



S2e-Leitlinie

Diagnostik und Therapie des

Benignen Prostatasyndroms (BPS)

Evidenztabelle

Registernummer: 043-034
Version 5.0 – Februar 2023





Inhaltsverzeichnis

1. Informationen zum Leitliniendokument.....	3
1.1. Herausgeber	3
1.2. Federführende Fachgesellschaft der Leitlinie.....	3
1.3. Finanzierung der Leitlinie.....	3
1.4. Kontakt	3
1.5. Zitierweise des Dokuments.....	3
1.6. Weitere Dokumente zur Leitlinie	3
1.7. Schema der Evidenzgraduierung (Level of Evidence) nach SIGN	5
1.8. Abkürzungsverzeichnis	6
2. Evidenztabellen zum Kapitel ‚Epidemiologie‘	12
3. Evidenztabellen zum Kapitel ‚Basisdiagnostik‘	24
4. Evidenztabellen zum Kapitel ‚Weiterführende Diagnostik‘	55
5. Evidenztabellen zum Kapitel ‚Prognosefaktoren für die Progression des BPS‘	100
6. Evidenztabellen zum Kapitel ‚Medikamentöse Therapie‘	128
7. Evidenztabellen zum Kapitel ‚Instrumentelle/operative Verfahren‘	204
8. Tabellenverzeichnis	258
9. Referenzen	259



1. Informationen zum Leitliniendokument

1.1. Herausgeber

Herausgeber dieses Leitlinienreports ist die Deutsche Gesellschaft für Urologie e. V. (DGU).

1.2. Federführende Fachgesellschaft der Leitlinie

Die Federführung und Erstellung der Leitlinie oblag dem Arbeitskreis Benignes Prostatasyndrom (BPS) der DGU.



1.3. Finanzierung der Leitlinie

Diese Leitlinie wurde finanziell durch die Deutsche Gesellschaft für Urologie e. V. unterstützt. Die Mitglieder der Leitliniengruppe arbeiteten ehrenamtlich ohne Honorar. Die wissenschaftliche und organisatorische Unterstützung erfolgte durch die Mitarbeiterinnen der DGU-Geschäftsstelle Berlin.

1.4. Kontakt

UroEvidence@Deutsche Gesellschaft für Urologie e. V.
Geschäftsstelle Berlin
Leitliniensekretariat
Martin-Buber-Straße 10
14163 Berlin
Tel.: +49 (0)30 8870833 0
E-Mail: urovidence@dgu.de

1.5. Zitierweise des Dokuments

Deutsche Gesellschaft für Urologie e. V. (Hrsg.): S2e-Leitlinie Diagnostik und Therapie des Benigen Prostatasyndroms (BPS), Evidenztabelle 5.0, 2020, AWMF-Registernummer: 043-035, <https://www.urologenportal.de/fachbesucher/wirueberuns/dgu/leitlinien-der-deutschen-gesellschaft-fuer-urologie.html> (abgerufen am: TT.MM.JJJJ).

1.6. Weitere Dokumente zur Leitlinie

Bei diesem Dokument handelt es sich um eine Ergänzung des Leitlinienreports der S2e-Leitlinie zur Diagnostik und Therapie des Benigen Prostatasyndroms (BPS), welche über folgende Seiten zugänglich ist:



- Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften (AWMF) (<http://www.awmf.org/leitlinien/aktuelle-leitlinien.html>)
- DGU (<https://www.urologenportal.de/fachbesucher/wirueberuns/dgu/leitlinien-der-deutschen-gesellschaft-fuer-urologie.html>)

Das Evidenztabellendokument ist die Grundlage für folgende Dokumente:

- Kurzfassung der Leitlinie
- Langfassung der Leitlinie

Die Erstellung der Evidenztabelle ist ausführlich beschrieben im

- Leitlinienreport



1.7. Schema der Evidenzgraduierung (Level of Evidence) nach SIGN

Tabelle 1: Schema der Evidenzgraduierung

Evidenzlevel	
1++	Qualitativ hochwertige Metaanalysen, Systematische Übersichten von RCTs, oder RCTs mit sehr geringem Risiko systematischer Fehler (Bias)
1+	Gut durchgeführte Metaanalysen, Systematische Übersichten von RCTs, oder RCTs mit geringem Risiko systematischer Fehler (Bias)
1-	Metaanalysen, Systematische Übersichten von RCTs, oder RCTs mit hohem Risiko systematischer Fehler (Bias)
2++	Qualitativ hochwertige systematische Übersichten von Fall-Kontroll- oder Kohortenstudien oder Qualitativ hochwertige Fall-Kontroll- oder Kohortenstudien mit sehr niedrigem Risiko systematischer Verzerrungen (Confounding, Bias, „Chance“) und hoher Wahrscheinlichkeit, dass die Beziehung ursächlich ist
2+	Gut durchgeführte Fall-Kontroll-Studien oder Kohortenstudien mit niedrigem Risiko systematischer Verzerrungen (Confounding, Bias, „Chance“) und moderater Wahrscheinlichkeit, dass die Beziehung ursächlich ist
2-	Fall-Kontroll-Studien oder Kohortenstudien mit einem hohen Risiko systematischer Verzerrungen (Confounding, Bias, „Chance“) und signifikantem Risiko, dass die Beziehung nicht ursächlich ist
3	Nicht-analytische Studien, z. B. Fallberichte, Fallserie
4	Expertenmeinung

1.8. Abkürzungsverzeichnis

Tabelle 2: Abkürzungsverzeichnis

Abkürzung	Bedeutung
5-ARI	5 α -Reduktase-Inhibitoren
AUA-SS/AUA-SI	<i>American Urologic Association Symptom Scale</i>
AUC	Fläche unter der Kurve (<i>Area Under the Curve</i>)
AUR	akuter Harnverhalt (<i>Acute Urinary Retention</i>)
ANV	aktuelle nächtliche Entleerungen (<i>Actual Nocturnal Voids</i>)
BoNT-A	Botulinum Neurotoxin Type A
B-TURP	Bipolare Transurethrale Resektion der Prostata
BipoLEP	Bipolare Enukleation der Prostata
BII	Benigne Prostatahyperplasie Impact Index
BMI	<i>Body Mass Index</i>
BOO	Blasenauslassobstruktion (<i>Bladder Outlet Obstruction</i>)
BOOI	Index zur Ermittlung einer Blasenauslassobstruktion (<i>Bladder Outlet Obstruction Index</i>)
BPE	Benigne Prostatavergrößerung (<i>Benign Prostatic Enlargement</i>)
BPEP	Bipolare Plasmakinetische Enukleation der Prostata
BPH	Benigne Prostatahyperplasie (<i>Benign Prostatic Hyperplasia</i>)
BPO	Benigne Prostataobstruktion (<i>Benign Prostatic Obstruction</i>)
BWT	Blasenwanddicke (<i>bladder wall thickness</i>)
CC	Korrelationskoeffizient (<i>Correlation Coefficient</i>)
CCM	Kondomkatheter-Methode (<i>Condom Catheter Method</i>)
CI	Konfidenzintervall (<i>Confidence Interval</i>)
CLV	Kontaktlaser-Vaporisation (<i>Contact Laser Vaporization</i>)
COI	Interessenkonflikt (<i>Conflict of Interest</i>)



DiLEP	Dioden-Laser-Enukleation der Prostata
DiLVP	Dioden-Laser-Vaporisation der Prostata
DRE	digito-rektale Untersuchung (<i>Digital Rectal Examination</i>)
DU	Detrusorunteraktivität
DWT	Detrusordickenmessung (<i>Detrusor Wall Thickness</i>)
FBC	funktionelle Blasenkapazität
FV	Volumenfrequenz
FVC	Volumenfrequenz-Diagramm (<i>Frequency Volume Chart</i>)
GP	Allgemeinarzt (<i>General Practitioner</i>)
h	hour
HDL	<i>High-density lipoprotein</i>
HoLAP	Holium-Laser-Ablation der Prostata
HoLEP	Holium-Laser-Enukleation der Prostata
HoLRP	Holium-Laser-Resektion der Prostata
HR	Hazard Ratio
HRQOL	Gesundheitsbezogene Lebensqualität (<i>Health-Related Quality Of Life</i>)
IIEF-5	Selbsttest zur Erektionsstörung (<i>International Index of Erectile Function</i>)
ILC	Interstitielle Laserkoagulation
IPP	Intraprostatische Protusion
IPSS	Internationaler Prostata-Symptomenscore (<i>International Prostate Symptom Score</i>)
IQR	Interquartilsabstand
KTP	Kaliumtitanylphosphat
LoE	Evidenzlevel (<i>Level of Evidence</i>)
LR	Wahrscheinlichkeitsverhältnisse (<i>Likelihood Ratio</i>)



LRP	Laproskopische Radikale Prostatektomie
LUTS	Symptome des unteren Harntrakts (<i>Lower Urinary Tract Symptoms</i>)
M-TURP	Monopolare Transurethrale Resektion der Prostata
MBS	störendste Symptome (<i>Most Bothersome Symptoms</i>)
MetS/MS	Metabolisches Syndrom
miRNA	Mikro-Ribonukleinsäure
MISP	Minimalinvasive einfache Prostatektomie (<i>Minimally Invasive Simple Prostatectomy</i>)
MD	Mittlere Differenz
mo	Monate
MSU	Mittelstrahlurin (<i>Midstream Urine</i>)
MW	Mittelwert
NIRS	Nahinfrarotspektroskopie
NPV	Negativer prädiktiver Wert (<i>Negative Predictive Value</i>)
NRE	Nichtrandomisierte experimentelle Studie
NUV	Nächtliches Urinvolumen
OAB	Überaktive Blase (<i>Overactive Bladder</i>)
OP	Operation
OR	Odds Ratio
OS	Gesamtüberleben (<i>Overall Survival</i>)
OSP	Offene einfache Prostatektomie (<i>Open Simple Prostatectomy</i>)
PAE	Prostata-Arterien-Embolisation
PCA	Prostatakarzinom
PCT	Penismanschettentest (<i>Penile Cuff test</i>)
PDE5-I	Phosphodiesterase-5-Inhibitoren
$p_{det}Q_{max}$	Detrusordruck bei maximaler Harnflussrate (<i>detrusor pressure at Q_{max}</i>)



PFS	Druck-Fluss-Studien (<i>Pressure Flow Studies</i>)
PKEP	Plasmakinetische Enukleation der Prostata
PKRP	Plasmakinetische Resektion der Prostata
PPBC	Patientenwahrnehmung des Blasenzustandes (<i>Patient Perception of Bladder Condition</i>)
PPV	Positiver prädiktiver Wert (<i>Positive Predictive Value</i>)
PSA	Prostata-spezifisches Antigen
PUL	<i>Prostatic Urethral Lift</i>
PKRP	Plasmakinetische Resektion der Prostata
PV	Prostatavolumen
PVP	Photo-Vaporization der Prostata
PVEP-XPS	Photoselektive Vapo-Enukleation der Prostata
PVR	Restharnvolumen (<i>Postvoid Residual Urine Volume</i>)
Q _{ave}	Durchschnittliche Durchflussrate (<i>average flow rate</i>)
Q _{max}	maximale Harnflussrate
QoL	Lebensqualität (<i>Quality of Life</i>)
RCT	Randomisierte kontrollierte Studien
RARP	Roboter-assistierte Radikale Prostatektomie
RASP	Roboter-assistierte einfache Prostatektomie
RF	Restfraktion
RNA	Ribonukleinsäure (<i>Ribonucleic Acid</i>)
RoB	Biasrisiko (<i>Risk of Bias</i>)
ROC	Grenzwertoptimierungskurve (<i>Receiver Operating Characteristic</i>)
RR	Relatives Risiko
RRP	Retropubische Radikale Prostatektomie
SD	Standardabweichung (<i>Standard Deviation</i>)



SI	Operative Intervention (<i>Surgical Intervention</i>)
SMD	Standardisierte Mittelwertdifferenz
SPUS	Suprapubischer Ultraschall
SR	Systematischer Review
TAUS	Transabdominaler Ultraschall
TOCAS	<i>Tamsulosin Oral Controlled Absorption System</i>
ThuVEP	Thulium-Laser-Vapoenukleation der Prostata
ThuVARP	Thulium-Laser-Vaporesektion der Prostata
TmLEP/ThuLEP	Thulium-Laser-Enukleation der Prostata
TmLRP/ThuLRP	Thulium-Laser-Resektion der Prostata
TUIP	Transurethrale Inzision der Prostata
TUNA	Transurethrale Nadelablation
TURis	Tranurethrale Resektion mit Kochsalzlösung (<i>Transurethral Resection in saline</i>)
TURP	Transurethrale Resektion der Prostata
TUVis	Tranurethrale Vaporisation mit Kochsalzlösung (<i>Transurethral Vaporisation in saline</i>)
TUVP	Transurethrale Elektrovaporisation der Prostata
TVZ	Übergangszone der Prostata (<i>Transition Zone of the prostate</i>)
UDS	Urodynamische Studien
UEBW	Mit Ultrasound gemessenes Blasengewicht (<i>Ultrasound Estimated Bladder Weight</i>)
UF	Uroflowmetrie
UK	<i>United Kingdom</i>
USA	<i>United States of America</i>
UTI	Harnwegsinfekt (<i>Urinary Tract Infection</i>)
VLAP	Visuelle Laserablation der Prostata



W	Watt
wbc	weißen Blutzellen (<i>white blood cell</i>)
wk	week
WMD	Gewichtete Mittelwert (<i>Weighted Mean Differences</i>)
y	year



2. Evidenztabelle zum Kapitel ‚Epidemiologie‘

Tabelle 3: Risikofaktoren

Schlüsselfrage						
Welche Risikofaktoren zur Entstehung einer BPS gibt es?						
Referenz	Studiencharakteristika	Patientenmerkmale	Ergebnisse	Schlussfolgerungen	Bemerkungen	LoE
Bradley, 2017, J Urol [1] SR	111 eingeschlossene Studien keine Angaben zu Anzahl eingeschlossene Patienten keine Angaben zu Ländern im Artikel oder in den Evidenztabelle Suchzeitraum bis Januar 2016	keine Angaben zu klinischen Merkmalen der Patienten	111 articles addressing: diet (28 studies) fluid intake (21) and caffeine (21) alcohol (26), tobacco use (44) The evidence grade was generally low (6% level 1, 24% level 2, 11% level 3 and 59% level 4).	Evidence of associations between lower urinary tract symptoms and diet, fluid intake and caffeine, alcohol and tobacco use is sparse and mostly observational. However, there is evidence of associations between increased fluid and caffeine intake and urinary frequency/urgency, and between modest alcohol intake and decreased benign prostatic hyperplasia diagnosis and lower urinary tract symptoms.	kritische Punkte in der Robis-Einschätzung: Identifikation und Auswahl der Studien: keine angemessene Anzahl an Datenbanken und keine zusätzlichen Quellen durchsucht Datenextraktion und Bewertung der Studien: keine Information, ob zwei Personen die Daten extrahiert haben, keine Angaben zur Einschätzung des Verzerrungsrisikos der Primärstudien, daher keine	LoE 1- bis LoE 2- Robis-Bewertung: High risk of Bias No direct or indirect commercial incentive associated with publishing this article. one author: Financial interest and/or other relationship with Medtronic Grants from the National Institute of Diabetes and Digestive and



					Information, ob das RoB zwei Personen durchgeführt haben	Kidney Diseases through cooperative agreements.
Gacci, 2015, BJU Int [2] SR + MA	8 eingeschlossene Studien observational studies 5403 eingeschlossene Patienten Suchzeitraum bis Oktober 2013 keine Angaben zu Ländern	mean age between 41.4 (5.2) y and 74 (8.1) y	Prostate volume mean difference, mL +1.8 mL, 95% CI 0.74–2.87; P<0.001 favours MetS transitional zone prostate volume, mean difference, mL +3.67mL 95% CI 1.31–6.03; P<0.001 favours MetS	Our results underline the exacerbating role of MetS-induced metabolic derangements in the development of BPE. Obese, dyslipidaemic, and aged men have a higher risk of having MetS as a determinant of their prostate enlargement.	kritische Punkte in der Robis-Einschätzung: Einschlusskriterien der Studien: keine Angaben zu den Einschlusskriterien Datensynthese und Ergebnisse: kein Funnel Plot oder Sensitivitätsanalyse und keine Diskussion des Verzerrungsrisikos der Primärstudien	LoE 2- Robis-Bewertung: High risk of Bias Conflict of Interest None declared no information about funding
Greco, 2019, Eur Urol Focus [3] SR + MA	37 eingeschlossene Artikel Oxford LoE A, B 1561 BPH Patienten Zeitraum der Veröffentlichung der eingeschlossene Studien 2007 – 2016 Schweden Czech Republic USA	mean age: 62 y - 72 y	64 miRNAs from 37 selected articles were ranked according to p values (p <0.05). Application of the robust rank aggregation method identified miR-221 as significantly associated with BPH (p = .013). relationship between benign prostate hyperplasia and microRNA-221 random effect-model used: effect size 1.16 (95% CI 0.61 – 1.71)	miR-221 has the potential to be used both as a biomarker and novel target in the early diagnosis and therapy of BPH. Technological advances should enable the synthesis of pre-RNA or anti-RNA molecules within carrier vehicles that can be safely delivered into patients. The development of such new pharmacologic therapies should be lastly investigated as possible therapy of one of	sehr kleine Studien haben hohe Effektmaße und die großen Studien zeigen keine Effekte, alle Konfidenzintervalle zeigen an, dass keine stat. Sign. vorliegt daher erscheint die Schlussfolgerung der Autoren sehr optimistisch	LoE 2- Robis-Bewertung: High risk of bias no funding no coi



	China Finland Greece Brasil Germany Serbia Italy Kolkata Bulgaria Turkey Bahrain Denmark Iran Spain Korea			the most common urologic diseases among elderly men.	kritische Punkte in der Robis-Einschätzung: Datenextraktion und Bewertung der Studien: keine Information zum Verzerrungsrisiko der Primärstudien Datensynthese und Ergebnisse: keine Diskussion des Verzerrungsrisikos der Primärstudien	
Minciullo, 2015, Urol Int [4] SR	13 eingeschlossene Studien 1620 eingeschlossene Patienten	keine Patientencharakteristika berichtet	Prostatic inflammation can cause the generation of free radicals. The extent of oxidative damage can be exacerbated by a decreased efficiency of antioxidant defense mechanisms. The balance between OS and the antioxidant component also has a role in developing prostate disease. Several works show the role of oxidant products and of depletion of antioxidant substances in BPH patients. It is accepted that free radicals play a role in carcinogenesis and that BPH should be considered a premalignant condition which may evolve into prostate cancer. High OS parameters and low antioxidant activity are more prominent in prostate cancer	Further studies are needed to clarify the potential role of antioxidants in BPH also in view of preventing the progression to prostate cancer	kritische Punkte in der Robis-Einschätzung Einschlusskriterien der Studien Identifikation und Auswahl der Studien: keine Beschreibung von vordefinierten Zielen und Einschlusskriterien, keine angemessene Anzahl an Datenbanken, keine Information zur Studienauswahl (2 unabhg. Reviewer)	LoE 2- Robis-Bewertung: High risk of bias no information about coi and funding



			patients compared with BPH and controls.		Datenextraktion und Bewertung der Studien keine Information, ob 2 unabhg. Reviewer die Daten extrahiert haben keine Information zum Verzerrungsrisiko der Primärstudien	
Russo, 2015, Aging Male [5] SR + MA	19 eingeschlossene Studien (1 experimental, 18 observational) 18 476 eingeschlossene Patienten Suchzeitraum bis Dez 2014 China Italien Korea Taiwan Japan USA Türkei	keine Patientencharakteristika berichtet	MD of IPSS MD=0.10 [95% CI -0.51 to 0.71]; p=0.75 favours MetS MD in PV MD=2.18 [95% CI 0.73 to 3.64] p=0.03 favours MetS MetS components and risk of moderate-to-severe LUTS: waist circumference WC >90 cm for Asian or >94 for Caucasian pooled ORs [95% CI] 1.13 [0.93–1.38] p=0.22 favours MetS HDL <40mg/dl pooled ORs [95% CI] 1.22 [0.91–1.64] p=0.19 favours HDL triglycerides >150 mg/dl pooled ORs [95% CI] 1.31 [1.01–1.71] p=0.04	Patients affected by MetS and LUTS/BPE are rising and emerging links have been postulated. However, current literature is limited to severe heterogeneity and ethnic disparities and results of the current meta-analysis demonstrated that MetS was not determinant in worsen LUTS/BPE. Moreover, among underlying pathways, diabetes and hypertriglyceridemia may represent significant MetS components able to more severe LUTS/BPE. Clinical connections between MetS and LUTS/BPE should be further investigated in order to set new preventive strategies and counteract the development of LUTS/BPE in men at risk.	12 der 19 eingeschlossenen Studien erreichten eine Qualitätsbewertung von mehr als 50%	LoE 2++ Robis-Bewertung: Low risk of bias no information about funding no conflict of interest



			<p>favours triglycerides</p> <p>patients with elevated fasting glucose (>6.1 mmol/L or 110 mg/dL)</p> <p>pooled ORs [95% CI] 1.77 [1.15–2.73] p=0.01)</p> <p>favours elevated fasting glucose</p>			
<p>Russo, 2015, Int J Urol</p> <p>[6]</p> <p>SR</p>	<p>19 eingeschlossene Studien</p> <p>nur nicht experimentelle Studien</p> <p>22540 eingeschlossene Patienten</p> <p>Suchzeitraum bis Dez 2014</p> <p>China Italien Frankreich Korea Taiwan Japan USA Türkei</p>	<p>keine Patientencharakteristika berichtet</p>	<p>The evidence synthesis showed a positive association between metabolic syndrome, number of components and lower urinary tract symptoms/bladder outlet obstruction. In particular, the major endocrine aberrations of this connection are central obesity and hypertriglyceridemia. The links between insulin resistance and lower urinary tract symptoms/bladder outlet obstruction should be better investigated. Ethnic disparities in all examined studies showed a different impact of metabolic syndrome on lower urinary tract symptoms/bladder outlet obstruction severity and such influence still remain unclear.</p>	<p>The relationship between metabolic syndrome and lower urinary tract symptoms/bladder outlet obstruction open the way for introducing physical activity and diet as recognized first-line interventions for treating lower urinary tract symptoms. However, this connection should be investigated in two different ethnic cohorts (i.e. Asian vs Caucasian) in order to better understand the impact of ethnic disparities on metabolic syndrome and lower urinary tract symptoms/bladder outlet obstruction severity.</p>	<p>kritische Punkte in der Robis-Einschätzung:</p> <p>Einschlusskriterien der Studien: keine Information zur Begründung der Einschlusskriterien</p>	<p>LoE 2-</p> <p>Robis-Bewertung: High risk of bias</p> <p>COI: None declared</p> <p>no information about funding</p>
<p>Siddiqui, 2019, J Urol</p> <p>[7]</p> <p>SR</p>	<p>125 eingeschlossene Studien</p> <p>keine Studiendesignangaben vorhanden</p>	<p>keine Patientencharakteristika berichtet</p>	<p>Of 6,150 citations identified 125 met the inclusion criteria. Most studies (93.6%) assessed biomarkers at 1 time point and were cross sectional in nature. Few studies adjusted for potentially confounding clinical variables or assessed biomarkers in an individual over time. No</p>	<p>Major deficiencies in the existing biomarker literature include poor reproducibility of laboratory data, unclear classification of patients with lower urinary tract symptoms and lack of adjustment for clinical covariates. Despite these</p>	<p>Studienstichproben bestehen aus Männern und Frauen</p>	<p>LoE 2++</p> <p>Robis-Bewertung: Low risk of bias</p> <p>Supported by the National Institute of</p>



			individual biomarkers are currently validated as diagnostic tools for lower urinary tract symptoms. Compared to controls, pathway analyses identified multiple immune response pathways that were enriched in overactive bladder syndrome and cell migration/cytoskeleton remodeling pathways that were enriched in female stress incontinence.	limitations we identified multiple putative pathways in which panels of biological markers need further research.		Diabetes and Digestive and Kidney Diseases through cooperative agreements No direct or indirect commercial, personal, academic, political, religious or ethical incentive is associated with publishing this article † Supported by Grant K23-DK110417 from the National Institute of Diabetes and Digestive and Kidney Diseases. ‡ Financial interest and/or other relationship with Ethicon, Inc.
Wang, 2016, Medicine [8]	8 eingeschlossene Studien in der Metaanalyse mit 3093 Patienten	Alters-MW in Jahren von 59 (50–83) bis 77.75 ±5.78	prostate growth rate mean difference 0.67 mL/y, P<0.001 95% CI 0.61 – 0.73	In conclusion, the results of this meta-analysis are consistent with literature indicating that BPH patients	falsche Beschriftung der Effektrichtung in den forest plots	LoE 2- Robis-Bewertung:



<p>SR + MA</p>	<p>cohort and case-control studies</p> <p>plus 1 Studie, die nur qualitativ ausgewertet wurde</p> <p>Suchzeitraum: bis März 2015</p> <p>Italien China Iran Türkei</p>	<p>BMI, kg/m² von 23.25 ±2.78 bis 29.8±4.3</p>	<p>favours met syndr</p> <p>prostate volume mean difference 6.8 mL, P=0.010 95% CI 1.65 – 11.95 favours met syndr</p> <p>IPSS mean difference 1.58 p=0.202 95% CI -0.85 – 4.01 Ergebnis stat. nicht sign</p> <p>PSA level mean difference 0.24 ng/mL, P= 0.056 95% CI -0.01 – 0.49 Ergebnis stat. nicht sign.</p> <p>maximal flow rate mean difference -1.41mL/s, P=0.345 95% CI -4.35 – 1.52 Ergebnis stat. nicht sign</p>	<p>with MS have a higher prostate growth rate and larger prostate volume than those without MS. However, measures of LUTS were not different between patients with and without MS. Further study is necessary to elucidate the association of BPH and metabolic disorder elements and the potential risk of disease progression in BPH patients with MS.</p>	<p>Beschreibung im Text jedoch richtig kritische Punkte in der Robis-Einschätzung:</p> <p>Identifikation und Auswahl der Studien: keine Information zu 2 unabhg. Reviewern, die die Studienauswahl durchgeführt haben</p> <p>Datenextraktion und Bewertung der Studien: keine Information zu 2 unabhg. Reviewer, um Fehler bei Datenerhebung zu minimieren</p>	<p>High risk of bias</p> <p>no coi</p> <p>medical writing and editorial assistance provided by Dr. Richard Sandore, MedCom Asia, Inc was funded by MSD China.</p>
<p>Xu, 2016, Medicine</p> <p>[9]</p> <p>SR + MA</p>	<p>8 eingeschlossene Studien</p> <p>6 cohort studies, 1 case-control study, and 1 cross-sectional study</p> <p>44100 eingeschlossene Patienten</p> <p>USA Griechenland</p>	<p>Altersangaben 40-79 Jahre</p>	<p>Nonsmokers vs ex-smokers no associated risk was found between the 2 groups: RR=0.99, 95% CI 0.94–1.05</p> <p>Nonsmokers vs current smokers smoking is not associated with increased risk of BPH RR=1.17, 95% CI 0.98–1.41</p> <p>Nonsmokers vs heavy and light smokers</p>	<p>In conclusion, our results suggest that there may be no significant association between smoking and risk of BPH. Strong evidence remains lacking for increased risk of BPH surgery among smokers, including ex-smokers and current smokers, though a marginally significant difference was observed in ever-smokers when compared with never-</p>	<p>kritische Punkte in der Robis-Einschätzung:</p> <p>Datenextraktion und Bewertung der Studien: keine Angaben zu 2 unabhg. Reviewer zur Bewertung des Verzerrungsrisikos</p>	<p>LoE 2-</p> <p>Robis-Bewertung: High risk of bias</p> <p>supported by grants from the Shanghai Pudong New Area Health and Family Planning Project (No. PW</p>



	Australien Suchzeitraum 1992 - 2010		no significant difference was observed between the 2 groups RR=1.02, 95% CI 0.84–1.24 Never-smokers vs ever-smokers no significance appeared when comparing never-smokers and ever-smokers RR=1.03, 95% CI 0.92–1.15	smokers. More studies are needed to detail the effects of smoking on risk of BPH.		2013D-3) and the program for outstanding medical academic leader no coi
Zou, 2016, World J Urol [10] MA	16 eingeschlossene Studien observational studies n=1895 cases of BHP patients with MetS n=2224 cases of BHP patients without MetS 2010-2014 China MetS	Age mean (SD) von 43.9 ± 2.4 bis 76.93 ± 5.85 Prostate volume (PV) (ml) Mean ± SD von 32.5 ± 3.6 bis 69.01 ± 8.77 PSA (ng/ml) Mean ± SD von 1.98 ± 2.17 bis 6.4 ± 5.1	Prostate volume differences patients with MetS have significantly higher total prostate volume than those without MetS WMD 10.15 ml 95 % CI 7.37–12.93 favours MetS Serum PSA level differences Patients with MetS have significantly higher serum PSA level than those without MetS WMD 0.53 ng/ml 95 % CI 0.17–0.88 favours MetS Annual prostate growth differences Patients with MetS have significantly higher prostate volume than those without MetS WMD 0.49 ml/year 95 % CI 0.24–0.73 favours MetS	This meta-analysis supports that the presence of MetS increases total prostate volume and annual prostate growth rate in Chinese BPH patients. Future studies are needed to explain the detailed underlying mechanisms.	die Daten der Metaanalyse stammen nur von chinesischen Patienten, daher ist die Generalisierung des Zusammenhangs des metabolischen Syndroms mit BPS evtl. auf Grund von kulturellen Unterschieden fraglich	LoE 2++ Robis-Bewertung: Low risk of bias no coi no information about funding



Tabelle 4: Progressionswahrscheinlichkeit

Schlüsselfrage								
Gibt es Nomogramme, welche die Progressionswahrscheinlichkeit im Vergleich zum empirischen/tatsächlichen Progressionsrisiko vorhersagen?								
Referenz	Studiencharakteristika	Patientenmerkmale	Nomogramm	Endpunkt	Effekte	Schlussfolgerung	Bemerkungen	LoE
Studien zu prognostischen Nomogrammen								
De Nunzio, 2018, Minerva Urologica e Nefrologica [11]	Prospective observational study n=232 April 2014 - March 2016 Italy 3 mo after TURP	men with lower urinary tract symptoms undergoing transurethral resection of prostate mean age/SD 68±9.6	Young Academic Urologists' benign prostatic obstruction nomogram Included variable in nomogram: Age Maximum urinary flow Residual urine Prostate volume Transitional zone volume IPSS Nomogram probability	predicting TURP outcome	Young Academic Urologists'-BPH nomogram: Younger age, higher preoperative IPSS scores, high nomogram probability were predictors of a better outcome after TURP AUC of 0.77; 95% CI: 0.70-0.83 At the best cut-off value 75% (nomogram probability): Sensitivity 62% Specificity 73% PPV 81% NPV 52%	In our experience, the Young Academic Urologists' nomogram was accurate to predict TURP outcome. Although our experience should be validated, it confirms that the YAU nomogram seems to be an easy and non-invasive tool to predict BPO, TURP success and to counsel patients before treatment.	prediction model was developed without any external or internal validation	LoE 2- Probast-RoB: High risk of bias No coi No information about funding



<p>Javle, 1998, The Journal of Urology</p> <p>[12]</p>	<p>prospective observational study</p> <p>n=53</p> <p>no information about time</p> <p>UK</p> <p>before and 3 months after surgery</p>	<p>men clinically determined suitable for transurethral prostatic resection</p> <p>Mean age was 68.5y (range 55 to 85)</p>	<p>I-PSS index, uroflowmetry, ultrasonography (prostatic size and residual urine volume measurement) and routine pressure flow study</p>	<p>success in treatment outcome after TURP</p> <p>A successful treatment outcome was defined: greater than 50% improvement in I-PSS index and/or score less than 7, greater than 50% and greater than 15 ml. per second improvement in maximum flow rate associated with a greater than 50% and less than 60 ml. decrease in residual urinary volume</p>	<p>urodynamic grading of benign prostatic obstruction: I-PSS index, maximum flow rate, residual urinary volume and detrusor contractility</p> <p>sensitivity 87% (20 of 23 pat) specificity 94% (16 of 17 pat) positive predictive value 95% (20 of 21)</p>	<p>Urodynamic grading of benign prostatic obstruction and detrusor contractility can reliably predict treatment outcome and, therefore, enable the urologist to identify a subgroup of patients who would not benefit from surgery.</p>	<p>sampling and analysis of the data might be biased</p>	<p>LoE 3</p> <p>Probast RoB high risk of bias</p> <p>no information about funding</p> <p>Supported by a grant from the Mersey Kidney Research Fund *Current address: Academic Department of Surgery, Postgraduate Medical School, Morriston Hospital, Swansea SA6 6NL, United Kingdom</p>
<p>Jeldres, 2009, Journal of Urology</p> <p>[13]</p>	<p>Prospective comparative observational study</p> <p>n=14.724</p> <p>January 1, 1989 - December 31, 2000</p>	<p>Men with BPH treated with TURP</p> <p>mean age 71 (43 to 99 y)</p>	<p>multivariable model: Age Charlson comorbidity index number of previous TURP procedures individual annual surgical volume</p>	<p>30-day mortality after TURP</p>	<p>Overall 30-day mortality occurred in n=58 patients (0.4%) undergoing transurethral resection of the prostate</p>	<p>Despite those limitations our model represents the first externally validated systematic tool to our knowledge for the quantification of 30-day mortality after TURP. Its excellent</p>		<p>LoE 2+</p> <p>Probast-Rob: low risk of bias</p> <p>Financial interest and/or other relationship with Pfizer, Bayer, Eli Lilly, Pierre Fabre, AMS and GSK.</p>



	Canada, Italy, France, Germany 30 days				<p>multivariable analyses: age (p<0.001) OR 1.11 (95% CI 1.06–1.17)</p> <p>Charlson comorbidity index (p<0.001) OR 1.36 (95% CI 1.19–1.56) age and Charlson comorbidity index based nomogram: ROC: 83%</p>	accuracy and good calibration properties warrant its use in clinical practice.		Supported by the University of Montreal Health Center Urology Associates, Fonds de la Recherche en Santé du Québec, the University of Montreal Department of Surgery and the University of Montreal Health Center (CHUM) Foundation.
Slawin, 2006, Urology [14]	<p>Post-hoc analysis of data from three 2-year multicenter, placebo-controlled, double-blind Phase III studies</p> <p>n =2167 dutasteride 0.5 mg/day</p> <p>n = 2158 placebo</p> <p>no information about date of data collection</p> <p>USA</p>	<p>men with BPH</p> <p>all men at least 50 y</p> <p>PSA level greater than 1.5 ng/mL, but less than 10 ng/mL</p> <p>enlarged prostate (30 cm³)</p>	<p>Development of a nomogram</p> <p>AUA-SI-Score</p> <p>BII</p> <p>prior use of selective alpha1-blockers, prostate volume</p> <p>PSA</p> <p>Qmax</p>	AUR and/or SI within 2 y	<p>Analysis of predictors of benign prostatic hyperplasia progression</p> <p>AUA-SI HR 1.17 (95% CI 0.95–1.45)</p> <p>BII HR 1.35 (95% CI 1.08–1.68)</p> <p>Prior alpha-blockers HR 1.58 (95% CI 1.20–2.09)</p> <p>Prostate volume (cm³)</p>	We constructed a nomogram for predicting the probability that a man would experience AUR or require SI within 2 years of benign prostatic hyperplasia diagnosis. At 24 months of follow-up, 7.4% of placebo patients and 3.7% of dutasteride patients had experienced AUR and/or SI, representing a 50% relative risk reduction and a	Outcome assessment has a potential of bias and analysis part has a potential of bias, therefore overall judgement: high risk of bias	<p>LoE 3</p> <p>Probst-RoB: High risk of bias</p> <p>No information about funding</p> <p>K. M. Slawin is a co-founder of Oncovance and is a study investigator partially funded by GlaxoSmithKline. M. W. Kattan is a co-founder of Oncovance. C. G. Roehrborn is a study investigator partially funded by, and is a paid</p>



	2 years				<p>HR 1.29 (95% CI 1.15–1.45)</p> <p>PSA (ng/mL) HR 1.35 (95% CI 1.12–1.62)</p> <p>Qmax (mL/s) HR 0.60 (95% CI 0.50–0.73)</p> <p>Dutasteride therapy HR 0.50 (95% CI 0.37–0.66)</p> <p>total number of points for all variables was used to determine the probability of AUR and/or SI within 2 years.</p> <p>nomogram was shown to discriminate well, concordance index of 0.71 (P <0.001)</p>	<p>3.7% absolute risk reduction. For the greatest risk patient randomized to the Phase III dutasteride trial, the nomogram predicted a maximal risk of 27%, significantly greater than the median risk of the placebo-treated patients</p>	<p>consultant to GlaxoSmithKline.</p>
--	---------	--	--	--	--	--	---------------------------------------



3. Evidenztabelle zum Kapitel ‚Basisdiagnostik‘

Tabelle 5: Psychometrische Eigenschaften des IPSS

Schlüsselfrage	
Wie sind die psychometrischen Eigenschaften des IPSS?	
Referenz	Ergebnisse
Badia, 1997, Eur Urol [15]	(1) production of forward translations; (2) quantification (rating) of their quality; (3) testing in target subjects; (4) back-translations into English, and (5) ratings for conceptual equivalence between the original and back-translations. A pilot run of this initial methodology was performed in one country (Spain) in order to test its feasibility and eventually refine any design issue.

Es erfolgte eine Suche nach der deutschen Version des IPSS. Von der deutschen Version gibt es keine Veröffentlichungen zur inhaltlichen Validität oder Reliabilität, daher wird hier nur die Quelle gezeigt, aus der die deutsche Übersetzung hervorging.



Tabelle 6: Minimal klinischer Unterschied des IPSS

Schlüsselfrage Wie groß ist der minimale klinisch wichtige Unterschied des IPSS? Gibt es Grenzwerte/Punktebereiche zur Stratifikation in Untergruppen?								
Referenz	Studien-design	Studien-charakterisitika	Patienten-merkmale	Diagnostischer Test	Referenz-Test	Ergebnisse	Bemerkungen	LoE
Barry, 1995, The journal of urology [16]	randomized, 4 arm blinded trial	n=1229 USA 1995	mean age 65 ys AUA symptom score 16 pts median peak urine flow rate 10,5 ml median post void residual urine volume 58 ml	AUA Symptom score Benign prostatic hyperplasia specific health status	global assessment with 5 points scoring	intra-class correlation coefficients AUA symptom index: BPH impact index: baseline 0.74 after 13 weeks 0.71 Internal consistencies AUA symptom and BPH impact index baseline 0.67 after 13 weeks 0.74 correlation between patient average baseline AUA symptom index and BPH impact index 0,54 (p <0.0001) AUA symptom index -Standard Effect Size* -0.74 BPH impact index -0.33 Guyatt's Responsiveness Statistic AUA -0.82 BPH impact Index -0.41 Subjects who rated themselves as being slightly improved had a mean decrease in AUA symptom index and BPH impact index scores of 3.1 and 0.4 points, respectively	Quadas-Bewertung: low risk of bias Bewertung der Domain V Responsiveness und VI Interpretability des Evaluating the Measurement of Patient-Reported Outcomes (EMPRO)-Tools: low risk of bias	1+



Tabelle 7: Einschränkung der Lebensqualität

Schlüsselfrage						
Wie stark ist die Lebensqualität der Patienten mit BPS eingeschränkt?						
Referenz	Studiencharakteristika	Patientenmerkmale	Fragebogen	Ergebnisse	Bemerkungen	LoE
Cizman, 2016, J Vasc & Interv Radiol [17] SR	n= 7 studies (n=6 prospective cohorts, 1 RCT) n=562 pat January 2006 – September 2013	patients with BPH	QoL score of the IPSS: (scored as de-lighted = 0, pleased = 1, mostly satisfied = 2, mixed-about equally satisfied and dissatisfied = 3, mostly dissatisfied =4, unhappy = 5, and terrible =6 ref to: Wang et al. BMC Urology (2015) 15:33	Einzelergbnisse: IPPS Quality of life score: 4.76 ± 0.98 at baseline 4.39 ±0.95 at baseline 2-6 Range	ROBIS-Bewertung: low risk of bias	LoE 2++
Coleman, 2002, Pharmacotherapy [18] SR	n=7 studies (RCT’s) n=2061 pat 1966-2002	patients with BPH	QoL score of the IPSS: (scored as de-lighted = 0, pleased = 1, mostly satisfied = 2, mixed-about equally satisfied and dissatisfied = 3, mostly dissatisfied =4, unhappy = 5, and terrible =6 (Coleman 2002)	Einzelergbnisse: IPPS Quality of life score: 3.63 at baseline 3.3 ±1.1 saw palmetto group at baseline 3.1 ±1.3 placebo group at baseline 3.0 ±0.8 placebo group at baseline 3.1 ±0.8 sitosterol group at baseline	no quality appraisal of the included studies ROBIS-Bewertung: low risk of bias	LoE 2++
Damiano, 2016, Archivio Italiano di Urologia e Andrologia [19] SR	n= 16 studies n=10 pre-clinical setting n= 6 clinical setting (RCT’s) n=4444 pat 1991-2015	patients with BPH	QoL score of the IPSS: (scored as de-lighted = 0, pleased = 1, mostly satisfied = 2, mixed-about equally satisfied and dissatisfied = 3, mostly dissatisfied =4, unhappy = 5, and terrible =6	Einzelergbnisse QoL Score des IPSS: 3.3. at baseline 4.2 at baseline 3.5 at baseline 4.2 at baseline	no quality appraisal of the included studies ROBIS-Bewertung: high risk of bias	LoE 2-



<p>Deng, 2018, World Journal of Urology</p> <p>[20]</p> <p>SR + MA</p>	<p>n=16 studies including nine randomized controlled trials (RCTs) and seven non-RCTs</p> <p>n= 855 cases of ThuVaRP, n= 583 cases of PKRP, and n= 325 cases of TURP</p> <p>2007-2015</p>	<p>patients with BPH</p> <p>mean age in included studies: from 61.4 ± 6.9 to 79.6 ± 8.4</p>	<p>QoL score of the IPSS: scored as de-lighted = 0, pleased = 1, mostly satisfied = 2, mixed-about equally satisfied and dissatisfied = 3, mostly dissatisfied =4, unhappy = 5, and terrible =6</p>	<p>Einzelergbnisse QoL Score des IPSS aus 26 Studien:</p> <p>IPSS-Score Werte aus den 26 Studien liegen zwischen 3.9 und 5.8 at baseline</p>	<p>ROBIS-Bewertung: high risk of bias</p>	<p>LoE 2-</p>
<p>Ding, 2013, Asian Journal of Andrology</p> <p>[21]</p> <p>SR + MA</p>	<p>n=4 RCT</p> <p>n= 2504 pat</p> <p>1109 in the silodosin group, 736 in the placebo group and 659 in the tamsulosin group</p> <p>1966-2011</p>	<p>patients with BPH</p> <p>mean age in included studies: from 64.7±8.1 to 67.5 ± 9.3</p>	<p>QoL score of the IPSS: (scored as de-lighted = 0, pleased = 1, mostly satisfied = 2, mixed-about equally satisfied and dissatisfied = 3, mostly dissatisfied =4, unhappy = 5, and terrible =6</p>	<p>Einzelergbnisse QoL Score des IPSS aus 4Studien:</p> <p>IPSS-Score Werte aus den 4 Studien liegen zwischen 3.7 und 4.9 at baseline</p>	<p>ROBIS-Bewertung: low risk of bias</p>	<p>LoE 2++</p>
<p>Haltbakk, 2003, BJU International</p> <p>[22]</p> <p>SR</p>	<p>n=51 publications, n=47 used the IPSS-QoL as a major result measure.</p> <p>n=4 overall QoL by the summed scores of validated or ad hoc generic indices</p> <p>1982 - 2001</p>	<p>patients with BPH</p> <p>Range of mean age: 62–74 ys</p>	<p>IPSS-QoL</p> <p>NHP, SF-36 or EuroQoL</p>	<p>IPSS-QoL-Score at baseline: Range of mean score: 3-6 in 47 studies</p> <p>NHP-Scores at baseline: Energy 20-26 Pain 8-14 Emotional role 7-16 Sleep 23-29 Social isolation 5-8 Physical mobility 9-14</p> <p>SF-36 at baseline: Physical role 63-70 Physical functioning: 68–78 General health perception: 65–72 Bodily pain: 72–80 Vitality energy: 59-67 Social functioning: 76–97</p>	<p>ROBIS-Bewertung: high risk of bias</p> <p>no pre-defined objectives and eligibility criteria, no efforts were made to minimise error in the study selection and data collection, no risk of bias assessment</p>	<p>LoE 2-</p>



				Mental health: 75–79 Emotional reaction: 66–84 BII, BPH Impact Index at baseline: 5-11		
Hwang, 2018, Cochrane Database of Systematic Reviews Cochrane Review [23] SR+MA	22 RCTs with 2223 randomised participants up to 8 October 2017	mean prostate volume: 35.4mL mean IPSS 18.3 Mean age: 67.8 ys	IPSS QoL Score scored as de-lighted = 0, pleased = 1, mostly satisfied = 2, mixed-about equally satisfied and dissatisfied = 3, mostly dissatisfied =4, unhappy = 5, and terrible =6	mean quality of life ranged from 2.7 to 3.1 (from 3 studies)	ROBIS-Bewertung: low risk of bias	LoE 2++
Jiang, 2016, Luts [24] SR + MA	n=6 studies (4 RCT, 2 clinical controlled trial) involving n=640 patients n=335 underwent TmLRP n= 305 underwent TURP 2008-2014	mean prostate volume (SD) in included studies from: 49.1 (17.4) ml to 66.5 (22) ml	IPSS QoL Score scored as de-lighted = 0, pleased = 1, mostly satisfied = 2, mixed-about equally satisfied and dissatisfied = 3, mostly dissatisfied =4, unhappy = 5, and terrible =6	QoL Mean (SD) at baseline in 4 studies: from 4.4(1.6) to 4.9(1.0)	ROBIS-Bewertung: low risk of bias	LoE 2++
Kuang, 2017, Cardiovasc Intervent Radiol [25] SR	n=10 studies (9 cohort studies, 1 RCT) n= 788 patients up to August 2015	mean age: 66.97 ys Mean PV (mL) 94.99 Mean IPSS 23.75	IPSS QoL Score scored as de-lighted = 0, pleased = 1, mostly satisfied = 2, mixed-about equally satisfied and dissatisfied = 3, mostly dissatisfied =4, unhappy = 5, and terrible =6	Mean QoL at baseline 4.63	ROBIS-Bewertung: high risk of bias no pre-defined objectives and eligibility criteria, no additional hand-search, no risk of bias assessment	LoE 2-



Lan, 2018, Lasers in Medical Science [26] SR + MA	n=5 studies (2 RCT, 3 clinical controlled trial) n=500 patients up to December 1, 2015	mean age (SD) in included studies from 69.02 ± 7.05 to 75.3 ± 8.1 prostate size: from 49.1 ± 17.4 to 115.04 ± 39.45	IPSS QoL Score scored as de-lighted = 0, pleased = 1, mostly satisfied = 2, mixed-about equally satisfied and dissatisfied = 3, mostly dissatisfied =4, unhappy = 5, and terrible =6	mean QoL (SD) at baseline in 4 studies from 4.47 ± 0.9 to 5.8 ± 0.9	ROBIS-Bewertung: high risk of bias no pre-defined objectives and eligibility criteria, no additional hand search	LoE 2-
Lin, 2016, World J Urol [27] SR + MA	n=9 studies (RCT's) n=758 patients 2002-2015		IPSS QoL Score scored as de-lighted = 0, pleased = 1, mostly satisfied = 2, mixed-about equally satisfied and dissatisfied = 3, mostly dissatisfied =4, unhappy = 5, and terrible =6	mean QoL (SD) score at baseline from 4.0 ± 1.2 to 5.2 ± 0.7	ROBIS-Bewertung: low risk of bias	LoE 2++
Malling, 2019, European Radiology [28] SR +MA	n=13 studies (2 of the included studies were RCTs) n= 1,254 patients 2014-2017	mean age in included studies: 60,4 – 77,9 ys men with BPH	IPSS QoL Score scored as de-lighted = 0, pleased = 1, mostly satisfied = 2, mixed-about equally satisfied and dissatisfied = 3, mostly dissatisfied =4, unhappy = 5, and terrible =6	mean QoL (95% CI) score at baseline 4.7 [4.5, 5.0]	ROBIS-Bewertung: low risk of bias	LoE 2++
Oeconomou, 2008, European Urology [29] literature review	n=10 included studies (1 RCT, 9 single arm studies) n=294 patients	LUTS due to BPE mean PV: from 19.6 ± 1.2 ml to 106 ml	IPSS QoL Score scored as de-lighted = 0, pleased = 1, mostly satisfied = 2, mixed-about equally satisfied and dissatisfied = 3, mostly dissatisfied =4, unhappy = 5, and terrible =6	mean QoL (SD) score at baseline from 1.6 ± 0.3 to 4.5 ± 2.7 in included studies	small-scale studies enrolling <30 patients ROBIS-Bewertung: high risk of bias study eligibility criteria not adequate described, no efforts were made to	LoE 2-



					minimise error in the study selection and data collection, no risk of bias assessment	
Pinto, 2016, Japan Journal of Nursing Science [30] literature review	n=16 included studies (RCT) (n = 3), descriptive comparative studies (n = 6), descriptive correlational studies (n = 2), simple descriptive studies (n = 2), retrospective studies (n = 2), and a prospective study (n = 1) 2002-2014	no information available	IPSSQ8 BII four-item BII, which addresses discomfort, worry, bother, and functional interference from any urinary problems. The BII scored by addition yielding a range from 0 (no impact) to 13 (great impact)	mean IPSS QoL (SD) score at baseline 4.51 ± 1.14 4.6 ± 1.0 3.9 Baseline BII scores: 5.3	ROBIS-Bewertung: high risk of bias no pre-defined objectives and eligibility criteria, no additional hand search, no efforts were made to minimise error in selection and data collection, no risk of bias assessment	LoE 2-
Pyo, 2017, Clinical Radiology [31] SR + MA	n=7 included studies RCT's n=642 included patients 2013-2016	mean age in included studies from 60.4 ±5.2 to 71. ±13.5	IPSS QoL Score scored as de-lighted = 0, pleased = 1, mostly satisfied = 2, mixed-about equally satisfied and dissatisfied = 3, mostly dissatisfied =4, unhappy = 5, and terrible =6	mean IPSS QoL (SD) score at baseline from 4.3 ±0.8 to 5.1 ±0.3 in included studies	ROBIS-Bewertung: high risk of bias no pre-defined objectives and eligibility criteria, no efforts were made to minimise error in the study selection and	LoE 2-



					risk of bias assessment	
Rieken, 2015, World J Urol [32] SR	n=17 included studies (9 RCT, 8 Serien) n=3196 patients 2009 - 2014	no information	IPSS QoL Score scored as de-lighted = 0, pleased = 1, mostly satisfied = 2, mixed-about equally satisfied and dissatisfied = 3, mostly dissatisfied =4, unhappy = 5, and terrible =6	mean IPSS QoL score at baseline 4 5	ROBIS-Bewertung: high risk of bias study eligibility criteria not adequate described, no efforts were made to minimise error in the selection, data collection and risk of bias assessment	LoE 2-
Schreuder, 2014, Cardiovasc Intervent Radiol [33] SR	n=9 articles (1 RCT, 8 cohort studies) with n=706 patients June 2008 – March 2013	BPH and moderate- to-severe LUTS mean age: from 63.4–74.1y	IPSS QoL Score scored as de-lighted = 0, pleased = 1, mostly satisfied = 2, mixed-about equally satisfied and dissatisfied = 3, mostly dissatisfied =4, unhappy = 5, and terrible =6	Pooled weighted mean QoL score at baseline: 4.34	ROBIS-Bewertung: high risk of bias no pre-defined objectives and eligibility criteria, no risk of bias assessment	LoE 2-
Teng, 2013, BJU International [34] SR + MA	n=9 studies included 5 RCT, 4 non-RCT n=1038 patients 2005 - 2012	no information	IPSS QoL Score scored as de-lighted = 0, pleased = 1, mostly satisfied = 2, mixed-about equally satisfied and dissatisfied = 3, mostly dissatisfied =4, unhappy = 5, and terrible =6	IPSS-QoL Score at baseline in included studies from 3.3 ± 1.7 to 5.08 ± 0.94	ROBIS-Bewertung: low risk of bias	LoE 2++
Uflacker, 2016, J Vasc Inter v Radiol	n=19 included in data collection	Mean Age (y)	IPSS QoL Score	IPSS-QoL Score at baseline in included studies from 4.33	ROBIS-Bewertung: low risk of bias	LoE 2++



[35] SR + MA	n=6 included in the meta-analysis case series November 2009 and December 2015	from 65.2 to 75.9	scored as de-lighted = 0, pleased = 1, mostly satisfied = 2, mixed-about equally satisfied and dissatisfied = 3, mostly dissatisfied =4, unhappy = 5, and terrible =6	to 6		
Zang, 2016, Lasers Med Sci [36] SR + MA	n=6 RCT including n=697 patients (347 treated with 120-W PVP and 350 with TURP	Mean prostate volume, mL (SD) from 43.4 (NR) to 67.3 (24.7)	IPSS QoL Score scored as de-lighted = 0, pleased = 1, mostly satisfied = 2, mixed-about equally satisfied and dissatisfied = 3, mostly dissatisfied =4, unhappy = 5, and terrible =6	Mean QoL (SD) at baseline from 3.60 (1.01) to 4.52 (0.27)	ROBIS-Bewertung: low risk of bias	LoE 2++
Zhu, 2015, World J Urol [37] SR + MA	n=7 studies included 4 RCT 3 non-RCT n=774 patients	mean age from 65.8 ± 8.4 to 74.5 ± 6.5 mean Prostate volume (mL) from 48 ± 18.3 to 66.5 ± 22	IPSS QoL Score scored as de-lighted = 0, pleased = 1, mostly satisfied = 2, mixed-about equally satisfied and dissatisfied = 3, mostly dissatisfied =4, unhappy = 5, and terrible =6	Mean QoL (SD) at baseline from 1.8 ± 0.9 to 4.9 ± 1	ROBIS-Bewertung: low risk of bias	LoE 2++



Tabelle 8: Urinanalyse

Schlüsselfrage Hilft die Urinanalyse einschließlich Dipstick bei der Differenzierung von BPS von anderen Erkrankungen?									
Referenz	Studiencharakteristika	Patientenmerkmale	Indextest	Referenztest	Endpunkt	Effekte	Schlussfolgerung	Bemerkungen	LoE
Chen, 1998, Chinese Medical Journal [38]	retrospective medical chart analysis n=2566 June 1993 – July 1994 Taiwan	n=1322 with BPH n=81 with complicated UTI	urine culture	no reference test	complicated UTI	urine culture positive rate 67,4% (n=60/81)	We concluded that the prognosis of complicated UTI is good if diagnosis and appropriate treatment are given promptly. Early drainage to relieve obstruction and intravenous antibiotics are initially necessary. Surgical intervention is required to resolve functional or structural abnormalities after the UTI has been controlled.		LoE 3 RoB Bewertung: high RoB no inclusion and exclusion criteria defined, intervention not clearly described, no statistical analysis no information about coi and funding
Demiray, 2016, Turkish Journal of Geriatrics [39]	retrospective evaluation of urine cultures Jan 2015 – Dec 2015 Turkey	n=506 outpatients with BPH mean age: 73.5 y	urine culture	no reference test	UTI	positive UTI: total: 16.6% (n=84) age group 65-74 y: n=42 (13.4%) age group 75-84 y:	Gram-negative bacteria, predominantly Escherichia coli, are the major causes of urinary tract infections in elderly men with benign prostatic hyperplasia. High resistance to frequently used drugs such as first generation cephalosporins and quinolones is an		LoE 3 RoB- Bewertung: high RoB no consecutive patient inclusion, no statistical



						n=34 (20.5%) age group >85 y: n=8 (30.8%) p=0.008	alerting situation. Also, contamination rates increase with advancing age; thus, urine sampling from these patients should be revised. Antimicrobial treatment should depend on local antimicrobial susceptibility testing results.		analysis, inclusion and exclusion criteria and patient characteristics only partially described no conflict of interest no financial support
Khasriya, 2010, Journal of urology [40]	prospective, blinded, observational trial n=508 midstream urine samples n=470 catheter urine samples UK	n=508 pat (432 women and 76 men) presenting with LUTS Mean (SD) daily frequency: 11.73 (5.4), daily incontinence episodes 1.2 (1.7) and mean urgency score: 3.79 (3), reflecting the widespread overactive bladder symptoms.	Leukocyte Esterase and Nitrite Tests Multistix® 8 SG	Routine culture method (gold standard) Enhanced culture method (enhanced reference standard)	Urinary Tract Infection	sensitivity for the gold standard: 56% for leukocyte esterase (95% CI 46-66), 10% for nitrite (95% CI 6-18) 56% for microscopic pyuria (95% CI 46-66) specificities of 66% (95% CI 61-70), 99% (95% CI 98-100) 72% (95% CI 67-76) sensitivity of leukocyte esterase for	This study was conducted in a normal clinical practice, giving it wide applicability through urological services where the limitations of these tests must be acknowledged. These tests should no longer be recommended for screening. Our understanding of the etiology of important conditions such as OAB may be seriously at fault.		LoE 2+ Quadas-Bewertung: low RoB Supported by Research into Ageing. no information about coi



		In fact 378 (74%) patients had OAB. Of these patients 132 (35%) had pyuria on microscopy, 90 (24%) with sterile pyuria and 79 (21%) had positive MSU cultures. Only 209 (55%) patients with OAB symptoms had normal urine.				microscopic pyuria: 81% (95% CI 75–87) specificity 83% (95% CI 78–87). Conclusion: Despite official guidelines and widespread use these tests cannot be considered appropriate for diagnosing urinary tract infection in patients with lower urinary tract symptoms, and should be abandoned in this context.		
Kupelian, 2013, BJU International [41]	observational study n=5081 MSU samples MSU 2008 – 2011 n=4375 samples were included in the final analysis	1223 patients (120 men and 1103 women; mean age 54 years; 95% CI 53–55) and 36 asymptomatic control subjects (eight men and 28	dipstick positive dipstick was defined as ≥‘trace’ leucocyte esterase	microscopy reference standard ≥10 wbc/mL	UTI urinary tract infection surrogate parameter: pyuria	diagnostic performance statistics for dipstick ≥ ‘trace’ leucocyte esterase in the detection of microscopic pyuria ≥10 wbc/μL: Dipstick ≥‘trace’ Sensitivity (95% CI)	Pyuria performs badly as a surrogate of UTI in patients with LUTS. This is exacerbated by cell loss during storage, and neither centrifugation, nor staining, appears to confer any diagnostic advantage. Clinicians should be alerted to the significant limitations of these tests.	LoE 2+ Quadas-Bewertung: Low RoB funded by project grants from the International Urogynecology Association, and Research into Ageing



		women; mean age 41 years; 95% CI 36–46)				0.38 (0.35– 0.40) Specificity (95% CI) 0.84 (0.83– 0.85) PPV (95% CI) 0.51 (0.48– 0.55) NPV (95% CI) 0.75 (0.73– 0.76)			no coi
Mohanty, 1996, Indian journal of pathology and microbiology [42]	comparative observational study pre and post operatively within at least 48 h of antibiotic cover n=100 with BPH	no description of patient characteristics	urine culture bacterial growth on culture of prostatic tissue	no reference test	urinary tract infection UTI	n=100 pat with BPH n=48 pre op UTI n=52 pre op no UTI n=42 pre op bact growth in prostatic tissue Davon: n=16 pre op UTI n=26 sterile urine culture n=58 pre op no bact growth in prost tissue Davon: n=32 positive urine culture n=26 sterile urine culture	Our data suggests that significant incidence (42%) of bacterial growth in prostatic tissue-occurs in patients with B.H.P. Pre- existing U.T.I. is not a reliable indicator by which this group could be identified pre-operatively and prostatic infection could be treated.	Die Ergebnisse des Vergleichs der Urinkulturen vor und nach der OP können verzerrt sein, da 36 der 48 Patienten mit UTI schon vor der OP einen Katheter hatten wesentliche Angaben zu Unterschieden wie p-Wert fehlen, Angaben zu Prozentwerten in Tabellen fehlerhaft	LoE 3 RoB- Bewertung: high risk of bias no consecutive patient inclusion, inclusion and exclusion criteria and patient characteristics not described, interventions partially described, no statistical analysis no information about funding and coi



Tabelle 9: Stellenwert des PSA

Schlüsselfrage									
Was ist der Stellenwert des Prostata-spezifischen Antigens (PSA)-Tests in der BPS-Diagnostik?									
Referenz	Studiencharakteristika	Patientenmerkmale	Index-test	Referenz-test	Endpunkt	Effekte	Schlussfolgerung	Bemerkungen	LoE
Antunes, 2006, Clinics [43]	Retrospective observational study n=218 no information about date of data collection Brazil	Mean age: 67.9 y (49 to 90) PSA < 4.0 72 (33.0%) 4.0 to 10.0 91 (41.7%) >10.0 55 (25.2%)	PSA	DRE	incidental carcinoma	For PSA-Test: PSA greater than 4.0 ng/mL Sensitivity 85.0%, Specificity 34.1% PPV 7.5% NPV 97.2%	Advanced age and the presence of a suspect digital rectal examination represent the most important risk factors for the diagnosis of an incidental carcinoma of the prostate. However, the low positive predictive values reflect the weak correlations among these variables.	Patient selection unclear No blinding of the investigator	LoE 2- Quadas RoB at risk No information about COI and funding
Carballido, 2011, International Journal of Clinical Practice [44]	prospective, epidemiological, multicentre observational study n= 768 no information about date of data collection Italy, France, UK, Spain	Consecutive male patients aged ≥ 50 years who spontaneously attended their regular GP office with LUTS n=666 per protocol population	GP visit 1: primary care clinic Medical history and disease symptoms assessment Possible diagnosis by GP (probability 0–100% and yes/no	Visit 3: specialist clinic, urologist Urologist reviews medical history and symptoms Physical examination (including DRE)	BPH	BPH diagnosis: visit 1 Sensitivity 84.1% 95% CI 80.3–87.4% Specificity 29.2% 95% CI 23.4–35.6% PPV 69.8% 95% CI 65.7–73.7% NPV 48.5% 95% CI 39.9–57.3%	A diagnostic algorithm including only objective variables (age, IPSS and PSA), easily implemented in any GP office, allows GPs to accurately diagnose BPH in approximately three-quarters of patients spontaneously reporting LUTS	Zum PSA-Test gibt es keine separate Schlussfolgerung! Alle Bewertungen im Quadas-Tool haben low RoB, bis auf die Tatsache, dass beim 3. Besuch (beim	LoE 2- Quadas-RoB: At risk of bias funded by GlaxoSmit hKline GSK COI: All authors without



		mean age (SD): 60.9 ± 7.9 (50–98)	IPSS and Bother Score questionnaires PSA analysis and urinalysis is requested Second visit to GP is scheduled GP visit 2: primary care clinic DRE is performed Possible diagnosis by GP (probability 0–100% and yes/no)	Review previous tests (IPSS/bother score/PSA/urinalysis) diagnostic tests (abdominal ultrasound/uroflowmetry) Urologist provides ‘gold-standard’ diagnosis		Visit 2: Sensitivity 80.0% 95% CI 75.9–83.6% Specificity 42.0% 95% CI 35.5–48.8% PPV 72.9% 95% CI 68.7–76.8% NPV 51.9% 95% CI 44.4–59.3% PSA-test by GP Sensitivity 55.2% Specificity 59.3% PPV 72.5% NPV 40.5% Age + IPSS + PSA as model: PPV 75.7% NPV 44.1% Sensitivity 58.9% Specificity 63.3%		Urologen als Gold-Standard) die Testergebnisse der vorherigen GP-Besuche 1 und 2 dem Urologen bekannt sind laut Studie Quadas fordert aber, dass der Untersucher des Gold-Standards keine Kenntnis über die Ergebnisse der ersten Tests haben soll, daher hier die Bewertung als high risk, somit ist die Gesamtbewertung: at risk of bias	first author consultant for GSK and / or AstraZeneca and Pierre Fabre Medicament. Almirall. Ramiro Castro and Martyn Gilson are employees of GSK.
Ho, 2014, Clinica Therapeutica [45]	Observational study n=79 March and October 2008 Malaysia	n=30 AUR n=32 LUTS men with bladder outlet obstruction with an underlying BPH enrolled mean age	PSA	Age IPSS PV BWT UEWB IPSS PV BWT UEBW	AUR	PSA cut-off <1.5/≥1.5 ng/ml PSA-test for AUR PPV (%) 58.1 NPV (%) 73.7 Sensitivity (%) 83.3 Specificity (%) 43.8	Combined with IPSS, ultrasound determined bladder characteristic, particularly UEBW, is a useful tool in predicting AUR in men with BPH By calculation, both high PV and	Autoren bezeichnen das Design der Studie als prospective und cross-sectional Widerspruch!	LoE 2+ Quadas RoB: low No information about COI and funding



		68 y mean PSA (ng/ml) (SD) 3.04 (5.67)				LR+: 1.48 LR -: 0.38	PSA (cut-off 1.5ng/ml) had the highest sensitivity (83.3%)	Cross sectional design	
Luo, 2017, Int urol and nephrol [46]	Retrospective observational study n=704 January 2013 – June 2016 China	BPH/LUTS patients n=112 DU group n= 592 control group mean (SD) age 69.72 (7.91 y)	totalPSA	physical examination, IPSS assessment, abdominal ultrasound measurement of PV, PVR, urodynamic examination	bladder detrusor underactivity	To predict bladder detrusor underactivity: totalPSA OR 1.036 95% CI 0.953 - 1.126 P=0.408 To predict the Pdet.max value: PSA (0-4ng/ml) AUC=0.727 Cut-off-value: 1.763ng/ml Sensitivity: 65.22% Specificity: 77.50%	Clinical factors were effective for predicting DU and could help improve the diagnostic accuracy for BPH/LUTS patients who cannot undergo urodynamic examinations.	Patient selection unclear, Blinding of investigators unclear	LoE 2- Quadas-RoB: At risk of bias No COI supported by Science and Technology Fund of Tianjin Provincial Commission of Health and Family Planning, Grant Number: 2015KR02
Yu, 1996, Journal of the Formosan Medical Association [47]	retrospective observational study n= 593 April 1993 – December 1995 Taiwan	Men who underwent prostatic surgery n=562 n=93 with PCa n=469 with BPH mean age:	PSA to detect PCa and to detect BPH		PCa	To detect PCa: PSA cut-off 4.0 ng/ml AUC 0.89 Sensitivity 94% Specificity 45% PPV 25% PSA cut-off 10.0 ng/ml	Our data confirmed the sensitivity of PSA in the detection of PCa in a country with low incidence of PCa. However, a considerable proportion of patients with BPH had elevated serum PSA levels caused by factors unrelated to		LoE 2- Quadas-RoB: low No information about



		69 y Range 48-96y				Sensitivity 85% Specificity 76% PPV 42%	malignancy. Raising the cut-off value of PSA or employing adjunct parameters derived from PSA determination may be helpful in improving the diagnostic efficacy of PSA.		COI and funding
Malati, 2006, Indian Journal of Clinical Biochemistry [48]	Observational study n=2325 no information about date of data collection India	n=583 healthy males, n=1090 patients of benign prostate hypertrophy (BPH), n= 651 patients of adenocarcinoma prostate mean age: healthy male group: 59 y range 19 y-86 y BPH group: Mean 63 y range 40-90y adenocarcinoma prostate group: 65 y	serum PSA quantitation Care was taken to collect serum samples for PSA determination before any kind of prostate manipulation	physical examination, digital rectal examination, TRUS, true cut prostate biopsy	BPH or PCa	serum PSA by selecting 2 ng/ml as cut off value for: Indian healthy males: specificity 77.2% BPH group sensitivity 52% serum PSA by selecting 4 ng/ml cut off value for: BPH group: Sensitivity: 31% serum PSA by selecting 2 ng/ml cut off value for AND 4 ng/ml cut off value for: Pretherapy adenocarcinoma prostate group: 100% sensitivity	This study clearly indicated rise of serum PSA with increasing burden of malignancy as almost all untreated patients and those with recurrence had very high PSA concentration.	Keine spezielle Schlussfolgerung für PSA bei BPS-Patienten Patient selection unclear, Blinding of investigators unclear	LoE 2- Quadas-RoB At risk of bias No information about COI and funding



Tabelle 10: Restharnmessung

Schlüsselfrage									
Bietet die Restharnmessung einen Vorteil bezüglich der Diagnostik einer BOO/BPO gegenüber der Druckflussmessung? Gibt es eine Grenzwertempfehlung für die Restharmenge?									
Referenz	Studiencharakteristika	Patientenmerkmale	Index-test	Referenz-test	Endpunkt	Effekte	Schlussfolgerung	Bemerkungen	LoE
ElSaied, 2013, African Journal of Urology [49]	observational study n= 50 March 2008 - December 2008 Egypt	men with LUTS Mean age 61.7y (53-76y)	uroflowmetry PVR PVR volume of >50 ml considered abnormal	PFS	BOO	PVR PPV 53.1% NPV 66.7% sensitivity 73.9% Specificity 44.4% Accuracy 58.0% LR+ 1.33 LR- 0.59	Detrusor wall thickness measurement can be used alone or in combination with other tests to diagnose and quantify bladder outlet obstruction non-invasively, with an accuracy approaching that of the standard pressure flow studies.	prospective recruitment of study participants, but cross sectional data analysis	LoE 2+ Quadas RoB Low no coi no information about funding
Kang, 2016, Urology [50]	retrospective observational study n=2494 October 2004 August 2013 Korea	LUTS/BPH patients who underwent urodynamic study n=2039 mean age (SD) 66.75 ± 7.46 y	measurement of PVR using ultrasound bladder scans	PFS	BOO	PVR Unadjusted OR 1.00 (95% CI) 1.00-1.01	Despite less common incidence of BOO in men with small prostates, they showed more severe symptoms and voiding indices with similar urodynamic outcomes for bladder abnormalities as compared to those with larger glands with BOO. Our study presents thought-provoking evidences	Patient enrolment is not reported if consecutive or random selected Blinding of investigators of both tests unclear no information provided of time interval	LoE 2- Quadas Rob: at risk of bias no coi no information about funding



							that LUTS/BPH patients with small prostates and refractory symptoms should be checked for bladder functions with urodynamic study. Finally, higher PSA and lower flow rates are predictive of outlet obstruction in men with small prostate glands.	between index test and reference test	
Ku, 2009, International Journal of Urology [51]	retrospective observational study n=212 no information about date of data collection Korea	Men that had LUTS median age 68, range 44–89 y	PVR: measured after uroflowmetry via a bladder scan RF= (PVR)/(voided volume +PVR) x 100 PVR	PFS	BOO	PVR (mL) >50ml OR (95% CI) 2.29 (1.54–5.52) Adjusted OR (95% CI) 0.51 (0.14–1.84) AUC for residual fraction (RF) 0.74 (0.67–0.81) (P<0.001) RF (%) Cutoff 10 PPV: 34.0% NPV: 91.5% Sensitivity: 91.2% Specificity: 34.8%	The presence or absence of BOO might be predicted using non-invasive methods. The residual fraction may help with patient management by better predicting the likely patient classification from pressure-flow studies.	Patient enrolment is not reported if consecutive or random selected Blinding of investigators of both tests unclear no information provided of time interval between index test and reference test	LoE 2- Quadas RoB: at risk of bias no information about coi and funding



						RF (%) Cutoff 20 PPV: 46.2% NPV: 88.2% Sensitivity: 75.4% Specificity: 67.7% RF (%) Cutoff 30 PPV: 42.9% NPV: 77.9% Sensitivity: 36.8% Specificity: 81.9%			
Lee, 2016, Investigative And Clinical Urology [52]	retrospective observational study n=517 2008 - 2014 Korea	final study sample included n=240 men: DU (n=111) BOO (n=129) mean age (±standard deviation): 65.3±9.2y	uroflowmetry PVR	UDS	DU BOO	to differentiate between DU and BOO PVR OR 0.99 (95% CI 0.98–0.99) AUC: PVR 0.796	We suggest DeltaQ as a novel post uroflowmetry calculated value to discriminate DU from BOO in men with obstructive lower urinary tract symptom. DeltaQ can be a reliable and useful tool to screen for differential diagnosis between DU and BOO before UDS.	Patient enrolment is not reported if consecutive or random selected Blinding of investigators of both tests unclear no information provided of time interval between index test and reference test	LoE 2- Quadas-RoB at risk of bias no coi no information about funding
Luo, 2017, Int Urol Nephrol [46]	retrospective observational study	men with BPH/LUTS	abdominal ultrasound measurement of PVR	urodynamic examination	bladder detrusor	bladder detrusor underactivity prediction	Clinical factors were effective for predicting DU and could help improve the diagnostic	Patient enrolment is not reported if consecutive or	LoE 2- Quadas RoB at risk of bias



	n=704 January 2013 – June 2016 China	n=112 detrusor underactivity group n=592 cases control group mean ± SD age: 69.72 ± 7.91 y			underactivity	PVR OR 1.004 (95% CI 1.001 - 1.007) AUC for PVR 0.716 threshold 147 mL: sensitivity 60.16% specificity 72.97%	accuracy for BPH/LUTS patients who cannot undergo urodynamic examinations.	random selected Blinding of investigators of both tests unclear no information provided of time interval between index test and reference test	no coi supported by Science and Technology Fund of Tianjin Provincial Commission of Health and Family Planning, Grant Number: 2015KR02
Oelke, 2007, European Urology [53]	prospective observational study n=160 1 January 2000 - 31 December 2001 Germany	men older than 40 yr with lower urinary tract symptoms and/or prostatic enlargement median age: 62 y range (40–89y)	7.5-MHz linear ultrasound array PVR	PFS	BOO	Postvoid residual urine <50/>50 ml PPV 52% (43–62) NPV 63% (51–76) Sensitivity 72% (62–82) Specificity 42% (32–53) Accuracy 56% LR + 1.25 (0.99–1.57) LR- 0.66 (0.43–1.33)	This study showed that sonographic measurements of DWT are an accurate alternative for pressure–flow measurements to assess the presence of BOO. DWT measurements show a higher diagnostic power than measurements of Qmax, Qave, postvoid residual urine, or prostate volume.		LoE 2+ Quadas-RoB: low no coi no information about funding
Shin, 2013, Korean Journal of Urology [54]	retrospective observational study n=239 May 2007 - December 2010	men with LUTS/BPH who underwent TURP mean age (SD):	urodynamic studies (PVR) post void residual urine	PFS	BOO	AUC PVR: 0.696 PVR OR 1.024 (95% CI 1.010. - 1.028)	In our study, an IPP exceeding 5.5 mm was significantly associated with BOO. The present findings define a specific degree of IPP associated with BOO. This knowledge should	Blinding of investigators of both tests unclear no information provided of time interval	LoE 2- Quadas Rob: at risk of bias no coi + no information about funding



	Korea	69.9±8.0 y	PVR (mL) <50 / >50				usefully guide the treatment of BOO in BPH/LUTS patients.	between index test and reference test	
--	-------	------------	--------------------	--	--	--	---	---------------------------------------	--



Tabelle 11: Harnblasenwanddickenmessung

Schlüsselfrage Bietet die Harnblasenwanddickenmessung einen Vorteil bezüglich der Diagnostik einer BOO/BPO gegenüber der Druckflussmessung? Gibt es eine Grenzwertempfehlung zur Harnblasenwanddicke?									
Referenz	Studien- charakteristika	Patienten- merkmale	Index- test	Referenz- test	Endpunkt	Effekte	Schlussfolgerungen	Bemerkungen	LoE
Systematische Übersichtsarbeiten									
Malde, 2017, European Urology [55]	n=42 eligible reports NRE recruiting a total of 4444 patients	adult men with LUTS	PCT UF DWT IPP NIRS	PFS	PCT/ Bladder Outlet Obstruction UF/ Bladder Outlet Obstruction DWT/ Bladder Outlet Obstruction IPP/ Bladder Outlet Obstruction NIRS/ Bladder Outlet Obstruction	detrusor wall thickness DWT 2mm Sensitivity Median (IQR): 82.7 (65.7–83) Range: 63.6–92 Specificity Median (IQR): 92.6 (76–95) Range: 68–97.3 Positive predictive value Median (IQR) 90.5 (81–94) Range: 65.7–95.5 Negative predictive value Median (IQR) 85 (76–86) Range: 75–86.2	Altered DWT and BWT may have a multifactorial basis, and further assessments in well-designed statistically powered trials are needed to assess wider application in clinical service delivery. According to the literature, a number of noninvasive tests have high sensitivity and specificity in diagnosing BOO in men. However, although the majority of studies have a low overall risk of bias, the available evidence is limited by heterogeneity. While several tests have shown promising		LoE 2+ ROBIS- Bewertung: low risk of bias no funding diverse coi of all authors



							results regarding noninvasive assessment of BOO, invasive urodynamics remain the gold standard.		
Primärstudien									
Aganovic, 2012, Med Arh. [56]	Prospective observational study n=111 2009-2010 Sarajevo, Bosnia and Herzegovina	Patients with LUTS and confirmed benign prostatic enlargement (BPE) mean age: 65.4 y (48-82y)	TAUS	PFS	BWT (bladder wall thickness) determined at the full bladder capacity to detect BOO	cut-off value of BWT: 5 mm Diagnostic acc. for BWT: AUC 0.61 Sensitivity 64.5% Specificity 59.2%	This study has demonstrated the use of assessing the intravesical prostatic protrusion in predicting infravesical obstruction in patients with BPE. It shows a good correlation of IPP with clinical and urodynamic variables, as well as high Specificity and positive predictive value in terms of obstruction by the IPP grade increase, while the determination of the bladder wall thickness shows this parameter to be only a modest indicator of bladder outlet obstruction.		LoE 2- Quadas-Bewertung: at risk of bias no coi no information about funding
EISaied, 2013, African Journal of Urology [49]	prospective diagnostic study n= 50 March 2008 and December 2008	men with LUTS Mean age 61.7 y (53-76 y)	TAUS	PFS	DWT to assess BOO	DWT to detect BOO PPV: 90.5% NPV: 86.2% Sensitivity: 82.7% Specificity: 92.6% Accuracy: 88%	Detrusor wall thickness is a theoretically rational and clinically practical tool to evaluate patients with lower urinary tract symptoms suspected of		LoE 2+ Quadas RoB Low no coi



	Egypt					LR+: 11.2 LR-: 0.19	having bladder outlet obstruction. Detrusor wall thickness measurement can be used alone or in combination with other tests to diagnose and quantify bladder outlet obstruction non-invasively, with an accuracy approaching that of the standard pressure flow studies.		no information about funding
Farag, 2017, Arab Journal of Urology [57]	Prospective diagnostic study n= 72 no information about time Netherlands, Egypt	adult men with LUTS Mean age (BOO): 62.3 y (SD 6.6 y) Mean age (no BOO): 65.1 (SD 12.3 y)	TAUS	PFS	BWT To detect BOO	BWT+ maximum urinary flow rate Correct classification: 61/72 patients (85%) Sensitivity: 92% Specificity: 65% PPV: 87% NPV: 76% Positive diagnostic likelihood ratio: 2.6	It was possible to combine BWT with the maximum urinary flow rate to create a new algorithm that could be used as a screening tool for BOO in men with lower urinary tract symptoms.		LoE 2- Quadas RoB At risk of bias no coi no funding
Franco, 2010, Journal of Urology [58]	prospective diagnostic study n= 100 Jan 2001-Jan 2002 Italy	men with LUTS due BPH Median age 66 y	Suprapubic ultrasound	Urodynamics PFS Qmax, detrusor pressure, Minimal urethral opening pressure	detrusor wall thickness to diagnose BOO bladder outlet obstruction	DWT PPV: 90% NPV: 50% Sensitivity: 73% Specificity: 82% Accuracy: 84% LR+: 4.05 LR-: 0.37 <u>Associated (IPP +/-or DWT)</u> PPV: 86.8% NPV: 66% Sensitivity: 90% Specificity: 63.1%	Suprapubic ultrasound of detrusor wall thickness and intravesical prostatic protrusion is a simple, noninvasive, accurate system to assess bladder prostatic obstruction in patients with lower urinary tract symptoms due to benign prostatic hyperplasia.	The study population was small and more than 70% of patients had bladder prostatic obstruction, which may partly explain our high positive predictive value.	LoE 2+ Quadas RoB Low no information about funding and coi



						Accuracy: 87% LR+: 2.4 LR-: 0.15			
Güzel, 2015, Urology [59]	Retrospective diagnostic study n= 236 no information about time Turkey	male patients who had LUTS-related benign prostatic enlargement with serum prostate-specific antigen level ≤4 ng/mL Mean age 62.5 y (39-77 y)	suprapubic ultrasonography	uroflowmetry and PVR presence of IPSS >19, maximum urine flow rate <15 mL/min, and postvoid resi >100 cm ³ were accepted as negative indicators of BOO	BWT Bladder wall thickness To detect BOO Bladder outlet obstruction	best cut-off value of BWT: 3.25 mm Sensitivity: 78.9% Specificity: 68.1% PPV: 57.6% NPV: 85.5% Accuracy: 71.9% mean BWT : 3.8 (1.4-8.7) mm In patients without BOO: BWT 2.9 mm; in the presence of 1, 2, or all 3 BOO indicators: BWT: 3.5, 4.1, 4.5 mm, respectively	BWT measurement gains value as a method with high diagnostic value and easy applicability.	Vergleich /Reference Test nicht wie in der PICO formuliert, daher indirekte Evidenz	LoE 2+ Quadas RoB low no information about funding and coi
Manieri, 1998, Journal of Urology [60]	Retrospective diagnostic study n= 174 no information about time Italy	men with LUTS Mean age 64.5 y (34-88 y)	suprapubic ultrasonography	Free uroflowmetry and pressure-flow studies	BWT To diagnose BOO	best cut-off value of BWT: 5 mm AUC: BWT 0.860 Versus 0.688 for peak flow rate 63.3% of patients with bladder wall thickness less than 5 mm were unobstructed	Measurement of bladder wall thickness appears to be a useful predictor of outlet obstruction with a diagnostic value exceeding free uroflowmetry although it does not represent a substitution to invasive urodynamics. These data support the hypothesis that the relationship between morphology and		LoE 2+ Quadas RoB low no information about funding and coi



						87.5% of those with a bladder wall thickness 5 mm or greater were obstructed	function are of clinical importance.		
						correlation ($r > 0.6$, $p \leq 0.007$) between bladder wall thickness and all parameters of the pressure-flow study			
Oelke, 2002, World J Urol [61]	Prospective diagnostic study n= 70 Feb 1999- Sep 1999 Germany	male patients with LUTS and (or prostate enlargement) Mean age 63 y (42-82 y)	suprapubic ultrasound	PFS Uroflowmetry, residual volume, prostate volume	DTW To detect BOO bladder outlet obstruction	<u>DTW (greater than or equal to 2mm)</u> Sensitivity: 63.6% Specificity: 97.3% PPV: 95.5% NPV: 75%	Measuring the thickness of the detrusor wall can be used as a screening test to detect BOO.		LoE 2- Quadas RoB: At risk of bias no information about funding and coi
Oelke, 2007, European Urology [53]	observational diagnostic study n=160 1 January 2000 -31 December 2001 Germany	men older than 40 yr with lower urinary tract symptoms and/or prostatic enlargement median age: 62 y range (40-89y)	7.5-MHz linear ultrasound array	PFS	BOO	DWT $<2/\geq 2$ mm PPV 94% (88-100) NPV 86% (79-93) Sensitivity 83% (74-91) Specificity 95% (91-100) Accuracy 89% LR+ 17.57% (6.71-45.98) LR- 0.18% (0.11-20.02)	This study showed that sonographic measurements of DWT are an accurate alternative for pressure-flow measurements to assess the presence of BOO. DWT measurements show a higher diagnostic power than measurements of Qmax, Qave, postvoid residual urine, or prostate volume.		LoE 2+ Quadas-RoB: low no coi no information about funding



Tabelle 12: Sonographie

Schlüsselfrage									
Bietet die transrektale Sonographie (TRUS) Vorteile gegenüber der abdominalen/suprapubischen Sonographie zur Bestimmung des Prostata-Volumens?									
Referenz	Studiencharakteristika	Patientenmerkmale	Index-test	Referenz-test	Endpunkt	Effekte	Schlussfolgerungen	Bemerkungen	LoE
Ajay I, 2013, Pan African Medical Journal [62]	prospective comparative study n=46 Nigeria	mean age: 69.0 ys IPSS ranged between 14 and 27	TAUS TRUS	prostate weight after surgery	volume of the TSV	Pearsons correlation of ultrasound (both TAUS and TRUS): total gland volume and TZV (r=0.958, p<0.001) Correlation of the enucleated prostate adenoma weight with the ultrasound estimated volumes revealed moderate significant positive correlation. (r=0.594, p<0.001)	The TZV estimation in patient with BPH is reliable and comparable on both TAUS and TRUS. Although, TRUS is more sensitive (higher correlation with enucleated adenoma) with better clarity, TAUS can be adequately utilized in poor resource regions.	Ergebnisse zum Vorteil einer US-Methode sind nicht berichtet	LoE 2- Quadas-Bewertung: RoB at risk of bias no coi +no information about funding indirekte Evidenz (nicht ganz passend zur PICO)
Chakraborty, 1990, Indian Journal of Radiology and Imaging [63]	observational study n=32 TRUS n=23 TAUS India	patients with benign prostatic enlargement no further patient characteristics	TRUS	TAUS	volume determination of the prostate	TAUS: enlargement Grade III in 9% enlargement in Grade I in 22% TRUS: enlargement in Grade III 25% enlargement in Grade I 16%	The transrectal approach gives a clear and complete view of the prostate and has proved to be simple, easily applicable and a reliable method for volume determination.		LoE 2- Quadas-Bewertung: RoB at risk of bias no information about coi and funding



						„average accuracy for weight determination by the transrectal method was 91% while that of the transabdominal method was 72% when compared to surgically determined weights!		
Feng, 2017, Urological Science [64]	observational study n=90 Taiwan	n=90 pat with LUTS mean age: 70 ys (range, 46-90 ys)	TRUS	SPUS	prostate Volume (mL)	Pearson Correlation: mean standard ± deviation (ml) SPUS 65.8 ± 46.5 TRUS 65.4 ± 43.9 r=0.944 (p < 0.001)	There was a strong correlation of prostate sizes measured by SPUS and TRUS. We believe that SPUS can be a reliable alternative for TRUS, especially in the patients with anal diseases. It can shorten the examination time and make the patient more comfortable	LoE 2+ Quadas-Bewertung: RoB low no funding no coi
Huang Foen Chung, 2004, European Urology [65]	observational pairwise comparative study (case control) n=100 The Netherlands	no information about patient characteristic	TAUS	TRUS	prostate volume	Prostate volume (cm3) TRUS (Bruel and Kæjr) Range: 12.6–194.2 Mean: 57.3 Median: 48.4 SD: 32.5 TAUS (SSD-1700) Range:23.1–200.1 Mean: 58.6 Median: 51.0 SD: 31.0	No statistically significant differences were found between the transabdominal-transrectal ultrasonography, two different transabdominal devices nor between different observers. However, for those using these measurements in everyday clinical practice, it is worth to point out that in our data a transabdominal scan and a transrectal scan in the same patient, on the	LoE 2+ Quadas-Bewertung: RoB low no information about coi Dutch Kidney Foundation Foundations “Vereniging Trust fonds Erasmus MC”,



						Pearson’s correlation coefficient, $r = 0.84$ $p < 0.001$	same day, differed more than 30% in one fourth of the patients and that two transabdominal scans in the same patient (with two different devices, on two different days) differed more than 30% in every fifth patient.		“Stichting Bevordering van Volkskracht”, “Stichting Aelwijn Florisz”, all in the Netherlands
Malemo, 2011, Int Urol and Nephrol [66]	observational study n=50 Uganda Nov 2009 – April 2010	n=50 pat with symptomatic BPH median age 70 ys (range 51–91 ys) BMI 23.3 kg/m ² (range 19.4–36.5)	SPUS	TRUS	prostate volume	Correlation between preoperative prostate volume measurement by (SPUS and TRUS): Spearman’s rank correlation coefficient $q = 0.98$, $P < 0.001$ sensitivity of SPUS to detect prostate volumes amenable to TRUS 21/22 = 95% [95% CI 78–99%]. SPUS specificity: 27/28 = 96% [95% CI 82–99%] PPV 95% [95% CI 78–99%] NPV 96% [95% CI 82–99%]	SPUS is accurate relative to TRUS in assessing preoperative volume of the prostate and can be used in the African context to assign patients to open prostatectomy or TURP.		LoE 2- Quadas-Bewertung: RoB at risk of bias no information about funding no coi
Prassopoulos, 1996, Abdominal Imaging [67]	observational study Greece n=95	n=95 consecutive patients, 47–85 ys (mean 69.7, SD 11.3)	SPUS	TRUS	total prostate gland volume TZP volume	Pearson correlation coefficient: mean volume of the prostate: $r = 0.948$, $p < 0.001$ TZP	According to the results of this study, SU appears to be as reliable as TU in assessing the size of the prostate and the TZP and may be used effectively in the evaluation of		LoE 2+ Quadas-Bewertung: RoB low



						r=0.953, p < 0.001	patients with BPH, as it is less cumbersome, better tolerated, and a widely available examination technique.		no information about coi or funding
--	--	--	--	--	--	--------------------	--	--	-------------------------------------



4. Evidenztabelle zum Kapitel ‚Weiterführende Diagnostik‘

Tabelle 13: Genauigkeit des Kreatinin-Wertes

Schlüsselfrage							
Wie ist die diagnostische Genauigkeit des Kreatinin-Wertes zur Beurteilung der globalen Nierenfunktion sowie zum Nachweis/Ausschluss einer Nierenfunktionsstörung?							
Referenz	Studien-design	Studien-charakterisitika	Patienten-merkmale	Messmethode	Ergebnisse/Schlussfolgerung	Bemerkungen	LoE
Lopez-Vargas, 2013, Nephrology [68]	SR of guidelines on chronic kidney disease I-III	One consensus statement 15 guidelines Australasia, Japan, France, Netherlands, Italy, UK, Canada, USA, Chile, Argentina, Spain 2002 - 2011	not available	GFR serum creatinine dipstick urinalysis morning urine 24h urine	Estimated glomerular filtration rate was the main diagnostic test recommended by all guidelines, while some also recommended serum creatinine and/or dipstick urinalysis as adjunct tests.		LoE 2+ ROBIS-Bewertung: low risk of bias
Rule, 2005, J Urol [69]	Systematic review	1966-2003	not available	usually based on a single presenting serum creatinine value without the differentiation of acute from chronic renal failure (serum creatinine cutoff of 1.5 to 3.0 mg/dl)	<ul style="list-style-type: none"> - wide range in prevalence estimates of renal failure in men with BPH based on inconsistent definition of renal failure - acuity of renal failure in most studies is unknown - comorbidities may be responsible for much of the chronic renal failure in men presenting with BPH symptoms - several studies do not show an association between lower urinary tract symptoms and renal function - no difference in the duration of symptoms in men with or without increased serum creatinine (n=1) - no correlation between lower urinary tract symptoms and serum creatinine (n=1) 	no overview of the number and characteristics of the included studies (and patients) no risk of bias assessment of the included studies no inclusion and exclusion criteria of study designs	LoE 2-



					<ul style="list-style-type: none"> - Half of all men with chronic urinary retention have increased serum creatinine or upper urinary tract dilatation (n=2) - chronic urinary retention show a strong correlation between bladder pressure and serum creatinine (n=2) - unclear: whether serum creatinine and residual urine volumes can be used reliably to screen patients for upper tract dilatation - presenting serum creatinine level was not a prognostic factor for chronic renal failure (n=1) - Men with large residual urine volumes (greater than 300 ml) are at higher risk for chronic renal failure 	ROBIS: high risk of bias	
--	--	--	--	--	---	--------------------------	--



Tabelle 14: Uroflowmetrie

Schlüsselfrage									
Bietet die Uroflowmetrie einen Vorteil bezüglich der Diagnostik einer Blasenauflassobstruktion (BOO)/gutartiger Prostataobstruktion (BPO) gegenüber der Druckflussmessung? Gibt es eine Grenzwertempfehlung zur Uroflowmetrie?									
Referenz	Studiencharakteristika	Patientenmerkmale	Indextest	Referenztest	Endpunkt	Effekte	Schlussfolgerung	Bemerkungen	LoE
Systematische Übersichtsarbeiten									
Malde, 2017, European Urology [55]	n=42 eligible reports NRE recruiting a total of 4444 patients	adult men with LUTS	PCT UV DWT IPP NIRS	PFS	PCT/BOO UF/BOO DWT/BOO IPP/BOO NIRS/BOO	UF 10ml/s Sensitivity Median (IQR): 68.3 (55.1–74.2) Range 29–100 Specificity Median (IQR): 70.5 (62.3–89.7) Range 37–100 PPV Median (IQR) 74.3 (66–89.5) 38.4–100 Negative predictive value Median (IQR) 68 (54–76) Range 46.5–100	Overall, the diagnostic accuracy of uroflowmetry in diagnosing BOO appears to be relatively limited compared to the other index tests. According to the literature, a number of noninvasive tests have high sensitivity and specificity in diagnosing BOO in men. However, although the majority of studies have a low overall risk of bias, the available evidence is limited by heterogeneity. While several tests have shown promising results regarding noninvasive assessment of BOO, invasive urodynamics remain the gold standard.		LoE 2++ ROBIS-Bewertung : low risk of bias no funding diverse coi of all authors



Primärstudien									
<p>Aganovic, 2004, Medicinski arhiv</p> <p>[70]</p>	<p>observational study</p> <p>n=102</p> <p>no information about date of data collection</p> <p>Bosnia</p>	<p>Men with proved BPE</p> <p>Qmax <10 ml/sec</p> <p>Mean age: 66,5 y (SD ±6,5)</p> <p>Qmax >10ml/sec:</p> <p>Mean age 62,7 y (±SD 8,9)</p>	<p>Uroflowmetry</p> <p>Cystometry</p>	PFS	BOO	<p>Qmax <10ml/sec n=52 (51%)</p> <p>Qmax >10ml/sec n=50 (49%)</p> <p>Qmax <10ml/sec</p> <p>Qmax 10-15 ml/sec</p> <p>Qmax >15ml/sec</p> <p>ROC 0.92 (p<0.00001)</p> <p>Linear passive urethral resistance relation >2 (urethral resistance factor >29cmH₂O)</p> <p>Sensitivity 72%</p> <p>Specificity 92%</p> <p>PPV 94%</p> <p>NPV 68%</p> <p>LR + 9.3</p> <p>LR - 0.27</p>	<p>Good allocation of the patients with BPE in the zone of the obstruction and analysis of symptom levels and other non-invasive variables increase accuracy of uroflowmetry (Qmax<10ml/sec). Using this way, high percent of invasive examinations can be avoided without causing significant diagnostic errors. Therefore, clinical decision making in treatment selection for an individual BPE patient is becoming easier.</p>	<p>Patient selection unclear</p> <p>No blinding of the investigator</p> <p>appropriate time interval between both tests not reported</p>	<p>LoE 2-</p> <p>Quadas-Rob: at risk of bias</p> <p>No information about coi and funding</p>
<p>Bøtker-Rasmussen, 1999, Neurourology and Urodynamics</p> <p>[71]</p>	<p>observational study</p> <p>n=29</p> <p>no information about date of data collection</p> <p>Denmark</p>	<p>healthy volunteers</p>	<p>uroflowmetry</p> <p>cystometry</p>	PFS	BOO	<p>Qmax <10 mL/s PPV 100%</p> <p>Sensitivity 33%</p> <p>Specificity 100%</p> <p>Qmax >10mL/s</p> <p>Qmax >15mL/s</p> <p>NPV <50%</p> <p>Sensitivity 60%</p> <p>Specificity 43%</p>	<p>correlation between BOO as demonstrated using pressure-flow and alternative diagnostic tests, i.e., flow rate, symptom score, and residual volume, was weak in this group of men. A possible explanation for the high frequency of BOO observed in the evaluated asymptomatic men could be that the</p>	<p>Blinding of investigators unclear</p> <p>small sample size</p>	<p>LoE 2-</p> <p>Quadas: at risk of RoB</p> <p>no information about coi and funding</p>



							values defining obstruction have been set too low.		
ElSaied, 2013, African Journal of Urology [49]	observational study n= 50 March 2008 - December 2008 Egypt	men with LUTS Mean age 61.7y (53-76y)	uroflowmetry	PFS	BOO	Qmax PPV 57.5% NPV 100% Sens 100% Spec 37.0% Acc 66.0% LR+ 1.59 LR- 0.0 Qave PPV 57.1% NPV 80.0% Sens 87.0% Spec 44.4% Acc 64.0% LR +1.56 LR -0.29	Detrusor wall thickness measurement can be used alone or in combination with other tests to diagnose and quantify bladder outlet obstruction non-invasively, with an accuracy approaching that of the standard pressure flow studies.		LoE 2+ Quadas RoB Low no coi no information about funding
Harding, 2004, Journal of Urology [72]	observational study n=150 full data of n=101 UK	men with LUTS who were referred for conventional PFS mean age 63 y (range 20 to 88)	Noninvasive penile cuff test uroflowmetry	PFS	BOO	Qmax less than 10 ml/second ⁻¹ Sens 81% Spec 64% PPV 51%	The results of this study suggest that the PCR index combines valid estimates of bladder contractility and the maximum flow rate, and it represents a clinically useful, noninvasive urodynamic parameter for the diagnosis of BOO.	critical issue in Rob: flow and timing	LoE 2- Quadas RoB at risk of bias
Hirayama, 2002, Journal of Urology [73] zusätzlich extrahiert	observational study n=36 prospective enrolment in April 1999 – June 2000	men who were treated for LUTS age range: 50 to 83 y mean: 67.6 y IPSS Mean SD	free-flowmetry Q max volume of residual urine	PFS	outflow obstruction detrusor contractility	positive predictive value (PPV) for outflow obstruction according to the Q max: PPV 65% at a max flow rate of 10 mL/s	The only parameter that was a clear indicator of outflow obstruction was Q. Other max indicators of detrusor contractility should be sought.	keine vollständigen Werte zur diagnostischen Genauigkeit, nur PPV berechnet	LoE 2- Quadas Rob: at risk of bias



<p><i>aus Malde-Review 2017</i></p>	<p>Japan</p>	<p>17. ± 4.9 range: 9-33 Prostate volume (mL) Mean SD 16.3±3.0 range: 10.0-19.8</p>				<p>PPV 100% at a flow rate of 5 mL/s IPSS, QOL index, and items related to TRUS and PSA values showed no significant differences positive predictive value for impaired detrusor contractility according to Qmax exhibits a log max normal distribution pattern with the peak flow rate at 9 mL/s</p>		<p>critical issue in Rob: patient selection interpretation of index and reference test</p>	<p>no information about coin and funding</p>
<p>Ku, 2009, International Journal of Urology [51] <i>zusätzlich extrahiert aus Malde-Review 2017</i></p>	<p>observational study prospective data collection and retrospective analysis n=212 no information about date of data collection Korea</p>	<p>Men that had LUTS median age 68 range 44-89 y median serum PSA level: 1.3 ng/mL (range 0.2 to 9.4) PV: 37.9 mL (range 11.3 to 148.0)</p>	<p>Free uroflowmetry voided volume Qmax residual fraction</p>	<p>pressure flow studies</p>	<p>bladder outlet obstruction</p>	<p>AUC for: Qmax 70.6% 95% CI, 63.1% to 78.1% P =0.001 RF 74.4% 95% CI, 67.2% to 81.7% P =0.001 Qmax cut-off of 12 mL/s or less: sensitivity 77.2% specificity 54.2% PPV: 38.3% NPV: 86.6%</p>	<p>The presence or absence of BOO might be predicted using non-invasive methods. The residual fraction may help with patient management by better predicting the likely patient classification from pressure-flow studies.</p>	<p>critical issue in Rob: patient selection interpretation of index and reference test</p>	<p>LoE 2- Quadas-RoB: at risk of bias no information about coin and funding</p>



						residual fraction < 20% sensitivity 75.4% specificity 67.7% PPV: 46.2% NPV: 88.2%			
Kuo, 1999, Urology [74] zusätzlich extrahiert aus Malde-Review 2017	observational study prospective consecutive enrolment from October 1997 to September 1998 n=324 Taiwan	men with LUTS age range: 45 to 88 y mean 67.8 ± 9.6	uroflowmetry flow rate, flow volume, Qmax clinical prostate score system: seven items: Qmax, flow pattern, voided volume, residual urine, TPV, TZI, and prostatic configuration	videourodynamic study	BPO	Prostate score: Qmax TPV voided volume residual urine Score ≥3: sensitivity 90.7% specificity 33% Prostate score: Qmax flow pattern voided volume residual urine TPV TZI prostatic configuration Score ≥3: sensitivity 87.2% specificity 60.8% Score ≥4: sensitivity 90.7% specificity 50.5% Score ≥5: sensitivity 97.6% specificity 38.2%	By combining uroflowmetry and transrectal sonography of the prostate, patients with LUTS can be diagnosed with a good sensitivity and specificity. Using the parameters in the uroflow and prostate measurements, a prostate score could be established and used as an indicator of BPO for selecting patients with LUTS who require further treatment or invasive VUDS.	critical issue in Rob: interpretation of index and reference test	LoE 2- Quadas-RoB: at risk of bias no information about coi and funding



						<p>Sensitivity and specificity of BPO diagnosis in patients with at least 1 favourable predictive factor</p> <p>Score ≥ 3: sensitivity 91.6% specificity 87.27%</p>			
<p>Lee, 2016, Investigative And Clinical Urology</p> <p>[52]</p>	<p>observational study</p> <p>N= 517 (charts review)</p> <p>2008 to 2014</p> <p>Korea</p>	<p>Total sample: N=240</p> <p>mean age (\pmSD) 65.3\pm9.2y</p>	<p>Uroflowmetry</p> <p>Values: Qmax, Qave, voiding volume, PVR index</p> <p>Qmax minus Qave (DeltaQ)</p>	UDS	<p>DU</p> <p>BOO</p>	<p>DU (n=111) BOO (n=129)</p> <p>Identifying DU: AUC: DeltaQ 0.806 Qmax 0.763 Qave 0.574 PVR 0.796</p> <p>cutoff Qmax 11.05 (mL/s) Sensitivity 69%, Specificity 68.5%</p> <p>cutoff DeltaQ 6.65 mL/s: Sensitivity 71.3% Specificity 70.3%</p> <p>cutoff PVR 84.5 mL Sensitivity 70.3% Specificity 75.2%</p>	<p>We suggest DeltaQ as a novel post uroflowmetry calculated value to discriminate DU from BOO in men with obstructive lower urinary tract symptom. DeltaQ can be a reliable and useful tool to screen for differential diagnosis between DU and BOO before UDS.</p>	<p>Patient selection unclear</p> <p>No blinding of the investigator</p> <p>appropriate time interval between both tests not reported</p>	<p>LoE 2-</p> <p>Quadas-RoB: at risk of bias</p> <p>No coi</p> <p>No information about funding</p>
<p>Oelke, 2002, World J Urol</p> <p>[75]</p>	<p>Prospective diagnostic study</p> <p>n= 70</p>	<p>male patients with LUTS and/or prostate enlargement</p>	<p>suprapubic ultrasound</p>	PFS	<p>DTW</p> <p>Detrusor wall thickness</p>	<p><u>DTW (greater than or equal to 2mm)</u></p> <p>Sensitivity: 63.6% Specificity: 97.3% PPV: 95.5%</p>	<p>Measuring the thickness of the detrusor wall can be used as a screening test to detect BOO.</p>		<p>LoE 2-</p> <p>Quadas RoB:</p>



<p><i>zusätzlich extrahiert aus Malde-Review 2017</i></p>	<p>Feb 1999- Sep 1999 Germany</p>	<p>Mean age 63 y (42-82 y)</p>		<p>Uroflowmetry residual volume, prostate volume</p>	<p>To detect BOO bladder outlet obstruction</p>	<p>NPV: 75% Qmax: Sensitivity: 100% Specificity: 25% PPV: 55% NPV: 100% Qave: Sensitivity: 93.6% Specificity: 22.2% PPV: 52.5% NPV: 80% Sensitivity: 81.3% Specificity: 43.2% PPV: 55.3% NPV: 72.7% AUC Qmax: 0.779 AUC Qave: 0.765 AUC residual urine: 0.699</p>			<p>At risk of bias no information about funding and coi</p>
<p>Oelke, 2007, European Urology [53]</p>	<p>observational study n=160 1 January 2000 -31 December 2001 Germany</p>	<p>men older than 40 yr with lower urinary tract symptoms and/or prostatic enlargement median age: 62 y range (40-89y)</p>	<p>free uroflowmetry Qmax Qave</p>	<p>PFS</p>	<p>BOO</p>	<p>Qmax (AUC: 0.84; 95%CI, 0.78-0.91) Nonobstructive/obstructive Qmax ≥15/<15 ml/s PPV 59% (50-67) NPV 97% (91-103) Sensitivity 99% (96-101) Specificity 39% (28-49) Accuracy 67% LR+ 1.61</p>	<p>This study showed that sonographic measurements of DWT are an accurate alternative for pressure-flow measurements to assess the presence of BOO. DWT measurements show a higher diagnostic power than measurements of Qmax, Qave, postvoid residual urine, or prostate volume.</p>		<p>LoE 2+ Quadas-RoB: low no coi no information about funding</p>



						<p>(1.36–1.91) LR- 0.03 (0–4.42)</p> <p>Nonobstructive/ obstructive Qmax ≥10/<10 ml/s</p> <p>PPV 69% (58–79) NPV 72% (63–82) Sensitivity 68% (57–78) Specificity 73% (63–82) Accuracy 70% LR+ 2.5 (1.7–3.68) LR - 0.44 (0.31–3.2)</p> <p>Qave (AUC: 0.82; 95%CI, 0.75–0.89)</p> <p>Nonobstructive/ obstructive 7/<7 ml/s PPV 59% (50–68) NPV 83% (72–94) Sensitivity 89% (82–96) Specificity 46% (35–56) Accuracy 66% LR+ 1.65 (1.34–2.04) LR- 0.23 (0.12–1.98)</p>			
Poulsen, 1994, Scandinavia	observational study	Men with symptomatic BPH	uroflowmetry	PFS	BOO	neither uroflowmetry, symptomatology nor prostate size	The disease entity of BPH is characterized by the interaction of prostate	Patient selection unclear	LoE 2-



<p>n Journal of Urology and Nephrology [76]</p>	<p>n=188 no information about date of data collection Denmark</p>	<p>Median age: 68y (32-90) n=153 free uroflowmetry and PFS</p>			<p>infravesical obstruction</p>	<p>correlated well with BOO</p>	<p>enlargement, the subjective symptom complex of prostatism, and the urodynamic infravesical obstruction. Since it is impossible to interpolate from one to another of these conditions, a comprehensive evaluation of a patient with symptomatic BPH should include an assessment of all these conditions.</p>	<p>No blinding of the investigator appropriate time interval between both tests not reported</p>	<p>Quadas-RoB: at risk of bias no information about coi and funding</p>
<p>Reynard, 1996, British Journal of Urology [77]</p>	<p>observational study n=165 December 1992 - February 1994 UK</p>	<p>men with LUTS suggestive of BPO median age 68y (range 50-84) n=148 (90%) voided four times</p>	<p>free uroflowmetry various thresholds of Qmax</p>	<p>PFS</p>	<p>BOO</p>	<p>Qmax <8 mL/s void 1: Sensitivity 43% Specificity 85% PPV 82% NPV 50% Qmax <10 mL/s void 1: Sensitivity 71% Specificity 71% PPV 79% NPV 61% Qmax <12 mL/s void 1: Sensitivity 84% Specificity 50% PPV 72% NPV 67% Qmax <15 mL/s void 1: Sensitivity 95% Specificity 35% PPV 69%</p>	<p>There was a significant increase in Qmax with each successive void when men with LUTS suggestive of BPO performed multiple free-flow measurements and consequently, single free-flow measurements substantially underestimated the maximum Qmax that these patients achieved. The specificity and PPV of Qmax for BOO can be improved considerably by performing multiple free-flow studies and by carefully selecting an appropriate threshold value (although whether pressure-flow studies are unnecessary will depend on what level of specificity and PPV is deemed acceptable in clinical practice). These findings should be considered if free-flow studies are to be used as</p>	<p>No blinding of the investigator</p>	<p>LoE 2- Quadas-RoB: at risk of bias no information about coi and funding</p>



						NPV 81% First, as would be expected, with an increasing threshold of Qmax (from 8 to 15 mL/s), the specificity and PPV decreased, while the sensitivity increased. Within the results for each threshold of Qmax, the specificity and PPV increased with each consecutive void.	the basis for deciding the clinical management of men with LUTS and may be particularly useful for urologists with limited facilities for pressure-flow studies.		
Reynard, 1998, British Journal of Urology [77]	observational study n=1271 2 y- period 12 centres in Europe, Australia, Canada, Taiwan and Japan	Men >45 y with LUTS and benign enlargement mean age 66.5 y range 45–88 y	uroflowmetry	PFS	BOO	Threshold Qmax (<10mL/s): (95% CI [n/N]) Sensitivity 47% (43–51) [252/540] Specificity 70% (65–75) [250/357] PPV 70% (65–75) [252/359] 1-NPV 54% (49–58) [288/539] Threshold Qmax (<15mL/s) (95% CI [n/N])	While uroflowmetry cannot replace pressure flow studies in the diagnosis of BOO, it can provide a valuable improvement over symptoms alone in the diagnosis of the cause of lower urinary tract dysfunction in men presenting with LUTS. This study provides performance statistics for Qmax with respect to BOO; such statistics may be used to define more accurately the presence or absence of BOO in men presenting with LUTS, so avoiding the need for formal pressure flow studies in everyday clinical practice, while improving the likelihood of a successful outcome from	Patient selection unclear No blinding of the investigator appropriate time interval between both tests not reported	LoE 2- Quadas- Rob: at risk of bias no information about coi and funding



						<p>Sensitivity 82% (79–85) [440/540]</p> <p>Specificity 38% (33–45) [136/357]</p> <p>PPV 67% (63–71) [446/661]</p> <p>1-NPV 42% (36–48) [100/236]</p>	<p>prostatectomy. This study also shows that low-volume uroflowmetry can provide useful diagnostic information and that, as such, the data from such voids should not be discarded.</p>		
<p>Schacterle, 1996, Neurology and Urodynamics [78]</p>	<p>observational study</p> <p>n= 134</p> <p>no information about date of data collection</p> <p>USA</p>	<p>mean age: 67.8 ±8.9 y</p> <p>Men with prostatism</p> <p>Adult male patients with lower urinary tract symptoms</p>	<p>American Urological Association symptom index (AUASI)</p>	<p>uroflowmetry</p> <p>video urodynamics incl. Micturitional urethral pressure profilometry</p>	<p>prostatic obstruction</p>	<p>Qmax < 15 ml/s + AUASI ≥ 20 Obstruction: Sensitivity % 73 Specificity % 74 PPV %70 NPV % 77 No obstructed n=16 (24%) No non-obstructed n=7 (10%)</p> <p>Qmax < 10 ml/s + AUASI ≥ 20 Obstruction: Sensitivity % 38 Specificity % 98 PPV % 93 NPV % 65 No obstructed n=13 (20%) No non-obstructed n= 1 (1%)</p> <p>Qmax < 15 ml/s + PVR ≥125 ml + AUASI ≥ 13 Obstruction:</p>	<p>Our analysis indicated that a threshold AUASI value of 20 or Qmax values of 10 or 15 ml/s for the prediction of bladder outlet obstruction results in several nonobstructed patients being classified as obstructed. Therefore, we suggest using two separate criteria for classifying patients as either obstructed or non-obstructed</p>	<p>Vergleich/Referenz-Test nicht wie in der PICO formuliert, daher indirekte Evidenz</p>	<p>LoE 2+</p> <p>Quadas RoB low</p> <p>No information about coifunding</p>



						<p>Sensitivity % 94 Specificity % 73 PPV % 85 NPV % 89 No obstructed n=17 (26%) No non-obstructed n=3 (4%)</p> <p>Qmax < 10 ml/s + PVR ≥ 125 ml + AUASI ≥ 13 Obstruction:</p> <p>Sensitivity % 60 Specificity % 100 PPV % 100 NPV % 64 obstructed n=12(18%) non-obstructed n=0</p>			
<p>Zhang, 2013, Urology [79]</p> <p><i>zusätzlich extrahiert aus Malde-Review 2017</i></p>	<p>observational study</p> <p>consecutive prospective enrollment</p> <p>n=94 enrolled n=87 with complete data sets</p> <p>no information about date of data collection</p> <p>China</p>	<p>men with LUTS</p> <p>mean age: 68.55±9.27 y (range 56-85)</p> <p>mean BMI 23.57 ± 2.61 (range 18.40-29.70)</p>	<p>uroflow examination</p> <p>Qmax PVR</p>	PFS	BOO	<p>Comparison of the maximum urine flow ± post void residual result and the Abrams-Griffiths number:</p> <p>sensitivity 33.3% specificity 87.5% positive predictive rate 87.5% negative predictive rate 33.3% coincidence rate 48.3%</p>	<p>Compared with the "maximum uroflow rate (Qmax), + PVR", NIRS can be more accurate and noninvasive for the diagnosis of BOO in men; this approach provides a new noninvasive method of high clinical value.</p>	<p>critical issue in RoB: flow and timing</p>	<p>LoE 2- Quadas-RoB: at risk of bias</p>



Tabelle 15: Kombinationen aus mehreren Untersuchungen

Schlüsselfrage Hat eine Kombination aus mehreren Untersuchungen (z.B. Uroflowmetrie plus Prostatavolumen plus Restharn) eine bessere Vorhersagekraft einer möglichen Obstruktion im Vergleich zum Goldstandard (Druckflussmessung)?									
Referenz	Studiencharakteristika	Patientenmerkmale	Index-test	Referenz-test	Endpunkt	Effekte	Schlussfolgerung	Bemerkungen	LoE
Aganovi. 2012, Acta Informatica Mediaca [80]	Prospective diagnostic study n=110 2009-2010 Bosnia and Herzegovina	patients with LUTS and confirmed BPE average age: 65.3 y (49-80)	Combination of: TAUS	PFS	PV IPP at the bladder volume of 150-200 ml BOOI BOON	Combination: BOON>-30 IPP >10mm AUC (95% CI): 0.752* (0.661-0.829) Sensitivity (%) (95% CI) 61.33 (49.4-72.4) Specificity (%) (95% CI) 80.56 (64.0-91.8) LR + (95% CI) 3.15 (2.5-4.0) LR - (95% CI) 0.48 (0.2-1.0) PPV (95% CI) 86.8 (74.5-94.6) NPV (95% CI) 50.0 (36.6-63.4)	The combination of cut-off values for BOON and IPP increases test accuracy according to BOO at the individual level, thus facilitating clinical decision making regarding diagnostics and optimal choice of therapy in patients with BPE . Owing to its good correlation with obstruction determinants, IPP can be included in the formula for BOON instead of prostate volume.	Patient enrollment is not reported if consecutive or random selected Blinding of investigators of both tests unclear	LoE 2- Quadas-RoB: At risk of bias No coi No information about funding



						Number Needed to Diagnose 2.4			
<p>Aganovic, 2012, Bosn J Basic Med Sci</p> <p>[81]</p>	<p>Prospective diagnostic study</p> <p>n=200</p> <p>2009-2011</p> <p>Bosnia and Herzegovina</p>	<p>patients with the lower urinary tract symptoms suggestive of benign prostatic enlargement</p> <p>average age of 64.4y (49-82)</p>	<p>TAUS</p> <p>Uroflowmetry</p>	<p>PFS</p>	<p>Qmax</p> <p>postvoid residual urine</p> <p>Bladder outlet obstruction number</p> <p>prostate volume in cubic centimeters - 3x maximal urinary free flow rate (in milliliters per second) -0.2 x mean voided volume (in milliliters, as estimated from frequency-volume charts)</p>	<p>Bladder outlet obstruction number >-20 (n=115)</p> <p>Sensitivity (%) 76.52 (67.71% to 83.92%)</p> <p>Specificity (%) 68.24 (57.24% to 77.92%)</p> <p>Positive Likelihood Ratio 2.41 (1.74 to 3.34)</p>	<p>The bladder outlet obstruction number may be used in daily urological practice as a valid, non-invasive indicator of infravesical obstruction in patients with BPE, with a possibility of correct classification of obstruction in approximately 75% of the cases. Transabdominal ultrasound has shown to be applicable to the bladder outlet obstruction number formula in determining prostate volume.</p>	<p>Patient enrolment is not reported if consecutive or random selected</p> <p>Blinding of investigators of both tests unclear</p>	<p>LoE 2-</p> <p>Quadas RoB</p> <p>At risk of bias</p> <p>No coi</p> <p>No information about funding</p>
<p>Caffarel, 2008, Neurology and Urodynamics</p> <p>[82]</p>	<p>Retrospective diagnostic study</p> <p>n=95</p>	<p>men with troublesome LUTS</p> <p>no information</p>	<p>uroflowmetry</p>	<p>PFS</p>	<p>Qmax alone and with the inclusion of additional variables (IPSS, PSA,</p>	<p>Bayes' all tests:</p> <p>Threshold for Chi² test 0.5</p> <p>Chi² 4.9</p> <p>p-value: 0.026</p>	<p>Although in our sample relevant additional tests do not improve the diagnostic power of Qmax as a predictor of BOO, we believe</p>	<p>We excluded 45 (47%) men due to inadequate voided volume (<150 ml)</p>	<p>LoE 2-</p> <p>Quadas RoB:</p> <p>At risk of bias</p> <p>No coi</p>



	September, 2001- August, 2002 UK	about mean age			and residual urine): Bayesian model to predict BOO	Bayes' Qmax only Threshold for Chi2 test 0.5 Chi ² 9.2 p-value: 0.002	the Bayesian approach is conceptually suited to modeling clinical decision making but may be better tested for a more clinically relevant outcome such as treatment response.	on the documented uroflowmetry tests, or because there were <2 additional parameters recorded These exclusions may have had an effect on our results since PVR in these men may have shown improved prediction for BOO Patient enrolment is not reported if consecutive or random selected Blinding of investigators of both tests unclear	No information about funding
Carballido, 2011, International	prospective, epidemiological, multicentre	Consecutive male patients	GP visit 1: medical history,	Visit 3: reference urologist	diagnosis of BPH	Age + IPSS + PSA + BPH probability as model:	A diagnostic algorithm including only objective		LoE 3



Journal of Clinical Practice [44]	observational study n= 768 no information about time Italy, France, UK, Spain	aged ≥ 50 years who spontaneously attended their regular GP office with LUTS were eligible for inclusion n=666 per protocol population mean age (SD): 60.9 ± 7.9 (50–98)	initial symptoms, IPSS and Bother Score Questionnaires , after which the GP recorded their BPH diagnosis GP: general practitioner GP visit 2: DRE and recorded their BPH diagnosis	surgery within 3 months of visit 2 patient’s symptoms and past medical history, performed a physical examination (including a DRE), reviewed the previous tests carried out by the GP and performed additional BPH diagnostic tests of abdominal ultrasound (with postvoid residual volume and prostate size estimation) and uroflowmetry.	benign prostate hypertrophy	PPV 77.1% NPV 46.8% Sensitivity 62.7% Specificity 63.7%	variables (age, IPSS and PSA), easily implemented in any GP office, allows GPs to accurately diagnose BPH in approximately three-quarters of patients spontaneously reporting LUTS		EPHPP-checklist Study quality: weak (at risk of bias) funded by GlaxoSmithKline coi: All authors without first author consultant for GSK and / or AstraZeneca and Pierre Fabre Medicament. Almirall. Ramiro Castro and Martyn Gilson are employees of GSK.
Farag, 2017, Arab Journal of Urology [57]	Prospective diagnostic study n= 72 no information about time	adult men with LUTS Mean age (BOO) 62.3 y (SD 6.6 y)	TAUS	PFS	BWT+ maximum urinary flow rate to detect BOO	BWT+ maximum urinary flow rate: Correct classification: 61/72 patients (85%) Sensitivity: 92% Specificity: 65%	It was possible to combine BWT with the maximum urinary flow rate to create a new algorithm that could be used as a screening tool for	Blinding of the investigators not reported Time between	LoE 2- Quadas RoB At risk of bias no coi



	Netherlands, Egypt	Mean age (no BOO) 65.1 y (SD 12.3 y)				PPV: 87% NPV: 76% Positive diagnostic likelihood ratio: 2.6	BOO in men with lower urinary tract symptoms.	both tests is not reported	no funding
Franco, 2010, Journal of Urology [58]	prospective diagnostic study n= 100 Jan 2001-Jan 2002 Italy	men with LUTS due BPH Median age 66 y	Suprapubic ultrasound	Urodynamics PFS	DWT intravesical prostatic protrusion Qmax, detrusor pressure, PMUO Minimal urethral opening pressure To detect BOO	Associated (IPP +/-or DWT) PPV: 86.8% NPV: 66% Sensitivity: 90% Specificity: 63.1% Accuracy: 87% LR+: 2.4 LR-: 0.15	Suprapubic ultrasound of detrusor wall thickness and intravesical prostatic protrusion is a simple, noninvasive, accurate system to assess bladder prostatic obstruction in patients with lower urinary tract symptoms due to benign prostatic hyperplasia.	The study population was small and more than 70% of patients had bladder prostatic obstruction, which may partly explain our high positive predictive value.	LoE 2+ Quadas RoB Low no information about funding and coi
Kuo, 1999, Urology [74]	prospective observational study n=324 October 1997 - September 1998 Taiwan	men with LUTS mean age 67.8y (45 to 88y)	uroflowmetry TRUS	PFS	BOO	Clinical prostate scoring system Prostate score = Qmax + TPV + voided volume +residual urine Score ≥3: sensitivity 90.7%, specificity 33% 2. Prostate score = Qmax + flow pattern + voided volume + residual urine + TPV + TZI + prostatic configuration	By combining uroflowmetry and transrectal sonography of the prostate, patients with LUTS can be diagnosed with a good sensitivity and specificity. Using the parameters in the uroflow and prostate measurements, a prostate score could be established and used as an indicator of BPO for selecting patients with LUTS	Blinding of investigators of both tests unclear Time between both tests is not reported	LoE 2- Quadas RoB at risk of bias no information about coi and funding



						<p>Score ≥ 3: sensitivity of BPO 87.2%, specificity 60.8%</p> <p>Score ≥ 4: sensitivity of BPO 90.7%, specificity 50.5%</p> <p>Score ≥ 5: sensitivity of BPO 97.6%, specificity 38.2%</p> <p>3. Sensitivity and specificity of BPO diagnosis in patients with at least 1 favorable predictive factor (n=148)</p> <p>Score ≥ 3: sensitivity of BPO 91.6%, specificity 87.27%</p> <p>4. Exclusion of patients with at least 1 favorable predictive factor (n=176)</p> <p>Score ≥ 3: sensitivity of BPO 68.9%, specificity 23.0%</p>	who require further treatment or invasive videourodynamic study		
Rademakers, 2017, Worl J Urol [83]	retrospective diagnostic study n= 143 no information about time Netherlands Germany	unselected, treatment-naïve male patients aged ≥ 40 y with uncomplicated, non-neurogenic LUTS Median age	Suprapubic ultrasound measurement	uroflowmetry, measurement transrectal ultrasound measurement multichannel computer urodynamic studies	DWT voiding sub-scores; maximum flow rate (Qmax), average flow rate (Qave), time to maximum urinary flow, and voiding	Noninvasive tests* to determine detrusor underactivity: threshold: 1.23 mm of DWT Sensitivity: 42% Specificity: 100% PPV: 100% NPV: 85%	This study showed that all men with ultrasound DWT ≤ 1.23 mm + bladder capacity >445 ml have detrusor underactivity. Combination of these two tests could help physicians to diagnose detrusor	Vergleich/Referenz-Test nicht wie in der PICO formuliert, daher indirekte Evidenz	LoE 2+ Quadas RoB: low No information about funding Coi: M. Oelke and G. A. van



		62 y (59-70 y)			time of free uroflowmetry; bladder capacity; voiding efficiency; prostate volume to detect Detrusor under-activity (incomplete bladder emptying (>30 ml) in the absence of bladder outlet obstruction or dysfunctiona l voiding)	LR likelihood ratio of a positive test result: 42 *model includes the following factors: age; total IPSS, IPSS storage, and voiding sub-scores; maximum flow rate (Qmax), average flow rate (Qave), time to maximum urinary flow, and voiding time of free uroflowmetry; bladder capacity; voiding efficiency prostate volume; and detrusor wall thickness	underactivity noninvasively in clinical practice.		Koevinge are consultants, speakers and trial participants of Astellas and have been rewarded with the Astellas European Foundation Grant 2012. K.L.J. Rademakers is employed from Astellas European Foundation Grant money.
Schacterl, 1996, Neurourology and Urodynamics [78]	Prospective diagnostic study n= 134 no information about time USA	mean age: 67.8 ±8.9 y Men with prostatism Adult male patients with lower urinary tract symptoms	AUASI	uroflowmetry video urodynamics incl. Micturitional urethral pressure profilometry	Qmax, PVR, AUASI prostatic obstruction	Qmax < 15 ml/s + AUASI ≥ 20 <i>Obstruction:</i> Sensitivity % 73 Specificity % 74 PPV %70 NPV % 77 No obstructed 16 (24%) No non-obstructed 7 (10%) Qmax < 10 ml/s + AUASI ≥ 20 <i>Obstruction:</i>	Our analysis indicated that a threshold AUASI value of 20 or Qmax values of 10 or 15 ml/s for the prediction of bladder outlet obstruction results in several nonobstructed patients being classified as obstructed. Therefore, we suggest using two	Vergleich/Referenz-Test nicht wie in der PICO formuliert, daher indirekte Evidenz	LoE 2+ Quadas RoB: low No information about coi and funding



						<p>Sensitivity % 38 Specificity % 98 PPV % 93 NPV % 65 No obstructed 13 (20%) No non-obstructed 1 (1%)</p> <p>Qmax < 15 ml/s + PVR ≥ 125 ml + AUASI ≥ 13 <i>Obstruction:</i></p> <p>Sensitivity % 94 Specificity % 73 PPV % 85 NPV % 89 No obstructed 17 (26%) No non-obstructed 3 (4%)</p> <p>Qmax < 10 ml/s + PVR ≥ 125 ml + AUASI ≥ 13 <i>Obstruction:</i> Sensitivity % 60 Specificity % 100 PPV % 100 NPV % 64 obstructed 12 (18%) non-obstructed 0</p>	<p>separate criteria for classifying patients as either obstructed or non-obstructed</p>		
--	--	--	--	--	--	---	---	--	--



Tabelle 16: Nicht-invasive Tests

Schlüsselfrage								
Welche nicht-invasiven Tests zur Bestimmung der BOO/BPO sind als Alternative zur urodynamischen Untersuchung geeignet?								
Referenz	Studiencharakteristika	Index-test	Referenz-test	Endpunkt	Effekte	Schlussfolgerung	Bemerkungen	LoE
Malde, 2017, European Urology [55]	n=42 eligible reports NRE recruiting a total of 4444 patients	PCT UF DWT IPP NIRS	PFS	PCT/ Bladder Outlet Obstruction UF/ Bladder Outlet Obstruction DWT/ Bladder Outlet Obstruction IPP/ Bladder Outlet Obstruction NIRS/ Bladder Outlet Obstruction	PCT Griffiths nomogram Sensitivity Median (IQR): 88.9 (76.4–94.4) Range: 64–100 Specificity Median (IQR): 75.7 (69.3–78.3) Range: 63–81 Positive predictive value Median (IQR) 67.7 (67.2–67.9) Range 66.7–68 Negative predictive value Median (IQR) 93 (85.5–96.5) Range 78–100 Uroflowmetry 10ml/s Sensitivity Median (IQR): 68.3 (55.1–74.2) Range	According to the literature, a number of noninvasive tests have high sensitivity and specificity in diagnosing BOO in men. However, although the majority of studies have a low overall risk of bias, the available evidence is limited by heterogeneity. While several tests have shown promising results regarding noninvasive assessment of BOO, invasive urodynamics remain the gold standard.		LoE 2++ ROBIS-Bewertung: low risk of bias no funding diverse coi of all authors



					29-100 Specificity Median (IQR): 70.5 (62.3-89.7) Range 37-100 Positive predictive value Median (IQR) 74.3 (66-89.5) 38.4-100 Negative predictive value Median (IQR) 68 (54-76) Range 46.5-100 detrusor wall thickness DWT 2mm Sensitivity Median (IQR): 82.7 (65.7-83) Range: 63.6-92 Specificity Median (IQR): 92.6 (76-95) Range: 68-97.3 Positive predictive value Median (IQR) 90.5 (81-94) Range: 65.7-95.5 Negative predictive value Median (IQR) 85 (76-86) Range: 75-86.2		
--	--	--	--	--	--	--	--



					<p>intravesical prostatic protrusion IPP 10mm Sensitivity Median (IQR): 67.8 (56.2–77) Range: 46–80 Specificity Median (IQR): 74.8 (67.4–84) Range: 65–92 Positive predictive value Median (IQR) 73.8 (72–94) Range: 69.6–94 Negative predictive value Median (IQR) 69.3 (63.2–71.9) Range: 46–78.9</p> <p>near-infrared spectroscopy NIRS algorithm Sensitivity Median (IQR): 85.71 (77–85.8) Range: 68.3–86 Specificity Median (IQR): 87.5 (75–88.1) Range: 62.5–88.9 Positive predictive value Median (IQR) 88.89 (85.7–89)</p>		
--	--	--	--	--	--	--	--



					Range: 82.7–89.2 Negative predictive value Median (IQR) 84 (63.4–84.8) Range: 42.9–85.71			
Presicce, 2017, Minerva Urologica e Nefrologica [84]	n=35 included references only not experimental designs n=3295 included patients Korea Poland Italy Turkey Germany Switzerland Iran Brazil Japan USA Australia Bosnia Malaysia China Jan 1995 until Febr 2016 (Angabe im Abstract) until Oct 2015 (Angabe im Methodenteil)	non invasive ultrasound measurements : BWT/DWT UEBW	pressure flow studies (PFS)	bladder outlet obstruction (BOO)	<p>UEBW as predictor of BOO 38.1±14.3 g^a 58.8±39.3 g^b 48.2±6.8 g^c accuracy (PPV): 87.9%*</p> <p>BWT as predictor of BOO 4.54±1.10 mm^d 2.2±0.06 mm^e 2.0±0.49 mm^f accuracy (AUC): 0.86*</p> <p>DWT as predictor of BOO 1.92±0.11 mm^g 6.6±2.1 mm^h accuracy (AUC): 0.93, (95% CI 0.88-0.98)*</p> <p>*Werte nur aus einer Studie, nicht aggregiert</p> <p>^a= Kojima et al., 1996 ^b= Almeida et al., 2010 ^c= Lee et al., 2008 ^d= Manieri et al., 1998 ^e= Jang et al., 2013 ^f= Blatt et al., 2008 ^g= Oelke et al., 2002 ^h= Franco et al. 2010</p>	The ultrasound evaluation of bladder/detrusor thickness appears to be simple, highly accurate and non-invasive technique to predict BOO and to evaluate the clinical outcomes after medical/surgical treatments for LUTS/BPH. The implementation of these techniques and their standardization will probably better define their role in the diagnostic algorithms of patients with LUTS and possibly reduce the number of unnecessary pressure flow-studies.	Angaben zum Suchzeitraum sind unterschiedlich genannt, Abweichung von Abstract und Methodenteil Bemerkungen aus der Robis-Bewertung: Unklarheit der Einschlusskriterien Unklarheiten in der Identifikation und Auswahl der Studien Unklarheiten in der Datenextraktion und Bewertung der Studien	LoE 2- Robis-Bewertung: high risk of bias no information about funding no coi



<p>Rieken, 2017, Minerva Urologica e Nefrologica [85]</p>	<p>n=28 eligible articles prospective and retrospective design n=19 reported articles in table 1-4 n=2807 included patients no information about countries 2005 - 2016</p>	<p>IPP measured by TRUS or TAUS</p>	<p>no information about reference tests</p>	<p>BOO</p>	<p>diagnostic accuracy (AUC): range of results from 9 studies: AUC 0.708 to 0.858 95% CI 0.615-0.791 to 95% CI 0.809 - 0.908</p>	<p>Analysis of IPP may be regarded as potential non-invasive alternative to standard PFS in the assessment of BOO. Patients with IPP>10 mm should be counselled regarding the high chance of need for surgical treatment following acute urinary retention.</p>	<p>Bemerkungen aus der Robis-Bewertung: Unklarheit der Einschlusskriterien Unklarheiten in der Identifikation und Auswahl der Studien Unklarheiten in der Datenextraktion und Bewertung der Studien</p>	<p>LoE 2- Robis-Bewertung high risk of bias no coi no information about funding</p>
<p>Sahai, 2013, Current Bladder Dysfunction Reports [86]</p>	<p>no information about included studies or included pat or countries of the studies Suchzeitraum: "Where possible we have focused on studies published within the last 2 years"</p>	<p>PVR Measurement Uroflowmetry Prostatic Imaging Studies Bladder/Detrusor Wall Thickness and Ultrasound Estimated Bladder Weight NIRS CCM</p>	<p>no information about reference tests</p>	<p>BOO</p>	<p>Several ultrasound based technique have shown promise and particularly in combination may increase diagnostic accuracy. However they are operator dependent and studies using such techniques need to be standardized. Certain cases, such as UEBW need studying in differing populations before firm conclusions can be made. BWT, DWT and RI all have their limitations and studies can be conflicting. Near infrared spectroscopy appears promising in small studies but further large</p>	<p>Despite a plethora of non-invasive tests available, none have been able to fully replace the gold standard of a pressure flow study in diagnosing BOO and poor detrusor contractility in the evaluation of LUTS. Although combination of techniques is likely to provide better diagnostic accuracy no one study so far has been able to replace invasive urodynamics which remains the gold standard.</p>	<p>Bemerkungen aus der Robis-Bewertung: Unklarheit der Einschlusskriterien Unklarheiten in der Identifikation und Auswahl der Studien Unklarheiten in der Datenextraktion und Bewertung der Studien</p>	<p>LoE 2- Robis Bewertung: high risk of bias public funding no coi</p>



		Penile Cuff Test and Newer Techniques Based on Compression			scale studies are required to validate its use. Non-invasive methods that measure isovolumetric bladder pressure correlate reasonably well with invasive studies but also have limitations such as effects of abdominal straining.			
--	--	--	--	--	--	--	--	--



Tabelle 17: Grenzwerte von urodynamischen Untersuchungen

Schlüsselfrage									
Welche Grenzwerte von urodynamischen Untersuchungen zur Feststellung einer BOO/BPO gibt es, die sich zur Bestimmung der Therapiebedürftigkeit eignen?									
Referenz	Studiencharakteristika	Patientenmerkmale	Indextest	Referenztest	Endpunkt	Effekte	Schlussfolgerung	Bemerkungen	LoE
Farag, 2017, Arab Journal of Urology [57]	prospective diagnostic study n= 72 no information about time of data collection The Netherlands, Egypt	adult men with LUTS Mean age (BOO):62.3 y (SD 6.6 y) Mean age (no BOO): 65.1 (SD 12.3 y)	TAUS BWT	PFS	BOO	BWT+ maximum urinary flow rate Correct classification: 61/72 patients (85%) Sensitivity: 92% Specificity: 65% PPV: 87% NPV: 76% Positive diagnostic likelihood ratio: 2.6	It was possible to combine BWT with the maximum urinary flow rate to create a new algorithm that could be used as a screening tool for BOO in men with lower urinary tract symptoms.	Blinding of the investigators not reported Time between both tests is not reported	LoE 2- Quadas RoB At risk of bias no coi no funding
Ko, 2017, Neurourology and Urodynamics [87]	prospective diagnostic study n=146 consecutive enrollment December 2013 and February 2015 Korea	men with (IPSS) >12 and lower urinary tract symptoms (LUTS) for >6 months Age, median (IQR) 67 (60-72)y	PCT	PFS	BOO	PCT sensitivity: 89.7%, PPV 54.2% specificity 71.8% NPV94.9% <i>There were no adverse events reported after PCT.</i>	Given its high NPV, PCT may be an efficient screening test for BOO in men. In addition, PCT is advantageous over PFS with regard to its short procedure time and acceptable tolerability.		LoE 2+ Quadas-Rob: low risk of bias Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by



									the Ministry of Health & Welfare, Republic of Korea no information about coi
Rademakers, 2017, Worl J Urol [83]	retrospective diagnostic study (pilot study) n= 143 patients	unselected, treatment-naïve male patients aged ≥40 years with uncomplicated non-neurogenic LUTS Median age 62 y (59-70 y)	ultrasound measurement of DWT uroflowmetry, measurement of PVR, transrectal ultrasound measurement of prostate volume	PFS	DU (incomplete bladder emptying (>30 ml) in the absence of bladder outlet obstruction or dysfunctional voiding)	Noninvasive tests* to determine detrusor underactivity:* threshold: 1.23 mm of DWT Sensitivity: 42% Specificity: 100% PPV: 100% NPV: 85% LR likelihood ratio of a positive test result: 42 *model includes the following factors: age; total IPSS, IPSS storage, and voiding sub-scores; Qmax, Qave, time to maximum urinary flow, and voiding time of free uroflowmetry; bladder capacity; voiding efficiency prostate volume; and DWT	This study showed that all men with ultrasound DWT ≤ 1.23 mm + bladder capacity >445 ml have detrusor underactivity. Combination of these two tests could help physicians to diagnose detrusor underactivity noninvasively in clinical practice.	Outcome nicht BOO, sondern DU	LoE 2+ Quadas-Bewertung: low risk of bias No information about funding Coi: M. Oelke and G. A. van Koeveringe are consultants, speakers and trial participants of Astellas and have been rewarded with the Astellas European



									Foundation Grant 2012. K.L.J. Rademakers is employed from Astellas European Foundation Grant money.
Van Mastricht, 2014, Neurourology and Urodynamics [88]	prospective diagnostic study n=71 The Netherlands November 2006 to August 2011	men who were considered necessary to decide if a TURP was indicated no information about age	condom catheter method	PFS according to International Continence Society standard	BOO	<p>maximum free flowrate Q_{max}: n=71 AUC: 0.78 (95% CI 0.67–0.89)</p> <p>non-invasive urethral resistance parameter AUC 0.68 (95% CI 0.55–0.80)</p> <p>cutoff urethral resistance parameter -17.4: sensitivity 0.62 specificity 0.62</p> <p>n=50 with P_{cond. Max.} higher than P_{det Q_{max}} :</p> <p>AUC 0.74 (95% CI 0.58–0.89) for diagnosing them on the basis of the maximum free flowrate Q_{max.free} and AUC 0.84</p>	In our population of TURP patients, the low flowrates affected the accuracy of the condom method to a degree that it did not perform better than a free flowrate measurement, which performed remarkably well. By excluding measurements in which the condom pressure underestimated the isovolumetric bladder pressure this method may contribute to a more accurate, patient friendly diagnosis of BOO in these patients. In the present study this exclusion was done by comparison with an invasive pressure measurement. A practical non-invasive test would necessitate a non-invasive exclusion criterion, which might be	patient selection not random or consecutive Time between both tests is not reported	LoE 2- Quadas-RoB: at risk of bias Nierstichting Nederland grant C05.2148 no coi



						(95% CI 0.72–0.95) using urethral resistance parameter	based on the risetime of the condom pressure.		
Zhang, 2014, Ultrasound in Medicine and Biology [89]	prospective diagnostic study n=55 November 2011 to May 2013 China	mean age: 65.7 ± 12.7 (range: 31–87) mean IPSS: 22.5 ± 5.8 (range: 13–33) mean quality of life: 4.1 ± 1.5 (range: 1–6)	TRUS shear wave sonoelastography	PFS	BOO	Elastic moduli of transitional zone: Sens 96.7% Spez 44.0% PPV 67.4% NPV 91.7% Acc 72.7% Elastic moduli > 32.4 kPa was defined as BOO Combination of total prostate volume or elastic modulus Sensitivity 97.2% Specificity 62.5% PPV 85.4% NPV 90.9% Acc 86.5% Total prostate volume >54.4 mL or elastic moduli > 32.4 Kilopascal was defined as BOO	The elastic modulus of the transitional zone is a promising indicator in the assessment of the severity of BOO. In addition, the combination of elastic modulus and total prostate volume was the most accurate indicator in the non-invasive diagnosis of BOO in patients with BPH.	patient selection not random or consecutive flow and timing of both tests unclear	LoE 2- Quadas-Rob: at risk of bias no information about coi Financial support obtained from National Natural Science Foundation of China



Tabelle 18: Blasentagebuch

Schlüsselfrage									
Ist das Blasentagebuch zur Objektivierung der Beschwerden bzw. zur Überwachung des Therapieerfolges geeignet?									
Referenz	Studiencharakteristika	Patientenmerkmale	Index-test	Referenz-test	Endpunkt	Effekte	Schlussfolgerungen	Bemerkungen	LoE
Blanker, 2000, Journal of Urology [90]	n=1688 „Krimpen study“ The Netherlands 3 days	n=1597 completed a 3-day FV chart FV n=1211 men with complete data	3 day FV chart IPSS	no nocturia	nocturia nocturnal polyuria 24 h urinary frequency number of voids	multivariate regression (OR 95% CI): 2 or more nocturnal BPH: OR 1.7 (1.2-2.4) 3 or more nocturnal: BPH: OR 3.1 (1.9-5.0) IPSS mild: OR 6.8 (3.5-13.3) IPSS moderate: OR 11.3 (5.5-22.9) IPSS. Severe: 17.1 (6.7-43.6)	Diurnal frequency is independent of age (median 5 voids, IQR 4-6) but higher in men with BPH. Nocturia increases with advancing age and is more frequent in men with nocturnal polyuria. BPH is an independent risk factor for nocturia and increased diurnal voiding frequency. In those with nocturia there is a great difference in subjective symptoms and objective data, indicating that the weight of the IPSS question on nocturia for making treatment decisions should be reconsidered.		LoE 3 Fallserien-RoB Bewertung: low risk of bias This study was funded by the Foundation for Urological Research Rotterdam, Rotterdam, The Netherlands
Blanker, 2001, Urology [91]	prospective single arm study 3924 men „Krimpen study“	n=1597 completed a 3-day FV chart FV 50 to 75 ys old	3-day FV chart on which each micturition was recorded in	no control group	FBC	multivariate analysis: <300 (reference)=1 FBC (mL) 300–400 ml OR 0.8 95% CI 0.6–1.2	Frequency volume charts are a valid, easy-to-use, noninvasive method to determine FBC as an aspect of urinary tract (dys)function in the evaluation of men with LUTS and to determine treatment options for		LoE 3 Fallserien-RoB Bewertung: low risk of bias



	The Netherlands Recruitment August 1995 - January 1998 3 days	1446 men constitute the basis for this report no separate description of BPH-characteristics	1-hour time units. On the third day, the volume of each voiding was recorded FBC was defined as the largest voided volume of the day			400–500 ml OR 0.6 95% CI 0.6–1.2 >500 ml OR 0.5 95% CI 0.4–0.8	LUTS		Foundation for Urological Research Rotterdam, Rotterdam, The Netherlands
Lee, 2011, Journal of Urology [92]	prospective, open label, single arm study n=136 men enrolled n= 94 completed the study As an intention to treat sample n=108 subjects were included in the analysis. Korea	Men 50 years old or older with LUTS/BPO and an I-PSS of 8 or greater	3 day voiding diary treated with 10 mg alfuzosin XL for 12 months	no control group	symptom specific goal achievement	Total MBS No. micturition episodes/24 hrs CC / p-value -0.155 / 0.148 No. urgency episodes/24 hrs CC / p-value -0.197 / 0.066 Storage MBS No. micturition episodes/24 hrs CC / p-value -0.361 / 0.024 No. urgency episodes/24 hrs CC / p-value -0.489 / 0.002 Voiding MBS	Assessing goal achievement for most bothersome symptoms can be a useful outcome measure in patients with benign prostatic obstruction with heterogeneous symptoms or goals reflecting change in quality of life.		LoE 3 Fallserien-RoB Bewertung low risk of bias Samsung Biomedical Research Institute Grant SBRI C-A7-218-3.



	no information about year 3 days for completing the voiding diary					No. micturition episodes/24 hrs CC / p-value 0.001 / 0.994 No. urgency episodes/24 hrs CC / p-value -0.072 / 0.664 Post-Micturition MBS No. micturition episodes/24 hrs CC / p-value 0.346 / 0.297 No. urgency episodes/24 hrs CC / p-value 0.398 / 0.225			
Matthiesen, 1999, BJU International [93]	two arm clinical trial Denmark no information about year 7 days	n=23 pat (mean age 62,8 years, range 42-78) with LUTS who were referred for the evaluation of potential BPH n=11 <i>healthy</i> men (control subjects,	7 day FV chart	no reference test	time and volume of each micturition day and night 24 h day time and volume of each fluid intake fluid intake and food intake was ad libitum	Nocturnal urine* (Vol ml/kg) controls 5.09 (0.34) patients 7.94 (0,55) 24-h urine* controls 18.41 (0.91) patients 24.11 (1.65) Nocturia episodes* controls 0	nocturia on a polyuric basis can be detected by using a FV chart	der Vergleich erfolgt zwischen Gesunden und Patienten, die alle ein Instrument (FV chart) ausfüllen	LoE 3 RoB-Tool for cross-sectional studies: high risk of bias no information about funding and coi



		mean age 63.3 years, range 58-69)				patients 1.66 (0,16) * <i>Statistical significance</i>			
Rajan P. 2010 British Journal of Medical and Surgical Urology [94]	observational study single arm Scotland, UK 2002 3 days	Age (years) mean/median 66.3/67.5 24-h urine volume (ml) 1796.0/1700 FBC (ml) 363.8/350 NUV (ml) 495.5/445 ANV (voids) 2.0/2	3-day FV-chart	no reference test	bladder outflow obstruction (LUTS/BOO) 24-h urine volume, daytime voids (frequency), FBC, ANV and NUV	no statistically significant differences in 24-h urine volume (p = 0.10) and FBC (p = 0.19) between each day of the FV chart significant differences identified between Days 1 and 2, and 1 and 3 for both NUV (p < 0.001) and ANV (p < 0.001).	data from a one-day FV chart is representative of a 3-day equivalent for the assessment of 24HUV and FBC in patients with LUTS/BOO	der Vergleich erfolgte nicht zwischen zwei Instrumenten, sondern zwischen den Ergebnissen einer Messung eines Tages und von drei Tagen	The authors declare that there are no conflicts of interest no information about funding LoE 3 RoB-Tool for cross-sectional studies: high risk of bias
van Doorn, 2011, Journal of Urology [95]	longitudinal, population based study, single arm the Krimpen study The Netherlands 3 days	n=1,597 men (95% of the responders) completed a 3-day FVC Median I-PSS (IQR) 4 (1-7) Median patient age: 60.9	3-day FVC participants recorded each micturition in 1-hour time units (first 2 days) and the volume of each void (third day).	IPSS nocturia question	Nocturia Determined From FVCs and IPSS	comparison of FVCs with I-PSS data on nocturia to establish whether men had a higher or lower estimated NVF baseline: 33.3% reported a lower NVF on FVCs	Based on the discrepancy between NVF on FVC and I-PSS, this study also emphasizes the importance of using an FVC as a confirmatory way of assessing nocturia before considering therapeutic interventions.	von einer Patientengruppe liegen Einschätzungen zu nocturia vor mit zwei Instrumenten vor, die verglichen werden beim Vergleich geht es um den Anteil der	LoE 3 Fallserien-Tool: low risk of bias two authors: † Financial interest and/or other relationship with Ferring.



		years (IQR 56.1–66.2)				60.3% scored an equal frequency 6.3% claimed a higher NVF on the I-PSS questionnaire than on the FVC most men did not estimate I-PSS-NVF to be higher than the recorded NVF on the FVC		Patienten, die ihre nocturia mit beiden Instrumenten gleich einschätzen es liegen keine Korrelationsmaße vor	‡ Financial interest and/or other relationship with Celon-Olympus and Ferring AG.
van Haarst, 2012, Journal of Urology [96]	prospective single arm study June 2008 to January 2009 The Netherlands 7 days for FVC frequency volume chart	n=398 forms n= 500 consecutive urological outpatients men and women 301 records were included, including those of 186 men and 115 women with a mean age of 56 years (60.0 and 49.1, respectively, range 19 to 87, p <0.001).	FVC for 7 days	I-PSS question 7 on nocturia (min 1 max 5 pts)	nocturia the date, the time and volume of each daily void, and the times of rising in the morning and going to sleep at night with FVC	I-PSS nocturia question 7 differed in men vs women (2.4 vs 1.9, p <0.009). mean I-PSS question 7 score: 2.2 mean FVC derived nocturia: 1.5 (p <0.001) Correlations were compared with the correlation of the 7-day FVC to I-PSS question 7 (r = 0.63)	The I-PSS nocturia score overestimated the nocturia derived from a 7-day FVC in most patients. When scoring the I-PSS, patients included a degree of bother. The correlation of I-PSS question 7 with mean nocturia increased with FVC duration until day 3. Longer duration FVCs did not improve this correlation. To analyze nocturia FVCs are obligatory but should be used to complement rather than verify the I-PSS.	Berechnungen für Männer und Frauen allerdings eine Berechnung für Männer mit BPH auch extra	LoE 3 Fallserien-Tool: low risk of bias 1 Autor: † Financial interest and/or other relationship with Celon-Olympus and Ferring AG.



						When we selected only men with BPH, the correlation of mean nocturia on the 7-day FVC with question 7 IPSS was only a little lower ($r = 0.60$)			
Yap, 2007, BJU International [97]	observational study design The study used baseline data collected for a randomized, controlled trial on the effectiveness of self-management for men with LUTS The Netherlands February 2003 and June 2004 3 days	n= 140 men with LUTS n=96 (69%) completed FVCs on all 3 days	three 1-day FVCs	no reference test	voiding behaviour FVC: from waking time and time to bed, and volume of urine voided to the closest hour 24-h frequency, daytime frequency, nocturnal frequency, number of urgent episodes, 24-h total voided volume, mean voided volume, maximum voided volume	test-retest-reliability Total voided (95% CI) volume/24 h, mL 0.78 (0.71–0.84) Nocturnal volume, mL 0.60 (0.50–0.70) Volume per void, mL 0.80 (0.73–0.86) Largest void, mL 0.74 (0.67–0.81) No. of voids/24 h 0.73 (0.66–0.81) No. of daytime voids 0.72 (0.64–0.80) No. of nocturnal voids 0.59 (0.49–0.70) No. of urgent voids 0.85 (0.80–0.89)	The measures of voiding behaviour derived from 1-day FVCs had sufficient test-retest reliability to differentiate between high and low levels of voiding symptoms. However, individual measurements could be imprecise, suggesting that, in men with LUTS, a 1-day FVC cannot be used for diagnosis, or monitoring changes in symptom scores after treatment.	nur bedingt zur Beantwortung der Schlüsselfrage geeignet Studie beschreibt Reliabilität des Instrumentes	LoE 3 RoB-Tool for cross-sectional studies: high risk of bias Coi: None declared no information about funding



					and nocturnal volume				
Yap, 2007 European Urology [98]	observational study UK February 2003 and June 2004 3 days	n=140 men with uncomplicated LUTS n=96 patients completed all 3 days	3 day FVC	IPSS	voiding behaviour FV charts: symptom-related measures, such as 24-h frequency, nocturnal frequency, daytime frequency, and number of urgent episodes, and volume-related measures, such as 24-h total intake, 24-h total voided volume, mean voided volume, maximum voided volume, and nocturnal volume.	correlation between IPSS and FVC: 24-h frequency (incomplete emptying) r = 0.25 frequency r = 0.33* Number of urgent episodes frequency r = 0.29* urgency r = 0.29* Nocturnal frequency r = 0.44* Nocturnal volume (ml) r = 0.32* * Correlations are significant at 0.01 level.	Weak associations were found between the self-rated I-PSS scores and FV measures of voiding, suggesting that the accurate assessment of LUTS requires self-reported measures of symptoms and objective measures of voiding behaviour.		LoE 3 RoB-Tool for quantitative studies: high risk of bias, because of the cross sectional study design no coi no information about funding
Yoo, 2018; PloS One [99]	observational study Korea	n=876 patients who underwent transurethral surgery for BPH	FVC IPSS	no reference test	global polyuria 24-hour urine output,	maximum voided volume and the number of daytime voids: related to Q2 IPSS	In this regard, the FVC needs to be used to accurately diagnose global polyuria in patients with BPH and LUTS. In the current study, diabetes	limitations: the results of the current study need to be verified in Western	LoE 3 RoB-Tool for quantitative studies:



	<p>January 2008 and January 2017</p> <p>FVC 72 h</p>	<p>n=214 patients who completed both FVC and I-PSS questionnaire assessments at any time</p> <p>n=193 patients finally included</p> <p>Number of patients, n (%) With global polyuria 19 (9.8)</p> <p>Age, years, mean ± SD 68.0 ± 8.5</p>			<p>nocturnal urine output, number of daytime voids,</p> <p>number of nocturnal voids,</p> <p>maximum voided volume</p> <p>Nocturnal polyuria index, nocturia index</p> <p>nocturnal bladder capacity index</p>	<p>(p = 0.001, p < 0.001), related to Q4 IPSS</p> <p>(p = 0.032, p = 0.010),</p> <p>number of nocturnal voids related to Q2 IPSS</p> <p>(p = 0.001), related to Q7 IPSS</p> <p>(p < 0.001)</p> <p>Nocturnal urine output and Nocturnal polyuria index related to Q7 IPSS</p> <p>(p = 0.041, p = 0.002)</p> <p>nocturia index related to Q2 (p < 0.001) related to Q7 (p < 0.001)</p> <p>nocturnal bladder capacity index related to Q7 (p < 0.001)</p>	<p>mellitus and increased number of voids, which could be easily assessed through history taking, were determined as the predictors of global polyuria. Therefore, in addition to patients with a predominant storage symptom or nocturia, FVC assessment needs to be considered in diabetic patients with BPH and increased number of voids to rule out the presence of global polyuria.</p>	<p>countries before being widely applied</p> <p>Ergebnisse nur bedingt geeignet zur Beantwortung der Schlüsselfrage, da es primär um inhaltliche Korrelationen von zwei Instrumenten geht (FVC und IPSS)</p>	<p>high risk of bias, because of the cross sectional study design</p> <p>no specific funding for this work</p> <p>no coi</p>
--	--	--	--	--	--	---	---	--	--



Tabelle 19: Druck-Fluss-Messung

Schlüsselfrage								
Wann soll eine Druck-Fluss-Messung durchgeführt werden?								
Referenz	Studiencharakteristika	Index-test	Referenz-test	Endpunkt	Effekte	Schlussfolgerung	Bemerkungen	LoE
Clement, 2015; Cochrane Database of Systematic Reviews [100]	n= 2 trials Randomised and quasi-randomised trials n= 339 men (of whom 188 underwent invasive urodynamic studies)	Invasive urodynamic	Clinical management Non-invasive uroynamics	Continuing symptoms of voiding dysfunction after treatment Number of men receiving conservative, drug or surgical treatment Number of men whose intended treatment was changed after invasive uroynamics Need for repeat or alternative treatment	Change management invasive: 24/188 (13%) non-invasive: 0/151 (0%) RR: 39.41 (95% CI 2.42 to 642.74) Undergo surgery invasive: 164/188 (87%) non-invasive: 151/151 (100%) RR: 0.87 (95% CI 0.83 to 0.92) Urine flow rate invasive: 140% non-invasive: 149% p= 0.13 IPSS score invasive: 58% non-invasive: 59% p= 0.22 No evidence was available to demonstrate whether differences in management equated to improved health	Although invasive urodynamic testing did change clinical decision making, we found no evidence to demonstrate whether this led to reduced symptoms of voiding dysfunction after treatment.	lack of outcome information for 24 men in one arm of the trial quality of the evidence of the included trials was low	LoE 1++ ROBIS-Bewertung: low risk of bias no funding



					outcomes (symptoms of voiding dysfunction, improved QoL, adverse effects with invasive urodynamic studies).		
Kim, 2017, PLOS One [101]	n= 19 articles prospective (n=7) and retrospective non-randomised studies (n= 12) n= 2321 patients	preoperative urodynamics	no preoperative urodynamics	BOO treatment outcome	BOO-positive patients was significant for better improvement of: - IPSS: pooled MD, 3.48; 95 % CI 1.72±5.24; p < 0.01) - QoL: pooled MD, 0.56; 95% CI, 0.14±1.02; p = 0.010) - Qmax: pooled MD, 3.86; 95% CI, 2.17±5.54; p < 0.01 - PVR: pooled MD, 32.46; 95% CI, 23.34±41.58 p < 0.01	Our meta-analysis results showed a significant association between urodynamic BOO and better improvements in all treatment outcome parameters. Preoperative UDS may add insight into postoperative outcomes after surgical treatment of benign prostatic hyperplasia.	LoE 2++ ROBIS-Bewertung: low risk of bias no funding
Malde, 2017, Eur Urol [55]	n=42 eligible reports NRE recruiting a total of 4444 patients	PFS	PCT UF DWT IPP NIRS	PCT/ Bladder Outlet Obstruction UF/ Bladder Outlet Obstruction DWT/ Bladder Outlet Obstruction IPP/ Bladder Outlet Obstruction NIRS/ NIRS/	PCT Griffiths Nomogram Sensitivity Median (IQR): 88.9 (76.4–94.4) Range: 64–100 Specificity Median (IQR): 75.7 (69.3–78.3) Range: 63–81 Positive predictive value Median (IQR) 67.7 (67.2–67.9) Range 66.7–68 Negative predictive value	The quality of the current data is insufficient to recommend the routine use of any noninvasive test over pressure-flow studies in diagnosing BOO in men with LUTS.	LoE 2++ ROBIS-Bewertung: low risk of bias no funding



				Bladder Outlet Obstruction	<p>Median (IQR) 93 (85.5–96.5) Range 78–100</p> <p>UF 10ml/s Sensitivity Median (IQR): 68.3 (55.1–74.2) Range 29–100 Specificity Median (IQR): 70.5 (62.3–89.7) Range 37–100 Positive predictive value Median (IQR) 74.3 (66–89.5) 38.4–100 Negative predictive value Median (IQR) 68 (54–76) Range 46.5–100</p> <p>DWT 2mm Sensitivity Median (IQR): 82.7 (65.7–83) Range: 63.6–92 Specificity Median (IQR): 92.6 (76–95) Range: 68–97.3 Positive predictive value Median (IQR)</p>		
--	--	--	--	----------------------------	--	--	--



					<p>90.5 (81–94) Range: 65.7–95.5 Negative predictive value Median (IQR) 85 (76–86) Range: 75–86.2</p> <p>IPP 10mm Sensitivity Median (IQR): 67.8 (56.2–77) Range: 46–80 Specificity Median (IQR): 74.8 (67.4–84) Range: 65–92 Positive predictive value Median (IQR) 73.8 (72–94) Range: 69.6–94 Negative predictive value Median (IQR) 69.3 (63.2–71.9) Range: 46–78.9</p> <p>NIRS algorithm Sensitivity Median (IQR): 85.71 (77–85.8) Range: 68.3–86 Specificity Median (IQR):</p>		
--	--	--	--	--	--	--	--



					87.5 (75–88.1) Range: 62.5–88.9 Positive predictive value Median (IQR) 88.89 (85.7–89) Range: 82.7–89.2 Negative predictive value Median (IQR) 84 (63.4–84.8) Range: 42.9–85.71			
--	--	--	--	--	---	--	--	--



5. Evidenztabelle zum Kapitel ‚Prognosefaktoren für die Progression des BPS‘

Tabelle 20: Prognostische Faktoren

Schlüsselfrage						
Welche prognostischen Faktoren für die Abschätzung der Progressionswahrscheinlichkeit gibt es?						
Referenz	Studien-Charakteristika	Patienten-merkmale	Ergebnisse	Schlussfolgerung	Bemerkungen	LoE
Systematische Übersichtsarbeiten						
Emberton M, 2008, BJU International [102]	16 eligible studies 12 158 patients included from placebo arms of randomized trials of medical therapy studies USA Europe New Zealand Mexico 1951–2005	range of mean age 62.6–66.5 ys	outcomes: change in prostate volume from baseline range 0.8–11.5 mL change in Q max from baseline range – 0.3 to 1.4 mL/s rates of surgery: 1–10% rates of AUR 0.4–6.6%	This systematic review confirms BPH disease progression in the form of increased prostate volume, reduction in maximum urinary flow rate and an increase in the risk of acute urinary retention and surgery. To provide quantitative estimates of effect, access to data from individual participants would be required.	keine Metanalyse möglich laut Autoren, die Daten seien zu heterogen	LoE 2- Robis-Bewertung: high risk of bias due to: only one reviewer for selection and critical appraising the references and no critical appraisal of the included studies funding by GlaxoSmithKline SA Coi: M.G.L. is an employee of GSK; M.E. is an Investigator in the GSK-sponsored Reduce trial in the UK. He has received lecture fees and has acted as a paid consultant for GSK. He is supported by the Comprehensive Biomedical Centre located at University College London and University College London Hospitals NHS Trust. J.M.F. and B.D. have acted as paid consultants for GSK. N.Q. is Director of OXON Epidemiology



						Limited, which carries out consultancy work for GSK.
--	--	--	--	--	--	--

Referenz	Studiencharakteristika	Patientenmerkmale	prognostischer Faktor	Endpunkt	statistische Analyse	Ergebnisse	Schlussfolgerung	LoE
Primärstudien								
Bosch, 2008, European Urology [103]	longitudinal community-based study (Krimpen study) n= 864 completed both rounds 4.2-y follow-up The Netherlands	men aged 50–78 y IPSS of 0–7, 8–19, and 20 points: 76.5%, 21.4%, and 2.1% median PV:30.2 cc (interquartile range, 24.9–37.8 cc)	PV measured by transrectal ultrasound TRUS	LUTS severity IPSS	OR with 95%CI for the 4.2-y incidence of clinically significant changes in symptom severity were calculated for men with real change in PV (with no real change in PV as reference).	n=173 of 864 men (20%) showed progression in terms of a significant increase of 4 IPSS points over a period of 4.2 y age-adjusted odds ratio: OR 1.38 [95%CI, 1.05–1.85]) increase in PV experienced a clinically significant rise in IPSS (>4 points) (26% or >10 cc) age-adjusted odds ratio: OR 1.50 [95%CI, 1.11–2.85]) without a real increase in PV experienced a clinically	Benign prostatic hyperplasia can be characterised as a progressive disease in a certain proportion of men older than 50 yr. Men with growing prostates are at a greater risk of symptomatic deterioration. Men who have prostates that do not grow significantly are more likely to improve symptomatically.	LoE 2- Quips-RoB: at risk of bias due to missing statistical model development research grant from GlaxoSmithKline no coi



						significant reduction in IPSS of 4 or more points than those with a real increase in PV		
Bosch, 2007, Prostate [104]	longitudinal community-based study (Krimpen study) n= 803 had prostate volume measurements from all three clinic visits 4.2-y follow-up The Netherlands	baseline age: 50 to 78 years (mean: 61.1; SD 6.6 y)	age BMI IPSS	three outcomes: log transition zone volume, log peripheral zone volume and log PSA	trivariate multilevel model	<p>rates of change of transition zone prostate volume and PSA with age (estimated correlation=0.9)</p> <p>transition zone prostate volume and PSA (estimated correlation =0.7)</p> <p>peripheral prostate volume and PSA (estimated correlation=0.5)</p> <p>rates of change of peripheral prostate volume and PSA with age (estimated correlation =0.7)</p> <p>Peripheral prostate volume and age (estimated correlation=0.8)</p> <p>transition zone volumes and age: (estimated correlation=0.7)</p>	This method establishes normal prostate volume values by age using prostate volume history in men without prostate cancer. The model provides baseline data from which disease progression might be detected.	LoE 2- Quips-RoB: at risk of bias due to missing of Important Confounders Measured and missing of Definition of the confounding factor no information about funding or coi



<p>Branche, 2018, The Journal of Urology [105]</p>	<p>RCT placebo arm of 2,588 men not receiving α-blockers or 5α-reductase inhibitors at baseline REDUCE study post hoc analysis n=2588 men in the placebo arm USA 4 year follow up</p>	<p>Median age: 62 years (IQR 58 e67) 90% white median MOS-Sleep score: 16.7 (IQR 6.7 e23.3) median BMI 26.8 kg/m2 (IQR 24.29.1) 8% diabetes 15% current smokers. Of the 2,588 men n=1,452 (56%) asymptomatic for urinary symptoms n=1,136 (44%) had LUTS at baseline, defined as I-PSS 8 or greater</p>	<p>sleep problems</p>	<p>lower urinary tract symptoms LUTS LUTS progression was defined as an I-PSS increase of 4 points or greater from baseline, any surgical procedure for BPH or the start of a new BPH drug.</p>	<p>Cox proportional hazards models</p>	<p>n= 580 (51%) with baseline LUTS demonstrated LUTS progression due to: increased IPSS n=442 medication n=114 surgery n= 24 sleep score (continuous) and baseline LUTS (IPSS 8 or greater) HR 1.06, 95% CI 1.01-1.12, p=0.029 quartile 4 sleep score HR 1.23 (95% CI 0.93-1.62) p=0.15 not getting enough sleep to feel rested in the morning (HR 1.04, 95% CI 1.0-1.07) p=0.027) having trouble falling asleep (HR 1.04, 95% CI 1.00-1.07) p=0.031)</p>	<p>Among men with lower urinary tract symptoms, worse sleep scores were associated with the progression of lower urinary tract symptoms and among asymptomatic men worse sleep scores were suggestively associated with the development of lower urinary tract symptoms. If confirmed, these data suggest that sleep problems may precede such symptoms. Whether treating sleep problems would improve lower urinary tract symptoms requires further testing.</p>	<p>LoE 2+ Quips-RoB: low risk of bias Supported by the Department of Veterans Affairs, GlaxoSmithKline and National Institutes of Health K24 CA160653 no coi</p>
<p>Burke, 2006, Urology [106]</p>	<p>prospective population-based</p>	<p>white men aged 40 to 79 y</p>	<p>diabetes mellitus</p>	<p>progression of BPH</p>	<p>least-squares regression line</p>	<p>All ages, diabetes median changes</p>	<p>The results of this study suggest that the presence of diabetes may be</p>	<p>LoE 2- Quips-RoB: at risk of bias</p>



	longitudinal study n=2115 1990 Follow-up for all BPH measures: biennially for 12 years (median follow-up 8.4) Olmsted County, Minnesota, USA	randomly selected n=111 had diabetes at baseline mean age (y): 63.0 ± 10.8 with diabetes mean age (ys): 54.0 ± 10.6 without diabetes		surrogate measures of benign prostatic hyperplasia: baseline questionnaire that assessed lower urinary tract symptom severity similar to those in the AUASI Qmax TRUS to measure PV PSA		AUA† +0.4 (p=0.04) PSA‡ +2.8 (p=0.75) Volume‡ +2.7 (p=0.48) Qmax‡ -4.7 (p=0.06) † Annual raw change ‡ Annual percentage of change	more closely associated with the dynamic components of lower urinary tract function than with benign prostatic hyperplasia progression, per se.	due to unclear prognostic factor measurement funded, in part, by research grants from Merck Research Laboratories as part of the BPH Natural History Study Group and the National Institutes of Health (AR30582). no information about coi
Burke, 2006, American Journal of Epidemiology [107]	prospective population-based longitudinal study n=2115 1990–2003 Follow-up for all BPH measures: biennially for 12 years (median follow-up 8.4)	Age (years) mean (SD) n=2,064 56.59 (10.55) Height (cm) n=1,800 176.56 (6.71) Weight (kg) n=1,799 89.74 (15.45) Body mass index (kg/m ²)	anthropometric measures: height, weight, waist and hip circumferences	progression of components of BPH measured by: AUASI Qmax TRUS to PV PSA	Logistic regression analyses least-squares regression line	Benign prostatic hyperplasia outcome: BMI (kg/m²) 25–29.9 AUASI* slope, >80th percentile¹ OR 0.96 (95% CI 0.69, 1.33) Qmax* slope, <20th percentile² OR 0.74 (95% CI 0.39, 1.39)	The authors conclude that anthropometric measures are not significantly associated with the presence or progression of BPH as measured by American Urological Association Symptom Index scores, peak urinary flow rate, prostate volume, or acute urinary retention. These data provide no evidence	LoE 2- Quips RoB: at risk of bias due to missing information about number and characteristics of men who dropped out funded, in part, by



	<p>Olmsted County, Minnesota, USA</p>	<p>n=1,798 28.75 (4.44)</p> <p>Waist (cm) n=1,800 102.11 (12.10)</p> <p>Hips (cm) n=1,800 104.69 (10.44)</p> <p>Prostate volume (ml) n=446 28.44 (11.81)</p> <p>Qmax* (ml/second) n=1,804 21.25 (9.76)</p> <p>Symptom score n=2,063 6.33 (5.50)</p>				<p>Pvol* slope, >80th percentile² OR 0.77 (95% CI 0.40, 1.46)</p> <p>Body mass index (kg/m²) ≥30 AUASI* slope, >80th percentile¹ OR 1.04 (95% CI 0.73, 1.48)</p> <p>Qmax* slope, <20th percentile² OR 1.04 (95% 0.52, 2.05)</p> <p>Pvol* slope, >80th percentile² OR 1.05 (95% CI 0.53, 2.07)</p> <p>Waist (cm) Second quartile (95–101) AUASI* slope, >80th percentile¹ OR 0.99 (95% CI 0.70, 1.38)</p> <p>Qmax* slope, <20th percentile² OR 1.29 (95% 0.66, 2.52)</p>	<p>of a consistent significant relation between anthropometric measures and BPH</p>	<p>research grants from Merck Research Laboratories as part of the BPH Natural History Study Group and from the National Institutes of Health (AR30582)</p> <p>Conflict of interest: Thomas Rhodes and Cynthia J. Girman are employed by and own stock in Merck & Co., Inc., which manufactures products for the treatment of benign prostatic hyperplasia. C. J. G. also owns stock in Amgen and Genentech</p>
--	---------------------------------------	---	--	--	--	--	---	---



						<p>Pvol* slope, >80th percentile² OR 0.91 (95% CI 0.46, 1.78)</p> <p>Waist (cm) Third quartile (102–109) AUASI* slope, >80th percentile¹ OR 0.84 (95% CI 0.59, 1.19)</p> <p>Qmax* slope, <20th percentile² OR 1.53 (95% 0.77, 3.04)</p> <p>Pvol* slope, >80th percentile² OR 1.22 (95% CI 0.62, 2.38)</p> <p>Waist (cm) Fourth quartile (>109) AUASI* slope, >80th percentile¹ OR 1.11 (95% CI 0.79, 1.56)</p> <p>Qmax* slope, <20th percentile² OR 1.28 (95% 0.62, 2.65)</p> <p>Pvol*</p>		
--	--	--	--	--	--	---	--	--



						<p>slope, >80th percentile² OR 1.08 (95% CI 0.54, 2.17)</p> <p>Waist/hip ratio Second quartile (0.94–0.98) AUASI* slope, >80th percentile¹ OR 0.96 (95% CI 0.68, 1.36)</p> <p>Qmax* slope, <20th percentile² OR 1.23 (95% 0.22, 7.00)</p> <p>Pvol* slope, >80th percentile² OR 0.74 (95% CI 0.12, 4.42)</p> <p>Waist/hip ratio Third quartile (0.99–1.02) AUASI* slope, >80th percentile¹ OR 1.08 (95% CI 0.76, 1.53)</p> <p>Qmax* slope, <20th percentile² OR 1.34 (95% 0.27, 6.70)</p>		
--	--	--	--	--	--	--	--	--



						<p>Pvol* slope, >80th percentile² OR 1.14 (95% CI 0.23, 5.54)</p> <p>Waist/hip ratio Fourth quartile (>1.02) AUASI* slope, >80th percentile¹ OR 1.03 (95% CI 0.72, 1.46)</p> <p>Qmax* slope, <20th percentile² OR 1.36 (95% 0.28, 6.65)</p> <p>Pvol* slope, >80th percentile² OR 0.97 (95% CI 0.20, 4.65)</p> <p>* AUASI; Qmax, peak urinary flow rate; Pvol, prostate volume.</p> <p>¹Annual raw change ²Annual percent change</p>		
Cahn, 2014, Current Urology [108]	retrospective chart analysis n = 44	males who had a diagnosis of BPH with 2 consecutive	prostate specific antigene (PSA) prostate volume	AUR development over a 24-month period	regression analysis	n=4 (9.1%) went on to develop AUR Age	In men with an elevated PVR, increased transrectal ultrasound prostate volume or PSA may	LoE 2- Quips-RoB: at risk of bias due to small



	<p>Albert Einstein Medical Center in Philadelphia, Pennsylvania</p> <p>USA</p> <p>men had 2 consecutive PVR determination greater than 100 ml over a 6-month period</p> <p>PVR</p>	<p>PVRs greater than 100 ml over a 6-month period</p> <p>mean age 58 years</p> <p>PVR (mean PVR 177 ml)</p> <p>PSA (mean PSA 1.65 ng/ml)</p> <p>TRUS prostate volume (mean TRUS volume 36 ml)</p>	<p>post void residual volume</p> <p>age</p>			<p>OR -0.02 (95% CI - 0.10-0.05)</p> <p>PVR OR -0.02 (95% CI - 0.10-0.05)</p> <p>PSA OR -0.02 (95% CI - 0.15-0.09)</p> <p>Prostate volume OR 0.19 (95% CI 0.07-0.31)</p>	<p>help predict which patients have an elevated risk of developing AUR within the next 24 months. This information may influence which patients need early surgical intervention versus medical therapy.</p>	<p>sample size, unclear prognostic factor measurement, and unclear management with confounding factors</p> <p>no information about funding and coi</p>
<p>Carter, 2005, Journal of Urology</p> <p>[109]</p>	<p>longitudinal observational study</p> <p>(Baltimore Longitudinal Study of Aging)</p> <p>n=704</p> <p>USA</p> <p>1958-2000</p>	<p><50 y: median age: 37.7 y (22.5-49.9)</p> <p>50-69.9 y: median age: 59.3 y (50.1-69.9)</p> <p><50ys: Ng/ml PSA 25th percentile:0.3</p> <p>50-69.9 y: Ng/ml PSA</p>	<p>prostate specific antigen PSA at baseline</p>	<p>lower urinary tract symptoms</p> <p>assessed by: medical history questionnaire and IPSS</p>	<p>mixed effects Poisson regression model</p>	<p>there was no statistically significant difference in symptom score distribution across PSA percentiles in men younger than 50 years (p = 0.87) or 50 to 69.9 years old (p = 0.59)</p> <p>when age was used as an independent variable in the model there was no statistically significant</p>	<p>These data suggest that PSA is not a useful predictor of the development of lower urinary tract symptoms in unselected, asymptomatic men.</p>	<p>LoE 2-</p> <p>Quips-Rob: at risk of bias due to missing outcome definition, due to reduced recognition of confounders</p> <p>supported by National Institute on Aging</p>



		<p>25th percentile:0.5</p> <p><50ys: Ng/ml PSA 50th percentile:0.5</p> <p>50-69.9 y: Ng/ml PSA 50th percentile:0.9</p> <p><50ys: Ng/ml PSA 75th percentile:0.8</p> <p>50-69.9 y: Ng/ml PSA 75th percentile:2.0</p>				relationship between baseline PSA and symptom score (p=0.38)		Intramural Research Program and a gift from GlaxoSmithKline no information about coi
<p>Crawfor, 2006, Journal of Urology</p> <p>[110]</p>	<p>RCT (MTOPS trial) placebo arm</p> <p>n=737 men who were randomized to placebo</p> <p>Average length of follow up 4.5 ys</p> <p>USA</p>	<p>Placebo group:</p> <p>Mean age (±SD) 62.5±7.5ys</p> <p>Mean AUA SS ±SD 16.8 ±5.9</p> <p>Mean Qmax (ml/sec) ±SD 10.5 ±2.6</p>	clinical and demographic characteristics	BPH progression defined as the first occurrence of an increase over baseline of at least 4 points in the AUA SS (confirmed by re-administration of the symptom	change in risk were determined using Cox proportional hazards regression analysis	<p>placebo group:</p> <p>overall clinical BPH progression rate: 4.5 events per 100 person-ys</p> <p>n=128 of 737 patients on placebo had a progression event, which corresponded to a 17% cumulative incidence during the study period.</p> <p>TotalPV</p>	Among men in the placebo arm, baseline TPV, PSA, Qmax, PVR and age were important predictors of the risk of clinical progression of BPH.	LoE 2- Quips-Rob: at risk of bias: due to uncomplete definition of prognostic factors, due to missing information about valid and reliable measurement of prognostic factors



		<p>Median +PV (ml) 30.6</p> <p>Mean PVR (ml) ± SD 69.6 ±82.1</p> <p>Mean PSA (ng/ml) ±SD 2.3 ±2.0</p>		<p>score questionnaire within 4 weeks), AUR, urinary incontinence, renal insufficiency or recurrent UTI.</p>		<p>baseline TPV of 31 ml or greater was associated with a significantly greater risk of BPH progression (p ,0.0001)</p> <p>baseline PSA of 1.6ng/dl or greater: significantly greater risk of overall clinical BPH progression (p=0.0009), significantly greater worsening over time of AUA SS (p=0.028), significantly greater risk of AUR (p=0.003) significantly greater need for invasive surgical treatment (p=0.018)</p> <p>Qmax with a baseline of less than 10.6 ml per second: significantly greater risk of BPH progression (p=0.011), significantly greater worsening over time of AUA SS (p=0.005)</p>	<p>Supported by National Institute of Diabetes and Digestive and Kidney Diseases</p> <p>Supported by the National Center for Minority Health and Health Disparities, National Institutes of Health. Financial support and drug products were provided by Merck and Pfizer.</p> <p>‡ Nothing to disclose. § Financial interest and/or other relationship with GlaxoSmith-Kline. I Financial interest and/or other relationship with</p>
--	--	---	--	--	--	--	--



						<p>significantly greater need for BPH related invasive therapy (p=0.033)</p> <p>PVR baseline PVR of 39ml or greater had a significantly greater risk of BPH progression (p=0.0008), significantly greater worsening over time of AUA SS (p=0.003) significantly greater need for BPH related invasive therapy (p=0.004)</p> <p>Age age at baseline 62 years or older significantly greater risk of BPH progression (p=0.0002) significantly greater worsening over time of AUA SS (p=0.0003)</p>		<p>GlaxoSmithKline, National Institutes of Health, Merck, Urology, MedReviews, Oncovance and Bellicum Pharmaceuticals.</p> <p>¶ Financial interest and/or other relationship with Merck.</p> <p>** Financial interest and/or other relationship with MSD, Pfizer, CALGB Clinical Trial Group, GlaxoSmithKline, Sanofi-Aventis, Urologix, Lilly Icos, NIDDK, Threshold Pharmaceuticals, GTX Inc., VA Corporate Studies and Southwest Oncology Group.</p> <p>Financial interest and/or other</p>
--	--	--	--	--	--	--	--	--



								relationship with Merck, Sanofi-Aventis Group, Auxilium, Oncura, Endocare, National Institutes of Health and University of Colorado Cancer Center
Fu, 2016, Urologia Internationalis [111]	longitudinal observational study n=525 April 2013 – April 2016 3-yr-follow up China	MetS group (n = 158) Age, years 65.72±8.53 Height, m 1.68±0.52 Weight, kg 72.4±8.95 BMI, kg/m ² 27.73±2.28	MetS diagnostic criteria of MetS were defined according to the updated National Cholesterol Education Program-Adult Treatment Panel III criteria for Asian Americans, with the presence of at least 3 of 5 characteristics: (1) BMI >30 kg/m ² ; (2) TG = 1.7 mmol/l; (3) HDL-C <1.03 mmol/l; (4) blood pressure = 130/85 mm Hg or use of antihypertensive	BPH clinical progression: increase at least 4 points in IPSS, AUR or the presence of renal insufficiency, recurrent urinary tract infection or urinary incontinence .	univariate and multivariate regression analysis	multivariate analyses for BPH clinical progression and the individual components of MetS Diabetes mellitus DM HR 1.37 (95% CI 1.12–1.59) Hyperlipidemia HR 0.91 (95% CI 0.65–1.26) Hypertension HR 1.50 (95% CI 1.08–1.94) Obesity HR 0.89 (95% CI 0.70–1.13)	The present results suggest that MetS, in particular, DM and hypertension, may accelerate the clinical progression of BPH in community-dwelling middle aged and older men.	LoE 2+ Quips-RoB: low risk of bias supported by the grant from the foundation of Shougang Corporation (No. 2013-20-1). no coi



			medications; and (5) FBG = 5.6 mmol/l, previous diagnosis of type 2 diabetes mellitus (DM) or use of antidiabetic medications or insulin					
Fukuta, 2011, Prostate [112]	longitudinal observational community-based study n=104 Japan 15 y follow up	suggestive of BPH in men aged 40–79 ys Baseline prostate volume (ml) median (range) 17.4 (7.9–36.0)	internal prostatic architecture Age decades PV	Prostatic Growth changes in PV over time	Multiple linear regression analysis	Multiple linear regression analysis: Age OR 0.125 (95% CI - 1.707–1.957) Prostate volume OR 2.657 (95% CI 0.303–5.011) Internal prostatic architecture OR 5.162 (95% CI 2.964–7.361)	This was the first study by longitudinal community-based study that the PV in Japanese men increased during 15 years. The internal prostatic architecture on TRUS is useful for predicting future prostatic growth.	LoE 2- Quips-RoB: at risk of bias due to not considering confounding factors Grant sponsor: Japan Society for the promotion of Science; Grant number: 19591862; Grant sponsor: Gohtaro Sugawara-Memorial Research Fund for Urologic Diseases no information about coi



<p>Lamb, 2011, BJU International [113]</p>	<p>longitudinal observational study (n=196) n=100 randomly selected n=96 analysed UK mean (range) follow-up 7 (7-8) ys</p>	<p>patients presenting for TRUS and biopsy of the prostate Age (years) Mean 73 Range 48-89</p>	<p>Immunohistochemistry CD4+ And CD8+ T-lymphocytes in a TRUS biopsy</p>	<p>marker of disease progression included: AUR 4 point rise in IPSS prescription of medical therapy (α-blocker or 5-α-reductase inhibitor) bladder outlet surgery</p>	<p>Jonckheere-Terpstra test to look for trends Pearsson-Clopper 95% exact CIs were calculated for specificity, sensitivity and predictive values.</p>	<p>Acute urinary retention No n=86 Yes n=10 +4point IPSS rise No n=89 Yes n=7 Addition of medication No n=64 Yes n=32 Bladder outlet surgery No n=85 Yes n= 11 Progression to acute urinary retention (AUR) according to a threshold mean of >1.35 + CD8+ cells per field No AUR < 1.35: n= 63 ≥ 1.35 n=23 AUR < 1.35: n= 4 ≥ 1.35 n=6 Fisher’s exact test for significance (P=0.04)</p>	<p>The present study, despite certain trends, shows no evidence for an association between CD4+ and CD8+ T-lymphocytes and the progression of LUTS in BPH.</p>	<p>LoE 2+ Quips-RoB: low risk of bias Alastair Lamb is a Clinical Research Fellow funded by GSK. Source of Funding for this study: Prostate UK.</p>
--	--	---	---	---	--	---	--	--



						<p>Progression characteristics and T-lymphocyte Acute Urinary Retention No retention (n = 86) AUR (n = 10) CD4: p=0.90 CD8: p=0.14</p> <p>>4 point increase in IPSS NO change (n=89) >4 point progression (n=7) CD4: p=0.98 CD8: p=0.24</p> <p>Medical Treatment No medication (n=64) Medication (n=32) CD4: p=0.15 CD8: p=0.55</p> <p>Bladder outlet surgery No surgery (n=85) Surgery (n=11) CD4: p=0.92 CD8: p=0.71</p>		
Marshall, 2014, Prostate Cancer & Prostatic Diseases [114]	longitudinal observational study Osteoporotic Fractures in Men Study	community-dwelling US men aged >65 ys men who had all four AUA-SI	Lifestyle, body mass index (BMI) mobility, mental health (Short-Form 12),	lower urinary tract symptoms LUTS Categories of LUTS	Multivariable logistic regression	mean (s.d.) change in the AUA-SI score from baseline to the fourth assessment: 1.0 (4.6)	Several non-urological lifestyle and health factors were independently associated with risk of LUTS progression in older men.	LoE 2- Quips-Rob: at risk of bias due to not considering confounding factors



	<p>n=1740 USA mean follow-up 6.9 (0.4) ys</p>	<p>assessments, who remained free from diagnosed prostate cancer, and who reported no treatment for LUTS or BPH</p> <p>mean age (SD) 71.4 (4.8)</p> <p>body mass index (BMI) 27.3 (3.7)</p> <p>AUA SI 6.0 (4.8)</p>	<p>medical history prescription medications</p>	<p>severity defined from the AUA-SI: mild (0-7 points), moderate (8-19 points) or severe (20-35 points)</p>		<p>Men in progressing compared with stable trajectories:</p> <p>mobility limitations OR 2.0, 95% CI: 1.0-3.8</p> <p>poor mental health OR 1.9, 95% CI: 1.1-3.4</p> <p>BMI >25.0 OR 1.7, 95% CI: 1.0-2.8</p> <p>hypertension OR 1.5, 95% CI: 1.0-2.4</p> <p>back pain OR 1.5, 95% CI: 1.0-2.4</p>	<p>This work was supported by the National Institute for Diabetes and Digestive and Kidney Diseases (Grant R21 DK083675 to LMM and JKP). The MrOS Study is supported by National Institutes of Health funding. The following institutes provide support: the National Institute on Aging (NIA), the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), the National Center for Advancing Translational</p>
--	---	---	---	---	--	---	--



								<p>Sciences (NCATS) and NIH Roadmap for Medical Research under the following grant</p> <p>Dr Parsons and Dr Marshall received funding as co-Principal Investigators for this research from the US National Institutes of Health under grant R21 DK083675. Dr Parsons also reports relationships with AMS and Sophiris outside the submitted work. All other authors declare no conflict of interests.</p>
Martin, 2014, Journal of Urology	longitudinal observational study	only men who had completed	metabolic, lifestyle and physical factors	LUTS progression AUA-SI	multinomial logistic regression models	Greater abdominal fat mass, lower income and a diagnosis of	Lower urinary tract symptoms may progress or remit. Even accounting for	LoE 2- Quips-RoB: at risk of bias



<p>[115]</p>	<p>FAMAS (Florey Adelaide Male Ageing Study) n=780 Australia mean follow up 5.0 ± 0.2 ys</p>	<p>the AUA-SI at T1 and T2 at baseline: men who reported mild LUTS: 81.9% moderate LUTS: 15.6% severe LUTS: 2.5%</p>				<p>depression were associated with progression of storage LUTS. Lower household income, lower plasma HDL cholesterol, higher estradiol, a diagnosis of depression and erectile dysfunction at baseline were associated with the progression of voiding symptoms <i>(konkrete Zahlen dazu nur in Schaubildern)</i></p>	<p>medication use, progression may be associated with modifiable disease, or metabolic or behavioral factors, which are also risk factors for type 2 diabetes and cardiovascular disease. These factors should be looked for and managed.</p>	<p>due to reduced recognition of confounders Supported by the Australian National Health and Medical Research Council (Project Grant #627227) no information about coi</p>
<p>Mondul, 2014, Journal of Urology [116]</p>	<p>longitudinal observational study Health Professionals Follow-up Study (HPFS) n=6,461 USA followed for over 16 years</p>	<p>included men: when they first experienced an IPSS of 8 to 14 International prostate symptom score (IPSS)</p>	<p>obesity weight gain height and weight BMI waist and hip circumference measurement assessed every 2y</p>	<p>LUTS progression: 1) a less stringent definition of "moderate or worse LUTS" defined as IPSS of =15 or surgery or medication use (n=1,680), and 2) a more stringent definition of "severe</p>	<p>Cox proportional hazards regression to estimate the HR and 95% CI of LUTS incidence or progression</p>	<p>Risk of LUTS (n=4,088) increased with increasing body mass index (BMI ≥35 vs 23-<25 kg/m2: HR=1.61; 95% CI 1.31-1.99, p-trend<0.0001) waist circumference (>42 vs ≤33 in: HR=1.39, 95% CI 1.19-1.63 p-trend<0.0001) weight gain from age 21 (≥50 lbs vs stable weight:</p>	<p>Men with higher total and abdominal adiposity or who gained weight were more likely to develop LUTS or experience progressive LUTS. Our findings support that obesity may be an important target for LUTS prevention and intervention.</p>	<p>LoE 2+ Quips-Rob: low risk of bias Funding: The Urologic Diseases in America Project (N01 DK70003) and by Public Service grants R01 DK45779 and P01 CA55075 (Harvard), and P50 DK082998</p>



				LUTS“ defined as IPSS of =20 or surgery or medication use (n=1,691).		HR=1.31, 95% CI 1.17-1.46 p-trend=<0.0001) Risk of LUTS progression n=1,691 increased with BMI (≥35 vs 23-<25 kg/m2: HR=1.44, 95% CI 1.04-2.00 p-trend=<0.0001) weight gain from 21 years of age (≥50 lbs vs stable weight: HR=1.35, 95% CI 1.14-1.60 p trend=<0.0001) waist circumference (>42 vs ≤33 in: HR=1.32, 95% CI 0.95-1.85 p trend=0.005		(Hopkins) from the Department of Health and Human Services, the National Institutes of Health no information about coi
Meigs JB, 1999, Journal of Urology [117]	longitudinal observational study Health Professionals Follow up Study n=6100 USA 1992 to 1995	no data about mean age etc provided	Baseline clinical risk factors Baseline medication use Baseline individual lower urinary tract symptoms	AUR requiring catheterization	multivariate adjusted logistic regression models	n=82 episodes of acute urinary retention requiring catheterization (crude incidence 5.2/1,000 person-years, (95% CI 4.1 to 6.4) sampling weighted incidence 4.5/1,000 person-years, (95% CI 3.1 to 6.2)	Acute urinary retention occurred relatively infrequently but older age, moderate or severe lower urinary tract symptoms, a diagnosis of benign prostatic hyperplasia and specific drug therapies significantly increased the risk of occurrence.	LoE 2- Quips-Rob: at risk of bias: due to selective sampling (only a certain group pf health professionals) Supported by Grants



						<p>between 1992 and 1995 (mean follow up 2.6 years, range 1.1 to 3.1)</p> <p>Age adjusted ratios for incident acute urinary retention by clinical and medication risk factors</p> <p>Baseline clinical risk factors</p> <p>Nonwhite race OR 1.1 (95% CI 0.4-3.6)</p> <p>Obesity OR 1.0 (95% CI 0.6-1.8)</p> <p>High waist-to-hip ratio OR 1.1 (95% CI 0.5-2.2)</p> <p>cigarette smokers OR 1.3 (95% CI 0.5-2.9)</p> <p>Diabetes mellitus OR 0.6 (95% CI 0.2-1.9)</p> <p>Hypertension OR 1.8 (95% CI 1.2-2.9)</p>	<p>DK45779, CA55075 and HL35464 from the National Institutes of Health, and by PORT I1 Grant HS 08397 from the Agency for Health Care Policy and Research.</p> <p>no information about coi</p>
--	--	--	--	--	--	--	--



						<p>History of prostatitis OR 1.0 (95% CI 0.5-1.7)</p> <p>Less than 3 ejaculation/mo OR 1.0 (95% CI 0.6-1.7)</p> <p>Elevated PSA test for prostate cancer screening OR 1.8 (95% CI 0.4-7.6)</p> <p>Baseline medication use: Calcium blocker OR 2.2 (95% CI 1.2-3.9)</p> <p>beta-blocker OR 1.9 (95% CI 1.1-3.3)</p> <p>Other (nondiuretic) antihypertensive OR 2.8 (95% CI 1.5-5.3)</p> <p>Antiarrhythmic OR 3.3 (95% CI 1.1-9.3)</p> <p>Age and multivariate adjusted odds ratios for incident acute urinary</p>	
--	--	--	--	--	--	--	--



						<p>retention among men with a clinical diagnosis of BPH by baseline lower urinary tract symptoms and 2-year symptom change:</p> <p>Sensation of incomplete bladder emptying OR 2.3 (95% CI 1.3-4.2)</p> <p>Having to void again after less than 2 hrs. OR 2.6 (95% CI 1.4-4.9)</p> <p>Stopping and starting several times during voiding OR 1.2 (95% CI 0.7-2.3)</p> <p>Difficulty postponing voiding OR 1.7 (95% CI 0.9-3.1)</p> <p>Weak urinary stream OR 1.9 (95% CI 1.02-3.5)</p> <p>Having to push or strain to begin voiding</p>	
--	--	--	--	--	--	---	--



						<p>OR 1.8 (95% CI 0.9-3.5)</p> <p>Typically got up 3 times/night or more to void during last mo OR 1.6 (95% CI 0.8-3.0)</p> <p>2-y change in overall lower urinary tract symptoms to more severe symptom score category: OR 1.3 (95% CI 0.6-2.8)</p> <p>2-y change in individual lower urinary tract symptoms: Sensation of incomplete bladder emptying OR 2.2 (95% CI 0.9-5.2)</p> <p>Having to void again after less than 2 hrs. OR 1.7 (95% CI 0.6-4.9)</p> <p>Stopping and starting several times during voiding OR 2.3 (95% CI 1.1-5.0)</p>	
--	--	--	--	--	--	--	--



						<p>Difficulty postponing voiding OR 2.5 (95% CI 1.1-5.9)</p> <p>Weak urinary stream OR 3.2 (95% CI 1.2-9.1)</p> <p>Having to push or strain to begin voiding OR 3.2 (95% CI 1.5-7.2)</p> <p>Typically got up 3 times/night or more to void during last mo OR 2.3 (95% CI 0.9-6.3)</p>		
<p>Patel, 2018, Prostate Cancer and Prostatic Diseases</p> <p>[118]</p>	<p>post-hoc analysis of the 4-year REDUCE study multicenter, randomized, double blind, placebo-controlled study</p> <p>n=1526 from placebo arm of REDUCE</p> <p>USA</p>	<p>mean age 62 y (SD = 6)</p> <p>PSA, ng/mL 5.7 (1.9) (SD)</p> <p>PSA-groups 2.5-4 ng/mL n=335 (21.8%)</p> <p>4.1-6 ng/mL n=589 (38.4%)</p> <p>6-10 ng/mL</p>	<p>prostate specific antigene PSA</p>	<p>Incident LUTS: defined as the first report of medical treatment, surgery, or sustained clinically significant LUTS among men who were asymptomatic at baseline.</p>	<p>Cox proportional hazards</p> <p>cumulative incidence curves, and the log-rank test</p>	<p>Baseline PSA (continuous) HR 1.08 (95% CI 1.00-1.17) p=0.040</p> <p>Baseline PSA 4.1-6.0 ng/mL HR 1.60 (95% CI 1.04-2.45) p=0.032</p> <p>Baseline PSA 6-10 ng/mL HR 1.68 (95% CI 1.10-2.57) p=0.016</p>	<p>Men with mild to no LUTS but increased baseline PSA are at increased risk of developing incident LUTS presumed due to benign prostatic hyperplasia.</p>	<p>LoE 2+</p> <p>Quips-RoB. low risk of bias</p> <p>REDUCE study was funded by GlaxoSmithKline.</p> <p>no coi</p>



		n=610 (39.8%)						
Roehrborn, 2000, Journal of Urology [119]	randomized, placebo controlled Proscar Long-Term Efficacy and Safety study n=164 placebo treated men in the subgroup USA follow up: 4 ys	men diagnosed with BPH Mean baseline SD (range) age 63ys ±6.1 (50 to 77) Mean baseline (ml.) prostate vol. SD (range) 54.6 ± 25.9 (14 to 222) Mean baseline (ng./ml.) PSA SD (range) 2.7 ± 2.1 (0.2 to 9.4)	age, baseline prostate volume PSA	prostate growth (absolute and percent volume change)	Multiple linear regression	absolute changes in prostate volume Age p= 0.88 Prostate volume p= 0.54 PSA p< 0.001 percent changes in prostate volume Age p= 0.58 Prostate volume p= 0.1 PSA p= 0.001 <i>(keine Wahrscheinlichkeitswerte HR, OR oder RR berichtet, nur statistische Signifikanz)</i> "Multiple linear regression was performed using absolute or percent volume change at 4 years as the dependent variable, and age, baseline volume and baseline PSA as independent variables."	Serum PSA is a stronger predictor of growth of the prostate in placebo treated patients than age or baseline prostate volume. Since prostate volume is a risk factor for acute urinary retention and the need for BPH related surgery, the ability of PSA to predict prostate growth may be an important factor when considering individual treatment options for BPH. Such use of PSA represents a shift in paradigm away from focusing solely on symptoms of BPH toward a more comprehensive approach with consideration of predicting and preventing risk factors of BPH related outcomes.	LoE 2+ Quips-Rob: low risk of bias Financial interest and/or other relationship with Merck. Financial interest and/or other relationship with Glaxo, Synthelabo, Abbott, U.S. Surgical, Vida Med, Dornier, Urologix and Pfizer. Financial interest and/or other relationship with Serono, Unimed, Biotek, Wyeth Ayerst, Organon and Smith Kline. Merck, West Point, Pennsylvania.



								no information about funding
--	--	--	--	--	--	--	--	------------------------------



6. Evidenztabelle zum Kapitel ‚Medikamentöse Therapie‘

Tabelle 21: Phytotherapeutika vs. Monotherapie

Schlüsselfrage										
Welche Effekte zeigen die Phytotherapeutika als Mono- oder Kombinationspräparate bei Patienten mit BPS im Vergleich zur Monotherapie?										
Referenz	Studien-design	Studien-charakteristika	Studienziel	Patienten-merkmale	Intervention	Kontrolle	Ergebnisse	Schlussfolgerung	Bemerkungen	LoE
Chinesische Kräutermedizin										
Ma, 2013, Asian Journal of Andrology [120]	Systematic review with meta-analysis	n=31 RCTs (n=11 RCTs for meta-analysis) Searched up to July 2011	This study aimed to evaluate the efficacy and side effects of Chinese herbal medicine versus placebo or active control in the treatment of symptomatic BPH.	n=2493 subjects sample size of included studies ranged from 40 to 160 patients prostate volumes varied from 22.8 to 52.4 ml	Chinese herbal medicine with or without adjuvant use with western medication	<ul style="list-style-type: none"> • Placebo <u>Western medication</u> • tamsulosin (n=3) • finasteride (n=1) • tamsulosin+ finasteride (n=1) • Pygeum africanum (n=1) • Saw palmetto (n=1) 	<p>QoL <u>Chinese herbal medicine vs. western medicine (n=3)</u> SMD -1.07 (-1.47, -0.68) p<0.00001 favours chinese herbal medicine</p> <p><u>Chinese herbal medicine vs. alpha-adrenic blocker (n=2)</u> SMD -1.13 (-1.70, -0.56) p=0.0001 favours chinese herbal medicine</p> <p><u>Chinese herbal medicine vs. phytotherapy (n=1)</u></p>	The evidence is too weak to support the efficacy of Chinese herbal medicine for BPH due to the poor methodological quality and small number of trials included.	no information about efforts were made to minimise error in risk of bias assessment Twenty-seven studies (87.1%) were carried out in China and published in Chinese language journals from 1997 to 2011. no conflict of interest declared The present study was supported by	LoE: 1++ RoB: low



						<p>SMD -0.88 (-1.53, -0.23) p=0.008 favours chinese herbal medicine</p> <p>Prostate volume <u>Chinese herbal medicine vs. western medicine (n=5)</u> SMD -0.31 (-0.58, -0.04) p=0.03 favours chinese herbal medicine</p> <p><u>Chinese herbal medicine vs. alpha-adrenic blocker (n=2)</u> SMD -0.57 (-0.95, -0.18) p=0.004 favours chinese herbal medicine</p> <p><u>Chinese herbal medicine vs. alpha-adrenic blocker+5ARI (n=1)</u> SMD -0.50 (-0.99, -0.01) p=0.05</p> <p><u>Chinese herbal medicine vs. phytotherapy (n=2)</u> SMD 0.00 (-0.33, 0.33) p=0.99</p>	<p>the Hospital Authority of Hong Kong, China</p> <p>results only shown for the comparison chinese herbal medicine vs. western medicine</p>	
--	--	--	--	--	--	---	--	--



							<p>Adverse events</p> <p><u>Chinese herbal medicine vs. western medicine (n=8)</u> RR 0.50 (0.32, - 0.78) p=0.003 favours chinese herbal medicine</p> <p><u>Chinese herbal medicine vs. alpha-adrenic blocker (n=4)</u> RR 0.67 (0.40,1.11) p=0.12</p> <p><u>Chinese herbal medicine vs. 5ARI (n=1)</u> RR 0.07 (0.00,1.15) p=0.06</p> <p><u>Chinese herbal medicine vs. phytotherapy (n=2)</u> RR 5.81 (0.25,134.73) p=0.27</p> <p><u>Chinese herbal medicine vs. alpha-adrenic blocker+5ARI (n=1)</u></p>		
--	--	--	--	--	--	--	--	--	--



							RR 0.28 (0.08,0.93) p=0.04 favours chinese herbal medicine			
							<u>Chinese herbal medicine+western medicine vs. western medicine (n=4)</u> RR 1.56 (0.53,4.60) p=0.42			
							<u>Chinese herbal medicine+ alpha- adrenic blocker vs. alpha-adrenic blocker (n=3)</u> RR 1.56 (0.53,4.60) p=0.42			
Eviprostat										
Hwang, 2018, Cochrane Database of Systematic Reviews [23]	Systematic review with meta- analysis	n=22 RCTs Searched up to 31 May 2018	To evaluate the effects of naftopidil for the treatment of LUTS associated with BPH.	n= 1 RCT with naftopidil vs. eviprostat 36 patients treated with naftopidil 13 patients treated with eviprostat	<ul style="list-style-type: none"> • Tamsulosin • Silodosin • Propiverine • Eviprostat 	Naftopidil	Naftopidil vs. eviprostat (n=1) <u>IPSS</u> MD -6.3 (95% CI -9.46; -3.14), p= 0.99 (Favours naftopidil) <u>IPSS-QoL</u>	Compared to Eviprostat, naftopidil likely resulted in a clinically important reduction in urological symptom scores and improved QoL.	no potential conflicts of interest, international support: Chonnam National University Medical School, Gwangju, Korea, South; Minneapolis VA Medical Center,	LoE: 1++ RoB: low



							MD -1.5 (95% CI -2.36; -0.64), p= 0.99 (Favours naftopidil)		Minneapolis, Minnesota, USA; University of Minnesota, Minneapolis, Minnesota, USA	
							0 treatment withdrawals for any reason or adverse events in both groups		only results for phytotherapy reported	
Pollenextrakte										
Antonelli, 2019, Phytotherapy Research [121]	Umbrella review (systematic review of systematic review)	n= 5 systematic reviews (one with meta-analysis) Searched up to January 27, 2019	The present umbrella review aims to qualitatively summarize results of existing systematic reviews about the therapeutic efficacy of orally administered pollen in the management of any nonallergic disease. A secondary aim of this work is to collect information from existing	n= 191 to 5217 patients n= 1 review with meta-analysis of patients with chronic prostatitis/chronic pelvic pain syndrome n= 3 reviews with LUTS/BPH/chronic prostatitis n= 1 review with all diseases	pollen extract	any type of comparison (placebo, usual care, other integrative treatments, or no control)	<u>pollen extract vs. placebo or other treatments</u> overall effect size significantly favored the pollen group (OR = 0.52 [0.34–0.81]); p = .02 for chronic prostatitis/chronic pelvic pain syndrome • flower pollen extract can significantly improve symptoms and QoL of patients affected by chronic prostatitis/chronic pelvic pain	In conclusion, results of the present umbrella review suggest that flower pollen extracts may be useful as a complementary remedy for the management of some nonallergic diseases, mainly symptomatic genitourinary problems like benign prostatic hyperplasia and chronic prostatitis.	no potential conflicts of interest and funding	LoE 1++ RoB: low



			reviews about pollen therapeutic dosage, toxicity, and tolerability.				syndrome (n=1) <ul style="list-style-type: none"> no significant adverse events were reported (n=1) positive results in favor of the efficacy of grass pollen extract (n=3) 			
Serenoa repens										
Cai, 2020, American Journal of Mens Health [122]	Systematic review with meta-analysis	n=4 RCTs 2002-2014 Searched up to May 2019	To assess the efficacy and safety of tamsulosin compared with Serenoa repens for the treatment of LUTS/BPH, this study performed a systematic review and metaanalysis of RCTs.	n=1080 patients with BPH/LUTS patients from Serbia, Europe, Turkey and Italy Quality level of the studies: low (n=3) to moderate (n=1)	Serenoa repens (320mg) n=543	Tamsulosin (0.4 mg) n=537	IPSS (n=4) MD: 0.63 (95% CI [-0.33, 1.59] p=0.2 QoL (n=3) MD: 1.51 (95% CI [-1.51, 4.52] p=0.33 Qmax (n=4) MD: 0.27 (95% CI [-0.15, 0.68] p=0.21 Postvoid residual volume (n=3) MD: -4.23 (95% CI [-22.97, 14.44] p=0.65 Prostate volume (n=3)	Serenoa repens had the same effect in treating BPH compared with tamsulosin in terms of IPSS, QoL, and PVR after at least 6-month treatment cycle. The latter had a greater improvement in prostate volume compared with the former. Serenoa repens did not increase the risk of adverse events especially with respect to ejaculation disorders and libido decrease.	no information if efforts were made to minimise error in study selection and data collection serious heterogeneity (I ² >75%) for QoL, PVR, PSA This work was supported by the National Nature Science Foundation of China. no potential conflicts of interest	LoE 1++ RoB: low



							<p>MD: -0.29 (95% CI [-0.41, -0.17] p<0.00001)</p> <p>PSA (n=4) MD: 0.46 (95% CI [-0.06, 0.97] p=0.08)</p> <p>Ejaculation disorders (n=3) MD: 12.56 (95% CI [3.83, 41.18] p<0.0001)</p> <p>Libido decrease (n=3) MD: 5.40 (95% CI [1.17, 24.87] p=0.03)</p>			
Russo, 2020, European Urology Focus [123]	Systematic review with network meta-analysis	n=22 RCTs Searched up to December, 31 2018	We aimed to compare the clinical efficacy of hexanic extract of serena repens versus non-hexanic extract of serona repens versus placebo versus alpha-blockers in patients affected by LUTS secondary to BPE through a	n=8564 patients Mean age: 64.27 y (SD 8.01 y) Mean IPSS: 18.23 (SD 4.64) Mean Qmax: 10.29 ml/s (SD 3.21) Postvoid residual: 68.99 ml (SD 49.58)	Serenoa repens (hexanic extract and non-hexanic extract)	<ul style="list-style-type: none"> • Placebo • Alpha-blocker 	<p><u>Overall mean changes in IPSS against placebo</u> Tamsulosin: -1.50, Silodosin: -2.16, Terazosin: -4.29, Alfuzosin: -1.75, Non-hexanic extract Serenoa repens: -1.60 Hexanic extract Serenoa repens: -1.24</p> <p><u>Overall mean changes in peak flow (ml/s) against placebo</u></p>	We demonstrated that Serenoa repens did not show clinically meaningful improvement in LUTS and peak flow.	<p>no information, if efforts were made to minimise error in the study selection and the risk of bias assessment</p> <p>no funding and no conflict of interests declared</p>	<p>LoE 1-</p> <p>RoB: high</p>



			network meta-analysis method.				<p>Tamsulosin: +1.45, Silodosin: +0.76, Terazosin: +1.35, Alfuzosin: +3.57, Non-hexanic extract Serenoa repens: +2.4 Hexanic extract Serenoa repens: +1.04</p> <p><u>SUCRA rankograms score</u> Terazosin (99.6%), Alfuzosin (53.7%), tamsulosin (42.3%), silodosin (68.5%), hexanic extract Serenoa repens (36.7%) non-hexanic extract Serenoa repens (47.3%)</p>			
Vela-Navarrete, 2018, BJUI [124]	Systematic review with meta-analysis	n=27 studies (15 RCTs, 12 cohort studies) Searched up to April 2017	To comprehensively evaluate the efficacy and safety of the hexanic extract of Serenoa repens (Permixon), at	n= 5800 patients	Permixon	<ul style="list-style-type: none"> • placebo • alpha-blocker • 5ARI 	<p>Permixon vs. alpha-blocker IPSS (n=4) WMD: 0.57 (-0.27;1.42) p=0.183</p> <p><u>Qmax (n=2)</u> WMD: -0.02 (-0.71; -0.66) p=0.946</p>	Permixon reduced nocturia and improved Qmax compared with placebo and had a similar efficacy to tamsulosin and short-term 5-ARI in relieving LUTS. Permixon appears to be an efficacious and	Detailed information to conflict of interest in the paper. This study was funded by Pierre Fabre Iberica, S.A, Barcelona, Spain	LoE Range 1++ to 2++ (mixed study designs)



			a dose of 320 mg daily, as monotherapy for the treatment of lower urinary tract symptoms associated with benign prostatic hyperplasia			<p><u>Prostate volume (n=2)</u> WMD: -0.87 (-2.64; -0.9) p=0.734</p> <p><u>PSA (n=2)</u> WMD: 0.05 (-0.13;0.22) p=0.603</p> <p>Permixon vs. 5ARI <u>IPSS (n=3)</u> WMD: 0.46 (-0.41;1.43) p=0.296</p> <p><u>PSA (n=2)</u> WMD: 0.97 (0.60;1.34) p<0.001</p> <p>Adverse drug reaction (Permixon) gastrointestinal disorders being the most frequent (3.8%)</p>	well-tolerated therapeutic option for the longterm medical treatment of LUTS/BPH.	results only shown for the comparison serenoa repens vs. monotherapy	RoB: low
Novara, 2016, European Urology Focus [125]	Systematic review with meta-analysis	n=12 RCTs Search date: January 2016	To evaluate the efficacy and safety of Permixon in the treatment of LUTS/BPH.	patients with LUTS/BPH	<ul style="list-style-type: none"> • Permixon vs. Placebo (n=7) • Permixon vs. Tamsulosin (n=2) • Permixon or combination 	<p><u>Permixon vs. tamsulosin</u> no statistical difference: • mean change in IPSS (WMD 1.15; 95% CI, -1.11 to 3.40; p = 0.32)</p>	Our meta-analysis showed that Permixon decreased nocturnal voids and Qmax compared with placebo and had efficacy in	no detailed inclusion and exclusion criteria, no information if efforts were made to minimise error in the risk of	LoE: 1- RoB: high



					<p>vs tamsulosin monotherapy (n = 2)</p> <ul style="list-style-type: none"> • Permixon vs. finasteride (n=1) 	<ul style="list-style-type: none"> • Qmax (WMD - 0.16; 95% CI, -0.60 to 0.28; p = 0.48) • adverse events (OR 0.95; 95% CI, 0.72–1.26; p = 0.72) <p><u>Permixon plus tamsulosin with tamsulosin alone</u></p> <ul style="list-style-type: none"> • mean IPSS significantly decreased (WMD 0.31; 95% CI 0.13–0.48; p < 0.01) • Qmax improvement (WMD 0.10; 95% CI, -0.02 to 0.21; p = 0.10) • Adverse events: favoring tamsulosin monotherapy was shown (OR 1.63; 95% CI, 0.94–2.84; p = 0.08) <p><u>Permixon vs. finasteride</u> similar efficacy:</p> <ul style="list-style-type: none"> • improvement in IPSS (-5.8 	<p>relieving LUTS similar to tamsulosin and short-term finasteride. Moreover, Permixon had a favorable safety profile with a very limited impact on sexual function, which is significantly affected by all other drugs used to treat LUTS/BPH.</p>	<p>bias assessment and no presentation of the assessment results</p> <p>serious heterogeneity (I²>75%) for IPSS (Permixon vs. Tamsulosin)</p> <p>no funding and no conflict of interests declared</p> <p>results only shown for the comparison phytotherapy vs. monotherapy</p>
--	--	--	--	--	---	---	---	--



							<p>with Permixon vs -6.2 with finasteride; p = 0.17)</p> <ul style="list-style-type: none"> • quality of life (-1.5 vs -1.4, respectively; p = 0.14) • increase in Qmax was slightly higher with finasteride (+2.7 vs +3.2, respectively; p = 0.035) • libido and impotence were less common in the Permixon arm • Sexual function score was significantly lower with Permixon than with finasteride (7.9 vs 9.3; p < 0.01) 			
Tacklind, 2012, Cochrane Database of Systematic Reviews [126]	Systematic review + meta-analysis	n=32 RCTs Searched up to January, 1 2012 Weighted mean follow-up:	This systematic review aimed to assess the effects and harms of Serenoa repens in the treatment of men with	n= 5666 men Weighted mean age: 64.6 y (40-90 y)	<ul style="list-style-type: none"> • Serenoa repens • Serenoa repens+ Urtica dioca • Serenoa repens+ tamsulosin 	<ul style="list-style-type: none"> • Placebo • Tamsulosin • Tamsulosin+Placebo 	<p>Serenoa repens vs. tamsulosin</p> <p><u>IPSS total score</u></p> <p><u>mean change from baseline</u></p> <p>(n=2)</p> <p>MD: -0.52 (95% CI: -1.91,0.88)</p>	Serenoa repens, at double and triple doses, did not improve urinary flow measures or prostate size in men with lower urinary tract symptoms	no conflict of interests declared partially funded by Grant Number R24 AT001293 from the National Center	LoE 1++ RoB: low



		29.2 wk (4-72 wk)	LUTS consistent with BPH.	Lost to follow-up: 10.4% (0%-21.4%)			<p><u>Peak urine flow change from baseline (n=2)</u> MD: -0.52 (95% CI: -1.91,0.88)</p> <p><u>Prostate size (n=2)</u> MD: -0.15 (95% CI: -1.44,1.13)</p> <p>Permixon+ tamsulosin vs. placebo+tamsulosin</p> <p><u>IPSS total score mean change from baseline (n=2)</u> MD: -0.61 (95% CI: -1.69,0.47)</p> <p><u>Peak urine flow change from baseline (n=2)</u> MD: 0.09 (95% CI: -0.8,0.98)</p>	consistent with BPH.	for Complementary and Alternative Medicine (NCCAM), and the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) Grant Number 1R01 DK063300-01A2.	
Verschiedene Behandlungsmöglichkeiten										
Fusco, 2018, Neurourology & Urodynamics [127]	Systematic review with meta-analysis	n=23 studies Searched up to June 2017	To perform a systematic review and meta-analysis of studies evaluating the urodynamic outcomes of alpha-1	n= 1044 patients	<ul style="list-style-type: none"> • alpha-1 adrenergic antagonists (n=18) • 5-alpha reductase inhibitors (n=3) 		Phytotherapeutic compounds (n=1 case serie, n= 1 RCT eviprostat vs. naftodil) <u>Bladder Outlet Obstruction</u>	PDE5is and phytotherapeutic compounds had no significant effects on urodynamic parameters.	no information if efforts were made to minimise error in study selection, risk of bias assessment and data collection,	LoE: 1- to 3 (mixed study designs)



			adrenergic antagonists, 5-ARIs, PDE5is, and phytotherapeutic compounds in patients with lower urinary tract symptoms related to benign prostatic obstruction.		<ul style="list-style-type: none"> • phytotherapeutic compounds (n=2) • PDE5I (n=1) 		<p>MD -2.33 (95% CI -18.56; 13.90), p= 0.78</p> <p><u>Detrusor pressure</u> MD -1.17 (95% CI -18.00; 15.66), p= 0.89</p> <p><u>Qmax change</u> MD 0.01 (95% CI -1.50; 1.51), p= 0.99</p>		<p>risk of bias assessment only for RCTs</p> <p>no information to funding or conflict of interest</p> <p>serious heterogeneity ($I^2 > 75\%$) for bladder outlet obstruction and detrusor pressure</p> <p>only results for phytotherapy reported</p>	RoB: high
--	--	--	---	--	---	--	--	--	---	-----------



Tabelle 22: Phytotherapeutika vs. Placebo/kontrolliertes Zuwarten

Schlüsselfrage										
Welche Effekte zeigen Phytotherapeutika und Phytotherapeutika in Kombination mit gängigen Monotherapien bei Patienten mit BPS im Vergleich zur Therapie mit Placebo/kontrolliertem Zuwarten?										
Referenz	Studien-design	Studien-charakteristika	Studienziel	Patienten-merkmale	Intervention	Kontrolle	Ergebnisse	Schlussfolgerungen	Bemerkungen	LoE
Chinesische Kräutermedizin										
Ma, 2013, Asian Journal of Andrology [120]	Systematic review with meta-analysis	n=31 RCTs (n=11 RCTs for meta-analysis) Searched up to July 2011	This study aimed to evaluate the efficacy and side effects of Chinese herbal medicine versus placebo or active control in the treatment of symptomatic BPH.	n=2493 subjects sample size of included studies ranged from 40 to 160 patients prostate volumes varied from 22.8 to 52.4 ml	Chinese herbal medicine with or without adjuvant use with western medication	<ul style="list-style-type: none"> • Placebo (n=2) • <u>Western medication</u> • tamsulosin (n=3) • finasteride (n=1) • tamsulosin+ finstaeride (n=1) • Pygeum africanum (n=1) • Saw palmetto (n=1) 	<p>Chinese herbal medicine vs. placebo</p> <ul style="list-style-type: none"> • did not detect any significant between-group difference in improving maximum flow rate and prostate volume (p>0.05). • IPSS, QoL and residual urine also did not show any group difference (p>0.05) <p><u>Adverse events</u> (n=6)</p>	This review showed that chinese herbal medicine, either as monotherapy or an adjuvant therapy with western medicine, was similar to either placebo or western medicine in the treatment of BPH. The frequency of adverse events of chinese herbal medicine was similar to that of placebo and even less than that of western medicine.	no information about efforts were made to minimise error in risk of bias assessment Twenty-seven studies (87.1%) were carried out in China and published in Chinese language journals from 1997 to 2011. no conflict of interest declared The present study was supported by the Hospital	LoE: 1++ RoB: low



							RR 0.76 (0.4;1.46) p=0.41		Authority of Hong Kong, China	
Pollenextrakte										
Antonelli, 2019, Phytotherapy Research [121]	Umbrella review (systematic review of systematic review)	n= 5 systematic reviews (one with meta-analysis) Searched up to January 27, 2019	The present umbrella review aims to qualitatively summarize results of existing systematic reviews about the therapeutic efficacy of orally administered pollen in the management of any nonallergic disease. A secondary aim of this work is to collect information from existing	n= 191 to 5217 patients n= 1 review with meta-analysis of patients with chronic prostatitis/chronic pelvic pain syndrome n= 3 reviews with LUTS/BPH/chronic prostatitis n= 1 review with all diseases	Grass pollen extract	any type of comparison (placebo, usual care, other integrative treatments, or no control)	<u>Grass pollen extract vs. placebo or other treatments</u> (n=1) overall effect size significantly favored the pollen group (OR = 0.52 [0.34–0.81]); p =.02 for chronic prostatitis/chronic pelvic pain syndrome • flower pollen extract can significantly improve symptoms and QoL of patients affected by chronic prostatitis/chr	In conclusion, results of the present umbrella review suggest that flower pollen extracts may be useful as a complementary remedy for the management of some nonallergic diseases, mainly symptomatic genitourinary problems like benign prostatic hyperplasia and chronic prostatitis.	no potential conflicts of interest and funding	LoE 1++ RoB: low



			reviews about pollen therapeutic dosage, toxicity, and tolerability.				<p>onic pelvic pain syndrome</p> <ul style="list-style-type: none"> no significant adverse events were reported <p><u>Grass pollen extract vs. placebo (n=1)</u></p> <ul style="list-style-type: none"> self-rated health improvement if compared with placebo (RR = 2.40 [1.21-4.75]) able to reduce nocturia if compared with placebo or Paraprost®. positive results in favor of the efficacy of grass pollen extract (n=3) 			
Serenoa repens										
Russo, 2020, European Urology Focus	Systematic review with network	n=22 RCTs Searched up to	We aimed to compare the clinical efficacy of hexanic	n=8564 patients	Serenoa repens • (hexanic extract and non-hexanic extract)	<ul style="list-style-type: none"> Placebo Alpha-blocker 	<u>Overall mean changes in IPSS against placebo</u> Tamsulosin: -1.50, Silodosin:	We demonstrated that in a short-term follow-up, no clinically meaningful improvement in IPSS	no information, if efforts were made to minimise error in the study	LoE 1- RoB: high



[123]	meta-analysis	December, 31 2018	extract of serona repens versus non-hexanic extract of serona repens versus placebo versus alpha-blockers in patients affected by LUTS secondary to BPE through a network meta-analysis method.	<p>Mean age: 64.27 y (SD 8.01 y)</p> <p>Mean IPSS: 18.23 (SD 4.64)</p> <p>Mean Qmax: 10.29 ml/s (SD 3.21)</p> <p>Postvoid residual: 68.99 ml (SD 49.58)</p>		<p>-2.16, Terazosin: -4.29, Alfuzosin: -1.75, Non-hexanic extract Serenoa repens: -1.60 Hexanic extract Serenoa repens: -1.24</p> <p><u>Overall mean changes in peak flow (ml/s) against placebo</u></p> <p>Tamsulosin: +1.45, Silodosin: +0.76, Terazosin: +1.35, Alfuzosin: +3.57, Non-hexanic extract Serenoa repens: +2.4 Hexanic extract Serenoa repens: +1.04</p> <p><u>SUCRA rankograms score</u></p> <p>Terazosin (99.6%), Alfuzosin (53.7%), tamsulosin (42.3%),</p>	or peak flow of serenoa repens has been demonstrated over placebo or alpha-blockers.	<p>selection and the risk of bias assessment</p> <p>no funding and no conflict of interests declared</p>	
-------	---------------	-------------------	---	---	--	---	--	--	--



							silodosin (68.5%), hexanic extract Serenoa repens (36.7%) non-hexanic extract Serenoa repens (47.3%)			
Vela-Navarrette, 2018, BJUI [124]	Systematic review with meta-analysis	n=27 studies (15 RCTs, 12 cohort studies) Searched up to April 2017	To comprehensively evaluate the efficacy and safety of the hexanic extract of Serenoa repens (Permixon), at a dose of 320 mg daily, as monotherapy for the treatment of lower urinary tract symptoms associated with benign prostatic hyperplasia	n= 5800 patients	Permixon	<ul style="list-style-type: none"> • placebo • alpha-blocker • 5ARI 	<p>Permixon vs. Placebo <u>Nocturia (n=7)</u> WMD: -0.64 (-0.98; -0.31) p=0.001 favors permixon</p> <p><u>Qmax (n=4)</u> WMD: 2.75 (0.57; -4.93) p=0.014 favors permixon</p> <p>Adverse drug reaction (Permixon) gastrointestinal disorders being the most frequent (3.8%)</p>	Permixon reduced nocturia and improved Qmax compared with placebo and had a similar efficacy to tamsulosin and short-term 5-ARI in relieving LUTS. Permixon appears to be an efficacious and well-tolerated therapeutic option for the longterm medical treatment of LUTS/BPH.	<p>Detailed information to conflict of interest in the paper.</p> <p>This study was funded by Pierre Fabre Iberica, S.A, Barcelona, Spain</p> <p>results only shown for the comparison serenoa repens vs. placebo</p>	<p>LoE Range 1++ to 2++ (mixed study designs)</p> <p>RoB: low</p>
Novara, 2016, European Urology Focus [125]	Systematic review with meta-analysis	n=12 RCTs Search date: January 2016	To evaluate the efficacy and safety of Permixon in the treatment of LUTS/BPH.	patients with LUTS/BPH	<ul style="list-style-type: none"> • Permixon vs. Placebo (n=7) • Permixon vs. Tamsulosin (n=2) • Permixon or combination 	<p><u>Permixon vs. Placebo</u> number of nocturnal voids at study end were significantly</p>	Our meta-analysis showed that Permixon decreased nocturnal voids and Qmax compared with placebo and had efficacy in relieving LUTS similar	no detailed inclusion and exclusion criteria, no information if efforts were made to	<p>LoE: 1-</p> <p>RoB: high</p>	



					vs tamsulosin monotherapy (n = 2) Permixon vs. finasteride (n=1)		lower with Permixon (WMD -0.31; 95% CI, -0.59 to -0.03; p = 0.03) Qmax was significantly higher in the patients treated with Permixon (WMD 3.37; 95% CI, 1.71–5.03; p < 0.0001) overall adverse event rates were similar for Permixon and placebo (OR 1.12; 95% CI, 0.13–9.75; p = 0.92)	to tamsulosin and short-term finasteride. Moreover, Permixon had a favorable safety profile with a very limited impact on sexual function, which is significantly affected by all other drugs used to treat LUTS/BPH.	minimise error in the risk of bias assessment and no presentation of the assessment results no funding and no conflict of interests declared results only shown for the comparison phytotherapy vs. placebo	
Tacklind, 2012, Cochrane Database of Systematic Reviews [126]	Systematic review + meta-analysis	n=32 RCTs Searched up to January, 1 2012 Weighted mean follow-up: 29.2 wk (4-72 wk)	This systematic review aimed to assess the effects and harms of Serenoa repens in the treatment of men with LUTS	n= 5666 men Weighted mean age: 64.6 y (40-90 y) Lost to follow-up: 10.4% (0%-21.4%)	<ul style="list-style-type: none"> • Serenoa repens • Serenoa repens+ Urtica dioica • Serenoa repens+ tamsulosin 	<ul style="list-style-type: none"> • Placebo • Tamsulosin • Tamsulosin +Placebo 	Serenoa repens vs. placebo <u>AUA total score (n=2)</u> MD: 0.25 (95% CI: -0.58,1.07) <u>Nocturia (n=9)</u> MD: -0.79 (95% CI: -1.28,0.29) favors serenoa repens	Compared with placebo, Serenoa repens, at double and triple the usual dose, provides no improvement for nocturia, peak urine flow, and symptom scores for men with benign prostatic hyperplasia.	no conflict of interests declared partially funded by Grant Number R24 AT001293 from the National Center for Complementary and Alternative	LoE 1++ RoB: low



			consistent with BPH.				<p><u>Peak urine flow change from baseline (n=3)</u> MD: 0.4 (95% CI: -0.3,1.09)</p> <p><u>Peak urine flow change at endpoint (n=6)</u> MD: 0.35 (95% CI: -1.5,1.76)</p> <p><u>Prostata size at endpoint (n=2)</u> MD: -2.2 (95% CI: -8.98,4.58)</p> <p><u>Prostata size from baseline (n=2)</u> MD: 1.1 (95% CI: -2.25,4.45)</p> <p><u>Adverse effects (n=4)</u> MD: 0.94 (95% CI: -0.27,3.19)</p> <p>Serenoa repens+Urtica dioica vs. placebo <u>Peak urine flow (mL/s) at endpoint (n=2)</u> MD: 2.48 (95% CI: -0.05,5.02) favors combination</p>	<p>Medicine (NCCAM), and the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) Grant Number 1R01 DK063300-01A2.</p> <p>Results only shown for the comparison phytotherapy vs. placebo.</p>
--	--	--	----------------------	--	--	--	---	--



							MD: -0.52 (95% CI: -1.91,0.88)			
Verschiedene Behandlungsmöglichkeiten										
Kim, 2012, Maturitas [128]	Umbrella review (systematic review of systematic review)	n= 6 systematic reviews Searched up to June 2012	The purpose of this overview of systematic reviews is to summarise the current evidence on the benefits and drawbacks of dietary supplements for treating BPH with LUTS. With this review, we aim to provide information on dietary supplements for patients and clinicians to aid in the clinical decision-making process.	n= 78 primary studies Data search dates between 1997-2012	<ul style="list-style-type: none"> • Serenoa repens (n=3) • beta-Sitosterol (n=1) • Pygeum africanum (n=1) • Cernilton (n=1) 	placebo	<p><u>Serenoa repens</u></p> <ul style="list-style-type: none"> • reported positive effects of Permixon in improving peak urine flow rate and reducing nocturia (n=1) • all types of Serenoa repens preparations: reported positive effects on urinary tract symptoms and flow measurements (n=1) • Serenoa repens did not improve urinary flow or prostate size (n=1, high-quality review) <p><u>beta-Sitosterol</u></p>	Several phytotherapeutic compounds, including beta-sitosterol, Pygeum africanum and Cernilton, showed specific effects on the symptoms and urinary flow measures related to BPH, but Serenoa repens did not. In terms of safety, all included compounds had mild and infrequent adverse effects.	no conflict of interest declared supported by the Korea Institute of Oriental Medicine grant numbers and by Korea Food Research Institute.	LoE: 1++ RoB: low



							<ul style="list-style-type: none"> • improved IPSS and urodynamic measurement including Qmax and PVR • no difference in adverse event rates <p><u>Pygeum africanum</u></p> <ul style="list-style-type: none"> • it improved self-rated symptoms, nocturia and PVR • adverse events were generally minor <p><u>Cernilton</u></p> <ul style="list-style-type: none"> • no significant improvement in urodynamic measures was observed 		
--	--	--	--	--	--	--	---	--	--



Tabelle 23: beta3-Agonisten vs. Placebo/kontrolliertes Zuwarten

Schlüsselfrage										
Welche Effekte zeigen beta3-Agonisten bei Patienten mit BPS im Vergleich zu Placebo/kontrolliertem Zuwarten?										
Referenz	Studien-design	Studien-charakteristika	Studienziel	Patienten-merkmale	Intervention	Kontrolle	Ergebnisse	Schlussfolgerungen	Be-merkungen	LoE
Systematische Übersichtsarbeiten mit Meta-Analysen										
Sebastianelli, 2018, International Journal of Urology [129]	Systematic review with meta-analysis	n= 8 RCTs (n= 7 with OAB patients, n= 1 LUTS patients) search up to 31 May 2016	To evaluate the efficacy and safety of mirabegron 50 mg and 100 mg in the treatment of storage lower urinary tract symptoms/o veractive bladder in comparison with a placebo and tolterodine 4 mg.	n= 10248 patients with storage lower urinary tract symptoms/o veractive bladder	<ul style="list-style-type: none"> • Mirabegron 25 mg (n= 600 patients) • Mirabegron 50 mg (n= 3168 patients) • Mirabegron 100 mg (n= 1986) 	<ul style="list-style-type: none"> • Tolterodine 4 mg (n=2138) • placebo (n=2356 patients) 	<p>Incontinence episodes per 24 h <u>Mirabegron 50 mg vs. placebo</u> WMD -0.38, P < 0.0001</p> <p><u>Mirabegron 100 mg vs. placebo</u> WMD -0.49, P < 0.0001</p> <p>Mean number of micturitions per 24 h <u>Mirabegron 50 mg vs. placebo</u> WMD -0.60, P < 0.0001</p> <p><u>Mirabegron 100 mg vs. placebo</u> WMD -0.72, P < 0.0001</p> <p>Increase of voided volume</p>	Mirabegron is an effective treatment for patients with storage lower urinary tract symptoms/ overactive bladder, providing a reduction of incontinence, urgency and frequency; an improvement of voided volume with a slight, but statistically, significant improvement of nocturia; with a good safety profile.	no information if efforts were made to minimise error in the study selection and the risk of bias assessment Several relations to pharmaceutical industries results only shown for the comparison beta 3 agonists vs. placebo	LoE 1++ RoB: low



							<p><u>Mirabegron 50 mg vs. placebo</u> WMD 12.67, P < 0.0001</p> <p><u>Mirabegron 100 mg vs. placebo</u> WMD 10.85, P < 0.0001</p> <p>Reduction of urgency episodes per 24 h</p> <p><u>Mirabegron 50 mg vs. placebo</u> WMD -0.53, P < 0.0001</p> <p><u>Mirabegron 100 mg vs. placebo</u> WMD -0.66, P < 0.0001</p> <p>Reduction of nocturia episodes</p> <p><u>Mirabegron 50 mg vs. placebo</u> WMD -0.13, P < 0.0003</p> <p><u>Mirabegron 100 mg vs. placebo</u> WMD -0.16, P = 0.05</p> <p>Treatment-emergent adverse event</p>		
--	--	--	--	--	--	--	--	--	--



						<p><u>Mirabegron 50 mg vs. placebo (n= 7)</u> OR: 0.94 (0.83, 1.06) p=0.32</p> <p><u>Mirabegron 100 mg vs. placebo (n= 4)</u> OR: 0.97 (0.81, 1.16) p=0.75</p> <p>Risk of hypertension <u>Mirabegron 50 mg vs. placebo</u> OR 1.02; P =0.90</p> <p><u>Mirabegron 100 mg vs. placebo</u> OR 1.41; P =0.08</p> <p>Cardiac arrhythmia <u>Mirabegron 50 mg vs. placebo</u> OR 1.0; P = 1.00</p> <p><u>Mirabegron 100 mg vs. placebo</u> OR 2.18; P =0.06</p> <p>Discontinuation <u>Mirabegron 50 mg vs. placebo</u> OR 0.97; P =0.80</p> <p><u>Mirabegron 100 mg vs. placebo</u> OR 0.89; P =0.63</p>		
--	--	--	--	--	--	--	--	--



Brasure, 2016, Agency for Healthcare Research and Quality [130]	Systematic review with meta-analysis	n= 62 (57 RCTs, 5 observational studies) search up to July 2015 n= 1 RCT compared Mirabegron vs. placebo	To assess the efficacy, comparative effectiveness, and adverse effects of newer drugs to treat LUTS attributed to benign prostatic hyperplasia.	patients with lower urinary tract symptoms attributed to BPH Mean age: 63 y	<ul style="list-style-type: none"> • Mirabegron 50 mg (n=70) • Mirabegron 100 mg (n=65) 	Placebo n=65	<u>Mean I-PSS score changes from baseline</u> 50mg Mirabegron: -6.2 100mg Mirabegron: -4.8 Placebo: -5.0 (not significant) The information provided was insufficient for effect size calculation or pooling across dose levels for any outcome or adverse effect (insufficient strength of evidence).	Evidence was insufficient to assess efficacy or adverse effects of mirabegron compared with placebo.	management for conflicts of interest described no information about funding results only shown for the comparison beta 3 agonists vs. placebo	LoE 1++ (for the comparison) RoB: low
Randomisierte kontrollierte Studien										
Nitti, 2013, Journal of Urology [131]	RCT (phase II study)	n= 200 men with LUTS and BOO	We investigated urodynamic parameters in men with lower urinary tract symptoms and bladder outlet obstruction treated with the b3	<u>Mean age</u> Mirabegron 50 mg: 64.3 - 8.80 y Mirabegron 100 mg: 63.3 - 10.17 y Placebo: 60.9 -8.35 y	<ul style="list-style-type: none"> • Mirabegron 50 mg (n=70) • Mirabegron 100 mg (n=65) 	Placebo n=65	Mean treatment-placebo difference (95% CI) <u>Qmax (full analysis set)</u> Mirabegron 50 mg: 0.40 (-0.63, 1.42) Mirabegron 100 mg: 0.62 (-0.43, 1.68) <u>Qmax (per protocol set)</u>	Mirabegron did not adversely affect voiding urodynamics (maximum urinary flow and detrusor pressure at maximum urinary flow) compared with placebo after 12 weeks of treatment.	no information about the randomization and allocation procedure Supported by Astellas Pharma Financial interest and/or other relationship with Allergan, Astellas, AMS,	LoE 1- RoB: high



			agonist mirabegron, a new therapy for overactive bladder symptoms.			<p>Mirabegron 50 mg: 1.09 (-0.12, 2.31) Mirabegron 100 mg: 0.28 (-0.97, 1.53)</p> <p><u>PdetQmax (full analysis set)</u> Mirabegron 50 mg: -5.94 (-13.98, 2.09) Mirabegron 100 mg: -1.39 (-9.73, 6.96)</p> <p><u>PdetQmax (per protocol set)</u> Mirabegron 50 mg: -5.99 (-15.87, 3.89) Mirabegron 100 mg: - 3.43 (-13.64, 6.78)</p> <p>Change from baseline to treatment end (full analysis set) <u>IPSS</u> Placebo: -5 Mirabegron 50 mg: -6.2 Mirabegron 100 mg: -4.8</p> <p><u>Voiding IPSS</u> Placebo: -2.8 Mirabegron 50 mg: -2.9 Mirabegron 100 mg: -2.4</p>	Coloplast, Medtronic, Pfizer, Serenity and Uroplasty and Astellas Pharma.
--	--	--	--	--	--	---	---



							<p><u>Storage IPSS</u> Placebo: -2.2 Mirabegron 50 mg: -3.3 (p<0.05 vs. placebo) Mirabegron 100 mg: -2.5</p> <p><u>PPBC</u> Placebo: -0.6 Mirabegron 50 mg: -0.9 Mirabegron 100 mg: -0.8</p> <p><u>Mean No. micturitions/24 hrs</u> Placebo: -0.31 Mirabegron 50 mg: -1.35 (p<0.05 vs. placebo) Mirabegron 100 mg: -1.37 (p<0.05 vs. placebo)</p> <p><u>Mean No. urgency episodes/24 hrs</u> Placebo: -0.33 Mirabegron 50 mg: -1.6 (p<0.01 vs. placebo) Mirabegron 100 mg: -0.93</p> <p><u>Mean No. incontinence episodes/24 hrs</u> Placebo: -0.96</p>		
--	--	--	--	--	--	--	--	--	--



							Mirabegron 50 mg: -0.89 Mirabegron 100 mg: -1.98 <u>Vol</u> <u>voided/micturition</u> <u>(ml)</u> Placebo: 5.4 Mirabegron 50 mg: 15.82 Mirabegron 100 mg: 15.8		
--	--	--	--	--	--	--	---	--	--



Tabelle 24: Kombinationstherapien vs. Placebo/Kontrolliertes Zuwarten

Schlüsselfrage										
Welche Effekte zeigen die Kombinationstherapien (nicht Phytotherapeutika) bei Patienten mit BPS im Vergleich zu Placebo/kontrolliertem Zuwarten?										
Referenz	Studien-design	Studien-charakteristika	Studienziel	Patienten-merkmale	Intervention	Kontrolle	Ergebnisse	Schlussfolgerung	Be-merkungen	LoE
Network meta-analysis										
Wang, 2014, PLoS One [132]	Systematic review with network meta-analysis	n=66 RCTs Search till June 2013	The aim of our study was to carry out a systematic review and network meta-analysis comparing the efficacy of different drug therapies for LUTS/BPH based on existing RCTs and ranking these regimens for practical consideration.	n=29384 participants	<ul style="list-style-type: none"> • alpha-blockers • alpha-blockers +PDE5-I • alpha-blockers + muscarinic receptor antagonists • alpha-blockers +5-ARI • 5a-reductase inhibitors • PDE5-I • muscarinic receptor antagonists • placebo 		<p>Alpha-blockers +5-ARI vs. placebo <u>Q_{max}</u> MD -1.98 (95% CI - 2.86,-1.12) p<0.01</p> <p><u>IPSS storage subscore</u> MD 0.43 (95% CI, - 1.61, 2.45) p=0.69</p> <p><u>IPSS voiding subscore</u> MD 1.63 (95% CI, 0.49, 2.77) p<0.01</p> <p>Alpha-blockers + muscarinic receptor antagonists vs. placebo <u>Q_{max}</u> MD -0.92 (95% CI - 1.59, -0.18) p=0.01</p>	Based on our novel findings, combination therapy, especially alpha-blockers plus PDE5-Is, is recommended for short-term treatment for LUTS/BPH.	<p>no information if efforts were made to minimise error in the study selection or the risk of bias assesment, no funnel plot or sensitivity analyses</p> <p>no conflict of interest declared</p> <p>supported by National Natural Science Foundation of China</p> <p>Results only shown for combination</p>	<p>LoE 1-</p> <p>RoB: high</p>



							<p><u>IPSS storage subscore</u> MD 1.33 (95% CI, 0.5, 2.14) p<0.01</p> <p><u>IPSS voiding subscore</u> MD 0.78 (95% CI, 0.23, 1.37) p<0.01</p> <p>Alpha-blockers +PDE5-I vs. placebo <u>Qmax</u> MD -1.90 (95% CI - 2.82, -0.99) p<0.01</p> <p><u>IPSS storage subscore</u> MD 2.20 (95% CI, 0.52, 3.90) p=0.01</p> <p><u>IPSS voiding subscore</u> MD 2.97 (95% CI, 1.69, 4.22) p<0.01</p> <p>Figure 7 shows the complete ranking</p>		therapy vs. placebo	
a-blocker und Antimuskarinikum										
Pang, 2021, Cochrane Database of	Systematic review with meta-analysis	n= 23 RCTs search up to 7	To assess the effects of combination therapy with anticholinergics and alpha-	n= 6285 men with LUTS secondary to BPO Mean age:	Alpha Blocker + Anticholinergic	placebo	Combination therapy vs. placebo <u>Urologic symptom scores</u> (n=4 RCTs)	Combination therapy versus placebo: combination therapy with anticholinergics and	serious heterogeneity (I ² ≥75%) for urologic symptom	LoE 1++ RoB: low



<p>Systematic Reviews [133]</p>		<p>August 2020</p>	<p>blockers in men with LUTS related to BPO.</p>	<p>65.7 y (54.4-73.9 y)</p>			<p>MD -2.73 (95% CI -5.55;0.08) p=0.06</p> <p><u>QoL</u> (n=2 RCTs) MD -0.97 (95% CI -2.11;0.16) p=0.09</p> <p><u>Adverse events</u> (n=3 RCTs) RR 1.24 (95% CI 1.04;1.47) p=0.01 favors placebo</p> <p><u>Acute urinary retention</u> (n=5 RCTs) RR 1.94 (95% CI 0.41;9.08) p=0.4</p>	<p>alpha-blockers was associated with little effect in urinary symptoms and uncertain improvement on quality of life, but combination therapy may increase unwanted side effects.</p>	<p>scores and QoL</p> <p>No conflict of interest.</p> <p>Funding: Guang An Men Hospital, China Academy of Chinese Medical Sciences, China Beijing Municipal Science & Technology Commission, China</p> <p>results only shown for the comparison combination therapy vs. placebo</p>	
-------------------------------------	--	--------------------	--	-----------------------------	--	--	--	---	--	--



<p>Li, 2015, Asian Journal of Andrology [134]</p>	<p>Systematic review with meta-analysis</p>	<p>n= 3 RCT published before January 14, 2014</p>	<p>To better make certain the efficacy and safety of this treatment method, we performed a meta-analysis of randomized clinical trials to define the effects of combination therapy solifenacin and TOCAS compared with placebo or TOCAS monotherapy.</p>	<p>n= 2036 patients with LUTS</p>	<p>solifenacin+T OCAS</p>	<p>placebo</p>	<p>Solifenacin 9 mg + TOCAS vs. placebo <u>IPSS</u> MD -1.50 (-2.30,-0.7) p=0.0002 <u>IPSS storage subscore</u> MD -0.71 (-1.18,-0.24) p=0.003 <u>IPSS voiding subscore</u> MD -0.15 (-0.79,0.5) p=0.66 <u>Total urgency and frequency score</u> MD -2.43 (-3.82,-1.5) p=0.0006 <u>Micturitions per 24 h</u> MD -0.81 (-1.13,-0.48) p<0.00001 <u>Volume voided per micturition</u> MD 28.13 (21.97, 34.30) p<0.00001 <u>Urgency episodes per 24h</u> MD -0.45 (-1.31,0.4)</p>	<p>Both combination treatments were well tolerated, with low incidence of urinary retention. Solifenacin 6 mg plus TOCAS significantly improved total IPSS, storage and voiding symptoms compared with placebo. Solifenacin 6 mg plus TOCAS also improved storage symptoms compared with TOCAS alone. There was no additional benefit of solifenacin 9 mg compared with 6 mg when used in combination with TOCAS.</p>	<p>no additional hand search, no information if efforts were made to minimise error in the study selection or data collection, no table 1 with study characteristics , risk of bias assessment performed, but not presented, no funnel plot Fig 7: Volume voided per micturition is greater in the experimental group no conflict of interest declared no information about support results only shown for the comparison combination</p>	<p>LoE 1- RoB: high</p>
---	---	---	---	-----------------------------------	---------------------------	----------------	--	---	--	---



							<p>p=0.30</p> <p><u>PVR</u> MD 14.81 (4.80,24.82) p=0.004</p> <p><u>Urinary retention</u> MD 5.56 (0.74,41.82) p=0.1</p> <p><u>Dry mouth</u> RR 8.62 (4.02,18.50) p<0.00001</p> <p>Solifenacin 6 mg+TOCAS vs. placebo</p> <p><u>IPSS storage subscore</u> MD -0.98 (-1.44,-0.52) p<0.0001</p> <p><u>IPSS voiding subscore</u> MD -0.70 (-1.32,-0.08) p=0.03</p> <p><u>Total urgency and frequency score</u> MD -3 (-4.36,-1.65) p<0.0001</p> <p><u>Micturitions per 24 h</u> MD -1.03 (-1.36,-0.71) p<0.01</p>	therapy vs. placebo	
--	--	--	--	--	--	--	---	----------------------------	--



							<p><u>Volume voided per micturition</u> MD 27.23 (21.25, 33.20) p<0.00001</p> <p><u>Urgency episodes per 24h</u> MD -0.64 (-1.05, -0.22) p<0.003</p> <p><u>PVR</u> MD 16.23 (6.31,26.15) p=0.001</p> <p><u>Urinary retention</u> MD 5.06 (0.24,104.99) p=0.29</p> <p><u>Dry mouth</u> RR 6.39 (2.94,13.91) p<0.00001</p>			
verschiedene Kombinationen										
Brasure, 2016, Agency for Healthcare Research and Quality [130]	Systematic review with meta-analysis	n= 62 (57 RCTs, 5 observational studies) search up to July 2015	To assess the efficacy, comparative effectiveness, and adverse effects of newer drugs to treat LUTS attributed to benign prostatic hyperplasia.	patients with lower urinary tract symptoms attributed to BPH	<ul style="list-style-type: none"> • Tolterodine +alpha-blocker • Solifenacin+ alpha-blocker 	placebo	<p>Tolterodine + alpha blocker vs. placebo (n=1 RCT)</p> <ul style="list-style-type: none"> • Combination therapy improved mean change in I-PSS (MD = -1.80) and I-PSS QoL more than placebo 	Anticholinergics (including tolterodine and solifenacin) combined with established alpha-blockers improved LUTS attributed to BPH more than placebo.	<p>management for conflicts of interest described</p> <p>no information about funding</p> <p>Results only shown for combination</p>	<p>LoE 1++ (for the comparison)</p> <p>RoB: low</p>



						<ul style="list-style-type: none"> • Rates of withdrawal due to adverse effects were higher with combination therapy than placebo <p>Solifenacin + alpha-blocker vs. placebo (n=3 RCT)</p> <p><u>I-PSS score (n=3)</u> WMD = -1.50 [-1.80 to -1.20] favors combination</p> <p><u>I-PSS QoL (n=1)</u> MD = -0.40 [-0.70 to -0.10] similar</p> <p><u>Overall withdrawals</u> RR = 1.20 [0.46 to 3.13] similar</p> <p><u>Withdrawals due to adverse effects</u> RR = 2.17 [0.72 to 6.55]</p> <p><u>Participants with ≥1 adverse effect</u> RR = 1.24 [0.99 to 1.55]</p>	therapy vs. placebo	
--	--	--	--	--	--	--	----------------------------	--



Tabelle 25: Monotherapien vs. Kombinationspräparaten

Schlüsselfrage										
Welche Effekte zeigen die Monotherapien (nicht Phytotherapeutika) bei Patienten mit BPS im Vergleich zu Kombinationspräparaten?										
Referenz	Studien-design	Studien-charakteristika	Studienziel	Patienten-merkmale	Intervention	Kontrolle	Ergebnisse	Schlussfolgerungen	Bemerkungen	LoE
Network meta-analysis										
Wang, 2014, PLoS One [132]	Systematic review with network meta-analysis	n=66 RCTs Search till June 2013	The aim of our study was to carry out a systematic review and network meta-analysis comparing the efficacy of different drug therapies for LUTS/BPH based on existing RCTs and ranking these regimens for practical consideration.	n=29384 participants	<ul style="list-style-type: none"> • alpha-blockers • alpha-blockers +PDE5-I • alpha-blockers + muscarinic receptor antagonists • alpha-blockers +5-ARI • 5a-reductase inhibitors • PDE5-I • muscarinic receptor antagonists • placebo 		<ul style="list-style-type: none"> • combination therapy with alpha-blockers plus PDE5-Is ranked highest on the assessment of IPSS total score, storage subscore and voiding subscore • alpha-blockers combined with 5ARIs ranked highest for Qmax, but alpha-blockers plus 5ARIs and alpha-blockers plus PDE5-Is had adjacent cumulative probabilities indicating that these two combination therapies had 	Based on our novel findings, combination therapy, especially alpha-blockers plus PDE5-Is, is recommended for short-term treatment for LUTS/BPH.	<p>no information if efforts were made to minimise error in the study selection or the risk of bias assesment, no funnel plot or sensitivity analyses</p> <p>no conflict of interest declared</p> <p>supported by National Natural Science Foundation of China</p>	LoE 1- RoB: high



							similar efficacy on improvement of Qmax <ul style="list-style-type: none"> combination therapies resulted in a relatively better effect than monotherapies <p>Figure 7 shows the complete ranking</p>			
Systematic reviews with meta-analysis										
α1-Blocker & Phosphodiesterase vs. monotherapy										
Sun, 2020, Minerva Urologica e Nefrologica [135]	Systematic review with meta-analysis	n=19 studies (17 RCTs, 2 retrospective studies) last update: October 2017	To systematically investigate the efficacy and safety of combination therapy in comparison with monotherapy.	n= 2472 patients with LUTS	Alpha-blocker + PDE5I	<ul style="list-style-type: none"> Alpha-blocker PDE5I 	<p>Alpha-blocker + PDE5I vs. alpha-blocker (n=11)</p> <p><u>IPSS</u> MD -0.68 (-1.21 to -0.15) p=0.01</p> <p><u>QoL</u> MD 5.33 (5.16-5.5) p<0.00001</p> <p><u>Qmax</u> MD 0.92 (0.56-1.29) p<0.00001</p> <p><u>PVR</u> MD -6.19 (-8.52 to -3.86) p<0.00001</p> <p><u>IIEF</u> MD 5.58 (4.69 to -6.46) p<0.00001</p>	Combination treatment is more effective than PDE5i or alphablockers alone, though the side effects are not significantly different.	<p>no information if efforts were made to minimise error in the study selection, data collection and risk of bias assessment</p> <p>no conflict of interest declared</p> <p>funding: National Natural Science Foundation of China</p> <p>results only shown for the comparison</p>	LoE 1- RoB: high



							<p><u>Total side effects</u> RR 2.25 (1.4-3.64) p= 0.0009</p> <p>Alpha-blocker + PDE5I vs. PDE5I (n=9) <u>IPSS</u> MD -1.30 (-1.39 to -1.2.15) p<0.0001</p> <p><u>QoL</u> MD -0.15 (-0.17 to -0.13) p<0.00001</p> <p><u>Qmax</u> MD 1.01 (0.89-1.13) p<0.00001</p> <p><u>PVR</u> MD 0.54 (0.03 - 1.06) p=0.04</p> <p><u>IIEF</u> MD -0.30 (-0.39 to -0.21) p<0.00001</p> <p><u>Total side effects</u> RR 1.29 (0.88-1.88) p= 0.2</p>	combination therapy vs. monotherapy		
Kallidonis, 2019, European Urology Focus [136]	Systematic review with meta-analysis	n=25 RCTs literature search was conducted in April 2018	To systematically investigate the efficacy and safety of combination therapy in comparison	patients with LUTS	• Alpha-blocker + PDE5I	• Alpha-blocker • PDE5I	<p>Alpha-blocker + PDE5I vs. alpha-blocker <u>IPSS at 3 mo</u> MD 1.46 (95% CI 0.49, 2.44) p=0.003 favours combination</p>	Treatment with combination therapy is more effective for the improvement of the IPSS. Less significant improvement was shown in Qmax. The beneficial effect of	no information if efforts were made to minimise error in the risk of bias assessment	LoE 1++ RoB: low



			with monotherapy.				<p><u>IPSS at the end of the eligible studies</u> MD 1.41 (95% CI 0.42, 2.41) p=0.005 favours combination</p> <p><u>IPSS changes of the eligible studies</u> MD -1.72 (-2.55, 0.89) p<0.0001 favours combination</p> <p><u>Qmax scores</u> MD -1.01 (-1.58, -0.43) p=0.0006 favours combination</p> <p><u>Qmax changes</u> MD -0.61 (-1.57, -0.34) p=0.21</p> <p><u>PVR scores</u> MD 0.65 (-5.37, 6.66) p=0.83</p> <p><u>PVR changes</u> MD -20.79 (-48.94, 7.37) p=0.15</p> <p><u>IIEF scores</u> MD -4.77 (-6.4, -3.14) p<0.0001 favours combination</p> <p><u>Adverse events</u></p>	<p>combination therapy regarding erectile dysfunction remains equivocal. The combination therapy seemed to be safe and well tolerated.</p>	<p>serious heterogeneity ($I^2 \geq 75\%$) for PVR</p> <p>no conflict of interest or funding declared</p>	
--	--	--	-------------------	--	--	--	--	--	--	--



							<p>RR 0.61 (0.44, 0.86) p<0.0001 favours alpha-blocker</p> <p>Alpha-blocker + PDE5I vs. PDE5I</p> <p><u>IIEF scores</u> MD 1.82 (-0.91, 4.54) p=0.19</p> <p><u>IIEF changes</u> MD 0.25 (-1.11, 1.62) p=0.72</p> <p><u>Adverse events</u> RR 1.87 (1.24, 2.81) p=0.003 favours PD5I</p>			
<p>Zhang, 2019, World Journal of Urology [137]</p>	<p>Systematic review with meta-analysis</p>	<p>n= 11 RCTs searched up to March 2018</p>	<p>We performed this meta-analysis to evaluate the role of combination therapy (α-blockers and PDE5-Is) in patients with LUTS/BPH.</p>	<p>n= 1038 patients</p>	<p>α-blockers + PDE5-Is</p>	<ul style="list-style-type: none"> α-blockers <p><u>IPSS</u> WMD -1.66 (95% CI -3.03, -0.29) p=0.000</p> <p><u>IPSS storage-system</u> WMD -0.18 (95% CI -0.58,0.2) p=0.417</p> <p><u>IPSS voiding-system</u> WMD -0.63 (95% CI -1.56,0.31) p=0.008</p> <p><u>QoL score</u></p>	<p>Our results indicated that combination therapy can significantly improve IPSS, Qmax, and IIEF in patients with LUTS/BPH. Combination therapy might be more suitable for these patients.</p>	<p>no information if efforts were made to minimise error in the study selection or risk of bias assessment</p> <p>serious heterogeneity (I²≥75%) for IPSS, QoL score, PVR and IIEF</p> <p>received research grants from the</p>	<p>LoE 1++</p> <p>RoB: low</p>	



							<p>WMD -0.32 (95% CI -0.84,0.2) p=0.000</p> <p><u>Q_{max}</u> WMD 0.94 (95% CI 0.24,1.64) p=0.000</p> <p><u>PVR</u> WMD -2.97 (95% CI -7.62,1.68) p=0.000</p> <p><u>IIFF</u> WMD 4.73 (95% CI -2.95,6.51) p=0.000</p>		National Natural Science Foundation of China (81671488) and the Beijing Natural Science Foundation (Grant no. 7162152).	
Choi, 2015, INJ [138]	Systematic review with meta-analysis	n=10 RCTs 2000-2014	To review the studies on α-1-adrenergic blocker monotherapy and combination therapy with long vs. short-acting PDE5Is in their use in LUTS and erectile dysfunction	n=584 patients	<p>Combination therapy</p> <ul style="list-style-type: none"> • Alfuzosin 10 mg/day + sildenafil 25 mg/day • Tamsulosin 0.4 mg/day + tadalafil 20 mg/day • Alfuzosin 10 mg/day + tadalafil 20 mg on alternative day • Tamsulosin 0.4 mg + sildenafil 25 mg 4 times/wk 	<p>Alpha blocker</p> <ul style="list-style-type: none"> • Alfuzosin 10 mg/day • Tamsulosin 0.4 mg/day • Doxazosin 2 mg/day 	<p>Short-acting PDE5I+alpha blockers vs. alpha-blocker</p> <p><u>IPSS</u> MD -1.70 (95% CI -2.62, -0.78) P=0.0003 favours combination</p> <p>Long-acting PDE5I+alpha blockers vs. alpha-blocker</p> <p><u>IPSS</u> MD -2.12 (95% CI -3.10, -1.14) P<0.0001 favours combination</p>	Combination PDE5I and α-1-adrenergic blocker could be a more effective treatment than α-1-adrenergic blocker monotherapy, and the differences between long and short-acting agents were minimal.	<p>no additional hand search, no information if efforts were made to minimise error in the risk of bias assessment, bias of the included studies were not addressed</p> <p>serious heterogeneity (I²≥75%) for residue urine (Long-acting PDE5I+alpha blockers vs. alpha-blocker)</p>	<p>LoE 1-</p> <p>RoB: high</p>



				<ul style="list-style-type: none"> • Tamsulosin 0.4 mg + vardenafil 10 mg • Tamsulosin 0.4 mg + tadalafil 5 mg/day • Doxazosin 2 mg + Sildenafil 50 mg/day • Alfuzosin 10 mg/day + tadalafil 10 mg/day • Tamsulosin 0.4 mg/day + tadalafil 10 mg/day 	<p>PDE5I+alpha blockers vs. alpha-blocker <u>IPSS</u> MD -1.93 (95% CI - 2.54, -1.32) P<0.0001 favours combination</p> <p>Short-acting PDE5I+alpha blockers vs. alpha-blocker <u>Qmax</u> MD 1.13 (95% CI - 0.28, -1.99) P=0.009 favours control</p> <p>Long-acting PDE5I+alpha blockers vs. alpha-blocker <u>Qmax</u> MD 0.14 (95% CI - 0.69, -0.97) p=0.74</p> <p>PDE5I+alpha blockers vs. alpha-blocker <u>Qmax</u> MD 0.71 (95% CI 0.08, 1.33) P=0.03 favours control</p> <p>Short-acting PDE5I+alpha</p>	<p>and IIEF (all comparison)</p> <p>no conflict of interest declared</p> <p>supported by the National Research Foundation of Korea (NRF) grant funded by the Korea government (MSIP)</p>
--	--	--	--	---	---	--



							<p>blockers vs. alpha-blocker <u>residual urine</u> MD -5.93 (95% CI -11.12, -0.74) P=0.03 favours combination</p> <p>Long-acting PDE5I+alpha blockers vs. alpha-blocker <u>residual urine</u> MD -18.83 (95% CI -45.97, 8.3) P=0.17</p> <p>PDE5I+alpha blockers vs. alpha-blocker <u>residual urine</u> MD -7.09 (95% CI -13.15, -1.04) P=0.02 favours combination</p> <p>Short-acting PDE5I+alpha blockers vs. alpha-blocker <u>IIEF</u> MD -4.85 (95% CI 2.81,6.88) P<0.00001 favours combination</p> <p>Long-acting PDE5I+alpha</p>		
--	--	--	--	--	--	--	---	--	--



							<p>blockers vs. alpha-blocker <u>IIEF</u> MD 2.85 (95% CI 0.46,5.24) P=0.02 favours combination</p> <p>PDE5I+alpha blockers vs. alpha-blocker <u>IIEF</u> MD 3.99 (95% CI -2.42,5.56) P<0.00001 favours combination</p>			
Wang, 2015, Asian Journal of Andrology [139]	Systematic review with meta-analysis	n=12 RCTs search up to January 2014	The aim of the present review was to compare the efficacy and safety of PDE5-Is and ABs used alone or combined for treating LUTS/BPH based on existing RCTs, so as to provide a more systematic and comprehensive assessment for	patients with LUTS due to benign prostatic hyperplasia	Alpha-blockers + PDE5I	<ul style="list-style-type: none"> • PDE5I • Alpha-blockers 	<p>Alpha-blockers + PDE5I vs. PDE5I <u>IPSS (n=5)</u> MD -3.97 (-5.40,-2.53) p<0.00001 favours combination</p> <p><u>Qmax (n=4)</u> MD -0.55 (-1.20,-0.10) p<0.00001 favours combination</p> <p><u>PVR (n=4)</u> MD -23.43 (-36.54,-10.32) p=0.0005 favours combination</p> <p><u>QoL (n=3)</u> MD -0.81 (-1.41,-0.21) p=0.008</p>	Our novel data demonstrated that PDE5-Is plus alpha-blockers ranked the highest on the improvement of LUTS/BPH. PDE5-Is monotherapy was also effective in this kind of disorder except less reduction of PVR than alpha-blockers. In addition, both combined- or mono-therapy were safe.	serious heterogeneity ($I^2 \geq 75\%$) for PVR, QoL (Alpha-blockers + PDE5I vs. PDE5I) and QoL (Alpha-blockers + PDE5I vs. alpha-blockers) no conflict of interest declared supported by National Natural Science Foundation of China	LoE 1++ RoB: low



			the use of PDE5-Is.			<p>favours combination</p> <p><u>IIEF (n=4)</u> MD 0.98 (-1.24, 3.20) p=0.39</p> <p>Alpha-blockers + PDE5I vs. alpha-blockers</p> <p><u>IPSS (n=8)</u> MD -1.86 (-2.45, -1.27) p<0.00001 favours combination</p> <p><u>Qmax (n=8)</u> MD 0.81 (0.37, 1.24) p=0.0003 favours combination</p> <p><u>PVR (n=7)</u> MD -5.37 (-10.14, -0.62) p=0.03 favours combination</p> <p><u>QoL (n=6)</u> MD 4.09 (2.92, 5.26) p=0.0007 favours combination</p> <p><u>IIEF (n=6)</u> MD 4.09 (2.92, 5.26) p<0.00001</p>		<p>results only shown for the comparison combination therapy vs. monotherapy</p>
--	--	--	---------------------	--	--	--	--	---



<p>Yan, 2014, Journal of Sexual Medicine [140]</p>	<p>Systematic review with meta-analysis</p>	<p>n= 7 RCTs search up to November 2013 Follow-up: 60 days to 3 months Italy, USA, Turkey, China, India</p>	<p>The purpose of this meta-analysis was to evaluate the efficacy of PDE5 inhibitors alone or in combination with alpha-blockers for the treatment of erectile dysfunction and LUTS.</p>	<p>n= 515 patients</p>	<p>PDE5 inhibitors and alpha-blockers</p>	<ul style="list-style-type: none"> • PDE5 inhibitors 	<p><u>Erectile dysfunction</u> MD: 2.25 (95% CI 0.07, 4.43) p=0.04 favours PDE5-I alone <u>IPSS</u> MD: -4.21 (95% CI -7.09, -1.32) p=0.004 favours combination <u>Qmax</u> MD: 1.43 (95% CI -0.38, 2.47) p=0.007 favours PDE5-I alone</p>	<p>In PDE5 inhibitors with alfablockers induce a statistically significant improvement in IIEF, IPSS, and Qmax values. The analysis suggests that PDE5 inhibitors plus alpha-blockers are significantly superior to PDE5 inhibitors alone for the treatment of erectile dysfunction and LUTS.</p>	<p>serious heterogeneity ($I^2 \geq 75\%$) for erectile dysfunction and IPSS no conflict of interest declared no information about funding Conclusion and Fig 3 and 4 are showing inconsistent results.</p>	<p>LoE 1++ RoB: low</p>
<p>Gacci, 2012, European Urology [141]</p>	<p>Systematic review with meta-analysis</p>	<p>n=12 RCTs Median follow-up: 12 weeks Search through September 2011</p>	<p>Perform a systematic review and meta-analysis of available prospective and cross-sectional studies on the use of PDE5-Is alone or in combination with a1-adrenergic blockers in patients with LUTS/BPH.</p>	<p>n=3430 patients</p>	<ul style="list-style-type: none"> • PDE5-Is vs. placebo (n=7 studies) • PDE5-Is + a1-adrenergic blockers vs. a1-adrenergic blockers (n=5 studies) 		<p>PDE5-Is+a1-adrenergic blockers vs. a1-adrenergic blockers (n=216 men) <u>IPSS</u> MD -1.85 (95% CI -3.73,0) p=0.05 <u>Qmax</u> MD 1.53 (95% CI 0.91,2.16) p < 0.0001 favour combination therapy <u>IIEF score</u></p>	<p>The meta-analysis of the available cross-sectional data suggests that PDE5-Is can significantly improve LUTS and erectile function in men with BPH. PDE5-Is seem to be a promising treatment option for patients with LUTS secondary to BPH with or without erectile dysfunction.</p>	<p>no information if efforts were made to minimise error in the study selection or data collection, no risk of bias assessment, no funnel plot or sensitivity analyses no conflict of interest or funding declared Results only shown for the</p>	<p>LoE 1 - RoB: high</p>



							MD 3.60 (95% CI 3.07,4.12) p < 0.0001 favour combination therapy		comparison combination therapy vs. monotherapy	
α1-Blocker & 5α-Reduktasehemmer vs. monotherapy										
Kang, 2017, clinical & Investigative Medicine [142]	Systematic review with meta-analysis	n= 6 RCTs Search up to May 2015 Mean follow-up: 6-54 mo	This study compared the efficacy of an α-blocker monotherapy alone with a combination of α-blocker plus 5α-reductase in treatment of BPH.	n= 6838 patients Mean age range: 63-66 y	α-blocker + 5α-reductase n=3438	α-blocker n=3400	<u>Acute urinary retention</u> OR: 0.286 (95% CI 0.199, 0.412) p=0.677 <u>Operation rate after intervention</u> OR: 0.277 (95% CI 0.2, 0.0384) p=0.342 <u>Prostate volume at 1-y after intervention</u> MD: -7.387 (95% CI -12.982, -1.791) p=0.006 <u>Urinary flow rate</u> MD: 0.527 (95% CI 0.052, 1.003) p=0.982 <u>Change in IPSS score at 1-year after intervention</u> MD: -0.087 (95% CI -0.231, 0.058) p=0.239	These findings indicate that combined α-blocker plus 5α-reductase therapy is more beneficial in treating benign prostatic hyperplasia in contrast to α-blocker monotherapy.	no information if efforts were made to minimise error in the risk of bias assessment serious heterogeneity (I ² ≥75%) for prostate volume Employee of MSD China Holding Company. The medical writing and editorial assistance was funded by MSD China. Cave: Errors in the Figure 5 description and the values in Figure 6 do not	LoE 1++ RoB: low



									match with the text	
Favilla, 2016, Aging Male [143]	Systematic review with meta-analysis	n= 5 RCTs search up to December 2015	The aim of this systematic review and meta-analysis was to evaluate the impact of combination therapy on erectile dysfunction and libido alterations from RCT.	n= 6131 patients	Alpha-blockers plus 5-ARI versus	<ul style="list-style-type: none"> • Alpha-blocker • 5-ARI 	<p>Combination therapy vs. alpha-blocker <u>Erectile dysfunction</u> OR 1.81 (95% CI 1.45, 2.26) p<0.00001 favours combination</p> <p><u>Libido alterations</u> OR 1.58 (95% CI 1.16, 2.14) p=0.003 favours combination</p> <p>Combination therapy vs. 5-ARI <u>Erectile dysfunction</u> OR 1.25 (95% CI 1.01, 1.53) p=0.04 favours combination</p> <p><u>Libido alterations</u> OR 1.03 (95% CI 0.77, 1.37) p=0.84</p>	We demonstrated that combination therapy with ABs and 5-ARIs was associated with significantly higher risk of erectile dysfunction and libido alterations compared with single monotherapy. Combination therapy showed similar risk of libido alterations compared with 5-ARI monotherapy.	<p>no information if efforts were made to minimise error in the risk of bias assessment, funnel plot and detailed risk of bias assessment for the included studies not shown</p> <p>no conflict of interest declared</p> <p>no information about funding</p> <p>Results only shown for the comparison combination therapy vs. monotherapy</p>	<p>LoE 1-</p> <p>RoB: high</p>
Gacci, 2014, Journal of Sexual medicine [144]	Systematic review with meta-analysis	n=23 RCTs Search date: January 2013	Ejaculatory dysfunction related to medical treatments for LUTS.	n= more than 4800 patients included in the combination therapy studies	<ul style="list-style-type: none"> • alpha-blockers vs. placebo (n=7) • 5ARIs vs. placebo (n=5) • 5ARI + alphablocker (n=4) 		<p>Ejaculation disorder <u>Combination vs. alpha-blocker</u> OR 3.75 (95% CI 2.81, 5) p<0.00001 favours alpha-blocker</p>	Combination therapy with alpha-blockers and 5ARIs resulted in a 3-fold increased risk of ejaculatory dysfunction related as compared with alpha-blockers or 5ARIs alone.	<p>no information if efforts were made to minimise error in the data collection, no risk of bias assessment, no funnel plot or</p>	<p>LoE 1-</p> <p>RoB: high</p>



					<ul style="list-style-type: none"> • alpha-blocker vs. alpha-blocker (n=3) • alpha-blocker vs. 5ARI (n=2) • 5ARI vs. 5ARI (n=1) others (n=1) 		<p><u>Combination vs. 5ARI</u> OR 2.76 (95% CI 1.20, 6.32) p=0.02 favours 5ARI</p>		<p>sensitivity analysis</p> <p>Several reactions to pharmaceutical industries</p> <p>serious heterogeneity ($I^2 \geq 75\%$) for combination therapy vs. 5ARI</p> <p>no information about funding</p> <p>Results only shown for the comparison combination therapy vs. monotherapy.</p>	
α1-Blocker & Muskarinrezeptorantagonisten vs. monotherapy										
Pang, 2021, Cochrane Database of Systematic Reviews [133]	Systematic review with meta-analysis	n= 23 RCTs search up to 7 August 2020	To assess the effects of combination therapy with anticholinergics and alpha-blockers in men with LUTS related to BPO.	n= 6285 men with LUTS secondary to BPO Mean age: 65.7 y (54.4-73.9 y)	Alpha Blocker + Anticholinergic	<ul style="list-style-type: none"> • alpha blocker • anticholinergics 	<p>Combination therapy vs. alpha-blocker (short term)</p> <p><u>Urologic symptom scores</u> (n=19 RCTs) MD -2.04 (95% CI -3.56; -0.52) p=0.009 favours combination</p> <p><u>QoL</u> (n=15 RCTs)</p>	<p><u>Combination therapy versus alpha-blockers:</u></p> <p>Combination therapy with anticholinergics and alpha-blockers may have uncertain effects on improvement of urinary symptoms and quality of life compared to alpha-</p>	serious heterogeneity ($I^2 \geq 75\%$) for Urologic symptom scores, QoL (alpha-blocker comparison), Urologic symptom scores	LoE 1++ RoB: low



						<p>MD -0.71 (95% CI -1.03; -0.38) p<0.0001 favors combination</p> <p><u>Adverse events</u> (n=12 RCTs) RR 1.10 (95% CI 0.9;1.34) p=0.34</p> <p><u>Acute urinary retention</u> (n=19 RCTs) RR 2.03 (95% CI 0.97;4.23) p=0.06</p> <p><u>Surgical intervention</u> (n=4 RCTs) RR 1.72 (95% CI 0.34;8.63) p=0.51</p> <p>Combination therapy vs. anticholinergics (short term) <u>Urologic symptom scores</u> (n=2 RCTs) MD -3.71 (95% CI -9.41;1.98) p=0.2</p> <p><u>QoL</u> (n=1 RCT) MD -1.49 (95% CI -1.88; -1.11) p<0.00001 favors combination</p> <p><u>Adverse events</u> (n=1 RCT)</p>	<p>blockers alone. Combination therapy may not increase unwanted side effects.</p> <p><u>Combination therapy compared to anticholinergics:</u> Combination therapy with anticholinergics and alpha-blockers may be associated with uncertain effects on urinary symptoms, but an improvement in quality of life in comparison with anticholinergics alone. Combination therapy may not increase unwanted side effects.</p>	<p>(anticholinergics) No conflict of interest.</p> <p>Funding: Guang An Men Hospital, China Academy of Chinese Medical Sciences, China Beijing Municipal Science & Technology Commission, China</p> <p>results only shown for the comparison combination therapy vs. monotherapy</p>
--	--	--	--	--	--	--	--	--



							RR 1.26 (95% CI 0.81;1.95) p=0.3 <u>Acute urinary retention</u> (n=3 RCTs) RR 0.55 (95% CI 0.11;2.65) p=0.46			
Kim, 2017, PloS ONE [145]	Systematic review with meta-analysis	n=16 RCTs search up to April 2016	The objective of this study was to determine the benefits and safety of initial combination treatment of an alpha blocker with anticholinergic medication in BPH/LUTS through a systematic review and meta-analysis.	n= 3548 Patients with Lower Urinary Tract Symptoms	Alpha Blocker + Anticholinergic n= 2195	alpha blocker n= 1353	IPSS total SMD -0.03 (95% CI -0.14, 0.08) IPSS storage SMD -0.28 (95% CI -0.4, -0.17) favours combination QoL SMD -0.29 (95% CI -0.5, -0.07) favours combination Qmax SMD 0.00 (95% CI -0.08, 0.08) PVR SMD 0.56 (95% CI 0.23, 0.89) favours alpha blocker	Initial combination treatment of an alpha blocker with anticholinergic medication is efficacious for in BPH/LUTS with improved measures such as storage symptoms and QoL without causing significant deterioration of voiding function.	no information if efforts were made to minimise error in the data collection or risk of bias assessment serious heterogeneity ($I^2 \geq 75\%$) for QoL, Qmax and PVR This study was partly supported by Astellas Pharma Korea, Inc. no further information about conflict of interest	LoE 1++ RoB: low
Yan, 2017, Urologia Internationalis	Systematic review with meta-analysis	n=7 RCTs 2000-February 2016	The purpose of this meta-analysis was to evaluate the	n= 710 patients	antimuscarinics + alpha-blocker	antimuscarinics	Total IPSS MD -3.26 (95% CI -4.16, -2.35) p<0.00001 favours combination	Our meta-analysis shows the beneficial effect of antimuscarinics alone in reducing	no information if efforts were made to minimise error in the risk of	LoE 1++ RoB: low



[146]		Median follow-up: 2wks	efficacy of antimuscarinics alone or in combination with alpha-blockers for the treatment of ureteral stent-related symptoms.				<p><u>QoL</u> MD -1.26 (95% CI -1.60, -0.93) p<0.00001 favours combination</p> <p><u>Visual Analogue Pain Scale</u> MD -0.70 (95% CI -1.92, -0.52) p=0.26</p> <p><u>Urinary symptoms</u> MD -3.63 (95% CI -7.78, 0.52) p=0.09</p> <p><u>body pain</u> MD -4.71 (95% CI -6.48, -2.94) p<0.00001 favours combination</p> <p><u>general health</u> MD -0.56 (95% CI -4.55, 3.44) p=0.79</p> <p><u>work performance</u> MD -0.96 (95% CI -1.61, -0.31) p=0.004 favours combination</p> <p><u>sexual matters index</u> MD -1.25 (95% CI -4.57, 2.06) p=0.46</p>	stent-related symptoms. The combined use of antimuscarinics and alpha-blockers results in additive favorable effects in patients with ureteral stent-related symptoms compared with antimuscarinics monotherapy. The alphablockers may enhance the efficacy of the antimuscarinics, which is beneficial for the treatment of ureteral stent-related symptoms.	<p>bias assessment, no results of sensitivity analysis shown</p> <p>serious heterogeneity ($I^2 \geq 75\%$) for visual analogue pain scale, urinary symptoms, general health and sexual matters index</p> <p>No competing financial interests exist.</p> <p>no information about funding</p> <p>results only shown for the comparison combination therapy vs. monotherapy</p>	
Hao, 2014, Urology	Systematic review	n= 18 RCTs	To assess the clinical	n= 4084 patients	Antimuscarinics and a-blockers	a-blockers n=1978	Storage IPSS	Antimuscarinics could and should be added	no funnel plots or sensitivity	LoE 1++



[147]	with meta-analysis	search up to June 2013	efficiency and safety of combination pharmacotherapy of antimuscarinics and α -blockers vs α -blockers monotherapy on patients with moderate to severe LUTS.		n=2106		<p>MD -1.51 (95% CI - 2.10, -0.91) p<0.00001 favours combination</p> <p>QoL MD -0.53 (95% CI - 0.27, 0.17) p=0.64</p> <p>Qmax MD -0.05 (95% CI - 0.27, 0.17) p=0.64</p> <p>PVR MD 6.53 (95% CI 3.06, 10.00) p=0.0002 favours monotherapy</p> <p>Total IPSS MD -0.88 (95% CI - 1.64, -0.12) p=0.02 favours combination</p> <p>Voiding IPSS MD 0.40 (95% CI - 0.34, 1.15) p=0.29</p> <p>Micturitions per 24h MD -1.14 (95% CI - 1.84, -0.45) p=0.0001 favours combination</p> <p>Urgency episodes per 24 hours</p>	to the drug regimen for patients with LUTS attributed to benign prostatic hyperplasia/bladder outlet obstruction, particularly are dominated by storage symptoms. For patients with increased acute urinary retention risk, they should be carefully monitored.	<p>analyses, bias of included studies not discussed</p> <p>serious heterogeneity ($I^2 \geq 75\%$) for Storage IPSS, QoL, PVR, total IPSS, voiding IPSS, Micturitions and urgency episodes</p> <p>no conflict of interest declared</p> <p>no information about funding</p>	RoB: low
-------	--------------------	------------------------	--	--	--------	--	--	---	---	----------



							MD -0.99 (95% CI -1.64, -0.51) p<0.0001 favours combination			
Filson, 2013, Journal of Urology [148]	Systematic review with meta-analysis	n= 7 RCTs searched up to September 12, 2012	To compare treatment with a-blockers and anticholinergics (ie combination therapy) to a-blocker monotherapy to clarify the efficacy and safety of this treatment approach among men with storage urinary symptoms related to benign prostatic hyperplasia.	n= 3629 patients	Anticholinergic + alphablocker	<ul style="list-style-type: none"> • Placebo Alpha-blocker monotherapy 	<p>Combination vs. monotherapy IPSS MD -0.73 (95% CI -1.09, -0.37) p<0.001</p> <p><u>Urinary frequency</u> MD -0.69 (95% CI -0.97, -0.41) p<0.001</p> <p><u>PVR</u> MD 11.60 (95% CI 8.50, 14.70) p<0.001</p> <p><u>Maximal urinary flow</u> MD -0.59 (95% CI -1.04, -0.14) p=0.01</p> <p><u>AUR (req. catheterization)</u> OR 2.44 (95% CI 0.81, 7.39) p=0.115</p> <p><u>AUR (overall)</u> OR 3.05 (1.54, 6.02)</p>	Combination treatment with a-blockers and anticholinergics significantly improved storage voiding parameters compared to men treated with a-blocker therapy alone. This treatment approach is safe with a minimal risk of increased post-void residual urine volume, decreased maximal urinary flow rate or acute urinary retention.	unclear if all relevant studies are included, because no presenting of the risk of bias assessment, which was used as inclusion criteria for the studies, no information if efforts were made to reduce errors in the assessment	LoE 1- RoB: high



									Medical, Endo Pharmaceutical s and Allergan.	
									Supported by the National Institutes of Health Training in Clinical Investigation in Urology grant	
Xin, 2013, Urology [149]	Systematic review with meta- analyses	n= 15 RCTs search up to January 30, 2013 Median follow-up: 12 wks (4- 52 wks)	The purpose of this meta-analysis was to assess the efficacy and safety of combination therapy vs alpha-blockers monotherapy for treatment of men with LUTS.	sample sizes ranged from 46-943 patients more than 4500 men included	Antimuscarinics +Alpha-blockers	Alpha- blockers	<u>Urgency episodes</u> MD -0.53 (95% CI - 0.73, -0.32) p<0.00001 favours combination <u>Micturitions</u> MD -0.79 (95% CI - 0.98, -0.6) p<0.00001 favours combination <u>Voided urine volume</u> WMD 30.34 (95% CI 12.08- 48.60, p<.01) <u>IPSS total score</u> WMD -0.94 (95% CI -1.66 to -0.21, P= .03) favours combination <u>IPSS QOL</u>	Combination therapy incorporating alpha- blockers and antimuscarinics is associated with greater benefit than alpha-blockers in treatment of men with substantial storage symptoms. Apart from an increased rate of dry mouth and constipation, addition of antimuscarinics seems to be well tolerated and relatively safe, although adverse effects associated with the long-term combination therapy are not available. These generalized	The authors declare that they have no relevant financial interests. no funding declared	LoE 1++ RoB: low



							<p>WMD -0.14 (95% CI -0.25 to -0.04 P <.01) favours combination</p> <p><u>IPSS storage subscore</u> WMD -0.82 (95% CI -1.10 to -0.53, P <.01) favours combination</p> <p><u>IPSS voiding subscore</u> WMD 0.09 (95% CI -0.36 to 0.54) P= .70</p> <p><u>Retention episodes</u> RR 0.01 (95% CI 0.00, 0.01) p= 0.009 favours alpha-blocker</p> <p>Overall adverse events were higher in patients receiving addition of antimuscarinics (50.1% vs 34.4%, RR 1.45, 95% CI 1.21-1.72, P <.01)</p>	findings likely obscure the heterogeneity in study populations, antimuscarinic type (doses), and measurement of efficacy.		
--	--	--	--	--	--	--	---	---	--	--



Mehrere Kombinationen										
Pattanaik, 2018, Cochrane Database of Systematic Review [150]	Systematic review with meta-analysis	n= 16 RCTs search up tp August 2018	To assess the effects of phosphodiesterase inhibitors compared to placebo and other standard of care drugs (alpha-blockers and 5-ARIs) in men with LUTS consistent with BPH.	patients with benign prostatic hyperplasia	<ul style="list-style-type: none"> phosphodiesterase inhibitors vs. placebo phosphodiesterase inhibitors vs. alpha-blockers phosphodiesterase inhibitors+alpha-blockers vs. alpha-blockers phosphodiesterase inhibitors+alpha-blockers vs. phosphodiesterase inhibitors phosphodiesterase inhibitors+5-ARI vs. 5-ARI 	<p>Phosphodiesterase inhibitors+alpha-blockers vs. alpha-blockers IPSS (n=4) MD -2.56 (-3.92,-1.19) p=0.00025 favour combination</p> <p><u>Adverse events</u> (n=4) RR 2.81 (1.53,5.17) p=0.00091 favours alpha blocker</p> <p>IPSS-QoL (n=2) MD -1.08 (-1.92, -0.23) p=0.013 favours combination</p> <p>Phosphodiesterase inhibitors+alpha-blockers vs. phosphodiesterase inhibitors IPSS (n=1) MD -2.40 (-6.47,1.67) p=0.25</p> <p>Phosphodiesterase inhibitors+5-ARI vs. 5-ARI IPSS (n=1)</p>	There appears to be no added benefit of phosphodiesterase inhibitors combined with alpha-blockers compared to phosphodiesterase inhibitors or AB alone or phosphodiesterase inhibitors combined with 5-ARI compared to ARI alone with regards to urinary symptoms. Most evidence was limited to short-term treatment up to 12 weeks and of moderate or low certainty.	no conflict of interest or funding declared Results only shown for the comparison combination therapy vs. monotherapy	LoE 1++ RoB: low	



							<p>1 at 4 weeks: MD - 2.0 (-2.48, 1.16) p<0.00001 2 at 12 weeks: MD -1.4 (-2.24, -0.56) favours combination 3 at 26 weeks: MD -1 (-1.83, -0.17) p=0.019 favours combination</p> <p><u>IPSS-QoL (n=1)</u> 1 at 4 weeks: MD -0.30 (-0.58, -0.02) p=0.034 favours combination 2 at 12 weeks: MD -0.2 (-0.48, 0.08) p=0.16 favours combination 3 at 26 weeks: MD -0.2 (-0.48, 0.08) p=0.16</p> <p><u>Adverse events (n=1)</u> RR 1.07 (95% CI 0.84, 1.36) p=0.59</p>			
Brasure, 2016, Agency for Healthcare Research and Quality	Systematic review with meta-analysis	n= 62 (57 RCTs, 5 observational studies)	To assess the efficacy, comparative effectiveness, and adverse effects of newer drugs to treat LUTS	patients with lower urinary tract symptoms	<ul style="list-style-type: none"> • Alpha Blockers • Anticholinergics • Beta 3 Agonists • PDE-5s 		<p>Tolterodine + alphablockers vs. alphablockers (n=4 RCTs, 1249 patients) <u>Responders (n=1 RCT)</u></p>	None of the drugs or drug combinations newly used to treat LUTS attributed to BPH showed outcomes superior to traditional alphablocker	management for conflicts of interest described study included mixed study designs	LoE 1++ RoB: low



[130]		search up to July 2015	attributed to benign prostatic hyperplasia.				<p>RR 2.7 (95% CI 1.55-4.70) favors combination</p> <p><u>IPSS score (n=4 RCTs)</u> WMD -0.19 (-1.08 to 0.69) similar</p> <p><u>IPSS QoL (n=3 RCTs)</u> WMD -0.34 (-1.14 to 0.46) similar</p> <p><u>Acute urinary retention (n=3 RCTs)</u> OR 2.69 (0.25-28.96)</p> <p><u>Participants with ≥1 adverse effect (n=1)</u> RR 1.26 (1-1.58)</p> <p>Tolterodine/ alphablockers or 5-ARI vs. alphablockers or 5-ARI (n=1 RCT) <u>Mean Change IPSS</u> tolterodine plus doxazosin/dutasteride: -8.9 doxazosin/dutasteride: -6.5</p> <p><u>Acute urinary retention</u></p>	<p>treatment. Combination therapies adding an anticholinergic to an established alphablockers offered no benefit over alphablockers monotherapy in improving LUTS and often increased the rate of adverse effects.</p>	<p>(observational studies and RCTs)</p> <p>no information about funding</p> <p>results only shown for combination therapy vs. monotherapy</p>
-------	--	------------------------	---	--	--	--	--	--	--



							<p>tolterodine plus doxazosin/dutasteride: 4% doxazosin/dutasteride: 3.5%</p> <p><u>Dry mouth</u> tolterodine plus doxazosin/dutasteride: 14% doxazosin/dutasteride: 6%</p> <p>Solifenacin alpha-blocker combination vs. monotherapy <u>IPSS score (n=6 RCTs)</u> WMD -0.29 (-0.88 to 0.30) similar</p> <p><u>IPSS QoL (n=4 RCTs)</u> WMD -0.18 (-0.39 to -0.03) similar</p> <p><u>Acute urinary retention (n=4 RCTs)</u> OR 3.75 (0.71-19.79)</p> <p><u>Participants with ≥1 adverse effect (n=1)</u> RR 1.21 (1.09-1.35)</p>		
--	--	--	--	--	--	--	---	--	--



							<p>Fesoterodine/alpha-blocker combination vs. alphablocker (n=2 RCTs) <u>IPSS (n=2)</u> Konstantinidis: MD -1.7 (95% CI -5.85 to 2.46) Kaplan: MD 0.00 (-0.83 to 0.083) similar</p> <p><u>Acute urinary retention (n=1 RCTs)</u> OR 1.00 (0.06-15.91)</p> <p><u>Participants with ≥1 adverse effect (n=1)</u> RR 1.46 (1.25-1.71)</p> <p>Oxybutynin+alpha blocker combination vs. alphablocker (n=1 RCTs) • combination therapy improved mean I-PSS scores more than monotherapy (WMD = -1.70) • participants with ≥1 adverse event were similar</p>		
--	--	--	--	--	--	--	--	--	--



							<p>Darifenacin/alpha-blocker vs. alpha-blocker (n=2 RCTs) <u>IPSS/AUA-SS (n=2)</u> Singh: -1.6 Ceylan: -3.47 unclear</p> <p><u>IPSS QoL (n=1)</u> MD = -0.8</p> <p><u>Acute urinary retention (n=1 RCTs)</u> RR = 4.00 [0.47 to 33.73]</p> <p>Trospium alpha-blocker vs. alpha-blocker (n=1 RCT) • Evidence was insufficient to assess efficacy for any outcome.</p> <p>Mirabegron+alpha-blocker vs. alpha-blocker (n=1) • evidence was insufficient for mean change in I-PSS score and adverse effects</p>		
--	--	--	--	--	--	--	--	--	--



							<p>Tadalafil+alphablocker vs. alphablocker (n=4) IPSS (n=4) WMD: -20.1 (-4.03 to 0.00)</p> <p>IPSS QoL (n=3) WMD: -0.44 (-0.73 to -0.15) similar (clinically)</p> <p>Tadalafil combination vs. 5-ARI Monotherapy or 5-ARI/alphablocker</p> <ul style="list-style-type: none"> • combined tadalafil/finasteride therapy improved mean I-PSS scores more than finasteride monotherapy (MD = -1.0) • IPSS QoL improvement was similar with combination and monotherapy (MD = -0.2) • Combined tadalafil/standard therapy also improved I-PSS QoL scores more 		
--	--	--	--	--	--	--	--	--	--



							<p>than standard therapy/placebo (MD = -0.6)</p> <p><u>I-PSS improvement</u> combination: 5.5 finasteride: 4.5</p> <p><u>Erectile dysfunction</u> combination: 1 finasteride: 5</p> <p><u>Improved I-PSS scores</u> tadalafil/standard therapy: 5.4 points tadalafil/standard therapy: 2.3 points</p> <p>Sildenafil+alpha blocker vs. alpha blocker (n=4) <u>IPSS (n=3)</u> WMD = -1.73 (95% CI -4.76 to 1.30) (n=1: MD -1)</p> <p><u>IPSS QoL (n=2)</u> Ozturk: MD -0.10 (95% CI -0.47 to 0.27) Tuncel: MD (95% CI -1.51 to -0.89)</p> <p>Vardenafil+ alpha blocker vs.</p>		
--	--	--	--	--	--	--	--	--	--



							<p>alphablocker (n=1)</p> <p><u>Mean recution in IPSS</u> combination: 5.8 monotherapy: 3.7 both achieving minimal detectable difference</p> <p><u>Adverse events</u> combination: 3 monotherapy: 2</p>			
--	--	--	--	--	--	--	--	--	--	--



Tabelle 26: Monotherapien vs. Monotherapien

Schlüsselfrage										
Welche Effekte zeigen die Monotherapien (nicht Phytotherapeutika) bei Patienten mit BPS im Vergleich zu den anderen Monotherapien?										
Referenz	Studien-design	Studien-charakterisitika	Studienziel	Patienten-merkmale	Intervention	Kontrolle	Ergebnisse	Schlussfolgerung	Bemerkungen	LoE
Netzwerk-Metanalyse										
Yuan, 2015, Medicine [151]	Systematic reviews with network meta-analysis	n= 124 RCTs up to February 2015	The objective of this study is to evaluate the comparative effectiveness and safety of monodrug therapies for BPH.	n= 58548 participants	<ul style="list-style-type: none"> • Finasteride • Dutasteride • Tadalafil • Vardenafil • Sildenafil • Tolterodine • Solifenacin • Fesoterodine • Naftopidil • Silodosin • Terazosin • Tamsulosin • Doxazosin • Alfuzosin 		<p><u>IPSS</u></p> <ul style="list-style-type: none"> • All drug therapies except tolterodine and solifenacin significantly improved the IPSS compared with placebo • improvement in the IPSS was comparable among silodosin, tamsulosin, alfuzosin, naftopidil, dutasteride, ardenafil, sildenafil, and tadalafil <p><u>Peak Urinary Flow Rate</u></p> <ul style="list-style-type: none"> • Doxazosin and dutasteride showed the greatest improvements • compared with placebo, doxazosin, dutasteride, terazosin, alfuzosin, tamsulosin, 	In conclusion, a-blockers, 5ARIs, and PDE5-Is are effective for BPH, with doxazosin and terazosin appearing to be the most effective agents. Drug therapies for BPH are generally safe and well-tolerated, with no major difference regarding the overall safety profile.	The authors have no funding and conflicts of interest to disclose	LoE 1++ RoB: low



							<p>naftopidil, and silodosin significantly increased the peak urinary flow</p> <ul style="list-style-type: none"> • doxazosin was significantly more effective than all other drug therapies • The effectiveness of dutasteride, terazosin, alfuzosin, tamsulosin, naftopidil, and silodosin was comparable • effectiveness of different classes of PDE5-Is was comparable in improving peak urinary flow <p><u>Safety</u></p> <ul style="list-style-type: none"> • Drug therapies were typically safe and well tolerated <p><u>primary specific adverse events</u></p> <ul style="list-style-type: none"> • among α-blockers: dizziness, headache, and asthenia • 5ARIs: impotence and decreased libido • muscarinic receptor antagonists: dry mouth, constipation, and dizziness 		
--	--	--	--	--	--	--	---	--	--



							• PDE5-I: headache and back pain			
Wang, 2014, PLoS One [132]	Systematic review with network meta-analysis	n=66 RCTs Search till June 2013	The aim of our study was to carry out a systematic review and network meta-analysis comparing the efficacy of different drug therapies for LUTS/BPH based on existing RCTs and ranking these regimens for practical consideration.	n=29384 participants	<ul style="list-style-type: none"> • alpha-blockers • alpha-blockers +PDE5-I • alpha-blockers + muscarinic receptor antagonists • alpha-blockers +5-ARI • 5a-reductase inhibitors • PDE5-I • muscarinic receptor antagonists • placebo 		<p>IPSS total score <u>Alphablocker vs. 5ARI</u> MD -0.96 (-1.8,-0.14) p=0.02</p> <p><u>Alphablocker vs. muscarinic receptor antagonists</u> MD -0.86 (-2.5,-0.77) p=0.30</p> <p><u>Alphablocker vs. PDE5-I</u> MD 0.11 (-0.53,0.75) p=0.74</p> <p><u>5ARI vs. muscarinic receptor antagonists</u> MD 0.1 (-1.69,1.9) p=0.04</p> <p><u>5ARI vs. PDE5-I</u> MD 1.07 (0.05,2.11) p=0.92</p> <p><u>Muscarinic receptor antagonists vs. PDE5-I</u> MD 0.98 (-0.75,2.72) p=0.72</p> <p>Qmax <u>Alphablocker vs. 5ARI</u> MD -0.12 (-0.75, -0.49) p=0.68</p>	Overall, combination therapies resulted in a relatively better effect than monotherapies	no information if efforts were made to minimise error in the study selection or the risk of bias assessment, no funnel plot or sensitivity analyses	LoE 1- RoB: high
									no conflict of interest declared	supported by National Natural Science Foundation of China
										only results shown for the comparison monotherapy vs. monotherapy



						<p><u>Alphablocker vs. muscarinic receptor antagonists</u> MD 1.36 (0.04,2.65) p=0.04</p> <p><u>Alphablocker vs. PDE5-I</u> MD 0.84 (0.05,1.63) p=0.04</p> <p><u>5ARI vs. muscarinic receptor antagonists</u> MD 1.46 (0.05,2.88) p=0.04</p> <p><u>5ARI vs. PDE5-I</u> MD 0.84 (0.05,1.63) p=0.04</p> <p><u>Muscarinic receptor antagonists vs. PDE5-I</u> MD -0.64 (-2.06,0.76) p=0.37</p> <p>IPSS-storage subscore <u>Alphablocker vs. 5ARI</u> MD -0.41 (-1.84, -1.07) p=0.6</p> <p><u>Alphablocker vs. muscarinic receptor antagonists</u> MD -0.75 (-3.08,1.55) p=0.52</p> <p><u>Alphablocker vs. PDE5-I</u> I</p>		
--	--	--	--	--	--	--	--	--



						<p>MD 0.3 (-0.48,1.09) p=0.45</p> <p><u>5ARI vs. muscarinic receptor antagonists</u> MD -0.35 (-3.12,2.34) p=0.78</p> <p><u>5ARI vs. PDE5-I</u> MD 0.7 (-0.94,2.36) p=0.4</p> <p><u>Muscarinic receptor antagonists vs. PDE5-I</u> MD 1.06 (-1.38,3.48) p=0.4</p> <p>IPSS-voiding subscore <u>Alphablocker vs. 5ARI</u> MD -0.51 (-1.33,0.32) p=0.23</p> <p><u>Alphablocker vs. muscarinic receptor antagonists</u> MD -1.72 (-4.08,0.65) p=0.16</p> <p><u>Alphablocker vs. PDE5-I</u> MD -0.05 (-0.58,0.46) p=0.82</p> <p><u>5ARI vs. muscarinic receptor antagonists</u> MD -1.22 (-3.67,1.24) p=0.33</p>			
--	--	--	--	--	--	--	--	--	--



							<p><u>5ARI vs. PDE5-I</u> MD 0.46 (-0.57,1.41) p=0.41</p> <p><u>Muscarinic receptor antagonists vs. PDE5-I</u> MD 1.67 (-0.76,4.04) p=0.18</p> <p>Figure 7 shows the complete ranking</p>			
Systematische Übersichtsarbeiten mit Metaanalysen										
Alphablocker vs. 5-Alpha Reduktase Inhibitoren										
Gacci, 2014, Journal of Sexual medicine [144]	Systematic review with meta-analysis	n=23 RCTs Search date: January 2013	Ejaculatory dysfunction related to medical treatments for LUTS.	n= more than 4800 patients included in the combination therapy studies	<ul style="list-style-type: none"> • alpha-blockers vs. placebo (n=7) • 5ARIs vs. placebo (n=5) • 5ARI + alphablocker (n=4) • alpha-blocker vs. alpha-blocker (n=3) • alpha-blocker vs. 5ARI (n=2) • 5ARI vs. 5ARI (n=1) • others (n=1) 		<p>Ejaculation disorder <u>Alpha-blocker vs. 5ARI</u> OR 0.7 (95% CI 0.30, 1.66) p=0.42</p> <p><u>Finasteride vs. 5ARI (n=5)</u> OR 0.5 (95% CI 0.18, 1.38) p=0.18</p> <p><u>Dusteride vs. 5ARI (n=1)</u> OR 1.75 (95% CI 0.93, 3.29) p=0.08</p>	In our systematic review and meta-analysis of the impact of medical treatments for LUTS due to BPH on ejaculatory function we demonstrated that alpha-blockers and 5ARI were both associated with significantly higher risk of ejaculation disorder than placebo. More the alpha-blocker is effective over time, greater is the incidence of ejaculation disorder. Finasteride has the same risk of	no information if efforts were made to minimise error in the data collection, no risk of bias assessment, no funnel plot or sensitivity analysis several realtions to pharmaceutical industries no information about funding Results only shown for the comparison combination	LoE 1- RoB: high



Phosphodiesterase-5-Hemmer vs. Alphablocker										
Sun, 2020, Minerva Urologica e Nefrologica [135]	Systematic review with meta-analysis	n=19 studies (17 RCTs, 2 retrospective cohort studies) last update: October 2017	To systematically investigate the efficacy and safety of combination therapy in comparison with monotherapy.	n= 2472 patients with LUTS n= 9 studies compared monotherapies	Alpha-blocker	PDE5I	<u>IPSS</u> MD -0.51 (-0.61 to -0.41) p<0.00001 <u>QoL</u> MD -0.15 (-0.22 to -0.08) p<0.00001 <u>Qmax</u> MD -0.07 (0.28-0.15) p<0.00001 <u>PVR</u> MD 9.09 (5.37-12.82) p<0.00001 <u>IIEF</u> MD 3.90 (2.91 to -4.89) p<0.00001 <u>Headache</u> RR 9.2 (0.51-165.99) p= 0.13 <u>Flushing</u> RR 5.11 (0.25-103.53) p= 0.29 <u>Dyspepsia</u> RR 9.2 (0.51-165.99) p= 0.13	PDE5I is better than is alpha-blockers in improving IPSS, QoL, PVR and IIEF.	no information if efforts were made to minimise error in the study selection, data collection and risk of bias assessment no conflict of interest declared funding: National Natural Science Foundation of China Results only shown for the comparison monotherapy vs. monotherapy	LoE 1- RoB: high



<p>Pattanaik, 2018, Cochrane Database of Systematic Review [150]</p>	<p>Systematic review with meta-analysis</p>	<p>n= 16 RCTs search up to August 2018</p>	<p>To assess the effects of phosphodiesterase inhibitors compared to placebo and other standard of care drugs (alpha-blockers and 5-ARIs) in men with LUTS consistent with BPH.</p>	<p>patients with benign prostatic hyperplasia</p>	<ul style="list-style-type: none"> • phosphodiesterase inhibitors vs. placebo • phosphodiesterase inhibitors vs. alpha-blockers • phosphodiesterase inhibitors+alpha-blockers vs. alpha-blockers • phosphodiesterase inhibitors+alpha-blockers vs. phosphodiesterase inhibitors • phosphodiesterase inhibitors+5-ARI vs. 5-ARI 		<p>Phosphodiesterase inhibitors vs. alpha-blockers <u>IPSS total (n=4)</u> MD 0.22 (-0.49, 0.93) p=0.54</p> <p><u>Benign Prostatic Hyperplasia Impact Index (n=2)</u> MD 0.03 (-1.10, 1.16) p=0.96</p> <p><u>IPSS QoL (n=4)</u> MD -0.1 (-0.48, 0.29) p=0.63</p> <p><u>Any adverse event with short-term use (n=4)</u> RR 1.35 (0.8,2.3) p=0.27</p> <p><u>Adverse events with short-term use related to vasodilatation (n=3)</u> RR 2.42 (1.05,5.56) p=0.038 favours alpha-blocker</p> <p><u>Adverse events with short-term use related to body pain (n=3)</u> RR 1.75 (0.38, 8.18) p=0.47</p> <p><u>Adverse events with short-term use related to upper</u></p>	<p>There is probably no difference between phosphodiesterase inhibitors and alpha-blockers when it comes to improving urinary symptoms, and there may be no difference with regards to how bothersome symptoms are, or unwanted drug effects.</p>	<p>serious heterogeneity ($I^2 \geq 75\%$) for Benign Prostatic Hyperplasia Impact Index</p> <p>no conflict of interest or funding declared</p> <p>Results only shown for the comparison monotherapy vs. monotherapy</p>	<p>LoE 1++ RoB: low</p>
--	---	--	---	---	---	--	--	---	--	--



							<p><u>gastrointestinal tract (n=3)</u> RR 4.87 (0.58, 41.22) p=0.15</p> <p><u>Adverse events with short-term use leading to treatment discontinuation (n=4)</u> RR 1.26 (0.31, 5.05) p=0.75</p>			
Wang, 2015, Asian Journal of Andrology [152]	Systematic review with meta-analysis	n=12 RCTs search up to January 2014	The aim of the present review was to compare the efficacy and safety of PDE5-Is and ABs used alone or combined for treating LUTS/BPH based on existing RCTs, so as to provide a more systematic and comprehensive assessment for the use of PDE5-Is.	patients with LUTS due to benign prostatic hyperplasia	Alpha-blockers	PDE5I	<p>IPSS MD 0.87 (-0.1, 1.84) p=0.08</p> <p>Qmax MD -0.55 (-1.2,0.1) p=0.09</p> <p>PVR MD 9.82 (3.80,15.85) p=0.001 favours alpha-blockers</p> <p>QoL MD -0.02 (-0.5,0.46) p=0.94</p> <p>IIEF MD 3.67 (1.56,5.77) p=0.0006 favours PDE5-Is</p> <p>Any adverse effects OR 1.05 (0.78,1.43) p=0.74</p> <p>Dizziness</p>	Our novel data demonstrated that PDE5-Is plus ABs ranked the highest on the improvement of LUTS/BPH. PDE5-Is monotherapy was also effective in this kind of disorder except less reduction of PVR than ABs. In addition, both combined- or mono-therapy were safe.	serious heterogeneity ($I^2 \geq 75\%$) for QoL no conflict of interest declared supported by National Natural Science Foundation of China results only shown for the comparison monotherapy vs. monotherapy	LoE 1++ RoB: low



							OR 0.56 (0.21,1.48) p=0.24 Dyspepsia OR 1.17 (0.35,3.89) p=0.8 Headache OR 1.38 (0.58,3.25) p=0.47 Nasopharyngitis OR 0.98 (0.39,2.44) p=0.96			
--	--	--	--	--	--	--	--	--	--	--



7. Evidenztabelle zum Kapitel ‚Instrumentelle/operative Verfahren‘

Tabelle 27: Laser-Verfahren

Schlüsselfrage										
Welche Effekte zeigen Laser-Verfahren bei Patienten mit BPS?										
Referenz	Studien-design	Studien-charakteristika	Studienziel	Patienten-merkmale	Intervention	Kontrolle	Ergebnisse	Schlussfolgerung	Bemerkungen	LoE
Metaanalyse										
Greenlight PVP vs. HoLEP										
Peng, 2020, Lasers in Medical Science [153]	Systematic review with meta-analysis	n=6 studies (2 RCTs, 4 retrospective cohort studies) Follow-up: 6-60 mo Search up to August 2019	This study aims to compare the efficacy and safety of holmium laser technologies and PVP for the treatment of BPH, and to perform a meta-analysis.	n=2014 patients with BPH	• PVP	<ul style="list-style-type: none"> • Holmium laser ablation (n=1 RCT) • HoLEP (n=1 RCT, 3 cohort studies) • holmium laser transurethral incision (n= 1 cohort study) 	HoLEP vs. PVP <ul style="list-style-type: none"> • HoLEP had better results in 1-, 3-, 6-month and 1-year Qmax, less PVR, less energy consumption, and lower conversion rate • HoLEP had similar performance in IPSS (P = 0.39), QoL (P = 0.74), catheterization time (P = 0.78), and overall adverse event rates (P = 0.83). 	Subgroup analysis of HoLEP vs. PVP suggested that HoLEP presented better results in 1-, 3-, 6-month and 1-year Qmax with less PVR, less energy consumption, and lower conversion rate. Compared with PVP, holmium laser therapies had higher 1-, 3-, and 6-month Qmax, less PVR, and less total energy consumption with a	no information if efforts were made to minimise error in the study selection, data collection and the risk of bias assessment, no funnel plot or sensitivity analysis no conflict of interest declared This study was funded by the	LoE 2- RoB: high



							<ul style="list-style-type: none"> • Statistical significant shorter operative time (MD = -3.67, P = 0.04), but not clinical relevant • PVP: high-risk patients with BPH regardless of the administration of anticoagulant therapy have a low blood transfusion rate • HoLEP: intermittent or continuous use of anticoagulant therapy did not adversely increase the risk of bleeding • HoLEP seems to be more cost-effective than PVP 	relatively lower risk of conversion rate. In subgroup analyses, HoLEP had shown better results in accordance with all holmium laser therapies.	National Natural Science Fund of China (grant no. 81770673) and 1.3.5. project for disciplines of excellence, West China Hospital, Sichuan University (grant no. ZY2017310). results only shown for HoLEP vs. PVP	
Netzwerk-Metaanalysen										
Huang, 2019, BMJ [154]	Systematic review with network meta-analysis	n=109 trials (106 two arms, 3 tree arms) Search date: from inception to 31 March 2019	To assess the efficacy and safety of different endoscopic surgical treatments for benign prostatic hyperplasia.	n=13676 patients with BPH	<ul style="list-style-type: none"> • Enucleation (Thulium, Holmium, Diode, bipolar) • Vapourisation (Diode, Greenlight, bipolar) • Resection (monopolar & bipolar TURP) 		<ul style="list-style-type: none"> • Enucleation achieved better Qmax and IPSS values than resection and vapourisation • Haemoglobin declination (n=68): vapourisation and enucleation methods were 	Eight new endoscopic surgical methods for benign prostatic hyperplasia appeared to be superior in safety compared with monopolar TURP. Among these new treatments,	no conflict of interest declared supported partly by a grant from the National Science Council in Taiwan	LoE 1++ RoB: low



							<p>ranked higher than bipolar TURP</p> <ul style="list-style-type: none"> • Clot retention and blood transfusion events: Vapourisation and enucleation methods using either laser or bipolar energy were ranked higher than bipolar TURP • Recurrence: Enucleation methods and bipolar TURP performed better than vapourisation methods 	enucleation methods showed better Qmax and IPSS values than vapourisation and resection methods.		
Sun, 2018, Medicine [155]	Systematic review with network meta-analysis	n= 88 RCTs 1995-2016	We made a network meta-analysis to compare the efficacy and safety of different transurethral procedures for BPH.	n=11187 enrolled patients with BPH	<ul style="list-style-type: none"> • diode laser vaporization • Nd:YAG • PVP • KTP/Nd:YAG • ILC • TURis • TmLRP • TmLEP • HoLEP • TURP • HoLRP • DiLEP • PKRP • PKEP • TUVV 	<p>Rank probability from the best to the worst</p> <p><u>IPSS</u> diode laser vaporization > Nd:YAG > PVP > KTP/Nd:YAG > ILC > TURis > TmLRP > TmLEP > HoLEP > M-TURP > HoLRP > DiLEP > PKRP > PKEP > TUVV</p> <p><u>Qmax</u> diode laser vaporization > PVP > Nd:YAG > KTP/Nd:YAG > ILC > HoLRP > TmLRP > TURis ></p>	Compared with other transurethral procedures, thulium, holmium and diode lasers were associated with better efficacy and fewer complications.	no additional hand-search, no information if efforts were made to minimise error in the study selection, no information about between-study variation, no funnel plots or sensitivity analysis no conflict of interest declared	LoE 1- RoB: high	



							<p>TmLEP>M-TURP>PKRP>HoLEP>DiLEP >PKEP>TUVP</p> <p><u>PVR</u> HoLEP > Nd:YAG > PVP > ILC > diode laser vaporization > PKRP > TURis > M-TURP > HoLRP > TmLRP > TmLEP > DiLEP > PKEP > TUVP > KTP/Nd:YAG</p> <p><u>Quality of Life</u> TmLRP > TmLEP > HoLEP > HoLRP > PVP > DiLEP > M-TURP > PKRP > PKEP> TUVP > TURis</p> <p><u>Operation time (fast to slow)</u> PKRP > DiLEP > M-TURP > Nd:YAG > KTP/Nd:YAG > TUVP > TURis > TmLRP > diode laser vaporization > PVP > PKEP > HoLEP > TmLEP > HoLRP</p> <p><u>Catheterization time (short to long)</u> diode laser vaporization > HoLRP > TmLRP > PVP > DiLEP>TmLEP>HoLEP>PKRP>PKEP>TUR</p>	no information about funding	
--	--	--	--	--	--	--	--	------------------------------	--



							is>TUVp>M-TURP > ILC > Nd:YAG			
							<p><u>Hospitalization time</u> (shortest to longest) HoLEP > PVP > TmLRP > TmLEP > HoLRP > DiLEP > diode laser vaporization > Nd:YAG > PKRP > M-TURP > PKEP > TUVp > TURIS</p>			
Li, 2016, Medicine [156]	Systematic review with network meta-analysis	n= 18 RCTs Searched up to August 2015	The aim of current study is to carry out a systematic review and network meta-analysis comparing the impact of different surgical treatments for LUTS/BPH on EF documented with IIEF-5 based on existing RCTs and ranking these regimens for	n=2433 participants with LUTS/BPH	PVP	<ul style="list-style-type: none"> • HoLEP • HoLRP • Laparoscopic simple prostatectomy • Open prostatectomy • PKEP • PKRP • TURP 	<p>Ranking Laparoscopic simple prostatectomy ranked highest on the variation of postoperative IIEF-5 score, followed by PKRP, HoLEP, TURP, Thulium laser, PKEP, PVP, HoLRP, and open prostatectomy.</p> <p>Subgroup analysis <u>Short term group (followed up 3 and 6 mo)</u></p> <ul style="list-style-type: none"> • PVP-patients suffered a decreased postoperative erectile function (P=0.014, SMD=-0.25, 95% CI -0.45 to -0.05, I2=0.0%, P=0.949), whereas patients underwent 	In subgroup analysis, only PVP was found lower postoperative erectile function in the short term and decreased baseline group, whereas TURP increased postoperative IIEF-5 score only for patients with normal baseline erectile function. HoLEP and PKEP showed pro-erectile effect even for patients with decreased baseline erectile function and short-term follow-up. Our novel data demonstrating surgical treatments for LUTS/BPH	no funnel plot or sensitivity analysis no conflict of interest declared supported by National Natural Science Foundation of China	LoE 1++ RoB: low



			practical consideration.			<p>HoLEP (P=0.009, SMD=0.22, 95% CI 0.06–0.39, I2=0.0%, P=0.402) and PKEP (P=0.002, SMD=0.31, 95% CI 0.12–0.50, I2=4.2%, P=0.372) had an increased postoperative IIEF-5 score.</p> <p><u>Group of normal baseline IIEF-5 score</u></p> <ul style="list-style-type: none"> patients who underwent HoLEP (P=0.006, SMD=0.39, 95% CI 0.11–0.66, I2=60.6%, P=0.038) and PKEP (P=0.000, SMD=0.29, 95% CI 0.19–0.39, I2=0.0%, P=0.515) had an increased postoperative IIEF-5 score PVP (P=0.045, SMD= -0.12, 95% CI -0.24 to -0.00, I2=0.0%, P=0.458) had a negative effect 	<p>showed no negative impact on postoperative erectile function except PVP. HoLEP and PKEP were found pro-erectile effect for all subgroups. New technologies, such as laparoscopic simple prostatectomy, PKRP, and Thulium laser, were ranked at top positions in the network analysis, although they had no pro-erectile effect in direct comparison due to limited original studies or poor baseline erectile function.</p>	
--	--	--	--------------------------	--	--	---	--	--



<p>Wang, 2016, Asian Pacific Journal of Cancer Prevention [157]</p>	<p>Systematic review with network meta-analysis</p>	<p>n= 27 RCTs Search up to April, 25, 2015</p>	<p>To compare and create hierarchies for efficacy and safety of TURP and laser surgeries for BPH</p>	<p>patients with benign prostate hyperplasia</p>	<ul style="list-style-type: none"> • TURP vs. HoLEP (n=6) • TURP vs, PVP (n=10) • TURP vs. HoLRP (n=1) • TURP vs. TmLRP (n=3) • TURP vs. DiLVP (n=1) • PVP vs. DiLVP (n=1) • HoLEP vs. PVP (n=2) • HoLEP vs. ThuLEP (n=1) • HoLAP vs. PVP (n=1) 		<p>IPSS at 6 mo HoLRP > TURP>DiLEP</p> <p>IPSS at 12 mo HoLEP> HoLRP>TURP</p> <p>Qmax at 6 mo HoLEP > HoLRP> TmLRP</p> <p>Qmax at 12 mo HoLEP > HoLRP >PVP</p> <p>Operative time TURP > TmLRP > DiLEP</p> <p>Cathedral removal time DiLEP > TmLRP >PVP</p> <p>Length of hospital stay TmLRP > PVP>HoLAP</p> <p>Urethral stricture HoLAP > TmLRP>PVP</p>	<p>TURP is considered the gold standard surgery for BPH, our network meta-analysis comparing 8 other BHP laser treatments and TURP showed that it may not be the best in terms of efficacy and safety, HoLEP is more competitive, IPSS at 12 months and Qmax at 6 months and 12 months especially.</p>	<p>no funnel plot or sensitivity analyses</p> <p>no information about conflict of interest and funding</p>	<p>LoE 1++</p> <p>RoB: low</p>
<p>Zhang, 2016, Scientific reports [158]</p>	<p>Systematic review with network meta-analysis</p>	<p>n= 36 RCTs search up to May 2015</p>	<p>A novel analysis method, network meta-analysis, might allow us to conduct a systematic review to compare the</p>	<p>n= 3831 patients with BPH</p>	<ul style="list-style-type: none"> • TURP • Diode laser vaporization • KTP/Nd:YAG vaporization • Nd:YAG vaporization • Thulium laser vaporesection 		<p>Rank probability from best to worst Qmax holmium laser (resection)> holmium laser (enucleation)> thulium laser (vapo-resection)> Nd:YAG (vaporization)> TURP> green light (vaporization)></p>	<p>To date, no completely or absolutely perfect laser technique could be found to take the place of TURP in the surgical treatment of BPH. Holmium laser and thulium laser may seem to be relatively better in</p>	<p>heterogeneity of the included studies not shown, no funnel plot or sensitivity analysis,</p> <p>no conflict of interest declared</p>	<p>LoE 1++</p> <p>RoB: low</p>



			efficacy and safety among different surgical treatments for BPH.		<ul style="list-style-type: none"> • Holmium laser resection • Holmium laser enucleation • Greenlight vapo-enucleation • Greenlight vaporization 	<p>diode laser (vaporization)> green light (vapo-enucleation)</p> <p><u>IPSS score</u> thulium laser (vapo-resection)> holmium laser (enucleation)> green light laser (vaporization)> TURP> green light laser (vapo-enucleation)> KTP/ Nd:YAG (vaporization)> Nd:YAG (vaporization)> diode laser (vaporization)</p> <p><u>PVR</u> holmium laser (enucleation)> thulium laser (vapo-resection)> KTP/Nd:YAG (vaporization)> diode laser (vaporization)> green light laser (vaporization)> TURP> green light laser (vapo-enucleation)> Nd:YAG (vaporization)</p> <p><u>Operating time</u></p>	terms of surgical efficacy and safety, so that these two lasers might be preferred in the selection of optimal laser surgery.	supported by Natural Science Foundation of China	
--	--	--	--	--	--	---	---	--	--



							<p>Nd:YAG (vaporization)> TURP> diode laser (vaporization)> green light laser (vaporization)> thulium laser (vaporesection)> green light laser (vaporization)> holmium laser (enucleation)> holmium laser (resection)</p> <p><u>Catheterization</u> diode laser(vaporization)> green light laser(vaporization)> thulium laser(vaporesection) > holmium laser(enucleation)> holmium laser(resection)> TURP> Nd:YAG(vaporization) > green light laser(vapo- enucleation)</p> <p><u>Hospitalization</u> thulium laser (vapo- resection)> green light laser (vaporization)> diode laser (vaporization)> holmium laser</p>		
--	--	--	--	--	--	--	--	--	--



							(enucleation)> holmium laser (resection)> green light laser (vapo-enucleation)> Nd:YAG (vaporization)> TURP			
--	--	--	--	--	--	--	---	--	--	--



Tabelle 28: Eukleationsverfahren

Schlüsselfrage										
Gibt es Unterschiede zwischen den Eukleationsverfahren?										
Referenz	Studien-design	Studien-charakteristika	Studienziel	Patienten-merkmale	Intervention	Kontrolle	Ergebnisse	Schlussfolgerung	Bemerkungen	LoE
Thulium Laser Eukleation vs. Holmium Laser Eukleation										
Xiao, 2019, Lasers in Medical Science [159]	Systematic review with meta-analysis	n=5 studies (2 RCTs, 3 cohort studies) before July 2018	To evaluate the clinical efficacy and safety of ThuEP* versus HoLEP in the management of BPH.	n=1010 patients with BPH	<ul style="list-style-type: none"> • ThuEP* (n=367) • TmLEP (n=116) 	HoLEP (n= 527)	<u>Operation time</u> MD: -4.44 (-13.13, 4.25) p= 0.32 <u>Enucleation time</u> MD: -7.73 (-14.39, -1.07) p= 0.02 favour thulium <u>Morcellation time</u> MD: 0.78 (-0.27, 1.82) p= 0.15 <u>Catherization time</u> MD: -0.01 (-0.09, 0.07) p= 0.82 <u>Hospital stay</u> MD: -0.27 (-0.87, 0.32) p= 0.37 <u>Hemoglobin decrease</u> MD: -0.10 (-0.23, 0.03) p= 0.14 <u>Sodium decrease</u>	ThuEP* showed higher enucleation efficacy and less intraoperative blood loss and may get a better outcome as compared to the HoLEP group in the early postoperative period with regard to Qmax/PVR and IPSS after the 1st and 12th months of the operation respectively.	no additional hand search, no information if efforts were made to minimise error in the risk of bias assessment serious heterogeneity (I ² >75%) for operation time, enucleation time, hospital stay, sodium decrease and PVR, IPSS, QoL (12 mo) The authors declare that they have no conflict of interest. supported by The National Natural Science Fund of China (81470927),	LoE 1++ to 2++ (mixed study designs) RoB:



							<p>MD: 0.29 (-0.98, 1.56) p= 0.66</p> <p><u>Qmax (12 mo postop)</u> MD: 0.22 (-0.72, 1.17) p= 0.64</p> <p><u>PVR (12 mo postop)</u> MD: -4.08 (-11.9, -3.74) p=0.31</p> <p><u>IPSS (12 mo postop)</u> MD: -1.29 (-2.39, -0.19) p=0.02 favours thulium</p> <p><u>QoL (12 mo postop)</u> MD: -0.39 (-1.02, 0.25) p=0.23</p> <p><u>Postoperative complications</u> no significant difference</p>		National Natural Science Fund of China (81800667), and 1.3.5 project for disciplines of excellence, West China Hospital, Sichuan University	
Plamakinetische Enukleation vs. Dioden-Enukleation										
Xiao, 2020, Lasers in Medical Science [160]	Systematic review with meta-analysis	n= 4 RCTs up to April 2019	To evaluate the clinical efficacy and safety of DiLEP versus bipolar prostate PKEP in the management of BPH.	n= 451 patients with BPH	DiLEP	PKEP	<p><u>Operative time</u> WMD: - 5.33 (-16.34, 5.68) p= 0.00001</p> <p><u>Enucleation time</u> WMD: 1.47 (- 0.17, 3.11) p= 0.68</p> <p><u>Enucleated tissue weight</u></p>	Both DiLEP and PKEP are safe and efficient methods for the treatment of BPH. DiLEP showed less perioperative hemoglobin decrease, less postoperative catheterization	no information if efforts were made to minimise error in the risk of bias assessment, no funnel plot or sensitivity analyses serious heterogeneity	LoE 1++ RoB: low



						<p>WMD: 1.73 (– 3.56, 7.02) p=0.54</p> <p><u>Percentage of enucleated tissue</u> WMD: 0.41 (– 4.49, 5.31) p= 0.06</p> <p><u>Decrease in hemoglobin</u> WMD: – 3.33 (– 5.08, – 1.59) p= 0.04 favors DiLEP</p> <p><u>Catheter duration</u> WMD: – 17.72 (– 32.74, – 2.9) p= 0.00001 favors DiLEP</p> <p><u>Postoperative bladder irrigation time</u> WMD: – 7.15 (– 13.67, – 0.62) p= 0.00001 favors DiLEP</p> <p><u>Hospital stay</u> WMD: – 0.29 (– 0.74, 0.16) p= 0.01</p> <p><u>Sodium decrease</u> WMD: – 0.82 (– 2.44, 0.79) p= 0.001</p> <p><u>Perioperative hemoglobin decrease</u> MD: – 3.33 (– 5.08, – 1.59) p= 0.0002 favors DiLEP</p>	<p>time, less postoperative irrigation time, and lower rates of postoperative irritative symptoms compared with the PKEP group.</p>	<p>(I²>75%) for operative time, catheter duration, postoperative irrigation time, sodium decrease, catheterization time and bladder irrigation time</p> <p>Funding: Project of the Health and Family Planning Committee of Sichuan Province, the popularization and promotion of ureteroscopic technique in the treatment of upper urinary tract stones in primary hospitals (No.16PI294); Project of Sichuan Provincial Health Department, Dual-source CT dual-energy urography and urolithiasis analysis in the early prevention and treatment of urolithiasis (No. ZH2017-101); Project of Science an Technology Department of</p>
--	--	--	--	--	--	--	---	---



						<p><u>Perioperative catheterization time</u> MD: - 17.82 (- 32.74, - 2.90) p= 0.02 favors DiLEP</p> <p><u>Postoperative bladder irrigation time</u> MD: - 7.15 (- 13.67, - 0.62) p= 0.03 favors DiLEP</p> <p><u>No significant differences between the groups for:</u></p> <ul style="list-style-type: none"> • IPSS (1 mo, 3 mo, 6 mo, 12 mo) • QoL (1 mo, 3 mo, 6 mo, 12 mo) • Qmax (1 mo, 3 mo, 6 mo, 12 mo) • PVR (3 mo, 6 mo, 12 mo) <p>Complications</p> <p><u>Irritative symptoms</u> OR 0.31 (0.14, 0.67) p=0.003 favors DiLEP</p> <p><u>Transitory incontinence</u> OR 0.72 (0.33, 1.56) p=0.41</p> <p><u>Retrograde ejaculation</u> OR 0.85 (0.23, 3.08) p=0.8</p>	<p>Chengdu, research and application of urogenital suspension mesh (No.2016-HM02-00020-SF); 1.3.5 project for disciplines of excellence, West China Hospital, Sichuan University (No. ZY2016104).</p> <p>The authors declare that they have no conflict of interest.</p>
--	--	--	--	--	--	---	--



							<p><u>Urethral stricture</u> OR 1.97 (0.35, 11.04) p= 0.44</p> <p><u>Capsule perforation</u> OR 1.00 (0.17, 5.91) p= 1</p>			
Netzwerk-Metaanalyse										
Huang, 2019, BMJ [154]	Systematic review with network meta-analysis	n=109 trials (106 two arms, 3 tree arms) Search date: from inception to 31 March 2019	To assess the efficacy and safety of different endoscopic surgical treatments for benign prostatic hyperplasia.	n=13676 patients with BPH	<ul style="list-style-type: none"> • Enucleation (Thulium, Holmium, Diode, bipolar) • Vapourisation (Diode, Greenlight, bipolar) • Resection (bipolar TURP) 	monopolar TURP	<p>Qmax at 12 mo best three (vs. TURP)</p> <ul style="list-style-type: none"> • bipolar enucleation (MD 2.42mL/s (95% CI 1.11 to 3.73)) • diode laser enucleation (1.86 (-0.17 to 3.88)) • holmium laser enucleation (1.07 (0.07 to 2.08)) <p><u>Worst</u></p> <ul style="list-style-type: none"> • diode laser vapourisation (-1.90 (-5.07 to 1.27)) <p>IPSS at 12 mo best three (vs. TURP)</p> <ul style="list-style-type: none"> • diode laser enucleation (MD -1.00 (-2.41 to 0.40)) • bipolar enucleation (0.87 (-1.80 to 0.07)) 	Eight new endoscopic surgical methods for benign prostatic hyperplasia appeared to be superior in safety compared with monopolar TURP. Among these new treatments, enucleation methods showed better Qmax and IPSS values than vapourisation and resection methods.	<p>further rankings for Qmax and IPSS at 6 mo, 24 mo, 36 mo in Fig 3</p> <p>no conflict of interest declared</p> <p>supported partly by a grant from the National Science Council in Taiwan</p>	<p>LoE 1++</p> <p>RoB: low</p>



						<ul style="list-style-type: none"> • holmium laser enucleation (-0.84 (-1.51 to 0.58)) <p><u>Worst</u></p> <ul style="list-style-type: none"> • diode laser vapourisation (1.30 (-1.16 to 3.76)) <p>Catherisation duration (hours) <u>best three (vs. TURP)</u></p> <ul style="list-style-type: none"> • DiLEP (MD -43.07 (-54.17 to -29.96)) • Diode laser vapourisation (MD -34.2 (-52.53 to -15.87)) • KTP laser vaporisation (MD -32.10 (-39.33 to 24.88)) <p><u>Worst</u></p> <ul style="list-style-type: none"> • Bipolar TURP (-10.8 (-15.44 to -6.14)) <p>Decline in Hb (10 g/L) <u>best three (vs. TURP)</u></p> <ul style="list-style-type: none"> • KTP laser vaporisation (MD -1.25 (-1.66 to 0.84)) • DiLEP (MD -0.86 (-1.31 to -0.41)) • ThuLEP (MD -0.8 (-1.13 to -0.46)) 		
--	--	--	--	--	--	---	--	--



						<p><u>Worst</u></p> <ul style="list-style-type: none"> • Bipolar TURP (-0.19 (-0.38 to -0.01)) <p>Blood transfusion best three (vs. TURP)</p> <ul style="list-style-type: none"> • Diode laser vapourisation (no events) • DiLEP (no events) • HoLEP (OR 0.05 (0.01 to 0.22)) <p><u>Worst</u></p> <ul style="list-style-type: none"> • Bipolar TURP (-0.42 (OR 0.28 to -0.61)) <p>Recatheterisation best three (vs. TURP)</p> <ul style="list-style-type: none"> • bipolar enucleation (OR 0.27 (0.11 to 0.69)) • ThuLEP (OR 0.37 (0.19 to 0.89)) • HoLEP (OR 0.42 (0.23 to 0.78)) <p><u>Worst</u></p> <ul style="list-style-type: none"> • Diode laser vapourisation (OR 2.17 (0.34 to 13.9)) <p>Clot retention best three (vs. TURP)</p>		
--	--	--	--	--	--	--	--	--



						<ul style="list-style-type: none"> • bipolar enucleation (OR 0.12 (0.02 to 0.76)) • KTP laser vaporisation (OR 0.16 (0.07 to 0.39)) • ThuLEP (OR 0.18 (0.06 to 0.48)) <p><u>Worst</u></p> <ul style="list-style-type: none"> • Bipolar TURP (OR 0.49 (0.32 to 0.74)) <p>Recurrence best three (vs. TURP)</p> <ul style="list-style-type: none"> • bipolar enucleation (OR 0.12 (0.02 to 0.76)) • HoLEP (OR 0.26 (0.06 to 1.28)) • Bipolar TURP (OR 0.87 (0.43 to 1.77)) <p><u>Worst</u></p> <ul style="list-style-type: none"> • ThuLEP (no event in TURP group) 			
Sun, 2018, Medicine [155]	Systematic review with network meta-analysis	n= 88 RCTs 1995-2016	We made a network meta-analysis to compare the efficacy and safety of different transurethral	n=11187 enrolled patients with BPH	<ul style="list-style-type: none"> • diode laser vaporization • Nd:YAG • PVP • KTP/Nd:YAG • ILC • TURis • TmLRP • TmLEP • HoLEP 	<p>Rank probability from the best to the worst</p> <p><u>IPSS</u></p> <p>diode laser vaporization > Nd:YAG > PVP > KTP/Nd:YAG > ILC > TURis > TmLRP > TmLEP > HoLEP</p>	Compared with other transurethral procedures, thulium, holmium and diode lasers were associated with better efficacy and fewer complications.	no additional hand-search, no information if efforts were made to minimise error in the study selection, no information about between-study variation, no	LoE 1- RoB: high



			procedures for BPH.		<ul style="list-style-type: none"> • TURP • HoLRP • DiLEP • PKRP • PKEP • TUVV 	<p>> M-TURP > HoLRP > DiLEP > PKRP > PKEP > TUVV</p> <p><u>Qmax</u> diode laser vaporization > PVP > Nd:YAG > KTP/Nd:YAG > ILC > HoLRP > TmLRP > TURis > TmLEP > M-TURP > PKRP > HoLEP > DiLEP > PKEP > TUVV</p> <p><u>PVR</u> HoLEP > Nd:YAG > PVP > ILC > diode laser vaporization > PKRP > TURis > M-TURP > HoLRP > TmLRP > TmLEP > DiLEP > PKEP > TUVV > KTP/Nd:YAG</p> <p><u>Quality of Life</u> TmLRP > TmLEP > HoLEP > HoLRP > PVP > DiLEP > M-TURP > PKRP > PKEP > TUVV > TURis</p> <p><u>Operation time (fast to slow)</u> PKRP > DiLEP > M-TURP > Nd:YAG > KTP/Nd:YAG > TUVV > TURis > TmLRP > diode laser</p>	<p>funnel plots or sensitivity analyses</p> <p>no conflict of interest declared</p> <p>no information about funding</p>	
--	--	--	---------------------	--	--	--	---	--



						<p>vaporization > PVP > PKEP > HoLEP > TmLEP > HoLRP</p> <p><u>Catheterization time</u> (short to long) diode laser vaporization > HoLRP > TmLRP > PVP > DiLEP > TmLEP > HoLEP > PKRP > PKEP > TURis > TUVP > M-TURP > ILC > Nd:YAG</p> <p><u>Hospitalization time</u> (shortest to longest) HoLEP > PVP > TmLRP > TmLEP > HoLRP > DiLEP > diode laser vaporization > Nd:YAG > PKRP > M-TURP > PKEP > TUVP > TURis</p>			
Li, 2016, Medicine [156]	Systematic review with network meta-analysis	n= 18 RCTs Searched up to August 2015p	The aim of current study is to carry out a systematic review and network meta-analysis comparing the impact of different surgical treatments for	n=2433 participants with LUTS/BPH	<ul style="list-style-type: none"> • HoLEP • HoLRP • Laprascopic simple prostatectomy • Open prostatectomy • PKEP • PKRP • TURP • PVP 	<p>Ranking Laprascopic simple prostatectomy ranked highest on the variation of postoperative IIEF-5 score, followed by PKRP, HoLEP, TURP, Thulium laser, PKEP, PVP, HoLRP, and open prostataectomy.</p> <p>Subgroup analysis</p>	HoLEP and PKEP showed pro-erectile effect even for patients with decreased baseline erectile function and short-term follow-up. Our novel data demonstrating surgical treatments for LUTS/BPH showed no negative impact on postoperative	no funnel plot or sensitiviy analysis no conflict of interest declared supported by National Natural Science Foundation of China	LoE 1++ RoB: low



			<p>LUTS/BPH on erectile function documented with IIEF-5 based on existing RCTs and ranking these regimens for practical consideration.</p>			<p><u>Short term group (followed up 3 and 6 mo)</u></p> <ul style="list-style-type: none"> • PVP-patients suffered a decreased postoperative erectile function (P=0.014, SMD=-0.25, 95% CI -0.45 to -0.05, I2=0.0%, P=0.949), whereas patients underwent HoLEP (P=0.009, SMD=0.22, 95% CI 0.06-0.39, I2=0.0%, P=0.402) and PKEP (P=0.002, SMD=0.31, 95% CI 0.12-0.50, I2=4.2%, P=0.372) had an increased postoperative IIEF-5 score. <p><u>Group of normal baseline IIEF-5 score</u></p> <ul style="list-style-type: none"> • patients who underwent HoLEP (P=0.006, SMD=0.39, 95% CI 0.11-0.66, I2=60.6%, P=0.038) and PKEP (P=0.000, SMD=0.29, 95% CI 0.19-0.39, 	<p>erectile function except PVP. HoLEP and PKEP were found pro-erectile effect for all subgroups. New technologies, such as laparoscopic simple prostatectomy, PKRP, and Thulium laser, were ranked at top positions in the network analysis, although they had no pro-erectile effect in direct comparison due to limited original studies or poor baseline erectile function.</p>	
--	--	--	--	--	--	--	---	--



							I ² =0.0%, P=0.515) had an increased postoperative IIEF-5 score			
Wang, 2016, Asian Pacific Journal of Cancer Prevention [161]	Systematic review with network meta-analysis	n= 27 RCTs Search up to April, 25, 2015	To compare and create hierarchies for efficacy and safety of TURP and laser surgeries for BPH.	patients with benign prostate hyperplasia	<ul style="list-style-type: none"> • TURP vs. HoLEP (n=6) • TURP vs, PVP (n=10) • TURP vs. HoLRP (n=1) • TURP vs. TmLRP (n=3) • TURP vs. DiLVP (n=1) • PVP vs. DiLVP (n=1) • HoLEP vs. PVP (n=2) • HoLEP vs. ThuLEP (n=1) • HoLAP vs. PVP (n=1) 		<p>IPSS at 6 mo HoLRP > TURP>DiLEP</p> <p>IPSS at 12 mo HoLEP> HoLRP>TURP</p> <p>Qmax at 6 mo HoLEP > HoLRP> TmLRP</p> <p>Qmax at 12 mo HoLEP > HoLRP > PVP</p> <p>Operative time TURP > TmLRP> DiLEP</p> <p>Cathedral removal time DiLEP > TmLRP >PVP</p> <p>Length of hospital stay TmLRP > PVP>HoLAP</p> <p>Urethral stricture HoLAP > TmLRP>PVP</p>	TURP is considered the gold standard surgery for BPH, our network meta-analysis comparing 8 other BHP laser treatments and TURP showed that it may not be the best in terms of efficacy and safety, HoLEP is more competitive, IPSS at 12 months and Qmax at 6 months and 12 months especially.	no funnel plot or sensitivity analyses no information about conflict of interest and funding	LoE 1++ RoB: low
Mehrere Vergleichsgruppen										
Li, 2015, Plos one	Systematic review with	n=7 RCTs	To evaluate the overall efficacy and	n= 735 patients with BPH	open prostatectomy	endoscopic enucleation	Open vs. endoscopic enucleation	Endoscopic enucleation is shown to have a	serious heterogeneity (I ² >75%) for	LoE 1++ RoB: low



[162]	meta-analysis	1998-27 July 2014	safety of endoscopic enucleation of the prostate vs open prostatectomy for large BPH.			<ul style="list-style-type: none"> • HoLEP (n=3) • BPEP (n=1) • PKEP (n=3) 	no significant differences in <ul style="list-style-type: none"> • IPSS (3 mo, 6 mo, 12 mo) • Qmax (3 mo, 6 mo, 12 mo) • QoL (3 mo, 6 mo, 12 mo) • PVR (3 mo, 6 mo, 12 mo) • IIEF-5 (3 mo, 6 mo, 24 mo) • Recatheterization • Urinary tract infection • Urinary incontinence • Bladder neck contracture/ Urethral strictures • Reintervention <p><u>IIEF-5 (12 mo)</u> WMD 1.00 [0.21, 1.78] p=0.01 favors endoscopic</p> <p><u>Blood transfusion</u> RR 0.22 (0.10, 0.47) p=0.00 favors endoscopic</p>	similar postoperative profile and comparable safety to open prostatectomy. By contrast, endoscopic enucleation may have a more desirable perioperative profile. endoscopic enucleation appears to be an effective and safe minimally invasive option for treating large prostates that requires only brief convalescence.	urinary incontinence no conflict on interest declared no funding	
indirekte Evidenz										
Zhang, 2016, Scientific reports	Systematic review with network	n= 36 RCTs	A novel analysis method, network meta-	n= 3831 patients with BPH	<ul style="list-style-type: none"> • TURP • Diode laser vaporization • KTP/Nd:YAG vaporization 		Rank probability from best to worst <u>Qmax</u> holmium laser (resection) > holmium	To date, no completely or absolutely perfect laser technique could be found to	heterogeneity of the included studies not shown, no funnel plot or	LoE 1++ RoB: low



[158]	meta-analysis	search up to May 2015	analysis, might allow us to conduct a systematic review to compare the efficacy and safety among different surgical treatments for BPH.		<ul style="list-style-type: none"> • Nd:YAG vaporization • Thulium laser vaporesection • Holmium laser resection • Holmium laser enucleation • Greenlight vapo-enucleation • Greenlight vaporization 	<p>laser (enucleation)> thulium laser (vapo-resection)> Nd:YAG (vaporization)> TURP> green light (vaporization)> diode laser (vaporization)> green light (vapo-enucleation)</p> <p><u>IPSS score</u> thulium laser (vapo-resection)> holmium laser (enucleation)> green light laser (vaporization)> TURP> green light laser (vapo-enucleation)> KTP/Nd:YAG (vaporization)> Nd:YAG (vaporization)> diode laser (vaporization)</p> <p><u>PVR</u> holmium laser (enucleation)> thulium laser (vapo-resection)> KTP/Nd:YAG (vaporization)> diode laser (vaporization)> green light laser (vaporization)> TURP> green light laser (vapo-enucleation)></p>	take the place of TURP in the surgical treatment of BPH. Holmium laser and thulium laser may seem to be relatively better in terms of surgical efficacy and safety, so that these two lasers might be preferred in the selection of optimal laser surgery.	sensitivity analysis, no conflict of interest declared supported by Natural Science Foundation of China	
-------	---------------	-----------------------	---	--	--	--	--	---	--



						<p>Nd:YAG (vaporization)</p> <p><u>Operating time</u> Nd:YAG (vaporization)> TURP> diode laser (vaporization)> green light laser (vaporization)> thulium laser (vaporesection)> green light laser (vaporization)> holmium laser (enucleation)> holmium laser (resection)</p> <p><u>Catheterization</u> diode laser(vaporization)> green light laser(vaporization)> thulium laser(vaporesection) > holmium laser(enucleation)> holmium laser(resection)> TURP> Nd:YAG(vaporization) > green light laser(vapo- enucleation)</p> <p><u>Hospitalization</u></p>		
--	--	--	--	--	--	---	--	--



							thulium laser (vapo-resection)> green light laser (vaporization)> diode laser (vaporization)> holmium laser (enucleation)> holmium laser (resection)> green light laser (vapo-enucleation)> Nd:YAG (vaporization)> TURP			
Lucca, 2015, World J Urol [163]	Systematic review with meta-analysis	n= 27 (23 case series, 4 non-randomized studies) 2004-2014	To assess the outcomes of MISP for the treatment of symptomatic benign prostatic hyperplasia in men with large prostates and (2) to compare them with OSP	n= 764 patients with BPH n= 16 studies conventional laparoscopy (595 patients) n= 8 studies robotic surgery (119 patients) n= 3 studies single-port technique (50 patients)	MISP • n= 163 patients	OSP n= 252 patients	MISP vs. OSP (n= 4 studies) • no significant differences were observed in the changes between preoperative and postoperative Qmax (WMD 3.78, 95 % CI -4.85 to 12.40, p = 0.39) and preoperative and postoperative IPSS (WMD 0.21, 95 % CI -6.82 to 7.24, p = 0.95) • Length of hospital stay (WMD -1.6 days, 95 % CI -2.9 to -0.2, p = 0.02) and length of catheter use (WMD -1.3 days, 95 % CI -2.5 to -0.06, p = 0.04)	MISP seems an effective and safe treatment option. It provides similar improvements in Qmax and IPSS as OSP. Despite taking longer, it results in less blood loss and shorter hospital stay.	no additional hand search, no information if efforts were made to minimise error in the study selection, no risk of bias assessment, no heterogeneity information for the comparison no conflict of interest declared supported by the development fund of the CHUV University Hospital	LoE: 2- (for the comparison) RoB: high



						<p>were significantly shorter in the MISIP group</p> <ul style="list-style-type: none"> • Duration of operation was longer than in the OSP group (WMD 37.8 min, 95 % CI 21.1–54.6, $p < 0.0001$) • Estimated blood loss was significantly lower in the MISIP group (WMD –187 ml, 95 % CI –338 to –36.1, $p = 0.015$) • no significant difference between both groups in the overall perioperative complication rate (OR 0.64, 95 % CI 0.4–1.03, $p = 0.066$) • Risk of incontinence was similar between the two groups (OR 0.59, 95 % CI –8.73 to –9.93) 		
--	--	--	--	--	--	--	--	--

* Thulium laser Enucleation of the Prostate or Thulium Vapoenucleation of the Prostate



Tabelle 29: Neue minimal-invasive Therapien vs. medikamentöse Therapie

Schlüsselfrage										
Welche Effekte zeigen neue minimal-invasive Therapien bei Patienten mit BPS im Vergleich zur medikamentösen Therapie?										
Referenz	Studien-design	Studien-charakteristika	Studienziel	Patienten-merkmale	Intervention	Kontrolle	Ergebnisse	Schlussfolgerung	Bemerkungen	LoE
Botulinum toxin										
Robert, 2018, World Journal of Urology [164]	RCT	n= 127 January 2011- November 2013 France last follow-up: May 2015	To explore efficacy and safety of BoNT-A prostatic injection in patients with LUTS due to benign prostatic hyperperplasia.	patients with LUTS Age BoNT-A: 64 y control: 63 y	BoNT-A n=64	medical therapy (e.g., plant extract, alpha blocker, 5 alpha reductase inhibitor, PDE-5 inhibitor, anti-muscarinic) n=63	Per-protocol analysis <u>IPSS score</u> BoNT-A: 12.0 ± 6.7 control: 11.8 ± 6.9 <u>IPSS-Q8</u> BoNT-A: 3.1 (SD 1.4) control: 3.1 (SD 1.4) <u>IIEF-5</u> BoNT-A: 14.9 (SD 8.3) control: 14.1 (SD 7.7) <u>International continence society score 1</u> BoNT-A: 1.1 (SD 2.2) control: 0.6 (SD 1.5) <u>International continence society score 1</u> BoNT-A: 1.2 (SD 2.4) control: 0.7 (SD 1.9) <u>Total PSA</u> BoNT-A: 4.6 (SD 3.2)	Four months after BoNT-A injection, most of the patients could interrupt LUTS-related medical treatments. In these patients, IPSS improvement was not inferior to optimized medical treatment, but the study design did not allow to conclude that this improvement was related with study drug rather than with sustained placebo effect.	open-label no conflict of interest declared This study was founded by an unrestricted grant of the French Ministry of Health	LoE 1- RoB: high



							<p>control: 2.7 (SD 2)</p> <p><u>Qmax</u> BoNT-A: 12.9 (SD 8.2) control: 12.2 (SD 6)</p> <p><u>Prostate volume</u> BoNT-A: 58.4 (SD 31.4) control: 51.8 (SD 30.2)</p> <p><u>PVR</u> BoNT-A: 59.7 (SD 77.2) control: 70.3 (SD 95.5)</p> <p><u>Most of the adverse events</u> BoNT-A: acute urinary retention, urinary tract infections, prostatitis, haematuria, haemospermia (83%) control: sexual side effects of the drugs (erectile and ejaculatory dysfunction, decreased sexual desire) (71%)</p>			
Rezüm										
Gupta, 2018, Journal of urology [165]	comparative analysis based on two RCTs (NCT019	n=1275	We evaluated the long-term outcomes of treatment of	patients with a prostate volume of 30 to 80 cc International Prostate	water vapor thermal therapy (Rezüm-System) n=129	<ul style="list-style-type: none"> doxazosin (n=368) finasteride (n=394) combination (n=384) 	<p>Subjective patient reported</p> <p><u>Thermal therapy vs. medicine</u></p> <ul style="list-style-type: none"> 3 mo: significantly greater mean improvement in I- 	A single water vapor thermal therapy procedure provided effective and durable improvements in symptom scores	Supported by NxThera, Inc. one author has financial interest and/or other	LoE: 2+ LoE: low



	12339, MTOPS)		lower urinary tract symptoms due to benign prostatic hyperplasia to compare a 1-time water vapor thermal therapy procedure with daily medical therapy in cohorts from the MTOPS study.	Symptom Score of 13 or greater Median age: 63.0 y			PSS vs. doxazosin (2.6, 95% CI 1.2-3.9, p <0.001) or finasteride (5.2, 95% CI 4.0-6.4, p <0.001) • 36 mo: doxazosin or finasteride showed little further IPSS improvement remained significantly less (1.8, 95% CI 0.4-3.2, p=0.02; 2.2, 95%CI 1.0-3.4, p<0.001) • 3 mo: combination drug had similar I-PSS improvements (1.4, 95% CI 0-2.8, p=0.05) • significant improvement in the BPHII QOL measure after thermal therapy vs.doxazosin at each visit during 36 months (p=0.02 to <0.001) and vs. finasteride during 24 mo (p=0.03 to <0.001) Objective clinical <u>Thermal therapy vs. medicine</u> • 3 to 12 mo: vs. doxazosin resulted in significantly greater	with lower observed clinical progression rates compared to daily long-term use of pharmaceutical agents.	relationship with NxThera	
--	---------------	--	--	--	--	--	--	--	---------------------------	--



							<p>improved peak flow (p=0.01 to 0.03) and greater improvements throughout 36 mo vs. finasteride (p <0.001 to 0.002)</p> <ul style="list-style-type: none"> Up to 12 mo: significantly improved Qmax vs. combination drug therapy (p <0.001 to 0.002) 6 to 24 mo: most consistent improvement in PVR occurred only after combination drug therapy (p <0.001 to 0.02) 			
<p>McVary, 2018, Journal of sexual medicine [166]</p>	<p>comparative analysis based on two RCTs (NCT01912339, MTOPS)</p>	<p>n=1295</p>	<p>To compare sexual function over 3 years after continuous daily treatment with pharmaceutical agents in the Medical Therapy of Prostatic Symptoms (MTOPS) study vs a single thermal</p>	<p>sexual active men with prostate volumes of 30-80 cm³ and IPSS ≥13 to ≤30</p>	<p>water vapor thermal therapy (Rezüm-System) n=86</p>	<ul style="list-style-type: none"> doxazosin (n=370) finasteride (n=391) combination (n=385) 	<p>Sexual desire through 3 years:</p> <ul style="list-style-type: none"> Men in the 3 drug groups had a worsening of sexual desire: - 6.7% doxazosin, -10.7% finasteride, -8.6% combination water vapor thermal therapy, subjects showed slight improvements (1.8% [-5.6, 9.2], P= .62) <p>Erectile Function</p> <ul style="list-style-type: none"> 3 drug groups showed significantly worsening erectile 	<p>With continued daily drug use, men experienced significant worsening of sexual desire, erectile and ejaculatory function with finasteride and combination drug therapy, and reduced desire and erectile function with doxazosin. Thermal therapy was not associated with significant negative changes in sexual function</p>	<p>slight differences in the baseline characteristics of the comparison groups</p> <p>Funding: This study was funded by NxThera Inc, Maple Grove, MN, USA.</p> <p>conflict of interest: detailed</p>	<p>LoE: 2+</p> <p>LoE: low</p>



			therapy procedure (Rezüm study) in subjects with matched criteria for LUTS severity and prostate size.				<p>function scores over time</p> <ul style="list-style-type: none"> • Rezüm: no significant mean changes over 3 years relative to baseline scores for the respective inventories (p=0.9) • minimal clinically important differences of improved scores for water vapor thermal therapy, occurred in 20 of 63 (32%) men at year 1 and 10 of 48 (21%) at year 3 <p>Ejaculatory Function</p> <ul style="list-style-type: none"> • Ejaculatory function worsened significantly in finasteride and combination drug groups over 3 years • thermal therapy showed a profile of decreasing, but no significant mean change in ejaculatory function at year 3, (-9.2% (-18.4, 0.0), P=0.05) <p>Overall Sexual Satisfaction</p> <ul style="list-style-type: none"> • The combination drug group had 	throughout 3 years after treatment.	description in the paper	
--	--	--	--	--	--	--	---	-------------------------------------	--------------------------	--



							decreases in overall sexual satisfaction at 1 and 2 years (-8.3%(-15.0,-1.6), P<.01 to -9.8% (-17.4, -1.7), P=0.01 • water vapor thermal therapy showed slight, nonsignificant improvements (4.6-6.0%) in the overall satisfaction domain score on the IIEF-15 compared with baseline (P≥ .17).			
Prostatic Urethral Lift										
Roehrborn, 2021, Eur Urol Fo [167]	Meta-analysis	n= 4 studies (2 RCTs (MTOPS, L.I.F.T), 1 cross-over study, 1 single-arm study)	To compare the long-term impact on sexual health of PUL or daily medical therapy of doxazosin or finasteride alone or in combination in BPH patients.	sexual active men with prostate volumes of 30-80 cm ³ and IPSS ≥13 to ≤30 Age: PUL: 64.6 ± 7.61 y Medicine: 62.4 ± 6.84 y (p = 0.0004) Prostate volumes PUL: 44.3 ± 11.7 cm ³	PUL n=188 patients	<ul style="list-style-type: none"> • doxazosin (n=223) • finasteride (n=211) • combination (n=221) 	Erectile function PUL was superior <ul style="list-style-type: none"> • compared to doxazosin at 12 mo (p = 0.02) and 24 mo (p = 0.05) • compared to finasteride at 24 mo (p = 0.02) and 48 mo (p = 0.03) • compared to combination therapy at 12 mo (p = 0.008) Ejaculatory function <ul style="list-style-type: none"> • only PUL significantly improved ejaculatory function at all time points 	Indirect comparison reveals that PUL is superior to BPH medical therapy in preserving erectile and ejaculatory function and sexual satisfaction.	no systematic search, differences in the baseline characteristics of the compared groups, no risk of bias assessment, no information about efforts were made to minimise error in the study selection and data collection sponsored by NeoTract Inc./Teleflex.	1- to 3 RoB: high



				Medicine: 38.7 ± 9.55 cm ³ (p < 0.0001)			Sexual satisfaction <ul style="list-style-type: none"> sexual satisfaction was significantly enhanced in men treated with PUL versus those treated with medical therapy 		The sponsor played a role in the collection, management, analysis, and interpretation of the data, and in manuscript preparation and review. Conflict of interest: paid consultants for NeoTract Inc./Teleflex.
--	--	--	--	---	--	--	---	--	--



Tabelle 30: Neue minimal-invasive Verfahren vs. TURP

Schlüsselfrage										
Welche Effekte zeigen neue minimal-invasive Verfahren bei Patienten mit BPS im Vergleich zur transurethrale Prostataresektion (TURP)?										
Referenz	Studien-design	Studien-charakteristika	Studienziel	Patienten-merkmale	Intervention	Kontrolle	Ergebnisse	Schlussfolgerung	Bemerkungen	LoE
Prostatic Urethral Lift										
Jung, 2019, Cochrane Database of Systematic reviews [168]	Systematic review with meta-analysis	n= 2 RCTs up until 31 January 2019	To assess the effects of PUL for the treatment of LUTS in men with BPH.	n= 297 men with BPH	PUL	<ul style="list-style-type: none"> TURP sham 	<p>PUL vs. TURP (n=1 RCT)</p> <p><u>QoL</u> MD 0.3 (95% -0.49,1.09) p=0.45</p> <p><u>Major adverse events</u> MD 0.64 (95% 0.18,2.19) p=0.47</p> <p><u>Retreatment</u> MD 1.19 (95% 0.21,6.75) p=0.84</p> <p><u>Erectile function</u> MD 0.8 (95% -1.5,3.1) p=0.5</p> <p><u>Ejaculatory function</u> MD 5 (95% 3.08,6.92) p<0.0001 favours PUL</p> <p><u>Minor adverse events</u> MD 0.88 (95% 0.7,1.09) p=0.23</p> <p><u>Acute urinary retention</u></p>	PUL appears less effective than TURP in improving urological symptoms both short-term and long term, while quality of life outcomes may be similar. The effect on erectile function appears similar but ejaculatory function may be better. We are uncertain about major adverse events short-term and found no long-term information. We are very uncertain about retreatment rates both short-term and long-term. We were unable to assess the effects of PUL in subgroups	serious heterogeneity ($I^2>75%$) for indwelling urinary catheter, hospital stay, QoL, erectile function, one author declared: Boston Scientific (consultant for endourology and stone management), Auris Health (consultant for robotic surgery and endourology) Source of support: Department of Urology, Yonsei	LoE 1++ RoB: low



						<p>RR 7.2 (95% 0.4,129.38) p=0.18</p> <p><u>Indwelling urinary catheter</u> RR 0.46 (0.25,0.84) p=0.01 favours PUL</p> <p><u>Hospital stay</u> MD -0.9 (-1.32,-0.48) p<0.0001 favours PUL</p> <p><u>Urological symptom scores (long term)</u> MD 6.1 (2.16,10.04) p=0 favours TURP</p> <p><u>QoL (long term)</u> MD 0.8 (0,1.6) p=0.05</p> <p><u>Retreatment (long term)</u> RR 2.39 (0.51,11.1) p=0.27</p> <p><u>Erectile function (long term)</u> MD 1.6 (95% 0.8,4) p=0.19</p> <p><u>Ejaculatory function (long term)</u> MD 4.3 (95% 2.17,6.43) p<0.0001 favours PUL</p> <p><u>Minor adverse events (long term)</u> RR 0.92 (95% 0.72,1.17) p=0.48</p>	<p>based on age, prostate size, or symptom severity and also could not assess how PUL compared to other surgical management approaches. Given the large numbers of alternative treatment modalities to treat men with LUTS secondary to BPH, this represents important information that should be shared with men considering surgical treatment.</p>	<p>University Wonju College of Medicine, Korea, South, Minneapolis VA Health Care System, USA., Department of Urology, University of Minnesota, USA.</p> <p>results only shown for the comparison PUL vs. TURP</p>
--	--	--	--	--	--	--	---	---



Botulinum neurotoxin A										
El-Dakhakhny, 2019, Arab Journal of Urology [169]	RCT	n= 92	To evaluate transperineal intraprostatic injection of BoNT-A in patients with LUTS secondary to BPH who failed to respond to 6-month medical treatment compared with TURP.	patients with LUTS secondary to BPH and failed to respond to conservative therapy for 6 months Mean age BoNT-A: 59 y (SD 5.5 y) TURP: 61.3 y (SD 6.1 y)	BoNT-A n=46	TURP n=46	<p>IPSS at 12 mo TURP: 12 (SD 2.5) BoNT-A: 13.1 (3.9) (significant difference vs. baseline) p=0.115</p> <p>Progress of prostate-related manifestations at 12 mo <u>TURP</u> improved: 0 static: 38 (82.6%) deteriorated: 8 (17.4%) <u>BoNT-A</u> improved: 8 (17.4%) static: 28 (60.9%) deteriorated: 10 (21.7%) p=0.027</p> <p>HRQOL at 12 mo TURP: 1.1 (SD 0.9) BoNT-A: 0.6 (SD 0.7) p=0.003</p> <p>IIIEF-5 at 12 mo TURP: 18.2 (SD 5) BoNT-A: 18.4 (SD 5) p=0.567</p> <p>Change in erectile function at 12 mo <u>TURP</u> improved: 2 (4.3%) static: 36 (78.3%) deteriorated: 8 (17.4%) <u>BoNT-A</u></p>	Intraprostatic BoNT-A injection reduced prostatic volume with subsequent increases in voided volume and Qmax, and decreases in PVR and serum tPSA level. Intraprostatic BoNT-A injection allowed surgery sparing in >70% and preserved erectile function in 91.3% of patients.	unclear allocation concealment, no information about blinding, unclear loss between enrolled eligible patients (n=118) and in the analysis included patients (n=92) No funding and no conflict of interest.	LoE 1- RoB: high



							improved: 3 (6.4%) static: 28 (91.4%) deteriorated: 1 (2.2%) p=0.047			
--	--	--	--	--	--	--	---	--	--	--



Tabelle 31: Prostata-Arterien-Embolisation vs. TURP

Schlüsselfrage										
Welche Effekte zeigt die Prostata-Arterien-Embolisation (PAE) bei Patienten mit BPS im Vergleich zu TURP?										
Referenz	Studien-design	Studien-charakteristika	Studienziel	Patienten-merkmale	Intervention	Kontrolle	Ergebnisse	Schlussfolgerungen	Bemerkungen	LoE
Jung, 2020, Cochrane Database of Systematic Reviews [170]	Systematic review with meta-analysis	n= 9 comparative studies (7 RCTs, 2 non-RCTs) up until 25 September 2020	To assess the effects of PAE compared to other procedures for treatment of LUTS in men with BPH.	n=820 participants Mean age: 66 y IPSS: 22.8 prostate volume: 72.8 ml	PAE	<ul style="list-style-type: none"> TURP sham 	<p>PAE vs. TURP Short term</p> <p><u>Urologic symptom score</u> (n=6 RCTs) MD 1.55 (95% CI -0.4,3.5) p=0.12</p> <p><u>QoL</u> (n=5 RCTs) MD 0.16 (95% CI -0.37,0.68) p=0.56</p> <p><u>Major adverse events</u> (n=4 RCTs) RR 0.71 (95% CI 0.16,3.10) p=0.64</p> <p><u>Retreatment</u> (n=3 RCTs) RR 3.64 (95% CI 1.02,12.98) p=0.05</p> <p><u>Erectile function</u> (n=2 RCTs) MD -0.03 (95% CI -6.35,6.29)</p>	Compared to TURP up to 12 months (short-term follow-up), PAE may provide similar improvement in urologic symptom scores and quality of life. While we are very uncertain about major adverse events, PAE may increase retreatment rates. We are uncertain about erectile function, but PAE may reduce ejaculatory disorders. Longer term (follow-up of 13 to 24 months), we are very uncertain as to how both procedures compare with regard to urologic symptom scores, but quality of life appears to be similar. We are very uncertain about major adverse events but PAE may increase retreatments. We did not find longer term evidence on erectile	serious heterogeneity ($I^2 > 75\%$) for urologic symptom scores, erectile function and ejaculatory disorder (short term) one author declares: Boston Scientific (consultant for endourology and stone management), Auris Health (consultant for robotic surgery and endourology) Sources of support: Department of Urology, Yonsei University Wonju College	LoE 1++ RoB: low



							<p>p=0.99</p> <p><u>Ejaculatory disorder</u> (n=3 RCTs) RR 0.26 (95% CI 0.06,1.19) p=0.08</p> <p><u>Minor adverse events</u> (n=3 RCTs) RR 0.83 (95% CI 0.41,1.69) p=0.61</p> <p><u>Acute urinary retention</u> (n=5 RCTs) RR 1.65 (95% CI 0.54,5.07) p=0.38</p> <p><u>Erectile function</u> (n=1 RCT) MD -2.00 (95% CI -2.55,-1.45) p<0.00001</p> <p><u>Hospital stay</u> (n=2 RCTs) MD -1.96 (95% CI -2.36,-1.57) p<0.00001</p> <p>Long term <u>Urologic symptom score</u> (n=1 RCT)</p>	<p>function and ejaculatory disorders.</p>	<p>of Medicine, Korea, South Minneapolis VA Health Care System, USA, Department of Urology, University of Minnesota, USA</p> <p>Results only shown for the comparison PAE vs. TURP and RCTs</p>	
--	--	--	--	--	--	--	---	--	--	--



							<p>MD 0.3 (95% CI -3.17,3.77) p=0.87</p> <p><u>QoL</u> (n=1 RCT) MD 0.206 (95% CI -0.49,0.89) p=0.57</p> <p><u>Major adverse events</u> (n=1 RCT) RR 1.96 (95% CI 0.63,6.13) p=0.25</p> <p><u>Retreatment</u> (n=1 RCT) RR 3.54 (95% CI 1.45,8.65) p=0.005</p> <p><u>Minor adverse events</u> (n=1 RCT) RR 1.66 (95% CI 0.94,2.94) p=0.08</p>			
<p>Knight, 2020, Cardiovasc Intervent Radiol [171]</p>	<p>Systematic review with meta-analysis</p>	<p>n= 6 comparative studies (3 RCTs, 3 non-RCTs) search date: 15 July 2020</p>	<p>To report a comparative systematic review and meta-analysis of PAE and TURP for the management of BPH.</p>	<p>n=598 patients with BPH</p>	<p>PAE</p>	<p>TURP</p>	<p>IPSS (n=6) MD: 2.19 (-1.14, 5.53) p=0.2</p> <p>IPSS-QoL (n=6) MD: -0.71 (-4.24, 2.83) p=0.7</p> <p>IIEF-5 (n=3) MD: 0.65 (-2.83, 4.12) p=0.72</p> <p>Qmax (n=6)</p>	<p>Subjective symptom improvement was equivalent between TURP and PAE. While TURP demonstrated larger improvements for some objective parameters, PAE was associated with fewer adverse events and shorter hospitalization times.</p>	<p>no information if efforts were made to minimise error in the study selection, data collection and risk of bias assessment, no funnel plot or sensitivity analyses</p>	<p>LoE: 1- to 2- (mixed study designs) RoB: high</p>



							<p>MD: 5.02 (2.66, 7.38) p<0.00001 favours TURP</p> <p>PVR (n=5) MD: 26.54 (-15.45, 68.52) p=0.05</p> <p>PV (n=6) MD: 15.59 (7.93, 23.25) p<0.00001 favours TURP</p> <p>PSA (n=4) MD: 1.02 (0.14, 1.89) p=0.02 favours TURP</p> <p>Hospital Length-of-Stay MD: -1.94 (-2.3, -1.59) p<0.00001 favours PAE</p> <p>Prodecursal/Operative time MD: 51.43 (16.06, 86.81) p=0.004 favours TURP</p> <ul style="list-style-type: none"> • RCTs only show the similar results 	<p>serious heterogeneity (I²>75%) for IPSS, IPSS-QoL, Qmax, PV and procedural/operative time</p> <p>no conflict of interest declared</p> <p>no funding</p>		
Jiang, 2019,	Systematic review with	n= 4 studies (2 RCTs, 2	To compare the clinical efficiency	n= 506 patients with BPH	PAE	TURP	postoperative IPSS (n=4)	TURP could achieve improved Qmax and QoL compared to PAE.	no additional hand search, no information if	LoE 1- to 2-



<p>BMC Urology [172]</p>	<p>meta-analysis</p>	<p>cohort studies) May 1998-2018</p>	<p>and safety of TURP and PAE for the treatment of BPH.</p>				<p>MD 1.56 [-0.67,3.78] p=0.17</p> <p>Postoperative Qmax (n=2) MD 4.66 [2.54,6.79] p<0.0001 favours PAE</p> <p>QoL (n=2) MD -0.53 [-0.88,-0.18] p<0.003 favour TURP</p> <p>Postoperative Prostate volume (n=2) MD -8.26 [-12.46,-3.88] p=0.0002 favours TURP</p> <p>Operative time (n=2) MD -10.55 [-16.92,-4.18] p=0.001 favours TURP</p> <p>Complications (n=2) OR 1.54 [1.00,2.38] p=0.05</p>	<p>For patients with BPH and LUTS, TURP was superior to PAE.</p>	<p>efforts were made to minimise error in the risk of bias assessment, no funnel plot or sensitivity analyses</p> <p>serious heterogeneity (I²>75%) for postoperative IPSS, Qmax, prostate volume, operative time and complications: „The four studies involved unilateral embolization, bilateral artery embolization or combined unilateral and bilateral embolization, which also increases the heterogeneity“</p> <p>Conclusion and Fig 5 are showing</p>	<p>(mixed study designs) RoB: high</p>
--------------------------	----------------------	--	---	--	--	--	---	--	---	--



									inconsistent results. no funding and no conflict of interest declared	
Xu, 2019, World Journal of Urology [173]	Systematic review with meta-analysis	n=9 comparative studies (2 RCTs, 7 cohort studies) up to June 2019	We conducted an updated meta-analysis to assess the efficacy and safety of PAE compared with TURP.	n=860 patients with BPH	PAE	TURP	<p>IPSS (n=9) MD 2.50 (95% CI 0.78, 4.21) p=0.004 favours TURP</p> <p>QoL (n=9) MD 0.40 (95% CI 0.09, 0.71) p=0.01 favours TURP</p> <p>Qmax (n=9) MD 2.54 (95% CI 1.02, 4.05) p=0.001 favours TURP</p> <p>PVR (n=8) MD 0.46 (95% CI -2.08, 3.00) p=0.72</p> <p>PV (n=9) MD 8.59 (95% CI 4.74, 12.44) p<0.0001 favours TURP</p> <p>Complications (n=7)</p>	PAE was inferior to TURP in the improvement of postoperative IPSS, QOL, PV, Qmax and TURP still remained the gold standard. However, PAE may be a valuable alternative to TURP in the treatment of BPH patients who refuse surgery or with surgery contraindication.	no information if efforts were made to minimise error in the selection of the studies and the risk of bias assessment serious heterogeneity (I ² >75%) for IPSS, Qmax, PV and complications no conflict of interest declared no information about funding	LoE 2++ RoB: low



							OR 0.57 (95% CI 0.21, 1.55) p=0.27			
							Sexual dysfunction (n=6) OR 0.24 (95% CI 0.15, 0.39) p<0.0001 favours PAE			
Zumstein, 2019, European Urology Focus [174]	Systematic review with meta-analysis	n= 5 studies (3 RCTs, 2 cohort studies) searched up to June 23, 2018	To perform a systematic review and meta-analysis of clinical trials comparing efficacy and safety of PAE versus established surgical therapies.	n=708 patients with BPH-LUTS	PAE	<ul style="list-style-type: none"> • TURP • Open prostatectomy 	PAE vs. TURP IPSS (n=3 RCTs) MD 2.09 (95% CI 0.61,3.56) p< 0.005 favour TURP <u>IPSS-QoL (n=3 RCTs)</u> MD 0.13 (95% CI -0.10,0.37) p=0.26 <u>IIEF-5 (n=2 RCTs)</u> MD 0.61 (95% CI -1.74,2.97) p=0.61 <u>Maximum flow rate (n=3 RCTs)</u> MD 2.23 (95% CI 1.35,3.11) p< 0.00001 favour TURP PVR (n=3 RCTs)	The results suggest that PAE is not as effective as established surgical therapies but has fewer side effects.	no funnel plot or sensitivity analyses no conflict of interest and no funding declared serious heterogeneity (I ² >75%) for IPSS, IPSS-QoL, IIEF-5, Maximum flow rate, PVR and procedure time Results only shown for the comparison PAE vs. TURP	LoE 1++ RoB: low



							<p>MD 6.76 (95% CI -15.43,28.94) p=0.55</p> <p><u>PV (n=3 RCTs, 1 cohort study)</u> MD 11.51 (95% CI 6.11,16.91) p<0.0001 favour TURP</p> <p><u>PSA (n=3 RCTs)</u> MD 0.56 (95% CI -0,1.12) p=0.05</p> <p><u>Hospitalization (n=3 RCTs)</u> MD -1.96 (95% CI -2.30,-1.59) p< 0.00001 favour PAE</p> <p><u>Procedure time (n=3 RCTs)</u> MD 23.51 (95% CI 18.21,28.81) p< 0.00001 favour TURP</p>			
Feng, 2017, Cardiovascu Intervent Radiol [175]	Systematic review with meta-analysis	n= 20 studies (case series, cohort studies, RCTs) Brazil, China, France,	To evaluate the clinical efficiency and safety of PAE treating moderate-to-severe LUTS related to BPH.	n=1318 patients require treatment due to moderate-to-severe LUTS Median age: 62-82.5y	PAE	TURP	<p>PAE vs. TURP both operations improved clinical outcomes of patients with BPH (n=2)</p> <p><u>Francisco C. Carnevale et al.'s study</u></p>	PAE should be considered to be the very promising alternative treatment for those who do not want or cannot tolerate surgical treatment, with its benefits on	no risk of bias assessment, no funnel plot or sensitivity analyses no conflict of interest declared	LoE 1- (for the comparison) RoB: high



		Italy, Portugal, USA Last search: April 2016				<p>Mean procedure time TURP: 61.7 ± 17.0 min PAE: 144.8 ± 50.1 min</p> <p>IPSS TURP: 6.1 ± 8.6 PAE: 12.8 ± 8.0</p> <p>QoL score TURP: 0.9 ± 1.4 PAE: 2.2 ± 1.2</p> <p>IIEF score TURP: 16.1 ± 5.7 PAE: 12.6 ± 7.7</p> <p>PV TURP: 32.0 ± 11.4 mL PAE: 50.9 ± 19.0 mL</p> <p>PSA level TURP: 1.6 ± 0.9 ng/mL PAE: 2.2 ± 1.1 ng/mL</p> <p>PVR TURP: 8.3 ± 11.9 mL PAE: 62.3 ± 71.0 mL</p> <p>Qmax TURP: 27.1 ± 8.7 mL/s</p>	IPSS, QoL score, PSA level, PV, Qmax, and PVR without affecting erectile function.	no specific Grant from any funding agency in public, commercial, or non-profit sectors Results only shown for the comparison PAE vs. TURP	
--	--	---	--	--	--	--	--	---	--



							<p>PAE: 10.1 ± 6.5 mL/s</p> <p><u>Yuanan Gao's study</u></p> <ul style="list-style-type: none"> no statistical difference in IPSS, QoL score, Qmax, and PVR PSA level: TURP 2.1, PAE 1.7, p=0.00116 PV: TURP 34.9, PAE 26.6, p=0.001 			
Shim, 2017, Journal of Urology [176]	Systematic review with meta-analysis and meta-regression	n=16 studies (3 comparative studies) 1966-January 2016	This study attempted to overcome the limitations of previous systematic reviews to determine the overall treatment efficacy and safety of prostatic arterial embolization compared with standard therapy.	patients with BPH/LUTS n= 149 patients treated with PAE n= 69 patients treated with TURP n= 80 patients treated with prostatectomy	PAE	<ul style="list-style-type: none"> TURP (n=2 RCTs) open prostatectomy (n=1 matched cohort study) 	<p>PAE vs. TURP or open prostatectomy</p> <p><u>IPSS</u> SMD: 0.88 (95% CI 0.10 to 1.66) favours control</p> <p><u>QoL</u> SMD: 0.25 (95% CI -0.28 to 0.77)</p> <p><u>Qmax</u> SMD: -1.44 (95% CI -2.30 to -0.58) favours control</p> <p><u>PVR</u> SMD: 0.14 (95% CI -0.18 to 0.46)</p> <p><u>IIEF</u></p>	Although there is growing evidence of the efficacy and safety of prostatic arterial embolization for benign prostatic hyperplasia, this systematic review using meta-analysis and meta-regression showed that prostatic arterial embolization should still be considered an experimental treatment modality.	<p>no keywords named, no information if efforts were made to minimise error in the data collection and the risk of bias assessment, no between-study variation addressed</p> <p>no conflict of interest declared</p> <p>Supported by the Next-generation Medical Device Development</p>	<p>LoE 1- (for the comparison)</p> <p>RoB: high</p>



							<p>SMD: 0.05 (95% CI -1.52 to 1.62)</p> <p><u>PSA</u> SMD: 0.46 (95% CI -0.02 to 0.95)</p> <p>PAE vs. TURP <u>Prostate volume</u> SMD: 0.48 (95% CI 0.14 to 0.82) favours control</p>		<p>Program for Newly-Created Market of the National Research Foundation funded by the Korean government, MSIP (No. 2015M3D5A106 5926), and the Soonchunhyang University Fund.</p> <p>only results shown for the comparison PAE vs. TURP</p>	
--	--	--	--	--	--	--	--	--	--	--



Tabelle 32: Aquablation vs. TURP

Schlüsselfrage										
Welche Effekte zeigt Aquablation im Vergleich zur TURP?										
Referenz	Studien-design	Studien-charakteristika	Studien-ziel	Patienten-merkmale	Intervention	Kontrolle	Ergebnisse	Schlussfolgerungen	Bemerkungen	LoE
Systematic Review										
Hwang, 2019, Cochrane Database of Systematic Reviews [177]	Systematic review	n= 1 RCT (WATER study) Last search date: 11 February 2019 Follow-up: 12 mo	To assess the effects of Aquablation for the treatment of lower urinary tract symptoms in men with benign prostatic hyperplasia.	n=184 men with benign prostatic hyperplasia Mean IPSS score: 22.6 Mean age: 65.9 y	Aquablation n=117 patients	TURP n=67 patients	IPSS MD -0.06, 95%CI -2.51 to 2.39 IPSS-QoL MD 0.27, 95% CI -0.24 to 0.78 Major adverse events RR 0.84, 95%CI 0.31 to 2.26 Retreatment RR 1.68, 95% CI 0.18 to 15.83 Erectile function MD 2.31, 95% CI -0.63 to 5.25 Ejaculatory function MD 2.57, 95% CI 0.60 to 4.53	Based on short-term (up to 12 months) follow-up, the effect of Aquablation on urological symptoms is probably similar to that of TURP (moderate-certainty evidence). The effect on quality of life may also be similar (low-certainty evidence). We are very uncertain whether patients undergoing Aquablation are at higher or lower risk for major adverse events (very low-certainty evidence). We are very uncertain whether Aquablation may result in little to no difference in erectile function but offer a small improvement in preservation of	one of the authors declared conflict of interest: Boston Scientific (consultant for endourology and stonemanagement), AurisHealth (consultant for robotic surgery and endourology). Funding: Minneapolis Veterans Administration Medical Center, USA. Salary support for Philipp Dahm, Chonnam National University Medical School, Korea, South. Salary support for Eu Chang Hwang,	LoE 1++ RoB: low



							<p>Minor adverse events RR 0.96, 95%CI 0.76 to 1.21</p> <p>Acute urinary retention RR 1.01, 95% CI 0.35 to 2.88</p> <p>Indwelling urinary catheter MD 6.00 hours, 95% CI -9.45 to 21.45</p> <p>Hospital stay MD 0.00 days, 95%CI-0.21 to 0.21</p>	ejaculatory function (both very low-certainty evidence).	Department of Urology, Yonsei University Wonju College of Medicine, Korea, South, Department of Urology, University of Minnesota, USA, Department of Urology, Chonnam National University Medical School, Korea, South	
Randomized Controlled Trials										
Gilling, 2020, Canadian Journal of Urology [178]	RCT (WATER study)	n=184 men with benign prostatic hyperplasia October 2015-December 2016 Australia/New Zealand, United Kingdom, United States	To compare 3-year efficacy and safety after prostate resection with Aquablation therapy or TURP for the treatment of lower urinary	Mean age Aquablation: 66.0 y (SD 7.3. y) TURP: 65.8 y (SD 7.2) Prostate size Aquablation: 54.1 gm (16.2 gm) TURP: 51.8 gm (13.8 gm)	Aquablation n=117 patients	TURP n=67 patients	<p>IPSS Aquablation: 14.4 (SD 6.8) TURP: 13.9 (SD 8.6) p=0.6848</p> <p>Qmax Aquablation: 11.6 cc/sec (SD 14 cc/sec) TURP: 8.2 cc/sec (SD 8 cc/sec) p=0.6848</p> <p>PVR</p>	Three-year BPH symptom reduction and urinary flow rate improvement were similar after TURP and Aquablation therapy. No subjects required surgical retreatment beyond 20 months postoperatively.	unclear allocation concealment no information about conflict of interests funded by PROCEPT BioRobotics	LoE 1+ RoB: low



		Follow-up: 36 mo	tract symptoms related to BPH.				Aquablation: 52 (SD 163) TURP: 53 (SD 224) p=0.9801 PSA was reduced significantly compared to baseline, but not statistical significant Aquablation: 0.9 TURP: 1.1 p=0.5983			
Gilling, 2019, Adv Thera [179]	RCT (Water study)	n=184 men with benign prostatic hyperplasia October 2015- December 2016 Australia/ New Zealand, United Kingdom, United States Follow-up: 24 mo	To compare 2-year safety and efficacy outcomes after Aquablatio n or TURP for the treatment of lower urinary tract symptoms related to BPH.	Mean age Aquablation: 66 y (SD 7.3. y) TURP: 65.8 y (SD 7.2) Prostate size Aquablation: 54.1 gm (16.2 gm) TURP: 51.8 gm (13.8 gm)	Aquablation n=117 patients	TURP n=67 patients	IPSS Aquablation: 14.7 (SD 7.1) TURP: 14.9 (SD 7.3) p=0.8304 IPSS QoL Aquablation: 3.2 (1.7) TURP: 3.3 (1.5) p=0.7007 Qmax Aquablation: 11.2 (SD 11) TURP: 8.6 (SD 12.2) p=0.188 PVR Aquablation: 57 cc (78 cc) TURP: 70 cc (101 cc) p=0.3894	Two-year efficacy outcomes after TURP and Aquablation were similar, and the rate of surgical retreatment was low and similar to TURP.	unclear allocation concealment Several reactions to pharmaceutical industries funded by PROCEPT BioRobotics	LoE 1+ RoB: low



							<p>PSA PSA was reduced significantly in both groups by 1 point (p=0.01)</p> <p>Anejaculation Aquablation: 10% TURP: 36% p=0.0003</p> <p>Retreatment rates Aquablation: 4.3% TURP: 1.5% p=0.4219</p>			
Pimentel, 2019, Urology [180]	RCT (WATER subgroup analysis)	n=66 men with benign prostatic hyperplasia Australia/ New Zealand, United Kingdom, United States Follow-up: 6 mo	To compare urodynamic outcomes between Aquablation vs TURP.	men aged 45-80 y old with prostate sizes from 30-80 grams, IPSS ≥ 12, and a Qmax <15 mL/s	Aquablation n= 43	TURP n= 23	<p>Detrusor pressure at maximal flow rates <u>Baseline to 6 mo</u> Aquablation: -36.1 p<0.001 TURP: -37.2 p<0.001</p> <p><u>Aquablation vs. TURP</u> 1.2 p=0.8919</p> <p>Qmax <u>Baseline to 6 mo</u> Aquablation: 5.5 p<0.001 TURP: 5.3 p<0.0012</p> <p><u>Aquablation vs. TURP</u></p>	In this trial, improvements after Aquablation in objective measures of bladder outlet obstruction were similar to those observed after TURP.	randomisation process only for the overall study population, no information about blinding funded by PROCEPT BioRobotics No author has a conflict of interest with PROCEPT BioRobotics	LoE 1- RoB: high



						<p>0.2 p=0.8904</p> <p>PVR <u>Baseline to 6 mo</u> Aquablation: -41.7 p=0.0406 TURP: -80.2 p=0.0113</p> <p><u>Aquablation vs. TURP</u> 38.5 p=0.4947</p> <p>Maximal Cystometric Capacity <u>Baseline to 6 mo</u> Aquablation: 63.1 p=0.0062 TURP: -38.3 p=0.32</p> <p><u>Aquablation vs. TURP</u> 101.4 p=0.0255</p> <p>Bladder Outlet Obstruction Index <u>Baseline to 6 mo</u> Aquablation: 79% to 22%, p<0.001 TURP: 96% to 22%, p<0.001</p>			
--	--	--	--	--	--	---	--	--	--



8. Tabellenverzeichnis

Tabelle 1:	Schema der Evidenzgraduierung	5
Tabelle 2:	Abkürzungsverzeichnis.....	6
Tabelle 3:	Risikofaktoren.....	12
Tabelle 4:	Progressionswahrscheinlichkeit	20
Tabelle 5:	Psychometrische Eigenschaften des IPSS	24
Tabelle 6:	Minimal klinischer Unterschied des IPSS.....	25
Tabelle 7:	Einschränkung der Lebensqualität	26
Tabelle 8:	Urinanalyse	33
Tabelle 9:	Stellenwert des PSA	37
Tabelle 10:	Restharnmessung	41
Tabelle 11:	Harnblasenwanddickenmessung	46
Tabelle 12:	Sonographie.....	51
Tabelle 13:	Genauigkeit des Kreatinin-Wertes	55
Tabelle 14:	Uroflowmetrie.....	57
Tabelle 15:	Kombinationen aus mehreren Untersuchungen	69
Tabelle 16:	Nicht-invasive Tests	77
Tabelle 17:	Grenzwerte von urodynamischen Untersuchungen.....	83
Tabelle 18:	Blasentagebuch	87
Tabelle 19:	Druck-Fluss-Messung.....	95
Tabelle 20:	Prognostische Faktoren.....	100
Tabelle 21:	Phytotherapeutika vs. Monotherapie.....	128
Tabelle 22:	Phytotherapeutika vs. Placebo/kontrolliertes Zuwarten	141
Tabelle 23:	beta3-Agonisten vs. Placebo/kontrolliertes Zuwarten	150
Tabelle 24:	Kombinationstherapien vs. Placebo/Kontrolliertes Zuwarten	157
Tabelle 25:	Monotherapien vs. Kombinationspräparaten	164
Tabelle 26:	Monotherapien vs. Monotherapien.....	194
Tabelle 27:	Laser-Verfahren	204
Tabelle 28:	Enukleationsverfahren	214
Tabelle 29:	Neue minimal-invasive Therapien vs. medikamentöse Therapie	231
Tabelle 30:	Neue minimal-invasive Verfahren vs. TURP	238
Tabelle 31:	Prostata-Arterien-Embolisation vs. TURP.....	242
Tabelle 32:	Aquablation vs. TURP	253



9. Referenzen

1. Bradley, C.S., et al., *Evidence of the impact of diet, fluid intake, caffeine, alcohol and tobacco on lower urinary tract symptoms: a systematic review*. J Urol, 2017. **198**(5): p. 1010-20.
2. Gacci, M., et al., *Metabolic syndrome and benign prostatic enlargement: a systematic review and meta-analysis*. BJU Int, 2015. **115**(1): p. 24-31.
3. Greco, F., et al., *The Potential Role of MicroRNAs as Biomarkers in Benign Prostatic Hyperplasia: A Systematic Review and Meta-analysis*. European Urology Focus, 2019. **5**(3): p. 497-507.
4. Minciullo, P.L., et al., *Oxidative stress in benign prostatic hyperplasia: a systematic review*. Urol Int, 2015. **94**(3): p. 249-54.
5. Russo, G.I., et al., *Connections between lower urinary tract symptoms related to benign prostatic enlargement and metabolic syndrome with its components: a systematic review and meta-analysis*. Aging Male, 2015. **18**(4): p. 207-16.
6. Russo, G.I., et al., *Emerging links between non-neurogenic lower urinary tract symptoms secondary to benign prostatic obstruction, metabolic syndrome and its components: A systematic review*. Int J Urol, 2015. **22**(11): p. 982-90.
7. Siddiqui, N.Y., et al., *Biomarkers Implicated in Lower Urinary Tract Symptoms: Systematic Review and Pathway Analyses*. J Urol, 2019. **202**(5): p. 880-889.
8. Wang, J.Y., Y.Y. Fu, and D.Y. Kang, *The Association Between Metabolic Syndrome and Characteristics of Benign Prostatic Hyperplasia: A Systematic Review and Meta-Analysis*. Medicine (Baltimore), 2016. **95**(19): p. e3243.
9. Xu, H., et al., *Smoking habits and benign prostatic hyperplasia: A systematic review and meta-analysis of observational studies*. Medicine (Baltimore), 2016. **95**(32): p. e4565.
10. Zou, C., et al., *Meta-analysis of metabolic syndrome and benign prostatic hyperplasia in Chinese patients*. World J Urol, 2016. **34**(2): p. 281-9.
11. De Nunzio, C., et al., *Young Academic Urologists' benign prostatic obstruction nomogram predicts clinical outcome in patients treated with transurethral resection of prostate: an Italian cohort study*. Minerva urologica e nefrologica = The Italian journal of urology and nephrology, 2018. **70**(2): p. 211-217.
12. Javllé, P., et al., *Grading of benign prostatic obstruction can predict the outcome of transurethral prostatectomy*. J Urol, 1998. **160**(5): p. 1713-7.
13. Jeldres, C., et al., *Development and External Validation of a Highly Accurate Nomogram for the Prediction of Perioperative Mortality After Transurethral Resection of the Prostate for Benign Prostatic Hyperplasia*. Journal of Urology, 2009. **182**(2): p. 626-632.
14. Slawin, K.M., et al., *Development of nomogram to predict acute urinary retention or surgical intervention, with or without dutasteride therapy, in men with benign prostatic hyperplasia*. Urology, 2006. **67**(1): p. 84-88.
15. Badia, X., M. Garcia-Losa, and R. Dal-Re, *Ten-language translation and harmonization of the International Prostate Symptom Score: developing a methodology for multinational clinical trials*. Eur Urol, 1997. **31**(2): p. 129-40.
16. Barry, M.J., et al., *Benign prostatic hyperplasia specific health status measures in clinical research: how much change in the American Urological Association symptom index and the benign prostatic hyperplasia impact index is perceptible to patients?* J Urol, 1995. **154**(5): p. 1770-4.
17. Cizman, Z., A. Isaacson, and C. Burke, *Short- to Midterm Safety and Efficacy of Prostatic Artery Embolization: A Systematic Review*. Journal of Vascular & Interventional Radiology, 2016. **27**(10): p. 1487-1493.e1.
18. Coleman, C.I., J.H. Hebert, and P. Reddy, *The effect of phytosterols on quality of life in the treatment of benign prostatic hyperplasia*. Pharmacotherapy, 2002. **22**(11): p. 1426-32.
19. Damiano, R., et al., *The role of Cucurbita pepo in the management of patients affected by lower urinary tract symptoms due to benign prostatic hyperplasia: A narrative review*. Arch Ital Urol Androl, 2016. **88**(2): p. 136-43.
20. Deng, Z., et al., *Thulium laser VapoResection of the prostate versus traditional transurethral resection of the prostate or transurethral plasmakinetic resection of prostate for benign*



- prostatic obstruction: a systematic review and meta-analysis.* World J Urol, 2018. **36**(9): p. 1355-1364.
21. Ding, H., et al., *Silodosin is effective for treatment of LUTS in men with BPH: a systematic review.* Asian Journal of Andrology, 2013. **15**(1): p. 121-8.
 22. Haltbakk, J., B.R. Hanestad, and S. Hunskaar, *Use and misuse of the concept of quality of life in evaluating surgical treatments for lower urinary tract symptoms.* BJU International, 2003. **91**(4): p. 380-8.
 23. Hwang, E.C., et al., *Naftopidil for the treatment of lower urinary tract symptoms compatible with benign prostatic hyperplasia.* Cochrane Database of Systematic Reviews, 2018. **10**: p. CD007360.
 24. Jiang, H. and Y. Zhou, *Safety and Efficacy of Thulium Laser Prostatectomy Versus Transurethral Resection of Prostate for Treatment of Benign Prostate Hyperplasia: A Meta-Analysis.* Luts, 2016. **8**(3): p. 165-70.
 25. Kuang, M., A. Vu, and S. Athreya, *A Systematic Review of Prostatic Artery Embolization in the Treatment of Symptomatic Benign Prostatic Hyperplasia.* Cardiovascular & Interventional Radiology, 2017. **40**(5): p. 655-663.
 26. Lan, Y., et al., *Thulium (Tm:YAG) laser vaporesction of prostate and bipolar transurethral resection of prostate in patients with benign prostate hyperplasia: a systematic review and meta-analysis.* Lasers in Medical Science, 2018. **33**(7): p. 1411-1421.
 27. Lin, Y., et al., *Transurethral enucleation of the prostate versus transvesical open prostatectomy for large benign prostatic hyperplasia: a systematic review and meta-analysis of randomized controlled trials.* World Journal of Urology, 2016. **34**(9): p. 1207-19.
 28. Malling, B., et al., *Prostate artery embolisation for benign prostatic hyperplasia: a systematic review and meta-analysis.* European Radiology, 2019. **29**(1): p. 287-298.
 29. Oeconomou, A., et al., *Is botulinum neurotoxin type A (BoNT-A) a novel therapy for lower urinary tract symptoms due to benign prostatic enlargement? A review of the literature.* Eur Urol, 2008. **54**(4): p. 765-75.
 30. Pinto, J.D., et al., *Health-related quality of life and psychological well-being in men with benign prostatic hyperplasia: An integrative review.* Jpn J Nurs Sci, 2016. **13**(3): p. 309-23.
 31. Pyo, J.S. and W.J. Cho, *Systematic review and meta-analysis of prostatic artery embolisation for lower urinary tract symptoms related to benign prostatic hyperplasia.* Clin Radiol, 2017. **72**(1): p. 16-22.
 32. Rieken, M. and A. Bachmann, *Update on Greenlight laser vaporization (PVP) 2014.* World J Urol, 2015. **33**(4): p. 531-7.
 33. Schreuder, S.M., et al., *The role of prostatic arterial embolization in patients with benign prostatic hyperplasia: a systematic review.* Cardiovasc Intervent Radiol, 2014. **37**(5): p. 1198-219.
 34. Teng, J., et al., *Photoselective vaporization with the green light laser vs transurethral resection of the prostate for treating benign prostate hyperplasia: a systematic review and meta-analysis.* BJU Int, 2013. **111**(2): p. 312-23.
 35. Uflacker, A., et al., *Meta-Analysis of Prostatic Artery Embolization for Benign Prostatic Hyperplasia.* Journal of Vascular & Interventional Radiology, 2016. **27**(11): p. 1686-1697.e8.
 36. Zang, Y.C., et al., *Photoselective vaporization of the prostate with GreenLight 120-W laser versus transurethral resection of the prostate for benign prostatic hyperplasia: a systematic review with meta-analysis of randomized controlled trials.* Lasers in Medical Science, 2016. **31**(2): p. 235-40.
 37. Zhu, Y., et al., *Thulium laser versus standard transurethral resection of the prostate for benign prostatic obstruction: a systematic review and meta-analysis.* World Journal of Urology, 2015. **33**(4): p. 509-15.
 38. Chen, S.S., et al., *Complicated urinary tract infection: analysis of 179 patients.* Zhonghua Yi Xue Za Zhi (Taipei), 1998. **61**(11): p. 651-6.
 39. Demiray, T., et al., *Microbiological Evaluation Of Urinary Tract Infections In Elderly Men With Benign Prostatic Hyperplasia.* Turkish Journal of Geriatrics, 2016.
 40. Khasriya, R., et al., *The Inadequacy of Urinary Dipstick and Microscopy as Surrogate Markers of Urinary Tract Infection in Urological Outpatients With Lower Urinary Tract Symptoms Without Acute Frequency and Dysuria.* Journal of Urology, 2010. **183**(5): p. 1843-1847.



41. Kupelian, A.S., et al., *Discrediting microscopic pyuria and leucocyte esterase as diagnostic surrogates for infection in patients with lower urinary tract symptoms: Results from a clinical and laboratory evaluation*. BJU International, 2013. **112**(2): p. 231-238.
42. Mohanty, N.K. and B.B. Jolly, *Prevalence of bacterial prostatitis in benign prostatic hyperplasia*. Indian J Pathol Microbiol, 1996. **39**(2): p. 111-4.
43. Antunes, A.A., et al., *Analysis of the risk factors for incidental carcinoma of the prostate in patients with benign prostatic hyperplasia*. Clinics (Sao Paulo), 2006. **61**(6): p. 545-50.
44. Carballido, J., et al., *Can benign prostatic hyperplasia be identified in the primary care setting using only simple tests? Results of the Diagnosis Improvement in Primary Care Trial*. Int J Clin Pract, 2011. **65**(9): p. 989-96.
45. Ho, C.C., et al., *Urinary bladder characteristics via ultrasound as predictors of acute urinary retention in men with benign prostatic hyperplasia*. Clin Ter, 2014. **165**(2): p. 75-81.
46. Luo, F., et al., *Assessment of noninvasive predictors of bladder detrusor underactivity in BPH/LUTs patients*. Int Urol Nephrol, 2017. **49**(5): p. 787-792.
47. Yu, H.J., et al., *Clinical efficacy of prostate-specific antigen testing in patients with prostate disease*. J Formos Med Assoc, 1996. **95**(10): p. 782-8.
48. Malati, T., et al., *Prostate specific antigen in patients of benign prostate hypertrophy and carcinoma prostate*. Indian J Clin Biochem, 2006. **21**(1): p. 34-40.
49. ElSaied, W., et al., *Detrusor wall thickness compared to other non-invasive methods in diagnosing men with bladder outlet obstruction: A prospective controlled study*. African Journal of Urology, 2013. **19**(4): p. 160-164.
50. Kang, M., et al., *Urodynamic Features and Significant Predictors of Bladder Outlet Obstruction in Patients With Lower Urinary Tract Symptoms/Benign Prostatic Hyperplasia and Small Prostate Volume*. Urology, 2016. **89**: p. 96-102.
51. Ku, J.H., S.Y. Cho, and S.J. Oh, *Residual fraction as a parameter to predict bladder outlet obstruction in men with lower urinary tract symptoms*. International Journal of Urology, 2009. **16**(9): p. 739-744.
52. Lee, K.S., P.H. Song, and Y.H. Ko, *Does uroflowmetry parameter facilitate discrimination between detrusor underactivity and bladder outlet obstruction?* Investigative and Clinical Urology, 2016. **57**(6): p. 437-441.
53. Oelke, M., et al., *Diagnostic Accuracy of Noninvasive Tests to Evaluate Bladder Outlet Obstruction in Men: Detrusor Wall Thickness, Uroflowmetry, Postvoid Residual Urine, and Prostate Volume*. European Urology, 2007. **52**(3): p. 827-835.
54. Shim, S.R., et al., *Is Tamsulosin 0.2 mg Effective and Safe as a First-Line Treatment Compared with Other Alpha Blockers?: A Meta-Analysis and a Moderator Focused Study*. Yonsei Medical Journal, 2016. **57**(2): p. 407-18.
55. Malde, S., et al., *Systematic Review of the Performance of Noninvasive Tests in Diagnosing Bladder Outlet Obstruction in Men with Lower Urinary Tract Symptoms*. Eur Urol, 2017. **71**(3): p. 391-402.
56. Aganovic, D., et al., *Which is a better indicator of bladder outlet obstruction in patients with benign prostatic enlargement--intravesical protrusion of prostate or bladder wall thickness?* Medicinski arhiv, 2012. **66**(5): p. 324-328.
57. Farag, F., et al., *A novel algorithm for the non-invasive detection of bladder outlet obstruction in men with lower urinary tract symptoms*. Arab Journal of Urology, 2017. **15**(2): p. 153-158.
58. Franco, G., et al., *Ultrasound Assessment of Intravesical Prostatic Protrusion and Detrusor Wall Thickness--New Standards for Noninvasive Bladder Outlet Obstruction Diagnosis?* Journal of Urology, 2010. **183**(6): p. 2270-2274.
59. Güzel, Ö., et al., *Can Bladder Wall Thickness Measurement Be Used for Detecting Bladder Outlet Obstruction?* Urology, 2015. **86**(3): p. 439-44.
60. Manieri, C., et al., *The diagnosis of bladder outlet obstruction in men by ultrasound measurement of bladder wall thickness*. J Urol, 1998. **159**(3): p. 761-5.
61. Oelke, M., et al., *Increase in detrusor wall thickness indicates bladder outlet obstruction (BOO) in men*. World J Urol, 2002. **19**(6): p. 443-52.
62. Ajayi, I., et al., *Correlation of transrectal and transabdominal ultrasound measurement of transition zone volume with post-operative enucleated adenoma volume in benign prostatic hypertrophy*. Pan African Medical Journal, 2013. **16**(no pagination).



63. Chakraborty, A., et al., *Transrectal ultrasonic volume determination of the prostate - a pre and postoperative study*. Indian Journal of Radiology and Imaging, 1990. **44**(1): p. 37-39.
64. Feng, K.K., et al., *Analysis of transrectal and suprapubic ultrasonography for prostate size evaluation*. Urological Science, 2017. **28**(3): p. 166-168.
65. Huang Foen Chung, J.W.N.C., et al., *Prostate volume ultrasonography: The influence of transabdominal versus transrectal approach, device type and operator*. European Urology, 2004. **46**(3): p. 352-356.
66. Malemo, K., et al., *Validation of supra-pubic ultrasonography for preoperative prostate volume measurement in sub-Saharan Africa*. Int Urol Nephrol, 2011. **43**(2): p. 283-8.
67. Prassopoulos, P., et al., *Suprapubic versus transrectal ultrasonography in assessing the volume of the prostate and the transition zone in patients with benign prostatic hyperplasia*. Abdominal Imaging, 1996. **21**(1): p. 75-77.
68. Lopez-Vargas, P.A., et al., *Prevention, detection and management of early chronic kidney disease: a systematic review of clinical practice guidelines*. Nephrology (Carlton), 2013. **18**(9): p. 592-604.
69. Rule, A.D., M.M. Lieber, and S.J. Jacobsen, *Is benign prostatic hyperplasia a risk factor for chronic renal failure?* J Urol, 2005. **173**(3): p. 691-6.
70. Aganovic, D., *The role of uroflowmetry in diagnosis of infravesical obstruction in the patients with benign prostatic enlargement*. Medicinski arhiv, 2004. **58**(1 Suppl 2): p. 109-111.
71. Botkor-Rasmussen, I., P. Bagi, and J.B. Jorgensen, *Is bladder outlet obstruction normal in elderly men without lower urinary tract symptoms?* Neurourology and Urodynamics, 1999. **18**(6): p. 545-552.
72. Harding, C., et al., *Predicting the outcome of prostatectomy using noninvasive bladder pressure and urine flow measurements*. Eur Urol, 2007. **52**(1): p. 186-92.
73. Hirayama, A., et al., *Comparison of parameters to determine the cause of urinary disturbance in men with prostate volume less than 20 milliliters*. International Journal of Urology, 2002. **9**(10): p. 554-559.
74. Kuo, H.C., *Clinical prostate score for diagnosis of bladder outlet obstruction by prostate measurements and uroflowmetry*. Urology, 1999. **54**(1): p. 90-96.
75. Oelke, M., et al., *Increase in detrusor wall thickness indicates bladder outlet obstruction (BOO) in men*. World journal of urology, 2002. **19**(6): p. 443-452.
76. Poulsen, A.L., et al., *Prostatic enlargement, symptomatology and pressure/flow evaluation: Interrelations in patients with symptomatic BPH*. Scandinavian Journal of Urology and Nephrology, Supplement, 1994(157): p. 67-73.
77. Reynard, J.M., et al., *The value of multiple free-flow studies in men with lower urinary tract symptoms*. British Journal of Urology, 1996. **77**(6): p. 813-8.
78. Schacterle, R.S., M.P. Sullivan, and S.V. Yalla, *Combinations of maximum urinary flow rate and American Urological Association symptom index that are more specific for identifying obstructive and non-obstructive prostatism*. Neurourology and Urodynamics, 1996. **15**(5): p. 459-472.
79. Zhang, P., et al., *Diagnosis of bladder outlet obstruction in men using a near-infrared spectroscopy instrument as the noninvasive monitor for bladder function*. Urology, 2013. **82**(5): p. 1098-102.
80. Aganovic, D., et al., *Does the combination of intravesical prostatic protrusion and bladder outlet obstruction number increase test accuracy according to benign prostatic obstruction at the individual level?* Acta Informatica Medica, 2012. **20**(3): p. 160-166.
81. Aganovic, D., et al., *Bladder outlet obstruction number-a good indicator of infravesical obstruction in patients with benign prostatic enlargement?* Bosnian Journal of Basic Medical Sciences, 2012. **12**(3): p. 144-150.
82. Caffarel, J., et al., *Modeling the clinical assessment of men with suspected obstructed voiding using Bayes' Theorem*. Neurourology and urodynamics, 2008. **27**(8): p. 797-801.
83. Rademakers, K.L., G.A. van Koeveeringe, and M. Oelke, *Ultrasound detrusor wall thickness measurement in combination with bladder capacity can safely detect detrusor underactivity in adult men*. World journal of urology, 2017. **35**(1): p. 153-159.
84. Presicce, F., et al., *Non-invasive ultrasound measurements in male patients with LUTS and benign prostatic obstruction: implication for diagnosis and treatment*. Minerva Urol Nefrol, 2017. **69**(3): p. 220-233.



85. Rieken, M., et al., *Clinical significance of intravesical prostatic protrusion in the management of benign prostatic enlargement: A systematic review and critical analysis of current evidence*. *Minerva Urologica e Nefrologica*, 2017. **69**(6): p. 548-555.
86. Sahai, A., et al., *Current State of the Art in Non-Invasive Urodynamics*. *Current Bladder Dysfunction Reports*, 2013. **8**(2): p. 83-91.
87. Ko, K.J., et al., *Diagnosing bladder outlet obstruction using the penile cuff test in men with lower urinary tract symptoms*. *Neurourol Urodyn*, 2017. **36**(7): p. 1884-1889.
88. van Mastrigt, R., et al., *Diagnostic power of the noninvasive condom catheter method in patients eligible for transurethral resection of the prostate*. *Neurourol Urodyn*, 2014. **33**(4): p. 408-13.
89. Zhang, M., et al., *Elastic modulus of the prostate: a new non-invasive feature to diagnose bladder outlet obstruction in patients with benign prostatic hyperplasia*. *Ultrasound Med Biol*, 2014. **40**(7): p. 1408-13.
90. Blanker, M.H., et al., *Normal voiding patterns and determinants of increased diurnal and nocturnal voiding frequency in elderly men*. *Journal of Urology*, 2000. **164**(4): p. 1201-5.
91. Blanker, M.H., et al., *Voided volumes: normal values and relation to lower urinary tract symptoms in elderly men, a community-based study*. *Urology*, 2001. **57**(6): p. 1093-8 discussion 1098-9.
92. Lee, Y.S., et al., *Most bothersome symptom and symptom specific goal achievement in patients with benign prostatic obstruction: a prospective open label study*. *Journal of Urology*, 2011. **185**(3): p. 1003-9.
93. Matthiesen, T.B., et al., *Nocturia and polyuria in men referred with lower urinary tract symptoms, assessed using a 7-day frequency-volume chart*. *BJU international*, 1999. **83**(9): p. 1017-1022.
94. Rajan, P., et al., *A one-day frequency-volume chart is representative of a 3-day chart in the assessment of lower urinary tract symptoms suggestive of bladder outflow obstruction*. *British Journal of Medical and Surgical Urology*, 2010. **3**(5): p. 194-197.
95. van Doorn, B., et al., *The natural history and predictive factors of voided volume in older men: the Krimpen Study*. *J Urol*, 2011. **185**(1): p. 213-8.
96. van Haarst, E.P., J.L. Bosch, and E.A. Heldeweg, *The international prostate symptom score overestimates nocturia assessed by frequency-volume charts*. *Journal of Urology*, 2012. **188**(1): p. 211-5.
97. Yap, T.L., et al., *The reliability of the frequency-volume chart in assessing lower urinary tract symptoms*. *BJU Int*, 2007. **100**(1): p. 111-5.
98. Yap, T.L., et al., *The relationship between objective frequency-volume chart data and the I-PSS in men with lower urinary tract symptoms*. *Eur Urol*, 2007. **52**(3): p. 811-8.
99. Yoo, S., et al., *Usefulness of the frequency-volume chart over the International Prostate Symptom Score in patients with benign prostatic hyperplasia in view of global polyuria*. *PLoS One*, 2018. **13**(7): p. e0197818.
100. Clement, K.D., et al., *Invasive urodynamic studies for the management of lower urinary tract symptoms (LUTS) in men with voiding dysfunction*. *Cochrane Database Syst Rev*, 2015(4): p. Cd011179.
101. Kim, M., C.W. Jeong, and S.J. Oh, *Diagnostic value of urodynamic bladder outlet obstruction to select patients for transurethral surgery of the prostate: Systematic review and meta-analysis*. *PLoS One*, 2017. **12**(2): p. e0172590.
102. Emberton, M., et al., *Progression of benign prostatic hyperplasia: systematic review of the placebo arms of clinical trials*. *BJU International*, 2008. **102**(8): p. 981-6.
103. Bosch, J.L., et al., *The long-term relationship between a real change in prostate volume and a significant change in lower urinary tract symptom severity in population-based men: the Krimpen study*. *European Urology*, 2008. **53**(4): p. 819-25; discussion 825-7.
104. Bosch, J.L., et al., *Establishing normal reference ranges for prostate volume change with age in the population-based Krimpen-study: prediction of future prostate volume in individual men*. *Prostate*, 2007. **67**(16): p. 1816-24.
105. Branche, B.L., et al., *Sleep Problems are Associated with Development and Progression of Lower Urinary Tract Symptoms: Results from REDUCE*. *J Urol*, 2018. **199**(2): p. 536-542.
106. Burke, J.P., et al., *Diabetes and benign prostatic hyperplasia progression in Olmsted County, Minnesota*. *Urology*, 2006. **67**(1): p. 22-5.



107. Burke, J.P., et al., *Association of anthropometric measures with the presence and progression of benign prostatic hyperplasia*. Am J Epidemiol, 2006. **164**(1): p. 41-6.
108. Cahn, D.B., et al., *Predicting acute urinary retention in patients with elevated post-void residuals*. Current Urology, 2014. **8**(2): p. 79-83.
109. Carter, H.B., et al., *Can a baseline prostate specific antigen level identify men who will have lower urinary tract symptoms later in life?* J Urol, 2005. **173**(6): p. 2040-3.
110. Crawford, E.D., et al., *Baseline factors as predictors of clinical progression of benign prostatic hyperplasia in men treated with placebo*. Journal of Urology, 2006. **175**(4): p. 1422-6; discussion 1426-7.
111. Fu, Y., et al., *The Relationship between the Clinical Progression of Benign Prostatic Hyperplasia and Metabolic Syndrome: A Prospective Study*. Urologia Internationalis, 2016. **97**(3): p. 330-335.
112. Fukuta, F., et al., *Internal prostatic architecture on transrectal ultrasonography predicts future prostatic growth: natural history of prostatic hyperplasia in a 15-year longitudinal community-based study*. Prostate, 2011. **71**(6): p. 597-603.
113. Lamb, A.D., et al., *CD4+ and CD8+ T-lymphocyte scores cannot reliably predict progression in patients with benign prostatic hyperplasia*. BJU International, 2011. **108**(2 Pt 2): p. E43-50.
114. Marshall, L.M., et al., *Lifestyle and health factors associated with progressing and remitting trajectories of untreated lower urinary tract symptoms among elderly men*. Prostate Cancer & Prostatic Diseases, 2014. **17**(3): p. 265-72.
115. Martin, S., et al., *Risk factors for progression or improvement of lower urinary tract symptoms in a prospective cohort of men*. J Urol, 2014. **191**(1): p. 130-7.
116. Mondul, A.M., E. Giovannucci, and E.A. Platz, *A prospective study of obesity, and the incidence and progression of lower urinary tract symptoms*. J Urol, 2014. **191**(3): p. 715-21.
117. Meigs, J.B., et al., *Incidence rates and risk factors for acute urinary retention: the health professionals followup study*. J Urol, 1999. **162**(2): p. 376-82.
118. Patel, D.N., et al., *PSA predicts development of incident lower urinary tract symptoms: results from the REDUCE study*. Prostate Cancer Prostatic Dis, 2018. **21**(2): p. 238-244.
119. Roehrborn, C.G., et al., *Serum prostate specific antigen is a strong predictor of future prostate growth in men with benign prostatic hyperplasia. PROSCAR long-term efficacy and safety study*. J Urol, 2000. **163**(1): p. 13-20.
120. Ma, C.H., et al., *Efficacy and safety of Chinese herbal medicine for benign prostatic hyperplasia: systematic review of randomized controlled trials*. Asian Journal of Andrology, 2013. **15**(4): p. 471-82.
121. Antonelli, M., D. Donelli, and F. Firenzuoli, *Therapeutic efficacy of orally administered pollen for nonallergic diseases: An umbrella review*. Phytotherapy Research, 2019. **33**(11): p. 2938-2947.
122. Cai, T., et al., *Comparison of Serenoa repens With Tamsulosin in the Treatment of Benign Prostatic Hyperplasia: A Systematic Review and Meta-Analysis*. American Journal of Mens Health, 2020. **14**(2): p. 1557988320905407.
123. Russo, G.I., et al., *Clinical Efficacy of Serenoa repens Versus Placebo Versus Alpha-blockers for the Treatment of Lower Urinary Tract Symptoms/Benign Prostatic Enlargement: A Systematic Review and Network Meta-analysis of Randomized Placebo-controlled Clinical Trials*. European Urology Focus, 2020. **15**: p. 15.
124. Vela-Navarrete, R., et al., *Efficacy and safety of a hexanic extract of Serenoa repens (Permixon[®]) for the treatment of lower urinary tract symptoms associated with benign prostatic hyperplasia (LUTS/BPH): systematic review and meta-analysis of randomised controlled trials and observational studies*. BJU International, 2018. **122**(6): p. 1049-1065.
125. Novara, G., et al., *Efficacy and Safety of Hexanic Lipidosterolic Extract of Serenoa repens (Permixon) in the Treatment of Lower Urinary Tract Symptoms Due to Benign Prostatic Hyperplasia: Systematic Review and Meta-analysis of Randomized Controlled Trials*. European Urology Focus, 2016. **2**(5): p. 553-561.
126. Tacklind, J., et al., *Serenoa repens for benign prostatic hyperplasia*. Cochrane Database of Systematic Reviews, 2012. **12**: p. CD001423.



127. Fusco, F., et al., *Alpha-1 adrenergic antagonists, 5-alpha reductase inhibitors, phosphodiesterase type 5 inhibitors, and phytotherapeutic compounds in men with lower urinary tract symptoms suggestive of benign prostatic obstruction: A systematic review and meta-analysis of urodynamic studies*. *Neurourology & Urodynamics*, 2018. **37**(6): p. 1865-1874.
128. Kim, T.H., et al., *Dietary supplements for benign prostatic hyperplasia: an overview of systematic reviews*. *Maturitas*, 2012. **73**(3): p. 180-5.
129. Sebastianelli, A., et al., *Systematic review and meta-analysis on the efficacy and tolerability of mirabegron for the treatment of storage lower urinary tract symptoms/overactive bladder: Comparison with placebo and tolterodine*. *Int J Urol*, 2018. **25**(3): p. 196-205.
130. Brasure, M., et al., *Newer Medications for Lower Urinary Tract Symptoms Attributed to Benign Prostatic Hyperplasia: A Review* Agency for Healthcare Research and Quality, 2016: p. 05.
131. Nitti, V.W., et al., *Urodynamics and safety of the β_3 -adrenoceptor agonist mirabegron in males with lower urinary tract symptoms and bladder outlet obstruction*. *J Urol*, 2013. **190**(4): p. 1320-7.
132. Wang, X., et al., *Comparative effectiveness of oral drug therapies for lower urinary tract symptoms due to benign prostatic hyperplasia: a systematic review and network meta-analysis*. *PLoS ONE [Electronic Resource]*, 2014. **9**(9): p. e107593.
133. Pang, R., et al., *Anticholinergics combined with alpha-blockers for treating lower urinary tract symptoms related to benign prostatic obstruction*. *Cochrane Database Syst Rev*, 2021. **2**: p. Cd012336.
134. Li, M.C., et al., *Efficacy and safety of solifenacin plus tamsulosin oral controlled absorption system in men with lower urinary tract symptoms: a meta-analysis*. *Asian Journal of Andrology*, 2015. **17**(1): p. 124-34.
135. Sun, Y., et al., *Study of phosphodiesterase 5 inhibitors and alpha-adrenoceptor antagonists used alone or in combination for the treatment of lower urinary tract symptoms due to benign prostatic hyperplasia*. *Minerva Urologica e Nefrologica*, 2020. **72**(1): p. 13-21.
136. Kallidonis, P., et al., *Combination Therapy with Alpha-blocker and Phosphodiesterase-5 Inhibitor for Improving Lower Urinary Tract Symptoms and Erectile Dysfunction in Comparison with Monotherapy: A Systematic Review and Meta-analysis*. *European Urology Focus*, 2019. **25**: p. 25.
137. Zhang, J., et al., *Alpha-blockers with or without phosphodiesterase type 5 inhibitor for treatment of lower urinary tract symptoms secondary to benign prostatic hyperplasia: a systematic review and meta-analysis*. *World Journal of Urology*, 2019. **37**(1): p. 143-153.
138. Choi, H., et al., *A Meta-Analysis of Long- Versus Short-Acting Phosphodiesterase 5 Inhibitors: Comparing Combination Use With alpha-Blockers and alpha-Blocker Monotherapy for Lower Urinary Tract Symptoms and Erectile Dysfunction*. *International neurourology journal*, 2015. **19**(4): p. 237-45.
139. Wang, K., et al., *Transurethral plasmakinetic resection of the prostate is a reliable minimal invasive technique for benign prostate hyperplasia: a meta-analysis of randomized controlled trials*. *Asian Journal of Andrology*, 2015. **17**(1): p. 135-42.
140. Yan, H., et al., *The efficacy of PDE5 inhibitors alone or in combination with alpha-blockers for the treatment of erectile dysfunction and lower urinary tract symptoms due to benign prostatic hyperplasia: a systematic review and meta-analysis*. *Journal of Sexual Medicine*, 2014. **11**(6): p. 1539-45.
141. Gacci, M., et al., *A systematic review and meta-analysis on the use of phosphodiesterase 5 inhibitors alone or in combination with α -blockers for lower urinary tract symptoms due to benign prostatic hyperplasia*. *Eur Urol*, 2012. **61**(5): p. 994-1003.
142. Kang, D., et al., *Combination of α -blocker and 5 α -reductase inhibitor for treatment of benign prostatic hyperplasia*. *Clin Invest Med*, 2017. **40**(5): p. E200-e210.
143. Favilla, V., et al., *Impact of combination therapy 5-alpha reductase inhibitors (5-ARI) plus alpha-blockers (AB) on erectile dysfunction and decrease of libido in patients with LUTS/BPH: a systematic review with meta-analysis*. *Aging Male*, 2016. **19**(3): p. 175-181.
144. Gacci, M., et al., *Impact of medical treatments for male lower urinary tract symptoms due to benign prostatic hyperplasia on ejaculatory function: a systematic review and meta-analysis*. *Journal of Sexual Medicine*, 2014. **11**(6): p. 1554-66.



145. Kim, H.J., et al., *Efficacy and Safety of Initial Combination Treatment of an Alpha Blocker with an Anticholinergic Medication in Benign Prostatic Hyperplasia Patients with Lower Urinary Tract Symptoms: Updated Meta-Analysis*. PLoS ONE [Electronic Resource], 2017. **12**(1): p. e0169248.
146. Yan, H., et al., *The Efficacy of Antimuscarinics Alone or in Combination with Alpha-Blockers for the Treatment of Ureteral Stent-Related Symptoms: A Systematic Review and Meta-Analysis*. Urologia Internationalis, 2017. **99**(1): p. 6-13.
147. Hao, N., et al., *Antimuscarinics and alpha-blockers or alpha-blockers monotherapy on lower urinary tract symptoms--a meta-analysis*. Urology, 2014. **83**(3): p. 556-62.
148. Filson, C.P., et al., *The efficacy and safety of combined therapy with alpha-blockers and anticholinergics for men with benign prostatic hyperplasia: a meta-analysis*. Journal of Urology, 2013. **190**(6): p. 2153-60.
149. Xin, Z., et al., *Addition of antimuscarinics to alpha-blockers for treatment of lower urinary tract symptoms in men: a meta-analysis*. Urology, 2013. **82**(2): p. 270-7.
150. Pattanaik, S., et al., *Phosphodiesterase inhibitors for lower urinary tract symptoms consistent with benign prostatic hyperplasia*. Cochrane Database of Systematic Reviews, 2018. **11**: p. CD010060.
151. Yuan, J.Q., et al., *Comparative Effectiveness and Safety of Monodrug Therapies for Lower Urinary Tract Symptoms Associated With Benign Prostatic Hyperplasia: A Network Meta-analysis*. Medicine, 2015. **94**(27): p. e974.
152. Wang, X.H., et al., *Systematic review and meta-analysis on phosphodiesterase 5 inhibitors and alpha-adrenoceptor antagonists used alone or combined for treatment of LUTS due to BPH*. Asian Journal of Andrology, 2015. **17**(6): p. 1022-32.
153. Peng, L., et al., *Holmium laser technologies versus photoselective greenlight vaporization for patients with benign prostatic hyperplasia: a meta-analysis*. Lasers in Medical Science, 2020. **14**: p. 14.
154. Huang, S.W., et al., *Comparative efficacy and safety of new surgical treatments for benign prostatic hyperplasia: systematic review and network meta-analysis*. BMJ, 2019. **367**: p. 15919.
155. Sun, H.Y., B. Lee, and J.H. Kim, *Factors affecting the efficacy and safety of phosphodiesterase 5 inhibitor and placebo in treatment for lower urinary tract symptoms: meta-analysis and meta-regression*. International Urology & Nephrology, 2018. **50**(1): p. 35-47.
156. Li, Z., et al., *The impact of surgical treatments for lower urinary tract symptoms/benign prostatic hyperplasia on male erectile function: A systematic review and network meta-analysis*. Medicine, 2016. **95**(24): p. e3862.
157. Wang, X.Y., H.T. Zong, and Y. Zhang, *Efficacy and safety of prostate artery embolization on lower urinary tract symptoms related to benign prostatic hyperplasia: a systematic review and meta-analysis*. Clinical Interventions In Aging, 2016. **11**: p. 1609-1622.
158. Zhang, X., et al., *Different lasers in the treatment of benign prostatic hyperplasia: a network meta-analysis*. Scientific Reports, 2016. **6**: p. 23503.
159. Xiao, K.W., et al., *Enucleation of the prostate for benign prostatic hyperplasia thulium laser versus holmium laser: a systematic review and meta-analysis*. Lasers in Medical Science, 2019. **34**(4): p. 815-826.
160. Xiao, K.W., et al., *Transurethral endoscopic enucleation of the prostate using a diode laser versus bipolar plasmakinetic for benign prostatic obstruction: a meta-analysis*. Lasers in Medical Science, 2020. **09**: p. 09.
161. Wang, L., et al., *Efficacy and Safety of Laser Surgery and Transurethral Resection of the Prostate for Treating Benign Prostate Hyperplasia: a Network Meta-analysis*. Asian Pacific Journal of Cancer Prevention: Apjcp, 2016. **17**(9): p. 4281-4288.
162. Li, M., et al., *Endoscopic enucleation versus open prostatectomy for treating large benign prostatic hyperplasia: a meta-analysis of randomized controlled trials*. PLoS ONE [Electronic Resource], 2015. **10**(3): p. e0121265.
163. Lucca, I., et al., *Outcomes of minimally invasive simple prostatectomy for benign prostatic hyperplasia: a systematic review and meta-analysis*. World Journal of Urology, 2015. **33**(4): p. 563-70.



164. Robert, G., A. de la Taille, and T. Herrmann, *Bipolar plasma vaporization of the prostate: ready to replace GreenLight? A systematic review of randomized control trials*. World Journal of Urology, 2015. **33**(4): p. 549-54.
165. Gupta, N., et al., *Three-Year Treatment Outcomes of Water Vapor Thermal Therapy Compared to Doxazosin, Finasteride and Combination Drug Therapy in Men with Benign Prostatic Hyperplasia: Cohort Data from the MTOPS Trial*. J Urol, 2018. **200**(2): p. 405-413.
166. McVary, K.T., et al., *Is Sexual Function Better Preserved After Water Vapor Thermal Therapy or Medical Therapy for Lower Urinary Tract Symptoms due to Benign Prostatic Hyperplasia?* J Sex Med, 2018. **15**(12): p. 1728-1738.
167. Roehrborn, C.G. and D.B. Rukstalis, *Prostatic Urethral Lift Versus Medical Therapy: Examining the Impact on Sexual Function in Men with Benign Prostatic Hyperplasia*. Eur Urol Focus, 2021.
168. Jung, J.H., et al., *Prostatic urethral lift for the treatment of lower urinary tract symptoms in men with benign prostatic hyperplasia*. Cochrane Database of Systematic Reviews, 2019. **5**: p. CD012832.
169. El-Dakhkhny, A.S., et al., *Transperineal intraprostatic injection of botulinum neurotoxin A vs transurethral resection of prostate for management of lower urinary tract symptoms secondary to benign prostate hyperplasia: A prospective randomised study*. Arab J Urol, 2019. **17**(4): p. 270-278.
170. Jung, J.H., et al., *Prostatic arterial embolization for the treatment of lower urinary tract symptoms in men with benign prostatic hyperplasia*. Cochrane Database Syst Rev, 2020. **12**: p. Cd012867.
171. Knight, G.M., et al., *Systematic Review and Meta-analysis Comparing Prostatic Artery Embolization to Gold-Standard Transurethral Resection of the Prostate for Benign Prostatic Hyperplasia*. Cardiovasc Intervent Radiol, 2021. **44**(2): p. 183-193.
172. Jiang, Y.L. and L.J. Qian, *Transurethral resection of the prostate versus prostatic artery embolization in the treatment of benign prostatic hyperplasia: a meta-analysis*. BMC Urol, 2019. **19**(1): p. 11.
173. Xu, X.J., et al., *An updated meta-analysis of prostatic arterial embolization versus transurethral resection of the prostate in the treatment of benign prostatic hyperplasia*. World Journal of Urology, 2019. **07**: p. 07.
174. Zumstein, V., et al., *Prostatic Artery Embolization versus Standard Surgical Treatment for Lower Urinary Tract Symptoms Secondary to Benign Prostatic Hyperplasia: A Systematic Review and Meta-analysis*. European Urology Focus, 2019. **5**(6): p. 1091-1100.
175. Feng, S., et al., *Prostatic Arterial Embolization Treating Moderate-to-Severe Lower Urinary Tract Symptoms Related to Benign Prostate Hyperplasia: A Meta-Analysis*. Cardiovascular & Interventional Radiology, 2017. **40**(1): p. 22-32.
176. Shim, S.R., et al., *Efficacy and Safety of Prostatic Arterial Embolization: Systematic Review with Meta-Analysis and Meta-Regression*. J Urol, 2017. **197**(2): p. 465-479.
177. Hwang, E.C., et al., *Aquablation of the prostate for the treatment of lower urinary tract symptoms in men with benign prostatic hyperplasia*. Cochrane Database of Systematic Reviews, 2019. **2**: p. CD013143.
178. Gilling, P., et al., *Three-year outcomes after Aquablation therapy compared to TURP: results from a blinded randomized trial*. Can J Urol, 2020. **27**(1): p. 10072-10079.
179. Gilling, P., et al., *Two-Year Outcomes After Aquablation Compared to TURP: Efficacy and Ejaculatory Improvements Sustained*. Adv Ther, 2019. **36**(6): p. 1326-1336.
180. Pimentel, M.A., O. Yassaie, and P. Gilling, *Urodynamic Outcomes After Aquablation*. Urology, 2019. **126**: p. 165-170.

Versionsnummer: 5.0

Erstveröffentlichung: 06/1999

Überarbeitung von: 02/2023

267 **Nächste Überprüfung geplant: 02/2028**



Die AWMF erfasst und publiziert die Leitlinien der Fachgesellschaften mit größtmöglicher Sorgfalt - dennoch kann die AWMF für die Richtigkeit des Inhalts keine Verantwortung übernehmen. **Insbesondere bei Dosierungsangaben sind stets die Angaben der Hersteller zu beachten!**

Autorisiert für elektronische Publikation: AWMF online