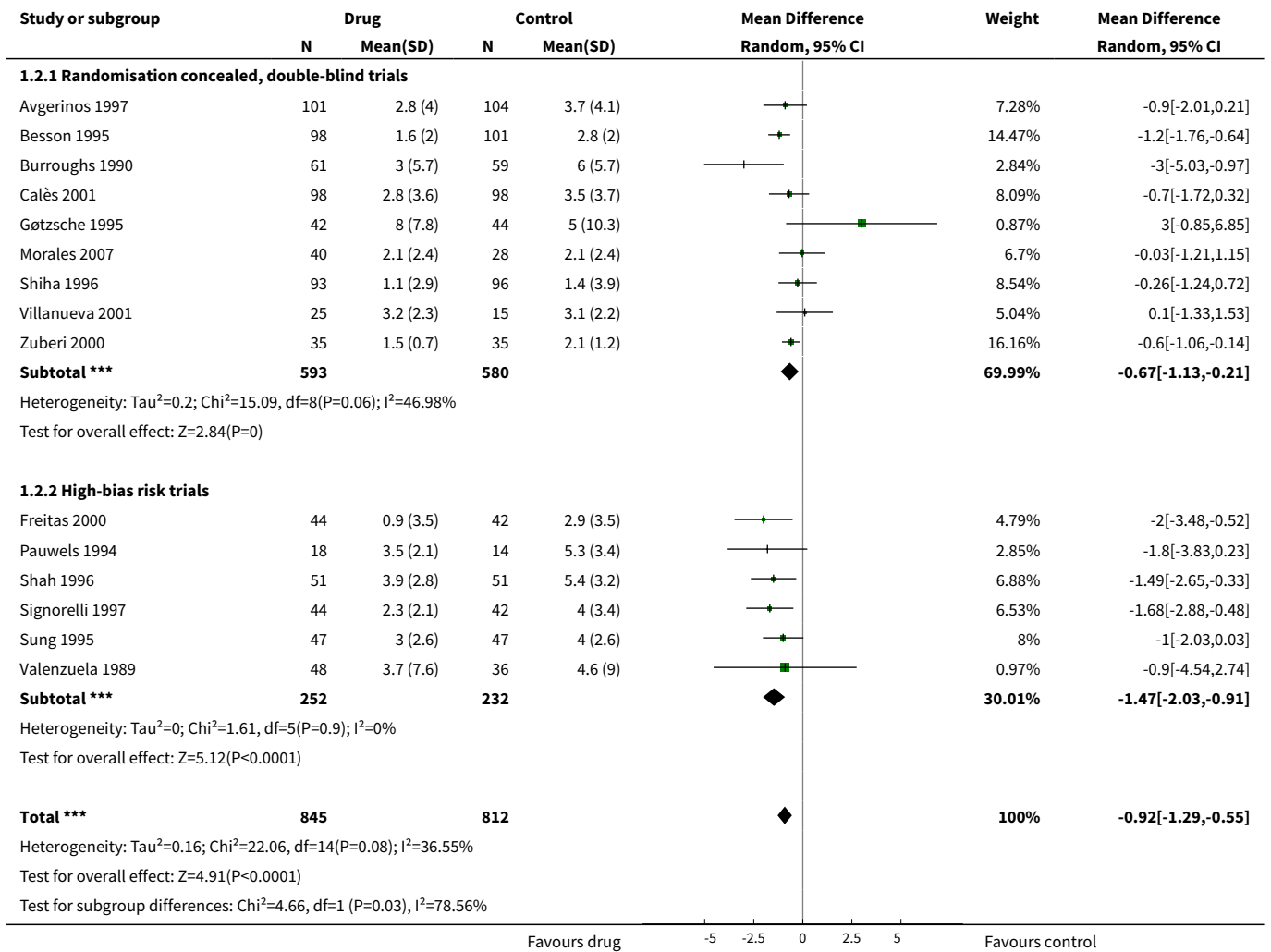
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
<b>1 Mortality</b>	16	2175	Risk Ratio (M-H, Fixed, 95% CI)	0.87 [0.74, 1.04]
1.1 Randomisation concealed, double-blind trials	8	1035	Risk Ratio (M-H, Fixed, 95% CI)	0.97 [0.75, 1.25]
1.2 High-bias risk trials	8	1140	Risk Ratio (M-H, Fixed, 95% CI)	0.80 [0.63, 1.01]
<b>2 Number of transfusions</b>	15	1657	Mean Difference (IV, Random, 95% CI)	-0.92 [-1.29, -0.55]
2.1 Randomisation concealed, double-blind trials	9	1173	Mean Difference (IV, Random, 95% CI)	-0.67 [-1.13, -0.21]
2.2 High-bias risk trials	6	484	Mean Difference (IV, Random, 95% CI)	-1.47 [-2.03, -0.91]
<b>3 Number with balloon tamponade</b>	7	804	Risk Ratio (M-H, Random, 95% CI)	0.72 [0.41, 1.29]
3.1 Randomisation concealed, double-blind trials	5	678	Risk Ratio (M-H, Random, 95% CI)	0.83 [0.49, 1.40]
3.2 High-bias risk trials	2	126	Risk Ratio (M-H, Random, 95% CI)	0.36 [0.03, 4.17]
<b>4 Number failing initial haemostasis</b>	17	1932	Risk Ratio (M-H, Random, 95% CI)	0.68 [0.54, 0.87]
4.1 Randomisation concealed, double-blind trials	9	1047	Risk Ratio (M-H, Random, 95% CI)	0.67 [0.49, 0.90]
4.2 High-bias risk trials	8	885	Risk Ratio (M-H, Random, 95% CI)	0.70 [0.46, 1.06]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
5 Number with rebleeding	13		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
5.1 Randomisation concealed, double-blind trials	6	606	Risk Ratio (M-H, Random, 95% CI)	0.84 [0.52, 1.37]
5.2 High-bias risk trials	7	757	Risk Ratio (M-H, Random, 95% CI)	0.36 [0.19, 0.68]

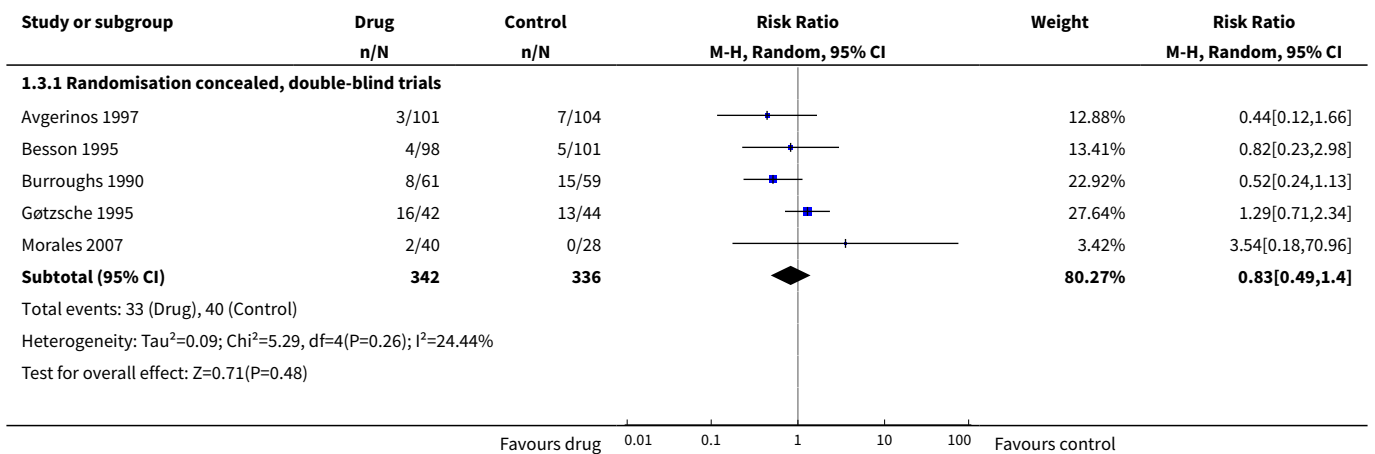
**Analysis 1.1. Comparison 1 Somatostatin analogues versus placebo or no treatment, Outcome 1 Mortality.**

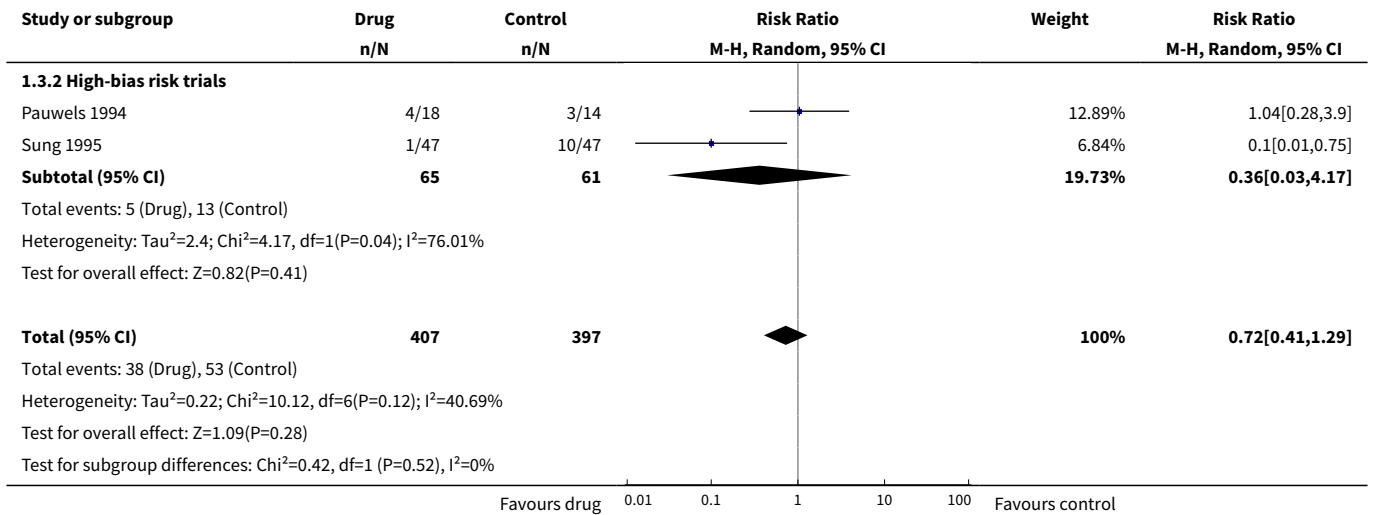


**Analysis 1.2. Comparison 1 Somatostatin analogues versus placebo or no treatment, Outcome 2 Number of transfusions.**

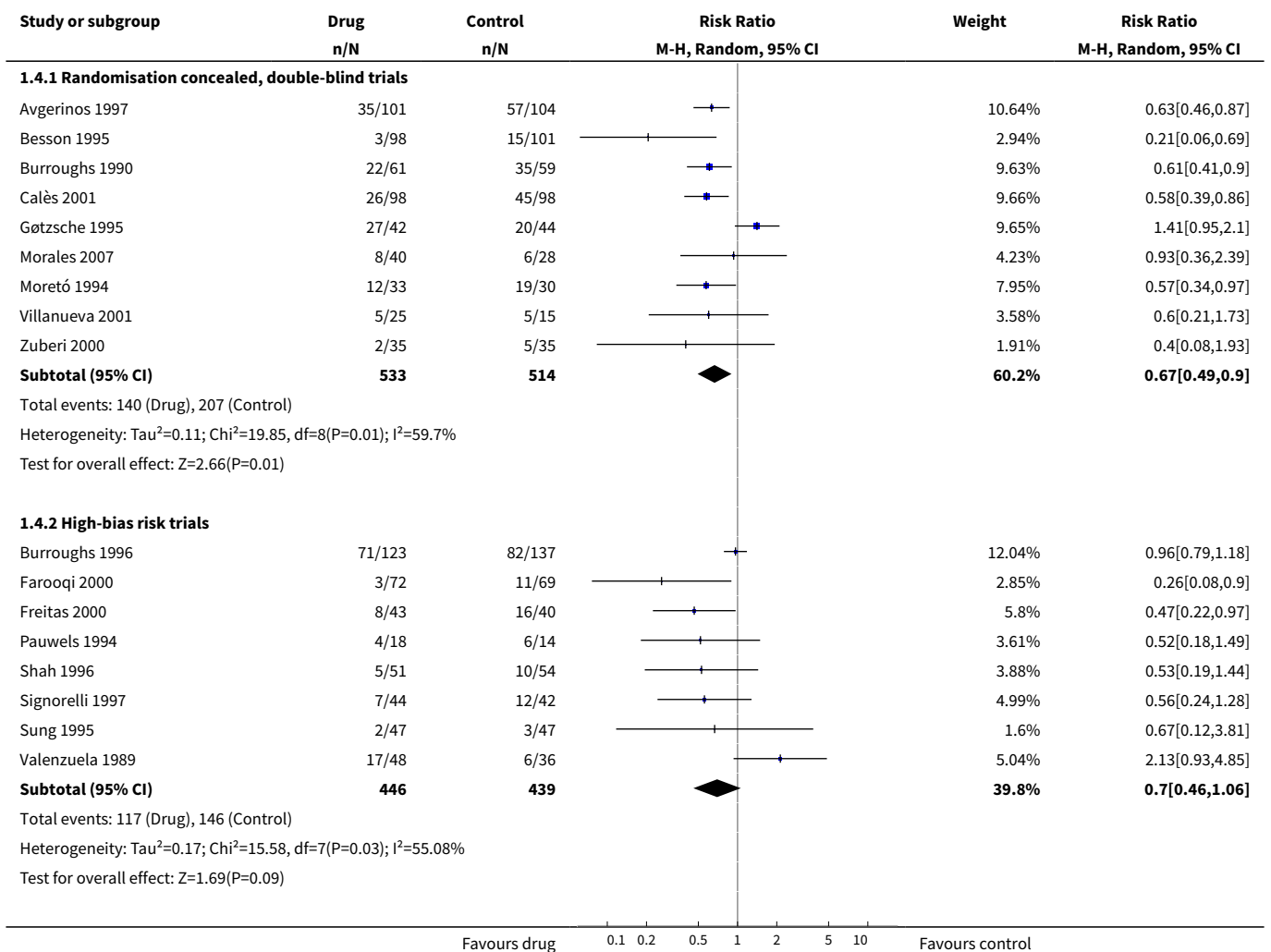


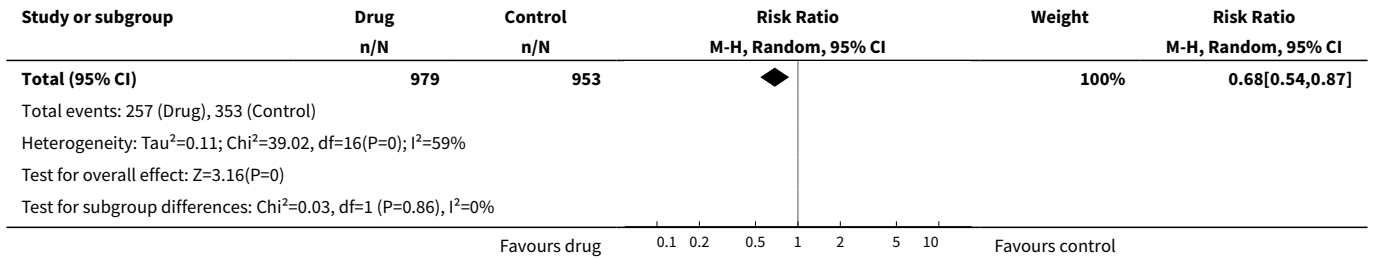
**Analysis 1.3. Comparison 1 Somatostatin analogues versus placebo or no treatment, Outcome 3 Number with balloon tamponade.**



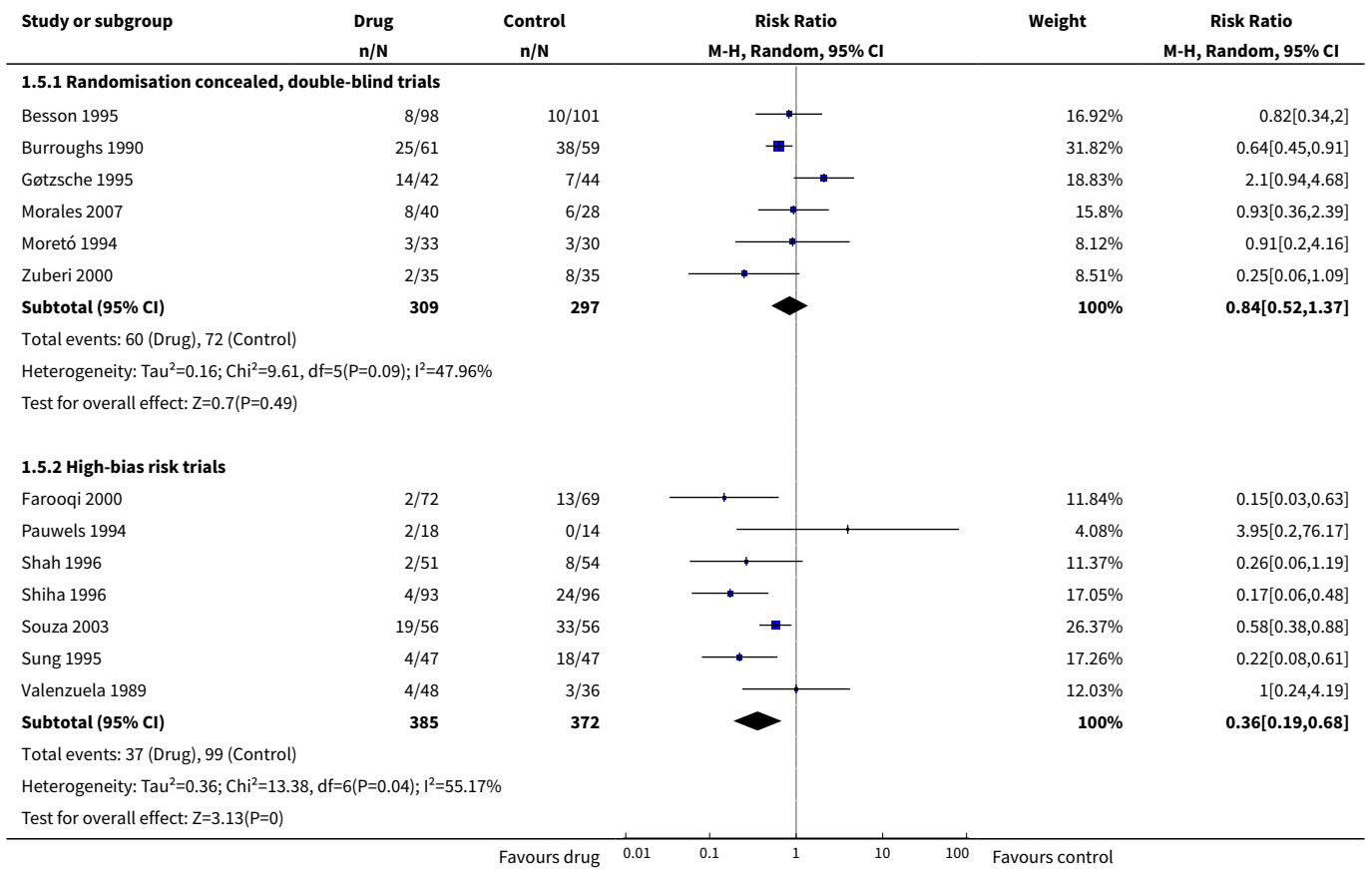


**Analysis 1.4. Comparison 1 Somatostatin analogues versus placebo or no treatment, Outcome 4 Number failing initial haemostasis.**





**Analysis 1.5. Comparison 1 Somatostatin analogues versus placebo or no treatment, Outcome 5 Number with rebleeding.**



**WHAT'S NEW**

Date	Event	Description
11 January 2012	New search has been performed	Updated, no new trials identified.
25 November 2011	Review declared as stable	No further trials are likely to be performed.

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## CONTRIBUTIONS OF AUTHORS

Peter Gøtzsche was the sole author of this review until the 2005 update for which update Asbjørn Hróbjartsson independently extracted data on the additional in- and excluded trials. Text prepared by Peter Gøtzsche and commented upon by Asbjørn Hróbjartsson. Peter Gøtzsche is guarantor.

## DECLARATIONS OF INTEREST

Peter Gøtzsche was the lead investigator of one of the included trials. Somatostatin was purchased at usual market price and the pharmaceutical company delivering coded drugs did not provide financial support to the trial and was not involved in its planning, execution, analysis, or publication.

## SOURCES OF SUPPORT

### Internal sources

- Rigshospitalet, Denmark.

### External sources

- No sources of support supplied

## INDEX TERMS

### Medical Subject Headings (MeSH)

Acute Disease; Blood Transfusion [statistics & numerical data]; Esophageal and Gastric Varices [\*drug therapy] [mortality]; Gastrointestinal Hemorrhage [\*drug therapy] [mortality]; Hemostatics [\*therapeutic use]; Liver Cirrhosis [complications]; Octreotide [\*therapeutic use]; Randomized Controlled Trials as Topic; Somatostatin [analogs & derivatives] [\*therapeutic use]

### MeSH check words

Humans