

Web appendix: Supplementary data

Supplement 1

Search strategy per database

PubMed

(`Contraceptives, Oral"[mesh] OR "Contraceptives, Oral"[Pharmacological Action] OR "oral contraceptives" OR "oral contraceptive" OR "Contraceptives, Oral, Combined"[Mesh] OR "combined oral contraceptives" OR "combined oral contraceptive" OR ((norethisterone OR norethisteron* OR norethindrone OR norethindron* OR "ethynodiol diacetate" OR lynestrenol OR lynestrenol* OR norethynodrel OR norethynodrel* OR dienogest OR dienogest* OR levonorgestrel OR levonorgestrel* OR norgestrel OR norgestrel* OR dl-norgestrel OR dl-norgestrel* OR desogestrel OR desogestrel* OR norgestimate OR norgestimat* OR gestodene OR gestoden* OR "medroxyprogesterone acetate" OR "chlormadinone acetate" OR nomegestrol OR nomegestrol* OR nestorone OR nestoron* OR "Cyproterone acetate" OR Drospirenone OR Drospirenon* OR oestrogen*[ti] OR estrogen[ti]) AND ("Ethinyl Estradiol"[mesh] OR "Ethinyl Estradiol" OR ethinylestradiol OR ethinylestradiol* OR Mestranol OR Mestranol* OR "estradiol valerate"[Supplementary Concept] OR "estradiol valerate" OR progestogen*[ti])) AND ("deep vein thrombosis"[ti] OR "deep venous thrombosis"[ti] OR "Venous Thrombosis"[ti] OR "Vein Thrombosis"[ti] OR "Venous Thrombosis"[mesh:noexp] OR "Thrombophlebitis"[mesh] OR "Upper Extremity Deep Vein Thrombosis"[mesh] OR Thrombophlebitis[ti] OR "pulmonary embolism"[ti] OR "pulmonary embolism"[mesh] OR "venous thromboembolism"[ti] OR "Venous Thromboembolism"[mesh] OR "venous thromboembolic disorders"[ti] OR (venous[ti] AND thromboembolic[ti] AND disorder[ti]) OR "venous thromboembolic diseases"[ti] OR "venous thromboembolic disease"[ti] OR "venous thrombotic"[ti] OR ("Thromboembolism"[mesh: noexp] AND (venous[tiab] OR vein[tiab] OR veins[tiab])) AND (risk OR risks OR risk factor OR risk factors) AND (women OR woman OR woman* OR women* OR girl OR girls OR female) NOT (animals NOT (human AND animals)))

EMBASE

(exp oral contraceptive agent/ OR "oral contraceptives".mp OR "oral contraceptive".mp OR "combined oral contraceptives".mp OR "combined oral contraceptive".mp OR (((norethisterone OR norethisteron* OR norethindrone OR norethindron* OR "ethynodiol diacetate" OR lynestrenol OR lynestrenol* OR norethynodrel OR norethynodrel* OR dienogest OR dienogest* OR levonorgestrel OR levonorgestrel* OR norgestrel OR norgestrel* OR dl-norgestrel OR dl-norgestrel* OR desogestrel OR desogestrel* OR norgestimate OR norgestimat* OR gestodene OR gestoden* OR "medroxyprogesterone acetate" OR "chlormadinone acetate" OR nomegestrol OR nomegestrol* OR nestorone OR nestoron* OR "Cyproterone acetate" OR Drospirenone OR Drospirenon*).mp OR oestrogen*.ti OR estrogen.ti) AND (("Ethinyl Estradiol" OR ethinylestradiol OR ethinylestradiol* OR Mestranol OR Mestranol* OR "estradiol valerate" OR "estradiol valerate").mp OR progestogen*.ti))) AND (("deep vein thrombosis" OR "deep venous thrombosis" OR "Venous Thrombosis" OR "Vein Thrombosis").ti OR exp deep vein thrombosis/ OR Vein Thrombosis/ OR Thrombophlebitis/ OR Thrombophlebitis.ti OR "pulmonary embolism".ti OR exp lung embolism/ OR "venous thromboembolism".ti OR exp Venous Thromboembolism/ OR "venous thromboembolic disorder*".ti OR "venous thromboembolic disease*".ti OR "venous thrombotic".ti) AND (exp risk/ OR risk*.mp OR exp risk factor/) AND ((women OR woman OR woman* OR women* OR girl OR girls OR female).mp OR exp female/) AND (exp human/ OR human.ti OR patient.ti OR patients.ti)

Web of Science

TS=("oral contraceptives" OR "oral contraceptive" OR combined oral contraceptive* OR ((norethisterone OR norethisteron* OR norethindrone OR norethindron* OR "ethynodiol diacetate" OR lynestrenol OR lynestrenol* OR norethynodrel OR norethynodrel* OR dienogest OR dienogest* OR levonorgestrel OR levonorgestrel* OR norgestrel OR norgestrel* OR dl-norgestrel OR dl-norgestrel* OR desogestrel OR desogestrel* OR norgestimate OR norgestimat* OR gestodene OR gestoden* OR "medroxyprogesterone acetate" OR "chlormadinone acetate" OR nomegestrol OR nomegestrol* OR nestorone OR nestoron* OR "Cyproterone acetate" OR Drospirenone OR Drospirenon*) AND ("Ethinyl Estradiol" OR ethinylestradiol OR ethinylestradiol* OR Mestranol OR Mestranol* OR "estradiol valerate" OR "estradiol valerate")))) AND TI=("deep vein thrombosis" OR "deep venous thrombosis" OR "Venous Thrombosis" OR "Vein Thrombosis" OR "Vein Thrombosis" OR Thrombophlebitis OR "pulmonary embolism" OR "venous thromboembolism" OR "venous thromboembolic disorder*" OR "venous thromboembolic disease*" OR "venous thrombotic") AND TS=risk* AND TS=(women OR woman OR woman* OR women* OR girl OR girls OR female)
Cochrane (<http://www3.interscience.wiley.com/cgi-bin/mrwhome/106568753/HOME>) ("oral contraceptives" OR "oral contraceptive" OR combined oral contraceptive* OR ((norethisterone OR norethisteron* OR norethindrone OR norethindron* OR "ethynodiol diacetate" OR lynestrenol OR lynestrenol* OR norethynodrel OR norethynodrel* OR dienogest OR dienogest* OR levonorgestrel OR levonorgestrel* OR norgestrel OR norgestrel* OR dl-norgestrel OR dl-norgestrel* OR desogestrel OR desogestrel* OR norgestimate OR norgestimat* OR gestodene OR gestoden* OR "medroxyprogesterone acetate" OR "chlormadinone acetate" OR nomegestrol OR nomegestrol* OR nestorone OR nestoron* OR "Cyproterone acetate" OR Drospirenone OR Drospirenon*) AND ("Ethinyl Estradiol" OR ethinylestradiol OR ethinylestradiol* OR Mestranol OR Mestranol* OR "estradiol valerate" OR "estradiol valerate")))) AND ("deep vein thrombosis" OR "deep venous thrombosis" OR "Venous Thrombosis" OR "Vein Thrombosis" OR "Vein Thrombosis" OR Thrombophlebitis OR "pulmonary embolism" OR "venous thromboembolism" OR "venous thromboembolic disorder*" OR "venous thromboembolic disease*" OR "venous thrombotic") AND risk* AND (women OR woman OR woman* OR women* OR girl OR girls OR female)

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TITLE/ABSTRACT/KEYWORD (oral contraceptives OR oral contraceptive OR combined oral contraceptive* OR ((norethisterone OR norethisteron* OR norethindrone OR norethindron* OR ethynodiol diacetate OR lynestrenol OR lynestrenol* OR norethynodrel OR norethynodrel* OR dienogest OR dienogest* OR levonorgestrel OR levonorgestrel* OR norgestrel OR norgestrel* OR dl-norgestrel OR dl-norgestrel* OR desogestrel OR desogestrel* OR norgestimate OR norgestimat* OR gestodene OR gestoden* OR medroxyprogesterone acetate OR chlormadinone acetate OR nomegestrol OR nomegestrol* OR nestorone OR nestoron* OR Cyproterone acetate OR Drospirenone OR Drospirenon*) AND (Ethinyl Estradiol OR ethinylestradiol OR ethinylestradiol* OR Mestranol OR Mestranol* OR estradiol valerate OR estradiol valerate))) AND (deep vein thrombosis OR deep venous thrombosis OR Venous Thrombosis OR Vein Thrombosis OR Vein Thrombosis OR Thrombophlebitis OR pulmonary embolism OR venous thromboembolism OR venous thromboembolic disorder* OR venous thromboembolic disease* OR venous thrombotic) AND risk* AND (women OR woman OR woman* OR women* OR girl OR girls OR female)

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(oral contraceptives OR oral contraceptive OR combined oral contraceptive* OR ((norethisterone OR norethisteron* OR norethindrone OR norethindron* OR ethynodiol diacetate OR lynestrenol OR lynestrenol* OR norethynodrel OR norethynodrel* OR dienogest OR dienogest* OR levonorgestrel OR levonorgestrel* OR norgestrel OR

norgestrel* OR dl-norgestrel OR dl-norgestrel* OR desogestrel OR desogestrel* OR norgestimate OR norgestimat* OR gestodene OR gestoden* OR medroxyprogesterone acetate OR chlormadinone acetate OR nomegestrol OR nomegestrol* OR nestorone OR nestoron* OR Cyproterone acetate OR Drospirenone OR Drospirenon*) AND (Ethinyl Estradiol OR ethinylestradiol OR ethinylestradiol* OR Mestranol OR Mestranol* OR estradiol valerate OR estradiol valerate))) AND (deep vein thrombosis OR deep venous thrombosis OR Venous Thrombosis OR Vein Thrombosis OR Vein Thrombosis OR Thrombophlebitis OR pulmonary embolism OR venous thromboembolism OR venous thromboembolic disorder* OR venous thromboembolic disease* OR venous thrombotic) AND risk* AND (women OR woman OR woman* OR women* OR girl OR girls OR female)

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TITLE((oral contraceptives OR oral contraceptive OR combined oral contraceptive* OR ((norethisterone OR norethisteron* OR norethindrone OR norethindron* OR ethynodiol diacetate OR lynestrenol OR lynestrenol* OR norethynodrel OR norethynodrel* OR dienogest OR dienogest* OR levonorgestrel OR levonorgestrel* OR norgestrel OR norgestrel* OR dl-norgestrel OR dl-norgestrel* OR desogestrel OR desogestrel* OR norgestimate OR norgestimat* OR gestodene OR gestoden* OR medroxyprogesterone acetate OR chlormadinone acetate OR nomegestrol OR nomegestrol* OR nestorone OR nestoron* OR Cyproterone acetate OR Drospirenone OR Drospirenon*) AND (Ethinyl Estradiol OR ethinylestradiol OR ethinylestradiol* OR Mestranol OR Mestranol* OR estradiol valerate OR estradiol valerate))) AND (deep vein thrombosis OR deep venous thrombosis OR Venous Thrombosis OR Vein Thrombosis OR Vein Thrombosis OR Thrombophlebitis OR pulmonary embolism OR venous thromboembolism OR venous thromboembolic disorder* OR venous thromboembolic disease* OR venous thrombotic) AND risk* AND (women OR woman OR woman* OR women* OR girl OR girls OR female))

Criteria for considering studies for this review

Types of studies

Observational studies in this review will include case-control, cohort and nested case-control designs. If available, randomized controlled trials will also be evaluated and included.

Types of participants

Participants will be healthy women taking combined oral contraceptives. We will exclude studies of women on hormone replacement therapy, studies of women taking non-oral or progestogen-only contraceptives and studies of women with recurrent venous thrombosis.

Types of interventions

Combined oral contraceptive use will be compared to non-use or to a reference combined oral contraceptive (for example, levonorgestrel with 30 µg of ethinylestradiol). We define a woman as a non-user when either she has never been exposed to a combined oral contraceptive or she was a former/previous combined oral contraceptive user. We will categorize the combined oral contraceptive type according to the estrogen type and dose and to the progestogen type.

Types of outcome measures

The outcome will be fatal or non-fatal first venous thrombosis event with the main focus on deep venous thrombosis or pulmonary embolism.

Supplementary table 1 Characteristics of excluded studies

Author	Year	Reason for exclusion
R.E.J. Roach ¹	2013	No data on progestogen type or ethinylestradiol dose
A. Bergendal ²	2012	No data on progestogen type or ethinylestradiol dose
K. Hall ³	2012	No data on venous thrombosis
S. Reed ⁴	2012	Compared with other contraceptives
M.K. Barsoum ⁵	2010	No data on progestogen type or ethinylestradiol dose
J.C. Dinger ⁶	2010	Included recurrent venous thrombosis
V. Tsankova ⁷	2010	Compared ever users versus never users
V. Tsankova ⁸	2010	No data on progestogen type or ethinylestradiol dose
H. Austin ⁹	2009	Other hormonal contraceptives, such as transdermal patch, vaginal ring, were included
Ø. Lidegaard ¹⁰	2009	Updated study from 2011 was included
P.G. Lindqvist ¹¹	2009	No data on progestogen type or ethinylestradiol dose
P.M. Eng ¹²	2008	Compared drospirenone versus other oral contraceptive users
J.C. Dinger ¹³	2007	Included recurrent venous thrombosis
C. Huerta ¹⁴	2007	No data on progestogen type or ethinylestradiol dose
J.D. Seeger ¹⁵	2007	Included recurrent venous thrombosis
C.C. Yang ¹⁶	2007	Exposed consisted of hormone replacement therapy users and oral contraceptive users
K. Hedenmalm ¹⁷	2005	Included recurrent venous thrombosis and cerebral vein thrombosis
H.M. Pearce ¹⁸	2005	No comparison was included
M. Primignani ¹⁹	2005	Included not only venous thrombosis
C. Worrall ²⁰	2005	Included recurrent venous thrombosis and no data on progestogen type or ethinylestradiol dose
A. Girolami ²¹	2004	Included not only venous thrombosis
P. Heuser ²²	2004	No extractable number of exposed and non-exposed women
H.E. Seaman ²³	2004	Included recurrent venous thrombosis
S. Sidney ²⁴	2004	Incomplete data on contraceptive use
H. Kieler ²⁵	2003	Included recurrent venous thrombosis
I. Martinelli ²⁶	2003	No data on progestogen type or ethinylestradiol dose
A. Tosetto ²⁷	2003	No data on progestogen type or ethinylestradiol dose
C. Legnani ²⁸	2002	Included recurrent venous thrombosis
Ø. Lidegaard ²⁹	2001	Review
L. N. Meurer ³⁰	2001	Review
J.P. Vallée ³¹	2001	Review
T. Amundsen ³²	2000	No data on progestogen type or ethinylestradiol dose
L.A. Heinemann ³³	2000	Report on Transnational study, already included
R. Lawrenson ³⁴	2000	Review
A.L. Nightingale ³⁵	2000	Commentary
M.S. Burnhill ³⁶	1999	Included progestogen-only contraceptives and retinal vein thrombosis
R.M. Herings ³⁷	1999	Data already included
M.A. Lewis ³⁸	1999	Report on Transnational study, already included
M.A. Lewis ³⁹	1999	Commentary
Ø. Lidegaard ⁴⁰	1998	Updated study from 2002 was included
Ø. Lidegaard ⁴¹	1998	Review
C. Bonifacj ⁴²	1997	Included recurrent venous thrombosis
R.D. Farmer ⁴³	1997	Ecologic study
M.A. Lewis ⁴⁴	1997	Report on Transnational study, already included

F.J. van der Meer ⁴⁵	1997	Review
J.P. Realini ⁴⁶	1997	Less than 10 venous thrombosis events
S. Suissa ⁴⁷	1997	Duration of contraceptive use
H. Ulmer ⁴⁸	1997	No data on progestogen type or ethinylestradiol dose
F. Grodstein ⁴⁹	1996	No data on progestogen type or ethinylestradiol dose
M. Pini ⁵⁰	1996	Included not only venous thrombosis and included recurrent venous thrombosis
N.R. Poulter ⁵¹	1996	Data already included
Y. Lis ⁵²	1993	Publication of study protocol
W.O. Spitzer ⁵³	1993	Publication of study protocol
D.A. Quinn ⁵⁴	1992	No data on progestogen type or ethinylestradiol dose
M. Thorogood ⁵⁵	1992	Included recurrent venous thrombosis and no data on progestogen type or ethinylestradiol dose
B.B. Gerstman ⁵⁶	1991	Incomplete data on contraceptive use
E. Hirvonen ⁵⁷	1990	No data on progestogen type or ethinylestradiol dose
WHO ⁵⁸	1989	No data on progestogen type or ethinylestradiol dose
H. Meinel ⁵⁹	1988	Included not only venous thrombosis and no data on progestogen type or ethinylestradiol dose
S.P. Helmrich ⁶⁰	1987	Incomplete data on contraceptive use
D. Bernstein ⁶¹	1986	No data on progestogen type or ethinylestradiol dose
R. Lambrekht ⁶²	1986	No data on venous thrombosis
K. Overgaard ⁶³	1986	No data on progestogen type or ethinylestradiol dose
M.P. Vessey ⁶⁴	1986	Incomplete data on contraceptive use
J.B. Porter ⁶⁵	1985	Less than 10 venous thrombosis events
J.B. Porter ⁶⁶	1982	Less than 10 venous thrombosis events
L.E. Bottiger ⁶⁷	1980	No data on ethinylestradiol dose
T.W. Meade ⁶⁸	1980	Included not only venous thrombosis
D.B. Petitti ⁶⁹	1979	No data on progestogen type or ethinylestradiol dose
A.W. Diddle ⁷⁰	1978	Less than 10 venous thrombosis events
RCGP ⁷¹	1978	Included not only venous thrombosis
IPPF ⁷²	1976	Communication to the editor
P.D. Stolley ⁷³	1975	Included not only venous thrombosis
M. Grounds ⁷⁴	1974	Included not only venous thrombosis
BCDS ⁷⁵	1973	No data on progestogen type or ethinylestradiol dose
A.Fuertes ⁷⁶	1971	Unclear reference group
W.H. Inman ⁷⁷	1970	No data on progestogen type or ethinylestradiol dose
H. Ludwig ⁷⁸	1970	Unclear what is defined as high progestogen
H.A. Siegel ⁷⁹	1969	No data on progestogen type or ethinylestradiol dose
M.P. Vessey ⁸⁰	1969	Included recurrent venous thrombosis
W.H. Inman ⁸¹	1968	No data on progestogen type or ethinylestradiol dose

Supplementary table 2 Overview of risk of bias per study

Author	Year	Source population	OC assessment	Outcome assesment	Follow-up
S.T. Bird	2013	NA	Low risk	High risk	Unclear
N. Gronich	2011	NA	Low risk	Unclear	Unclear
Ø. Lidegaard	2011	NA	Low risk	High risk	Unclear
S.S. Jick	2011	Low risk	Low risk	Unclear	NA
L. Parkin	2011	Low risk	Low risk	High risk	NA
L.A.J. Heinemann	2010	Low risk	High risk	High risk	NA
A. van Hylckama Vlieg	2009	Low risk	High risk	Low risk	NA
S.S. Jick	2006	Low risk	Low risk	Unclear	NA
E. Samuelsson	2004	NA	Low risk	Low risk	Unclear
K. Hedenmalm	2004	NA	Low risk	High risk	Unclear
L.A.J. Heinemann	2002	High risk	High risk	High risk	NA
Ø. Lidegaard	2002	Low risk	High risk	High risk	NA
L. Parkin	2000	Low risk	High risk	High risk	NA
R.D.T. Farmer	2000	NA	Low risk	High risk	Unclear
R.M.C. Herings	1999	NA	Low risk	Unclear	Unclear
J.C. Todd	1999	NA	Low risk	High risk	Unclear
I. Martinelli	1999	Low risk	Unclear	Unclear	NA
K.W.M. Bloemenkamp	1999	Low risk	High risk	Low risk	NA
R.D.T. Farmer	1998	Low risk	Low risk	Unclear	NA
B.S. Andersen	1998	Low risk	Low risk	Low risk	NA
M.A. Lewis	1996	High risk	High risk	Unclear	NA
R. Farmer	1996	NA	Low risk	Unclear	Unclear
K.W.M. Bloemenkamp	1995	Low risk	High risk	Low risk	NA
WHO	1995	High risk	Low risk	High risk	NA
WHO1	1995	High risk	Low risk	High risk	NA
WHO2	1995	High risk	Low risk	High risk	NA

NA, not applicable due to cohort design in case of source population or due to case-control design in case of follow-up

Supplementary table 3 Included publications with data on generation of progestogens and reference group non-use

Design	Study	Study design	Non-use n event/ n total	1st n event/ n total	2nd n event/ n total	3rd n event/ n total
1	Lidegaard 2011	Cohort	1812/4960730	21/34203	198/233912	1747/2049368
	Hylckama 2009	Case-control	421/1523	55/81	382/672	412/582
	Heinemann 2002	Case-control	246/2115	45/190	131/865	28/195
	Bloemenkamp 1999	Case-control	83/511	18/46	8/22	33/67
	Bloemenkamp 1995	Case-control	46/150	8/13	20/38	37/52
	WHO1 1995	Case-control	168/855	29/74	156/392	53/104
	WHO2 1995	Case-control	505/2220	26/65	153/337	18/25
2	Heinemann 2010	Case-control	70/1215	-	61/245	62/238
	Lidegaard 2002	Case-control	458/3196	-	98/296	351/1204
	Parkin 2000	Case-control	9/95	-	3/11	12/27
	WHO 1995	Case-control	397/1916	-	137/340	71/127
3	Samuelsson 2004	Cohort	32/171206	-	-	17/14819
	Martinelli 1999	Case-control	41/179	-	-	43/79
	Andersen 1998	Case-control	27/133	-	-	16/23
4	Hedenmalm 2004	Cohort	-	36/1898899	74/6343562	83/1739393
	Farmer 2000	Cohort	-	12/39421	98/307070	161/374129
5	Gronich 2011	Cohort	-	-	23/33187	384/651455
	Jick 2006	Nested case-control	-	-	70/386	211/950
	Herrings 1999	Cohort	-	-	29/121411	49/88295
	Todd 1999	Cohort	-	-	32/76993	53/92052
	Farmer 1998	Case-control	-	-	27/116	15/79
	Lewis 1996	Case-control	-	-	96/419	156/451
	Farmer 1996	Cohort	-	-	14/76600	15/65100

Total can be total number of women in the group, or the total follow-up time; Design refers to the type and number of direct comparisons provided in a single study. Studies with the same design provide direct comparisons of exactly the same generations or same individual oral contraceptives

Supplementary table 4 Study specific adjusted risk estimates: generations of contraceptives

Study	Comparison					
	1st vs non-use	2nd vs non-use	3rd vs non-use	1st vs 2nd	3rd vs 2nd	1st vs 3rd
	RR (95%CI)	RR (95%CI)	RR (95%CI)	RR (95%CI)	RR (95%CI)	RR (95%CI)
Lidegaard2011	-	-	-	-	-	-
Hylckama2009	-	-	-	-	-	-
Heinemann2002	8.1 (5.3-12.5)	4.9 (3.5-6.9)	4.3 (2.6-7.2)	-	0.9 (0.6-1.4)	-
Bloemenkamp1999	-	-	-	-	-	-
Bloemenkamp1995	-	-	-	-	-	-
WHO1 1995	-	-	-	-	-	-
WHO2 1995	-	-	-	-	-	-
Heinemann2010	-	6.9 (4.3-10.9)	8.1 (5.0-13.1)	-	-	-
Lidegaard2002	4.1 (2.4-7.1)	2.9 (2.2-3.8)	4.0 (3.2-4.9)	1.5 (0.9-2.7)	1.3 (1.0-1.8)	-
Parkin2000	-	-	-	-	-	-
WHO1995	-	-	-	-	-	-
Samuelsson2004	-	-	-	-	-	-
Martinelli1999	-	-	-	-	-	-
Andersen1998	-	-	48.6 (5.6-423.0)	-	-	-
Hedenmalm2004	-	-	-	-	-	-
Farmer2000	-	-	-	-	-	-
Gronich2011	-	-	-	-	-	-
Jick2006	-	-	-	-	-	-
Herings1999	-	-	-	-	3.5 (1.4-8.8)	-
Todd1999	-	-	-	-	-	-
Farmer1998	-	-	-	-	-	-
Lewis1996	6.2 (3.8-10.2)	3.4 (2.4-4.6)	5.4 (3.9-7.3)	-	1.6 (1.2-2.2)	-
Farmer1996	-	-	-	-	-	-

Supplementary table 5 Included publications with data on the 10 selected contraceptives and reference group non-use

Design	Study	Study design	Non-use	20LNG	30LNG	50LNG	20GSD	30GSD	20DSG	30DSG	35NRG	35CPA	30DRSP
			n event/ n total	n event/ n total	n event/ n total	n event/ n total	n event/ n total	n event/ n total	n event/ n total	n event/ n total	n event/ n total	n event/ n total	n event/ n total
1	Hylckama 2009	Case-control	421/1523	8/14	485/858	60/80	14/32	119/186	58/85	289/397	9/13	125/187	19/33
2	Lidegaard 2011	Cohort	1812/4960730	-	78/104251	31/23691	321/472118	738/668355	322/470982	201/170249	165/267664	109/120934	266/286859
3	Parkin 2000	Case-control	9/95	-	2/6	0/2	-	5/10	4/9	3/8	-	2/3	-
4	Lidegaard2002	Case-control	458/2738	-	-	12/28	6/36	206/692	58/187	63/153	18/118	-	-
5	Bloemenkamp 1999	Case-control	83/511	-	18/46	-	-	5/9	6/7	22/51	-	-	-
6	Bloemenkamp 1995	Case-control	46/150	-	20/38	-	-	-	-	37/52	-	-	-
7	Farmer 2000	Cohort	-	-	64/190191	-	-	63/143581	18/37584	65/152524	15/40440	16/25709	-
8	Todd 1999	Cohort	-	-	22/49484	-	-	21/41947	9/10426	23/39679	-	-	-
9	Farmer 1996	Cohort	-	-	5/35800	-	-	5/30500	-	10/34600	-	-	-
10	Jick 2006	Nested case-control	-	-	70/386	-	-	-	-	87/315	124/635	-	-
11	Bird2013	Cohort	-	30/28782	56/58356	-	-	-	-	-	-	-	151/96217
	Jick 2011	Nested case-control	-	20/151	45/282	-	-	-	-	-	-	-	121/434
12	Parkin 2011	Nested case-control	-	-	44/233	-	-	-	-	-	-	-	17/43
13	Lewis 1996	Case-control	-	-	-	-	-	-	15/51	64/174	19/50	-	-

Design refers to the type and number of direct comparisons provided in a single study. Studies with the same design provide direct comparisons of exactly the same generations or same individual oral contraceptives

Supplementary table 6 Study specific adjusted risk estimates: per combined oral contraceptive

Comparison	Study													
	Hylckama2009	Lidegaard2011	Parkin2000	Lidegaard2002	Bloemenkamp1999	Bloemenkamp1995	Farmer2000*	Todd1999	Farmer1996	Jick2006	Bird2013	Jick2011	Parkin2011	Lewis1996
	RR (95%CI)	RR (95%CI)	RR (95%CI)	RR (95%CI)	RR (95%CI)	RR (95%CI)	RR (95%CI)	RR (95%CI)	RR (95%CI)	RR (95%CI)	RR (95%CI)	RR (95%CI)	RR (95%CI)	RR (95%CI)
20LNG vs non-use	-	-	-	-	-	-	-	-	-	-	-	-	-	-
30LNG vs non-use	3.6 (2.9-4.6)	2.2 (1.7-2.8)	-	-	3.7 (1.9-7.2)	3.8 (1.7-8.4)	-	-	-	-	-	-	-	-
50LNG vs non-use	-	3.5 (2.5-5.1)	-	5.3 (2.3-12.3)	-	-	-	-	-	-	-	-	-	-
20GSD vs non-use	-	3.5 (3.1-4.0)	-	2.0 (0.7-5.7)	-	-	-	-	-	-	-	-	-	-
30GSD vs non-use	5.6 (3.7-8.4)	4.2 (3.9-4.6)	-	3.5 (2.8-4.5)	5.2 (1.3-20.6)	-	-	-	-	-	-	-	-	-
20DSG vs non-use	-	3.3 (2.9-3.7)	-	4.8 (3.2-7.1)	24.7 (2.8-213.5)	-	-	-	-	-	-	-	-	-
30DSG vs non-use	7.3 (5.3-10.0)	4.2 (3.6-4.9)	-	5.4 (3.6-8.0)	4.9 (2.5-9.4)	8.7 (3.9-19.3)	-	-	-	-	-	-	-	-
35NRG vs non-use	5.9 (1.7-21.0)	2.6 (2.2-3.0)	-	1.7 (1.0-3.1)	-	-	-	-	-	-	-	-	-	-
35CPA vs non-use	6.8 (4.7-10.0)	4.1 (3.4-5.0)	17.6 (2.7-113.0)	3.3 (1.4-7.6)	-	-	-	-	-	-	-	-	-	-
30DRSP vs non-use	6.3 (2.9-13.7)	4.5 (3.9-5.1)	-	-	-	-	-	-	-	-	-	-	-	-
30LNG vs 20LNG	0.9 (0.3-2.5)	-	-	-	-	-	-	-	-	-	-	-	-	-
50LNG vs 20LNG	-	-	-	-	-	-	-	-	-	-	-	-	-	-
20GSD vs 20LNG	-	-	-	-	-	-	-	-	-	-	-	-	-	-
30GSD vs 20LNG	-	-	-	-	-	-	-	-	-	-	-	-	-	-
20DSG vs 20LNG	-	-	-	-	-	-	-	-	-	-	-	-	-	-
30DSG vs 20LNG	-	-	-	-	-	-	-	-	-	-	-	-	-	-
35NRG vs 20LNG	-	-	-	-	-	-	-	-	-	-	-	-	-	-
35CPA vs 20LNG	-	-	-	-	-	-	-	-	-	-	-	-	-	-
30DRSP vs 20LNG	-	-	-	-	-	-	-	-	-	-	-	3.2 (1.8-5.5)	-	-
50LNG vs 30LNG	2.2 (1.3-3.7)	-	-	-	-	-	-	-	-	-	-	-	-	-
20GSD vs 30LNG	-	-	-	-	-	-	-	-	-	-	-	-	-	-
30GSD vs 30LNG	-	-	-	-	-	-	1.3 (0.9-1.9)	-	-	-	-	-	-	-
20DSG vs 30LNG	-	-	-	-	-	-	1.4 (0.8-2.4)	-	-	-	-	-	-	-
30DSG vs 30LNG	-	-	-	-	-	-	1.3 (0.9-1.8)	-	1.5 (0.3-8.3)	1.7 (1.2-2.4)	-	-	-	-

[illegible]

35CPA vs 35NRG	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
30DRSP vs 35NRG	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
30DRSP vs 35CPA	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

* Unadjusted estimates were reported

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