



TEKRARLAYAN GEBELİK KAYIPLARINDA HEPARİN VE ASPİRİN KULLANIMI

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TEKRARLAYAN GEBELİK KAYBI

- 2 VE DAHA GEBELİK KAYBI %5
ACOG 2001, NVOG2007

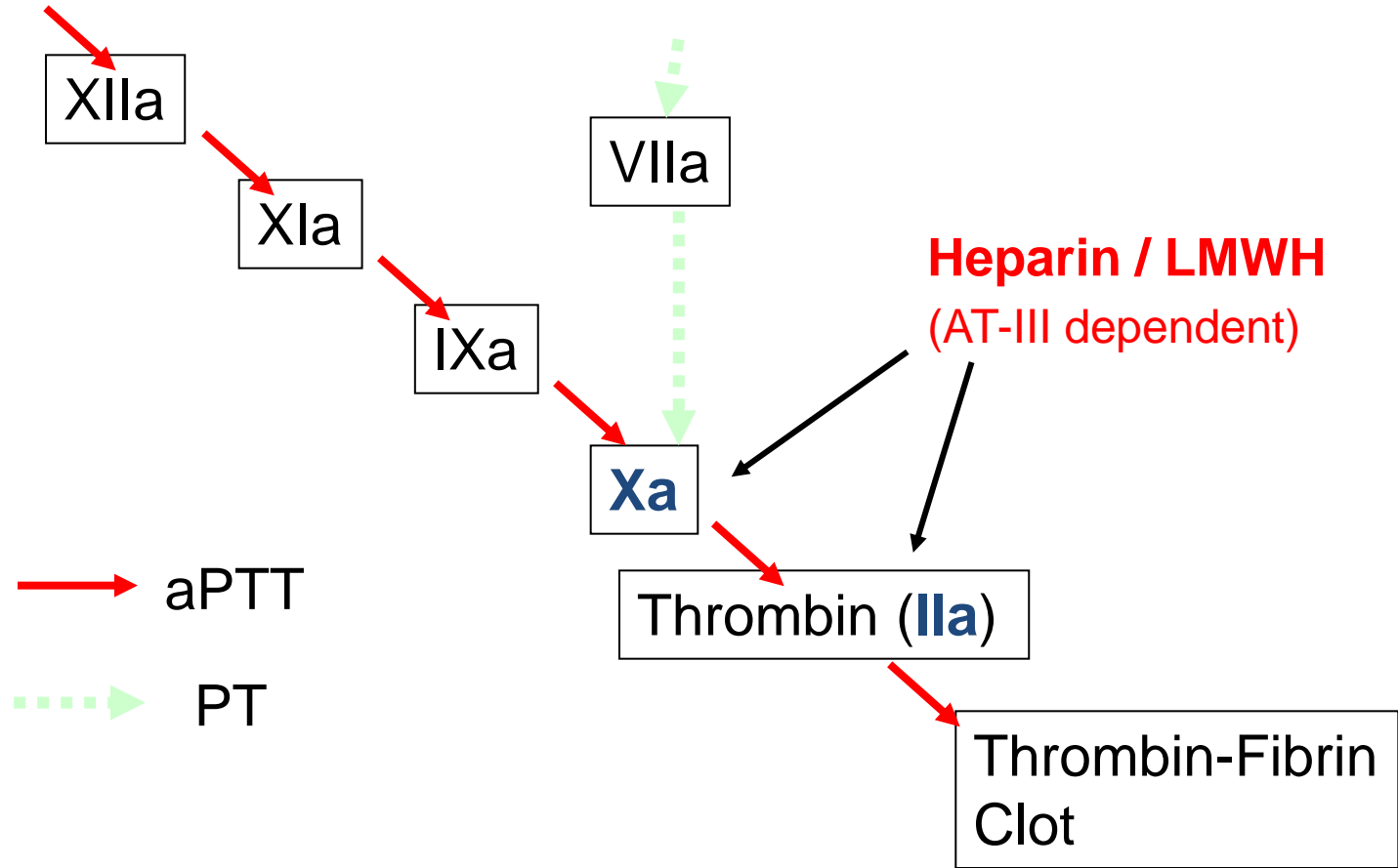
- 3 VE DAHA FAZLA GEBELİK KAYBI %1-2
WHO1997, ESHRE 2007

FETAL TROMBOTİK VASKULOPATİ??

Kuagulasyon Sistemi

Intrinsik Yol

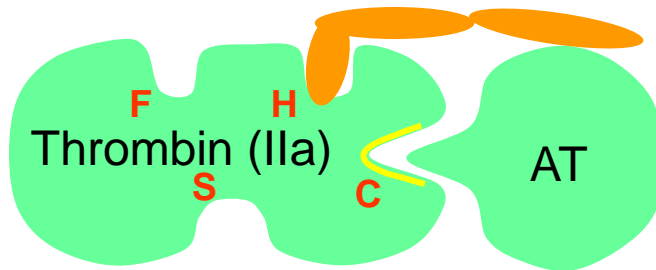
Extrinsik Yol



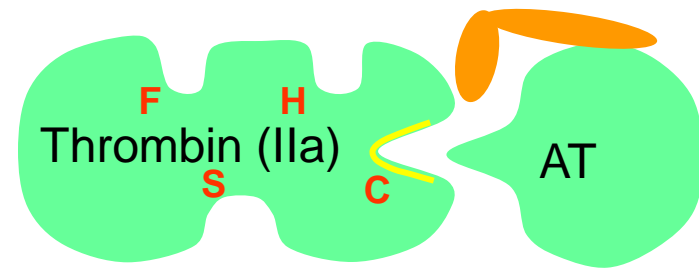
Heparin

- beta 2 glycoprotein 1e bağlanmaktadır.
- Antikompleman aktivasyonu inhibe eder.
(fondaparinox ve hirodin hariç)
- C3 ün deziduada birikimini engeller.
- Antiinflamatuvar etki (aktive Th1i aktive Th2ye çevirmektedir.)

Unfractionated Heparin



LMWH



Hem UH Xa aktivitesini inhibe eder.

LMWH hem faktör Xa hem de faktör IIa yı inhibe eder.

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Low-Molecular-Weight Heparins

Anti-Facotr Xa : Anti - Factor IIa Ratios

Agent	Trade	Xa:IIa	Mol Wt (d)
Enosaparin	Lovenox	3.8 : 1	4,200
Dalteparin	Fragmin	2.7 : 1	6,000
Ardeparin	Normiflo	1.9 : 1	6,000
Nadroparin		3.6 : 1	4,500
Reviparin		3.5 : 1	4,000
Tinzaparin		1.9 : 1	4,500

APS harici tekrarlayan Düşüklerde Heparin ve Aspirin Kullanımı

- Bar J 2000
- Bar 2001
- Bick 2000
- Brenner 2000
- Brenner 2005Live enox çalışması
- Carp 2003
- Grandone 2002
- Gris 1995
- Gris 2004
- Li 2003
- Ogasawaran 2001
- Rai 2000
- Reznikoff 1999
- Sarig 2003
- Sarto 2001
- Sorenson 2000
- Tzaffettas 2002
- Younis 2000
-

Dolitzky 2006

Heparin(40mg/
gün)ve
aspirin(100mg/
gün)

107 hasta

Tulppala 1997

Aspirin (50mg/gün)
ve plasebo

54 hasta



COCHRANE 2009

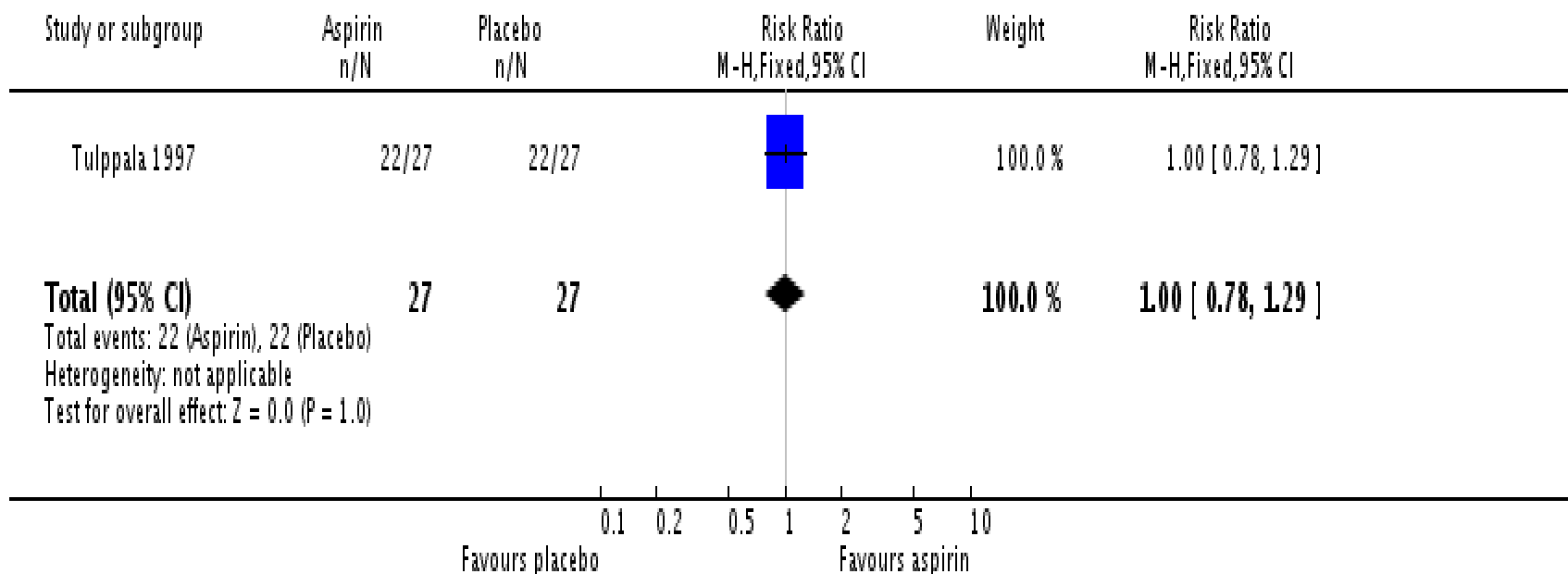
Comparison 1. Aspirin versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Live-birth rate	1	54	Risk Ratio (M-H, Fixed, 95% CI)	1.0 [0.78, 1.29]

Comparison 2. Enoxaparin versus aspirin

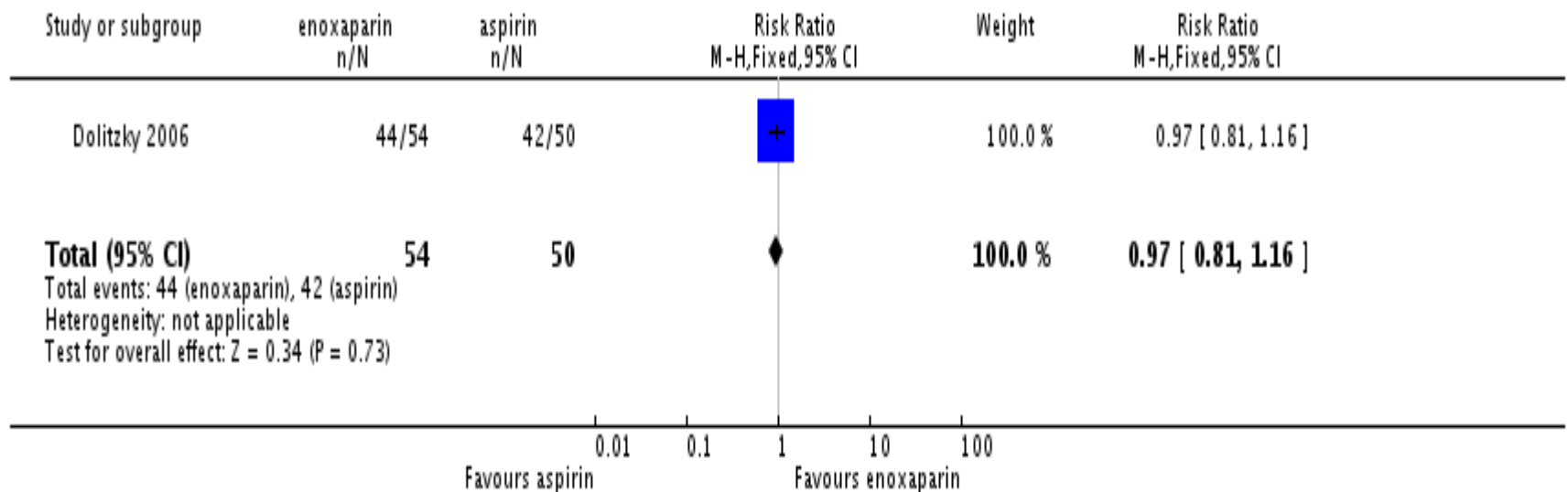
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Live-birth rate	1	104	Risk Ratio (M-H, Fixed, 95% CI)	0.97 [0.81, 1.16]
2 Preterm delivery	1	104	Risk Ratio (M-H, Fixed, 95% CI)	0.93 [0.28, 3.01]
3 Obstetric complications: pre-eclampsia	1	104	Risk Ratio (M-H, Fixed, 95% CI)	0.13 [0.01, 2.50]
4 Obstetric complications: intrauterine growth restriction	1	104	Risk Ratio (M-H, Fixed, 95% CI)	2.78 [0.12, 66.75]

Review: Aspirin or anticoagulants for treating recurrent miscarriage in women without antiphospholipid syndrome
 Comparison: 1 Aspirin versus placebo
 Outcome: 1 Live-birth rate



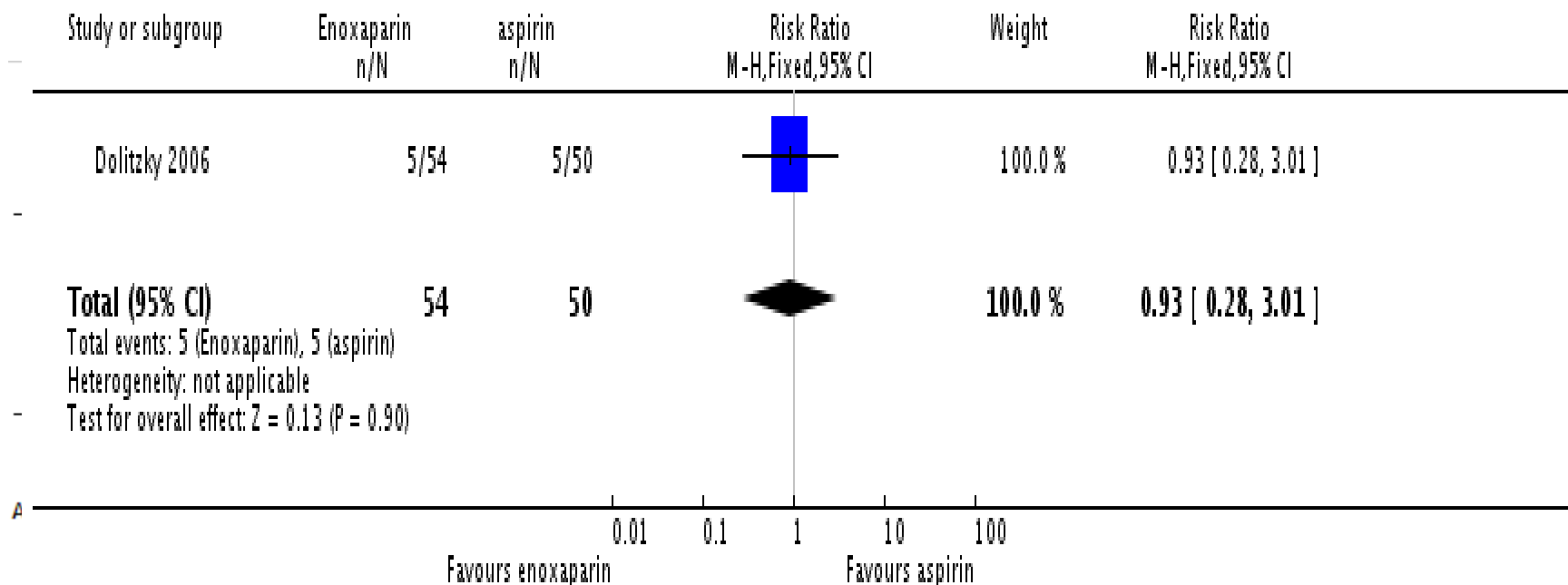
Analysis 1.1. Comparison 1 Aspirin versus placebo, Outcome 1 Live-birth rate.

Review: Aspirin or anticoagulants for treating recurrent miscarriage in women without antiphospholipid syndrome
 Comparison: 2 Enoxaparin versus aspirin
 Outcome: 1 Live-birth rate



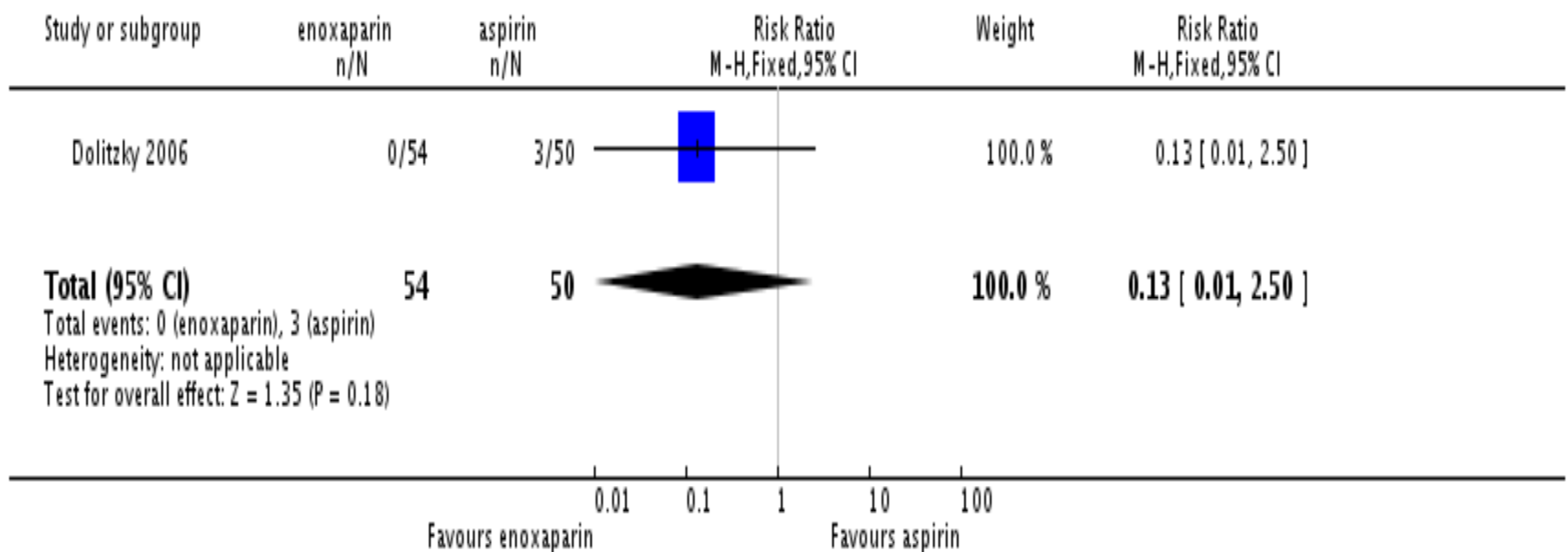
Analysis 2.1. Comparison 2 Enoxaparin versus aspirin, Outcome 1 Live-birth rate.

Review: Aspirin or anticoagulants for treating recurrent miscarriage in women without antiphospholipid syndrome
 Comparison: 2 Enoxaparin versus aspirin
 Outcome: 2 Preterm delivery



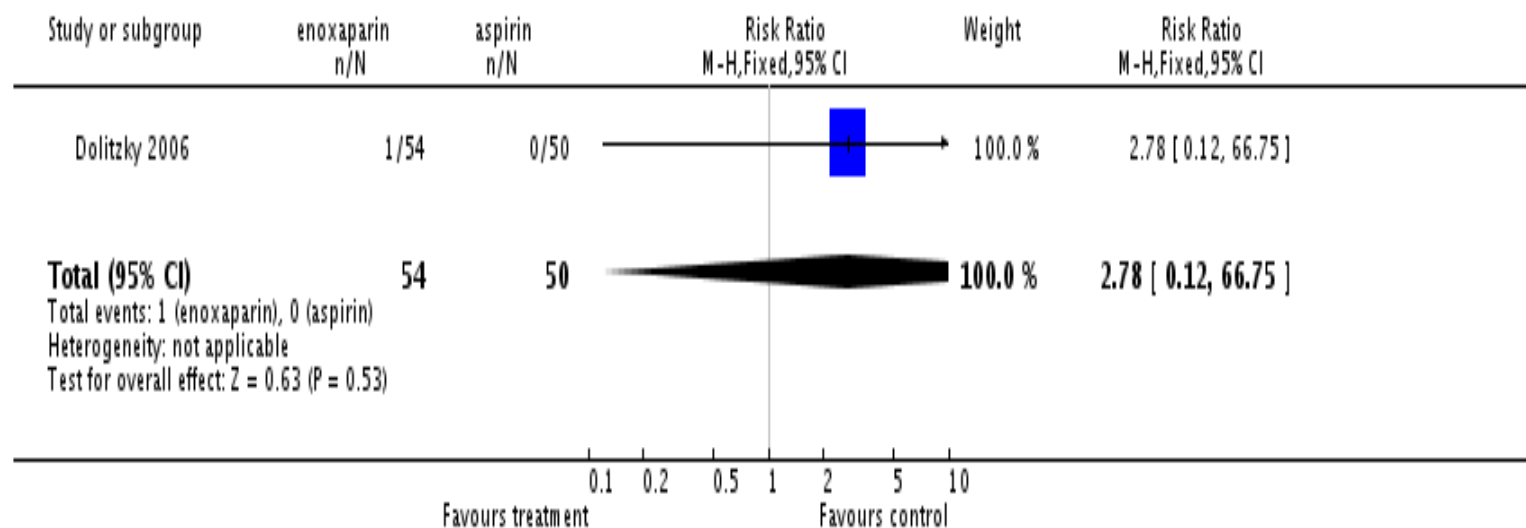
Analysis 2.2. Comparison 2 Enoxaparin versus aspirin, Outcome 2 Preterm delivery.

Review: Aspirin or anticoagulants for treating recurrent miscarriage in women without antiphospholipid syndrome
 Comparison: 2 Enoxaparin versus aspirin
 Outcome: 3 Obstetric complications; pre-eclampsia



Analysis 2.3. Comparison 2 Enoxaparin versus aspirin, Outcome 3 Obstetric complications; pre-eclampsia.

Review: Aspirin or anticoagulants for treating recurrent miscarriage in women without antiphospholipid syndrome
 Comparison: 2 Enoxaparin versus aspirin
 Outcome: 4 Obstetric complications; intrauterine growth restriction



[Analysis 2.4]

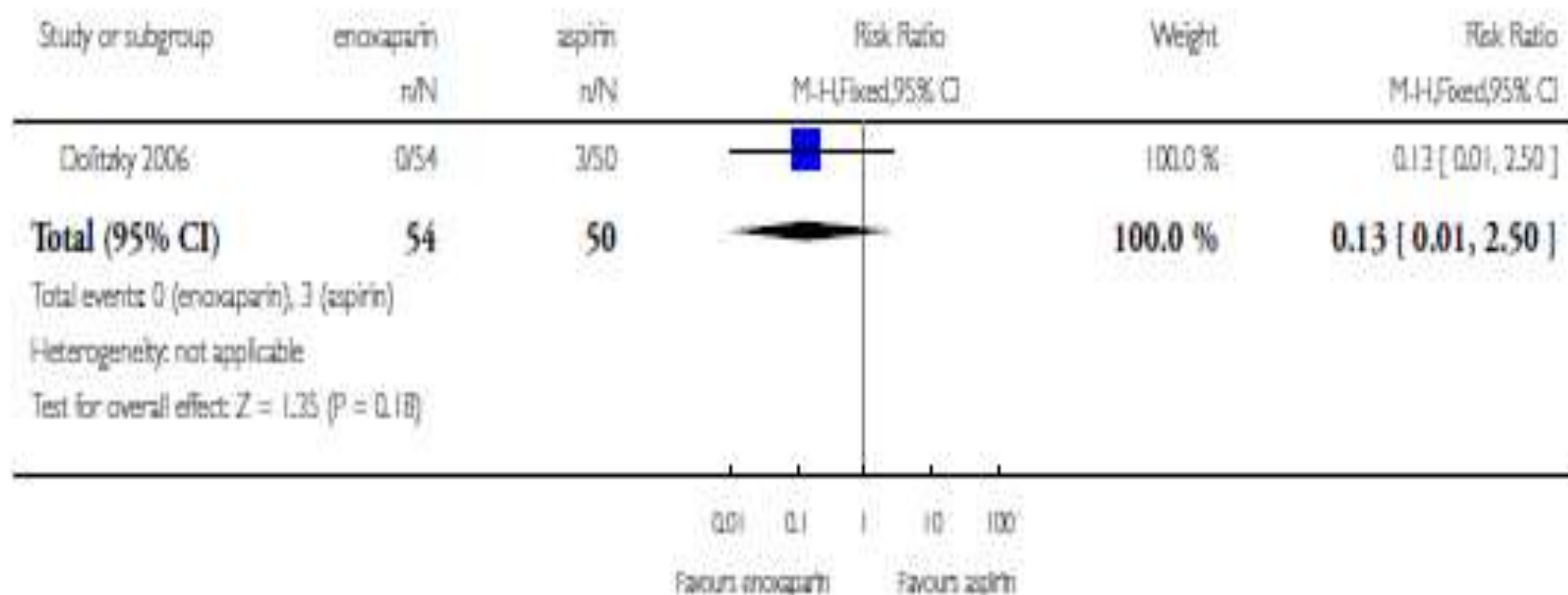
Analysis 2.4. Comparison 2 Enoxaparin versus aspirin, Outcome 4 Obstetric complications; intrauterine growth restriction.

Analysis 2.3. Comparison 2 Enoxaparin versus aspirin, Outcome 3 Obstetric complications; pre-eclampsia.

Review: Aspirin or anticoagulants for treating recurrent miscarriage in women without antiphospholipid syndrome

Comparison: 2 Enoxaparin versus aspirin

Outcome: 3 Obstetric complications; pre-eclampsia

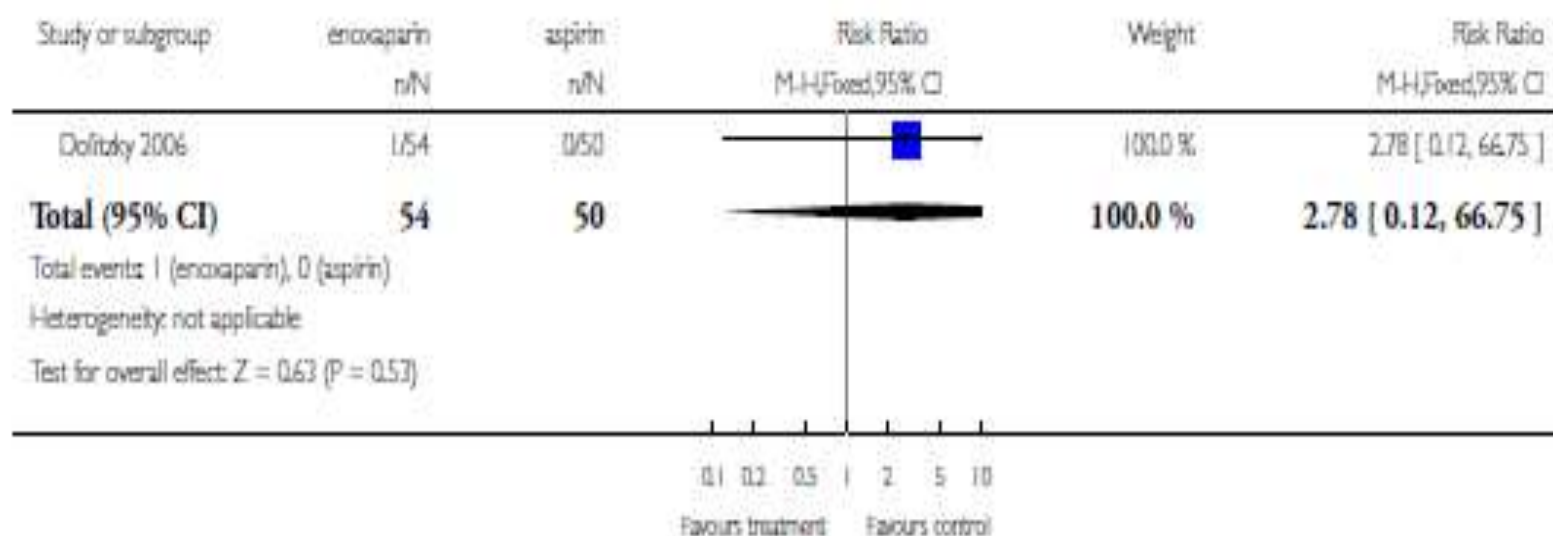


Analysis 2.4. Comparison 2 Enoxaparin versus aspirin, Outcome 4 Obstetric complications; intrauterine growth restriction.

Review: Aspirin or anticoagulants for treating recurrent miscarriage in women without antiphospholipid syndrome

Comparison: 2 Enoxaparin versus aspirin

Outcome: 4 Obstetric complications; intrauterine growth restriction



ALIFE

SPIN

ETHGII

TIPPS

ALIFE

- Norveç
- 2004-2008 yılları arası
- 123 kombine tedavi, 120 aspirin, 121 plasebo
- 2 ve üstü tekrarlayan düşük
- 100mg aspirin, 2850 IU fraxiheparin
- 6 hafta-doğum
- “Ne aspirin grubunda ne enoxaparin grubunda ne de kombine tedavide canlı doğum oranı değişmemektedir.”

N Engl J Med 2010;362:1586-96

SPIN (Scottish Pregnancy Intervention)

- Yeni zellanda, İngiltere
- 294 hasta
- 147 hasta enoxaparin 40 mg subcutaneously and 75 mg aspirin
- 2 ve üstü tekrarlayan düşük
- “Ne aspirin grubunda ne enoxaparin grubunda ne de kombine tedavide canlı doğum oranı değişmemektedir.”

Blood. 2010 May 27;115(21):4162-7.

HABENOX

- Enoxaparin 40 mg (n=68), enoxaparin 40 mg ve aspirin 100 mg (n=63) ve aspirin 100 mg (n=76)
- 3 ve üstü trombofilisi olan ve olmayan
- “Ne aspirin grubunda ne enoxaparin grubunda ne de kombine tedavide canlı doğum oranı değişmemektedir.”

[Thromb Haemost.](#) 2011 Feb;105(2):295-301

- **Low-molecular weight heparin in patients with recurrent early miscarriages of unknown aetiology.**
- [Badawy AM,](#)
- 340 gebe
- LMWH (Enoxaparin) 20 mg, kalp atışından 34 haftaya kadar
- Erken düşük oranı 4.1% - 8.8% ve geç düşük oranı 1.1%- 2.3%
- Gebelik komplikasyonlarında fark yoktur.

[J Obstet Gynaecol.](#) 2008 Apr;28(3):280-4

- **Treatment options and pregnancy outcome in women with idiopathic recurrent miscarriage: a randomized placebo-controlled study.**
- [Fawzy M,](#)
- 70 gebe.
- enoxaparin tek, prednisone, aspirin, ve progesterone ile kombine ve placebo.
- %81, %85, %48 üç grupta canlı bebek oranı oranı

[Arch Gynecol Obstet.](#) 2008 Jul;278(1):33-8.

Etkisiz

Etkili

SPIN

COCHRANE

ALIFE

BADAWAY

FAWAY



Kalıtımsal Trombofili

- Rey 2003 Lancet
- Dudding 2004 Thromb Haemost
- Preston 1996 Lancet
- Lissade-Lavigne G 2005- J Thromb Haemost
- Dizon-Townson 2005 Obstet Gynecol
- Silver 2010 Obstet Gynecol (faktör 5 ve protrombin)

ACOG Bulten 2011

- Metaanaliz ve retrospektif kohort çalışmalarda kalıtsal trombofili ve birinci trimester gebelik kaybı ile ilgisi var deniyor.

ANCAK

- RCT çalışmalarda bu ilgi gösterilememiştir.
- TEDAVİ???????????????

- [Odiari EA,](#)
- [Hum Reprod.](#) 2012 Oct;27(10):2933-40.
- **Pravastatin does not prevent antiphospholipid antibody-mediated changes in human first trimester trophoblast function.**

- [Carroll TY,](#)
- [Am J Reprod Immunol.](#) 2011 Oct;66(4):286-96.
- **Modulation of trophoblast angiogenic factor secretion by antiphospholipid antibodies is not reversed by heparin.**

HEPARIN???????

- Trofoblast invasyon
 - implantasyon
 - Vaskularisasyon