

**Disease activity and maternal–fetal outcomes in pregnant women with prolactinoma: a
systematic review and meta-analysis**

Supplementary File

Diego Barata Bandeira¹; Letícia Santana Alves¹; Andrea Glezer²; Cesar Luiz
Boguszewski³; Vania dos Santos Nunes-Nogueira¹

¹Department of Internal Medicine, Medical School, São Paulo State University/UNESP, Botucatu,
São Paulo, Brazil.

²Neuroendocrine Unit, Division of Endocrinology and Metabolism, Hospital das Clínicas,
University of São Paulo Medical School, São Paulo, Brazil.

³Endocrine Division (SEMPR), Department of Internal Medicine, Federal University of Paraná,
Curitiba, Brazil.

Corresponding Author information:

Nunes-Nogueira VS, PhD, MD

Department of Internal Medicine, São Paulo State University (UNESP)/Medical School, Brazil,
São Paulo, Botucatu

Email: vania.nunes-nogueira@unesp.br

Phone: +55 14 3880 11 71

Orcid: 0000-0001-9316-4167

Table I. Excluded studies and reasons.....	3
Table II. Risk of bias evaluation of included studies.....	4
Figure I. Meta-analysis findings: Frequency of participants using dopamine agonist at conception.....	6
Figure II. Meta-analysis findings: Frequency of participants using dopamine agonist during pregnancy.....	7
Figure III. Meta-analysis findings: Frequency of participants submitted to neurosurgery for prolactinoma treatment before pregnancy.....	8
Figure IV. Meta-analysis findings: Frequency of gestational diabetes mellitus.....	9
Figure V. Meta-analysis findings: Frequency of prolactinoma remission.....	10
Figure VI. Meta-analysis findings: Frequency of breastfeeding.....	11
Figure VII. Meta-analysis findings: Frequency of apoplexy.....	12
Figure VIII. Meta-analysis findings: Frequency of perinatal mortality	13
Figure IX. Meta-regression of spontaneous abortion and covariate year of manuscript publication.....	14
Search Strategies	19

Table I. Excluded studies and reasons

Study	Year of publication	Country	Reasons
Badawy et al.	1997	USA	Not found.
Badawy et al.	1982	USA	No outcomes of interest.
Bergh et al.	1981	Sweedden	No outcomes of interest.
Bonneville et al.	1982	France	No outcomes of interest.
Bricaire et al.	1988	France	Duplicated.
Cacelli et al.	2015	Brazil	Partial results of full article already included (Sant'Anna et al., 2020).
Cannavò et al.	1999	Italy	No outcomes of interest.
Chen et al.	2002	China	Not found.
Cristiani et al.	1981	Italy	Not found.
Crosignani et al.	1989	Italy	Duplicated.
de Wit et al.	1984	Netherlands	Duplicated.
Decoudier et al.	2011	France	Partial results of full article already included (Barraud et al., 2020).
Dietemann et al.	1983	France	Duplicated.
Divers et al.	1983	USA	Duplicated.

Ericsson et al.	2012	Sweeden	No outcomes of interest.
Fossati et al.	1994	France	Not found.
Galvão et al.	2016	Portugal	Duplicated.
Grossman et al.	1984	UK	No outcomes of interest.
Gsponer et al.	1999	Switzerland	No outcomes of interest.
Helie et al.	1996	France	No outcomes of interest.
Hoffmann et al.	1983	Germany	Less than 3 participants.
Holmgren et al.	1986	Sweeden	Duplicated.
Ibuki et al.	1986	Japan	Not found.
Jin et al.	1990	China	Not found.
Kim et al.	2014	South Korea	Abstract.
Kondo et al.	1989	China	No outcomes of interest.
Kuhn et al.	2021	France	No outcomes of interest.
Lasolle et al.	2021	France	No outcomes of interest.
Laws Jr et al.	1983	USA	Duplicated.
Leal Cerro et al.	1985	Italy	No outcomes of interest.
Lian et al.	2017	China	No outcomes of interest.
López et al.	1988	Chile	Not found.
Mikina et al.	2014	Poland	Abstract.
Rees et al.	2016	UK	Partial results of full article already included (Lambert et al., 2017).
Samaan et al.	1986	USA	No outcomes of interest.
Sant' Anna et al.	2020	Brazil	Duplicated.
Seshadri et al.	1993	India	Not found.
Tankirilu et al.	2021	Turkey	Duplicated.
Ventz et al.	1985	Germany	Not found.
Verhelst et al.	1998	Belgium	No outcomes of interest.
Větr et al.	1990	Czech Republic	Not found.
Yi et al.	2018	China	No outcomes of interest.

Table II. Risk of bias evaluation of included studies

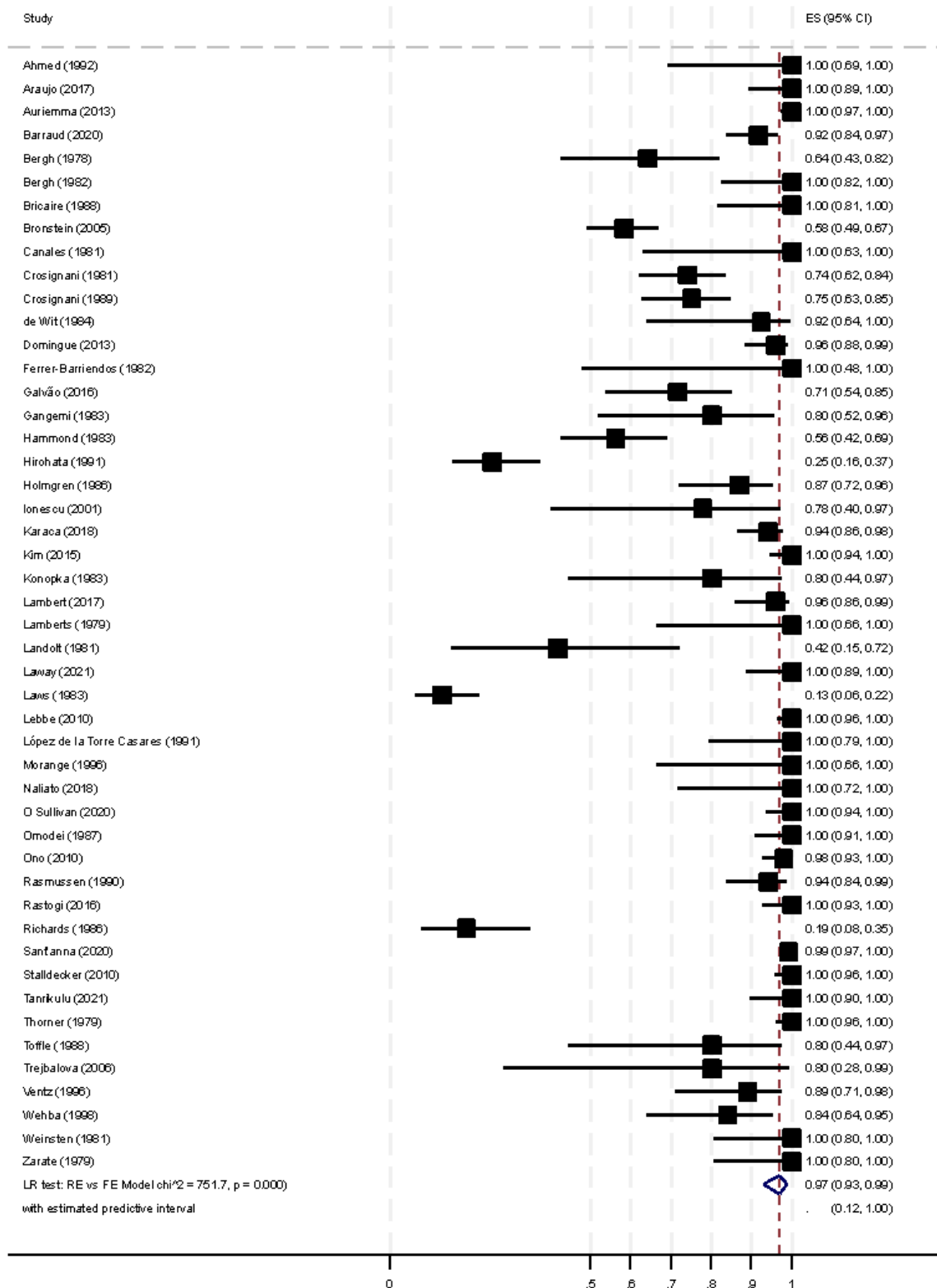
Study	Year	1. Were there clear criteria for inclusion in the review?	2. Was the condition measured in a valid way?	3. Were valid methods used for identification of the condition?	4. Did the case series have consecutive inclusion?	5. Did the case series have complete inclusion?	6. Was there clear reporting of the demographics of the cases?	7. Was there clear reporting of clinical outcomes?	8. Were the outcomes or follow-up results of cases reported?	9. Was there clear reporting of the presenting signs and symptoms?	10. Was appropriate statistical analysis performed?
Ahmed et al.	1992	Y	Y	Y	N	Y	N	Y	Y	NA	NA
Araujo et al.	2017	Y	Y	Y	Y	Y	N	Y	Y	NA	NA
Auriemma et al.	2013	Y	Y	Y	N	Y	N	Y	Y	NA	NA
Barraud et al.	2020	Y	Y	Y	N	Y	N	Y	Y	NA	NA
Bergh et al.	1978	Y	Y	Y	Y	Y	N	Y	Y	NA	NA
Bergh et al.	1982	Y	Y	Y	N	N	N	Y	Y	NA	NA
Bricaire et al.	1988	Y	Y	Y	U	Y	N	Y	Y	NA	NA
Bronstein et al.	2005	N	U	U	U	U	N	Y	Y	NA	NA
Canales et al.	1981	Y	Y	Y	U	Y	N	Y	Y	NA	NA
Crosignani et al.	1981	Y	Y	Y	Y	Y	N	Y	Y	NA	NA
Crosignani et al.	1985	Y	Y	Y	Y	N	N	Y	Y	NA	NA
Crosignani et al.	1989	Y	Y	Y	U	Y	Y	Y	Y	NA	NA
De Wit et al.	1984	Y	Y	Y	U	Y	N	Y	Y	NA	NA
Divers et al.	1983	Y	Y	Y	U	Y	Y	Y	Y	NA	NA
Domingue et al.	2014	Y	Y	Y	Y	Y	Y	Y	Y	NA	NA
Ferrer-Barriendos et al.	1982	Y	Y	Y	U	Y	Y	Y	Y	NA	NA
Galvão et al.	2016	Y	Y	Y	Y	N	Y	Y	Y	NA	NA
Gangemi et al.	1983	Y	Y	Y	U	Y	Y	Y	Y	NA	NA
Hammond et al.	1983	Y	Y	Y	Y	Y	Y	Y	Y	NA	NA
Hirohata et al.	1991	Y	Y	Y	N	Y	N	Y	Y	NA	NA

Holmgren et al.	1986	Y	Y	Y	U	Y	N	Y	Y	NA	NA
Ionescu et al.	2001	Y	N	N	Y	U	Y	Y	Y	NA	NA
Karaca et al.	2018	Y	U	U	U	Y	Y	Y	Y	NA	NA
Kim et al.	2015	Y	Y	Y	Y	Y	Y	Y	Y	NA	NA
Konopka et al.	1983	U	U	U	U	Y	Y	Y	Y	NA	NA
Kupersmith et al.	1994	Y	Y	Y	Y	Y	Y	Y	Y	NA	NA
Lambert et al.	2017	Y	Y	Y	N	Y	Y	Y	Y	NA	NA
Lamberts et al.	1979	Y	Y	Y	U	Y	Y	Y	Y	NA	NA
Landolt et al.	1981	Y	Y	Y	N	Y	Y	Y	Y	NA	NA
Laway et al.	2021	Y	Y	Y	N	Y	Y	Y	Y	NA	NA
Laws et al.	1983	Y	Y	Y	N	Y	N	Y	Y	NA	NA
Lebbe et al.	2010	Y	Y	Y	N	Y	Y	Y	Y	NA	NA
López de la Torre Casares et al.	1991	Y	Y	Y	U	Y	N	Y	Y	NA	NA
Morange et al.	1996	Y	U	U	N	Y	Y	Y	Y	NA	NA
Naliato et al.	2018	Y	Y	Y	N	Y	Y	Y	Y	NA	NA
O Sullivan et al.	2020	Y	Y	Y	Y	Y	Y	Y	Y	NA	NA
Omodei et al.	1987	Y	Y	Y	N	Y	Y	Y	Y	NA	NA
Ono et al.	2010	Y	Y	Y	N	Y	N	Y	Y	NA	NA
Rasmussen et al.	1990	Y	Y	Y	U	U	Y	Y	Y	NA	NA
Rastogi et al.	2016	Y	Y	Y	N	Y	Y	Y	Y	NA	NA
Richards et al.	1986	Y	Y	Y	N	Y	N	Y	Y	NA	NA
Sant'anna et al.	2020	Y	Y	Y	N	Y	Y	Y	Y	NA	NA
Stalldecker et al.	2010	Y	Y	Y	N	Y	Y	Y	Y	NA	NA
Tanrikulu et al.	2021	Y	Y	Y	N	Y	Y	Y	Y	NA	NA
Thorner et al.	1979	Y	Y	Y	Y	Y	N	Y	Y	NA	NA
Toffle et al.	1988	Y	Y	Y	Y	Y	N	Y	Y	NA	NA
Trejbalova et al.	2006	N	Y	Y	N	Y	Y	Y	Y	NA	NA
Ventz et al.	1996	Y	Y	Y	U	Y	Y	Y	Y	NA	NA

Wehba et al.	1998	N	U	U	U	U	N	Y	Y	NA	NA
Weinsten et al.	1981	Y	Y	Y	U	Y	Y	Y	Y	NA	NA
Woosley et al.	1982	Y	Y	Y	N	Y	Y	Y	Y	NA	NA
Zarate et al.	1979	Y	Y	Y	U	Y	Y	Y	Y	NA	NA

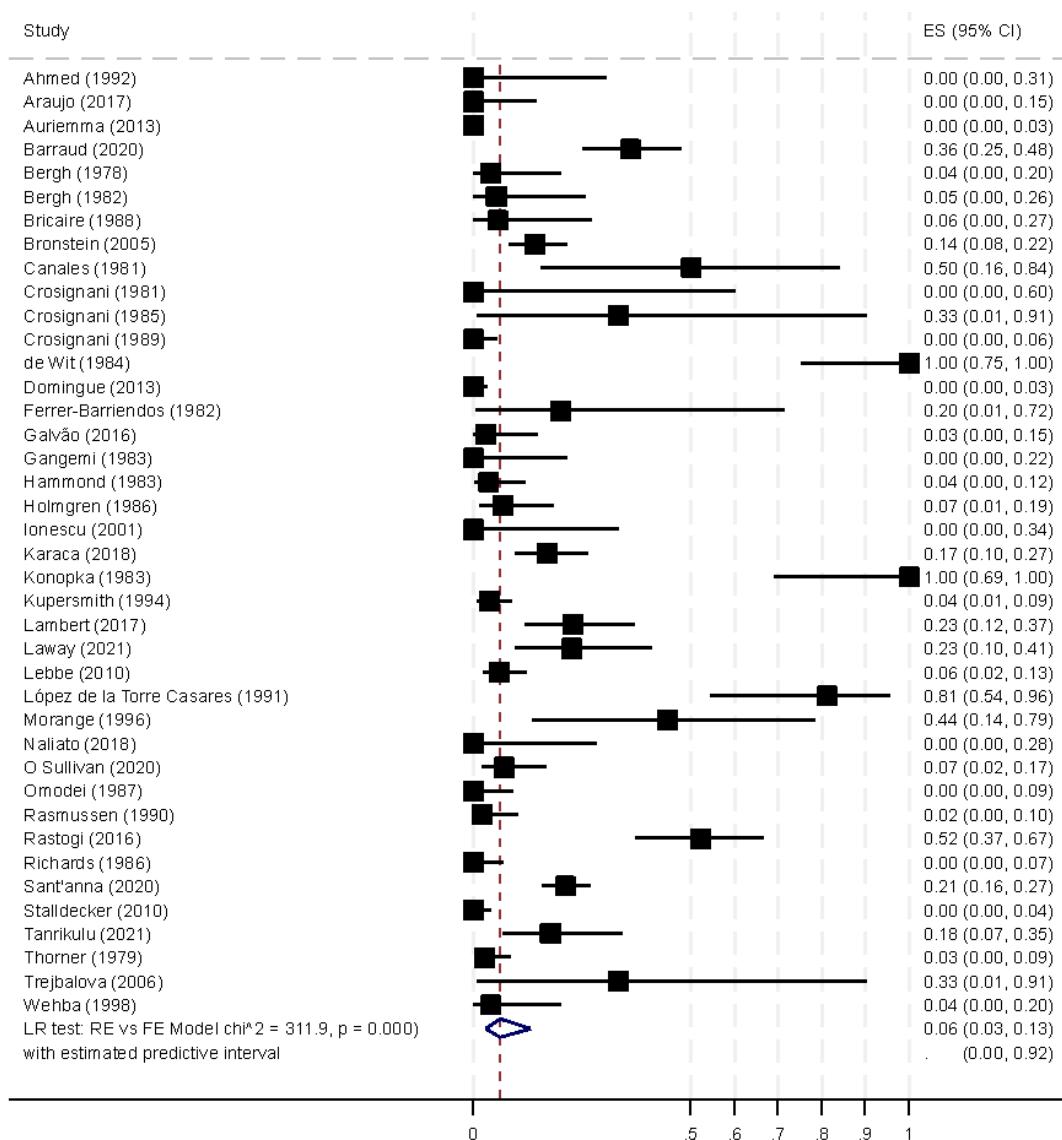
N: no; NA: not applicable; U: unclear; Y: yes.

Figure I. Meta-analysis findings: Frequency of participants using dopamine agonist at conception



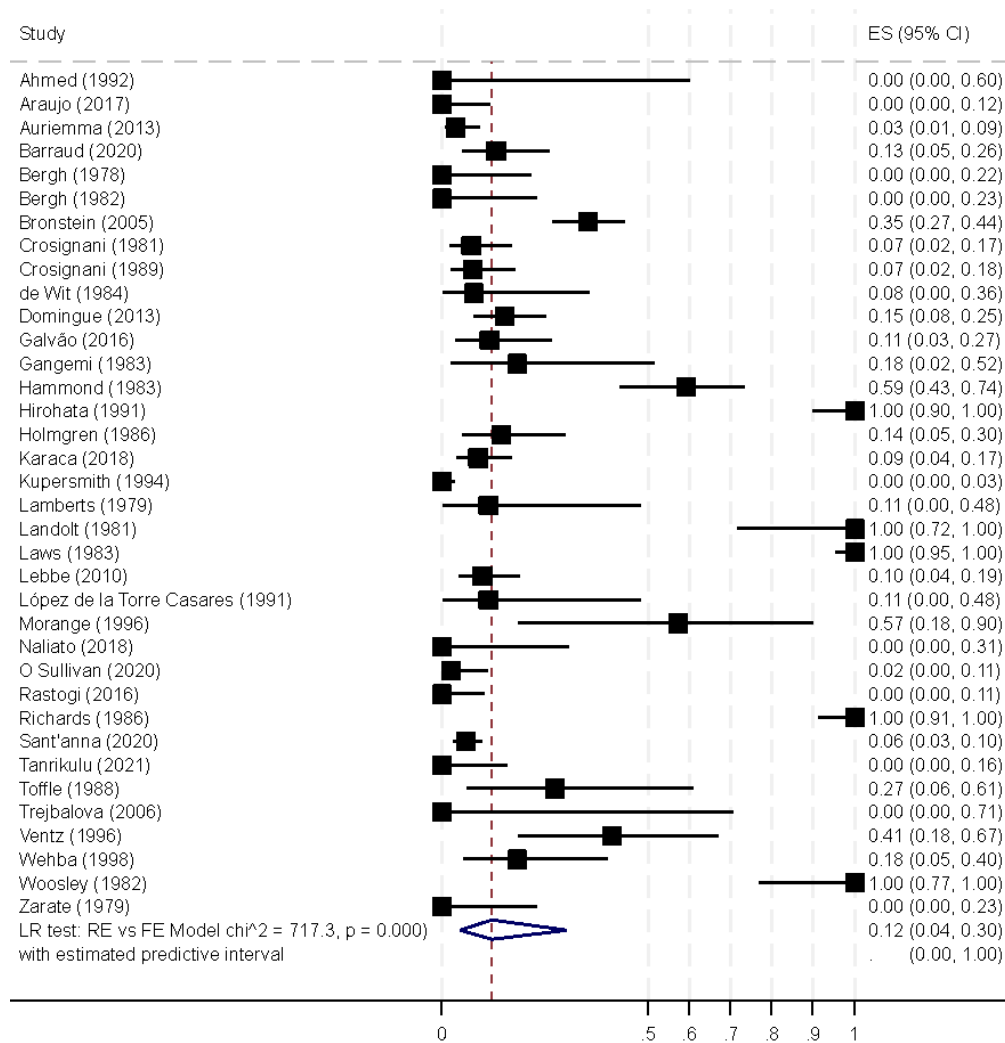
ES, effect size; FE, fixed effects; LR, likelihood ratio; RE, random effects; 95% CI, 95 confidence intervals.

Figure II. Meta-analysis findings: Frequency of participants using dopamine agonist during pregnancy



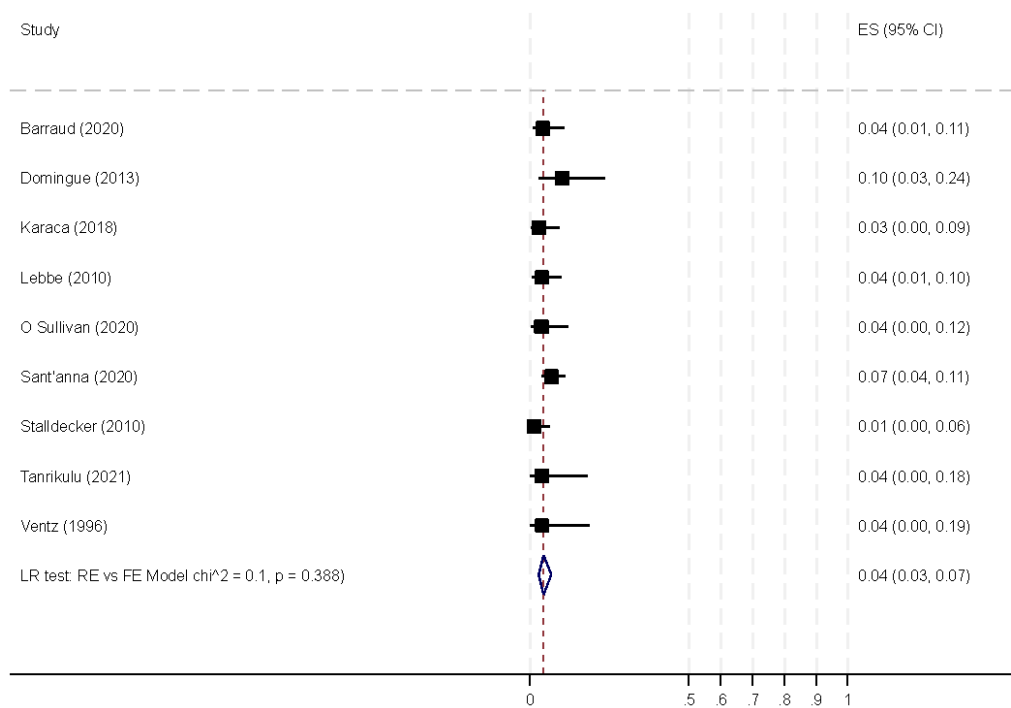
ES, effect size; FE, fixed effects; LR, likelihood ratio; RE, random effects; 95% CI, 95 confidence intervals.

Figure III. Meta-analysis findings: Frequency of participants submitted to neurosurgery for prolactinoma treatment before pregnancy



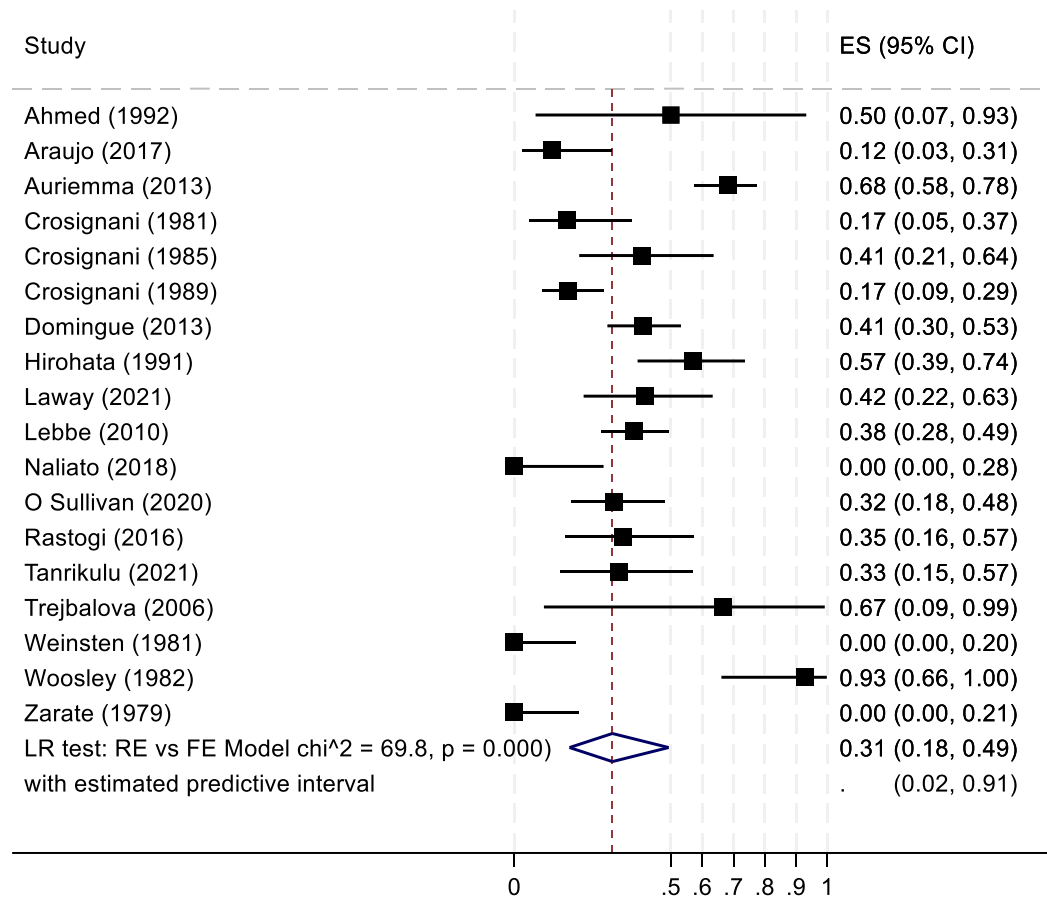
ES, effect size; FE, fixed effects; LR, likelihood ratio; RE, random effects; 95% CI, 95 confidence intervals.

Figure IV. Meta-analysis findings: Frequency of gestational diabetes mellitus



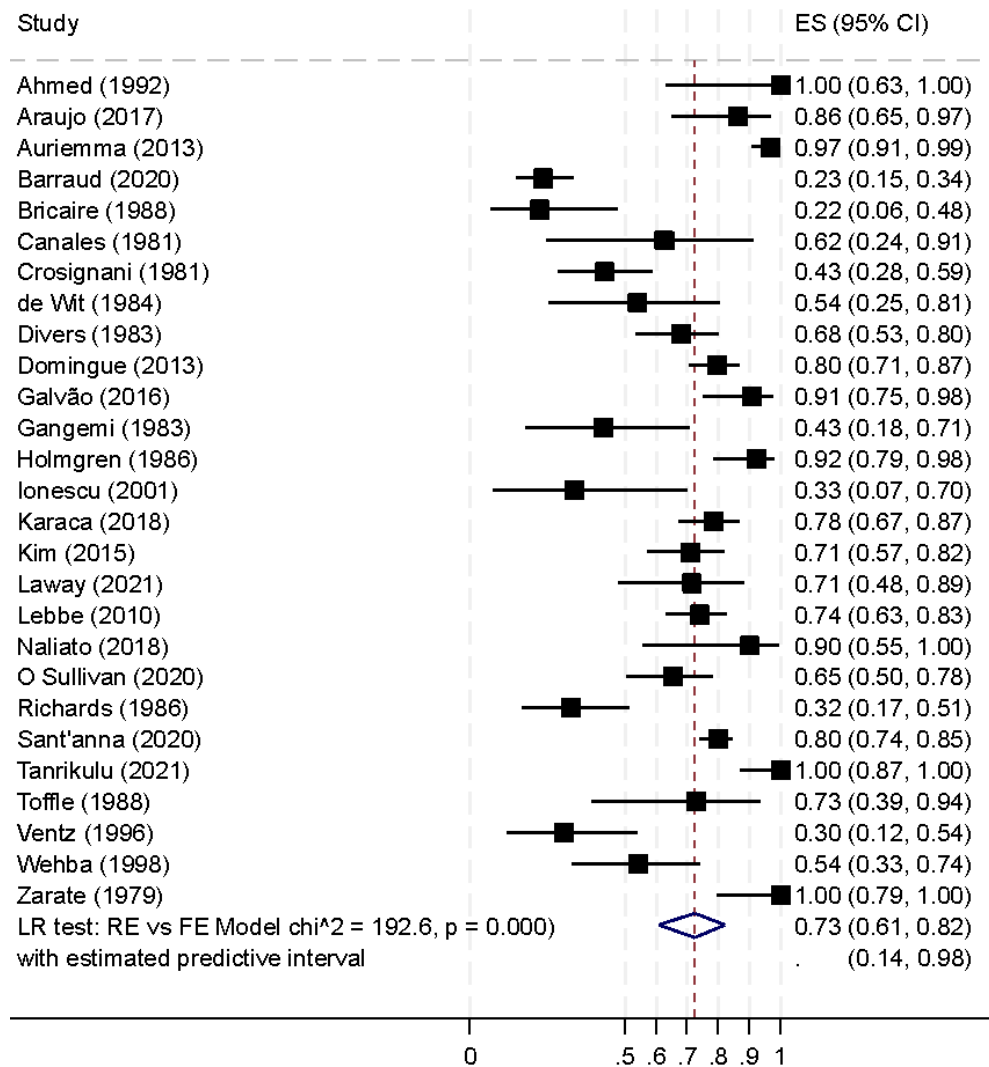
ES, effect size; FE, fixed effects; LR, likelihood ratio; RE, random effects; 95% CI, 95 confidence intervals.

Figure V. Meta-analysis findings: Frequency of prolactinoma remission



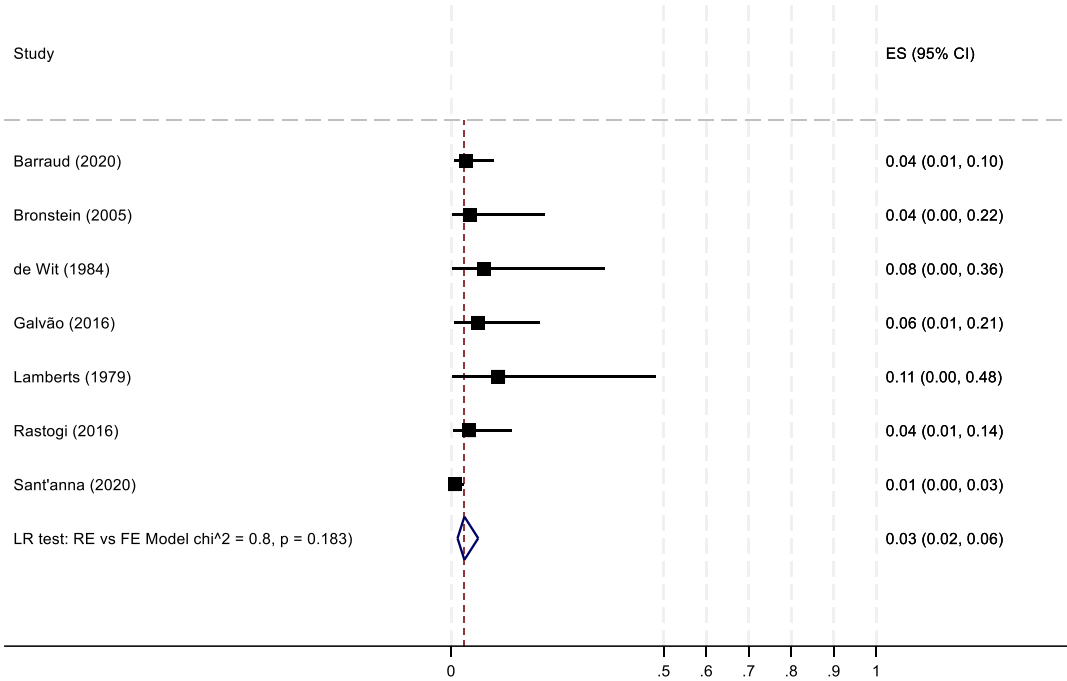
ES, effect size; FE, fixed effects; LR, likelihood ratio; RE, random effects; 95% CI, 95 confidence intervals.

Figure VI. Meta-analysis findings: Frequency of breastfeeding



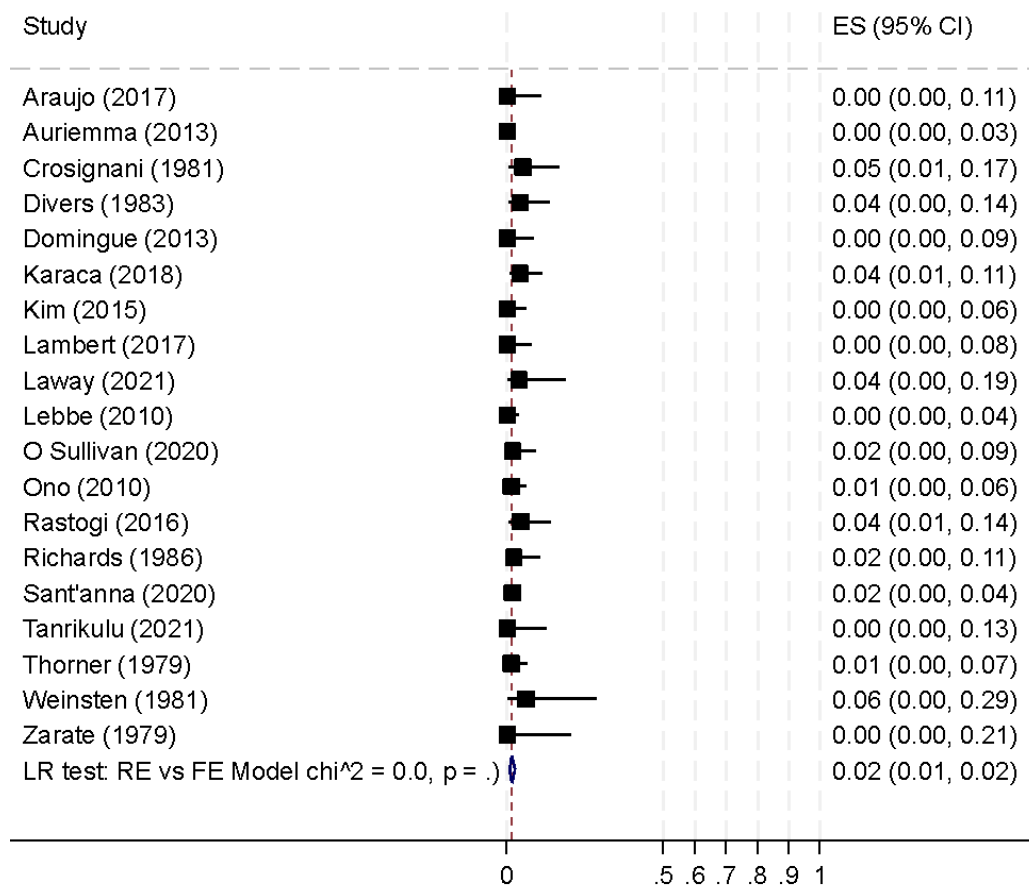
ES, effect size; FE, fixed effects; LR, likelihood ratio; RE, random effects; 95% CI, 95 confidence intervals.

Figure VII. Meta-analysis findings: Frequency of apoplexy



ES, effect size; FE, fixed effects; LR, likelihood ratio; RE, random effects; 95% CI, 95 confidence intervals.

Figure VIII. Meta-analysis findings: Frequency of perinatal mortality



ES, effect size; FE, fixed effects; LR, likelihood ratio; RE, random effects; 95% CI, 95 confidence intervals.

Figure IX. Meta-regression of spontaneous abortion and covariate year of manuscript publication.

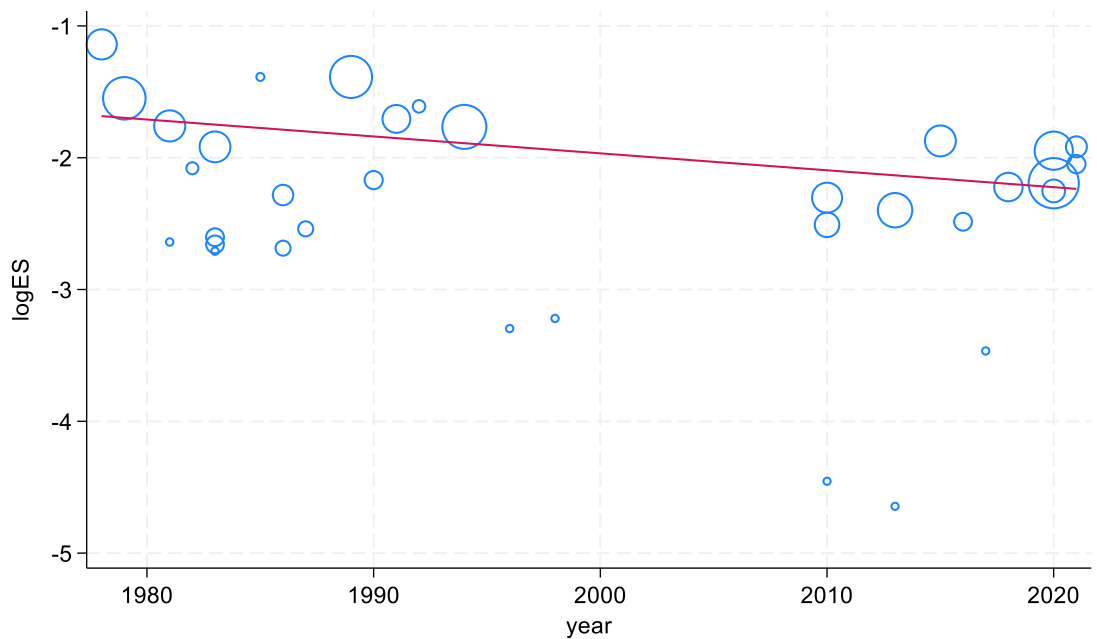
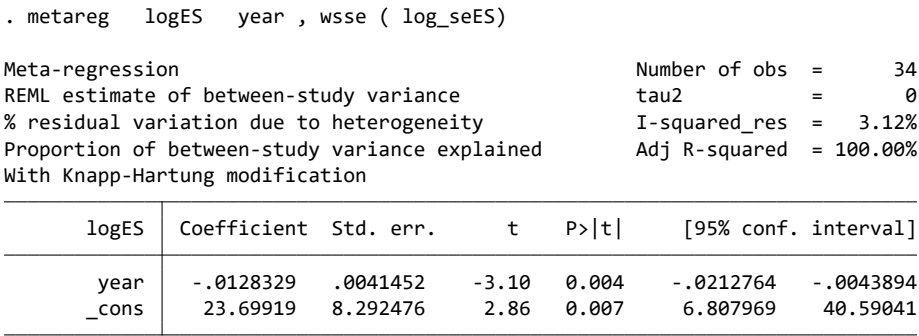
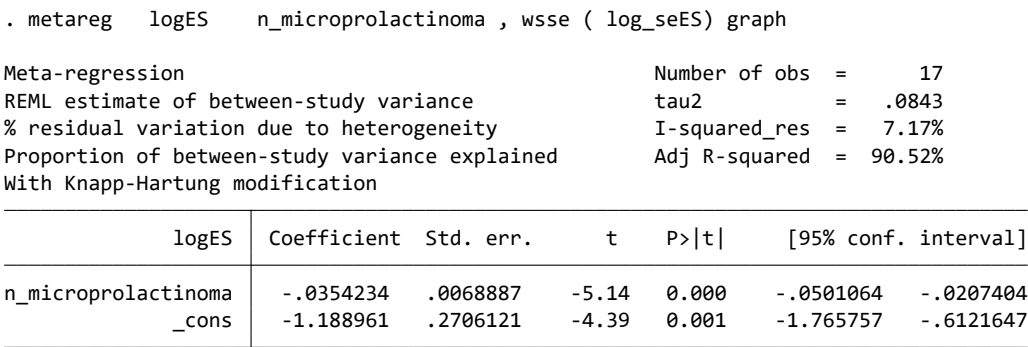
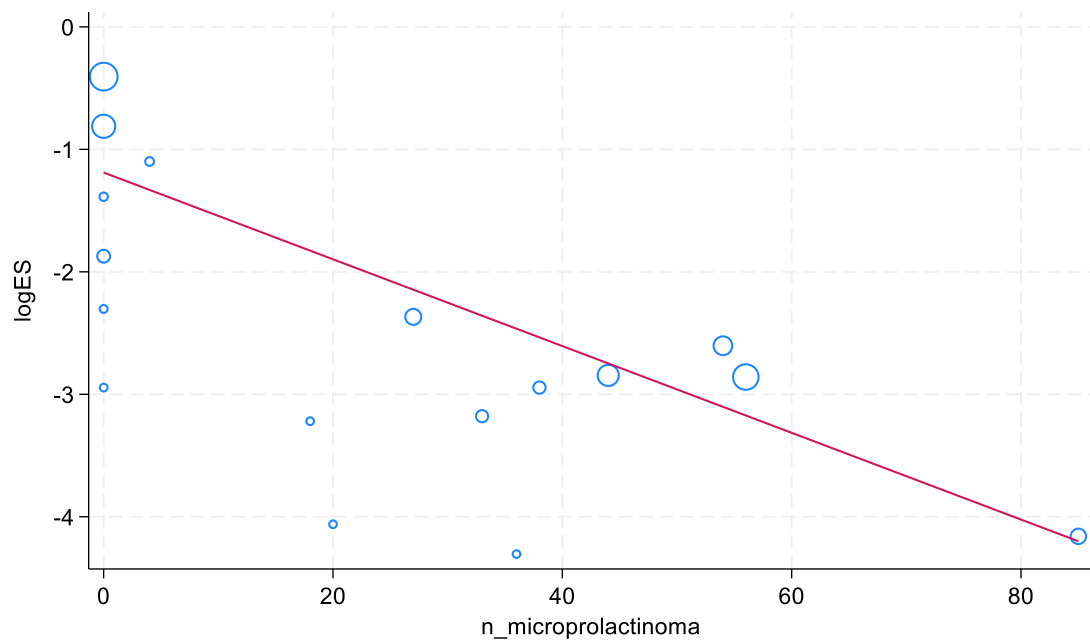


Figure X. Meta-regression of visual impairment and covariate number of pregnant women with microprolactinoma of manuscript publication.





Search Strategies

PubMed

1 "Prolactinoma"[Mesh] OR (Prolactinomas) OR (Lactotroph Adenoma) OR (Adenoma, Lactotroph) OR (Adenomas, Lactotroph) OR (Lactotroph Adenomas) OR (Prolactinoma, Familial) OR (PRL-Secreting Pituitary Adenoma) OR (PRL Secreting Pituitary Adenoma) OR (PRL-Secreting Pituitary Adenomas) OR (Pituitary Adenoma,

PRL-Secreting) OR (Pituitary Adenomas, PRL-Secreting) OR (Prolactin-Producing Pituitary Adenoma) OR (Pituitary Adenoma, Prolactin-Producing) OR (Pituitary Adenomas, Prolactin-Producing) OR (Prolactin Producing Pituitary Adenoma) OR (Prolactin-Producing Pituitary Adenomas) OR (Prolactin-Secreting Pituitary Adenoma) OR (Prolactin Secreting Pituitary Adenoma) OR (Adenoma, Prolactin-Secreting, Pituitary) OR (Pituitary Adenoma, Prolactin-Secreting) OR (Pituitary Adenoma, Prolactin Secreting) OR (Pituitary Adenomas, Prolactin-Secreting) OR (Prolactin-Secreting Pituitary Adenomas) OR (Microprolactinoma) OR (Microprolactinomas) OR (Macroprolactinoma) OR (Macroprolactinomas)

#2 "Pregnancy"[Mesh] OR (Pregnancies) OR (Gestation) OR (Pregnant women) OR (Pregnant) OR (Lactating women) OR (Maternal iodine intake) OR (Postpartum) OR (Pregnant patient)

#1 AND #2 = 715

Embase

'prolactinoma'/exp OR 'lactotroph adenoma' OR 'lactotroph adenomas' OR 'macroprolactinoma' OR 'macroprolactinomas' OR 'microprolactinoma' OR 'microprolactinomas' OR 'prl producing adenoma' OR 'prl producing adenomas' OR 'prl producing pituitary adenoma' OR 'prl producing pituitary adenomas' OR 'prl producing pituitary tumor' OR 'prl producing pituitary tumors' OR 'prl producing pituitary tumour' OR 'prl producing pituitary tumours' OR 'prl producing tumor' OR 'prl producing tumors' OR 'prl producing tumour' OR 'prl producing tumours' OR 'prl secreting adenoma' OR 'prl secreting adenomas' OR 'prl secreting pituitary adenoma' OR 'prl secreting pituitary tumor' OR 'prl secreting pituitary tumors' OR 'prl secreting pituitary tumour' OR 'prl secreting pituitary tumours' OR 'prl secreting tumor' OR 'prl secreting tumour' OR 'prl secreting tumours' OR 'prolactin producing adenoma' OR 'prolactin producing adenomas' OR 'prolactin producing pituitary adenoma' OR 'prolactin producing pituitary adenomas' OR 'prolactin producing pituitary tumor' OR 'prolactin producing pituitary tumors' OR

'prolactin producing pituitary tumour' OR 'prolactin producing pituitary tumours' OR 'prolactin producing tumor' OR 'prolactin producing tumors' OR 'prolactin producing tumour' OR 'prolactin producing tumours' OR 'prolactin secreting adenoma' OR 'prolactin secreting adenomas' OR 'prolactin secreting pituitary adenoma' OR 'prolactin secreting pituitary adenomas' OR 'prolactin secreting pituitary tumor' OR 'prolactin secreting pituitary tumors' OR 'prolactin secreting pituitary tumour' OR 'prolactin secreting pituitary tumours' OR 'prolactin secreting tumor' OR 'prolactin secreting tumors' OR 'prolactin secreting tumour' OR 'prolactin secreting tumours' OR 'prolactinomas'

#2 'pregnancy'/exp OR 'child bearing' OR 'childbearing' OR 'gestation' OR 'gravity' OR 'intrauterine pregnancy' OR 'labor presentation' OR 'labour presentation' OR 'pregnancy maintenance' OR 'pregnancy trimesters'

#1 AND #2=479

Latin American and Caribbean Health Sciences Literature (by Virtual Health Library)

#1 MH: "Prolactinoma" OR (Adenoma Pituitário Secretor de PRL) OR (Adenoma Pituitário Secretor de Prolactina) OR (Adenoma Pituitário Secretório de Prl) OR (Adenoma Pituitário Secretório de Prolactina) OR H:C04.557.470.035.625\$ OR MH:C04.588.322.609.792\$ OR MH:C10.228.140.617.738.675.800\$ OR MH:C19.344.609.792\$ OR MH:C19.700.734.792\$

#2 MH: "Gravidez" OR (Gestação) OR MH: G08.686.784.769

#1 AND #2=18

CENTRAL

ID Search Hits

#1 MeSH descriptor: [Prolactinoma] explode all trees 40

#2 (pregnancy): ti,ab,kw (Word variations have been searched) 62479

#3 #1 AND #2 2

#4 (prolactinoma):ti,ab,kw (Word variations have been searched) 88

#5 #1 OR #4 88

#6 #2 AND #5 7