Pathologie Vasculaire Placentaire
EBM et aspirine

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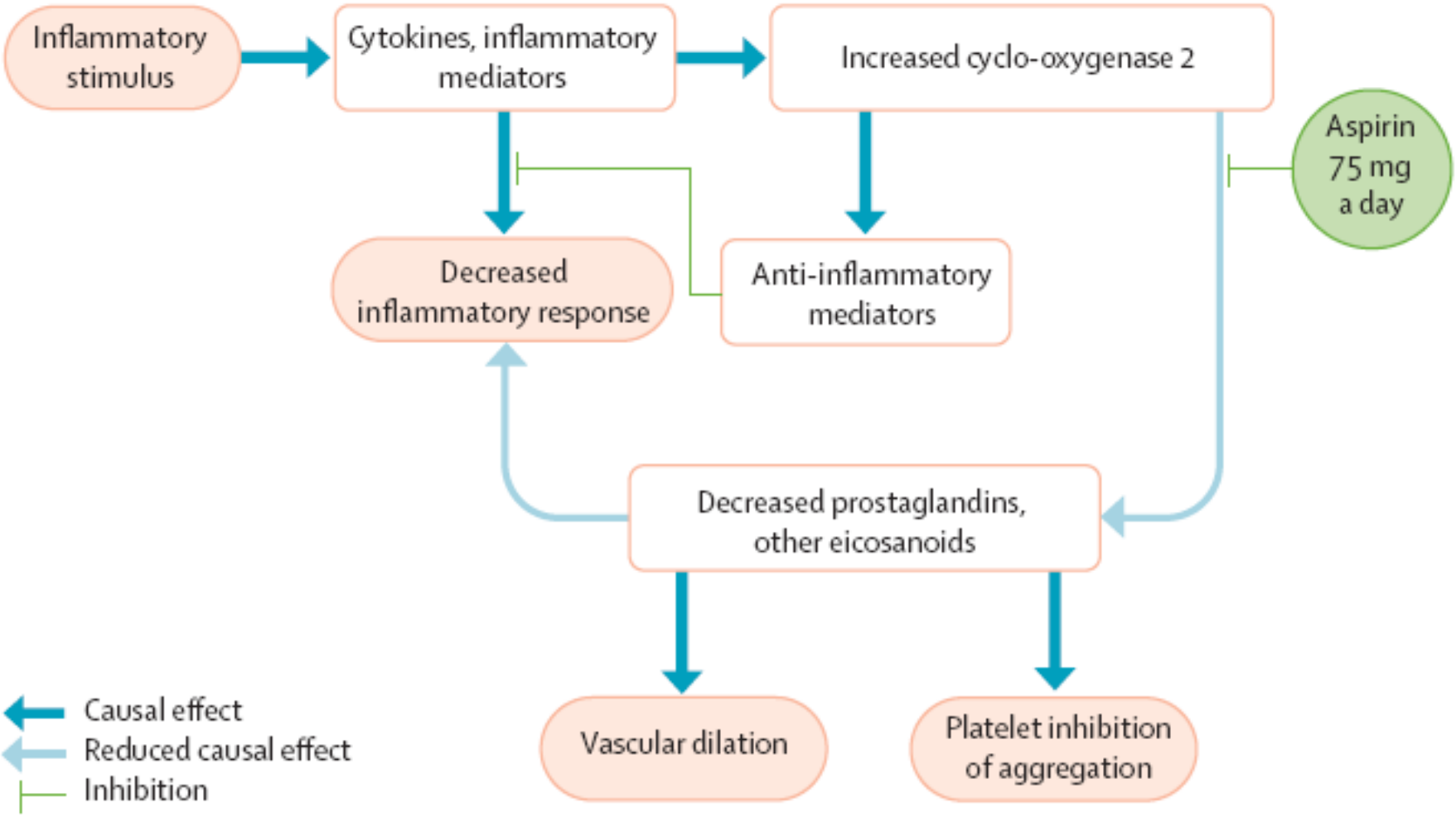
Effets de l'aspirine

- Effets anti-aggrégant plaquettaire
  - Effet sur les thromboses placentaires
  - Effet sur l'activation plaquettaire précoce en rapport avec le syndrome maternel
- Effets la balance vasoconstrictrice-vasodilatarice
  - Augmentation des PGI2
  - Diminution de TXA2

Effets de l'aspirine



Aspirine

- Modalités de prescription
  - 100 à 160 mg
  - A partir de 8-12 SA lorsque l'indication est liée aux ATCD obstétricaux
  - Avant en cas de lupus ou SAPL
  - Pas de surveillance de la coagulation

Aspirine (risque général)

Subtil D et al. BJOG 2003

Table 2. Frequency of pre-eclampsia and related complications. Percentages are in parentheses.

	Aspirin	Placebo	RR (95% CI)
Mothers	(n = 1634)	(n = 1640)	
Hypertension	151/1632 (9.3)	131/1637 (8.0)	1.16 (0.92–1.45)
Pre-eclampsia	28/1632 (1.7)	26/1637 (1.6)	1.08 (0.64–1.83)
With birth ≤32 weeks	3/1632 (0.2)	5/1637 (0.3)	0.60 (0.14–2.51)
With birth <37 weeks	8/1632 (0.5)	14/1637 (0.9)	0.57 (0.24–1.36)
Severe	9/1632 (0.6)	10/1637 (0.6)	0.90 (0.37–2.22)
HELLP syndrome	11/1625 (0.7)	5/1632 (0.3)	2.21 (0.77–6.35)
Placental abruption	13/1623 (0.8)	9/1628 (0.6)	1.45 (0.62–3.38)
Children[a]	(n = 1645)	(n = 1660)	
Induced preterm delivery	47/1642 (2.9)	42/1655 (2.5)	1.13 (0.75–1.70)
Birthweight ≤ 3rd centile	47/1643 (2.9)	28/1660 (1.7)	1.70 (1.07–2.69)
Birthweight ≤ 10th centile	199/1643 (12.1)	189/1657 (11.4)	1.06 (0.88–1.28)
Perinatal death	12/1645 (0.7)	11/1660 (0.7)	1.11 (0.49–2.50)
In utero	9 (0.5)	8 (0.5)	
Neonatal	3 (0.2)	3 (0.2)	
Vascular cause	6 (0.4)	6 (0.4)	
Non-vascular cause	4 (0.2)	5 (0.3)	
Unknown cause	2 (0.1)	0 (0.0)	

[a] Births ≥22 weeks, medically indicated termination of pregnancy excluded.

Meta analyse (PE – Bas risque)

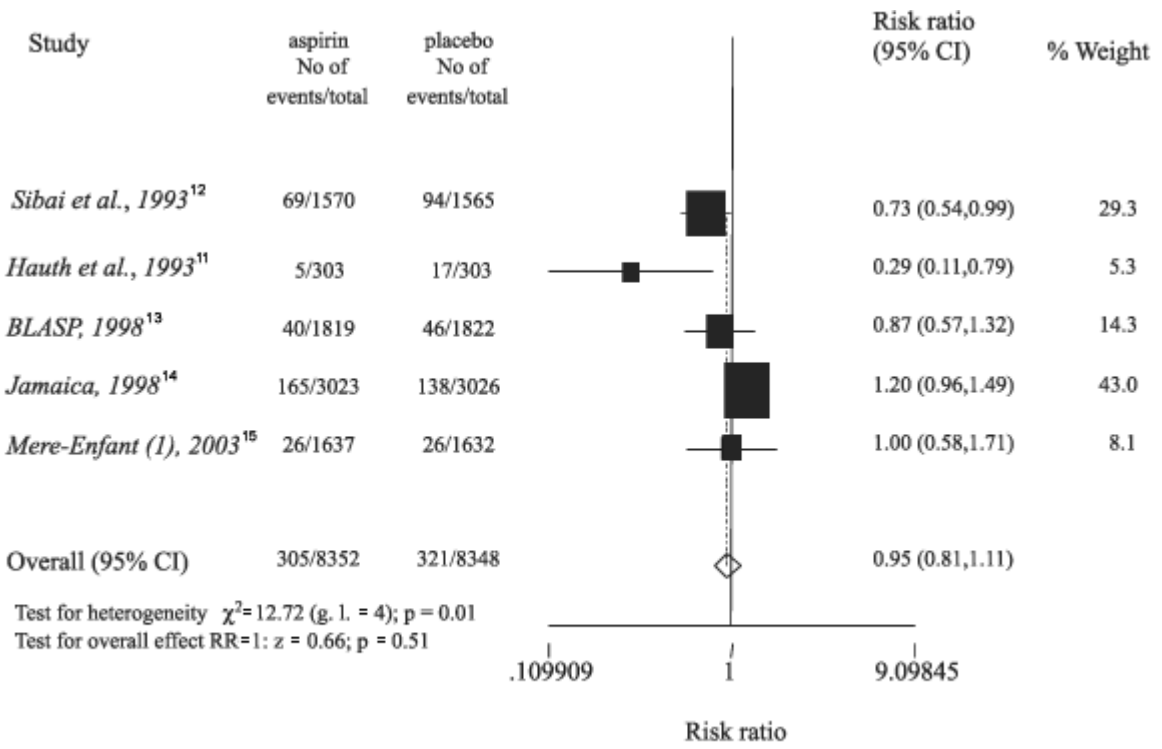


Figure 1 - Effect of low-dose aspirin in the expected outcome in women at low risk for preeclampsia

Ruano R et al. Clinics 2005

Meta analyse (PE – Haut risque)

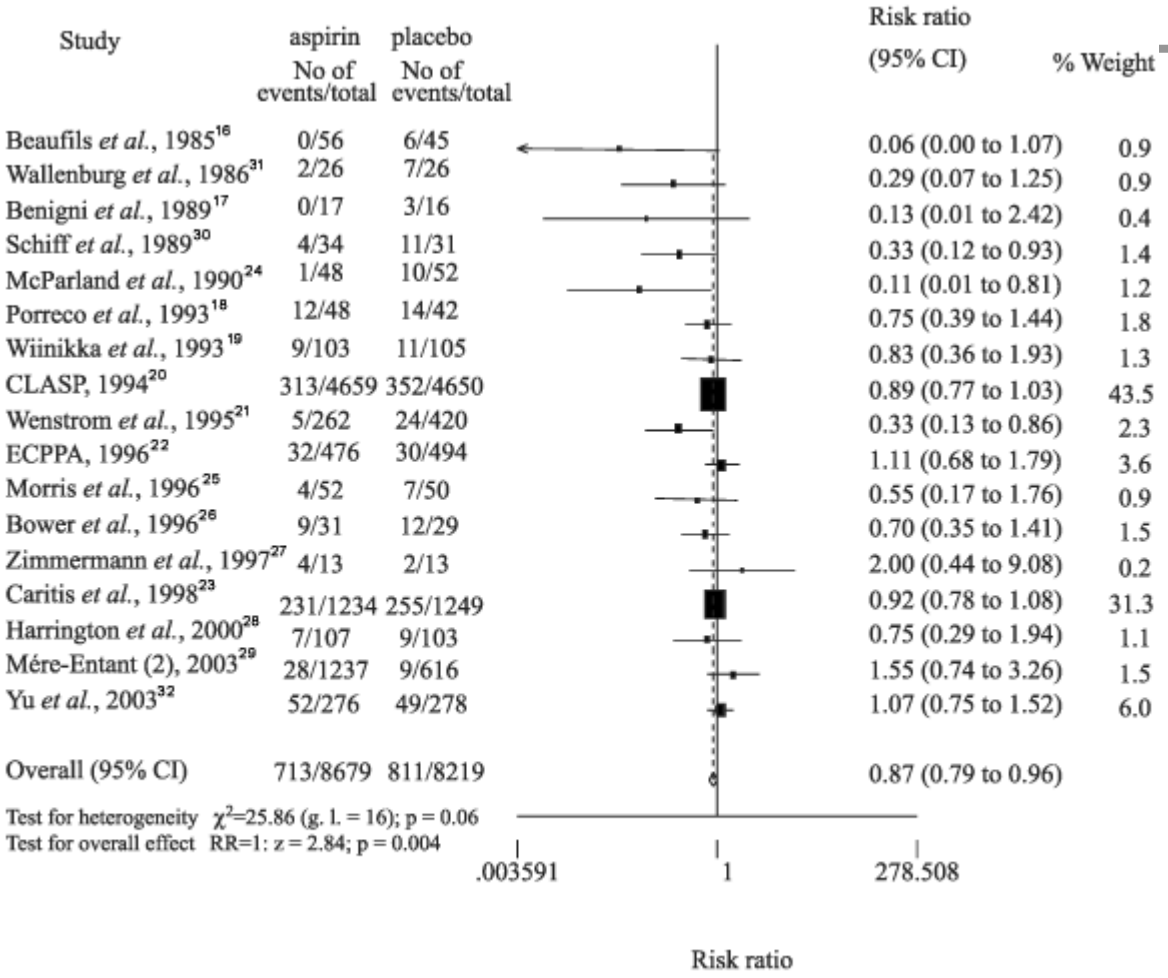


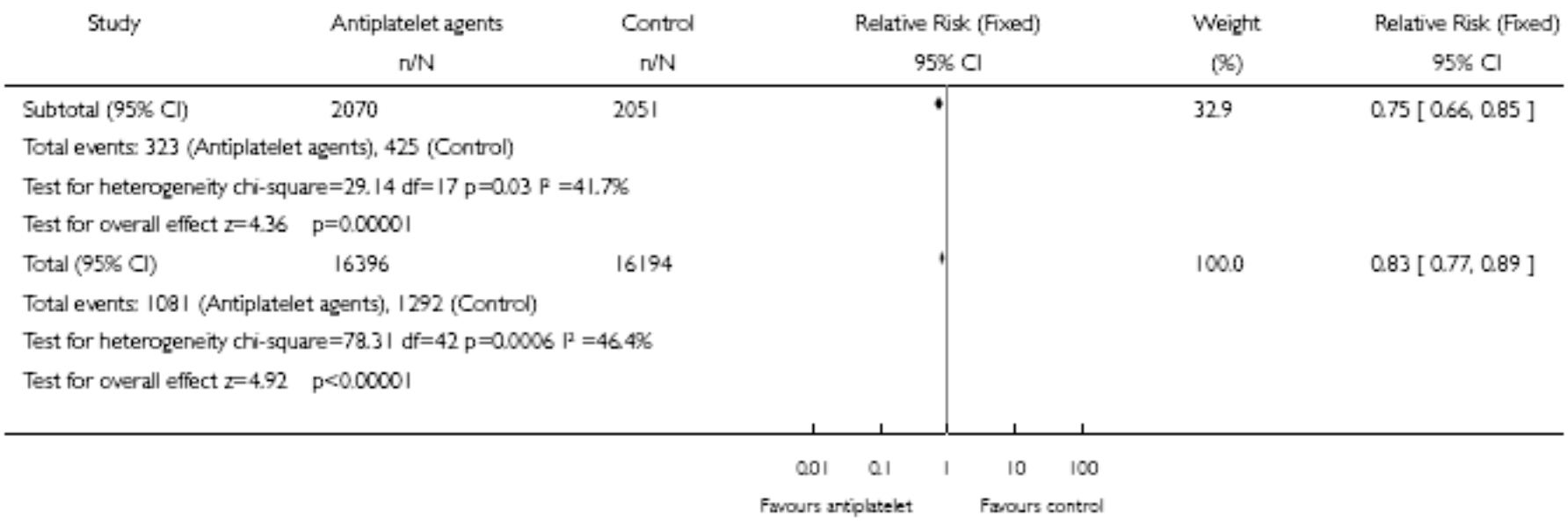
Figure 2 - Effect of low-dose aspirin in the expected outcome in women at high risk for preeclampsia

Ruano R et al. Clinics 2005

Données divergentes des MA

- Modèles variables selon l'hétérogénéité des essais pris en compte
- Inclusion de petites études
- Inclusion des études anciennes
- Données agrégées ou individuelles

Aspirine (risque global)



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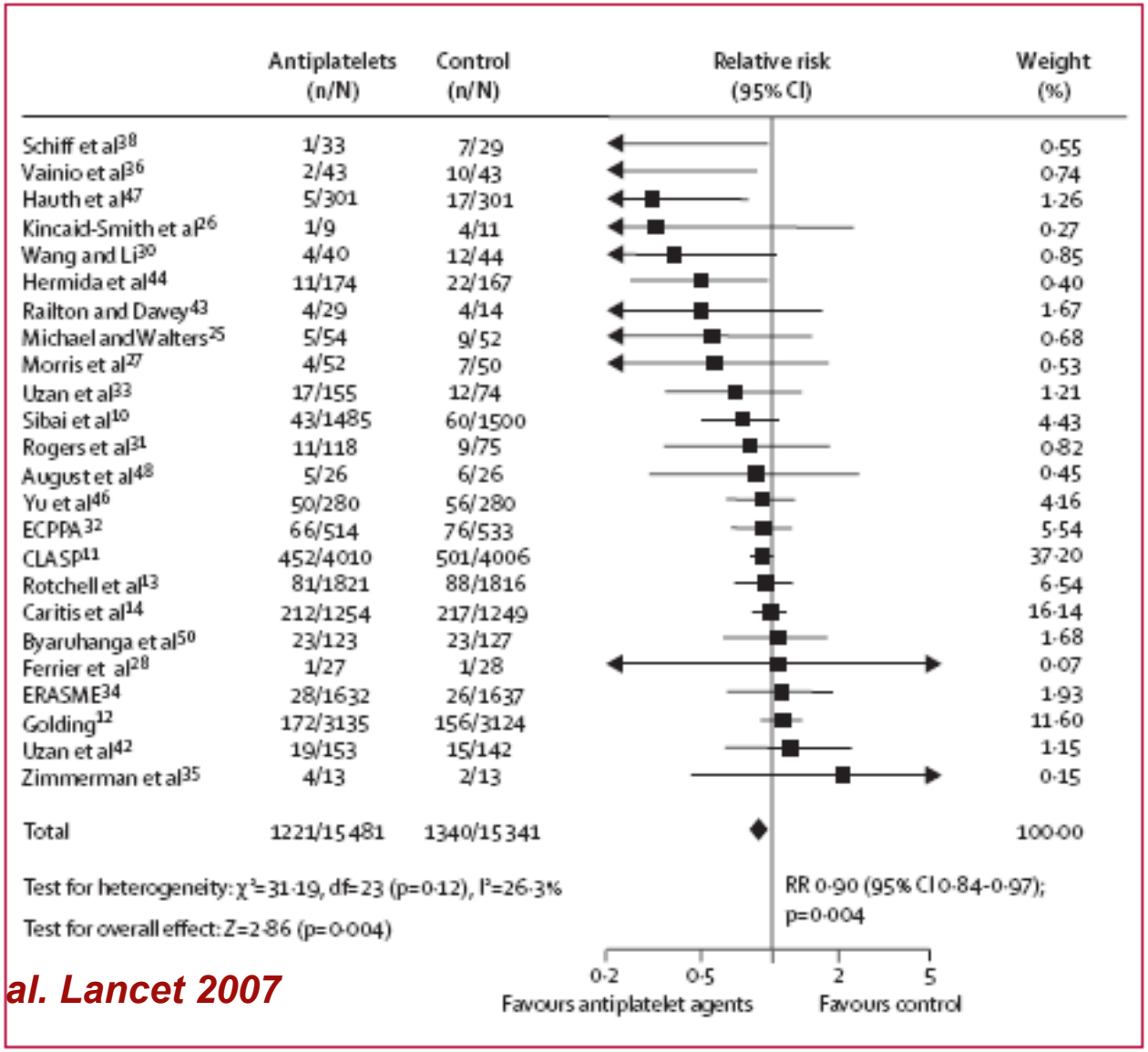
Aspirine (risque global)



	Antiplatelets (n/N)	Control (n/N)	Weight (%)
Schiff et al[38]	1/33	7/29	0·55
Vainio et al[36]	2/43	10/43	0·74
Hauth et al[47]	5/301	17/301	1·26
Kincaid-Smith et al[26]	1/9	4/11	0·27
Wang and Li[30]	4/40	12/44	0·85
Hermida et al[44]	11/174	22/167	0·40
Railton and Davey[43]	4/29	4/14	1·67
Michael and Walters[25]	5/54	9/52	0·68
Morris et al[27]	4/52	7/50	0·53
Uzan et al[33]	17/155	12/74	1·21
Sibai et al[10]	43/1485	60/1500	4·43
Rogers et al[31]	11/118	9/75	0·82
August et al[48]	5/26	6/26	0·45
Yu et al[46]	50/280	56/280	4·16
ECPPA[32]	66/514	76/533	5·54
CLASP[11]	452/4010	501/4006	37·20
Rotchell et al[13]	81/1821	88/1816	6·54
Caritis et al[14]	212/1254	217/1249	16·14
Byaruhanga et al[50]	23/123	23/127	1·68
Ferrier et al[28]	1/27	1/28	0·07
ERASME[34]	28/1632	26/1637	1·93
Golding[12]	172/3135	156/3124	11·60
Uzan et al[42]	19/153	15/142	1·15
Zimmerman et al[35]	4/13	2/13	0·15
Total	1221/15 481	1340/15 341	100·00

Test for heterogeneity: χ^2=31·19, df=23 (p=0·12), I^2=26·3%

Test for overall effect: Z=2·86 (p=0·004)

RR 0·90 (95% CI 0·84–0·97); p=0·004

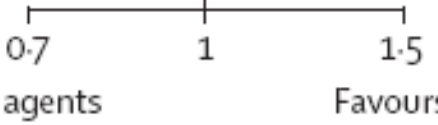
0·2 0·5 2 5

Favours antiplatelet agents Favours control

Askie LM et al. Lancet 2007

Aspirine (risque global)

	Antiplatelets n/N	Control n/N	Number of trials	Relative risk (95% CI)	Relative risk (95% CI)
Pre-eclampsia	1221/15481	1340/15341	24		0·90 (0·84–0·97)
Delivery <34 weeks' gestation	1018/15709	1111/15523	26		0·90 (0·83–0·98)
Fetal/baby death before discharge	484/15412	524/15260	23		0·91 (0·81–1·03)
Small for gestational age infant	568/10772	624/10654	20		0·90 (0·81–1·01)
Pregnancy with serious adverse outcome*	1552/8684	1716/8698	13		0·90 (0·85–0·96)



Askie LM et al. Lancet 2007

Effet selon la dose d'aspirine

- Pas de lien entre la dose d'aspirine et la réduction du risque de PE

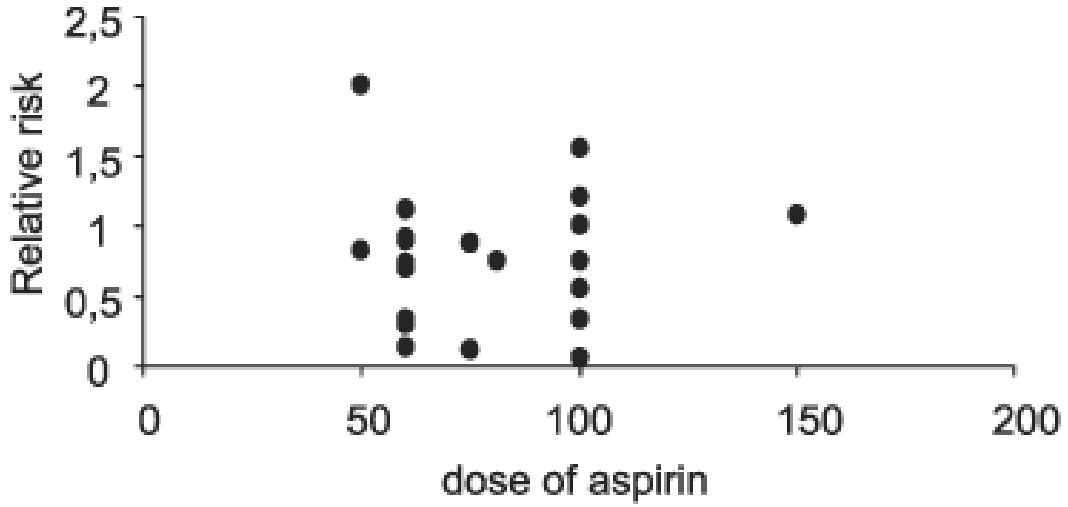


Figure 3 - Correlation between dose of aspirin and relative risk for preeclampsia in each trial

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Effet Dose

Table 1 Primary Prevention Trials: Prevention of MI and Stroke

Trial	Ref	ASA dose/day	MI	*P*	Stroke	*P*
WHS	4	50 mg*	+2%	ns	−17%	.04
HOT	5	75 mg Men	−42%	.001	−1%‡	ns
		75 mg Women	−19%	ns		
PPP	6	100	−31%	ns	−33%	ns
PHS	7	160†	−44%	<.001	+22%	ns
UK	8	500 mg/D	−3%	ns	+17%	ns

ASA = aspirin; WHS = Women's Health Study; HOT = Hypertension Optimal Treatment study; PPP = Primary Prevention Project; PHS = Physician's Health Study; UK = British physician study.

*50 mg/day = 100 mg QOD.

†160 mg/day = 325 mg QOD.

‡Stroke data for men and women combined.

Table 2 Lowest Effective Dose (mg/day)

Primary prevention	
MI in men age 50+	160
MI in women age 50+	>100
Stroke in men 50+	Unknown
Stroke in women 50+	>100
Stroke in men/women with AF	325
Secondary prevention	
MI in men/women with CAD	75
MI/death in men/women with AMI	160
Stroke in men/women with HX stroke/TIA	50
Stroke/death in men/women with acute stroke	160

MI = myocardial infarction; AF = atrial fibrillation; CAD = coronary artery disease; AMI = acute mycardial infarction; HX = history of; TIA = transient ischemic attack.

Dalen JE et al. AM J Med 2006

ATCD

- Pas de variation de l'effet ASP selon les ATCD

Subgroup	Category	Antiplatelets n/N	Control n/N	Relative risk (95% CI)	Interaction p value
Pregnancy and medical history					
First pregnancy with or without any high risk factor	With	195/1194	212/1176	0·90 (0·76–1·08)	0·71
	Without	287/7335	327/7288	0·87 (0·75–1·02)	
Second or subsequent pregnancy with or without any high risk factor	With	659/5375	720/5281	0·89 (0·81–0·99)	0·56
	Without	79/1545	79/1556	0·98 (0·73–1·33)	
Second or subsequent pregnancy with or without history of HDP	With	449/3116	497/2991	0·86 (0·77–0·97)	0·25
	Without	289/3799	302/3849	0·96 (0·82–1·12)	
Pre-existing renal disease	Yes	21/240	31/210	0·63 (0·38–1·06)	0·23
	No	814/11131	896/11072	0·90 (0·82–0·96)	
Pre-existing diabetes	Yes	60/439	82/466	0·76 (0·56–1·04)	0·26
	No	1053/12707	1138/12601	0·91 (0·84–0·99)	
Pre-existing hypertension	Yes	293/1678	295/1625	0·97 (0·84–1·12)	0·28
	No	849/11641	958/11603	0·88 (0·81–0·96)	
Previous infant small for gestational age	Yes	187/1635	160/1491	1·05 (0·86–1·28)	0·27
	No	308/3419	370/3498	0·85 (0·73–0·98)	
	No previous infant	482/8529	539/8464	0·89 (0·79–0·99)	

Askie LM et al. Lancet 2007

Effet ASP selon la prévalence

- Pas de variation de l'effet ASP selon les sous groupes

Subgroup	Category	Antiplatelets n/N	Control n/N	Relative risk (95% CI)	Interaction p value
Current pregnancy					
Maternal age (years)	<20	158/3593	161/3593	0·97 (0·78–1·20)	0·35
	20–35	924/10 935	1038/10 777	0·87 (0·80–0·95)	
	>35	139/911	139/927	1·02 (0·83–1·26)	
Pregnancy type	Singleton	1114/14 325	1206/14 187	0·91 (0·84–0·98)	0·67
	Multiple	57/544	71/577	0·85 (0·61–1·18)	
Trial factors					
Gestation treatment started (weeks)	<20	686/9171	776/9023	0·87 (0·79–0·96)	0·24
	≥20	534/6263	560/6260	0·95 (0·85–1·06)	
Intended aspirin dose* (mg/day)	≤75	1065/12 766	1163/12 784	0·92 (0·85–0·99)	0·23
	>75	115/2369	142/2316	0·77 (0·61–0·97)	

Askie LM et al. Lancet 2007

Meta analyse Cochrane

- PE :
  - Réduction de 17% (46 trials, 32,891 women)
  - RR 0.83, (95% CI : 0.77- 0.89)
  - NNT 72 (52, 119)
    - Haut risque (risk difference (RD) -5.2% (-7.5, -2.9), NNT 19 (13, 34)
    - Risque modéré (RD -0.84 (-1.37, -0.3), NNT 119 (73, 333)
- Naissance prématurée :
  - réduction de 8% (29 trials, 31,151 women)
  - RR 0.92, (95% CI : 0.88 - 0.97)
  - NNT 72 (52, 119)
- MFIU et DC néonatal
  - Réduction de 14% (40 trials, 33,098 women,
  - RR 0.86, 95% CI 0.76 - 0.98)
  - NNT 243 (131, 1,666)
- Hypotrophie
  - Réduction de 10% (36 trials, 23,638 women)
  - RR 0.90, (95% CI : 0.83 - 0.98).

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Conclusions de la Cochrane

- « Les anti aggrégants plaquettaires ont des effets modérés sur la prévention de la PE et des ses conséquences. D'autres essais seront nécessaires pour déterminer les patientes chez lesquelles le TT est le plus efficace, quand il doit être débuté et à quelle dose »

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NNT selon la prévalence attendue

	Sample baseline event rate	PARIS relative risk (95%CI)	Number needed-to-treat (95% CI)
Pre-eclampsia	18%	0·90 (0·84–0·97)	56 (35–185)
	6%		167 (104–556)
	2%		500 (313–1667)
Preterm <34 weeks	20%	0·90 (0·83–0·98)	50 (29–250)
	10%		100 (59–500)
	2%		500 (294–2500)
Perinatal death	7%	0·91 (0·81–1·03)	159 (75–476)
	4%		278 (132–833)
	1%		1111 (526–3333)
Small for gestational age baby	15%	0·90 (0·81–1·01)	67 (35–667)
	10%		100 (53–1000)
	1%		1000 (526–10 000)
Pregnancy with serious adverse outcome	25%	0·90 (0·85–0·96)	40 (27–100)
	15%		67 (44–167)
	7%		143 (95–357)

Table 4: PARIS number needed-to-treat with sample baseline event rates

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Conclusion

- Confirmation d'un effet faible mais bien réel de l'aspirine (10-15%)
- Nécessité de poursuivre des essais de forte puissance afin de préciser les sous groupes qui en tireront l'effet le plus important
- Utilisation de la posologie la plus forte/ inoffensive sur la mère et le fœtus (160mg)