APPENDIX

UTEROTONIC AGENTS FOR PREVENTING POSTPARTUM HAEMORRHAGE. A NETWORK META-ANALYSIS.

Supplementary Appendix

Figure 1. Network diagram for prevention of PPH ≥ 500 mL by mode of birth (vaginal birth). The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison.

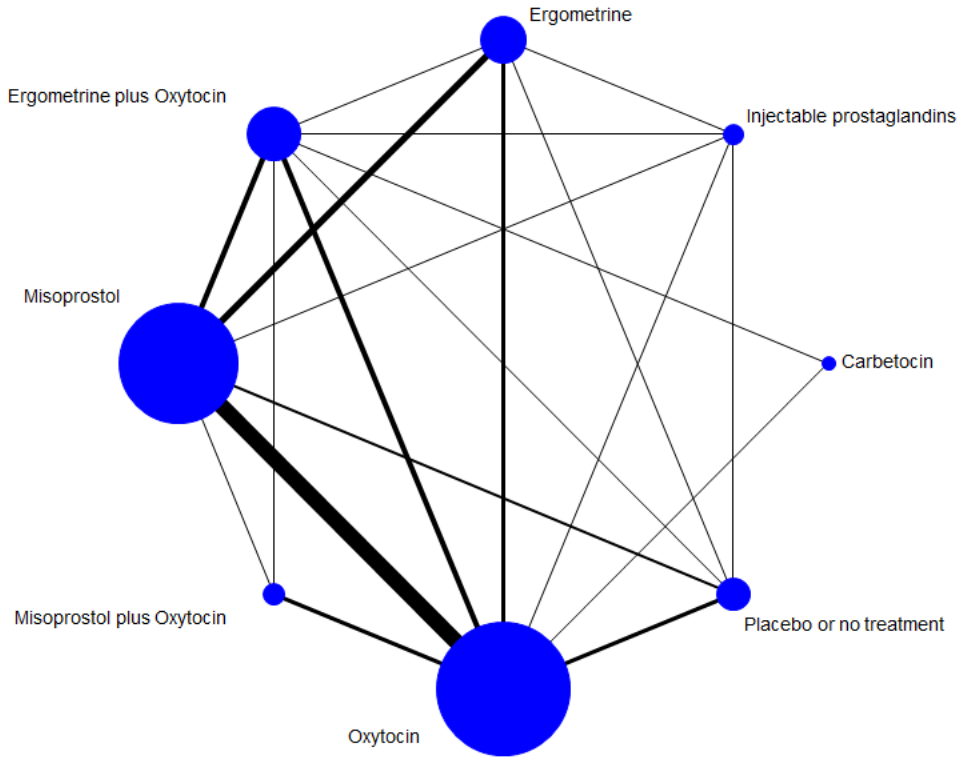


Figure 2. Forest plot with relative risk ratios and 95% CIs from pairwise, indirect and network (combining direct and indirect) analysis for prevention of PPH ≥ 500 mL by mode of birth (vaginal birth).

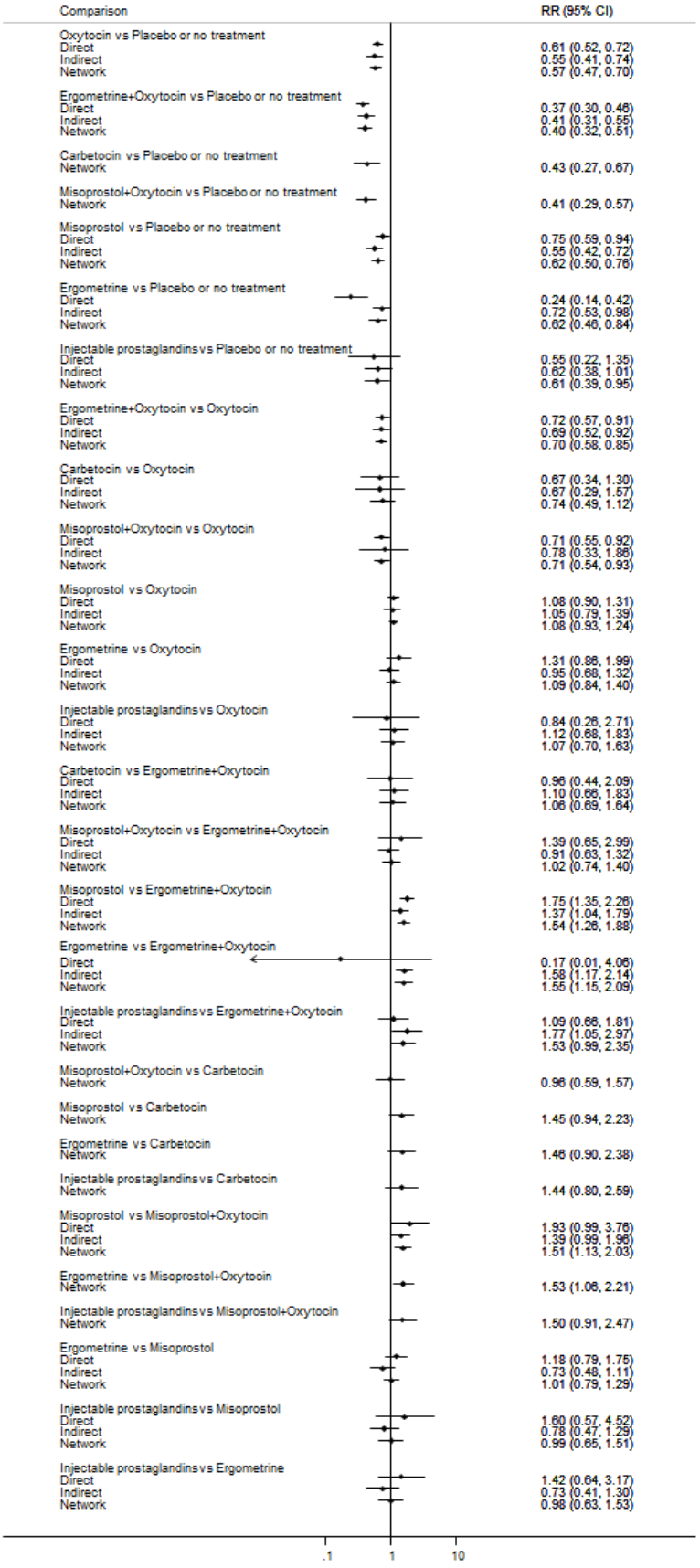


Figure 3. Cumulative rankograms comparing each of the uterotonic drugs for prevention of PPH ≥ 500 mL by mode of birth (vaginal birth). Ranking indicates the cumulative probability of being the best drug, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SUrface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available drug options.

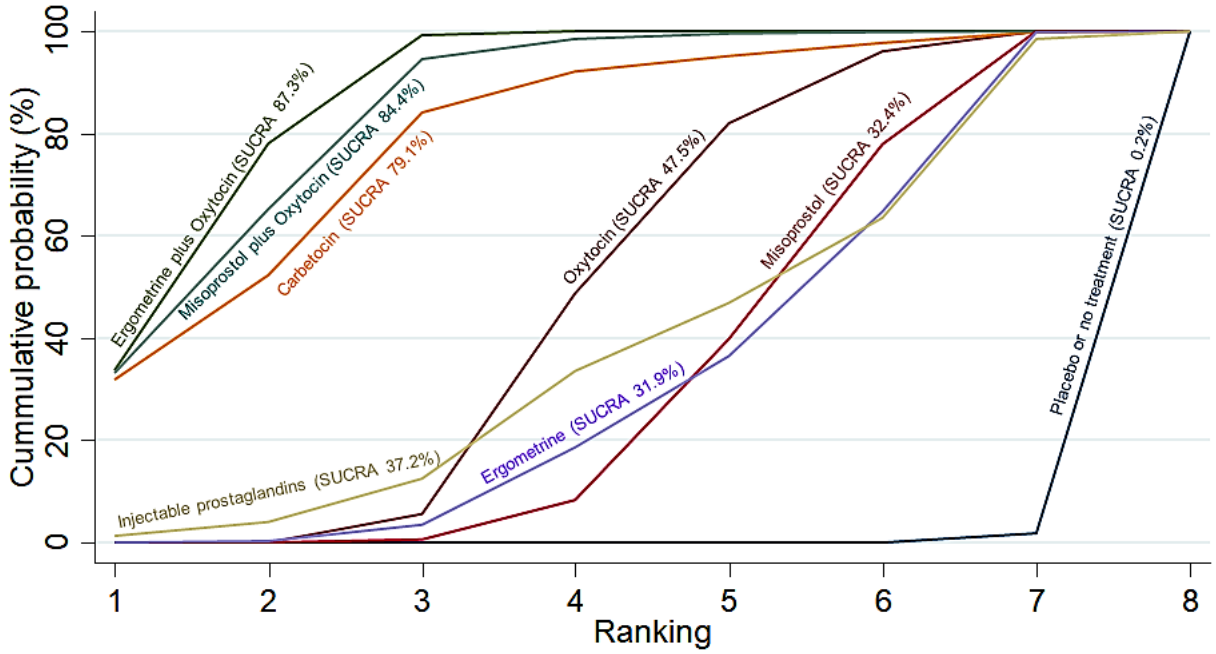


Figure 4. Network diagram for prevention of PPH ≥ 1000 mL by mode of birth (vaginal birth). The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison.

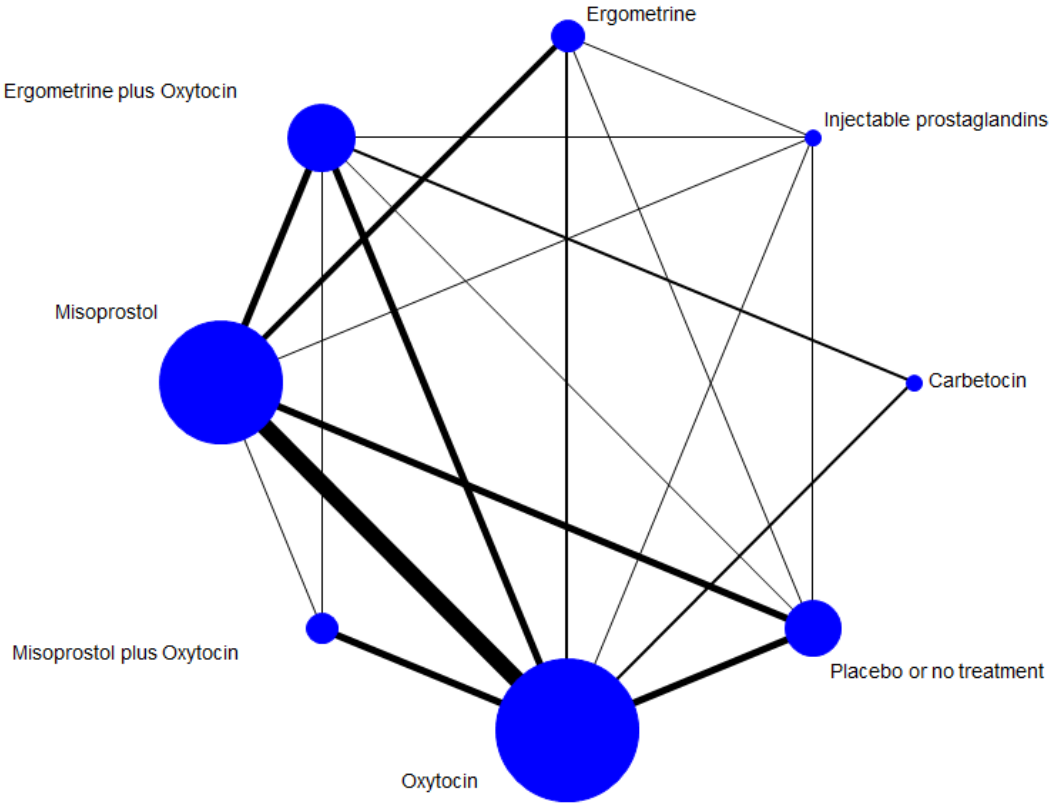


Figure 5. Forest plot with relative risk ratios and 95% CIs from pairwise, indirect and network (combining direct and indirect) analysis for prevention of PPH ≥ 1000 mL by mode of birth (vaginal birth).

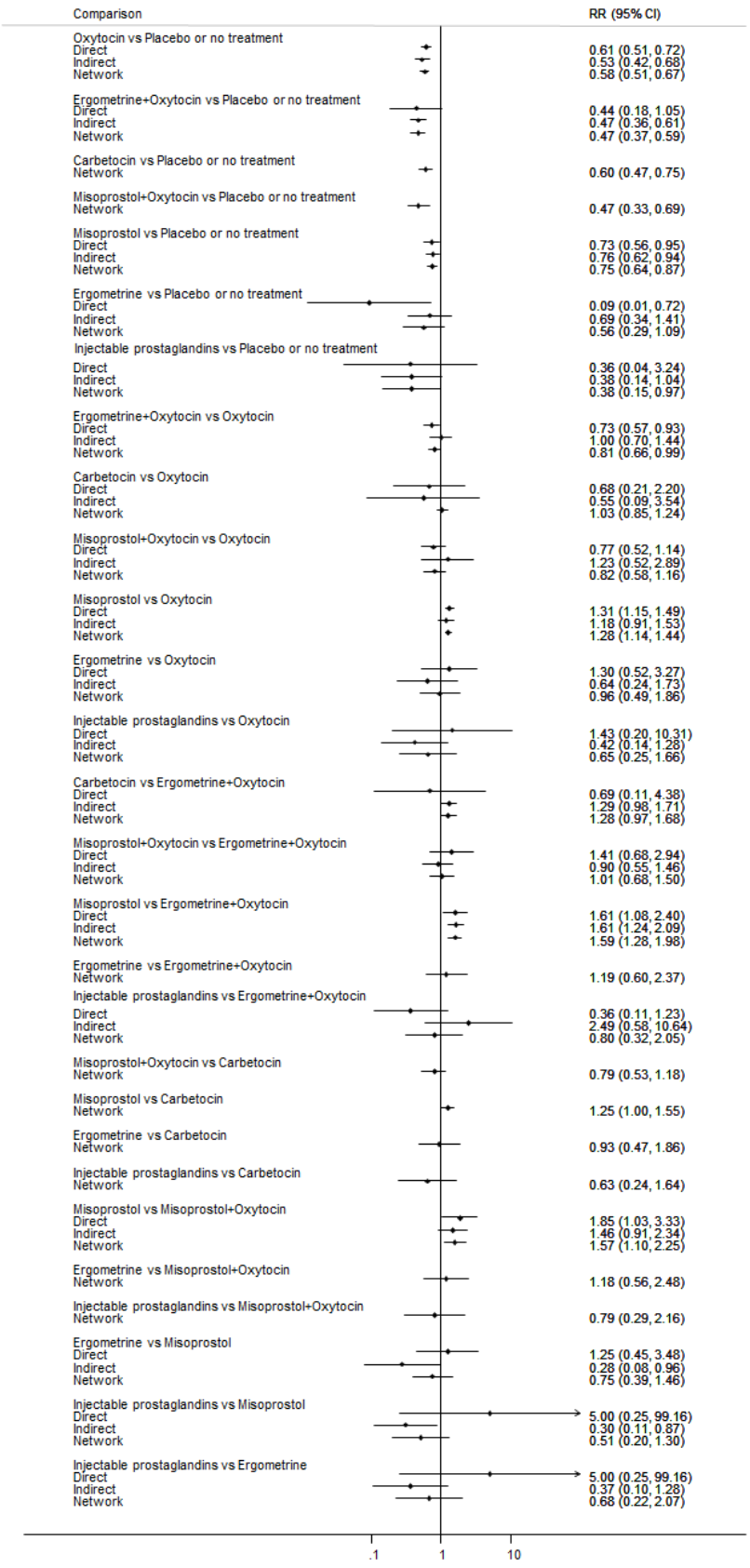


Figure 6. Cumulative rankograms comparing each of the uterotonic drugs for prevention of PPH ≥ 1000 mL by mode of birth (vaginal birth). Ranking indicates the cumulative probability of being the best drug, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SUrface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available drug options.

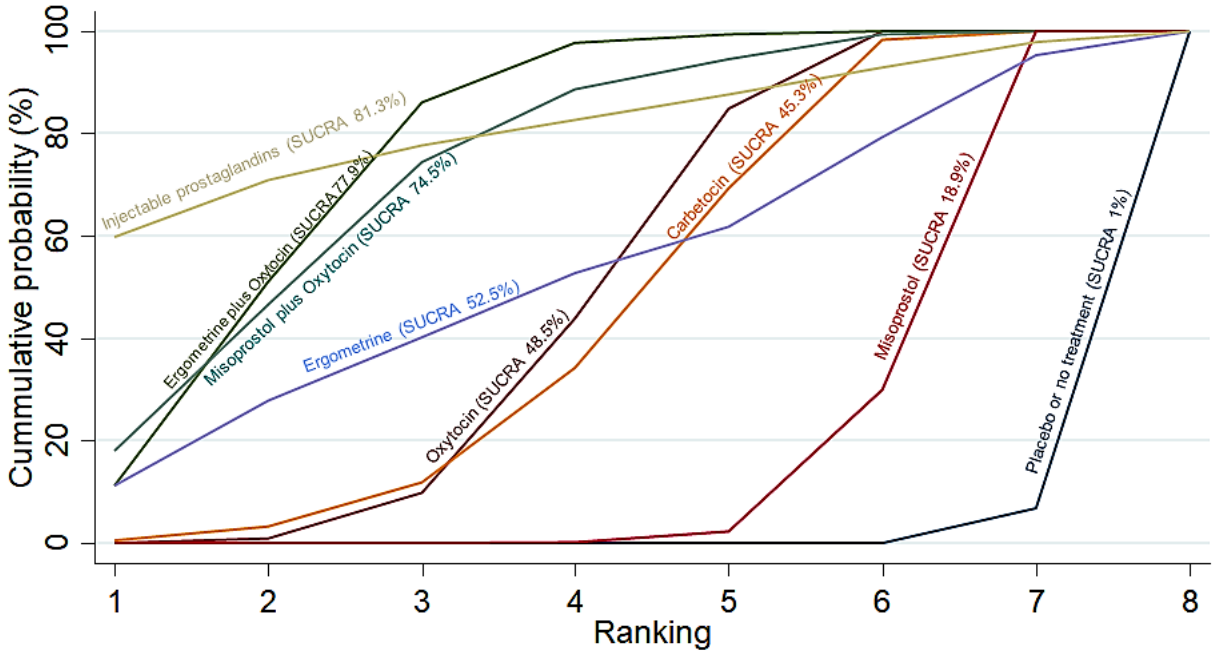


Figure 7. Network diagram for prevention of PPH ≥ 500 mL by mode of birth (caesarean section). The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison.

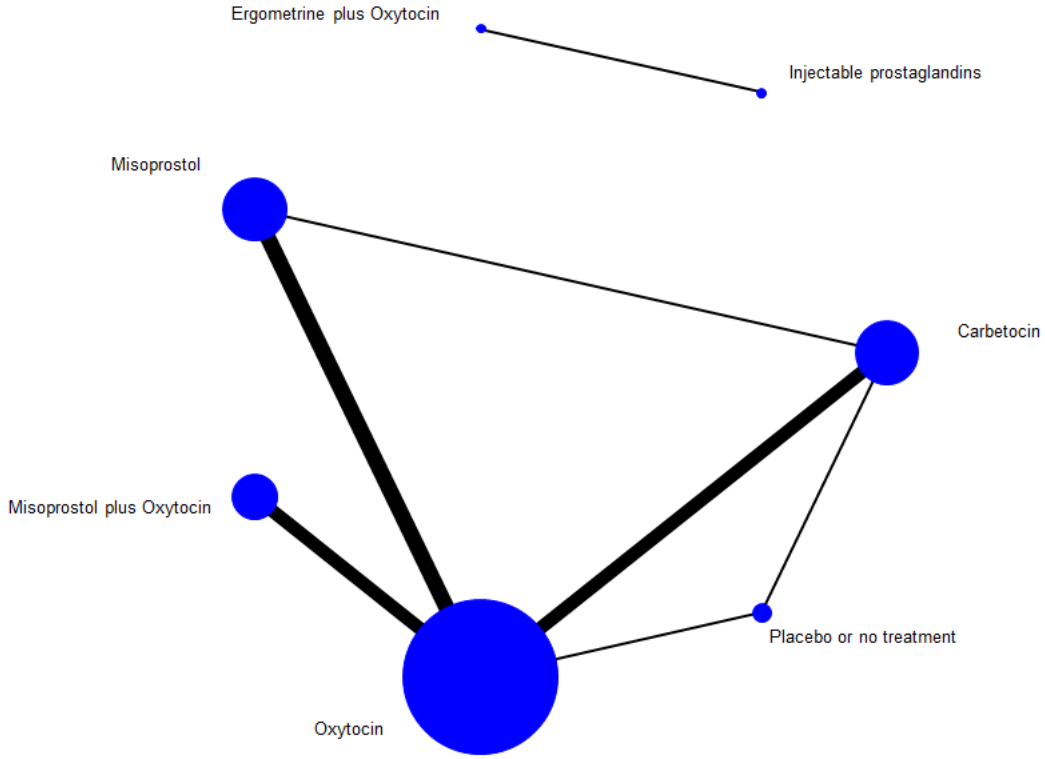


Figure 8. Forest plot with relative risk ratios and 95% CIs from pairwise, indirect and network (combining direct and indirect) analysis for prevention of PPH ≥ 500 mL by mode of birth (caesarean section).

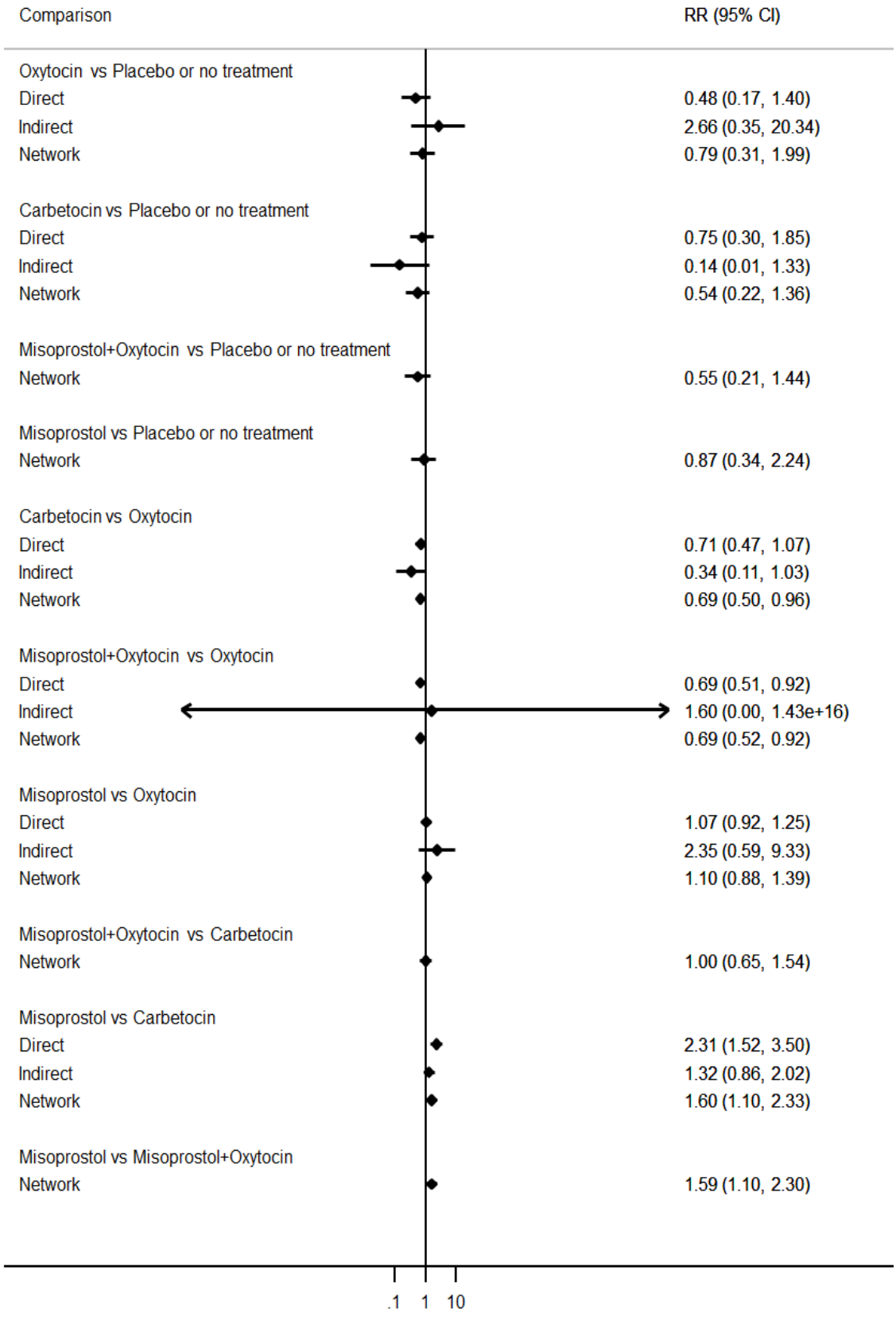


Figure 9. Cumulative rankograms comparing each of the uterotonic drugs for prevention of PPH ≥ 500 mL by mode of birth (caesarean section). Ranking indicates the cumulative probability of being the best drug, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SUrface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available drug options.

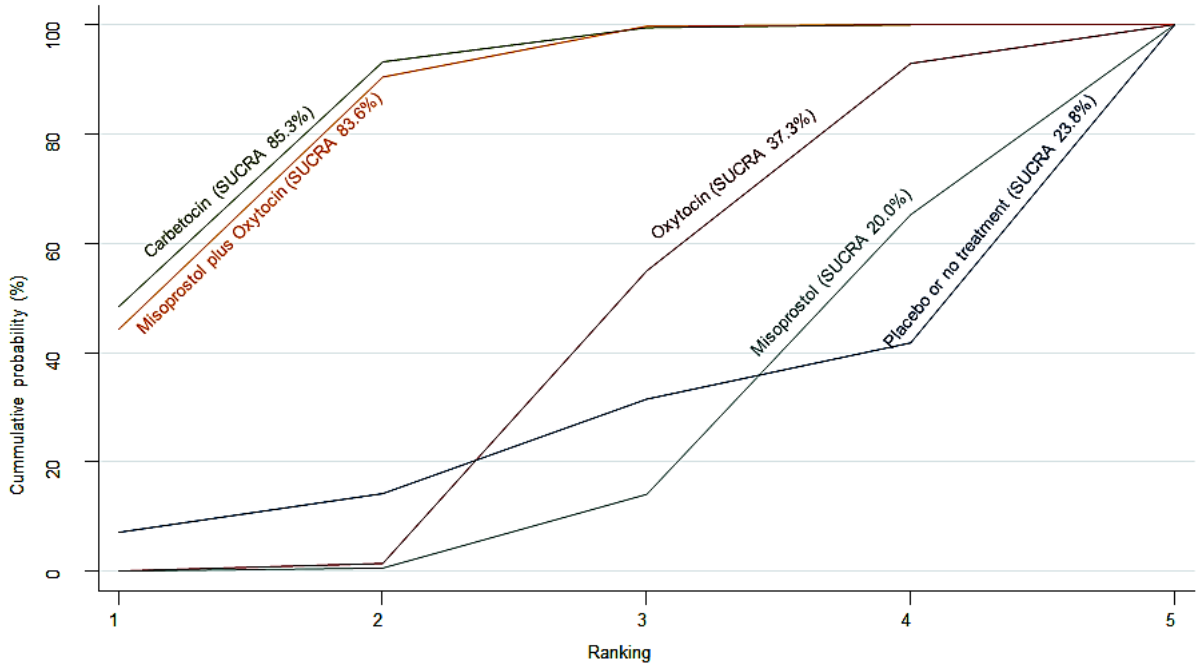


Figure 10. Network diagram for prevention of PPH ≥ 1000 mL by mode of birth (caesarean section). The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison.

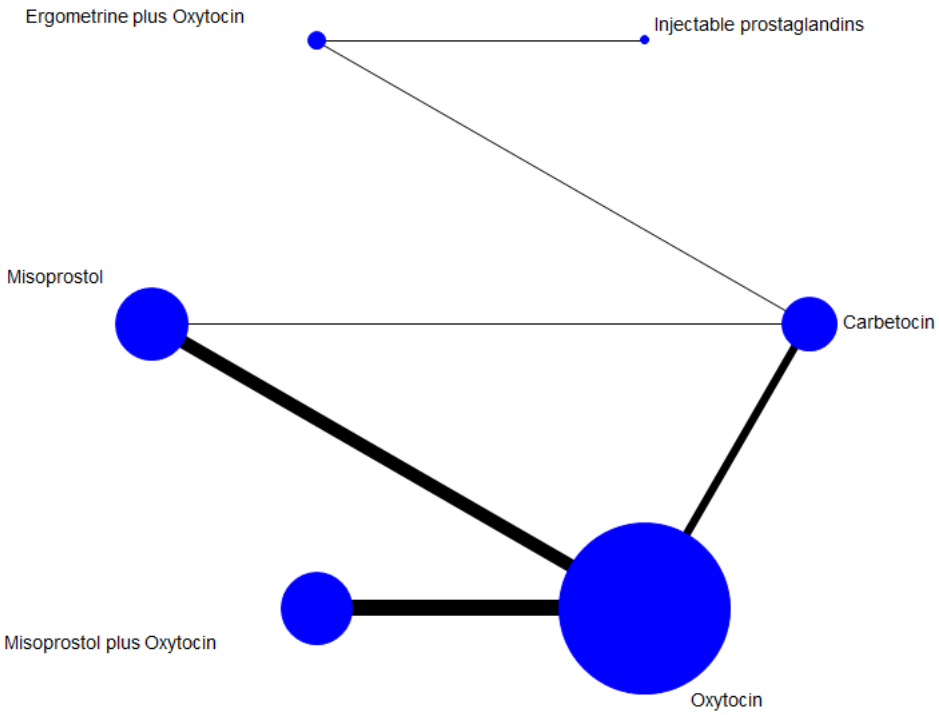


Figure 11. Forest plot with relative risk ratios and 95% CIs from pairwise, indirect and network (combining direct and indirect) analysis for prevention of PPH ≥ 1000 mL by mode of birth (caesarean section).

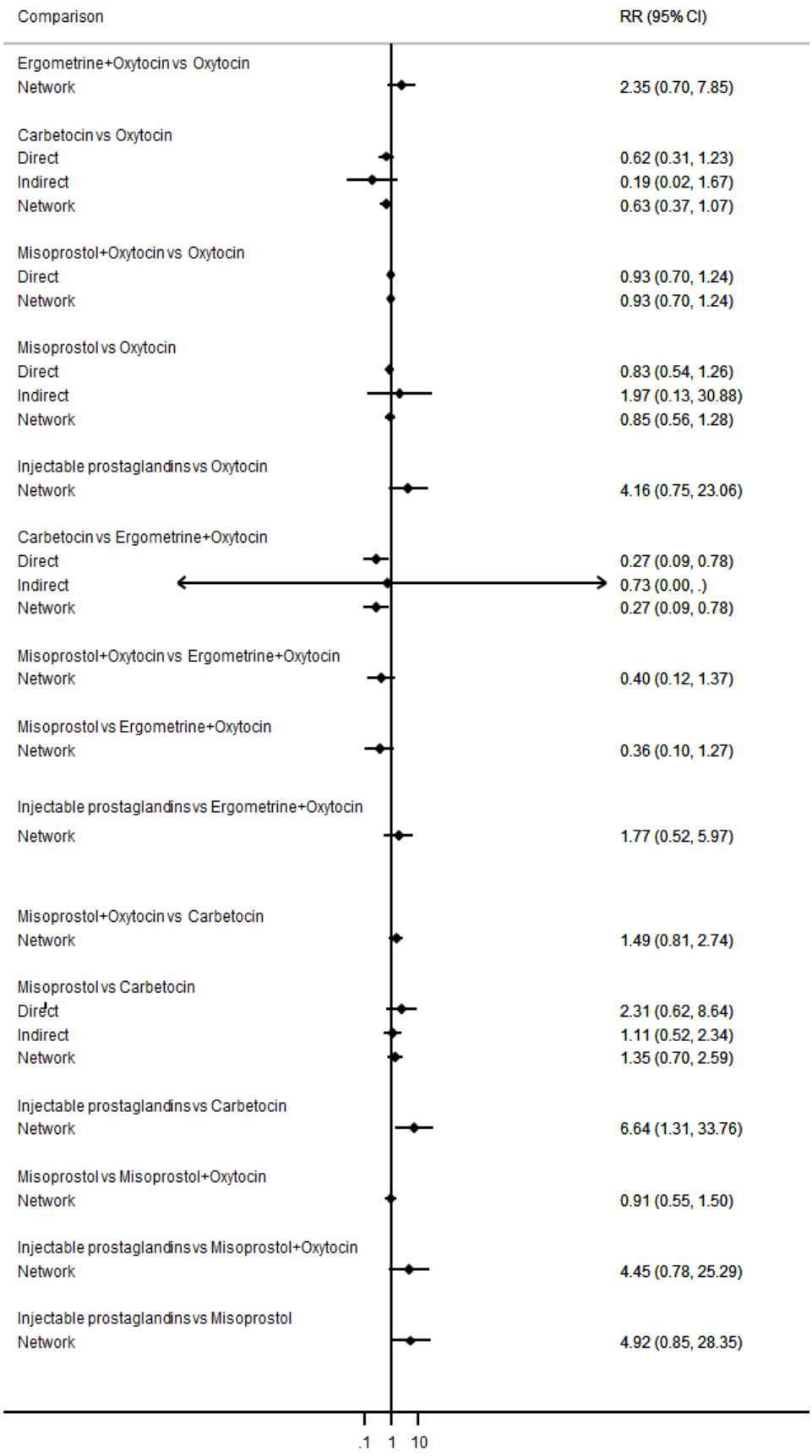


Figure 12. Cumulative rankograms comparing each of the uterotonic drugs for prevention of PPH ≥ 1000 mL by mode of birth (caesarean section). Ranking indicates the cumulative probability of being the best drug, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SUrface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available drug options.

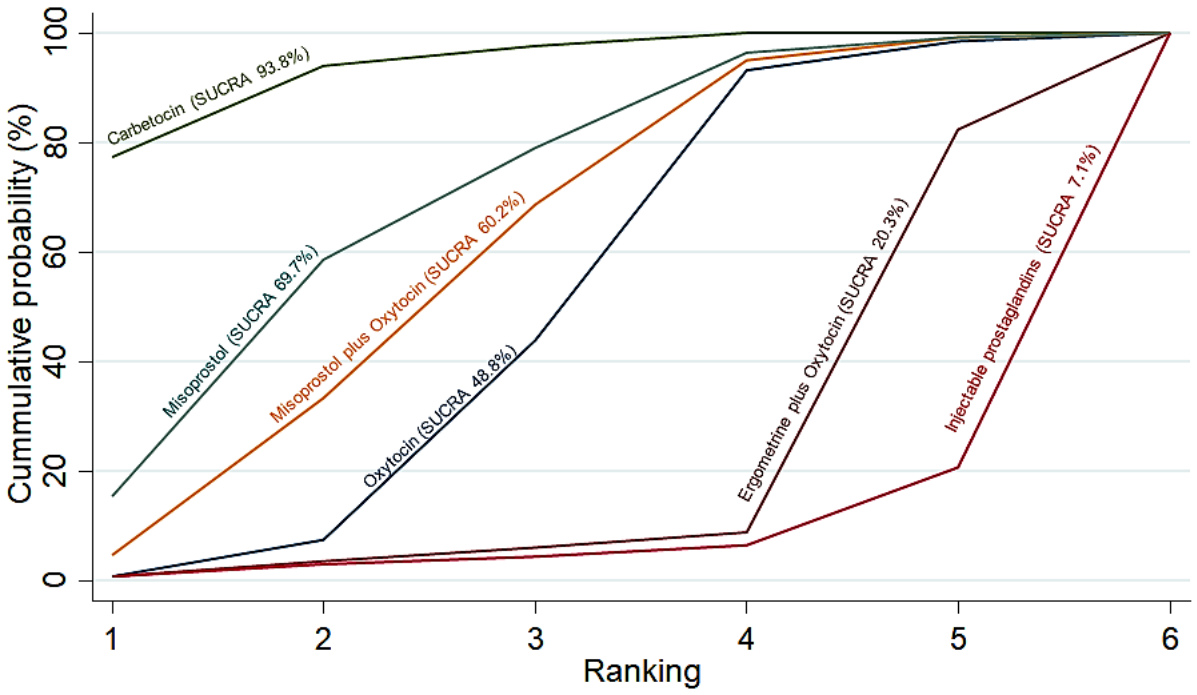


Figure 13. Network diagram for prevention of PPH ≥ 500 mL by prior risk for postpartum haemorrhage (low risk). The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison.

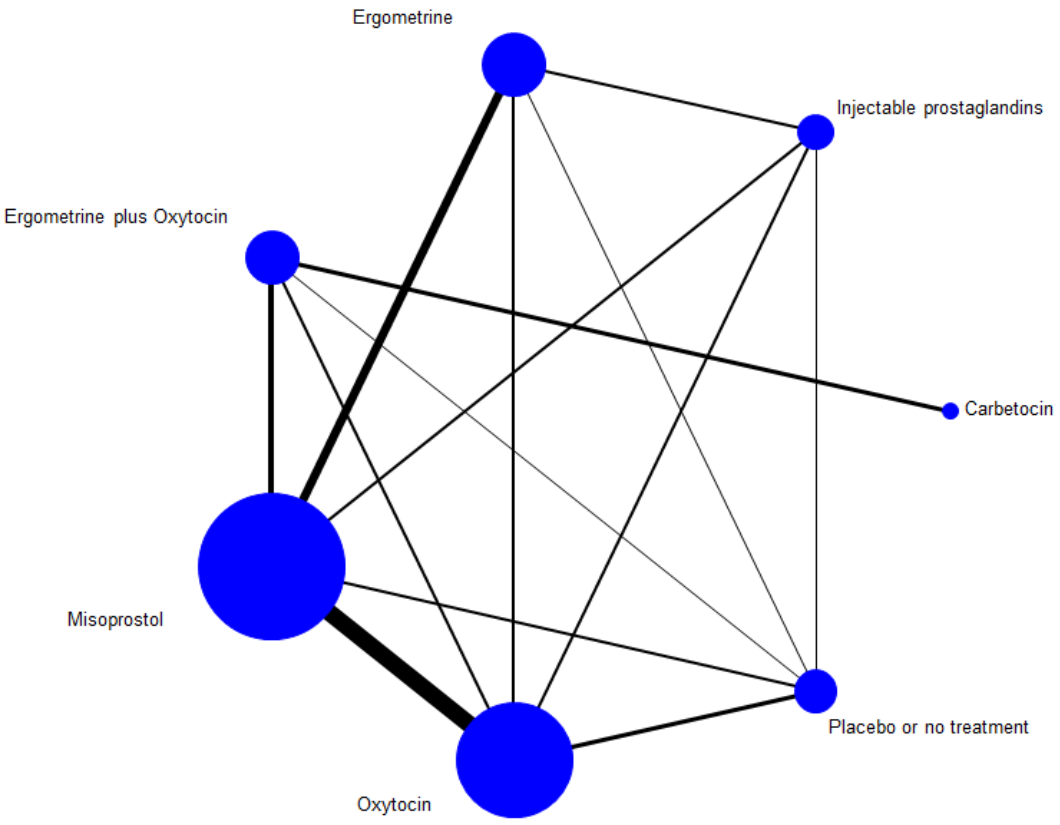


Figure 14. Forest plot with relative risk ratios and 95% CIs from pairwise, indirect and network (combining direct and indirect) analysis for prevention of PPH ≥ 500 mL by prior risk for postpartum haemorrhage (low risk).

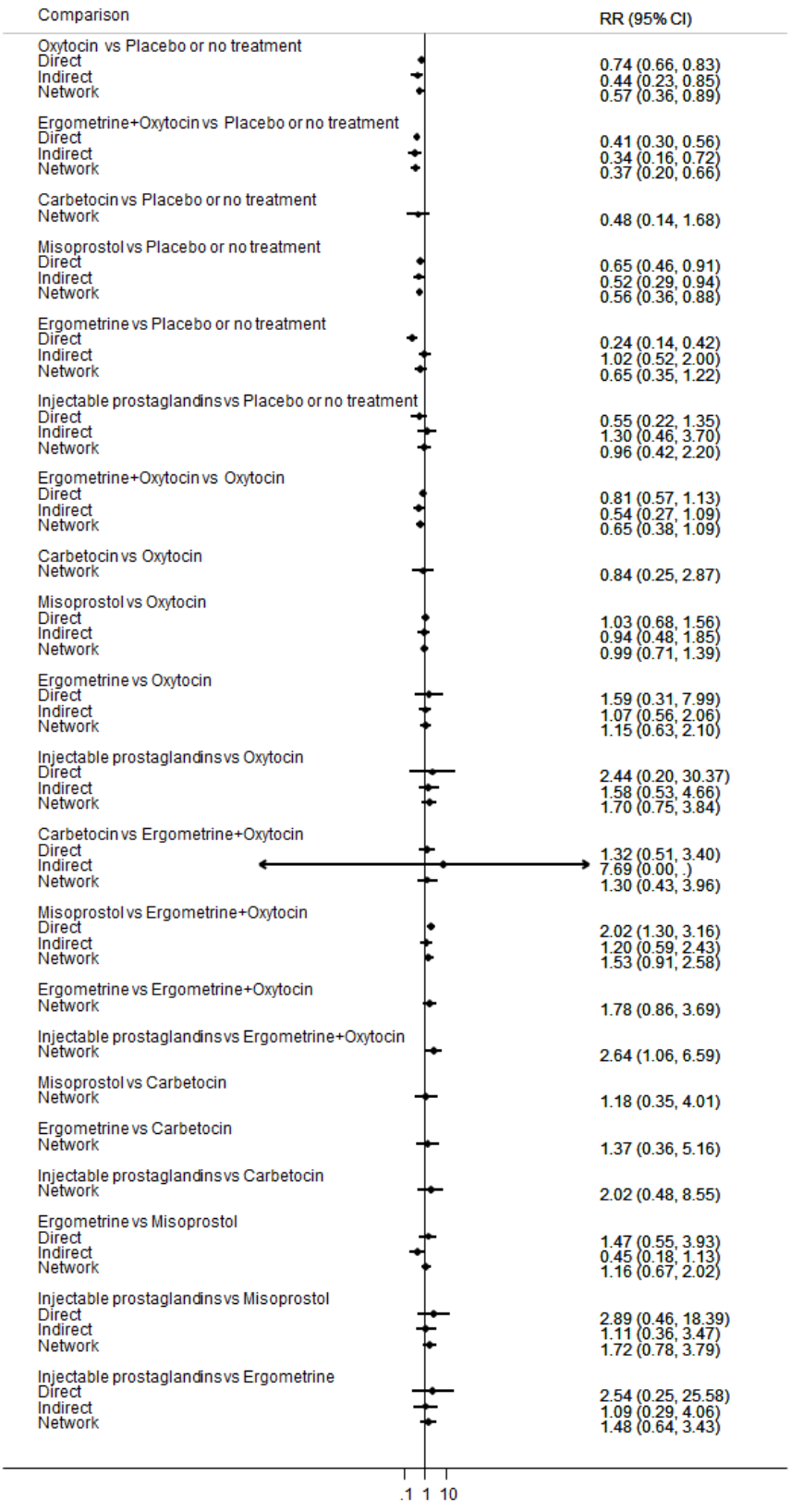


Figure 15. Cumulative rankograms comparing each of the uterotonic drugs for prevention of PPH ≥ 500 mL by prior risk for postpartum haemorrhage (low risk). Ranking indicates the cumulative probability of being the best drug, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SUrface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available drug options.

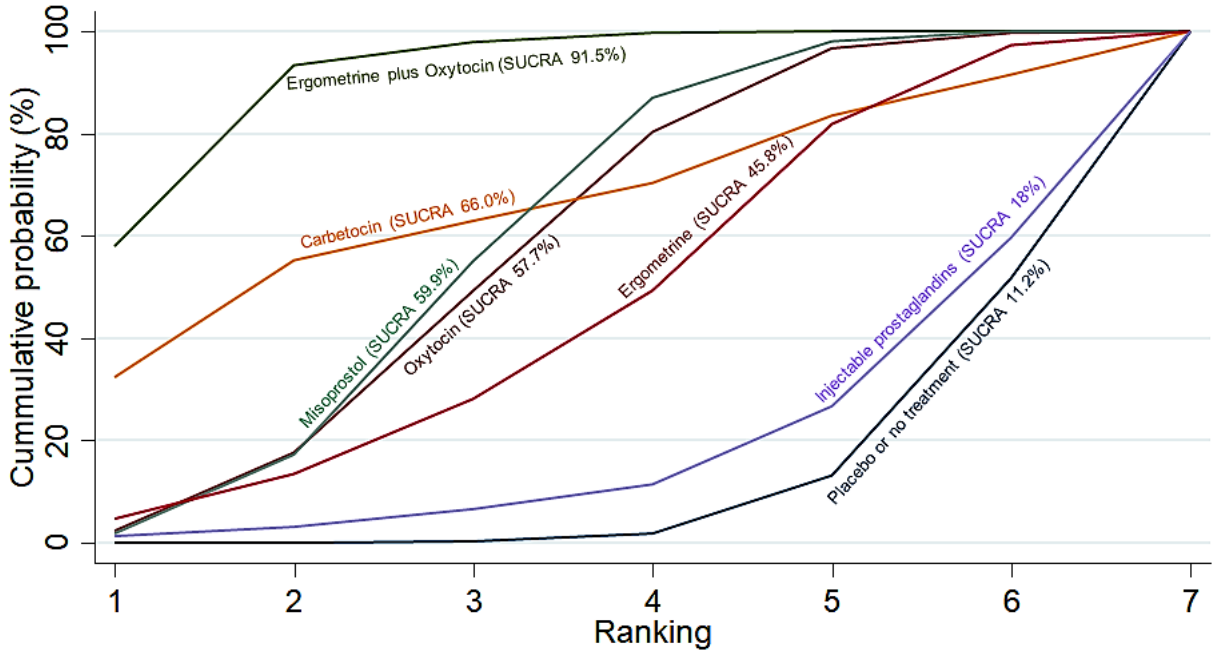


Figure 16. Network diagram for prevention of PPH ≥ 1000 mL by prior risk for postpartum haemorrhage (low risk). The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison.

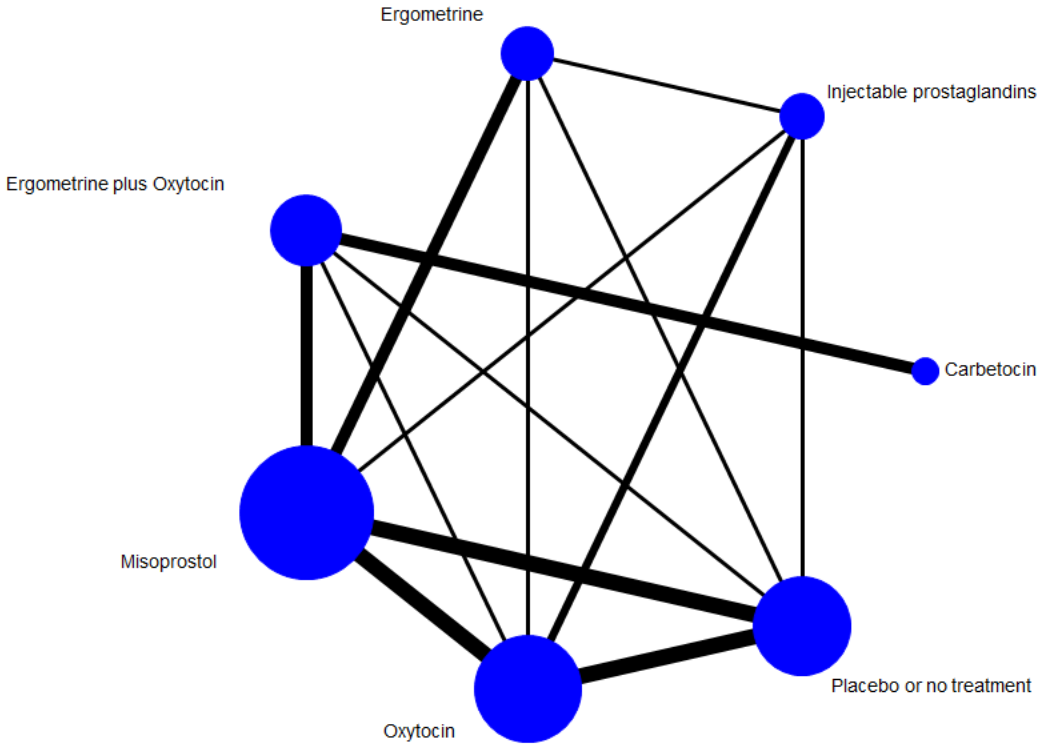


Figure 17. Forest plot with relative risk ratios and 95% CIs from pairwise, indirect and network (combining direct and indirect) analysis for prevention of PPH ≥ 1000 mL by prior risk for postpartum haemorrhage (low risk).

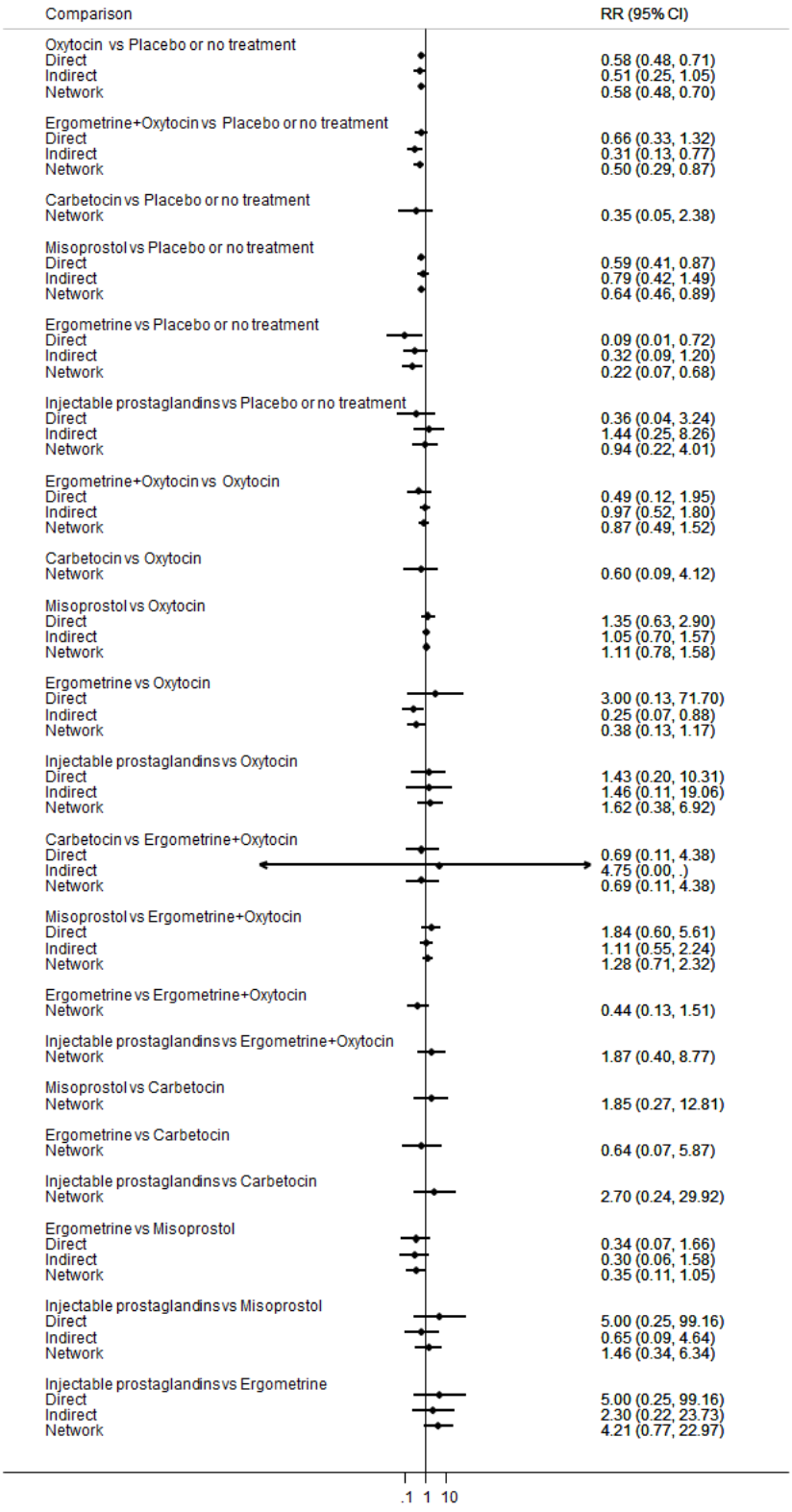


Figure 18. Cumulative rankograms comparing each of the uterotonic drugs for prevention of PPH ≥ 1000 mL by prior risk for postpartum haemorrhage (low risk). Ranking indicates the cumulative probability of being the best drug, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SUrface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available drug options.

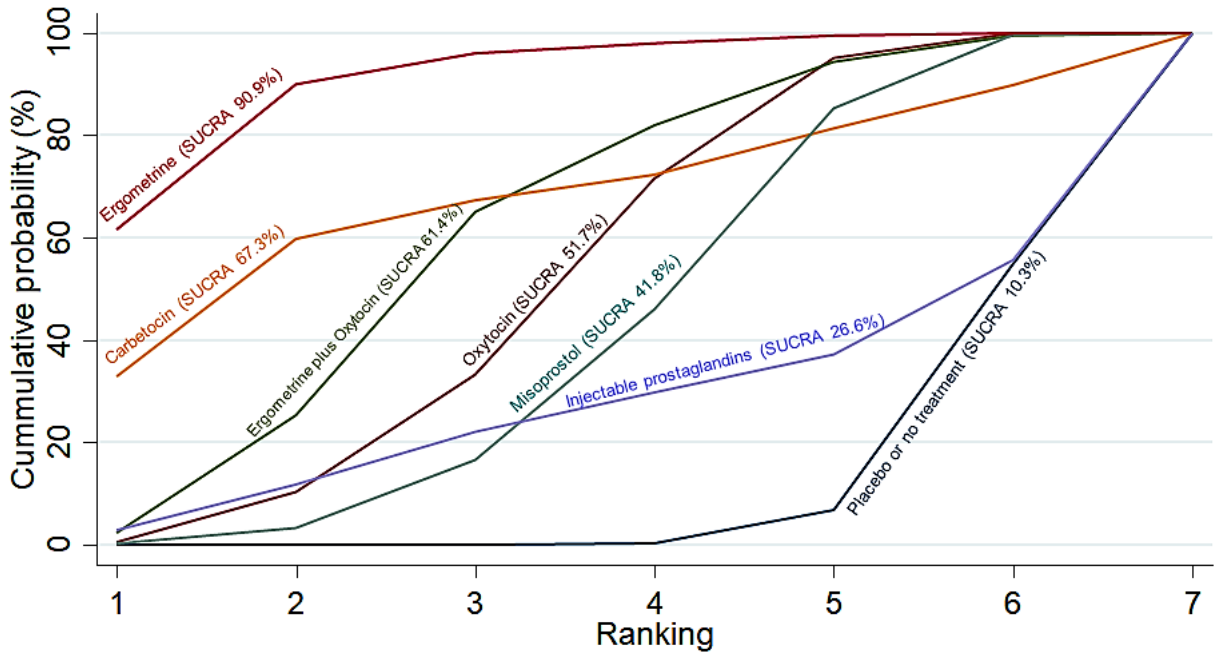


Figure 19. Network diagram for prevention of PPH ≥ 500 mL by prior risk for postpartum haemorrhage (high risk). The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison.

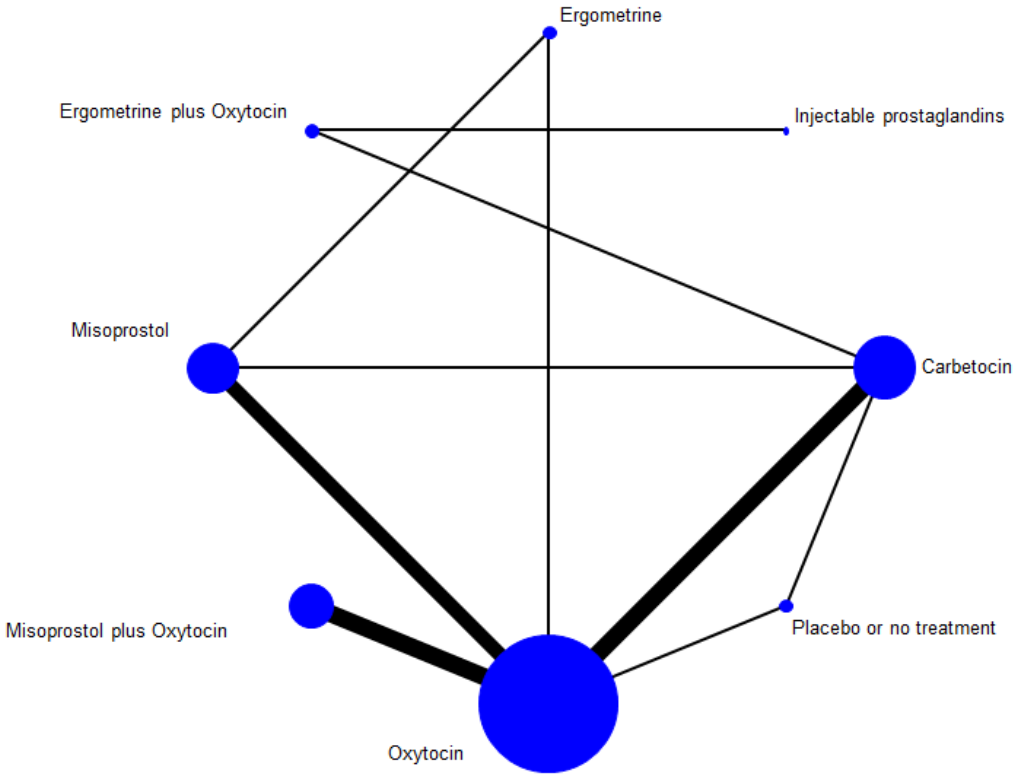


Figure 20. Forest plot with relative risk ratios and 95% CIs from pairwise, indirect and network (combining direct and indirect) analysis for prevention of PPH ≥ 500 mL by prior risk for postpartum haemorrhage (high risk).

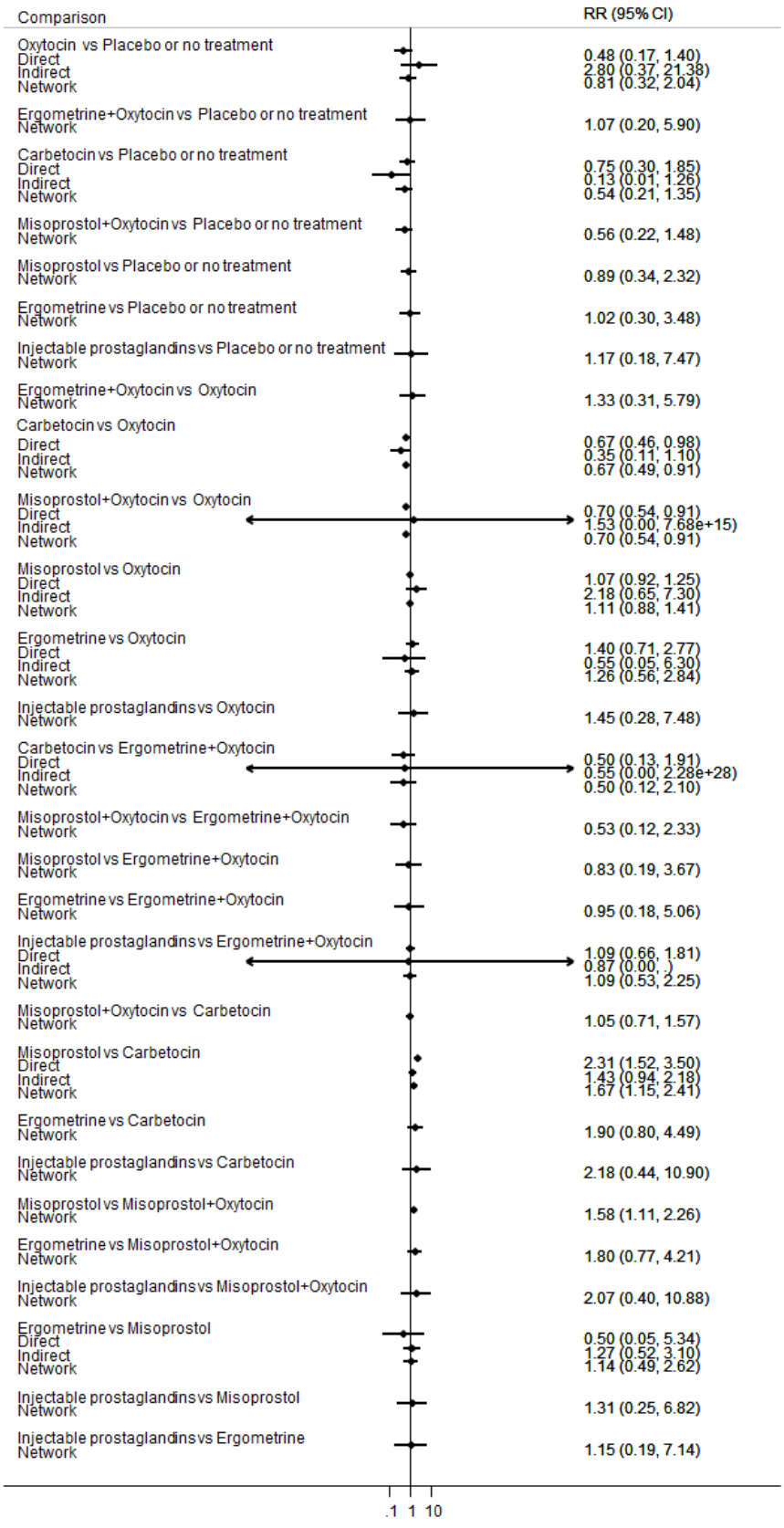


Figure 21. Cumulative rankograms comparing each of the uterotonic drugs for prevention of PPH ≥ 500 mL by prior risk for postpartum haemorrhage (high risk). Ranking indicates the cumulative probability of being the best drug, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SUrface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available drug options.

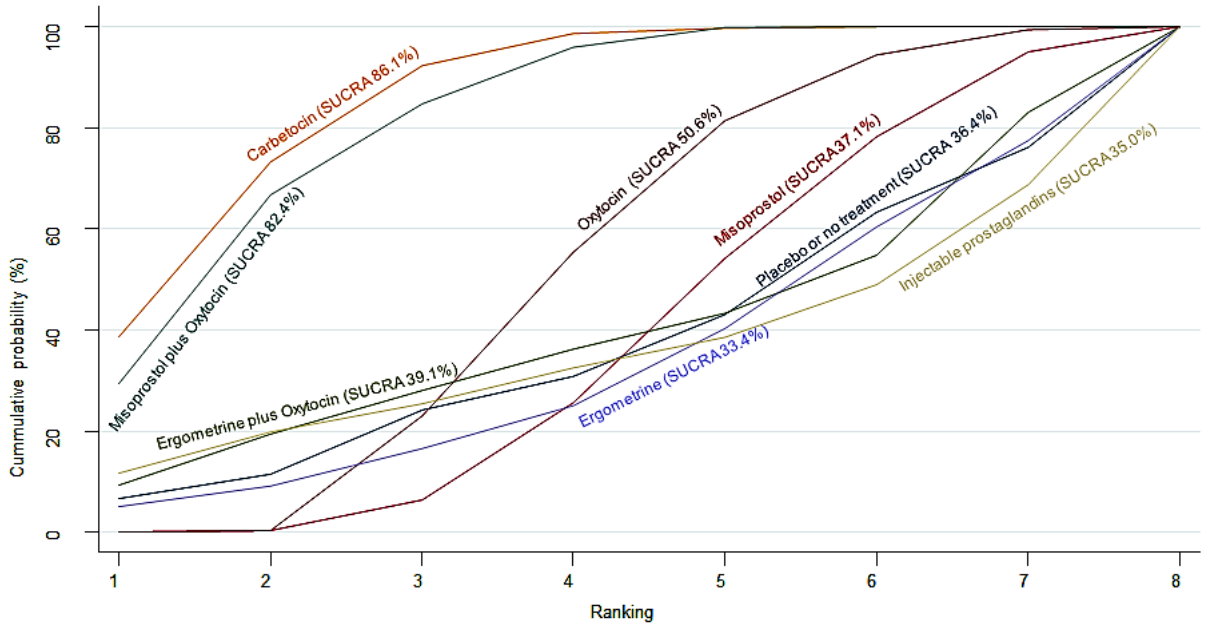


Figure 22. Network diagram for prevention of PPH ≥ 1000 mL by prior risk for postpartum haemorrhage (high risk). The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison.

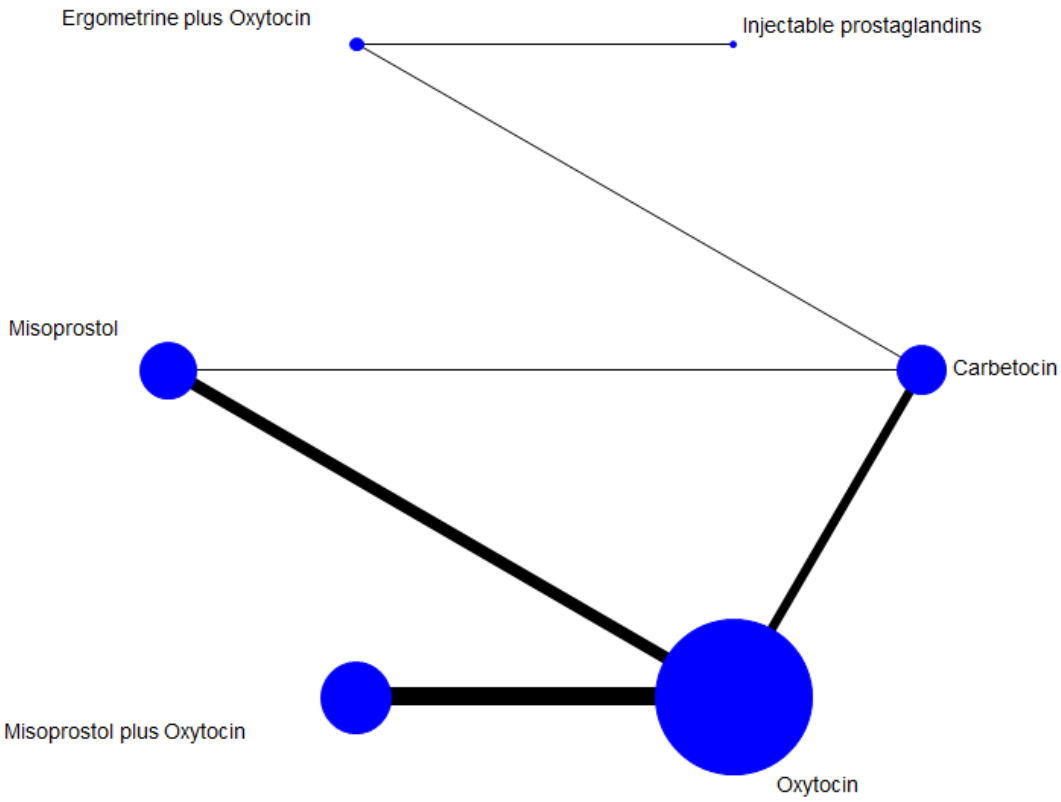


Figure 23. Forest plot with relative risk ratios and 95% CIs from pairwise, indirect and network (combining direct and indirect) analysis for prevention of PPH ≥ 1000 mL by prior risk for postpartum haemorrhage (high risk).

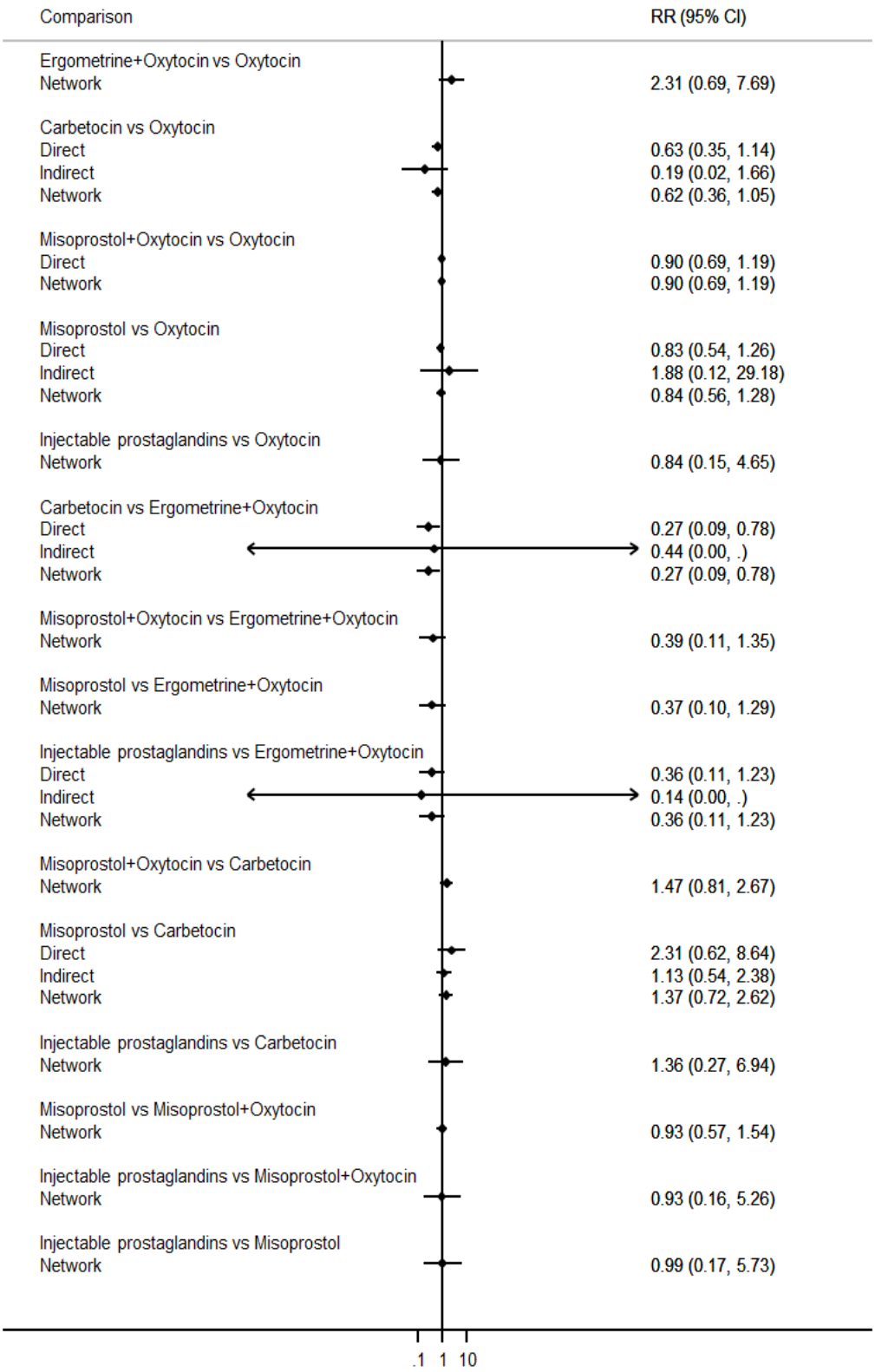


Figure 24. Cumulative rankograms comparing each of the uterotonic drugs for prevention of PPH ≥ 1000 mL by prior risk for postpartum haemorrhage (high risk). Ranking indicates the cumulative probability of being the best drug, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SUrface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available drug options.

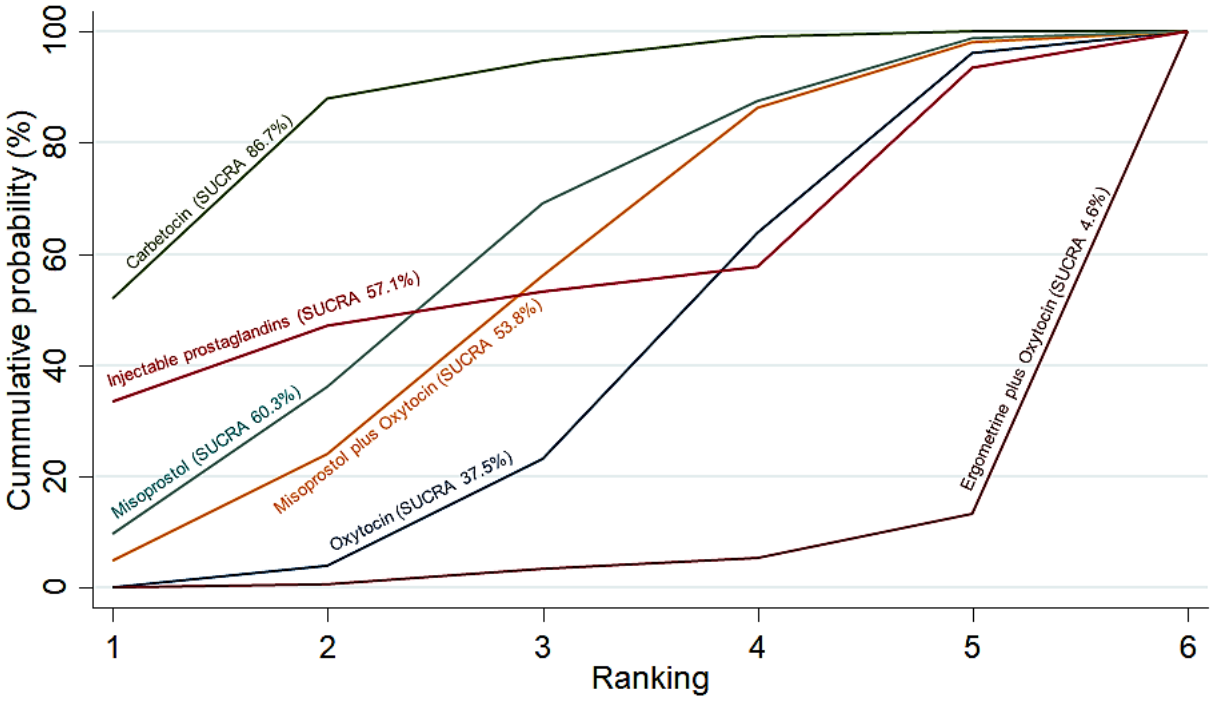


Figure 25. Network diagram for prevention of PPH ≥ 500 mL by healthcare setting (hospital setting). The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison.

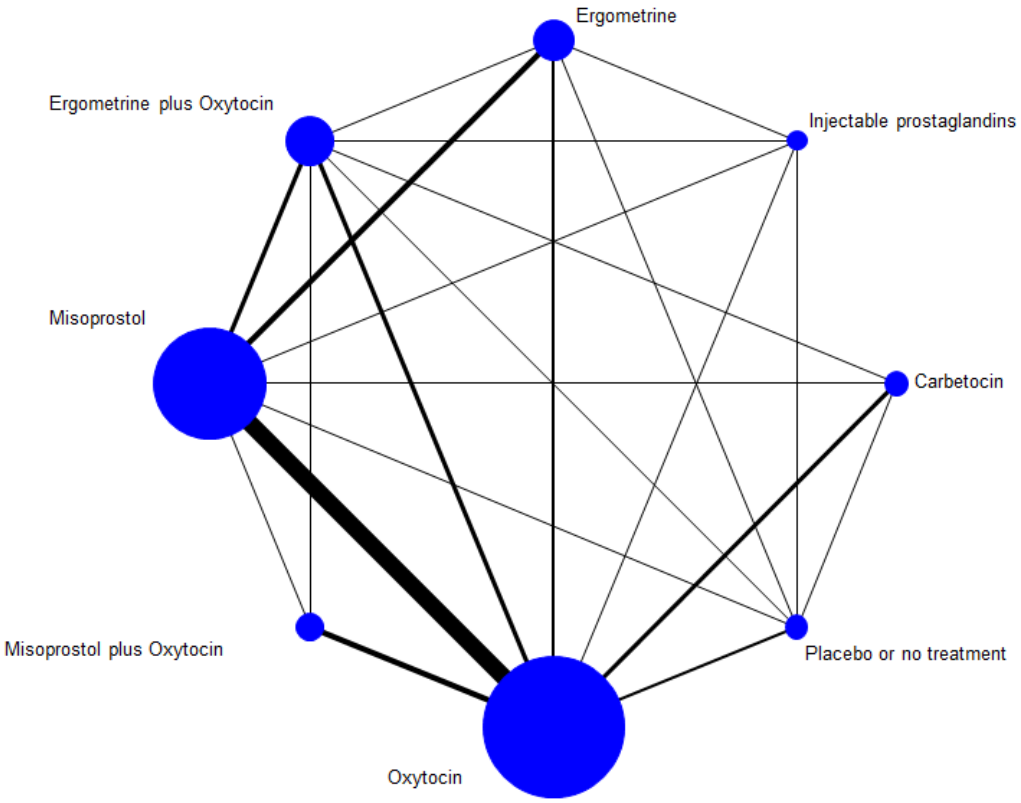


Figure 26. Forest plot with relative risk ratios and 95% CIs from pairwise, indirect and network (combining direct and indirect) analysis for prevention of PPH ≥ 500 mL by healthcare setting (hospital setting).

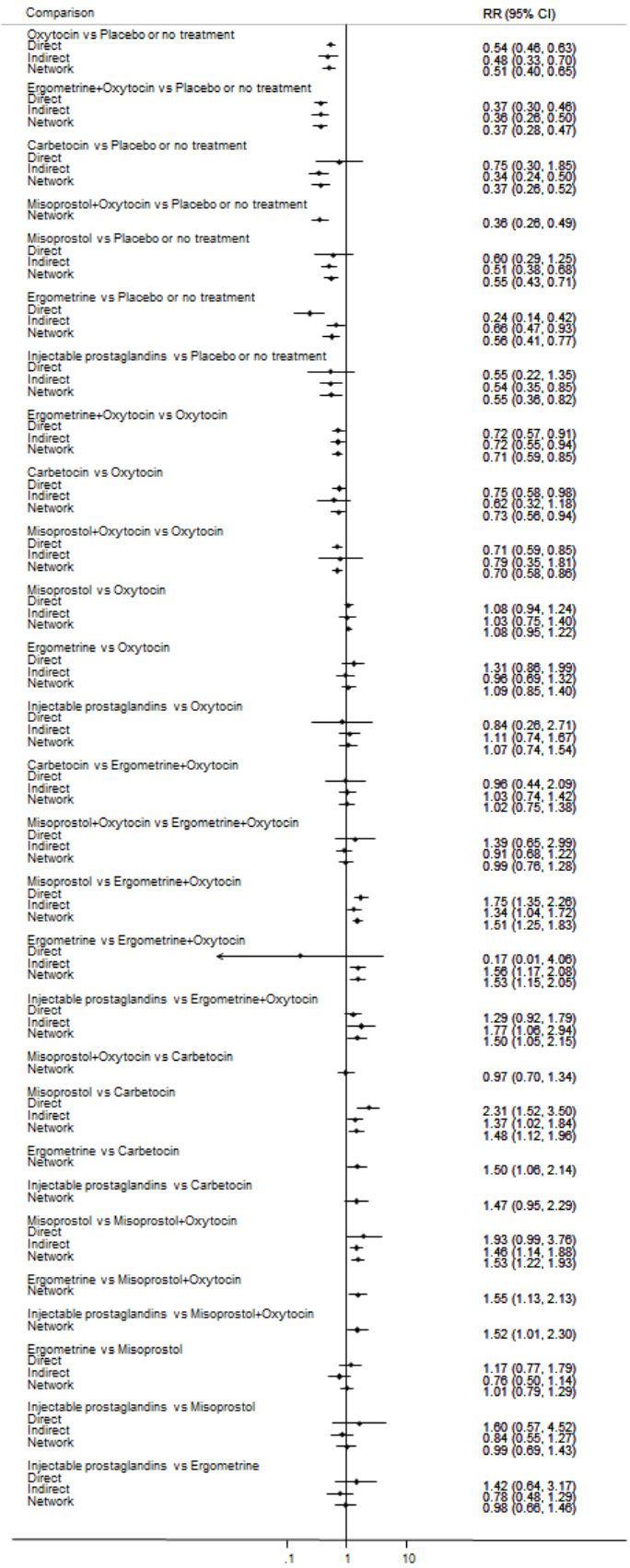


Figure 27. Cumulative rankograms comparing each of the uterotonic drugs for prevention of PPH ≥ 500 mL by healthcare setting (hospital setting). Ranking indicates the cumulative probability of being the best drug, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SUrface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available drug options.

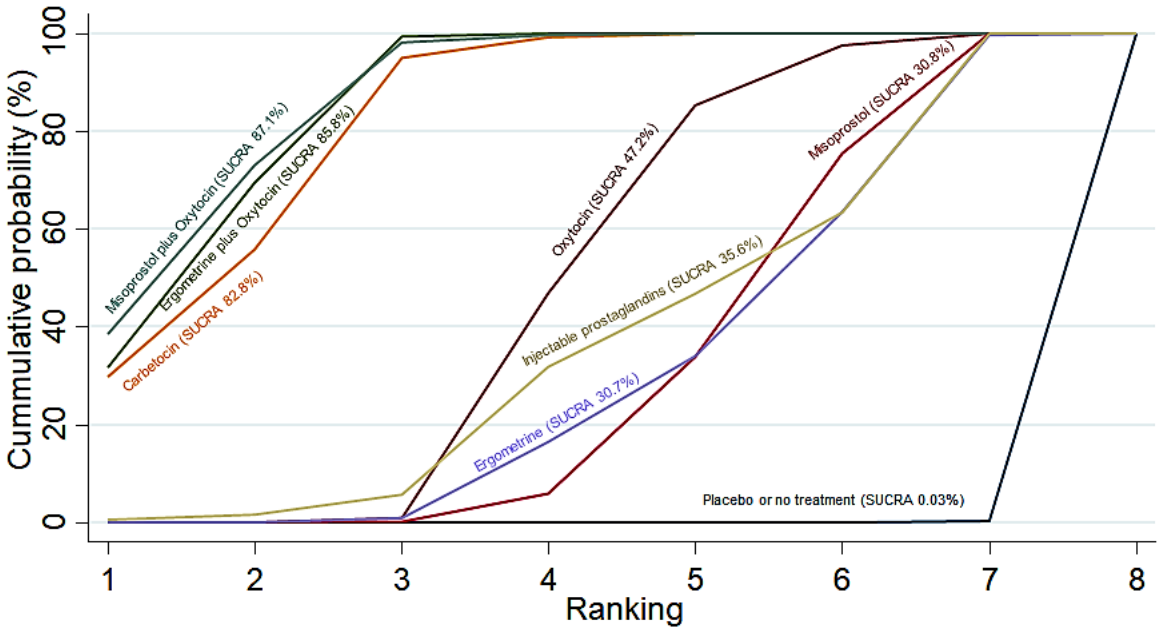


Figure 28. Network diagram for prevention of PPH ≥ 1000 mL by healthcare setting (hospital setting). The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison.

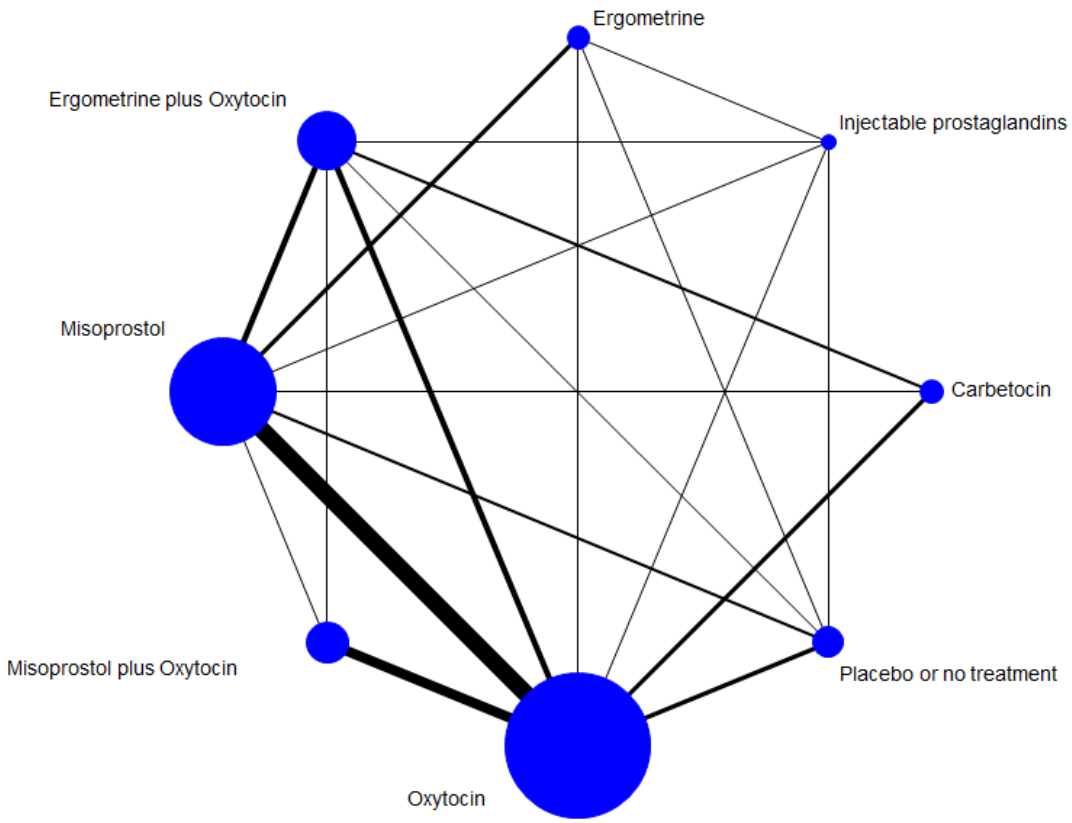


Figure 29. Forest plot with relative risk ratios and 95% CIs from pairwise, indirect and network (combining direct and indirect) analysis for prevention of PPH ≥ 1000 mL by healthcare setting (hospital setting).

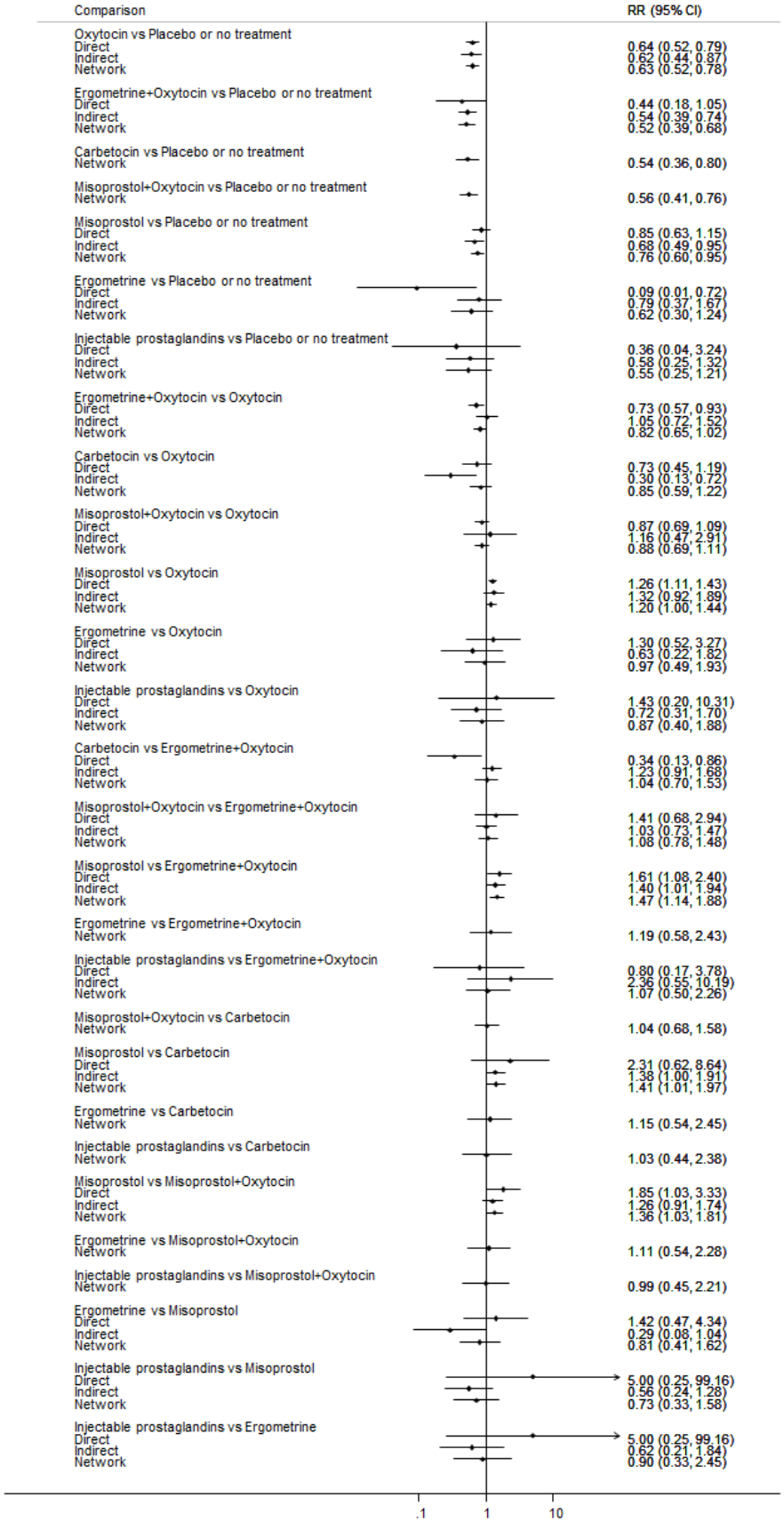


Figure 30. Cumulative rankograms comparing each of the uterotonic drugs for prevention of PPH ≥ 1000 mL by healthcare setting (hospital setting). Ranking indicates the cumulative probability of being the best drug, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SUrface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available drug options.

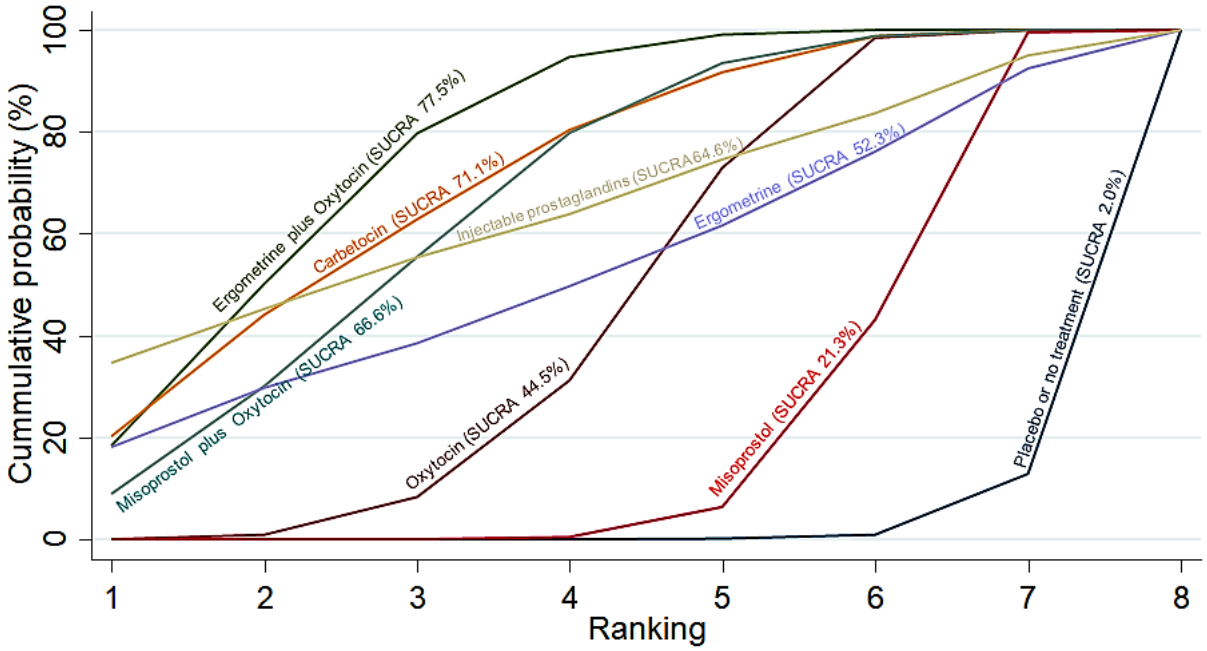


Figure 31. Network diagram for prevention of PPH ≥ 500 mL by healthcare setting (community setting). The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison.

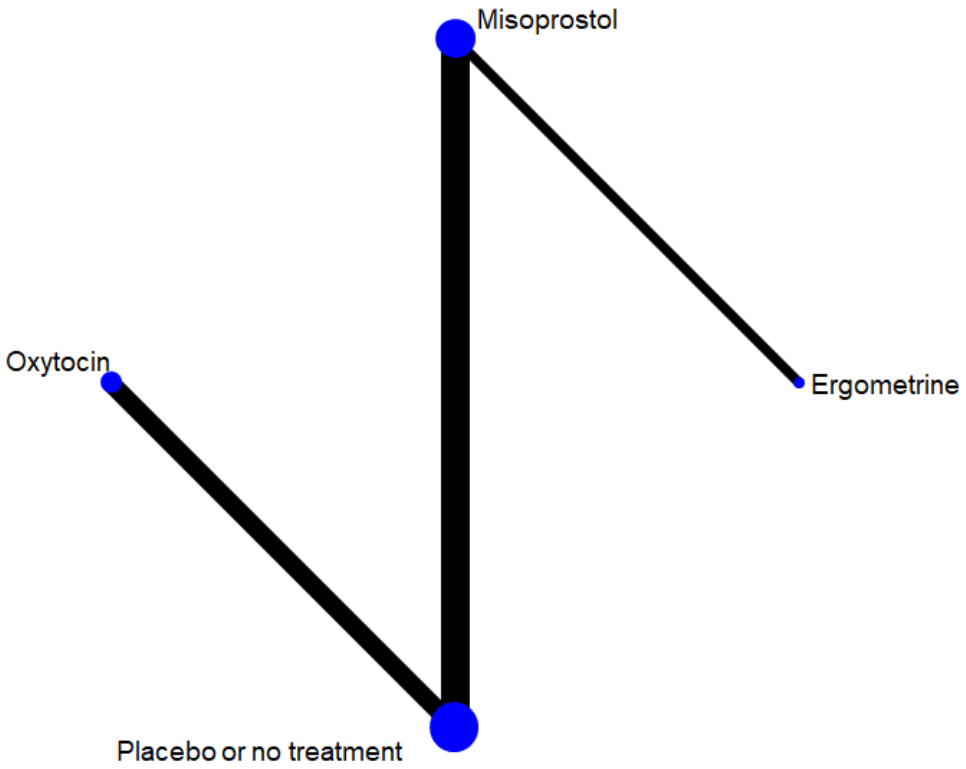


Figure 32. Forest plot with relative risk ratios and 95% CIs from pairwise, indirect and network (combining direct and indirect) analysis for prevention of PPH ≥ 500 mL by healthcare setting (community setting).

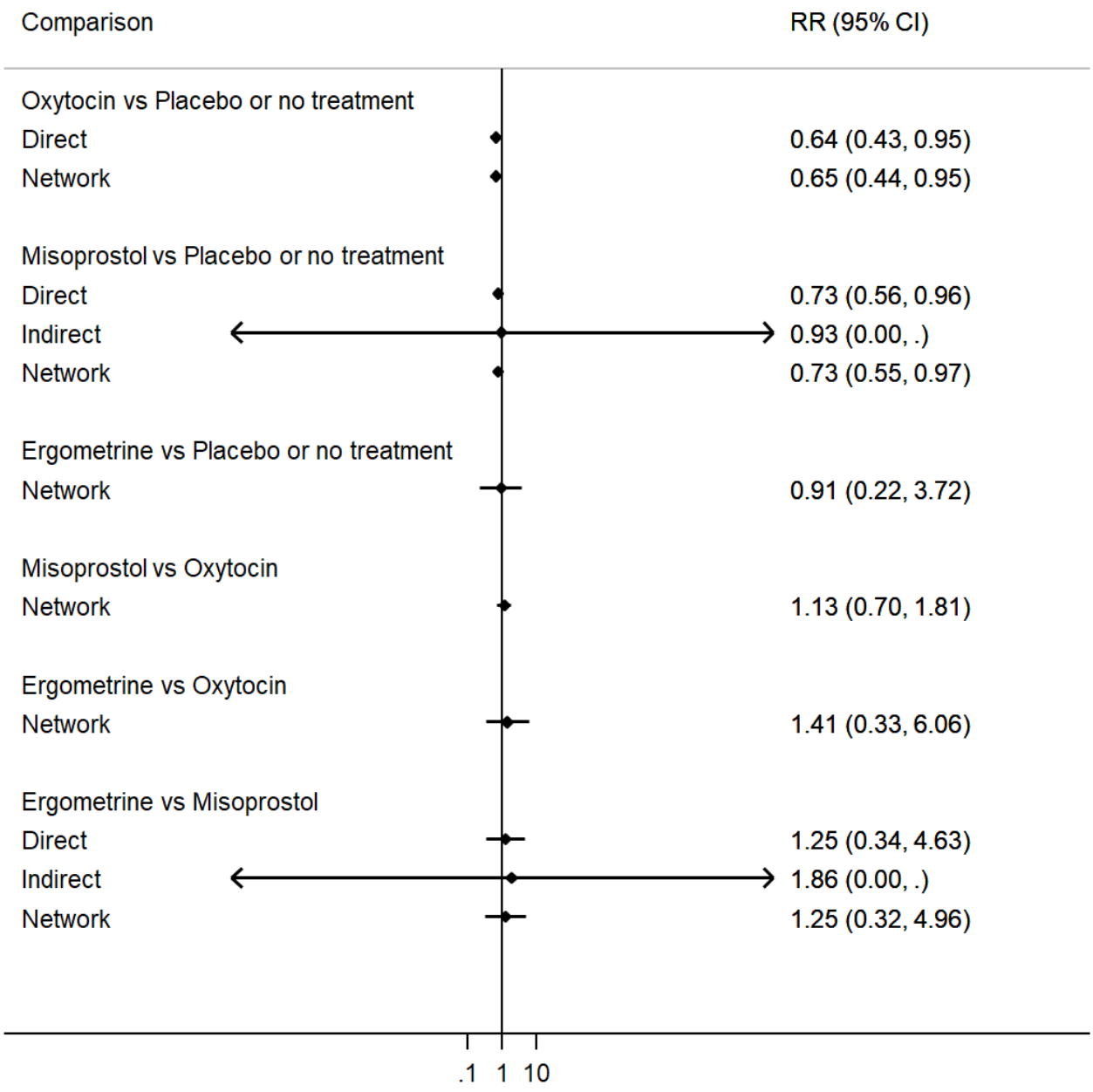


Figure 33. Cumulative rankograms comparing each of the uterotonic drugs for prevention of PPH ≥ 500 mL by healthcare setting (community setting). Ranking indicates the cumulative probability of being the best drug, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SUrface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available drug options.

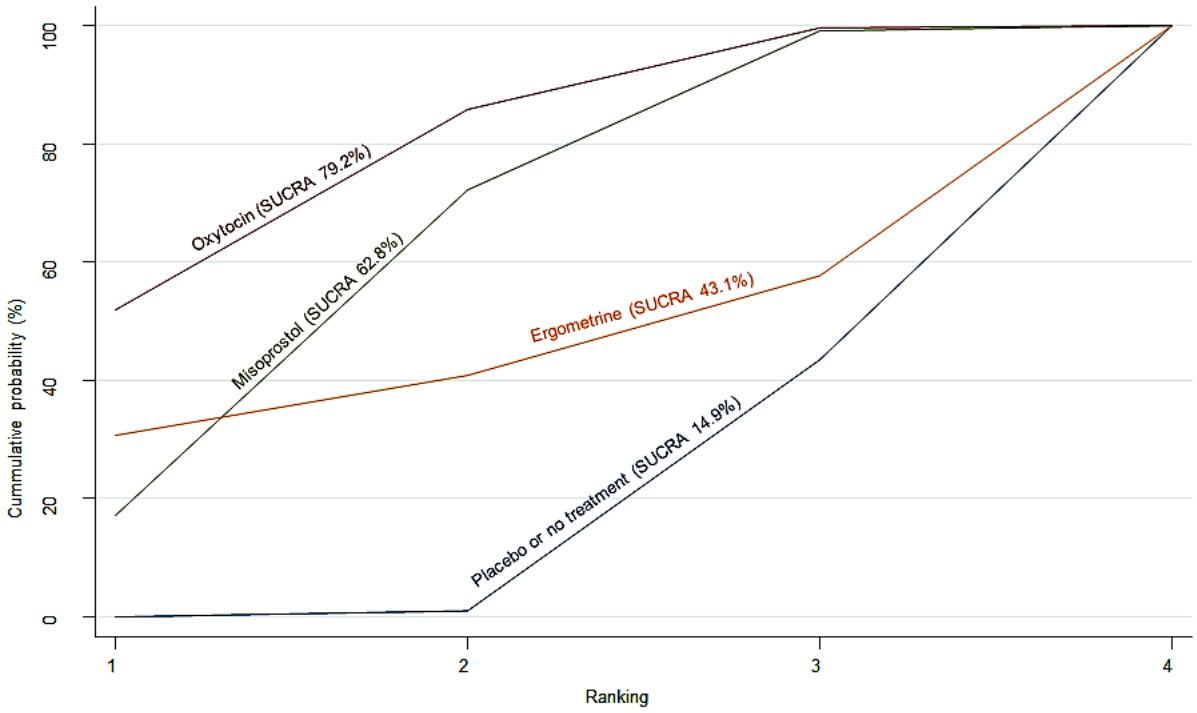


Figure 34. Network diagram for prevention of PPH ≥ 1000 mL by healthcare setting (community setting). The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison.

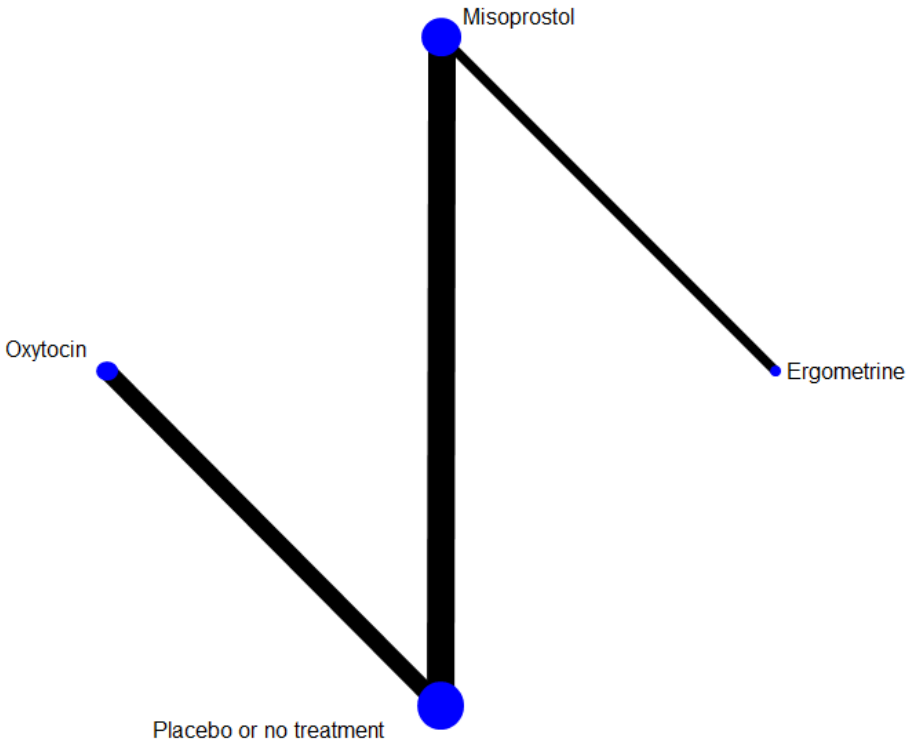


Figure 35. Forest plot with relative risk ratios and 95% CIs from pairwise, indirect and network (combining direct and indirect) analysis for prevention of PPH ≥ 1000 mL by healthcare setting (community setting).

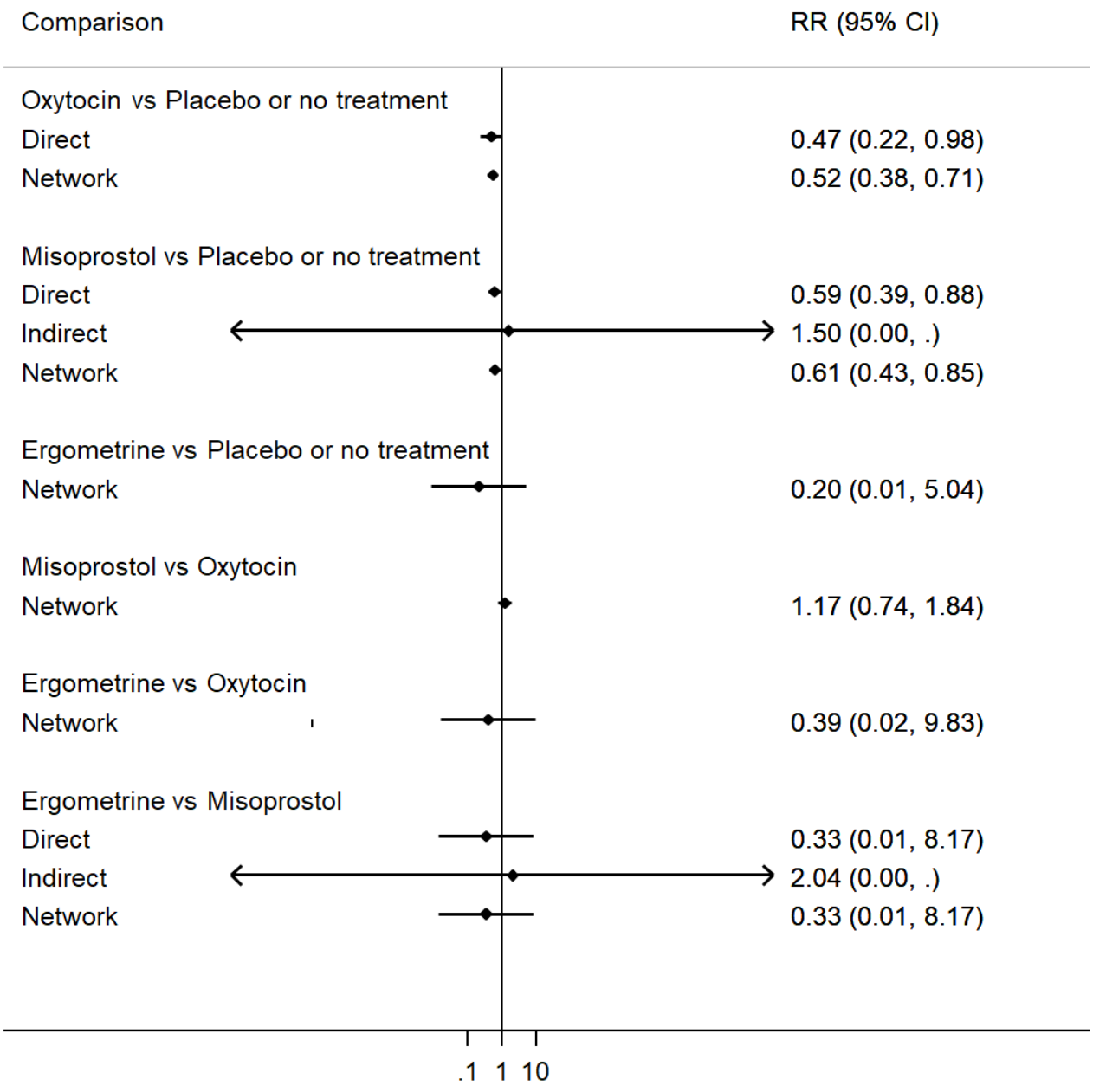


Figure 36. Cumulative rankograms comparing each of the uterotonic drugs for prevention of PPH ≥ 1000 mL by healthcare setting (community setting). Ranking indicates the cumulative probability of being the best drug, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SUrface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available drug options.

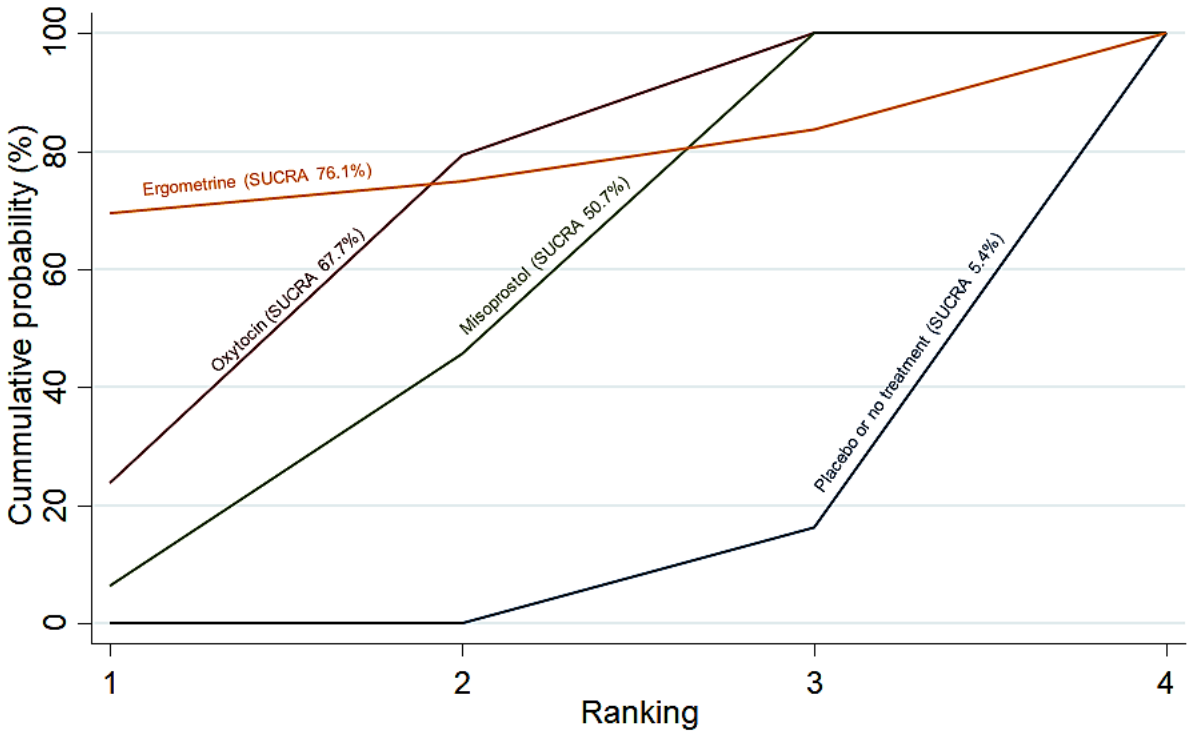


Figure 37. Network diagram for prevention of PPH ≥ 500 mL restricted to misoprostol studies that use a low dose (less or equal to 500 mcg). The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison.

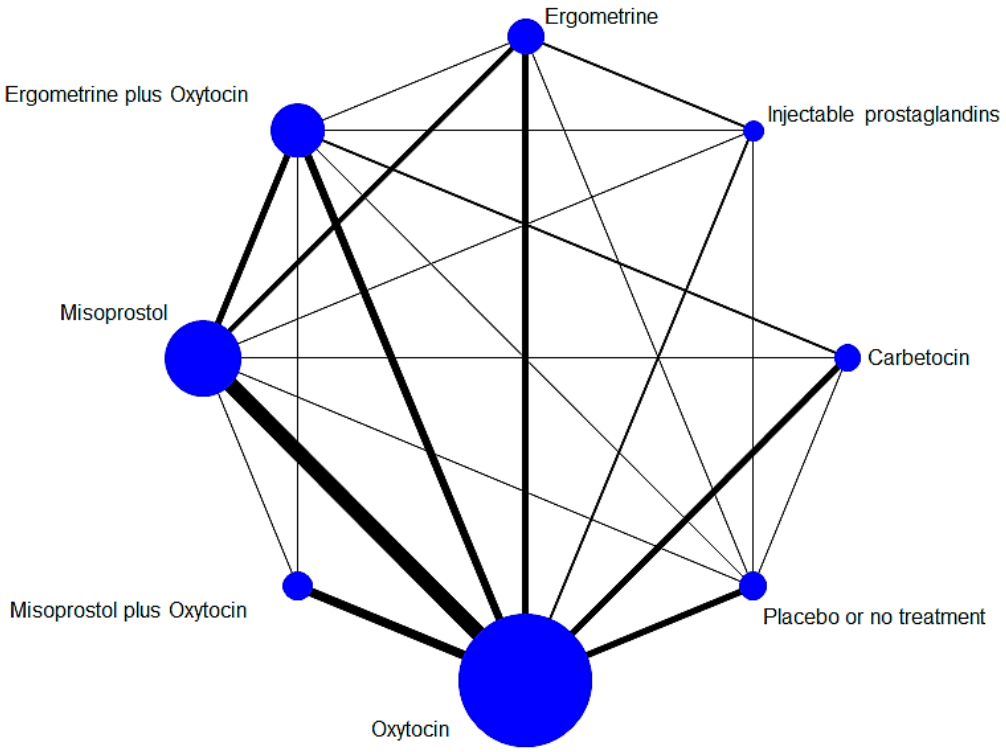


Figure 38. Forest plot with relative risk ratios and 95% CIs from pairwise, indirect and network (combining direct and indirect) analysis for prevention of PPH ≥ 500 mL restricted to misoprostol studies that use a low dose (less or equal to 500 mcg).

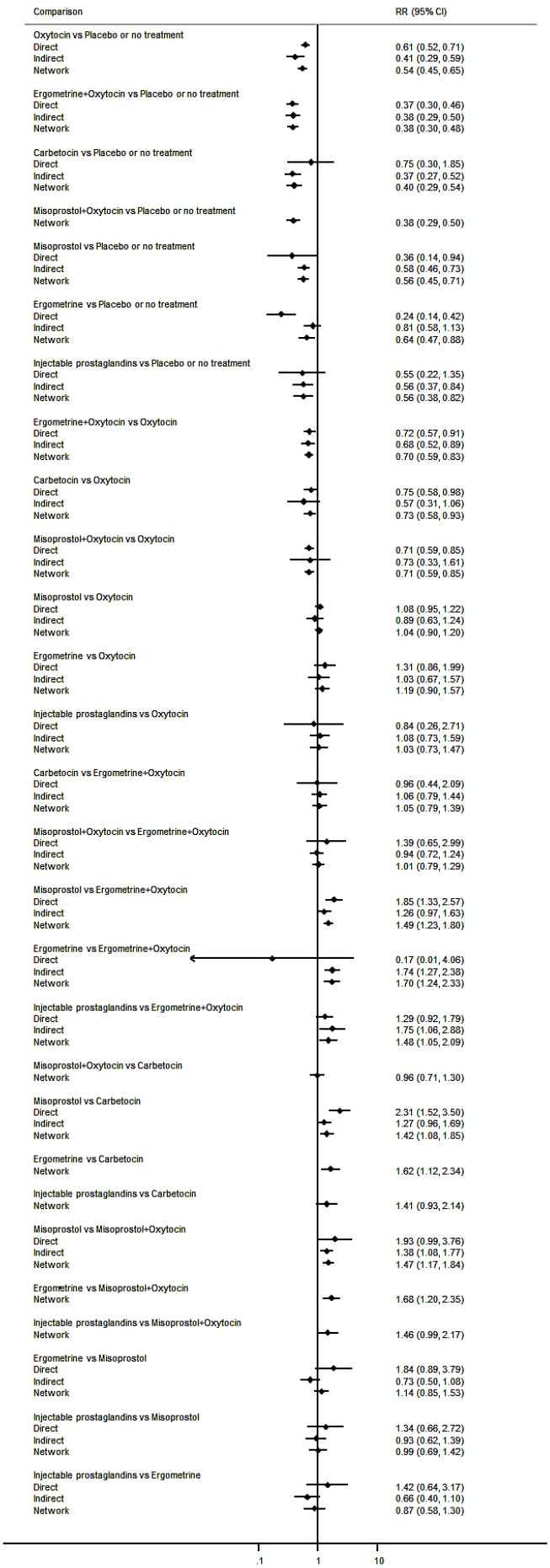


Figure 39. Cumulative rankograms comparing each of the uterotonic drugs for prevention of PPH ≥ 500 mL restricted to misoprostol studies that use a low dose (less or equal to 500 mcg). Ranking indicates the cumulative probability of being the best drug, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SUrface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available drug options.

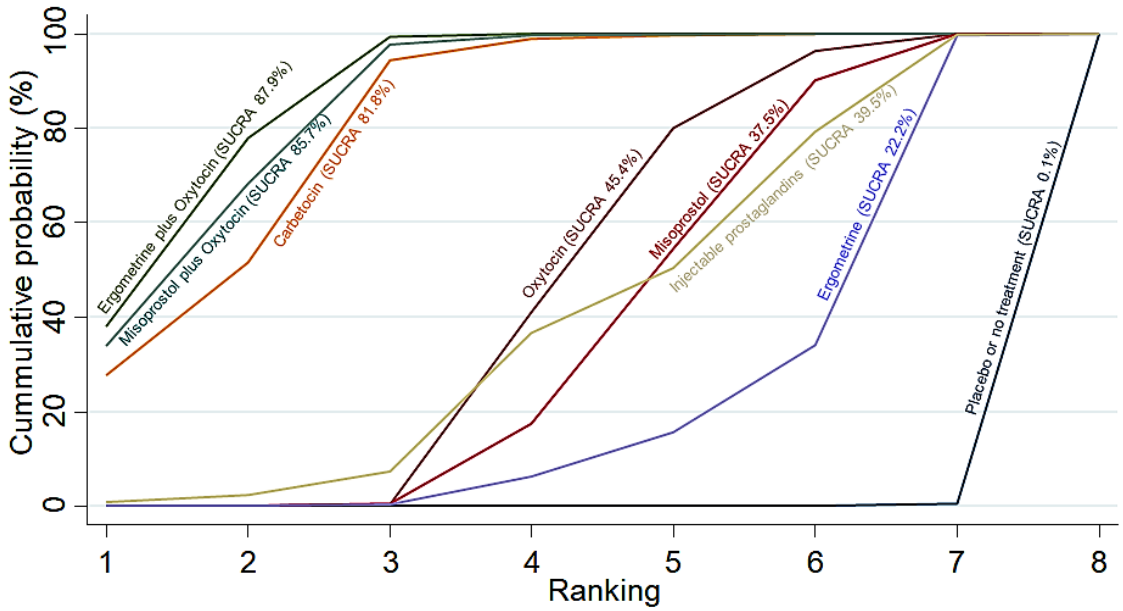


Figure 40. Network diagram for prevention of PPH ≥ 1000 mL restricted to misoprostol studies that use a low dose (less or equal to 500 mcg).The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison.

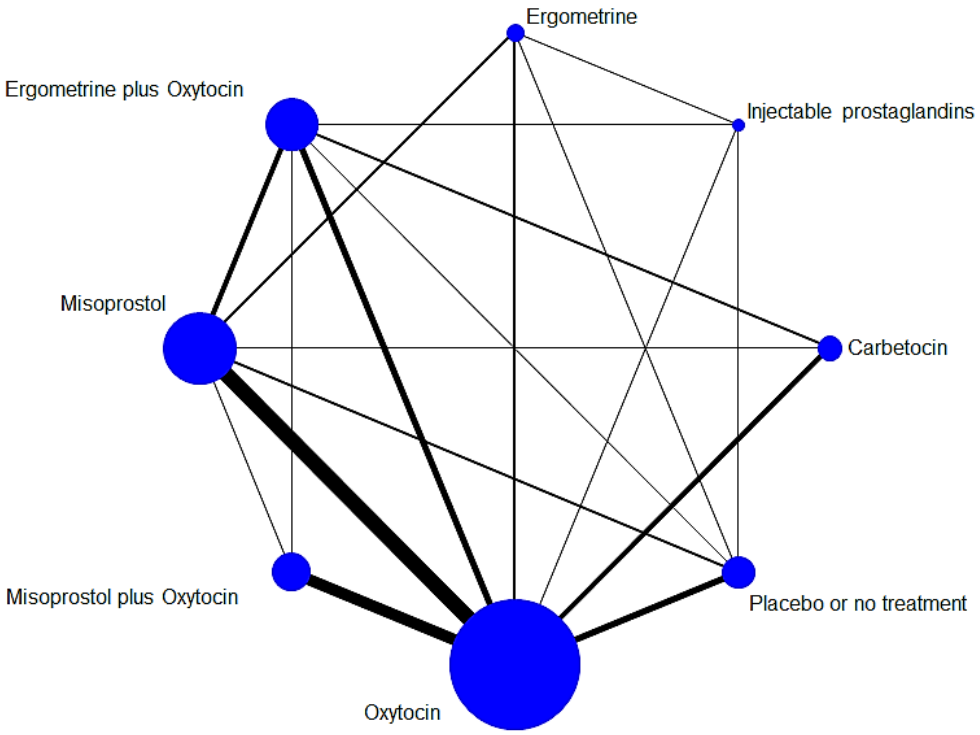


Figure 41. Forest plot with relative risk ratios and 95% CIs from pairwise, indirect and network (combining direct and indirect) analysis for prevention of PPH ≥ 1000 mL restricted to misoprostol studies that use a low dose (less or equal to 500 mcg). Figure 66. Figure

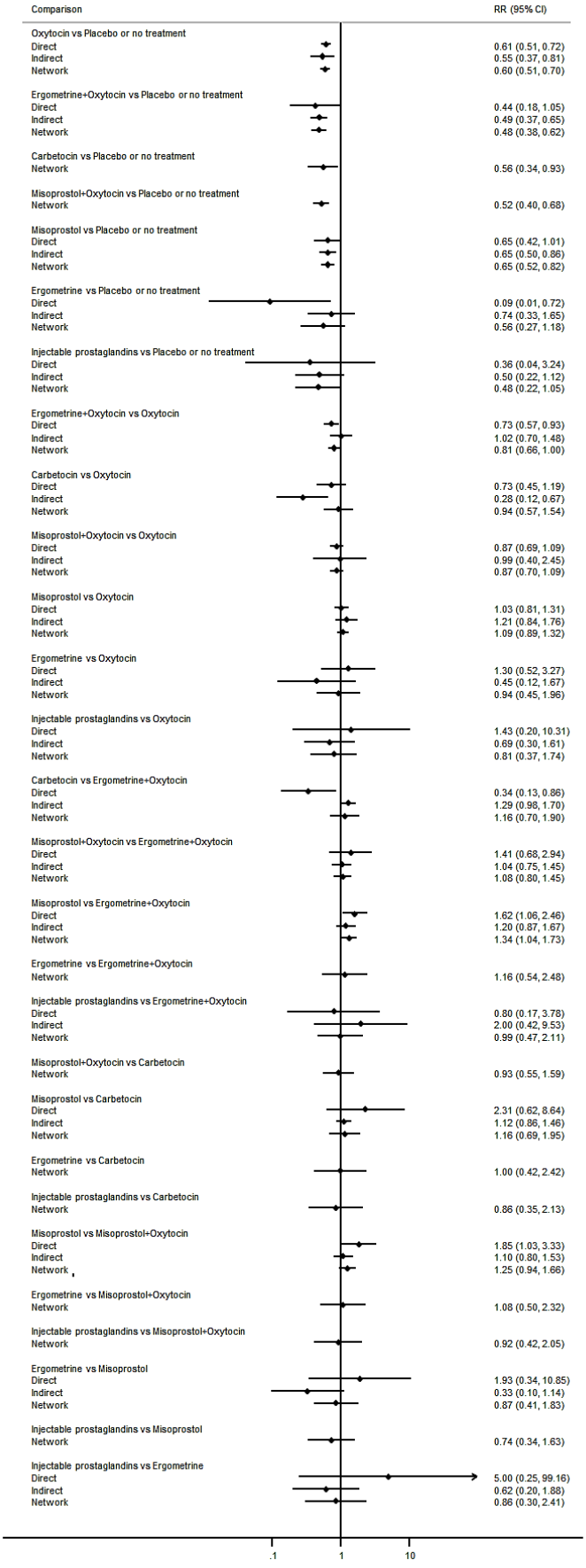


Figure 42. Cumulative rankograms comparing each of the uterotonic drugs for prevention of PPH ≥ 1000 mL restricted to misoprostol studies that use a low dose (less or equal to 500 mcg). Ranking indicates the cumulative probability of being the best drug, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SURface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available drug options.

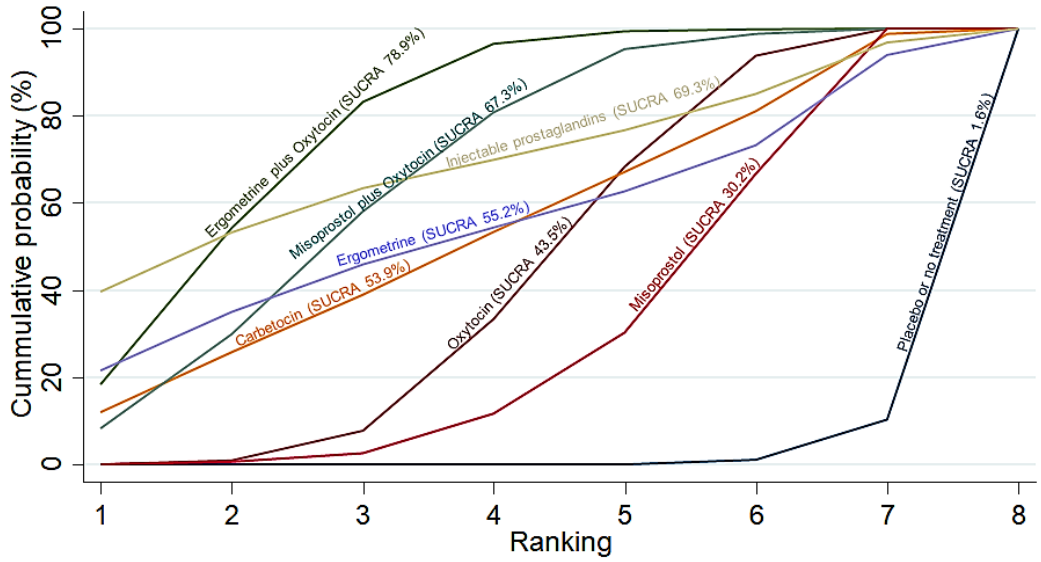


Figure 43. Network diagram for prevention of PPH ≥ 500 mL restricted to misoprostol studies that use a high dose (600 mcg or more). The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison.

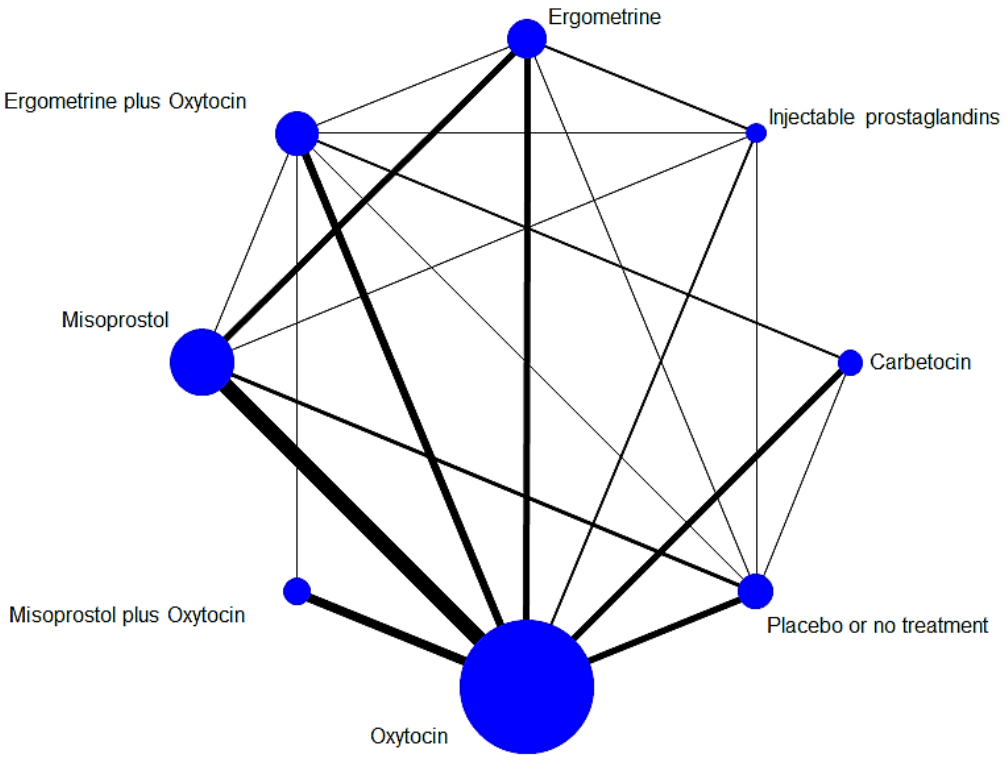


Figure 44. Forest plot with relative risk ratios and 95% CIs from pairwise, indirect and network (combining direct and indirect) analysis for prevention of PPH ≥ 500 restricted to misoprostol studies that use a high dose (600 mcg or more).

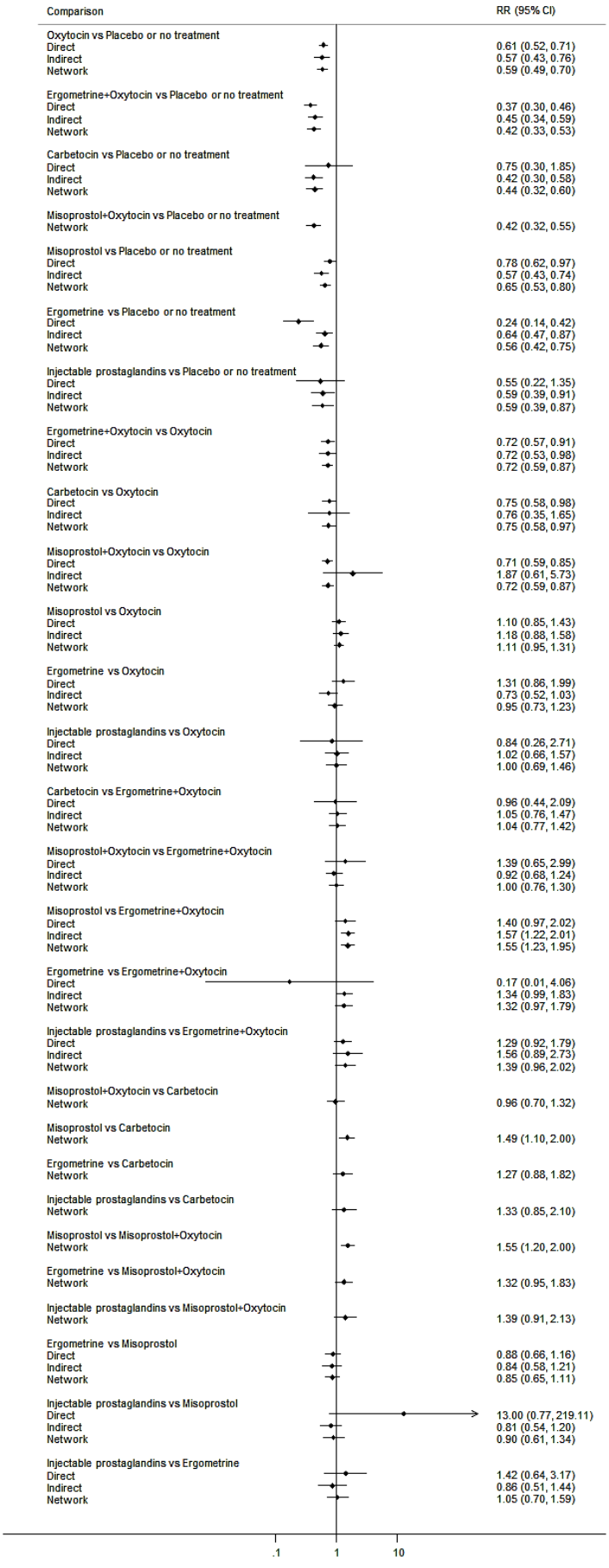


Figure 45. Cumulative rankograms comparing each of the uterotonic drugs for prevention of PPH ≥ 500 mL restricted to misoprostol studies that use a high dose (600 mcg or more). Ranking indicates the cumulative probability of being the best drug, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SUrface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available drug options.

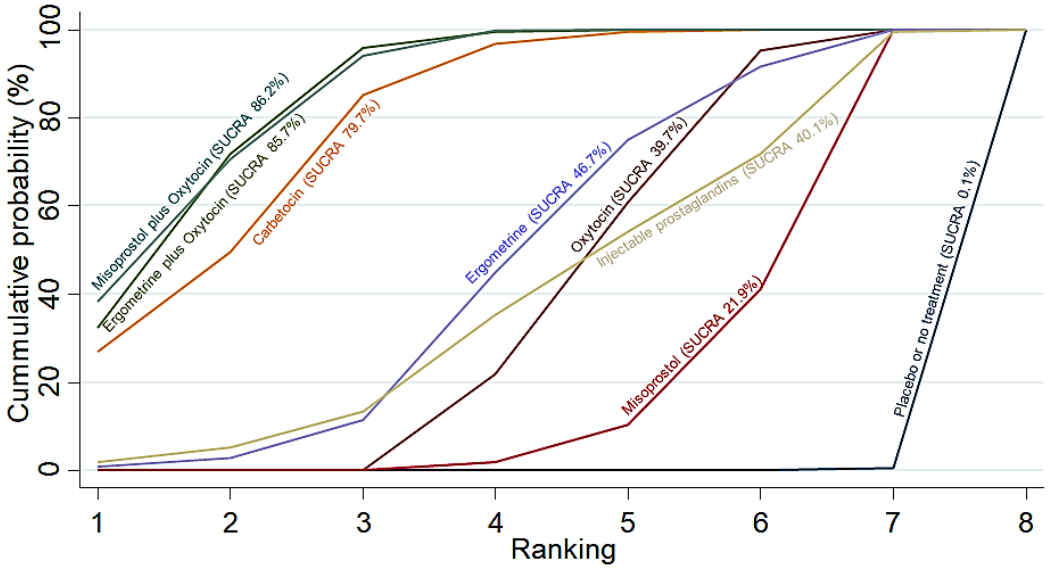


Figure 46. Network diagram for prevention of PPH ≥ 1000 mL restricted to misoprostol studies that use a high dose (600 mcg or more). The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison.

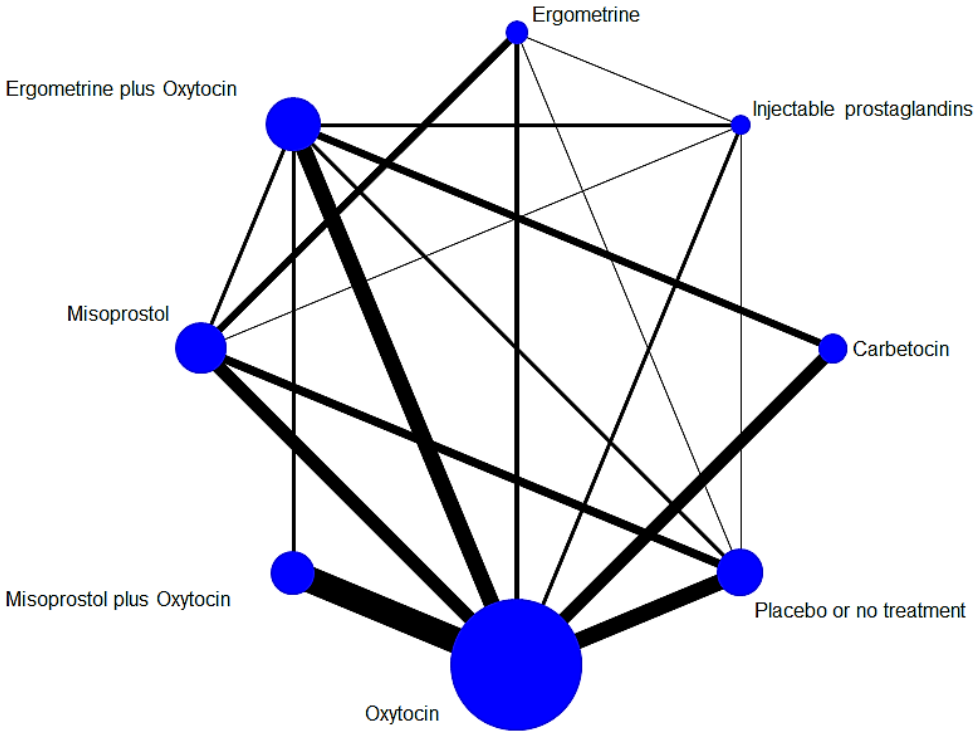


Figure 47. Forest plot with relative risk ratios and 95% CIs from pairwise, indirect and network (combining direct and indirect) analysis for prevention of PPH ≥ 1000 mL restricted to misoprostol studies that use a high dose (600 mcg or more).

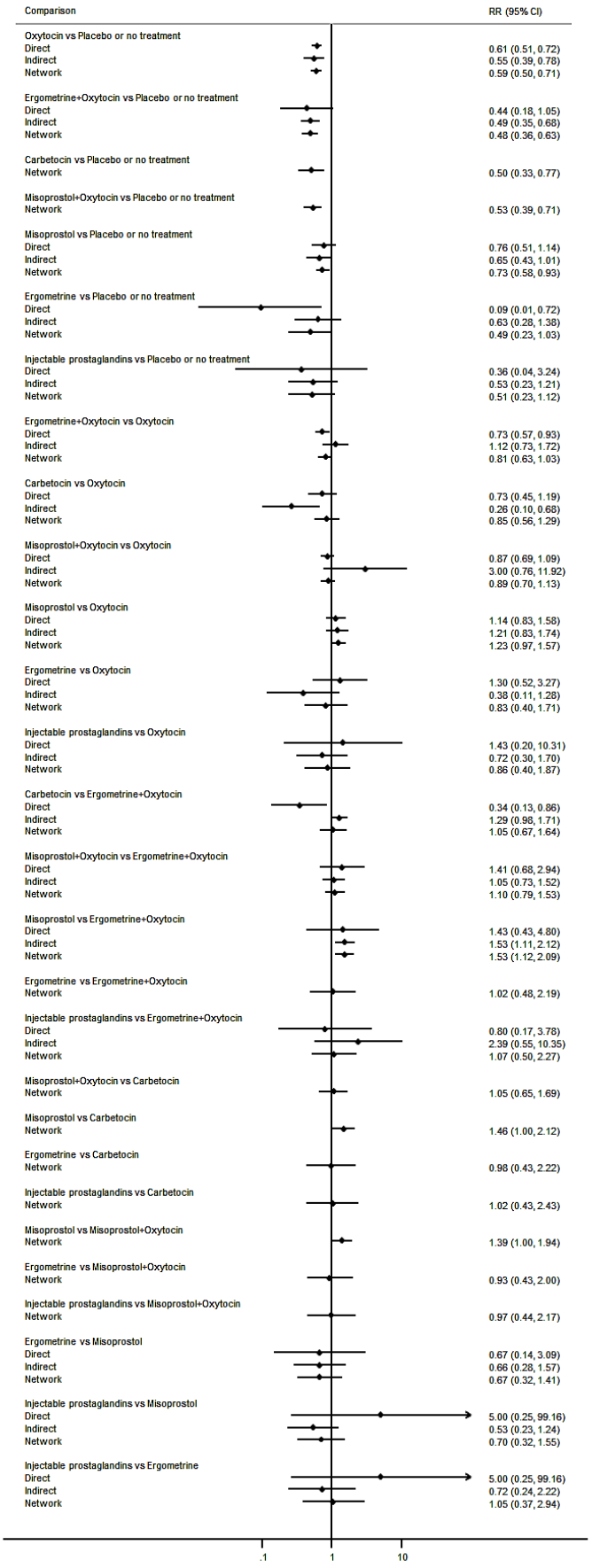


Figure 48. Cumulative rankograms comparing each of the uterotonic drugs for prevention of PPH ≥ 1000 mL restricted to misoprostol studies that use a high dose (600 mcg or more). Ranking indicates the cumulative probability of being the best drug, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SUrface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available drug options.

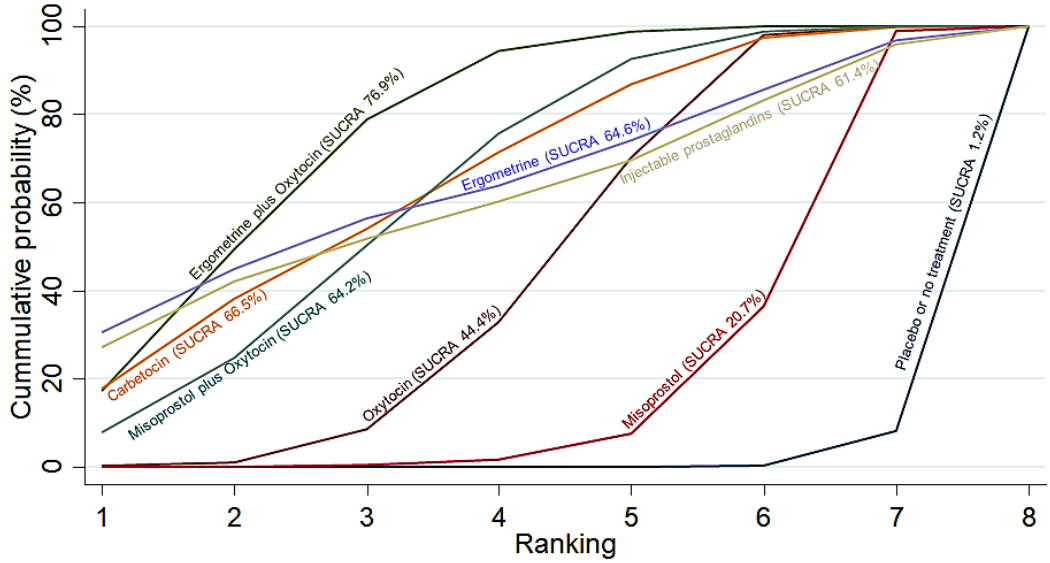


Figure 49. Network diagram for prevention of PPH ≥ 500 mL restricted to oxytocin studies that used an intramuscular or intravenous bolus of any dose. The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison.

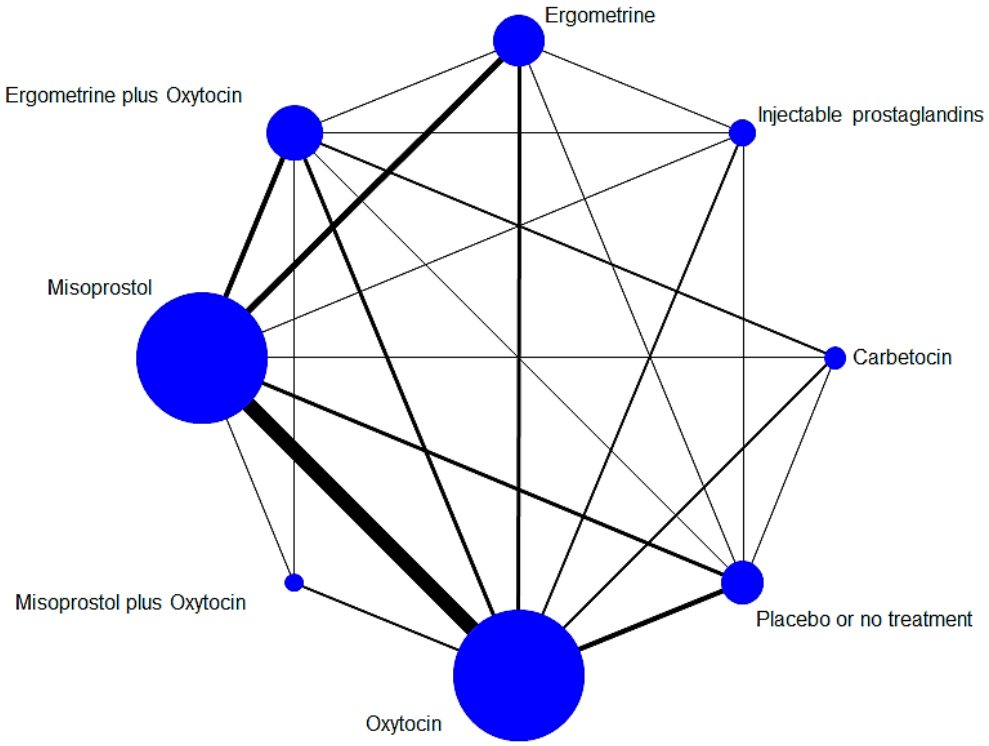


Figure 50. Forest plot with relative risk ratios and 95% CIs from pairwise, indirect and network (combining direct and indirect) analysis for prevention of PPH ≥ 500 restricted to oxytocin studies that used an intramuscular or intravenous bolus of any dose.

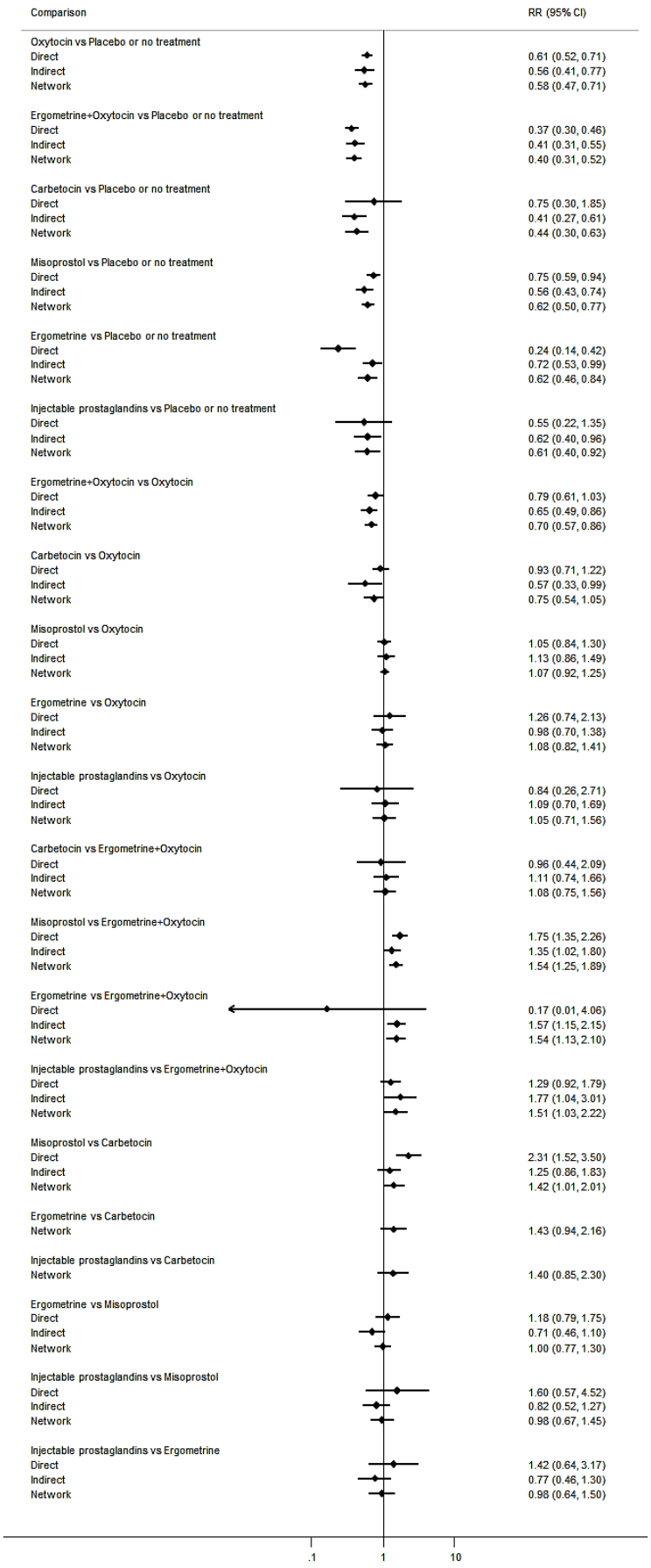


Figure 51. Cumulative rankograms comparing each of the uterotonic drugs for prevention of PPH ≥ 500 restricted to oxytocin studies that used an intramuscular or intravenous bolus of any dose. Ranking indicates the cumulative probability of being the best drug, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SUrface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available drug options.

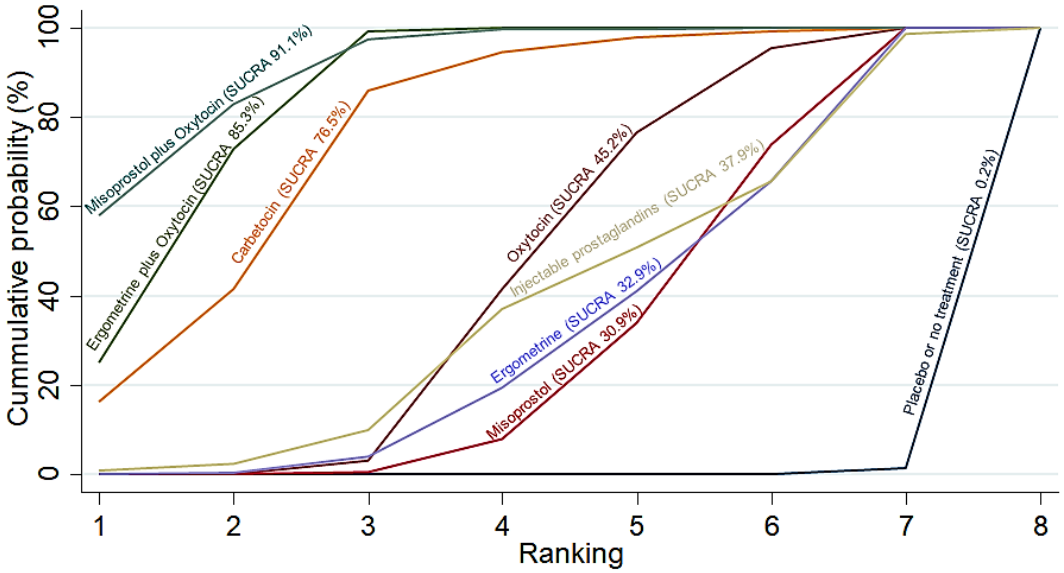


Figure 52. Network diagram for prevention of PPH ≥ 1000 mL restricted to oxytocin studies that used an intramuscular or intravenous bolus of any dose. The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison.

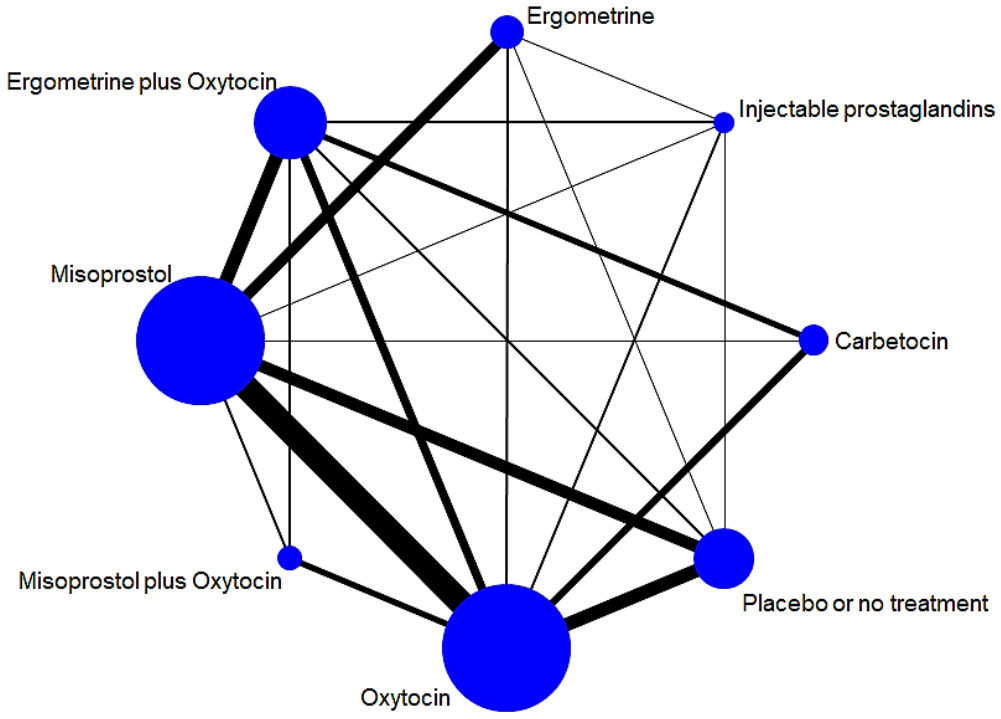


Figure 53. Forest plot with relative risk ratios and 95% CIs from pairwise, indirect and network (combining direct and indirect) analysis for prevention of PPH ≥ 1000 restricted to oxytocin studies that used an intramuscular or intravenous bolus of any dose.

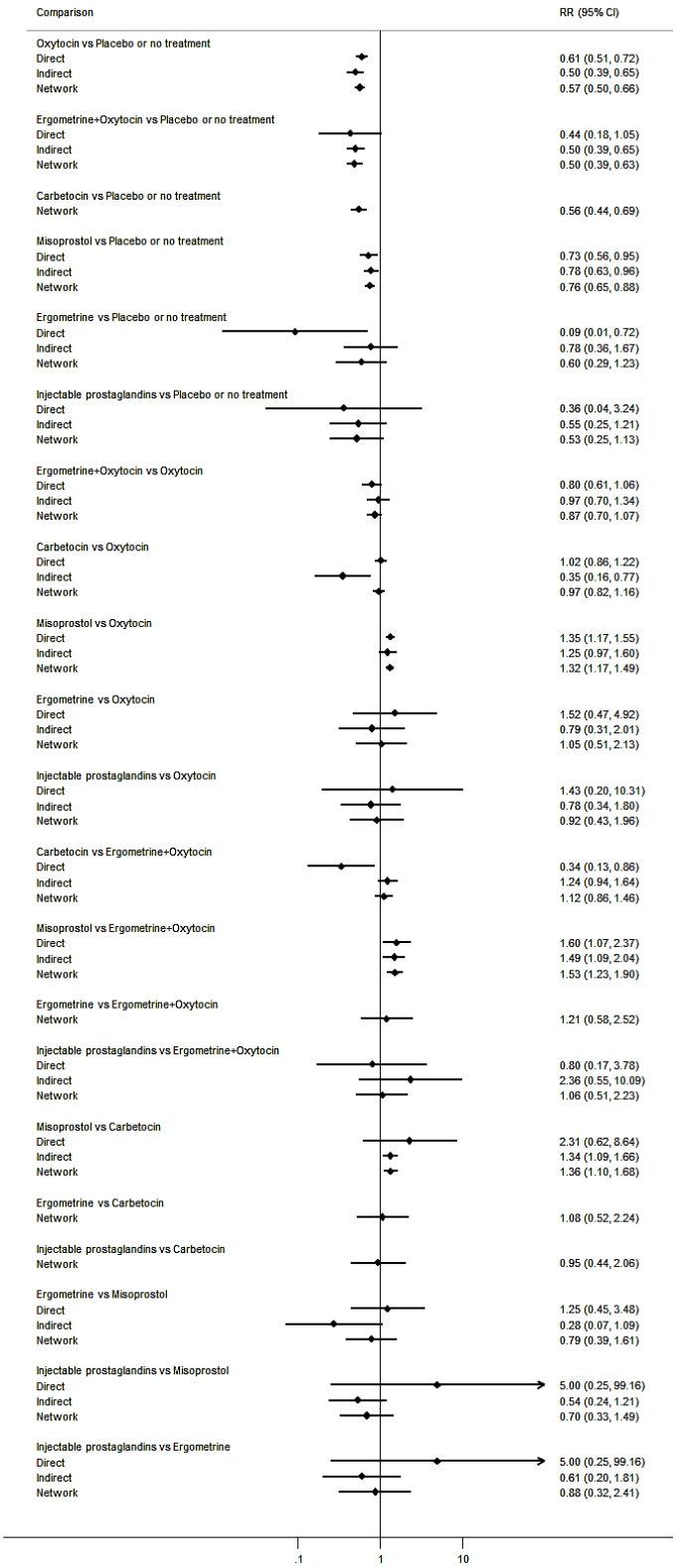


Figure 54. Cumulative rankograms comparing each of the uterotonic drugs for prevention of PPH ≥ 1000 restricted to oxytocin studies that used an intramuscular or intravenous bolus of any dose. Ranking indicates the cumulative probability of being the best drug, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SURface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available drug options.

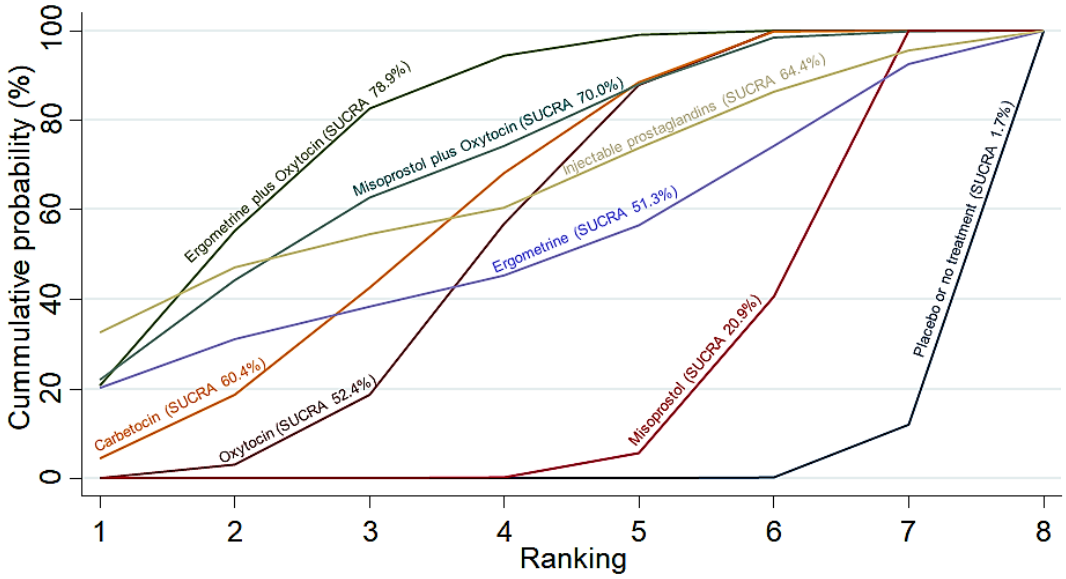


Figure 55. Network diagram for prevention of PPH ≥ 500 mL restricted to oxytocin studies that used an intravenous bolus plus an infusion of any dose. The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison.

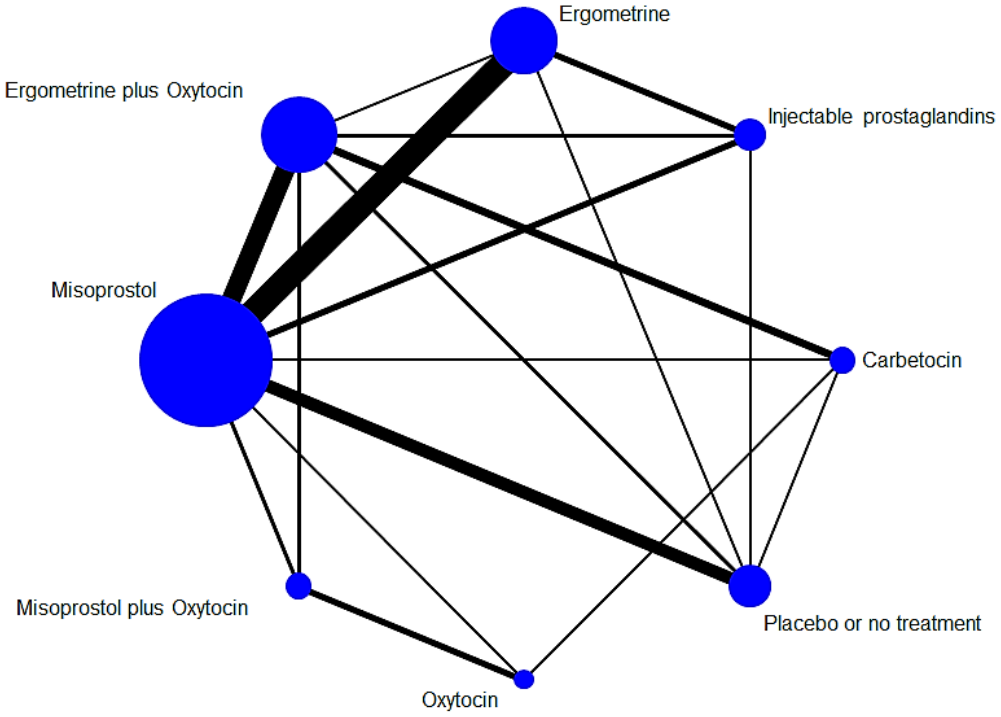


Figure 56. Forest plot with relative risk ratios and 95% CIs from pairwise, indirect and network (combining direct and indirect) analysis for prevention of PPH ≥ 500 restricted to oxytocin studies that used an intravenous bolus plus an infusion of any dose.

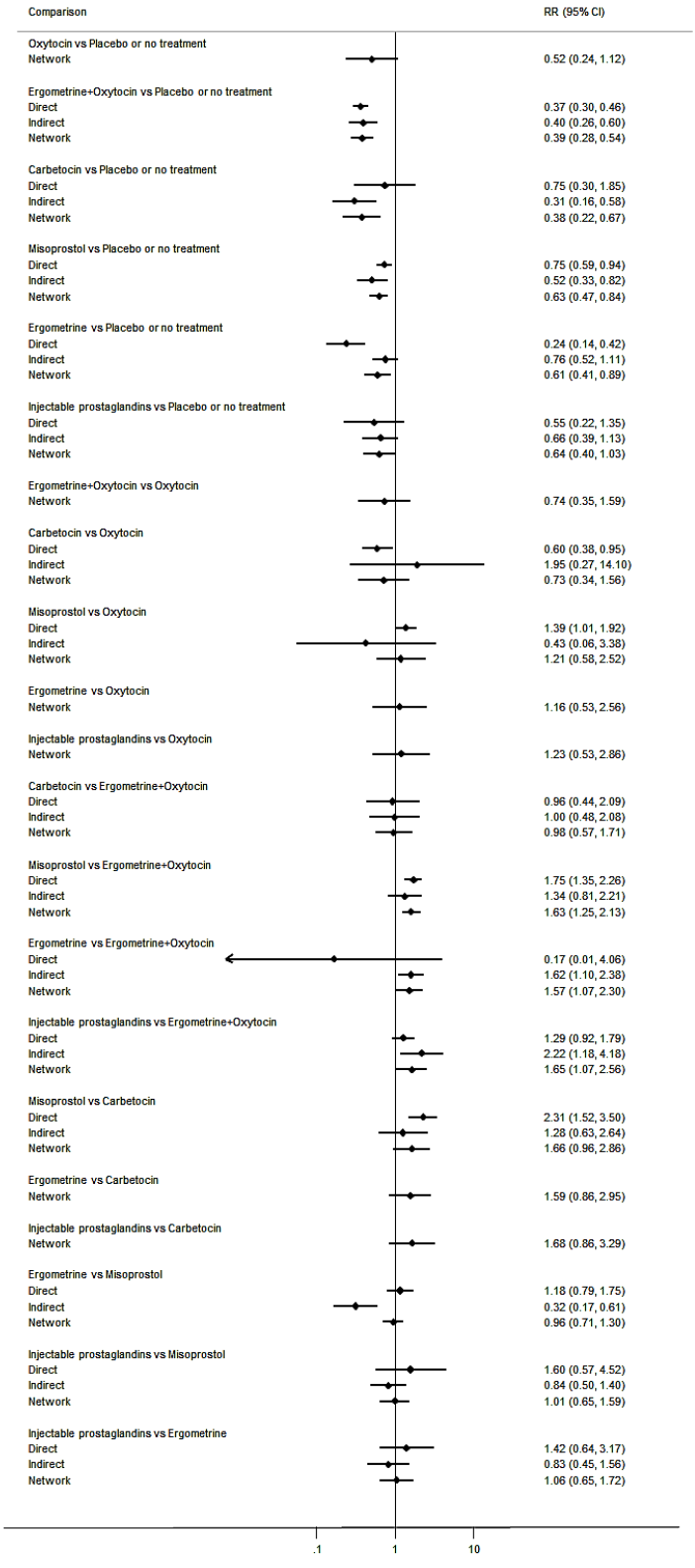


Figure 57. Cumulative rankograms comparing each of the uterotonic drugs for prevention of PPH ≥ 500 restricted to oxytocin studies that used an intravenous bolus plus an infusion of any dose. Ranking indicates the cumulative probability of being the best drug, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SUrface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available drug options.

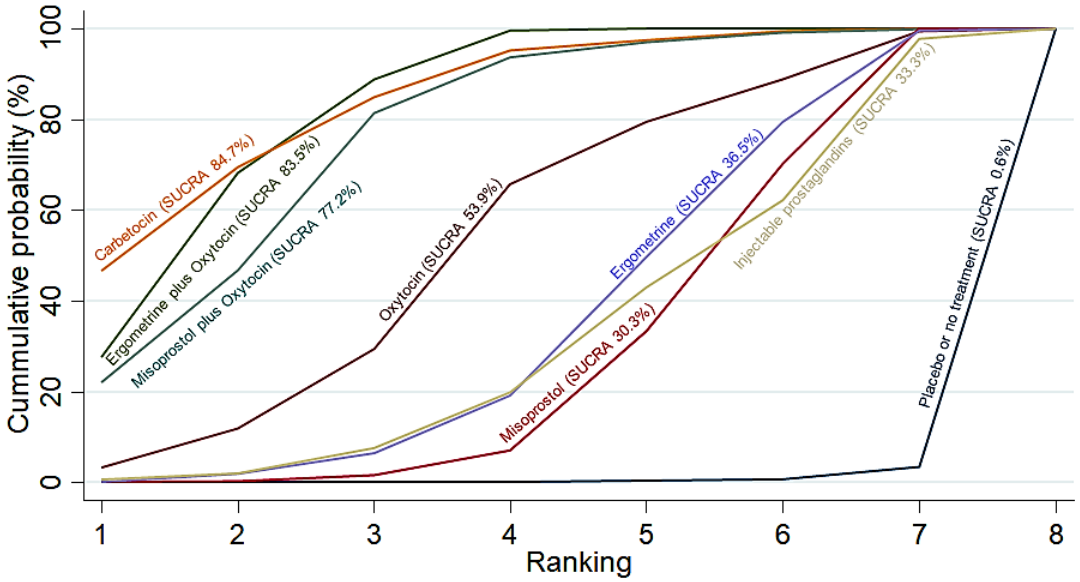


Figure 58. Network diagram for prevention of PPH ≥ 1000 mL restricted to oxytocin studies that used an intravenous bolus plus an infusion of any dose. The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison.

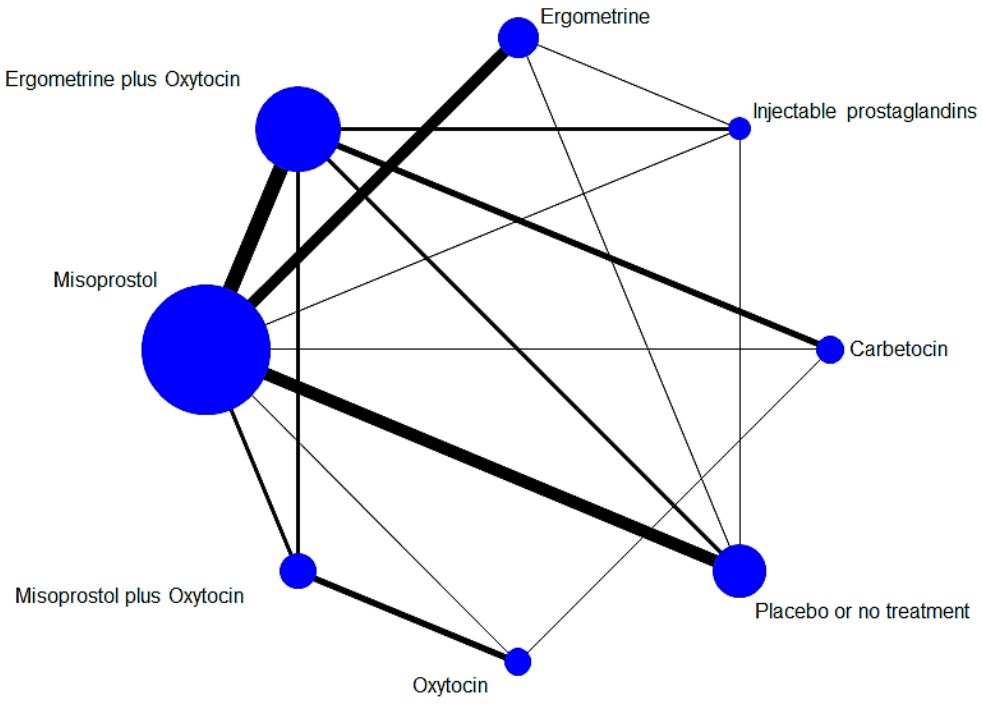


Figure 59. Forest plot with relative risk ratios and 95% CIs from pairwise, indirect and network (combining direct and indirect) analysis for prevention of PPH ≥ 1000 restricted to oxytocin studies that used an intravenous bolus plus an infusion of any dose.

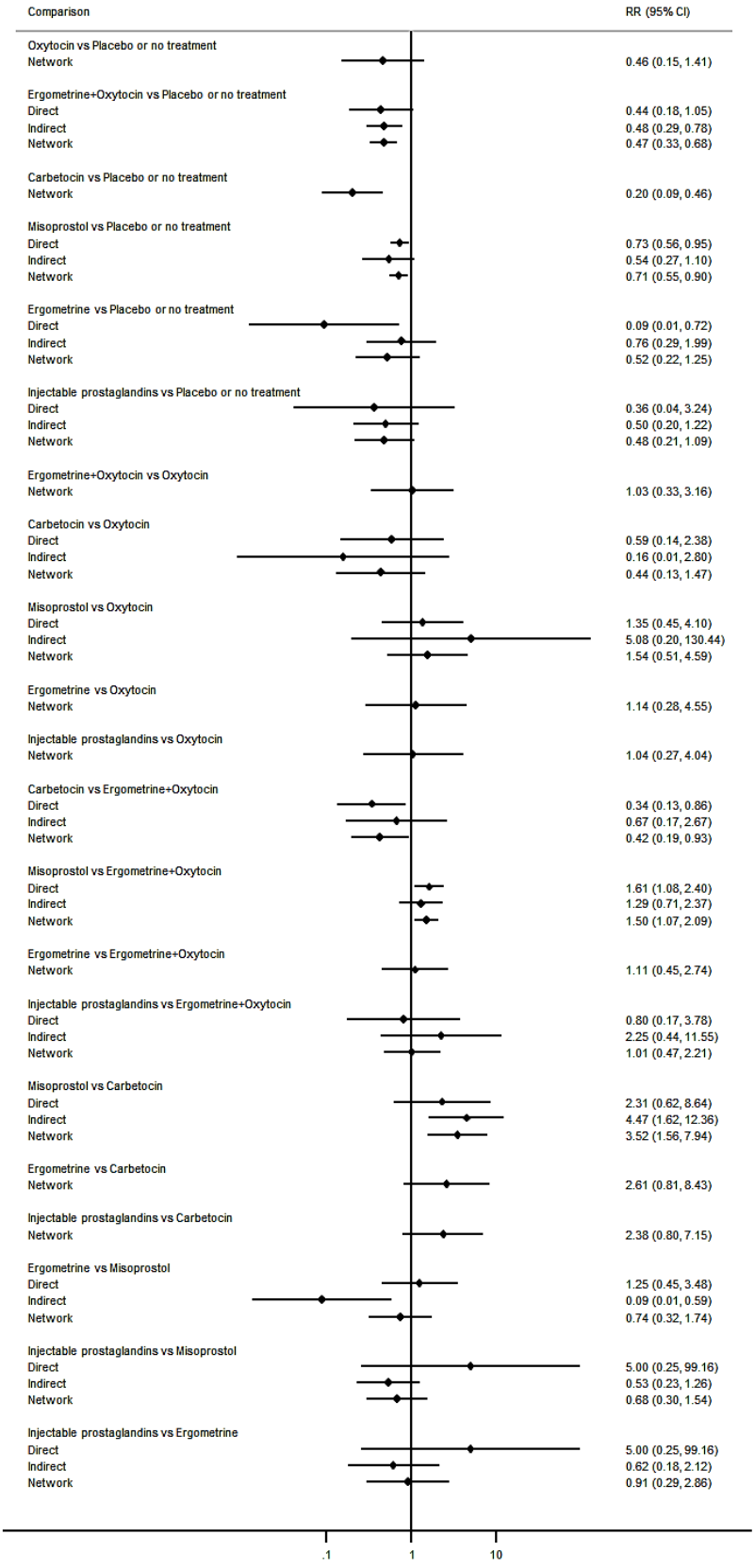


Figure 60. Cumulative rankograms comparing each of the uterotonic drugs for prevention of PPH ≥ 1000 restricted to oxytocin studies that used an intravenous bolus plus an infusion of any dose. Ranking indicates the cumulative probability of being the best drug, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SUrface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available drug options.

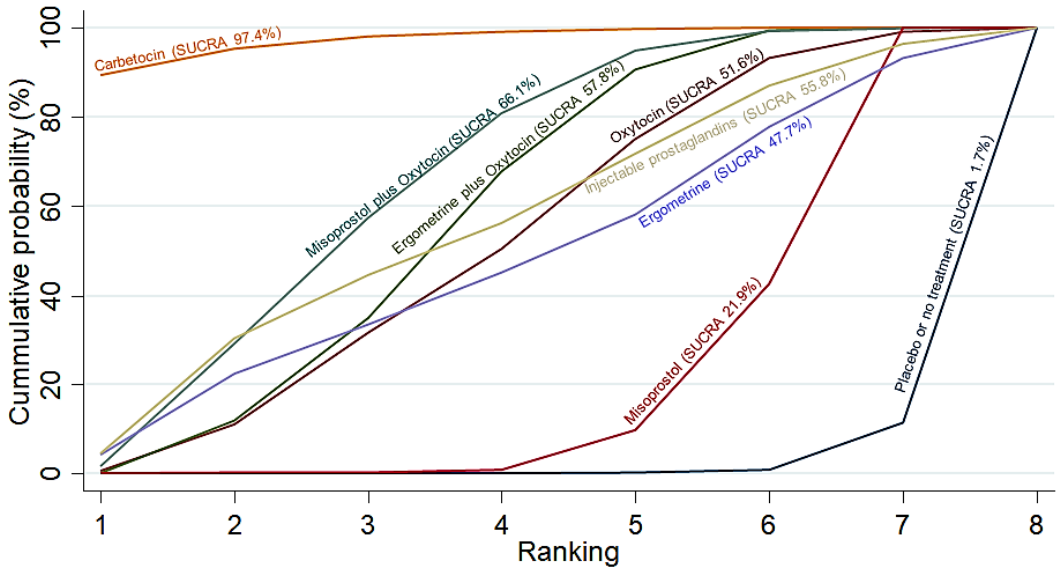


Figure 61. Network diagram for prevention of PPH ≥ 500 mL restricted to oxytocin studies that used an intravenous infusion only of any dose. The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison.

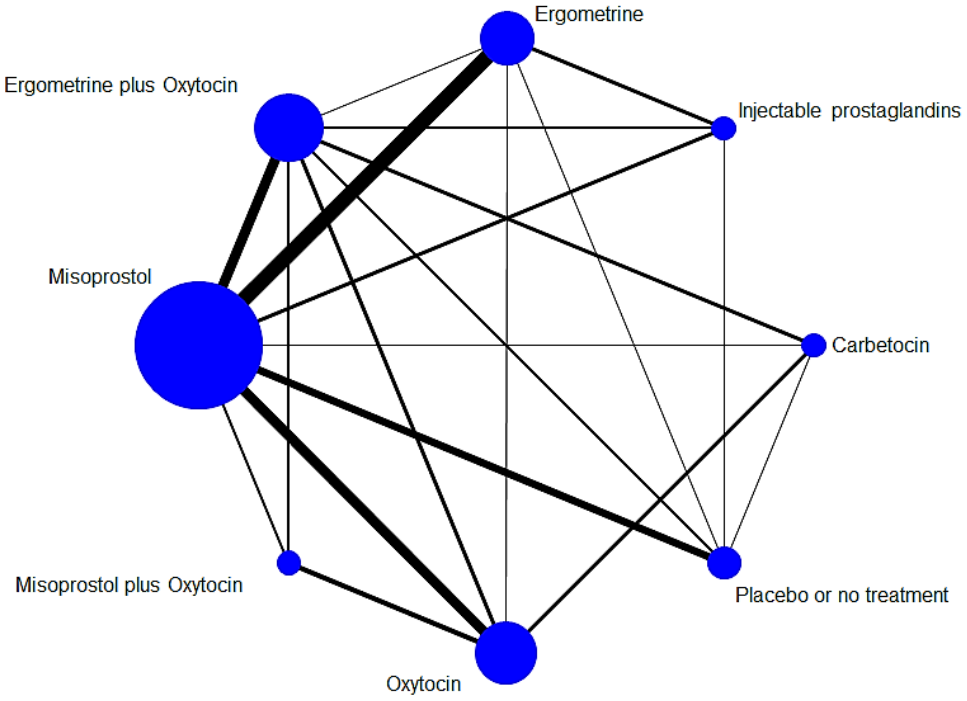


Figure 62. Forest plot with relative risk ratios and 95% CIs from pairwise, indirect and network (combining direct and indirect) analysis for prevention of PPH ≥ 500 restricted to oxytocin studies that used an intravenous infusion only of any dose.

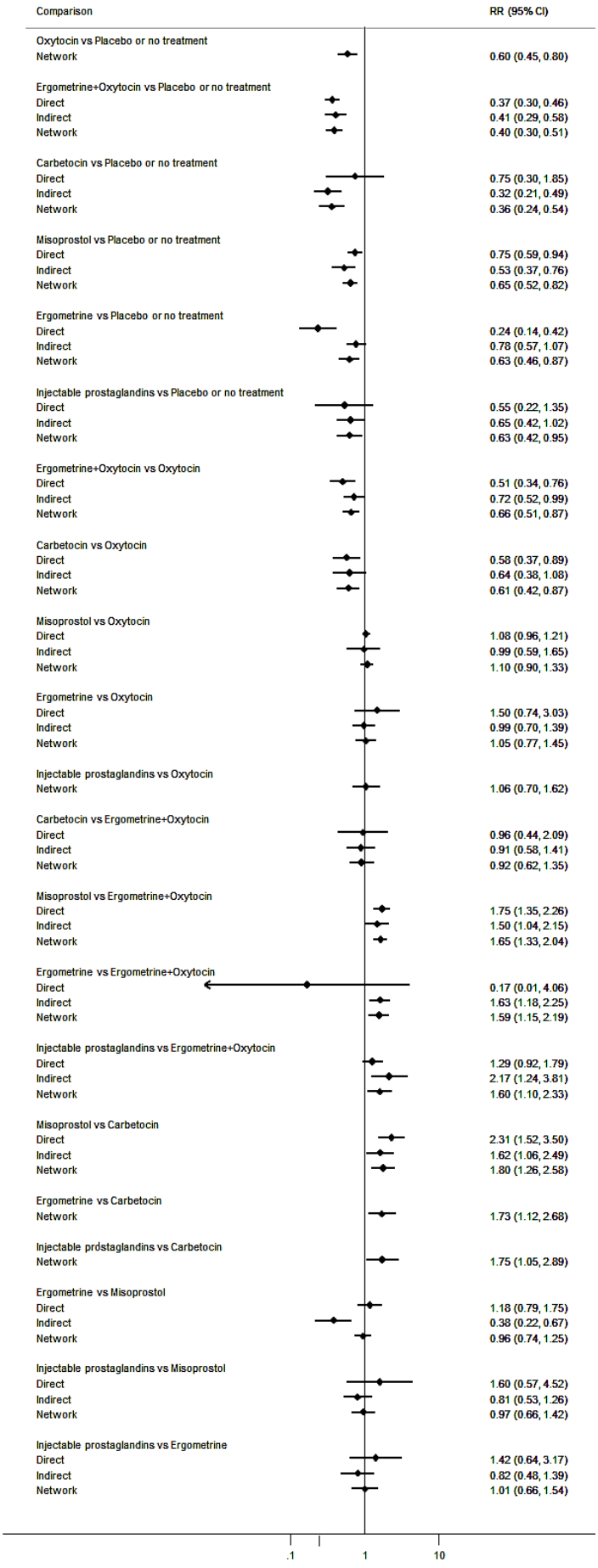


Figure 63. Cumulative rankograms comparing each of the uterotonic drugs for prevention of PPH ≥ 500 restricted to oxytocin studies that used an intravenous infusion only of any dose. Ranking indicates the cumulative probability of being the best drug, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SURface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available drug options.

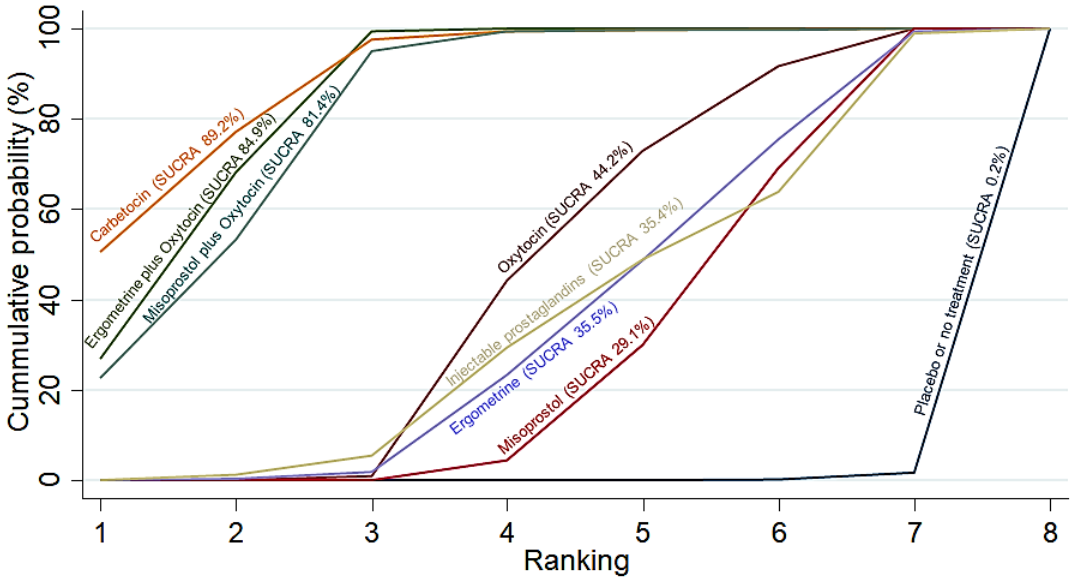


Figure 64. Network diagram for prevention of PPH ≥ 1000 mL restricted to oxytocin studies that used an intravenous infusion only of any dose. The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison.

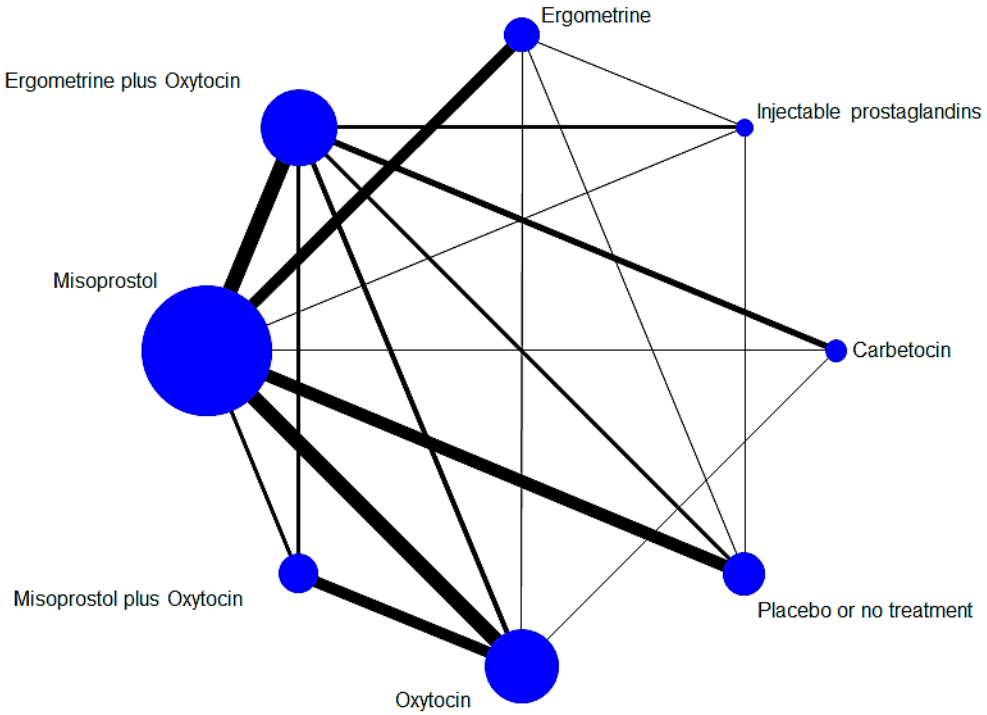


Figure 65. Forest plot with relative risk ratios and 95% CIs from pairwise, indirect and network (combining direct and indirect) analysis for prevention of PPH ≥ 1000 restricted to oxytocin studies that used an intravenous infusion only of any dose.

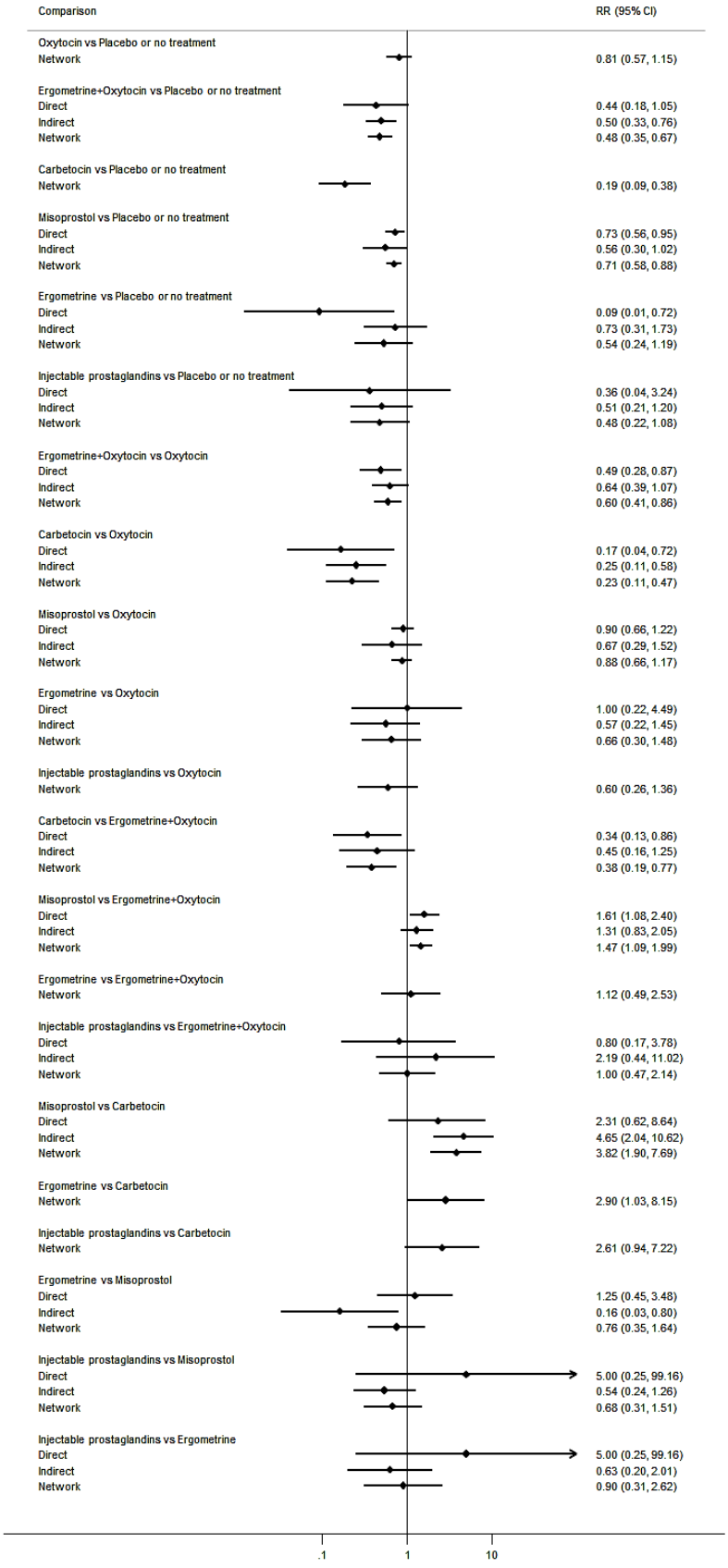


Figure 66. Cumulative rankograms comparing each of the uterotonic drugs for prevention of PPH ≥ 1000 restricted to oxytocin studies that used an intravenous infusion only of any dose. Ranking indicates the cumulative probability of being the best drug, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SUrface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available drug options.

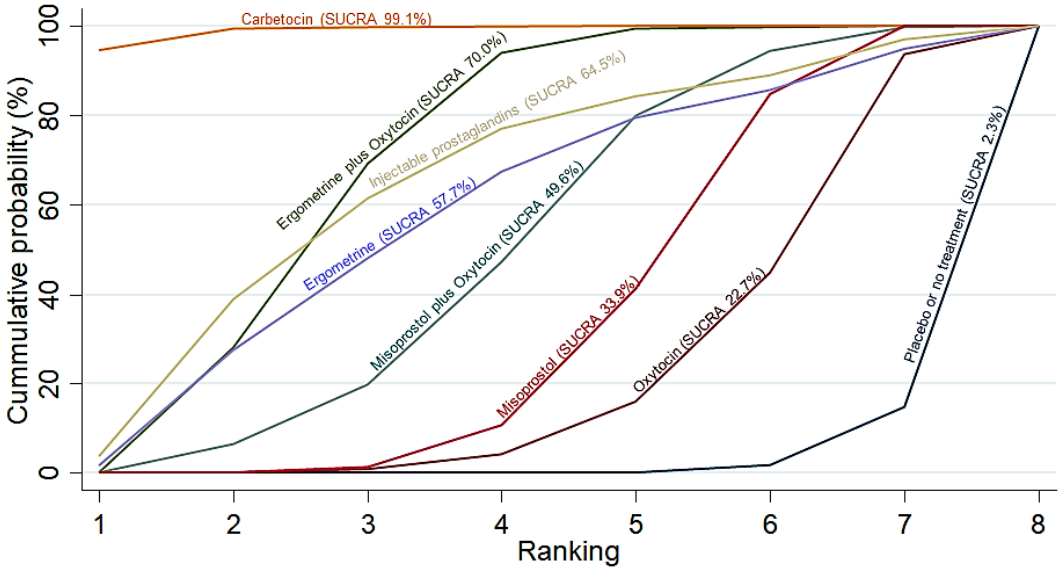


Figure 67. Network diagram for prevention of PPH ≥ 500 mL by quality of studies (high quality trials). The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison.

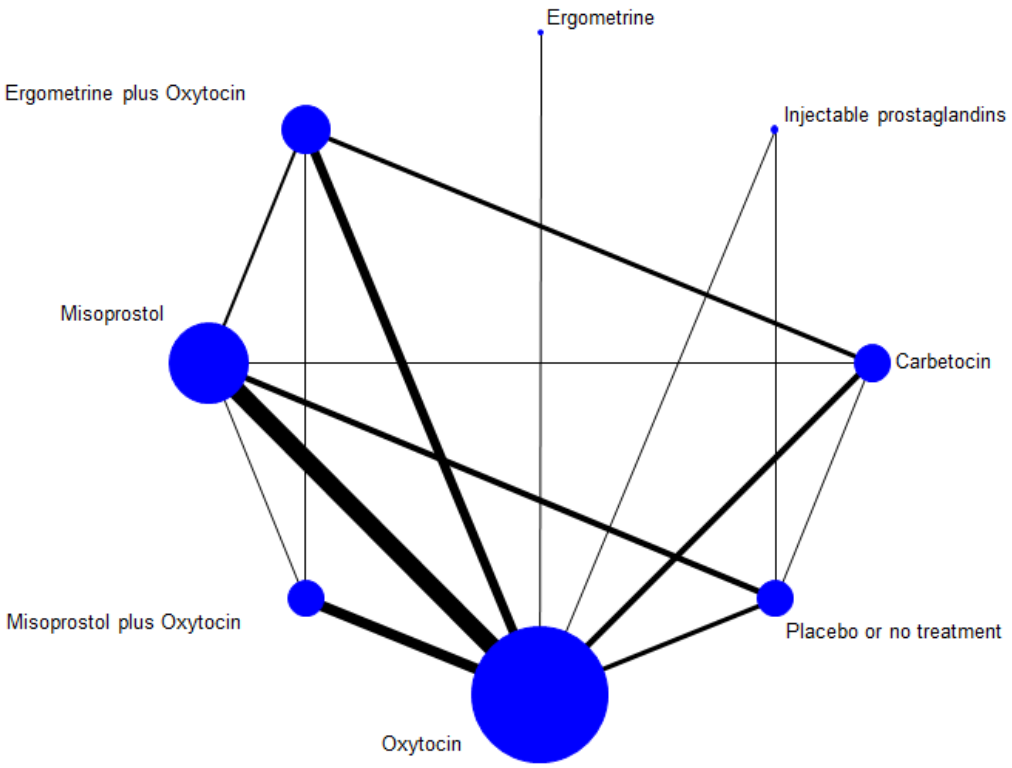


Figure 68. Forest plot with relative risk ratios and 95% CIs from pairwise, indirect and network (combining direct and indirect) analysis for prevention of PPH ≥ 500 mL by quality of studies (high quality trials).

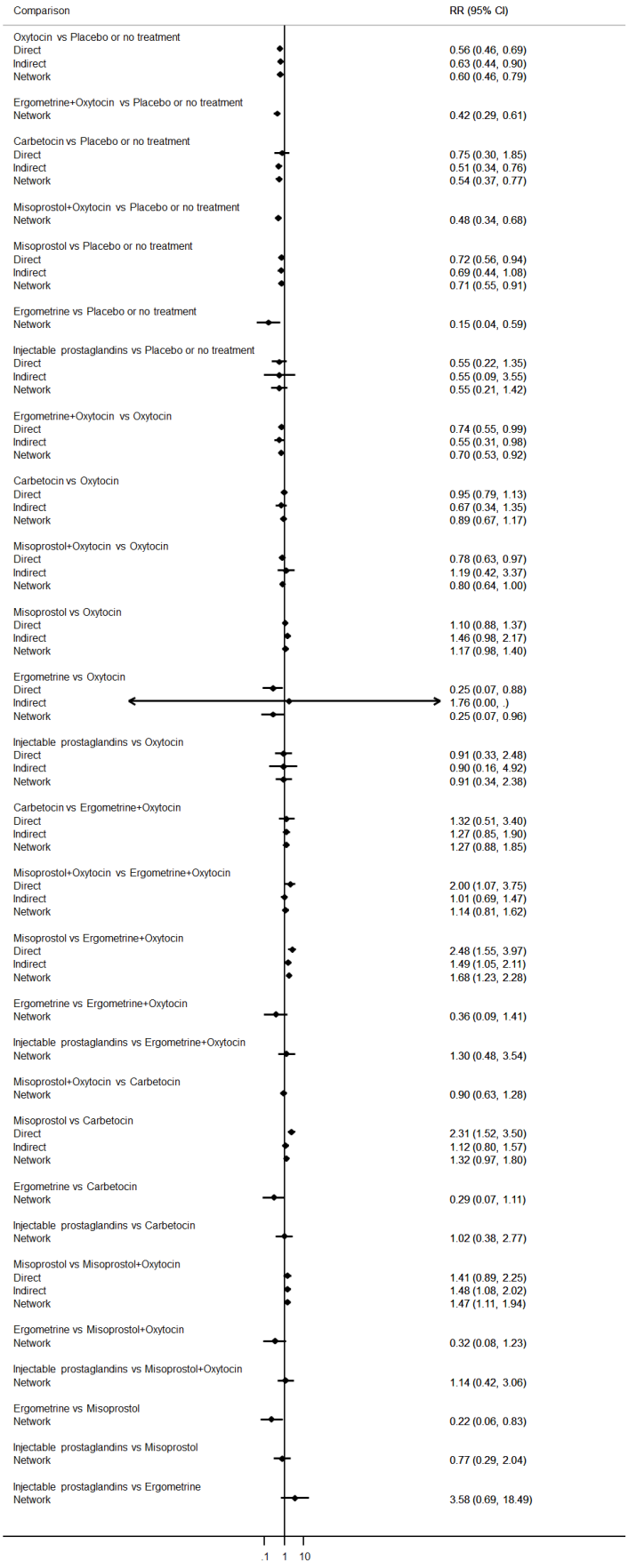


Figure 69. Cumulative rankograms comparing each of the uterotonic drugs for prevention of PPH ≥ 500 mL by quality of studies (high quality trials). Ranking indicates the cumulative probability of being the best drug, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SUrface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available drug options.

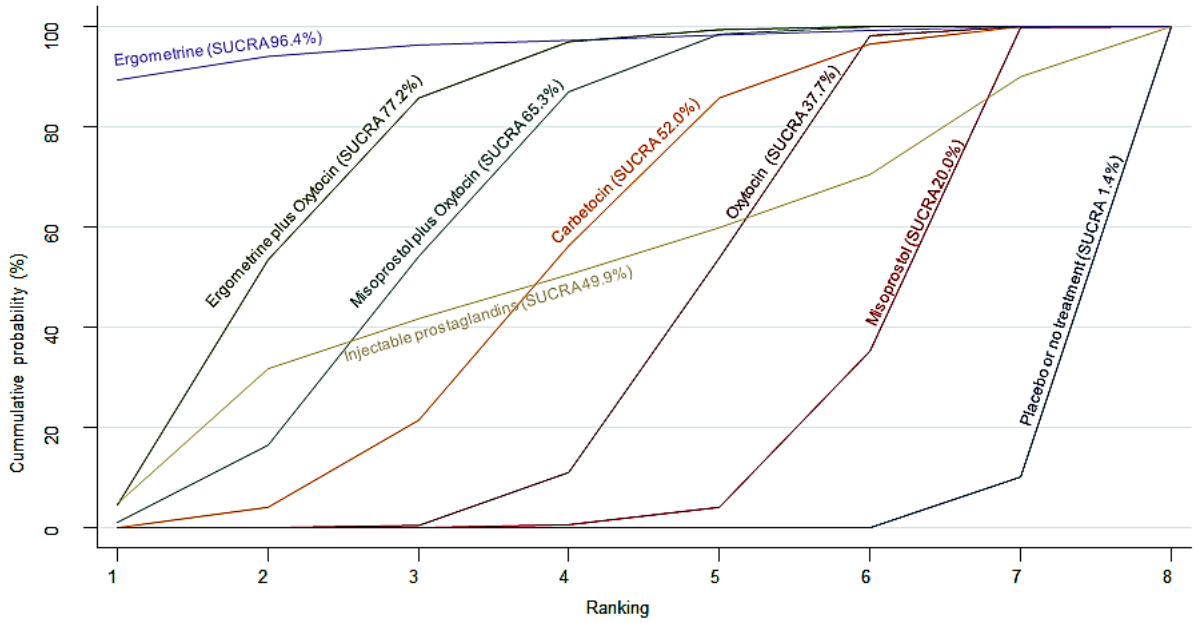


Figure 70. Network diagram for prevention of PPH ≥ 1000 mL by quality of studies (high quality trials). The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison.

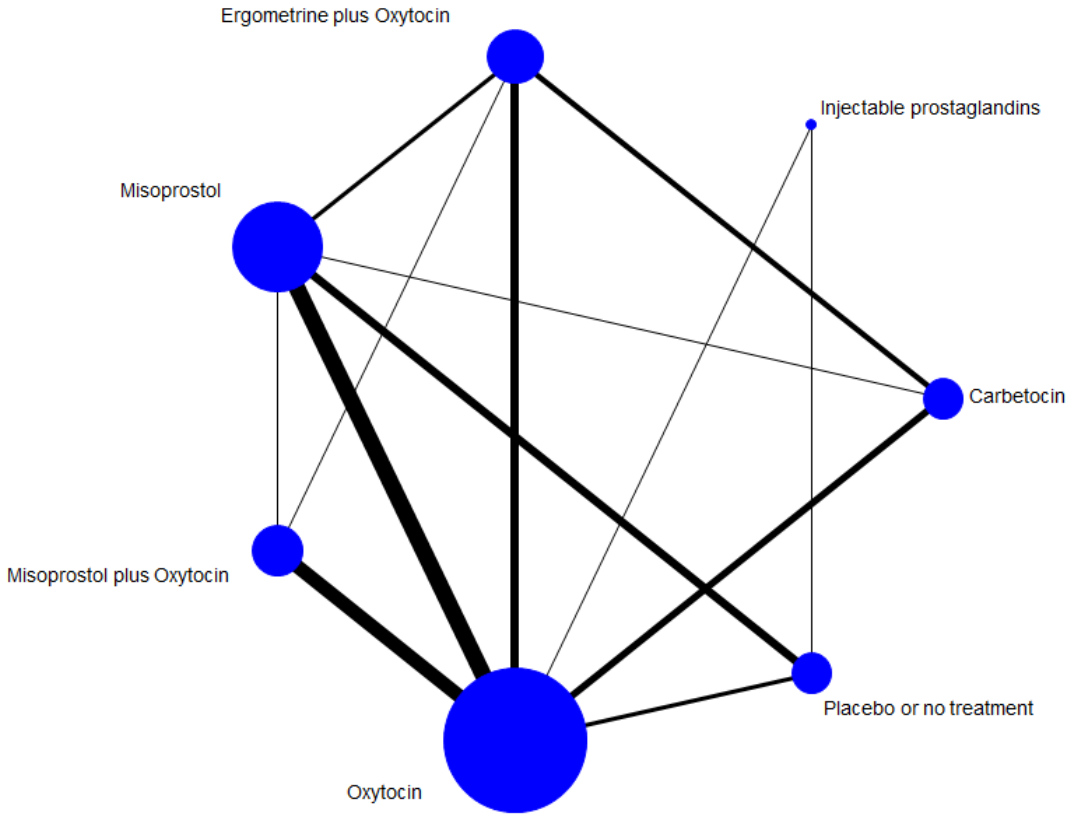


Figure 71. Forest plot with relative risk ratios and 95% CIs from pairwise, indirect and network (combining direct and indirect) analysis for prevention of PPH ≥ 1000 mL by quality of studies (high quality trials).

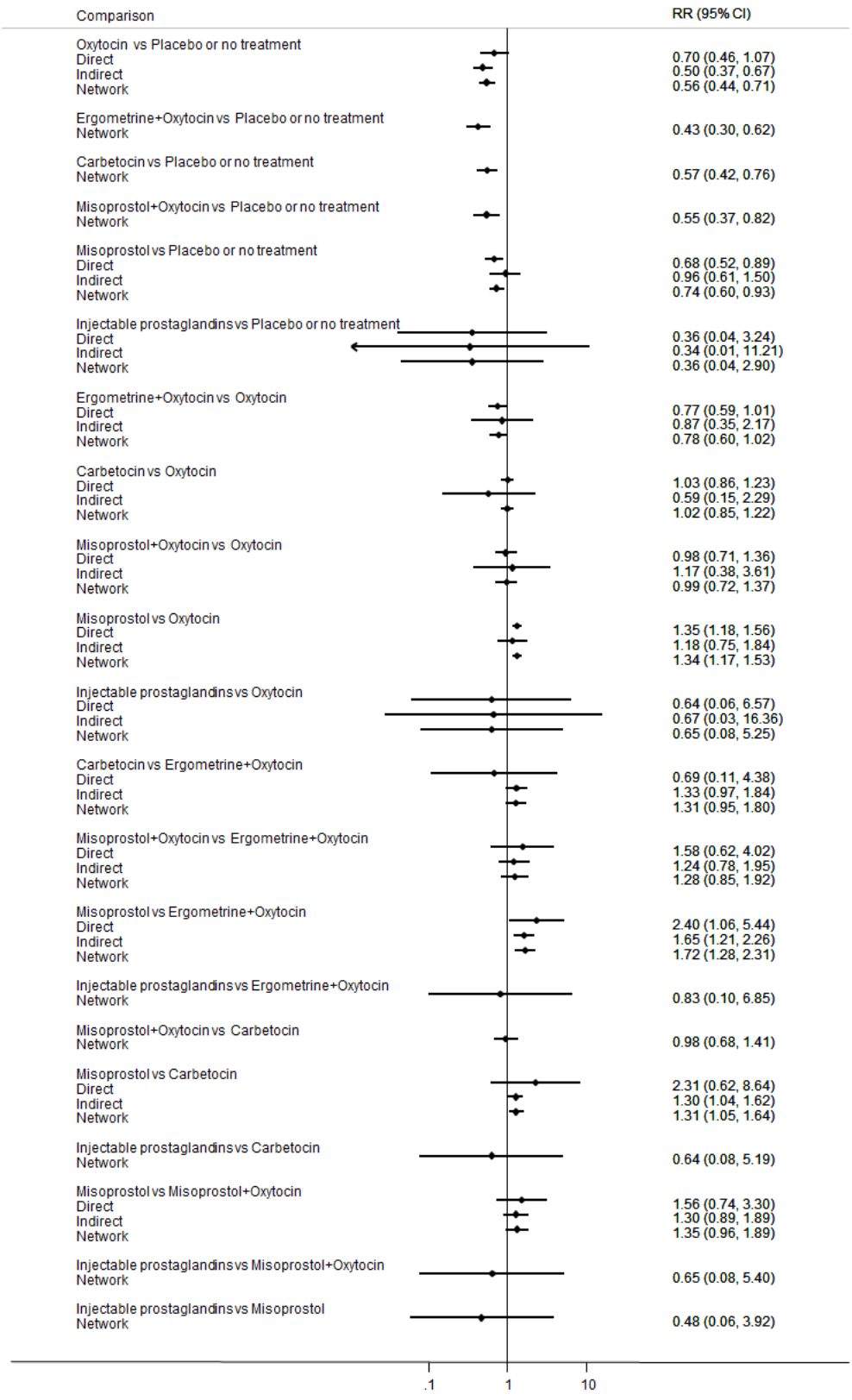


Figure 72. Cumulative rankograms comparing each of the uterotonic drugs for prevention of PPH ≥ 1000 mL by quality of studies (high quality trials). Ranking indicates the cumulative probability of being the best drug, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SUrface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available drug options.

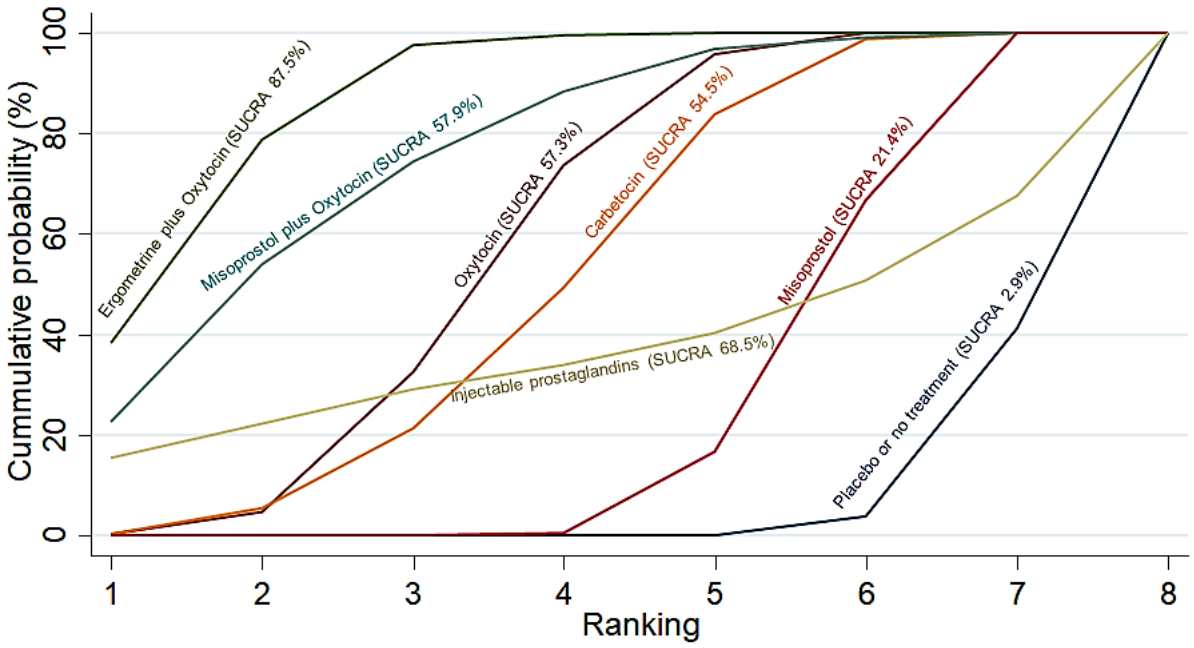


Figure 73. Network diagram for prevention of PPH ≥ 500 mL restricted to studies with funding source at low risk of bias (public or no funding). The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison.

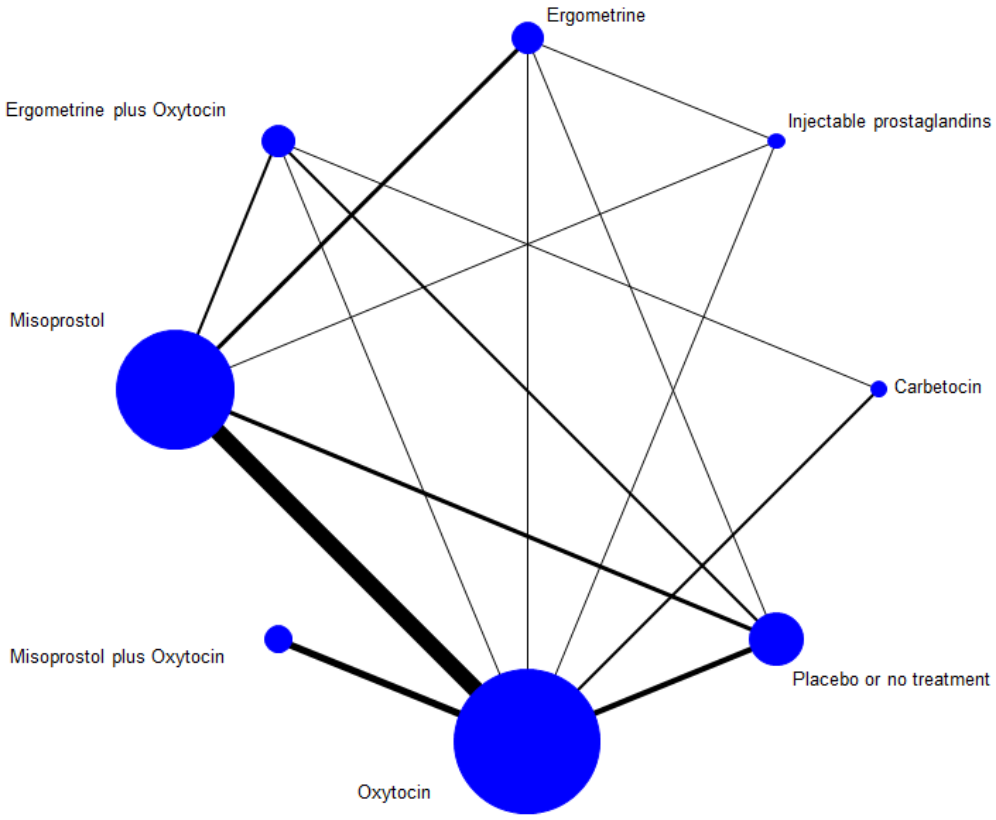


Figure 74. Forest plot with relative risk ratios and 95% CIs from pairwise, indirect and network (combining direct and indirect) analysis for prevention of PPH ≥ 500 mL restricted to studies with funding source at low risk of bias (public or no funding).

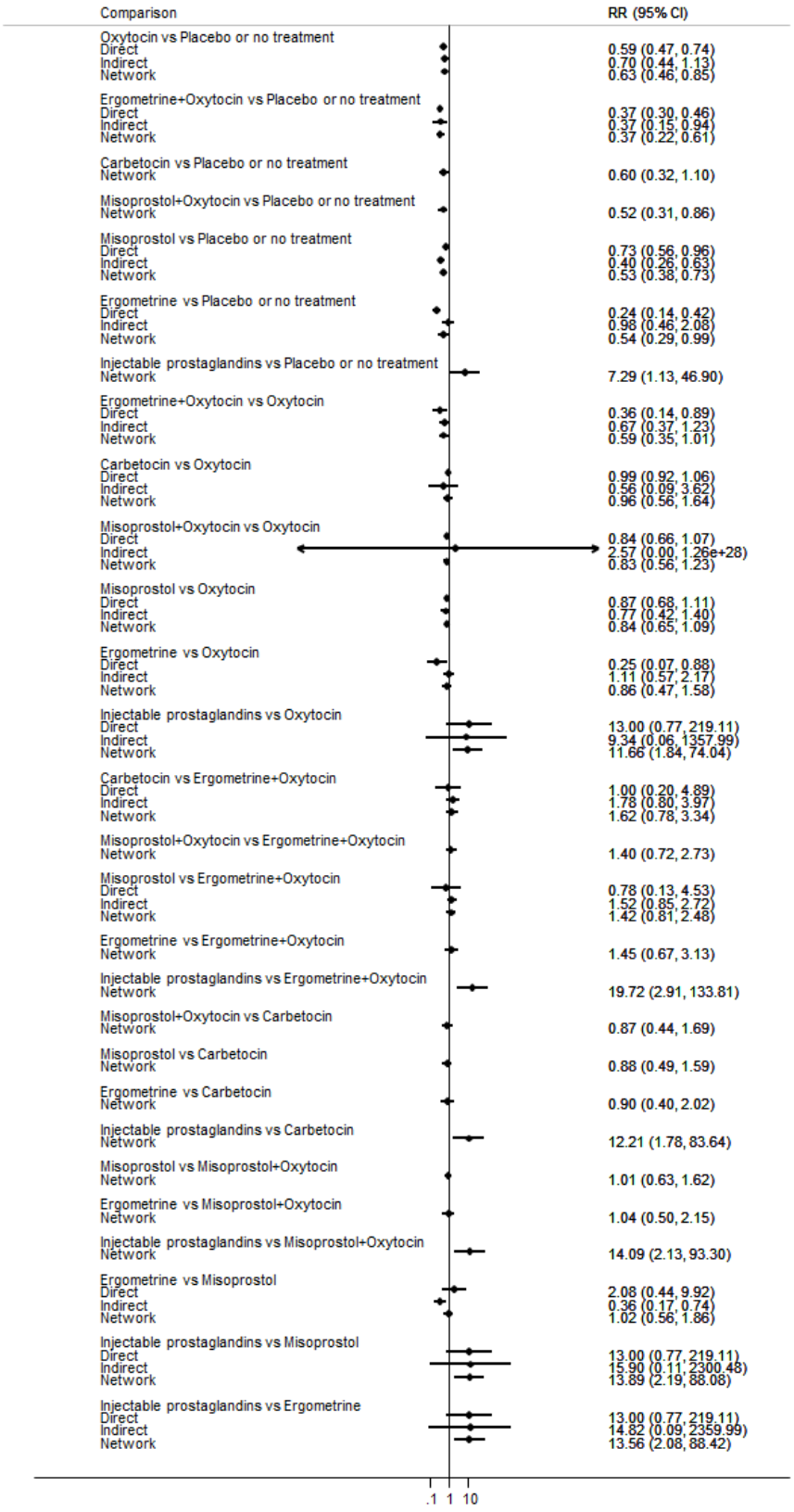


Figure 75. Cumulative rankograms comparing each of the uterotonic drugs for prevention of PPH ≥ 500 mL restricted to studies with funding source at low risk of bias (public or no funding). Ranking indicates the cumulative probability of being the best drug, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SUrface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available drug options.

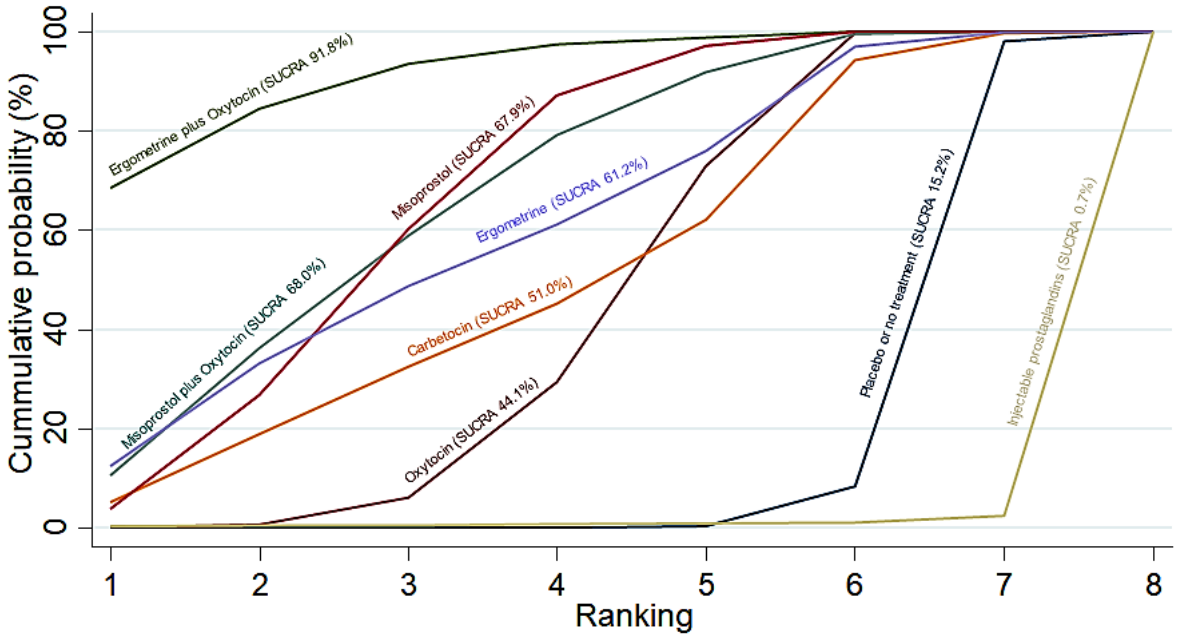


Figure 76. Network diagram for prevention of PPH ≥ 1000 mL restricted to studies with funding source at low risk of bias (public or no funding). The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison.

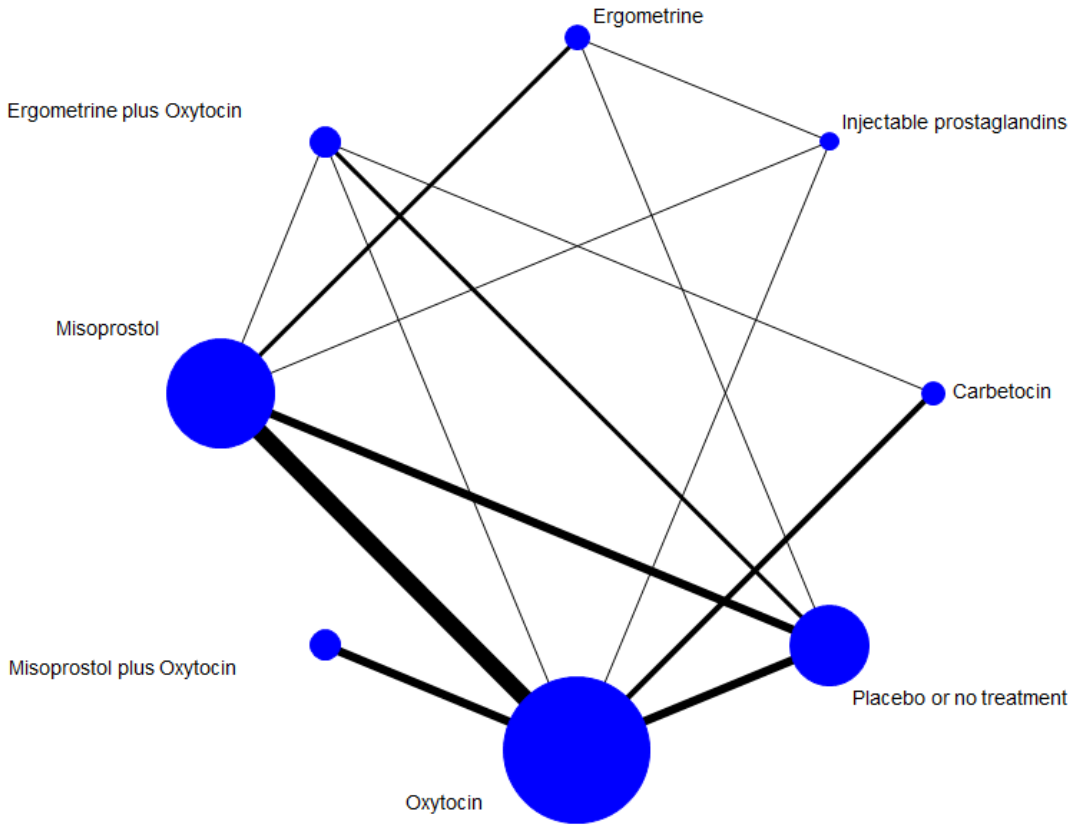


Figure 77. Forest plot with relative risk ratios and 95% CIs from pairwise, indirect and network (combining direct and indirect) analysis for prevention of PPH ≥ 1000 mL restricted to studies with funding source at low risk of bias (public or no funding).

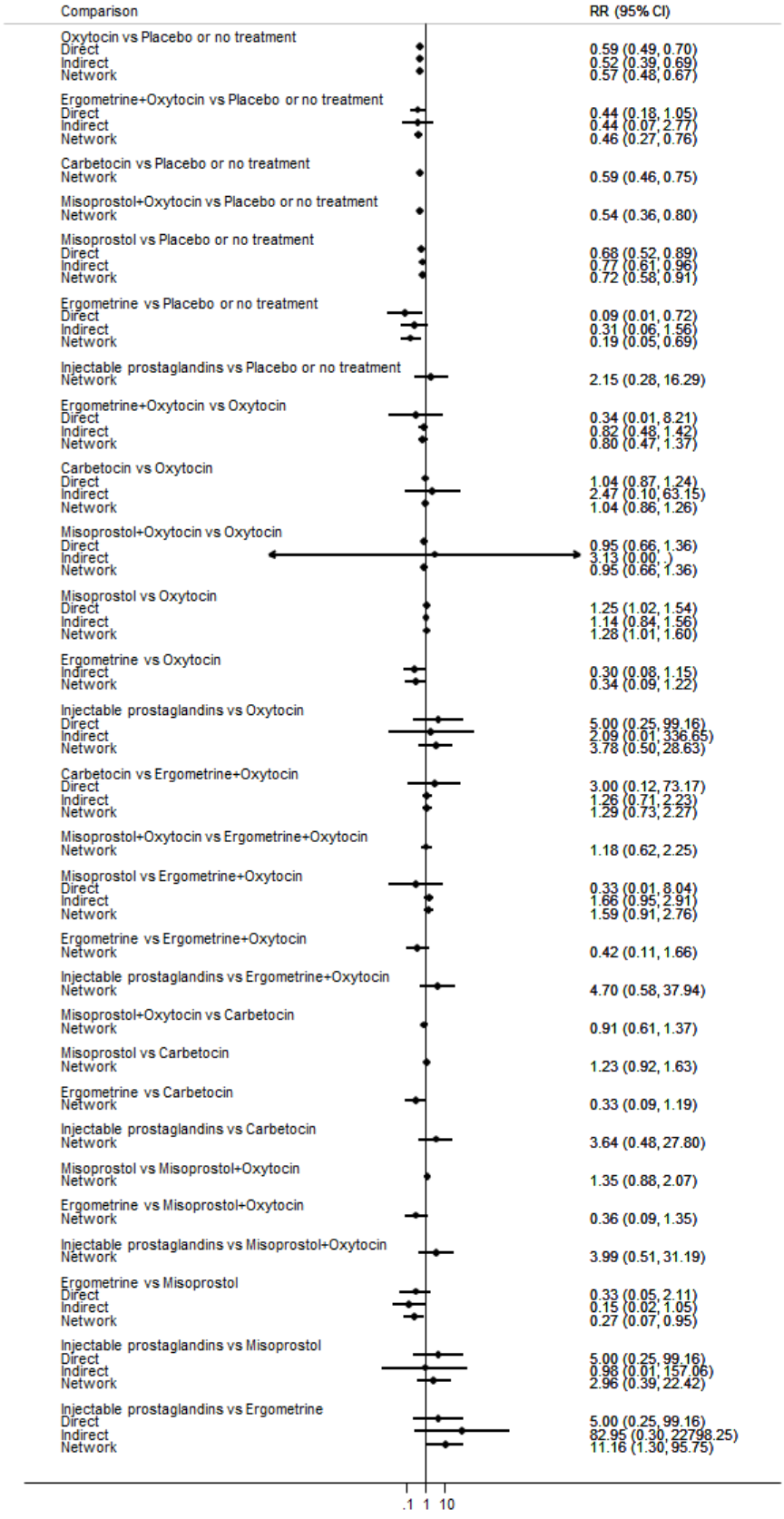


Figure 78. Cumulative rankograms comparing each of the uterotonic drugs for prevention of PPH ≥ 1000 mL restricted to studies with funding source at low risk of bias (public or no funding). Ranking indicates the cumulative probability of being the best drug, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SUrface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available drug options.

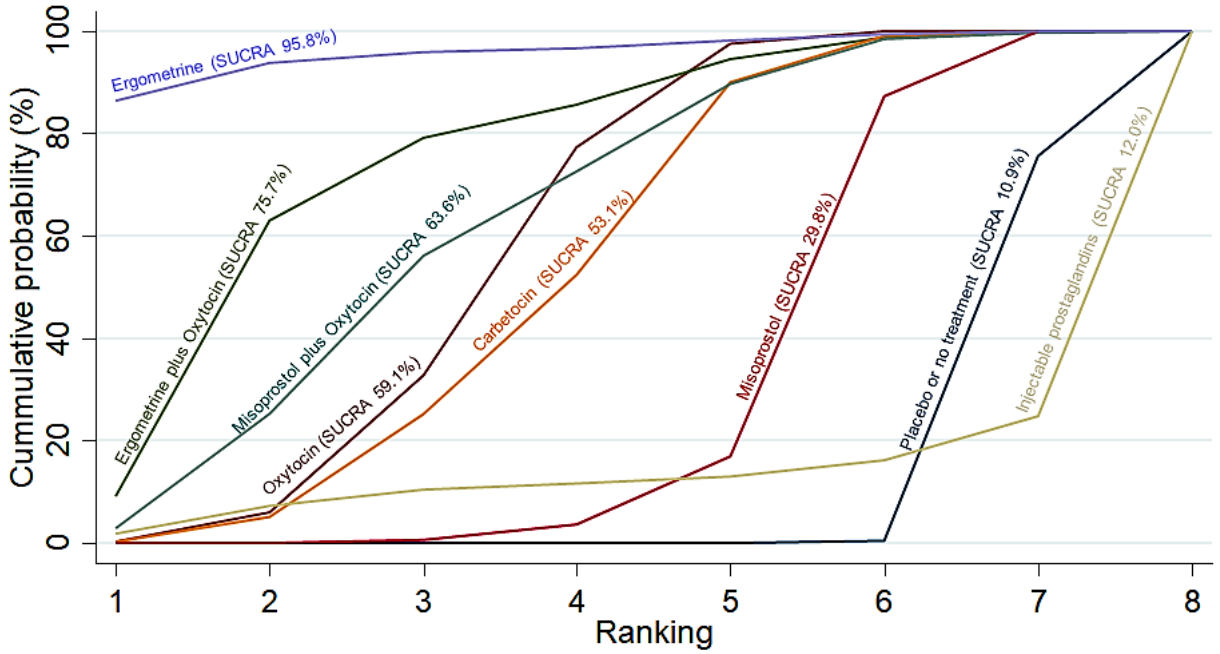


Figure 79. Network diagram for prevention of PPH ≥ 500 mL restricted to studies with an objective method of measuring blood loss. The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison.

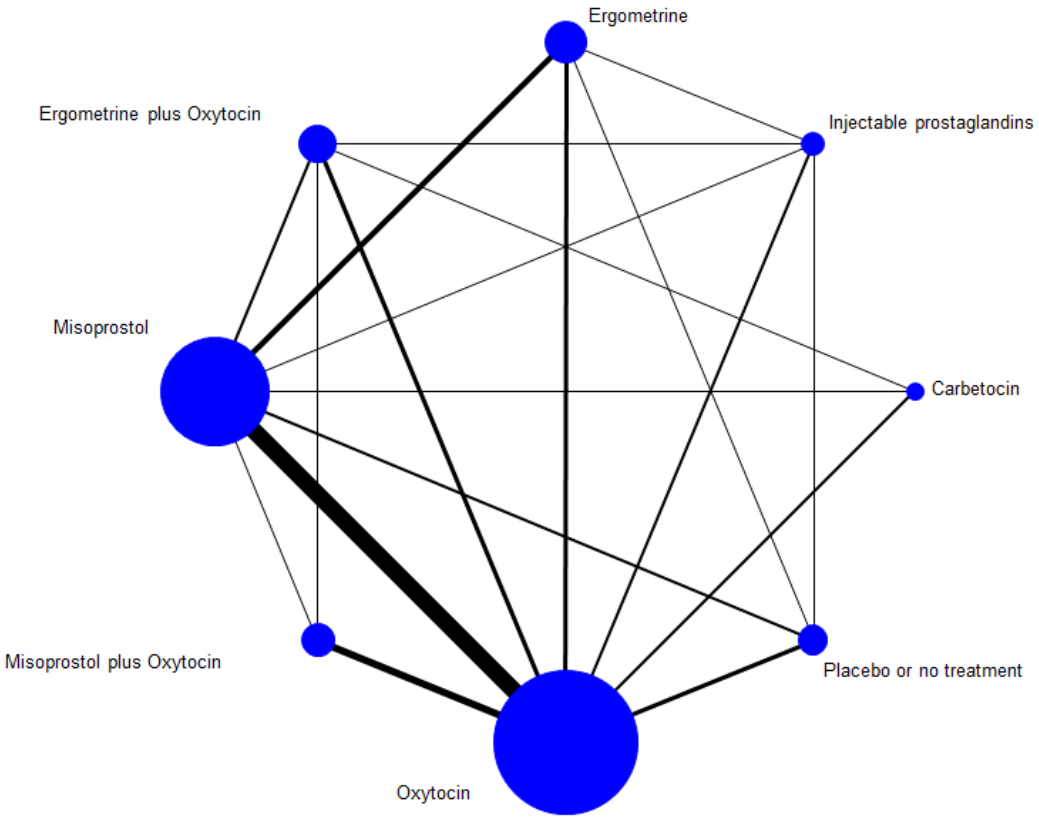


Figure 80. Forest plot with relative risk ratios and 95% CIs from pairwise, indirect and network (combining direct and indirect) analysis for prevention of PPH ≥ 500 mL restricted to studies with an objective method of measuring blood loss.

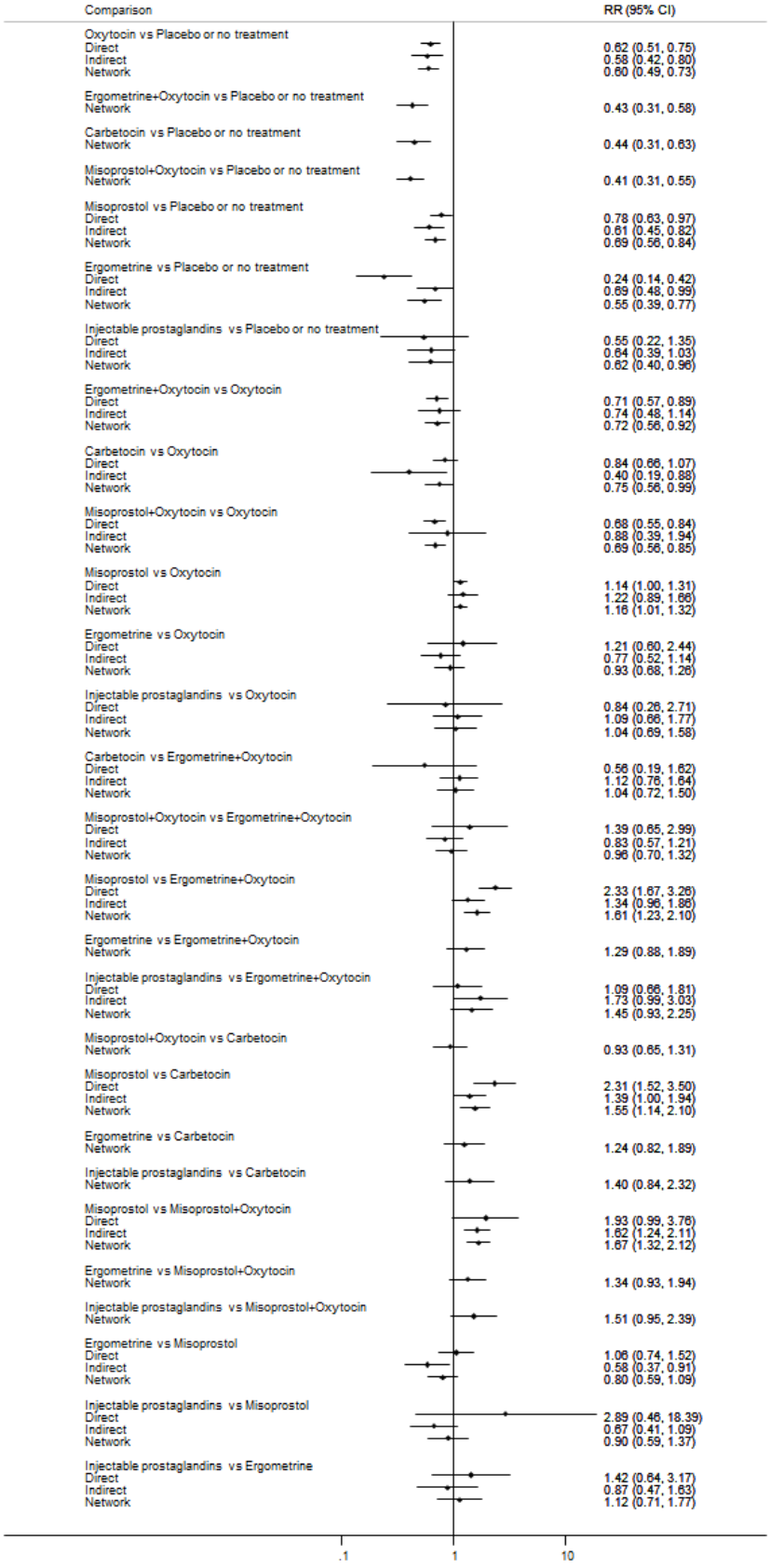


Figure 81. Cumulative rankograms comparing each of the uterotonic drugs for prevention of PPH ≥ 500 mL restricted to studies with an objective method of measuring blood loss. Ranking indicates the cumulative probability of being the best drug, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SUrface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available drug options.

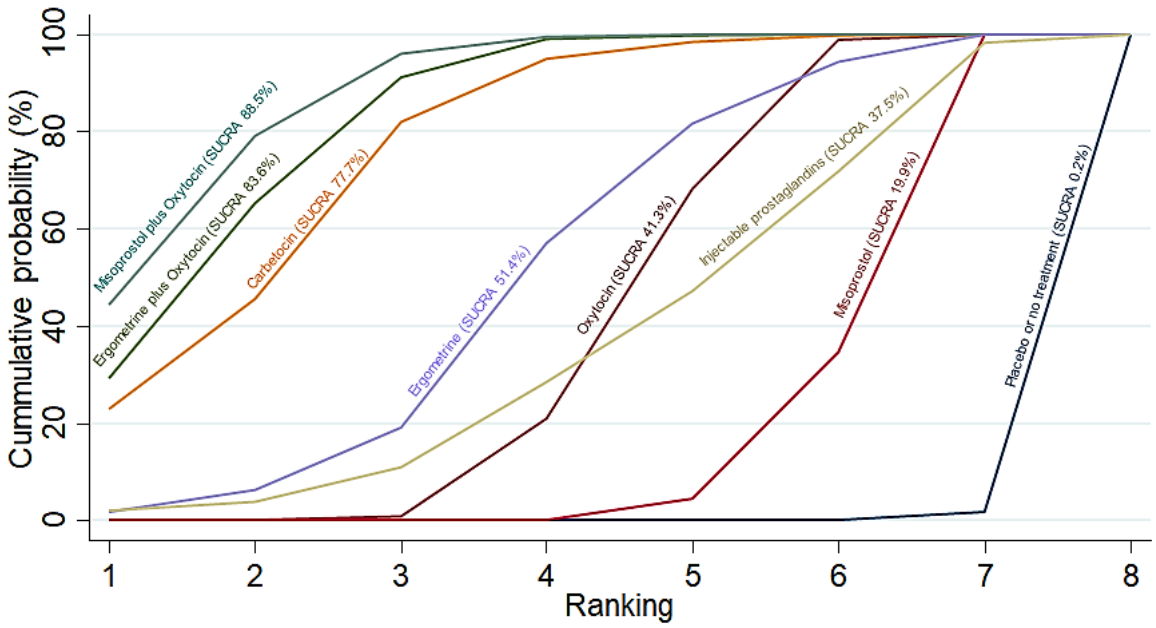


Figure 82. Network diagram for prevention of PPH ≥ 1000 mL restricted to studies with an objective method of measuring blood loss. The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison.

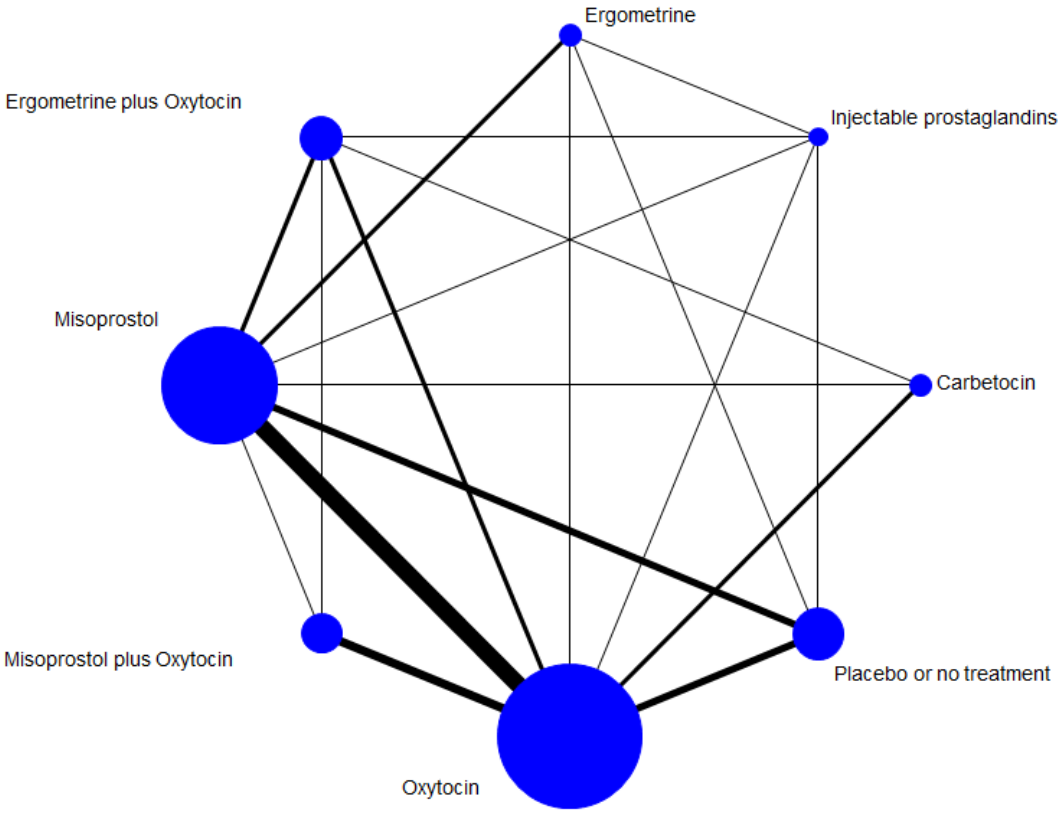


Figure 83. Forest plot with relative risk ratios and 95% CIs from pairwise, indirect and network (combining direct and indirect) analysis for prevention of PPH ≥ 1000 mL restricted to studies with an objective method of measuring blood loss.

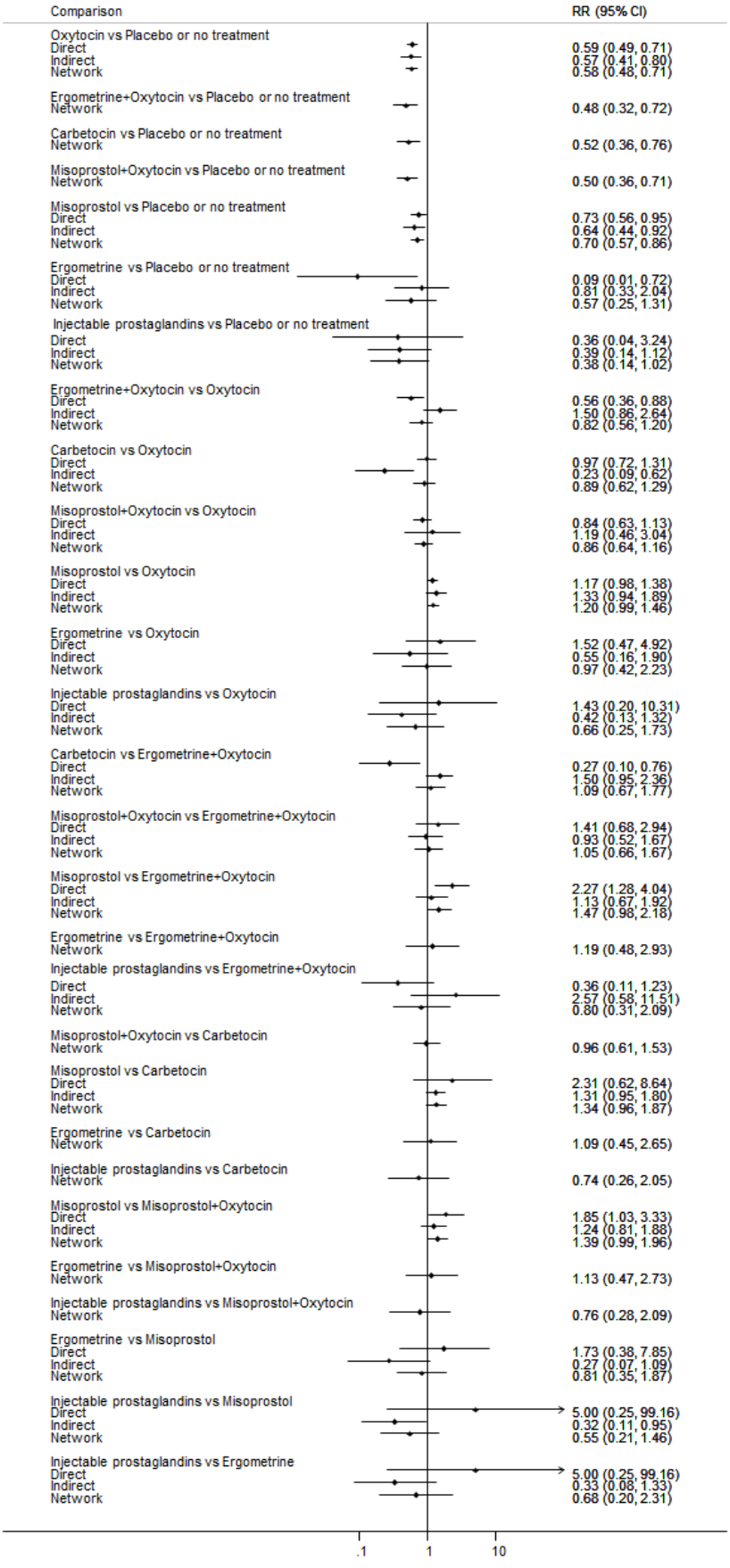


Figure 84. Cumulative rankograms comparing each of the uterotonic drugs for prevention of PPH ≥ 1000 mL restricted to studies with an objective method of measuring blood loss. Ranking indicates the cumulative probability of being the best drug, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SUrface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available drug options.

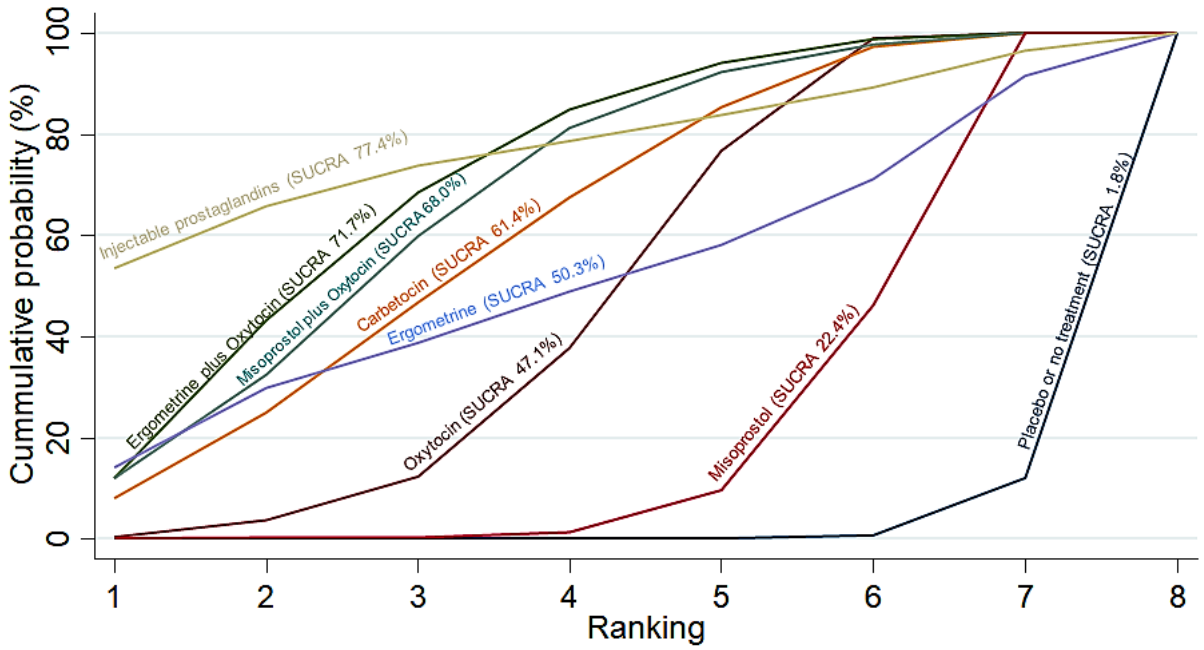


Figure 85. Network diagram for prevention of PPH ≥ 500 mL restricted to large studies (> 400 participants). The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison.

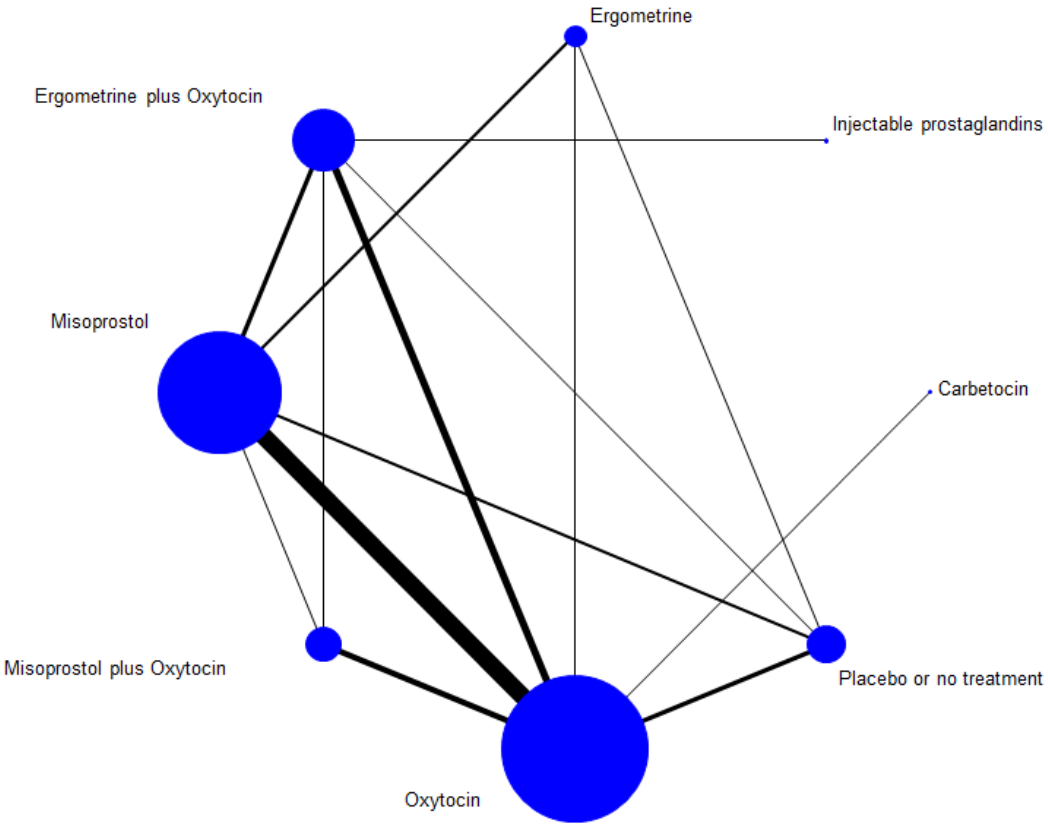


Figure 86. Forest plot with relative risk ratios and 95% CIs from pairwise, indirect and network (combining direct and indirect) analysis for prevention of PPH ≥ 500 mL restricted to large studies (> 400 participants).

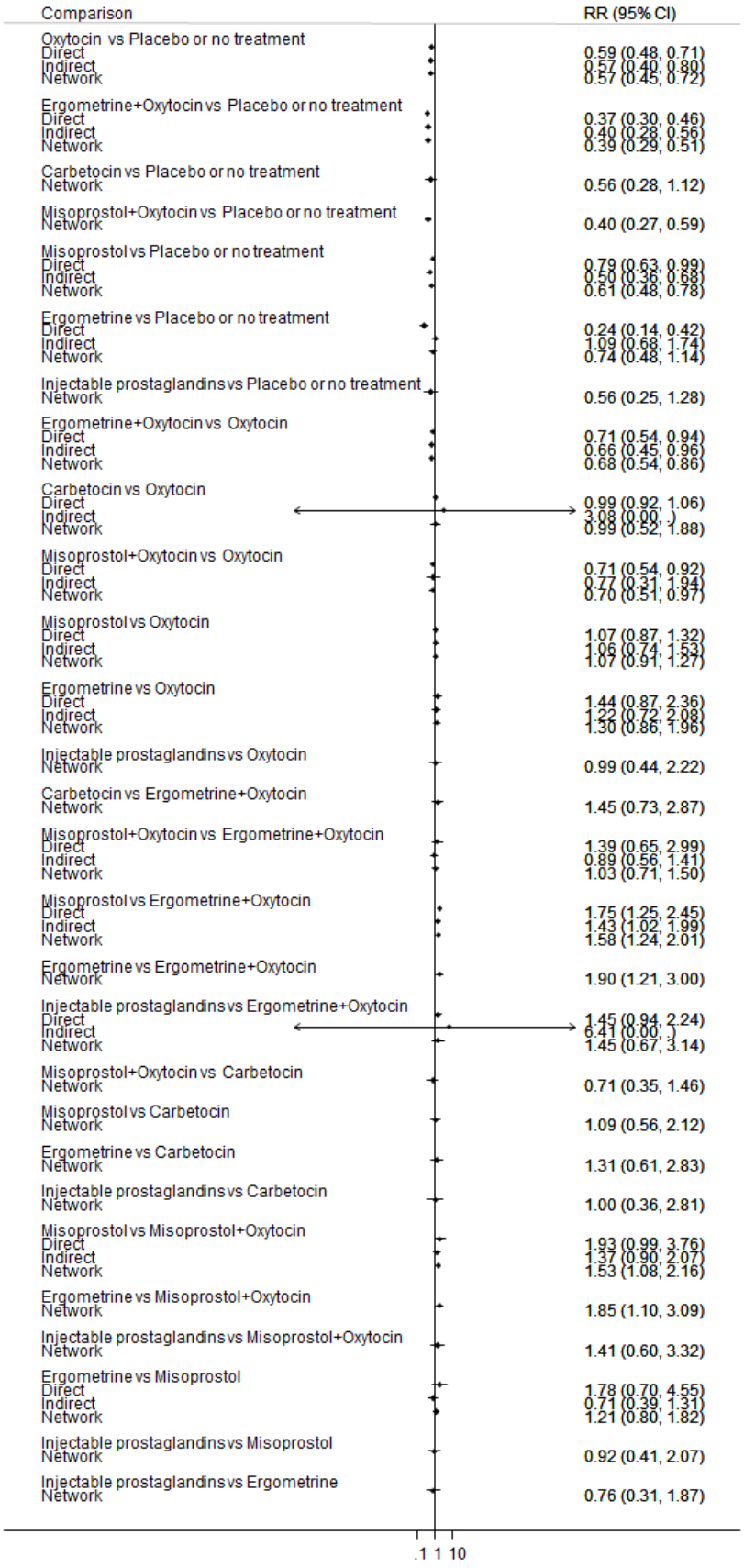


Figure 87. Cumulative rankograms comparing each of the uterotonic drugs for prevention of PPH ≥ 500 mL restricted to large studies (> 400 participants). Ranking indicates the cumulative probability of being the best drug, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SUrface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available drug options.

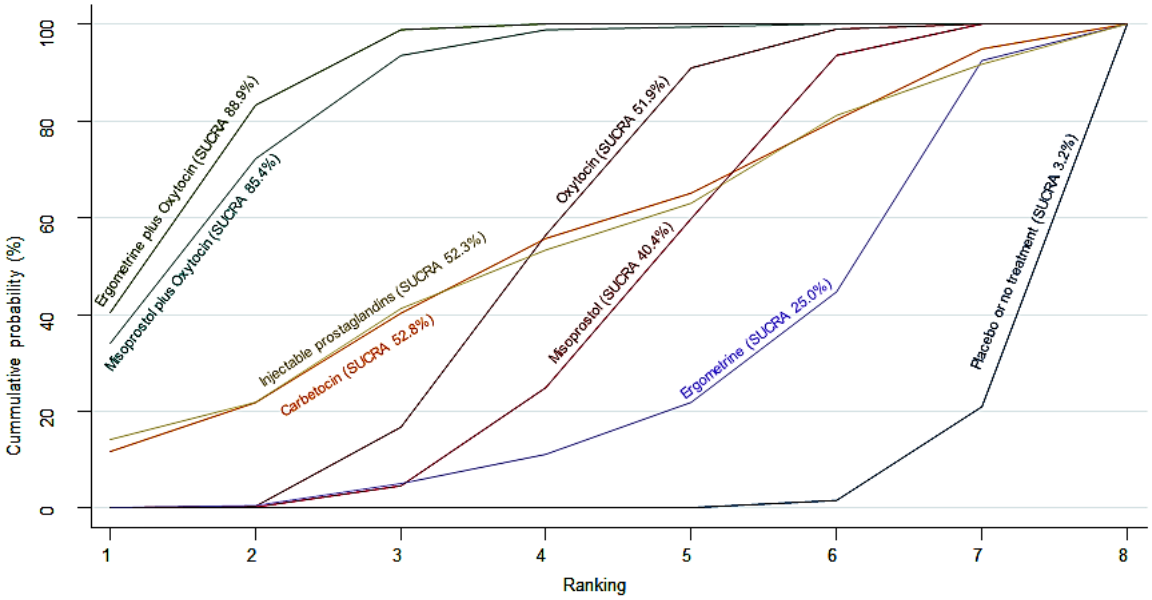


Figure 88. Network diagram for prevention of PPH ≥ 1000 mL restricted to large studies (> 400 participants). The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison.

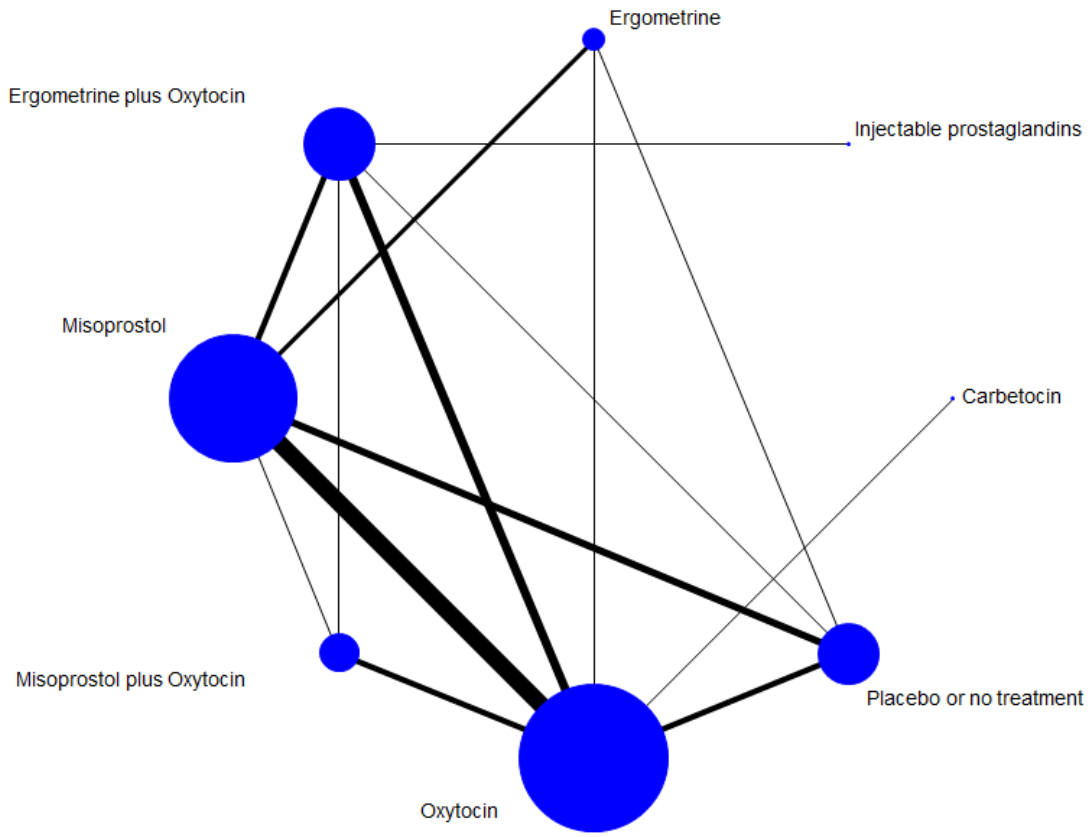


Figure 89. Forest plot with relative risk ratios and 95% CIs from pairwise, indirect and network (combining direct and indirect) analysis for prevention of PPH ≥ 1000 mL restricted to large studies (> 400 participants).

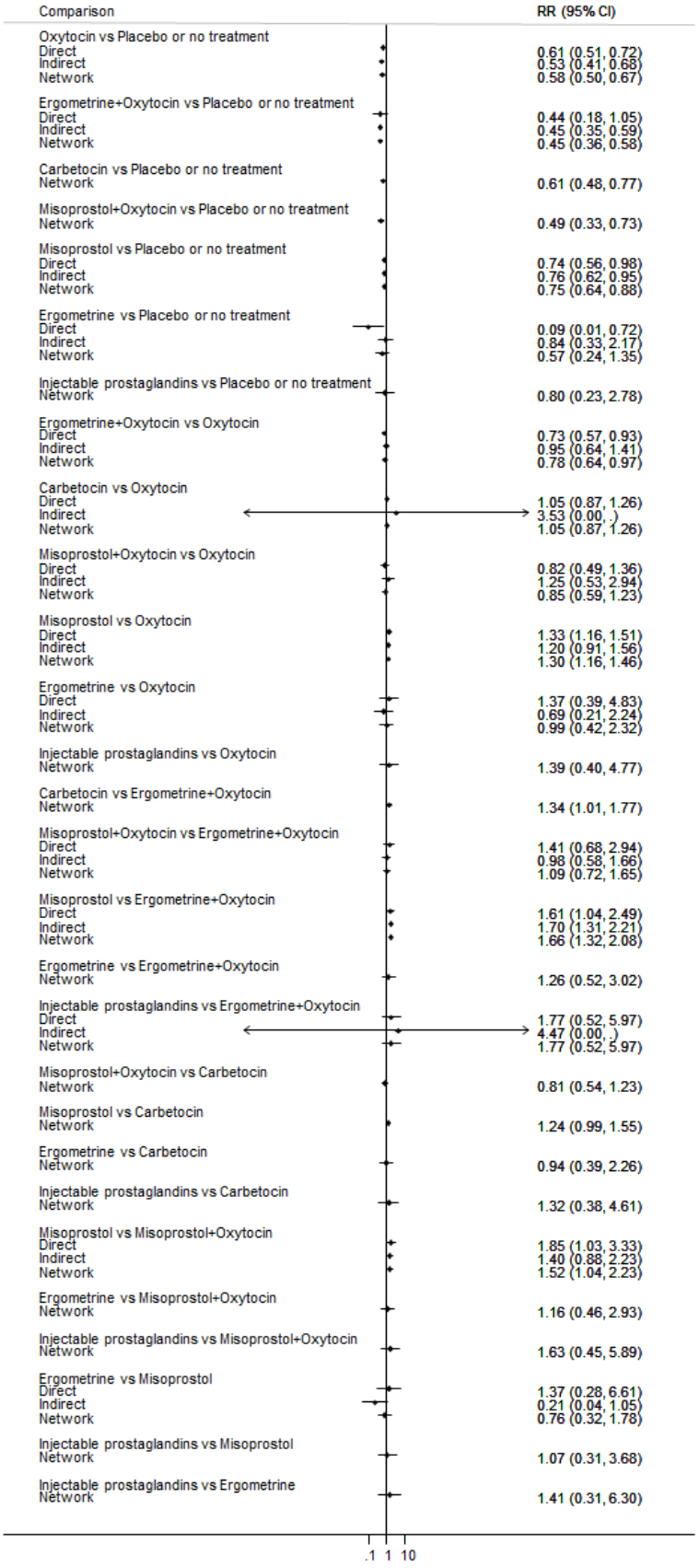


Figure 90. Cumulative rankograms comparing each of the uterotonic drugs for prevention of PPH ≥ 1000 mL restricted to large studies (> 400 participants). Ranking indicates the cumulative probability of being the best drug, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SUrface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available drug options.

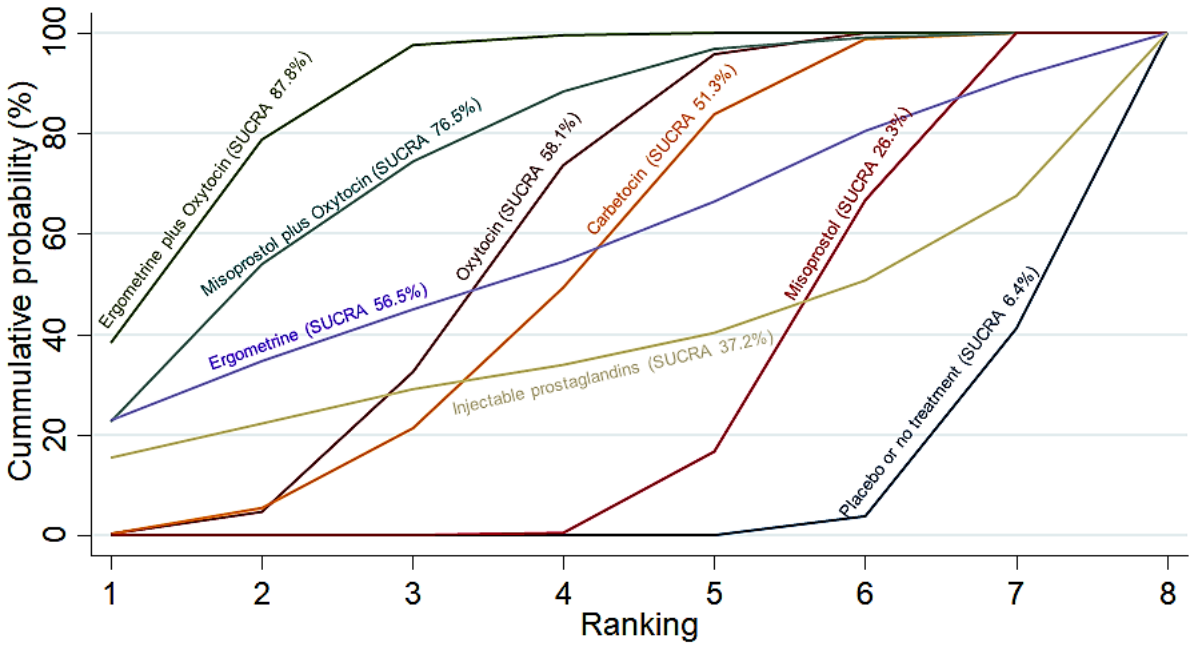


Figure 91. Forest plot with relative risk ratios and 95% CIs from pairwise, indirect and network (combining direct and indirect) analyses for prevention of PPH ≥ 500 mL (all comparisons).

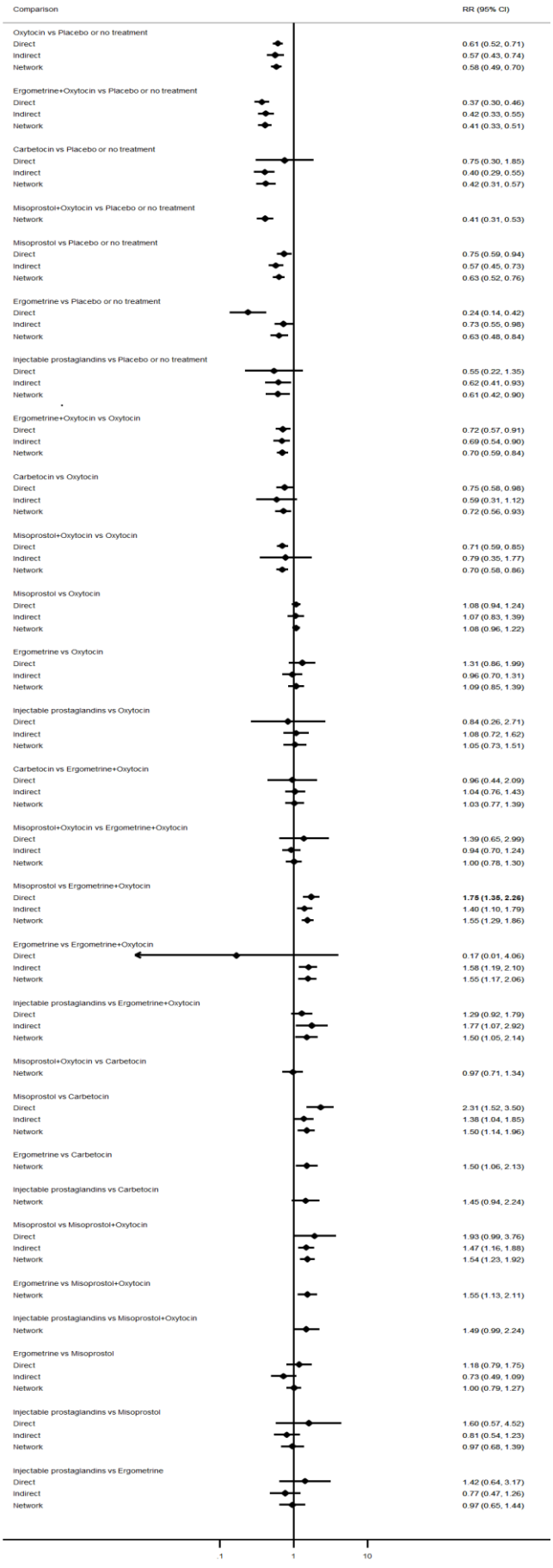


Figure 92. Forest plot with relative risk ratios and 95% CIs from pairwise, indirect and network (combining direct and indirect) analyses for prevention of PPH ≥ 1000 mL (all comparisons).

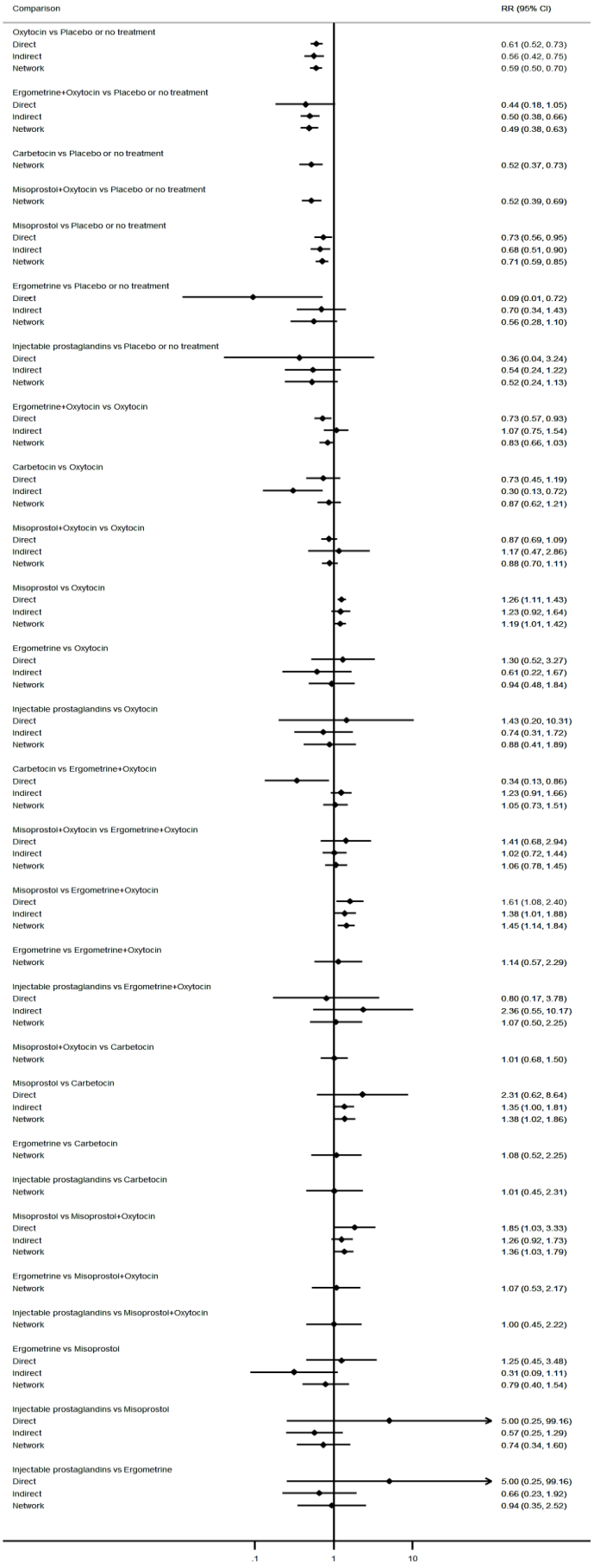


Figure 93. Forest plot with relative risk ratios and 95% CIs from pairwise, indirect and network (combining direct and indirect) analyses for prevention of maternal death (all comparisons).

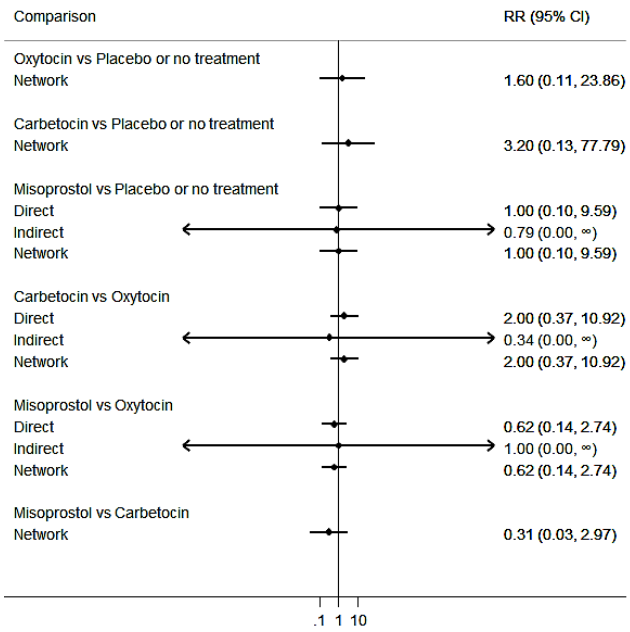


Figure 94. Forest plot with relative risk ratios and 95% CIs from pairwise, indirect and network (combining direct and indirect) analyses for prevention of severe maternal morbidity: Intensive care admissions (all comparisons).

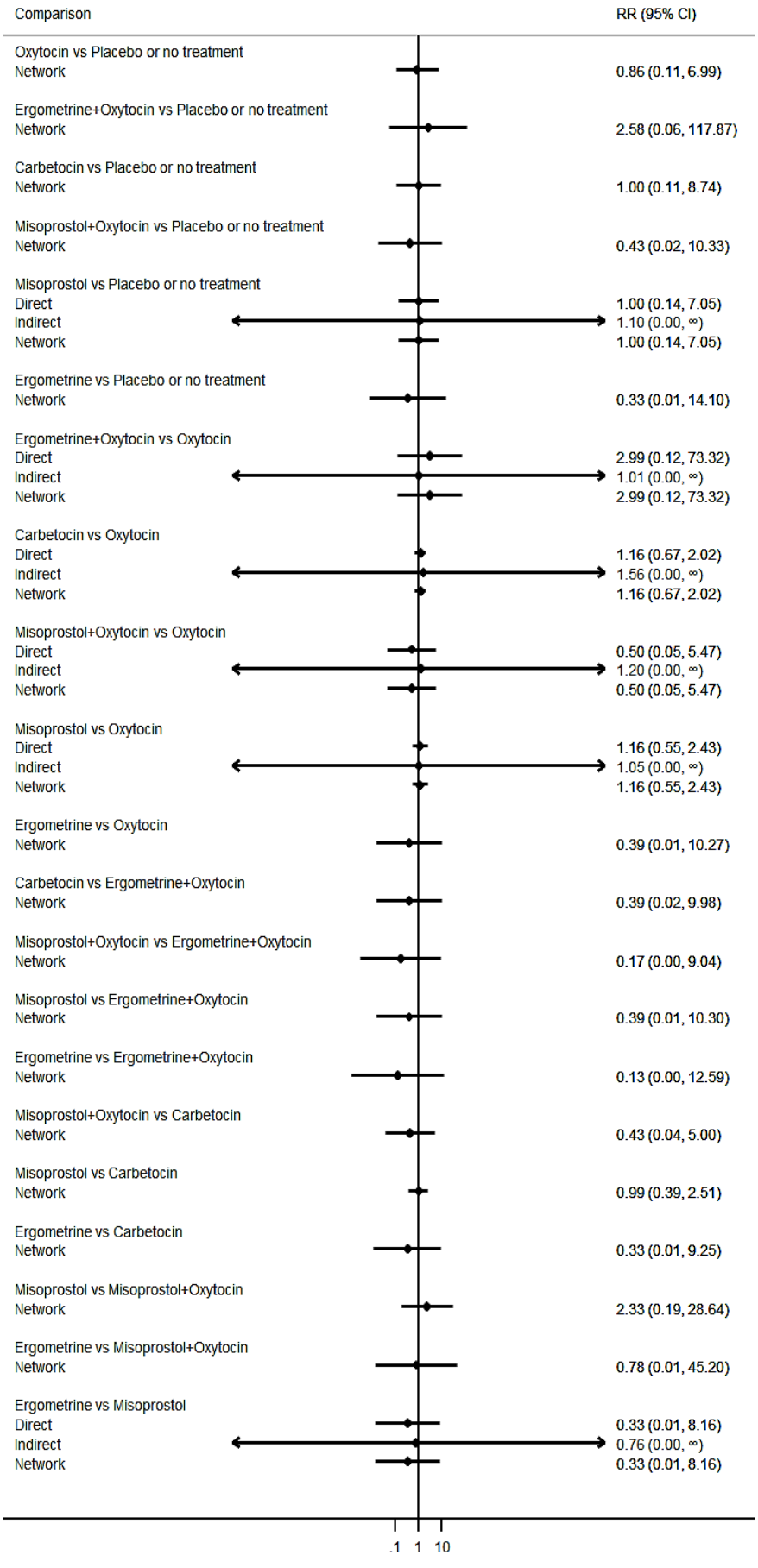


Figure 95. Forest plot with relative risk ratios and 95% CIs from pairwise, indirect and network (combining direct and indirect) analyses for additional uterotonics (all comparisons).

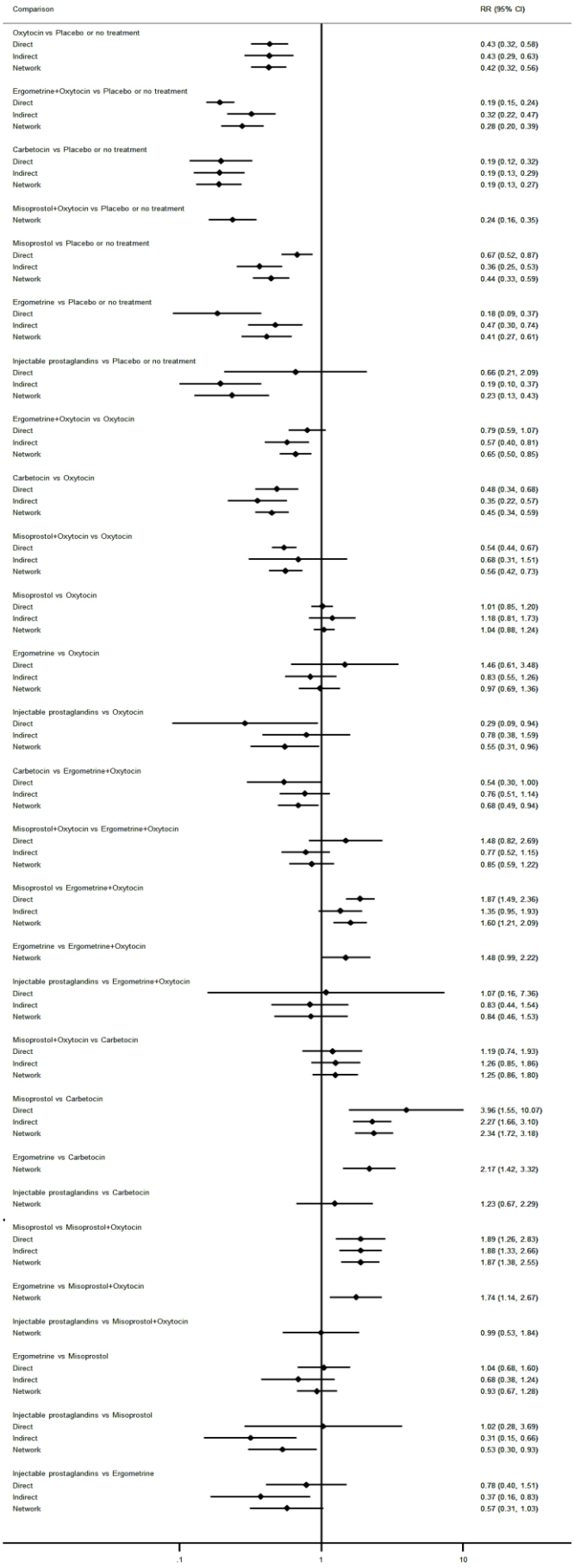


Figure 96. Forest plot with relative risk ratios and 95% CIs from pairwise, indirect and network (combining direct and indirect) analyses for blood transfusion (all comparisons).

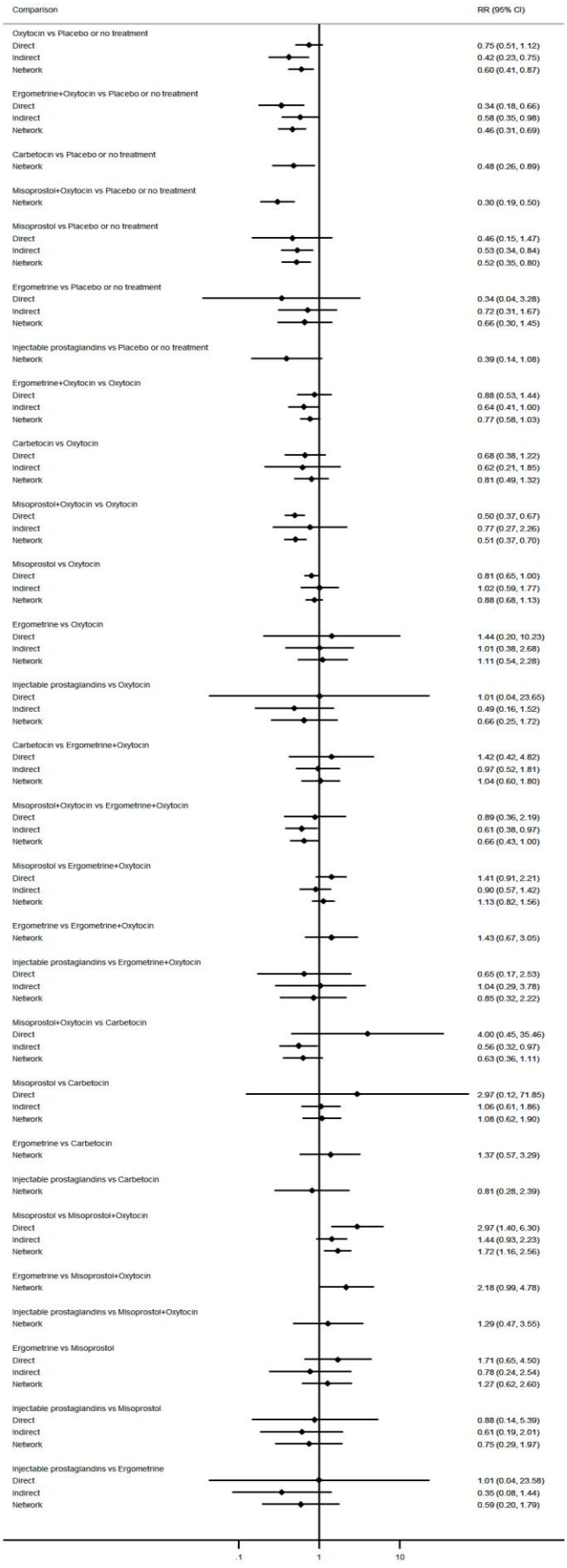


Figure 97. Forest plot with relative risk ratios and 95% CIs from pairwise, indirect and network (combining direct and indirect) analyses for mean blood loss (ml) (all comparisons).

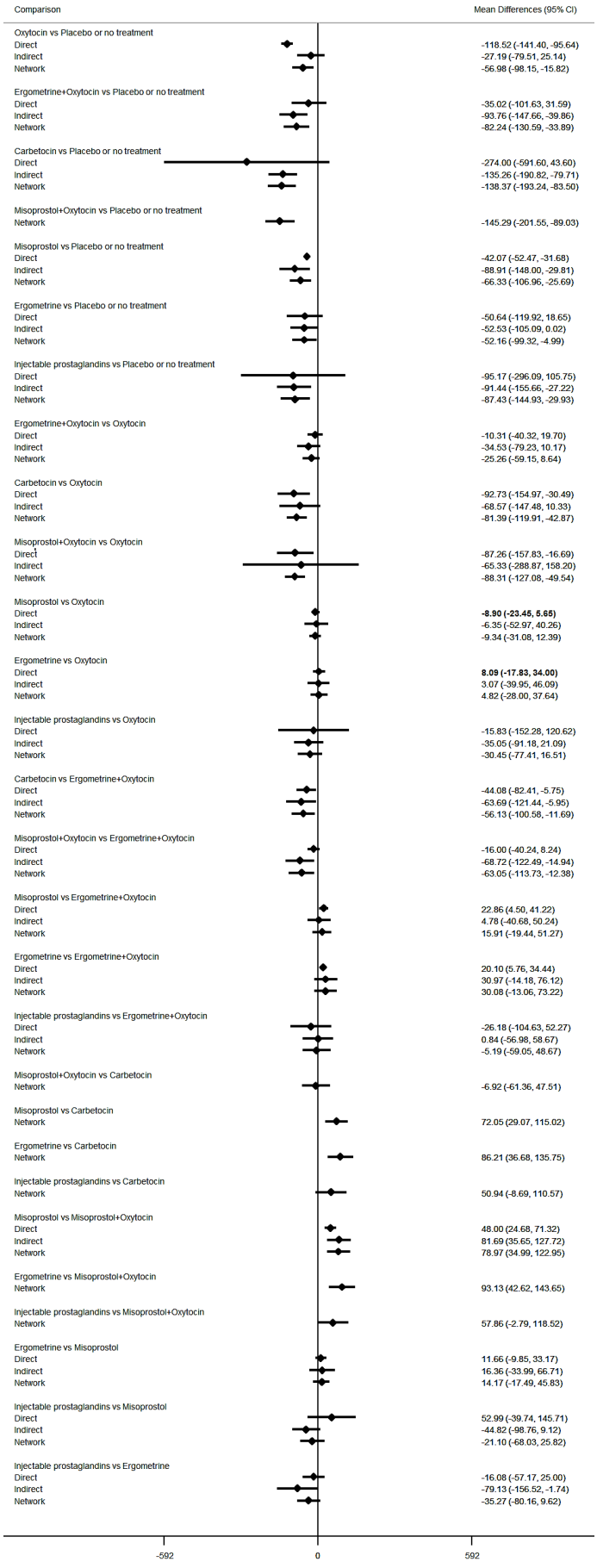


Figure 98. Forest plot with relative risk ratios and 95% CIs from pairwise, indirect and network (combining direct and indirect) analyses for change in haemoglobin measurements before and after birth (g/L) (all comparisons).

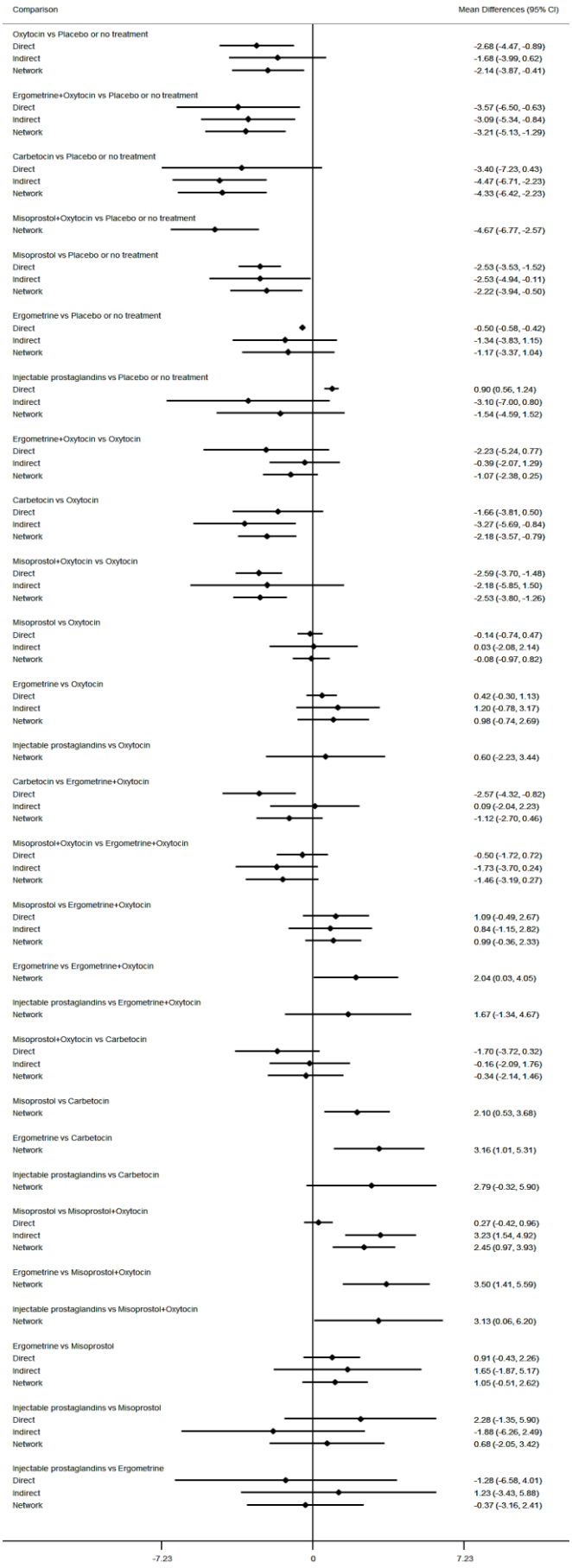


Figure 99. Forest plot with relative risk ratios and 95% CIs from pairwise, indirect and network (combining direct and indirect) analyses for breastfeeding at discharge (all comparisons).

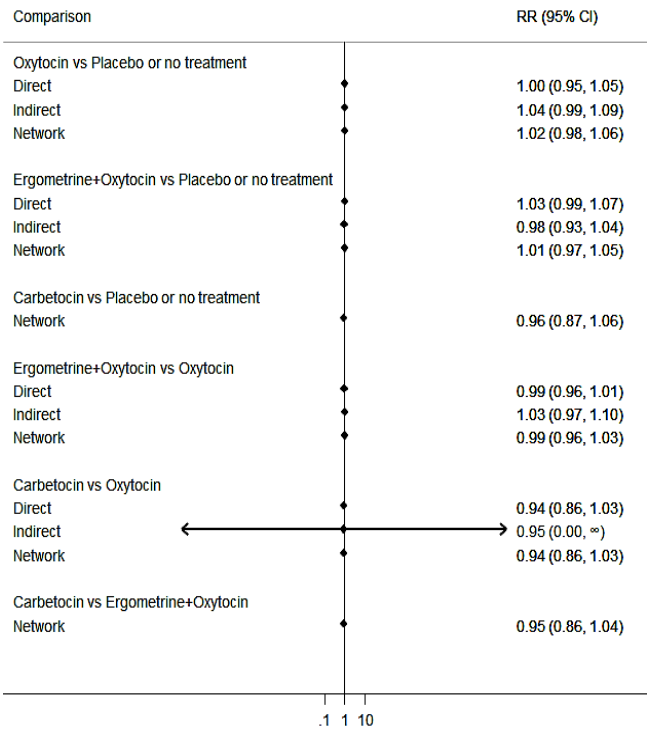


Figure 100. Forest plot with relative risk ratios and 95% CIs from pairwise, indirect and network (combining direct and indirect) analyses for nausea (all comparisons).

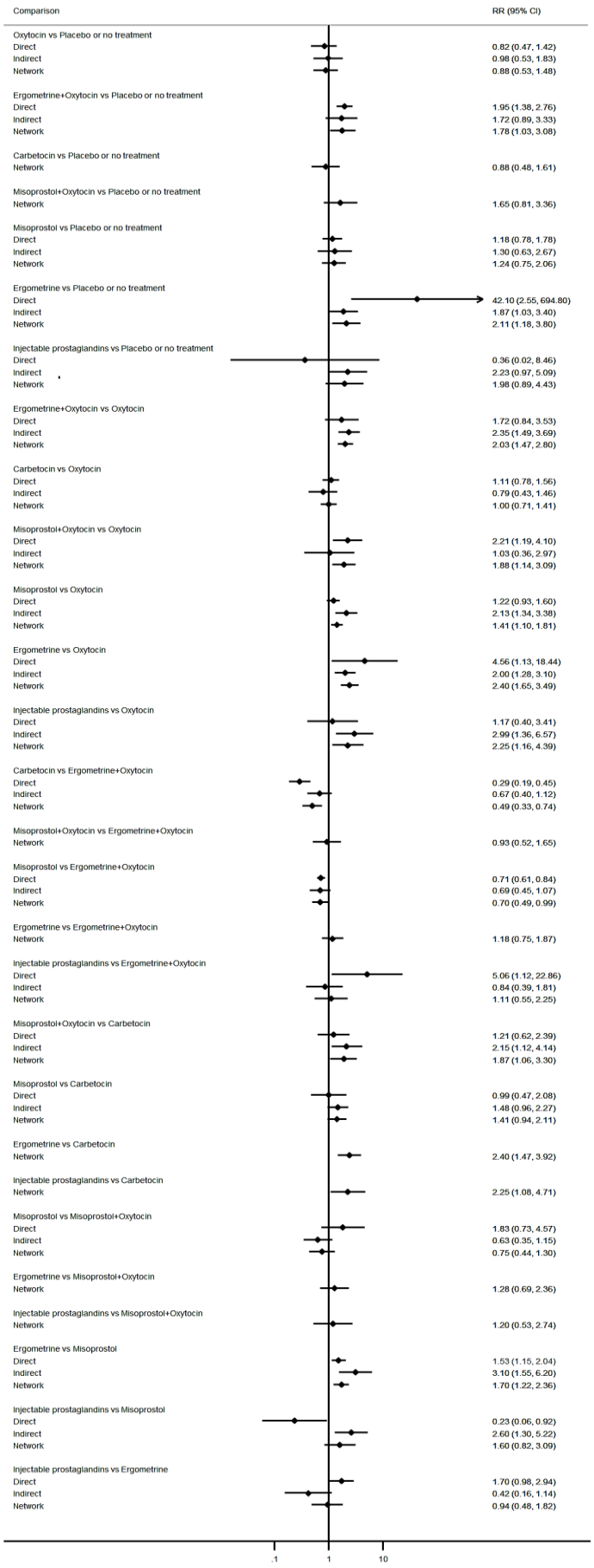


Figure 101. Forest plot with relative risk ratios and 95% CIs from pairwise, indirect and network (combining direct and indirect) analyses for vomiting (all comparisons).

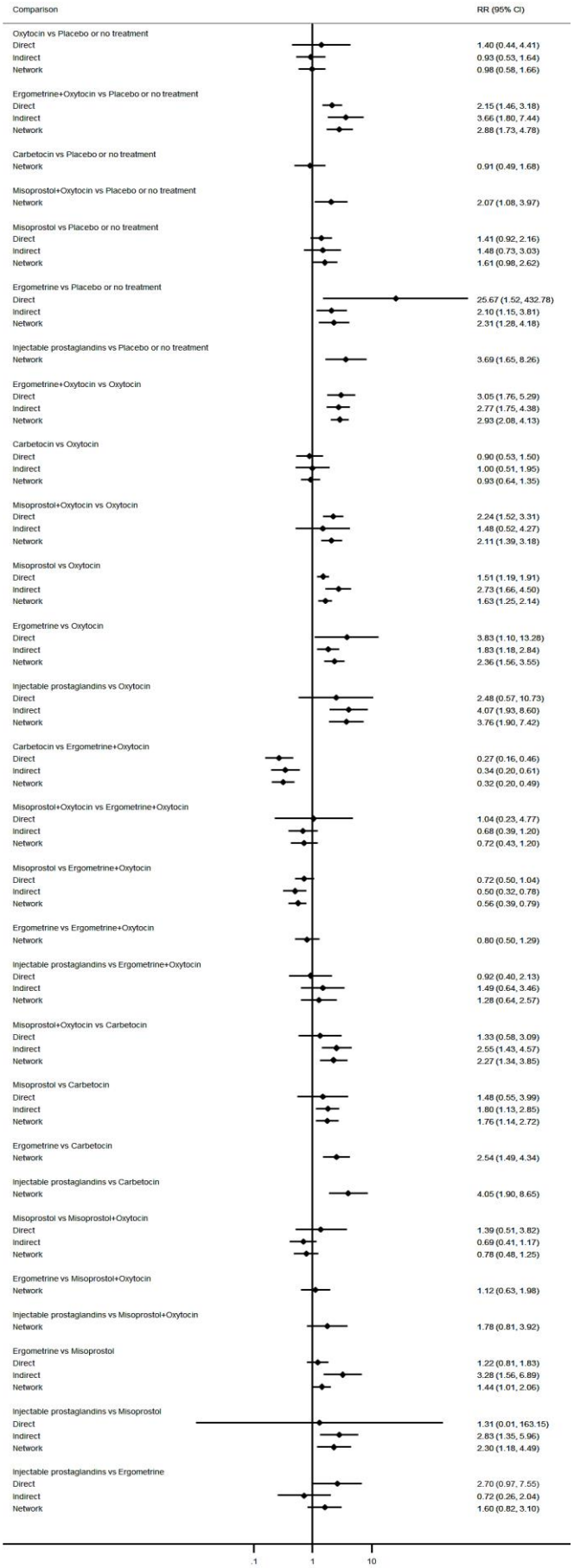


Figure 102. Forest plot with relative risk ratios and 95% CIs from pairwise, indirect and network (combining direct and indirect) analyses for hypertension (all comparisons).

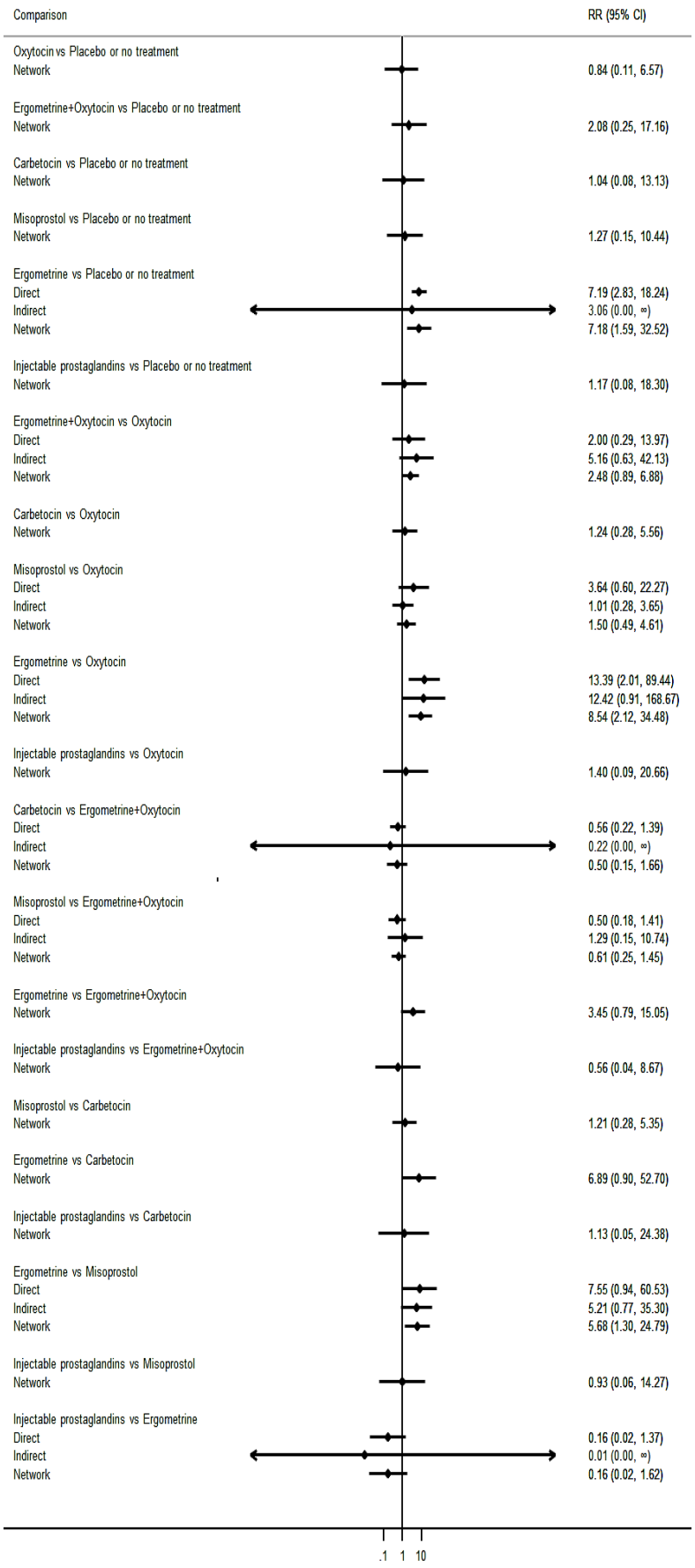


Figure 103. Forest plot with relative risk ratios and 95% CIs from pairwise, indirect and network (combining direct and indirect) analyses for headache (all comparisons).

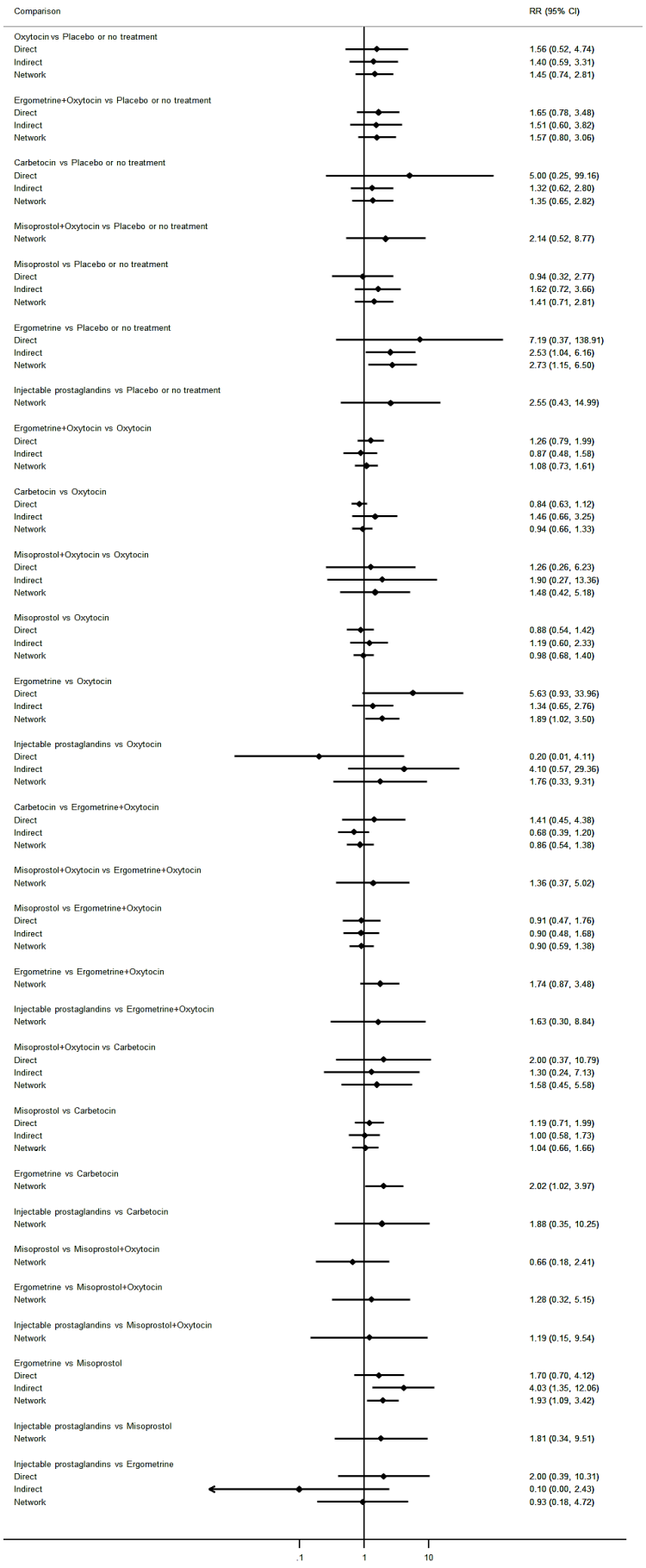


Figure 104. Forest plot with relative risk ratios and 95% CIs from pairwise, indirect and network (combining direct and indirect) analyses for fever (all comparisons).

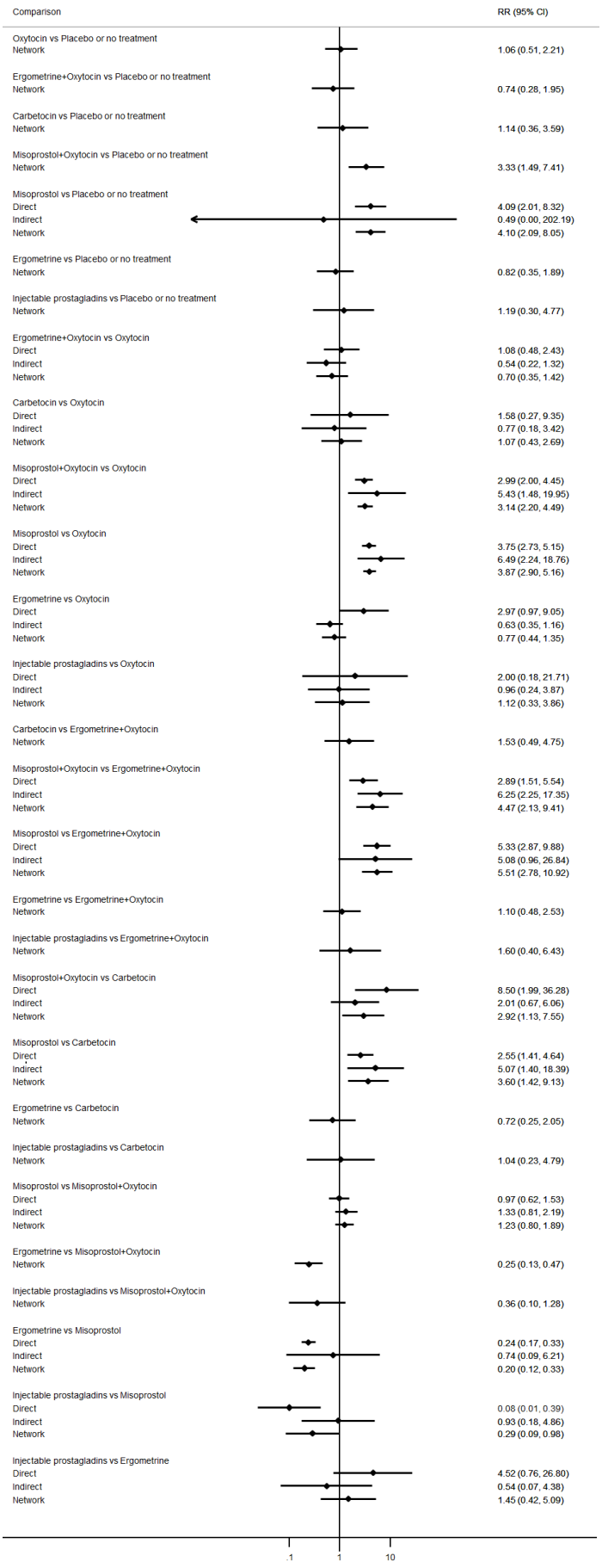


Figure 105. Forest plot with relative risk ratios and 95% CIs from pairwise, indirect and network (combining direct and indirect) analyses for shivering (all comparisons).

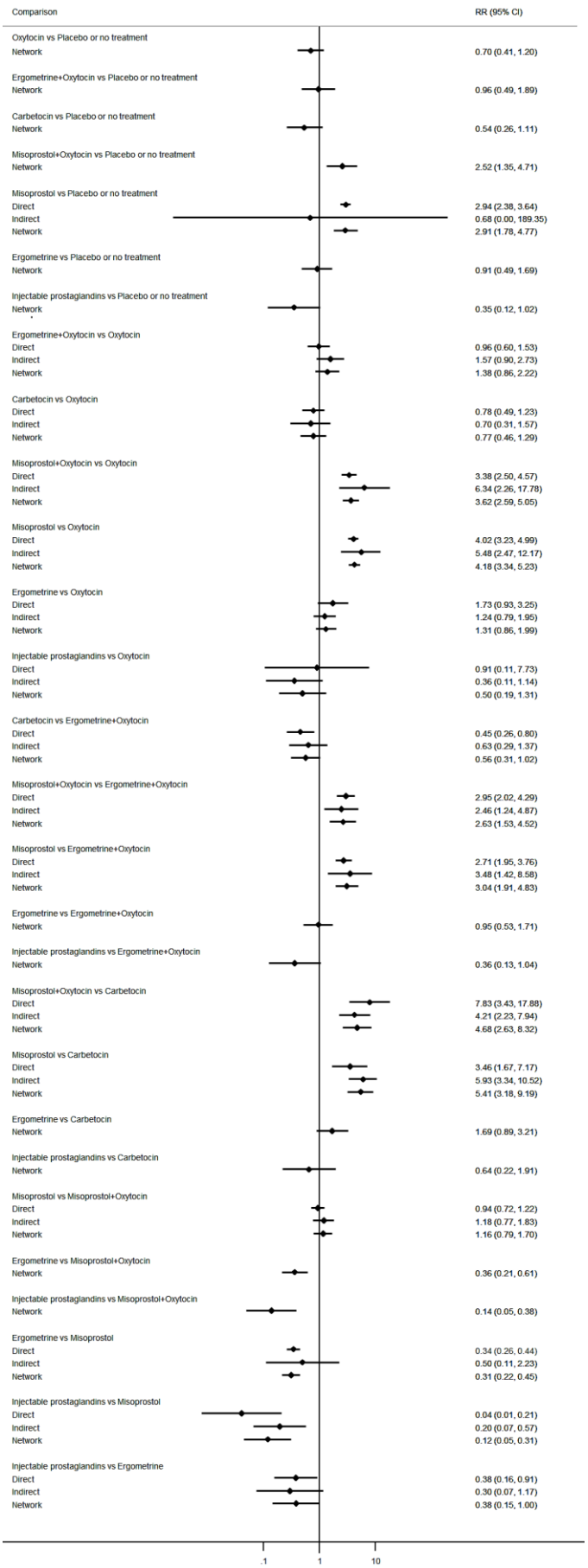


Figure 106. Forest plot with relative risk ratios and 95% CIs from pairwise, indirect and network (combining direct and indirect) analyses for abdominal pain (all comparisons).

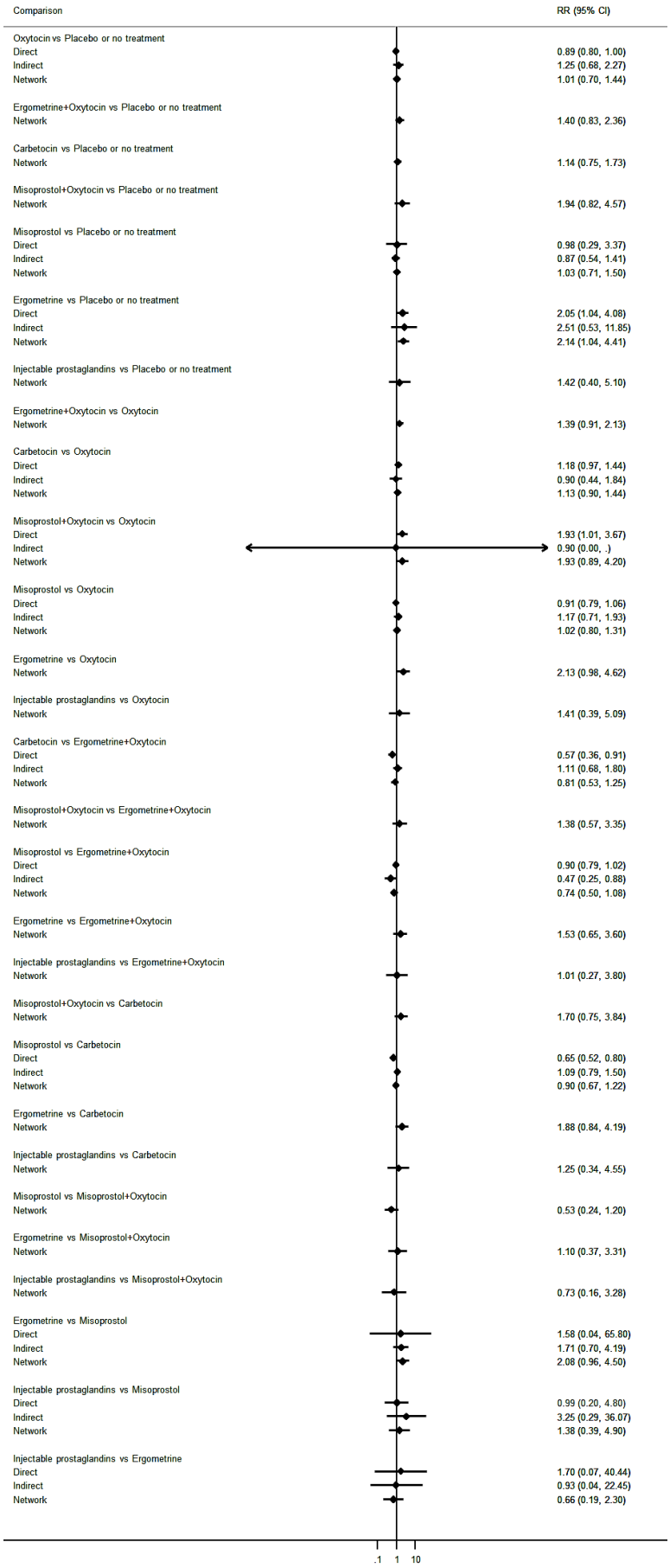
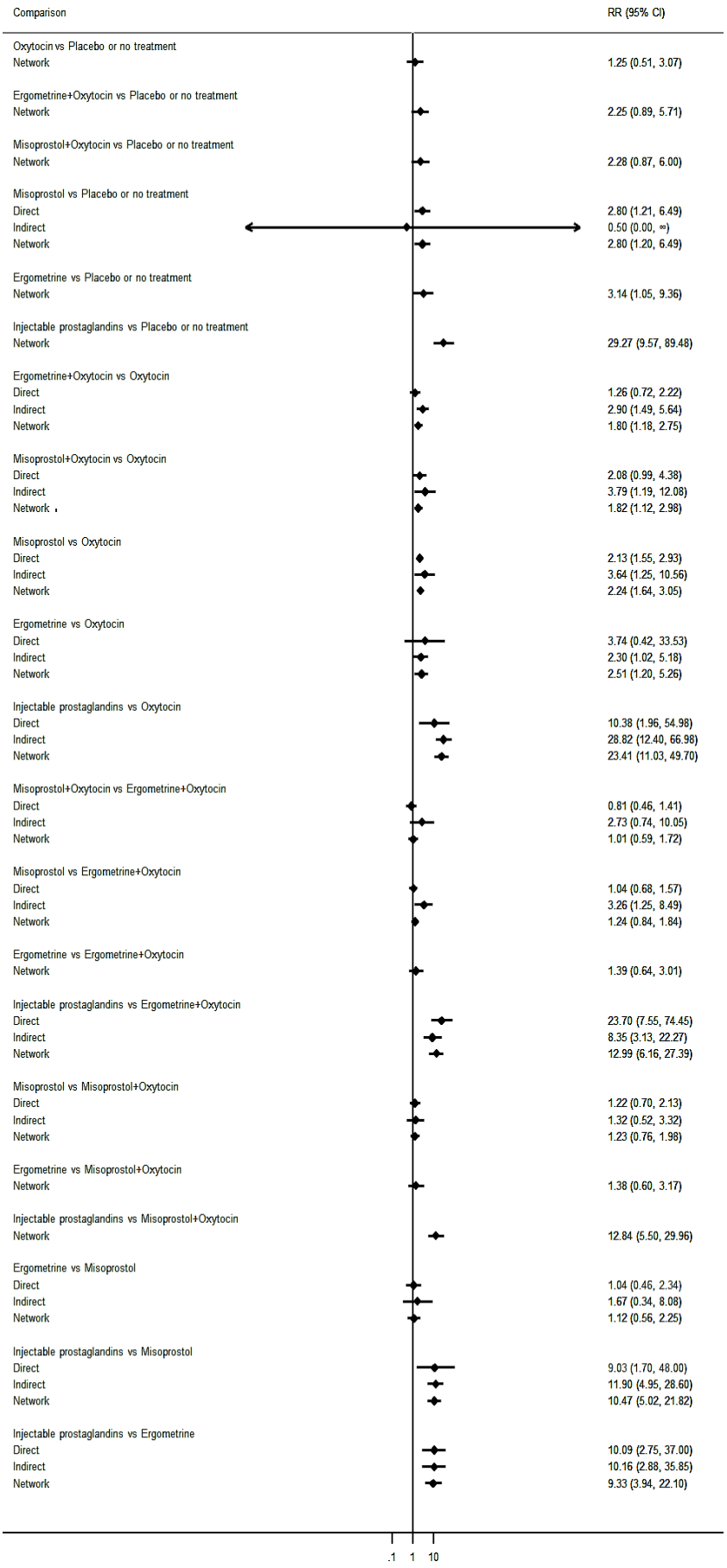


Figure 107. Forest plot with relative risk ratios and 95% CIs from pairwise, indirect and network (combining direct and indirect) analyses for diarrhea (all comparisons).



Additional data from trialists

First Author	Pub Year	Additional data
Adanikin	2012	Additional data retrieved from Adanikin A, Orji E, Adanikin P, Olaniyan O. Comparative study of rectal misoprostol to oxytocin in preventing postpartum haemorrhage post caesarean section. International Journal of Gynecology and Obstetrics 119S3 (2012) S825: Objectives: In patients with risk factors for primary postpartum haemorrhage, it is generally considered good practice to administer an adjunctive uterotonic agent after the active management of the third stage of labour. Oxytocics that have been used in this adjunctive context include oxytocin infusion or rectal misoprostol as practised in our centre. Although this practise is popular in our environment, objective comparative assessment of these prophylactic measures is lacking. This study thus set out to compare the efficacy of both measures, the result of which may engender a change in the current practice in our centre and elsewhere or indeed strengthen it. Materials: Oxytocin, Rectal misoprostol. Placebo (Lactose tablet; Normal saline). Methods: In this comparative study, 218 parturients who delivered by caesarean section received 5 IU of intravenous oxytocin after cord clamping and were further randomized to receive either 600mcg rectal misoprostol and a placebo infusion intravenously or placebo rectally and an oxytocin infusion. 4 hours post-operative blood loss was estimated by application of pads of known weight. Results: The mean immediate 4 hours post-operative blood loss was not significantly different between the rectal misoprostol and oxytocin infusion group (106.65±30.64 ml versus 109.02±27.55 ml; p=0.553) and the change between the pre-operative and postoperative hematocrit was similar. No patient developed primary postpartum haemorrhage in the study. There was no statistically significant difference in the incidence of pyrexia and shivering. Conclusions: Post-caesarean section rectal misoprostol has comparative efficacy to oxytocin infusion in preventing postpartum haemorrhage after caesarean section. Misoprostol which can be stored at high temperatures and has a shelf life of several years should be favoured as ideal adjunctive uterotonic in developing countries with a tropical climate and limited refrigeration capabilities that is needed to maintain the potency of oxytocin.
Al-Sawaf	2013	Response to email queries: PPH > 500 ml — No. Events — Total No. Women Control — 8 — 39 Misoprostol — 3 — 28 Oxytocin — 2 — 37 PPH > 1000 ml — No. Events — Total No. Women Control — 6 — 39 Misoprostol — 2 — 28 Oxytocin — 1 — 37

		Change in Hb after Delivery (g/dl) Mean Hb Change SD Total No. Women Control 1.3 0.6 39 Misoprostol 1.3 0.9 28 Oxytocin 1.2 0.9 37
Amin	2014	Response to email queries: Thanks for including my study in urban met analysis. The answers to u r questions are . 1.all pt included in the study were admitted through emergency and ops. After complet history and examination pt with history of privious c . section. ,traumatic ppq. ,bleeding disorders. ,history of prolonged difficult labour, placenta previa, placetal abruption, history of pph. ,multiple gestation and women having BMi more than 30 were excluded. However all other pt with full term pregnancy and who came to labour room in spontaneous onset of labour resulting in spontaneous vaginal delivery without episiotomy were included in the study. 2.as I expand before that high risk pt were not included in study so no death and major morbidity been noted.
Askar	2011	Response to email queries: Hypertension 3rd Stage 30-60 mins 3rd Stage 60-120 mins Total of Patients Intervention (Carbetocin) 0 0 0 Control (Syntometrine) 7 7 7 (these are the same patients)
Attilakos	2010	Response to email queries: Carbetocin Oxytocin 1 Nausea 2Nausea 2 Nausea+Flushed 3 Vomiting 1 Nausea+Headache 1 Vomiting+Trigeminy 1 Nausea+Abdominal pain 1 Nausea+Headache 2 Nausea+Vomiting 2 Nausea+Vomiting 1 Nausea+Vomiting+Sweating 1 Nausea+Vomiting+SOB 1 Nausea+Vomiting+Tremors 1 Nausea+Flushed+Tremors 1 Nausea+Vomiting+Flushed+Hypotension 1 Nausea+Vomiting+Flushed+Tremors 1 Tightness throat 2 Dizziness 2 Dizziness 1 Dizziness+Flushed+Sweating 1 Flushed 2 Hypotension 2 Hypotension 2 Tremors 1 Hypotension+SOB 1 SOB 1 ST Depression 1 Blurred vision 1 Tachycardia 1 Metallic taste 1 Tremors+Tachycardia 1 Pain in arm 1 Metallic taste+SOB+Wheezing 1 Abdominal pain+SOB 1 Metallic taste+POF 1 Backache 1 Headache 1 Headache n = 22 n = 26

		SOB = Shortness OF Breath POF = Pressure Over Forehead
Atukunda	2014	Attachment to response to email queries: Vomiting (generally) Events Total Misoprostol 35(6.1) 569 Oxytocin 19(3.3) 570 Vomiting (severe) Events Total Misoprostol 8(1.4) 569 Oxytocin 3(0.5) 570 Morbidity (extensive vaginal repair) Events Total Misoprostol 11(1.9) 570 Oxytocin 8(1.4) 570
Bambigoye, Hofmeyr	1998	Response to email queries: We did not document the routine drugs used in the active management of labour in each case. At two sites in South Africa (East London and Dora Nginza, Port Elizabeth), and in Uganda the routine was oxytocin 10u IM. At the third site in SA (Rob Ferreira) oxytocin 5u IM was used in 60/155 and oxytocin-ergometrine (5u/0.5mg) was used in 85/155. In Nigeria either oxytocin or ergometrine was used, but we don't have the details. As this was a randomized trial, we expected the routine management to be evenly distributed between the randomized groups.
Begley	1990	Response to email queries: Random number tables were used from the statistical text-book by Fleiss (1981). The first number was selected from the table by a disinterested observer and the numbers were then allocated in blocks of 100, following in sequence. Duration 3rd Stage Mins 0-20 21-40 41-60 61-80 81-100 102-120 >120 Mean SD/CI Total Intervention (Active) 674 11 4 0 2 8 6 11.26 19.62 705 Control (Physiological) 670 41 7 1 4 1 0 11.56 8.41 724 Change in Hb (g/dl) Mean Change SD/CI Total Number of Patients Intervention (Active) +0.91 1.19 618 Control (Physiologocal) +0.47 1.27 645
Bellad	2012	Response to email queries: Four women in the misoprostol group and none in the oxytocin group experienced fever (defined as ?38º C); this was entered onto the form as a dichotomous variable and we have no information regarding the actual temperature (or whether any woman experienced a temperature of ?40º C). One woman in the oxytocin group had retained placenta and a blood transfusion; this was the only case of

		transfusion and required ICU admission for monitoring. There were no other complications (e.g., organ failure) and no maternal deaths. 58/329 women receiving oxytocin (17.6%) had second stage of labor >=30 minutes. 53/323 women receiving sublingual misoprostol (16.4%) had second stage of labor >=30 minutes. 1 woman receiving oxytocin and no women receiving sublingual misoprostol had a third stage of labor >=30 minutes.
Bhullar	2004	Response to email queries: I don't have the raw data anymore, but I am certain we did not have any maternal deaths.
Bugalho	2001	Additional data extracted from published Cochrane review(s)
Chaudhuri	2012	Additional data extracted from published Cochrane review(s)
Chhabra	2008	Response to email queries: You know this was low dose study in low risk cases for prophylaxis. So the answers are: The number of women (n/N) in each study group (if any) who needed major surgery - nil The number of women (n/N) in each study group (if any) who needed ICU admission - nil The number of women (n/N) in each study group (if any) who had hyperpyrexia (T>40) - nil The number of women (n/N) in each study group (if any) who had vital organ failure - nil The number of women (n/N) in each study group (if any) who had an estimated blood loss >1000mls - nil The number of women (n/N) in each study group (if any) who died - nil
Dansereau	1999	Response to email queries: Thank you again for your interest. What I meant to clarify previously is that the paper should have stated that "two patients in each group had a [severe] postpartum hemorrhage [requiring blood transfusion]". Because of the difficulty in assessing estimated blood loss, we had decided -before the beginning of the study- to not use that variable but rather, to use the judgment of the surgeon (blinded to the study drug), as to whether the patient needed additional oxytocic (required in all cases of PPH). Clearly more than two patients per group had a PPH greater than 500 or even 1000 ml. The exact number is not available though as we decided not to use that outcome of PPH in our study.
El Behery	2015	Response to email queries: PPH > 500 ml Events Carbetocin 6 Oxytocin 19

		Major morbidity or death Carbetocin 0 Oxytocin 3 I confirm that we actually excluded cases listed below from our study: congenital fetal anomalies, placenta previa, diabetes, hypertension, preeclampsia, cardiac disorders, general anaesthesia
El Tahan	2012	Response to email queries: I will address below your queries as follows: Any maternal deaths: no Maternal ICU admissions: no Hysterectomies: no Maternal fever >40C: there were 16/179 cases developed pyrexia <40 C in misoprostol group; none exceeded 40C. Blood loss of >1000mls: yes some cases in the placebo group had a total perioperative blood loss >1000 ml
Enakpene	2007	Response to email queries: There was no death recorded in either group None of the study participants required additional surgery such as hysterectomy or arterial ligation to treat massive postpartum hemorrhage. There was only one ICU admission in the misoprostol group for non-hemorrhage related condition but due to postpartum eclampsia. No participants in each study group developed hyperpyrexia of temperature > 40oC No participants developed major organ failure Three participants from the oral misoprostol group had massive postpartum hemorrhage greater than 1000ml while only one participants in the methylergometrine group developed massive postpartum hemorrhage. However, all the four patients who developed massive hemorrhage responded very well with additional oxytocics and did not require surgical interventions.
Fawole	2011	There were no women who experienced hyper-pyrexia (T 40) or vital organ failure, or who needed ICU admission, in either the intervention or control group.
Fenix	2012	Additional data retrieved from an unpublished text entitled “Double-blind randomized controlled trial comparing the effect of carbetocin with oxytocin for the prevention of postpartum hemorrhage among high risk women following vaginal delivery.” **Results** The study was conducted over a 4-month period (from May 2011 to August 2011). There were a total of 272 deliveries in our hospital during the study period, of which, 111 delivered vaginally. 75 women

were finally recruited into the study. Nine women in the carbetocin group and six women in the oxytocin group failed to have a paired hemoglobin test to measure the change in hemoglobin 24 hours after delivery because they refused further blood extraction. These 15 women were excluded, and we therefore had 30 women each in the carbetocin and oxytocin arm in the analysis that was randomly assigned to receive either of the two different interventions.

There was no significant difference between the two groups in their demographic characteristics (Table 1). Most of the participants were college degree holders with an average age of 30 years. The average age of gestation was 38 weeks for the carbetocin group while almost 39 weeks in the oxytocin group. It was also observed that about two thirds were multigravid women for both groups.

The average hemoglobin count 24 hours after delivery of the participants for the oxytocin group (-1.1) seems to have a greater drop than those in the carbetocin group (-0.6) (Table 2).

Participants in the carbetocin group exhibited a relatively lower average estimated blood loss than those in the oxytocin group (296 cc and 493 cc respectively). There was no case of postpartum hemorrhage between the two groups. The distribution of exposure to additional agents revealed that 9 out of 10 patients in the oxytocin group needed additional uterotonic agents. In contrast, 90% of the participants in the carbetocin group did not need any additional agent after drug administration. In addition, it was noted that almost all of the patients in the oxytocin group needed a uterine massage compared to a negligible number of those in the carbetocin group. Meanwhile, none of the patients needed blood transfusion. (Table 3)

Carbetocin immediately (1min) took effect to the patients in the carbetocin group while those patients in the oxytocin group waited for some time (30 min or more) for oxytocin to take effect (Table 3).

Adverse effects are presented in Table 4. The incidences of headache and hypogastric pain were similar in between groups. There were no nausea, vomiting, facial flushing or pain in the injection site noted.

20% percent or 6 out of 30 women in the carbetocin group had tachycardia (defined as maternal pulse ‡100) within 60 minutes postdelivery and were significantly higher than the 10% (3 out of 30) recorded in the oxytocin group however, the difference was statistically insignificant. The mean blood pressure values at different intervals after delivery of each group are also shown in Table 4 though no statistical difference was observed between the two interventions.

To determine if there is a significant difference between the two drugs, we will need to perform independent sample T-Test. Prior to performing the test, we need to satisfy its assumptions which is as follows: (a) normality of the data, (b) homogeneity / constancy of variance. (Appendix A).

Based on the results in Table 5, we can conclude that there's a significant difference between the Carbetocin and Oxytocin since the p-values for the Estimated Mean Blood Loss and Mean difference of the Hemoglobin count are approximately zero (< LOS = 0.05).

Looking at the mean difference of the hemoglobin count, having a value of 0.57 implies that carbetocin garnered a significantly lower change in the hemoglobin count after 24 hours.

The mean difference of the estimated blood loss, with value of -197.33, denotes statistically lower blood loss for patients exposed to carbetocin than those who were exposed to oxytocin.

Table 1 Baseline Characteristics of Patients

Characteristics		Carbetocin (N = 30)	Oxytocin (N = 30)
Age *		30	30
Age of Gestation *		38.3	38.6
Epidural Analgesia **		100	100
Previous Postpartum Hemorrhage **		6.7	6.7
Augmentation with syntocinon **		76.7	73.3
Episiotomy **		100	100
Normal Vaginal Delivery **		100	100
Educational Level **	College Grad	56.7	73.3
	College Undergrad	26.7	23.3
	High School Grad	3.3	0
	High School UnderGrad	3.3	0
	Post Grad	10	3.3
Gravidity **	Primigravida	33.3	26.7
	Multigravida	66.7	73.3

** - Based on Mean*
*** - Based on Percentages (%)*

Table 2 Primary outcome (peripartum hemoglobin concentration)

Characteristics	Carbetocin (N = 30)	Oxytocin (N = 30)	Mean Difference
Mean Hemoglobin count on admission (g / dl) *	11.8	12.1	-0.3
Mean Hemoglobin count 24 hrs after delivery (g / dl) *	11.2	11	0.2
Mean fall in hemoglobin (g / dl) *	***-0.6***	***-1.1***	***0.5***

** - Based on Mean*

Table 3 Secondary outcomes

Characteristics		Carbetocin (N = 30)	Oxytocin (N = 30)
Estimated Blood Loss *			
Mean Estimated Blood Loss (cc)		296	493.3
Blood loss > 500mL		-	-
Blood loss > 1000mL		-	-
Additional agent **			
Methergin		6.7	90
None		90	0
Oxytocin		3.3	10
Uterine Massage **	No	90	16.7
	Yes	10	83.3
Blood Transfusion **	No	100	100
Time drug has effected **	Upon Drug Injection	-	6.7
	1 Min	43.3	3.3
	5 Min	30	3.3
	15 Min	3.3	16.7
	30 Min	-	23.3
	1 Hr	-	10
	6 Hr	-	26.7
	24 Hr	23.3	-

**Data are presented as mean (SD).*
***Data are presented as n (%).*

Table 4 Adverse reactions

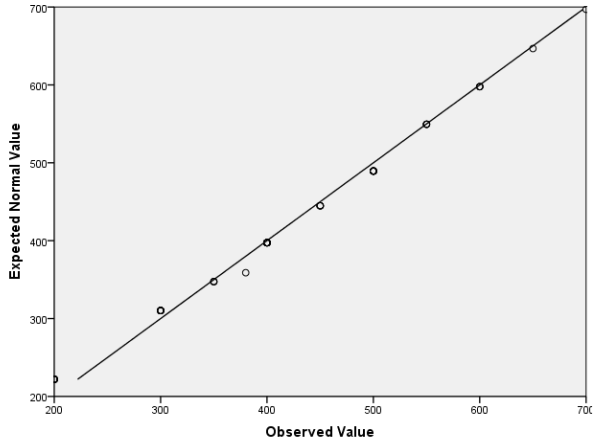
Characteristics	Carbetocin (N = 30)	Oxytocin (N = 30)
Headache *	3.3	3.3
Hypogastric Pain *	23.3	26.7
Mean systolic blood pressure immediately after delivery **	116.9 (17)	118.2 (14)
Mean diastolic blood pressure immediately after delivery **	66.8 (9.7)	67.5 (7.5)
Mean systolic blood pressure 5 minutes after delivery **	113.8 (9.1)	116.3 (8.5)
Mean diastolic blood pressure 5 minutes after delivery **	64 (5.9)	63.5 (4.9)
Mean systolic blood pressure 30 minutes after delivery **	114.1 (9)	115.8 (9.8)
Mean diastolic blood pressure 30 minutes after delivery **	64.5 (5.9)	65.4 (6.4)
Mean systolic blood pressure 60 minutes after delivery **	114.6 (10.1)	114.1 (12.2)
Mean diastolic blood pressure 60 minutes after delivery **	66.3 (8.2)	65.6 (6.4)
Pulse Rate after delivery **	88.6 (8.8)	82.6 (8.7)
Pulse Rate 30 minutes after delivery **	87.4 (8.6)	83.2 (11.7)
Pulse Rate 60 minutes after delivery **	86.3 (8.2)	84 (10.5)

** - Based on Percentages (%)*
*** - Based on Mean (Std Dev)*

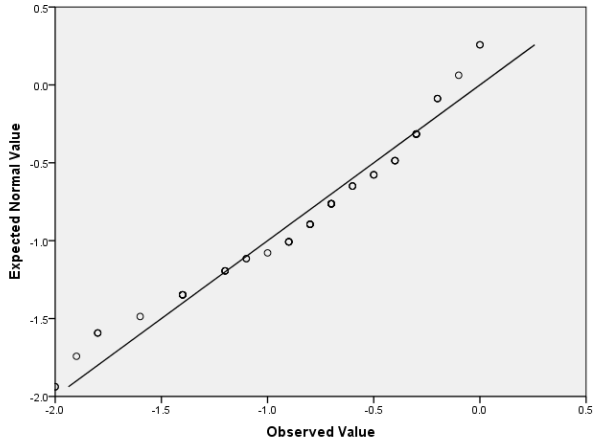
Table 5 T-Test for independent samples means

Independent Samples T - Test for Equality of Means				
	T Test Statistic	Degrees of Freedom	P- Value	Mean Difference
Difference of Hemoglobin Count	4.99	58	< 0.001	0.57
Estimated Blood Loss (cc)	-8.93	58	< 0.001	-197.33

Appendix A Q-Q plot of estimated blood loss



Appendix A Q-Q plot of difference of preoperative hemoglobin count and 24 hours hemoglobin count



		Response to email queries: Regarding your query on the incongruity on 30 parturients receiving oxytocin with mean blood loss of 493ml but 0 cases more than 500ml, it was because the estimated blood loss during delivery was measured only through eyeballing of the gauzes used. And in the estimation, we did not include the bleeding coming from repair of the laceration. That is why one of our recommendations for future studies is to measure the actual blood loss using a more accurate device of measurement. And also, since the estimation of blood loss is often inaccurate during delivery, it was agreed that a fall in hemoglobin be used as a primary outcome assessing the efficacy of the uterotonic agents in reducing postpartum hemorrhage.
Gavilanes	2015	Response to email queries: PPH 500- 1000 ml Events Total Misoprostol 33 50 Oxytocin 26 50 PPH > 1000 ml Events Total Misoprostol 12 50 Oxytocin 13 50 None of our patients had major morbidity. There were no deaths neither.
Gulmezoglu	2001	Additional data extracted from published Cochrane review(s)
Hofmeyr	1998	Response to email queries: Misoprostol (n=36) Placebo (n=37) RR 95% CI p > 500ml 8 (22%) 15 (41%) 0.55 0.27-1.13 0.15 > 1000ml 2 (5.6%) 5 (14%) 0.41 0.09-1.98 0.23 Add.oxytocic 2 (5.6%) 7 (19%) 0.29 0.07-1.32 0.08
Hofmeyr	2011	Response to email queries: I've checked the original data: all 9 pyrexias were between 39 and 39.9, none 40 or more. The only severe morbidity we recorded were the 9 laparotomies, of whom one had hysterectomy. There was no overlap of data. The Nigeria site in Hofmeyr 2011 was University College Hospital, Ibadan. Fawole 2011 included two other hospitals in Ibadan and other Nigerian sites. Univ college hospital occurs in the title as that is bukola's base, but was not a site. Additional data also retrieved from Hofmeyr GJ, Gülmezoglu AM, Novikova N, Linder V, FerreiraS, Piaggio G. Misoprostol to prevent and treat postpartum haemorrhage: a systematic review and meta-analysis of maternal deaths and dose-related effects. Bulletin of the World Health Organization 2009;87:666-677.

		Additional data also retrieved from Hofmeyr GJ, FerreiraS, Nikodem VC, Mangesi L, Singata M, Jafta Z, Maholwana B, Mlokoti Z, Walraven G, Gülmezoglu AM. Misoprostol for treating postpartum haemorrhage: a randomized controlled trial [ISRCTN72263357]. BMC Pregnancy and Childbirth 2004, 4:167.
Jerbi	2007	Response to email queries: No blood loss more than 1000ml in any group. No transfusion or maternel death in the 2 groups.
Lapaire	2006	Response to email queries: “Calculated” blood loss: Misoprostol (n=24) Oxytocin (n=19) > 500 ml 18 15 >1000 ml 13 11 “Estimated” blood loss: Misoprostol (n=28) Oxytocin (n=28) > 500 ml 18 10 >1000 ml 1 14
Musa	2015	Response to email queries: There was on postpartum blood loss > 1000ml in both group. Range of blood loss was 20-790ml in misoprostol group and 40-790 in oxytocin group. There was no maternal death recorded though participants were followed up only in the early puerperium. There was no major morbidity. The only morbidity recorded was retained placenta that warranted manual removal of placenta. The two cases occur in oxytocin group and none in misoprostol group.
Nasr	2009	Response to email queries: Regarding your queries, I write to confirm that NO women in either group needed major surgery or ICU admission, nor did any have hyperpyrexia, massive bleeding over 1000 mL or major organ failure.
Ortiz-Gomez	2013	Response to email queries: The method of randomisation was made by our Statistical department, and I believe it was a computer-generated sequence.
Owonikoko	2011	Response to email queries: PPH > 500 ml Events Sublingual Misoprostol 34 Intravenous Oxytocin 27 PPH > 1000 ml Events Sublingual Misoprostol 4 Intravenous Oxytocin 5

		Blood loss (ml) Mean SD/CI Total Sublingual Misoprostol 667.12mls 213.38 50 Intravenous Oxytocin 649.90mls 251.15 50 Change in Hb (%) Mean SD/CI Total Sublingual Misoprostol 4.5 3.3 50 Intravenous Oxytocin 4.3 2.97 50
Parsons	2007	Response to email queries: Duration of 3rd Stage >30 Mins Mean (Mins) SD CI Total Intervention 3 6.95 6.11(SD) 6.13-7.76 (CI) 218 Control 2 6.18 4.62(SD) 5.57-6.79(CI) 222
Rosseland	2013	Response to email queries: The data on estimated blood loss is the visually estimated blood loss in the OR. As you can read in the article we believe these data are of limited value and have based our analyses of blood loss on change in Hb instead. A strict perioperative IV fluid protocol was followed, of course. PPH > 500 ml Events Total Oxytocin 4 26 Carbetocin 6 25 Placebo 8 25 PPH > 1000 ml Events Total Oxytocin 0 26 Carbetocin 0 25 Placebo 0 25 Change in Hb (g/dl) Mean SD/CI Total Oxytocin -0.82 0.67 26 Carbetocin -0.50 0.82 25 Placebo -0.84 0.53 25 Change in Hb (%) Mean SD/CI Total Oxytocin 27.9 14.1 26 Carbetocin 25.6 13.6 25 Placebo 15.7 16.5 25
Sadiq	2011	Response to email queries: For fever, there wasn't any patient lost to follow up because each round of study lasted only 24 hours, and throughout this period, the patients were hospitalized (admitted). For fever, we have full data set, but some of the data were published elsewhere (an act that will probably sound strange to you). There wasn't death in the study (another fact that may probably sound

		strange, despite the global reports on maternal mortality in Nigeria). There were differences in baseline characteristics like age, parity, etc. however, we thought to have minimize the effects of these differences through randomization of treatment - even though what was done was not the literary meaning of the term 'randomization' since we did not initially consider a specific patient population. However, we suggested further studies (in my reports) whereby baseline characteristics are made uniform between the two groups. In case of baseline treatment with oxytocin; there is clear demarcation in that the Misoprostol group had no pretreatment with oxytocin.
Samimi	2013	Response to email queries: Because our aim of this study was prevention of PPH not treatment of PPH, therefore we had not mortality or morbidity in our study population, also we used of hemoglobin as indicator of blood loss instead of measurement of blood loss volume.
Shrestha	2011	Response to email queries: We did not find hyperpyrexia (T>40), vital organ failure, ICU admission, surgery, or who died, in either the intervention or control group of this study.
Tewatia	2014	Response to email queries: PPH > 500 ml: Events Misoprostol 0 Oxytocin o PPH > 1000 ml: Events Misoprostol 0 Oxytocin 0 Death: Events Misoprostol 0 Oxytocin 0 Morbidity: Events Misoprostol fever 13, shivering 10,nausea 1, vomiting 1 Oxytocin nausea 1, vomiting 1
Ugwu	2014	Response to email queries: PPH > 500ml Event Total Misoprostol 15 60 Oxytocin 33 60 PPH> 1000ml Event Total misoprostol 1 60 oxytocin 2 60

		Death Event Total Misoprostol 0 60 Oxytocin 0 60 Morbidity Events Total Misoprostol 0 60 Oxytocin 0 60
Walley	2000	Response to email queries: 3rd stage >30 mins Mean (mins) SD CI misoprostol 6.15 3.76 5.62-6.69 oxytocin 7.30 13.08 5.40-9.19 3rd stage >30 mins Events Total Misoprostol 0 194 Oxytocin 2 185
Whigham	2014	Response to email queries: Carbetocin vs oxytocin in non-elective C/S PPH>500ml Events total Carbetocin 42 59 Oxytocin 37 53 PPH>1000ml Events Total Carbetocin 6 59 Oxytocin 6 53 Active labour at time of C/S PPH>500ml Events Total Carbetocin 22 30 Oxytocin 19 28 PPH>1000ml Events Total Carbetocin 4 30 Oxytocin 3 28
Zachariah	2006	Response to email queries: We did not have any maternal deaths in any of the study groups.