

Gravidanza e patologie cardiovascolari

TERAPIA ANTIIPERTENSIVA GUIDATA DALL'EMODINAMICA MATERNA: REVISIONE SISTEMATICA DELLA LETTERATURA E METANALISI

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- L'**ipertensione in gravidanza** riguarda il 5 -15% delle donne.
- Il **trattamento** dei disordini ipertensivi in gravidanza oggi si basa sull'impiego di farmaci raccomandati dalle LG, scelti sulla base della preferenza del clinico.
- Il **target** è la riduzione dei valori di pressione arteriosa materna a prescindere dai **meccanismi fisiopatologici sottostanti**.

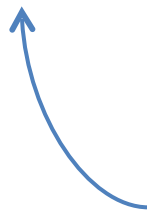


La pressione arteriosa media (MAP) è la risultante di due componenti:

l'output cardiaco



$$\text{MAP} = \text{CO} \times \text{TPVR}$$



resistenze vascolari
Periferiche totali



Tramite metodiche diagnostiche **non invasive** è possibile inquadrare il profilo emodinamico delle pazienti come:

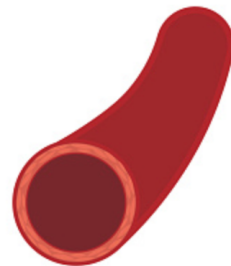
IPODINAMICO

(Basso CO ed alta TPVR)



IPERDINAMICO

(Alto CO e basse TPVR)



Trattamento

Labetalolo^a o metoprololo p.o.^b
(Classe I)

Labetalolo i.v., nicardipina i.v.,
urapidil i.v., Mg⁺⁺ i.v.
(Classe I)

Metildopa p.o.^c
(Classe I)

Nifedipina p.o.^d
(Classe I)

De Backer J, Haugaa KH, Hasselberg NE, de Hosson M, Brida M, Castelletti S, Cauldwell M, Cerbai E, Crotti L, de Groot NM, Estensen M, Goossens ES, Haring B, Kurpas D, McEniery CM, Peters SA, Rakisheva A, Sambola A, Schlager O, Schoenhoff FS, Simoncini T, Steinbach F, Sudano I, Swan L, Valente AM, ESC Scientific Document Group. Linee guida ESC 2025 per il trattamento delle malattie cardiovascolari in gravidanza. *G Ital Cardiol* 2026;27(2 Suppl. 1):e1-e113. doi 10.1714/4637.46475



A quadri emodinamici diversi dovrebbero corrispondere differenti scelte terapeutiche

Farmaci in gravidanza

- ❖ β -bloccanti ($\downarrow$ CO)
- ❖ vasodilatatori come nitroderivati e calcioantagonisti ($\downarrow$ TPVR)
- ❖ **Monoterapia:** labetalolo o metildopa
- ❖ **Monoterapia:** nifedipina
- ❖ **Monoterapia:** in assenza di labetalolo, metoprololo o oxprenololo





IPODINAMICO
(Basso CO ed alta TPVR)

No Beta-bloccanti:
riducono l'output cardiaco

Si Calcio-antagonisti o
nitroderivati:
riducono le resistenze vascolari periferiche



IPERDINAMICO
(Alto CO e basse TPVR)

No calcio-antagonisti:
riducono le resistenze vascolari periferiche

Si beta-bloccanti: riducono
l'output cardiaco



(Oltre alla pressione arteriosa è importante considerare anche la frequenza cardiaca!)

Table 4 Maternal hemodynamic profile and proposed pharmacological approach

Parameter	Hyperdynamic circulation	Hypodynamic circulation
Heart rate ³⁵	>90 beats/min Alpha and beta blockers (alpha methyldopa, labetalol), calcium channel blockers (amlodipine, diltiazem)	<70 beats/min Calcium channel blockers (nifedipine), NO donors + oral fluids
Cardiac output ³⁵	>8 L/min Alpha and beta blockers (alpha methyldopa, labetalol)	<5 L/min Calcium channel blockers (nifedipine), NO donors + fluids
Total peripheral vascular resistance ³⁵	<800 dynes.s.cm ⁻⁵ Alpha and beta blockers (alpha methyldopa, labetalol)	>1,300 dynes.s.cm ⁻⁵ Calcium channel blockers (nifedipine), NO donors + fluids
Mean arterial pressure/Heart rate ³⁶	<1.1 Labetalol	>1.4 Nifedipine, NO donors + oral fluids

Source: Adapted from Vasapollo et al³⁵ and Mulder et al.³⁶

AIPE-SIMP Position Statement on Maternal Hemodynamics Vasapollo et al.



Table 4 Hemodynamic parameters and proposed therapeutic approach according to maternal hemodynamic profile

<i>Parameter</i>	<i>Hypodynamic circulation</i>	<i>Normodynamic circulation</i>	<i>Hyperdynamic circulation</i>
HR (bpm)	< 70	70–90	> 90
CO (L/min)	< 5	5–8	> 8
TPVR ($\text{dynes} \times \text{s} \times \text{cm}^{-5}$)	> 1300	800–1300	< 800
MAP/HR ratio (mmHg/bpm)	> 1.4	1.1–1.4	< 1.1
First-line therapy	Dihydropyridine calcium-channel blocker (e.g. nifedipine, amlodipine, lercanidipine) or non-dihydropyridine calcium-channel blocker (diltiazem)*	α -methyldopa	Labetalol or α -methyldopa†
Second-line therapy	α -methyldopa, optionally with first-line agent	Non-dihydropyridine calcium-channel blocker (diltiazem) or dihydropyridine calcium-channel blocker (amlodipine), optionally with first-line agent	Non-dihydropyridine calcium-channel blocker (diltiazem) or dihydropyridine calcium-channel blocker (amlodipine), optionally with first-line agent

*Requires agents that induce direct vasodilation of smooth muscle; β -blockers may provoke bradycardia and hypoperfusion in these patients. Observational studies^{9,10,12,19–21,35} report that adding fluid therapy and nitric oxide donors to standard antihypertensive management may help to correct hypovolemia and increased vascular tone characteristic of hypodynamic circulation, which is linked frequently to fetal growth restriction; however, this approach is not endorsed by current international guidelines. †Requires agents that target cardiac output (CO), often associated with tachycardia, rather than vasculature; dihydropyridine calcium-channel blockers may be poorly tolerated. HR, heart rate; MAP, mean arterial pressure; TPVR, total peripheral vascular resistance.



Hemodynamics-guided treatment of hypertensive disorders of pregnancy: systematic review and meta-analysis

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T. GHI⁸, F. MECACCI⁹, N. CHIANCHIANO¹⁰, G. CASTELLINI¹¹, T. STAMPALIJA^{12,13} 
and Collaborators[†]



Obiettivo

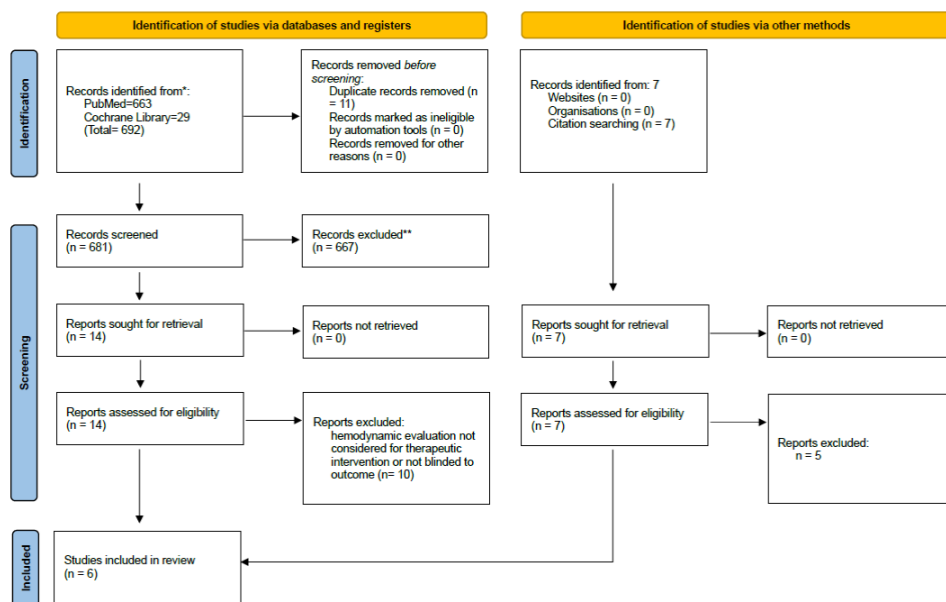
Valutare, dai dati presenti in letteratura, se il **trattamento antipertensivo** guidato da una **valutazione emodinamica materna non invasiva** riduca gli esiti **avversi materni e perinatali** rispetto alla gestione standard basata sulla pressione arteriosa.



Metodi

- Sono stati consultati PubMed/MEDLINE e la Cochrane Library dalla loro origine fino al 15 giugno 2025.
- HDP con valutazione emodinamica non invasiva (ecocardiografia, USCOM)
- Terapia guidata dall'emodinamica vs terapia standard
- **Outcome:** preeclampsia, HELLP, ipertensione severa, FGR, parto <34 sett, morte perinatale





**6 studi inclusi:
(1 RCT, 5 osservazionali/case-control)**

intervention group: 418 - 614 patients,
control group: 546 - 731 patients.



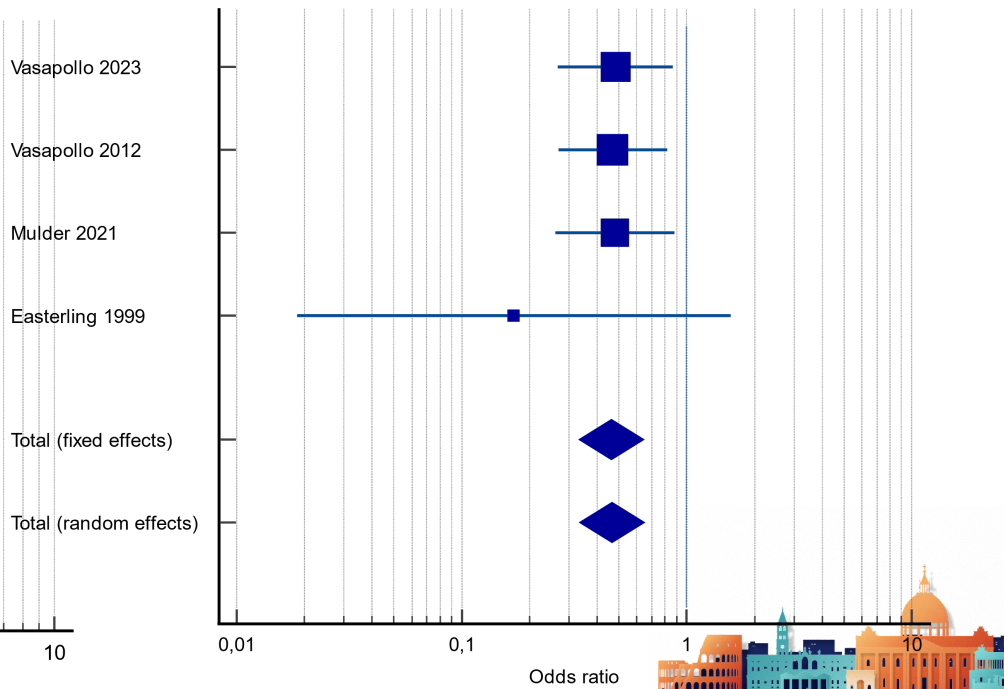
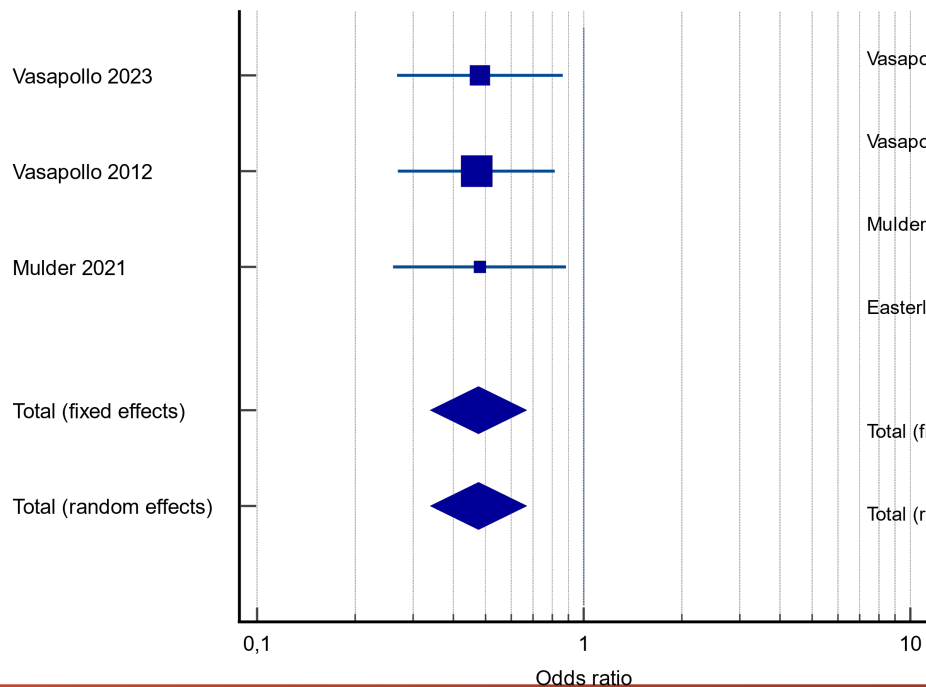
Table 1 Characteristics of six studies included in systematic review and meta-analysis of hemodynamics-guided management of hypertensive disorders of pregnancy

<i>Study</i>	<i>Design</i>	<i>Cases (n)*</i>	<i>Controls (n)*</i>	<i>Study population</i>	<i>Hemodynamic assessment</i>	<i>Therapeutic management</i>	<i>Outcome(s) reported</i>
Easterling (1999) ¹³	Randomized controlled trial	28	28	Pregnant women at risk for PE with hyperdynamic circulation (CO > 7.4 L/min at 22–25 weeks)	Single measurement of CO using Doppler monitor (UltraCOM®)	Randomization to atenolol <i>vs</i> placebo	PE
Vasapollo (2012) ⁹	Non-randomized interventional study	100	300	Pregnant women with early-onset hypodynamic mild hypertension (TPVR > 1350 dynes × s × cm ⁻⁵ at 22–27 weeks)	Single measurement of TPVR using transthoracic echocardiography	Sequential allocation to SC (nifedipine) <i>vs</i> SC + NO donor <i>vs</i> SC + oral fluids <i>vs</i> SC + NO donor + oral fluids	PE, HELLP syndrome, severe hypertension, FGR, placental abruption, PTB, PND
Stott (2017) ¹¹	Non-randomized interventional study	52	50	Pregnant women with hypertension	Serial monitoring of SV and CO using bioreactance CO monitor (NICOM®)	Cases received labetalol or labetalol + vasodilator according to prediction model; controls received labetalol universally	Severe hypertension
Mulder (2021) ⁶	Non-randomized interventional study	157	157	Pregnant women with previous PE at risk of recurrence	Serial monitoring of CO, TPVR and BP using transthoracic echocardiography (cases only)	Cases with ≥ 2 hemodynamic parameters outside GA-normalized physiological reference range treated with labetalol, α-methyldopa or nifedipine, according to hemodynamic profile, with potential for adjustment at each clinical visit	PE, eclampsia, HELLP syndrome, FGR, placental abruption, PTB, PND
Vasapollo (2023) ¹⁰	Non-randomized interventional study	161	160	Pregnant women with chronic hypertension and hypodynamic circulation (TPVR > 1300 dynes × s × cm ⁻⁵ at 24 weeks)	Single measurement of TPVR using transthoracic echocardiography	Allocation to SC (α-methyldopa + nifedipine or amlodipine) <i>vs</i> SC + NO donor + oral fluids	PE, HELLP syndrome, severe hypertension, FGR, placental abruption, PTB, PND
di Pasquo (2024) ⁸	Multicenter observational cohort study	116†	36†	Pregnant women with <i>de-novo</i> hypertension or PE at 22–38 weeks	Single measurement of CO, HR, SVR and SV using continuous-wave Doppler monitor (USCOM 1A®)	Clinician blinded to hemodynamic profile prescribed vasodilator or β-blocker; therapy was considered appropriate retrospectively if hypodynamic profile (CO ≤ 5 L/min and/or SVR ≥ 1300 dynes × s × cm ⁻⁵) received vasodilator and hyperdynamic profile (CO > 5 L/min and/or SVR < 1300 dynes × s × cm ⁻⁵) received labetalol	Severe hypertension

Only first author is given for each study. *Cases denote patients treated according to maternal hemodynamic profiling, while controls are patients who received standard care (SC). †Cases denote patients determined retrospectively to have received hemodynamically appropriate therapy, while controls are patients who received inappropriate therapy. BP, blood pressure; CO, cardiac output; FGR, fetal growth restriction; GA, gestational age; HR, heart rate; NO, nitric oxide; PE, pre-eclampsia; PND, perinatal death; PTB, preterm birth; SV, stroke volume; SVR, systemic vascular resistance; TPVR, total peripheral vascular resistance.

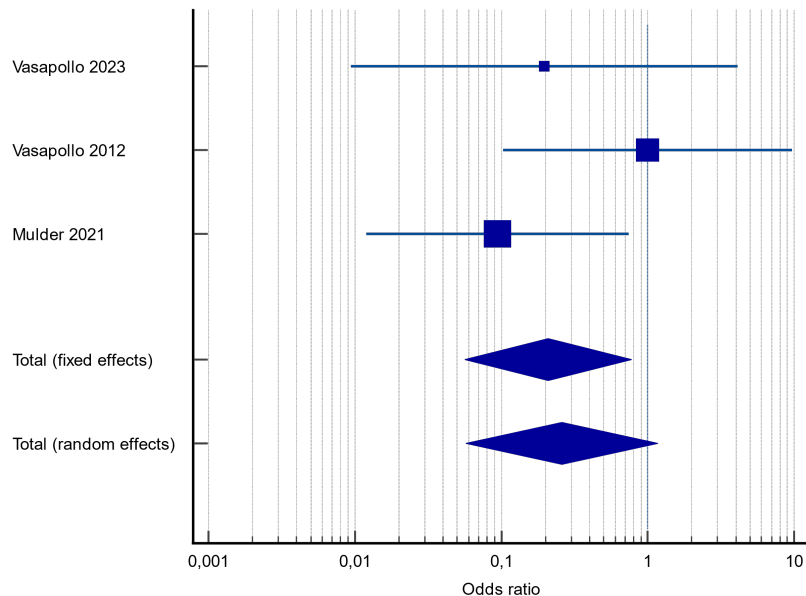
Preeclampsia

Riduzione rischio del 52%
OR 0.48 (95% CI 0.34–0.67)



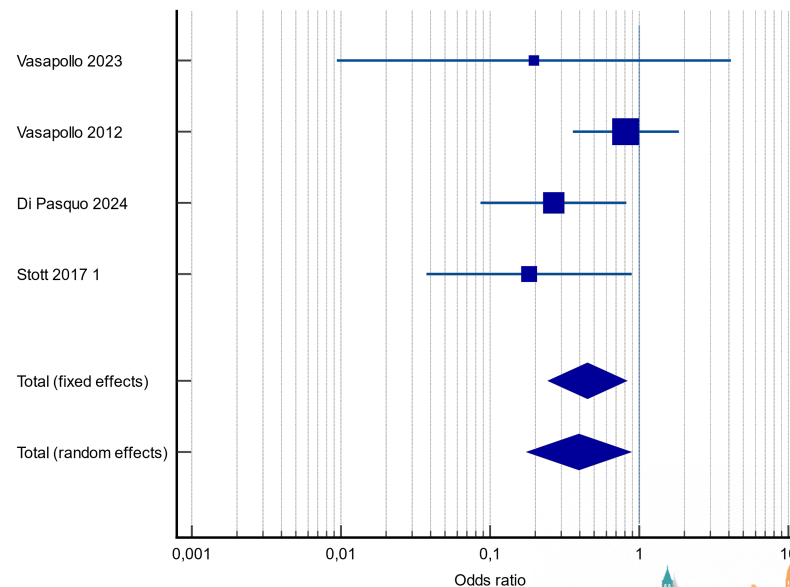
HELLP:

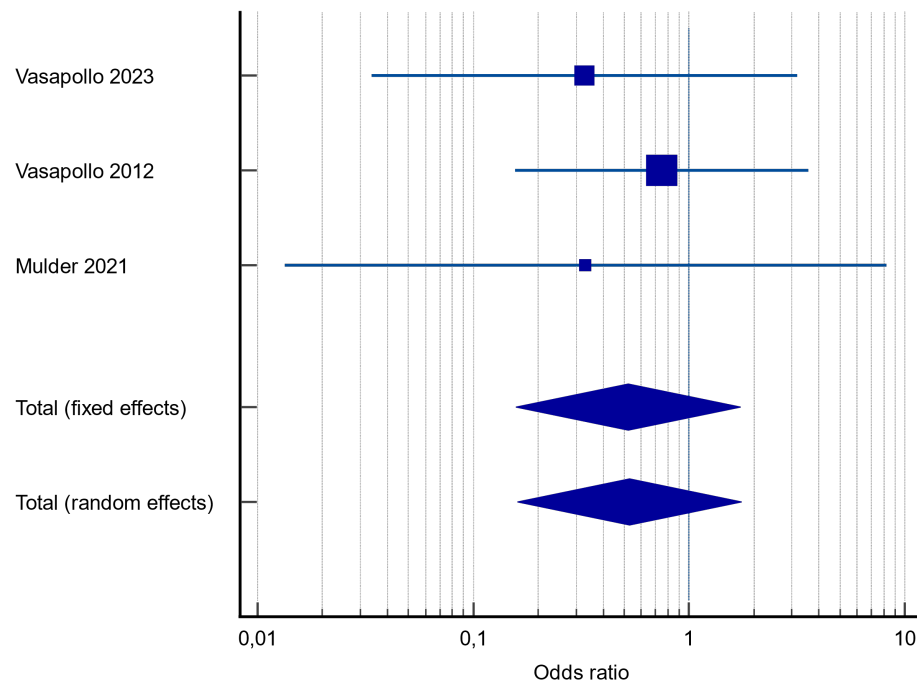
OR 0.21 (0.06–0.78) → –79%



Iipertensione severa:

OR 0.45 (0.25–0.82) → –55%



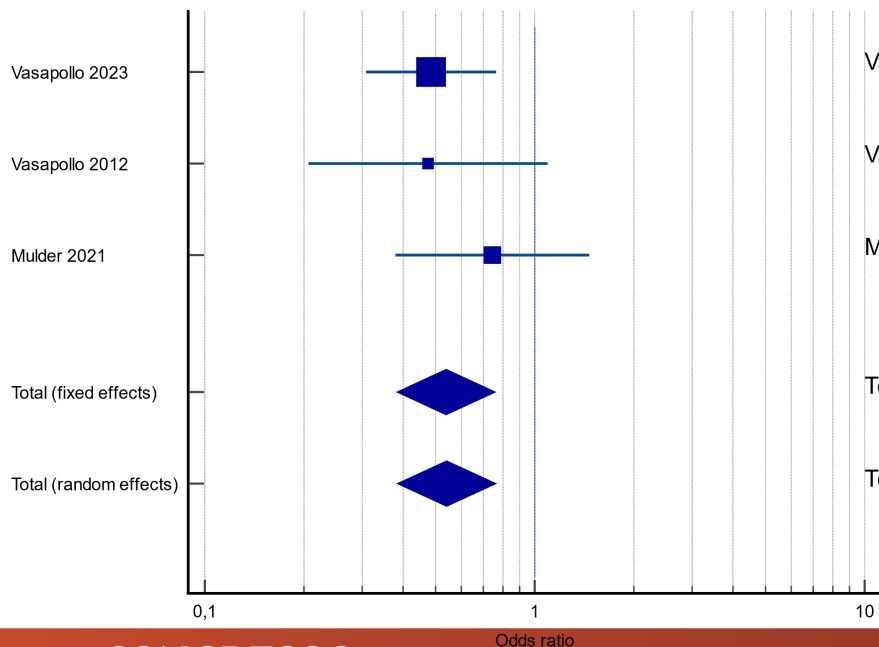


Abruption placentae:
OR 0.53 (0.16–1.75) → NS



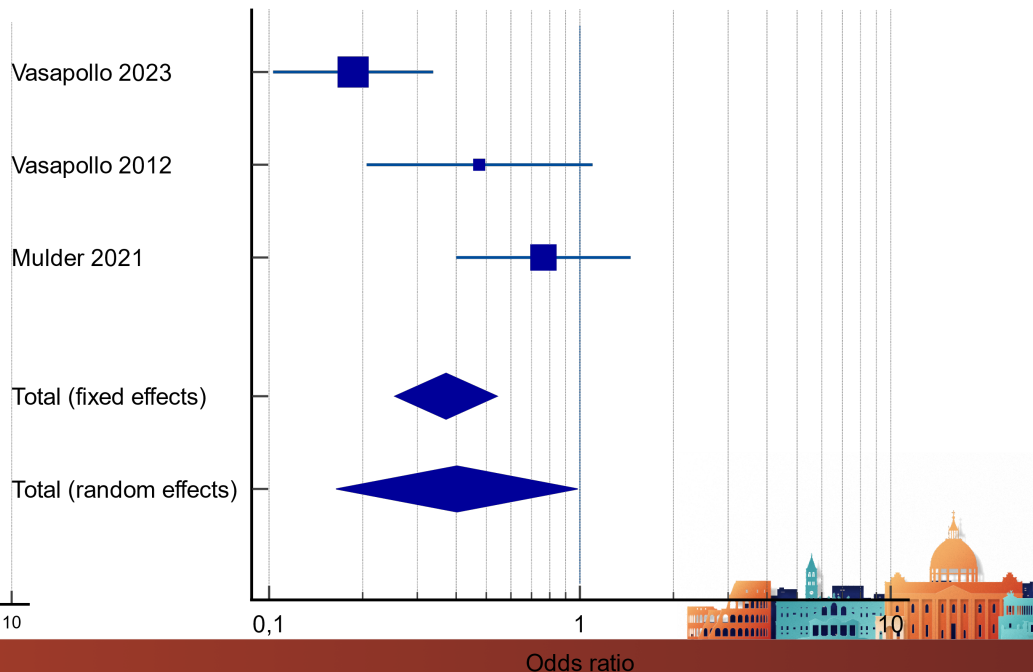
Fetal Growth Restriction:

OR 0.54 (0.38–0.76) → –46%



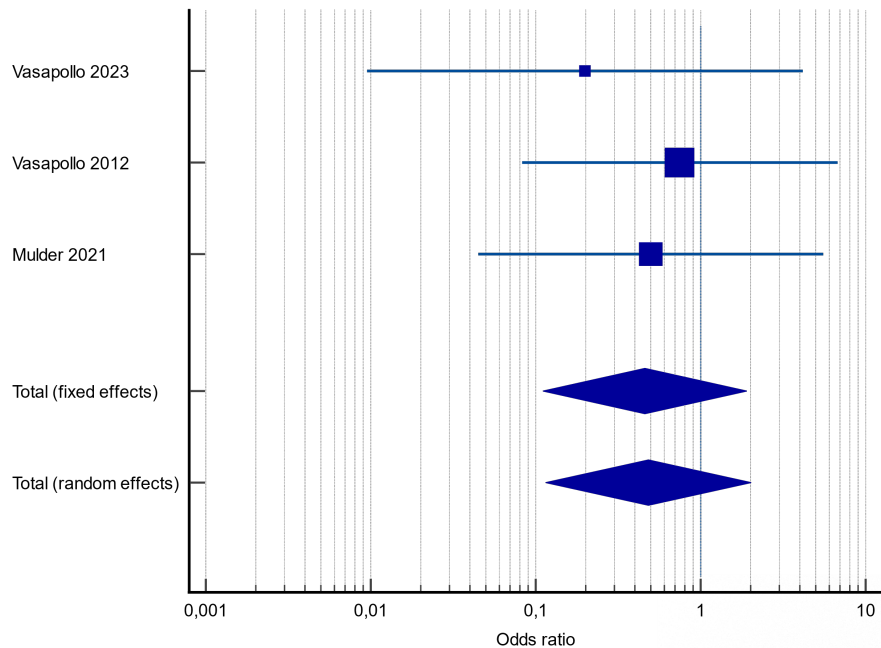
Parto <34 sett.:

OR 0.37 (0.25–0.54) → –63%



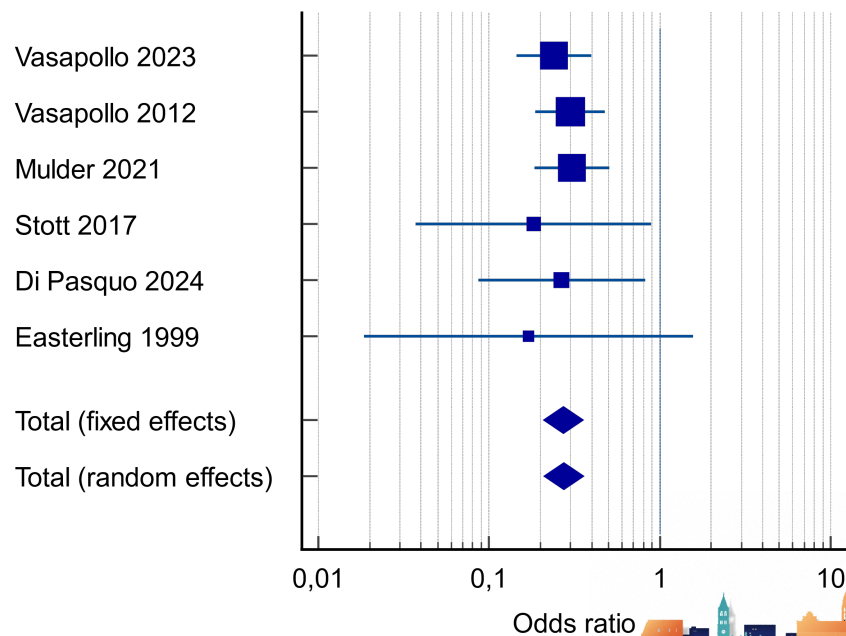
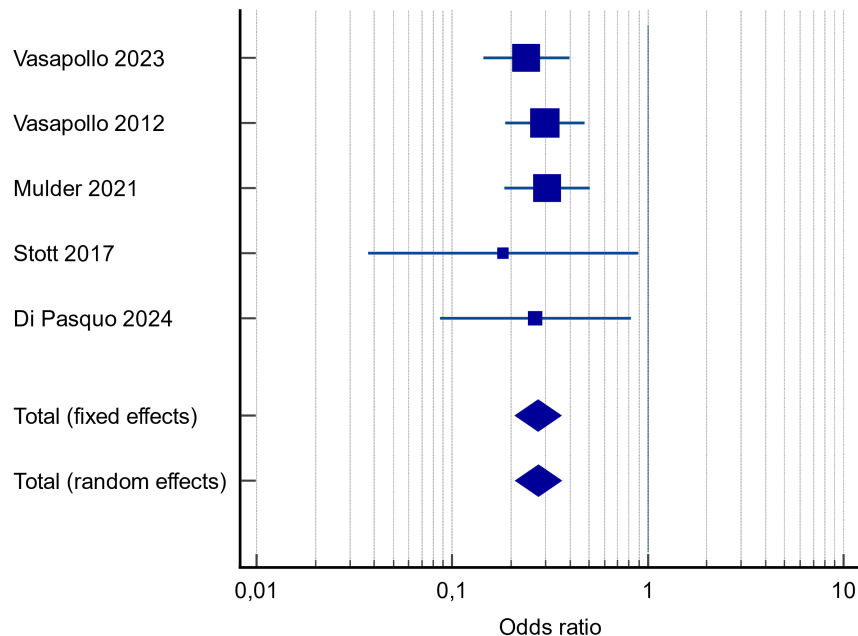
Morte perinatale:

OR 0.46 (0.11–1.90) → NS



OR complessivo 0.28 (95% CI 0.21–0.36)

Riduzione di circa 70% del rischio di eventi avversi globali



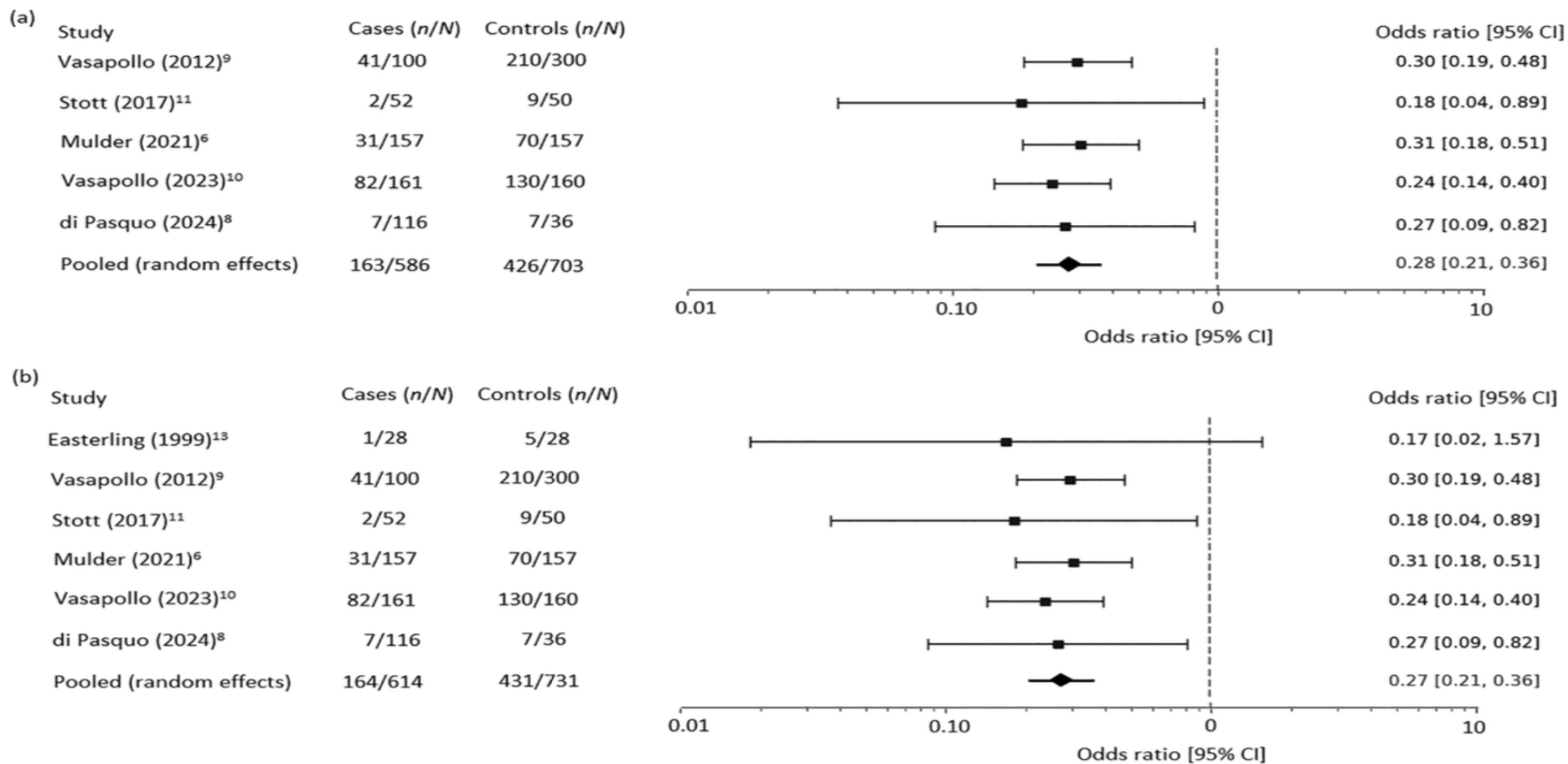


Figure 2 Forest plots showing prevalence of composite adverse outcome in women managed by hemodynamics-guided antihypertensive therapy *vs* standard care, excluding (a) and including (b) randomized controlled trial of Easterling *et al.*¹³. Only first author is given for each study.

Conclusioni

Questi risultati supportano
l'utilizzo del **monitoraggio emodinamico non invasivo** per personalizzare
il trattamento nelle gravidanze complicate da ipertensione.

Personalizzare la terapia antipertensiva sulla base del profilo
emodinamico materno migliora significativamente l'outcome composito
materno-fetale.





Vi aspettiamo!

