

# The Effectiveness of Anticholinergic Therapy for Overactive Bladders: Systematic Review and Meta-Analysis

# Eficácia da terapia anticolinérgica na bexiga hiperativa: revisão sistemática e metanálise

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# Abstract

The overactive bladder (OAB) has a significant negative impact on the quality of life of patients. Antimuscarinics have become the pharmacological treatment of choice for this condition. The objective of this systematic review and meta-analysis is to examine the evidence from randomized clinical trials about the outcomes of the antimuscarinic drugs available in Brazil on OABs. We searched MEDLINE and the Cochrane Central Register of Controlled Trials from the inception of these databases through to September 2015. The primary outcome measures were the mean decrease in urge urinary incontinence episodes and the mean decrease in the frequency of micturition. The results suggest that there is a moderate to high amount of evidence supporting the benefit of using anticholinergic drugs in alleviating OAB symptoms when compared with placebo. It is still not clear whether any of the specific drugs that are available in Brazil offer advantages over the others. These drugs are associated with adverse effects (dry mouth and constipation), although they are not related to an increase in the number of withdrawals.

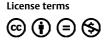
# Keywords► overactive bladder

- urge incontinence
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- urinary frequency and antimuscarinics

# Resumo

A bexiga hiperativa determina um impacto negativo na qualidade de vida dos nossos pacientes. Os antimuscarínicos tornaram-se o tratamento farmacológico de escolha para essa condição. O objetivo desta revisão sistemática e metanálise é examinar as melhores evidências científicas sobre estas medicações disponíveis no Brasil no tratamento de mulheres com bexiga hiperativa. As bases de dados utilizadas foram MEDLINE e a biblioteca da Cochrane, das quais selecionamos os ensaios clínicos

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# **Palavras chaves**

- bexiga hiperativaincontinência de
- urgência
   frequência urinária e antimuscarínicos

randomizados até setembro de 2015. Os principais desfechos analisados foram a diminuição dos episódios de incontinência urinária de urgência e a diminuição da frequência de micção. Os resultados sugerem que as drogas existentes no Brasil sustentam o benefício dos anticolinérgicos no alívio dos sintomas da bexiga hiperativa quando comparadas com o placebo. Em termos de eficácia, as medicações apresentam resultados semelhantes no controle dos sintomas. Essas drogas estão associadas a efeitos adversos importantes, tais como boca seca e constipação, e esses efeitos adversos não influenciaram no uso da medicação.

# Introduction

Overactive bladder (OAB) is defined by the International Continence Society as the presence of urinary urgency, usually accompanied by frequency and nocturia, with or without urge urinary incontinence (UUI), in the absence of a urinary tract infection or another obvious pathology.<sup>1</sup> Overactive bladder is a highly prevalent disease in both men and women, affecting 12–17% of the adult population. This condition has a significant negative impact on the quality of life of patients, affecting emotional, physical, social, occupational, and domestic functions.<sup>2–4</sup>

Overactive bladder symptoms are thought to develop as a result of inappropriate contractions of the bladder detrusor during the filling phase of the micturition cycle. Normal and abnormal bladder contractions occur via cholinergic activation of the muscarinic receptors. As is the case in other chronic conditions, OAB typically requires long-term persistence and adherence to therapy.<sup>5</sup> Behavior modification, which includes education about the disorder, lifestyle changes (, such as avoiding caffeinated beverages, for example), as well as pelvic floor muscle training and bladder retraining, represent the first-line therapy options for this condition. However, when these approaches are insufficient, second-line therapy involves pharmacological treatment, and antimuscarinic agents are the treatment of choice.<sup>6–8</sup>

Although anticholinergic medications have been shown to improve patients' symptoms, they create a widespread blockade of cholinergic activity that often results in side effects such as dry mouth, cognitive changes, constipation, urinary retention, blurred vision, and dyspepsia.<sup>9</sup> These problems can be difficult to manage, and may contribute to poor patient adherence to treatment.<sup>10</sup>

The objective of this systematic review and meta-analysis was to examine the currently available evidence from randomized clinical trials (RCTs) about the outcomes of the pharmacological management of OAB, and to summarize the comparative effectiveness of the drugs available in Brazil. Only antimuscarinic agents commercialized in Brazil were included in the analysis, since this meta-analysis is the basis for the development of Brazilian urogynecology guidelines.<sup>11</sup>

# Methods

This study was exempt from institutional review board approval, given that it was a systematic review and metaanalysis; it did not involve the use of any interventions on humans. To report the results of this meta-analysis, we utilized the Preferred Reporting Items for Systematic reviews and Meta-Analysis (PRISMA) statement.<sup>12</sup>

# Search Strategy

An exhaustive electronic search was performed using the MEDLINE database, as well as the Cochrane Central Register of Controlled Trials, with the dates of the included articles spanning from the inception of these databases through to September 2015. We also searched the references of the identified articles and restricted the search to articles published in English. The search combined relevant terms and descriptors related to OAB, anticholinergic drugs, oxybutynin, darifenacin, tolterodine, solifenacin, and RCTs.

#### **Eligibility Criteria and Data Extraction**

The review only included RCTs featuring adult male and female patients diagnosed with OAB or with a diagnosis of detrusor over activity, and who were also submitted to any of the anticholinergic treatments available in Brazil. The selection criteria are described in **-Table 1**. In a first screening, two independent authors (AMRMF and MVCM) assessed all of the abstracts retrieved from the search; they then obtained the full manuscripts of the citations that met the inclusion criteria. These authors evaluated the studies' eligibility and quality, and extracted the data subsequently. Any discrepancies were solved by agreement, and, if needed, the authors reached a consensus with a third author (MR). The meta-analysis included studies that provided accurate data related to those primary outcomes that could be analyzed. Thus, only studies that provided the mean, sample size, and standard deviation (SD) values of the primary outcomes were included in the analysis. Otherwise, when the available data were expressed as the median, it was necessary that the study provided the range values (lowest and highest values) to extrapolate the mean. If only the ranges of continuous variables were reported, we would estimate the SD by dividing the range by four. Dose escalation and crossover studies were excluded, as it was not possible to abstract the data related to our primary outcomes.

#### **Outcome Measures**

The primary outcomes of interest for this systematic review and meta-analysis were the mean decrease in the number of UUI episodes per day and the mean decrease in the number

	Included	Excluded
Population	Symptomatic diagnosis of overactive bladder (OAB) or a urodynamic diagnosis of detrusor over activity	OAB as consequence of surgery
Intervention	Anticholinergic drugs available in Brazil (oxybutynin 5 mg and 10 mg; darifenacin 7.5 mg and 15 mg; tolterodine 1 mg, 2 mg, and 4 mg; solifenacin 5 mg and 10 mg)	Anticholinergic drugs not available in Brazil or with different doses or routes of administration that are not available in Brazil
Comparison	Placebo, comparison between different drugs, or comparison between different doses of the same drug	
Outcomes	<ul> <li>Primary outcomes <ul> <li>Mean decrease in urge urinary incontinence (UUI)</li> <li>episodes per day</li> </ul> </li> <li>Mean decrease in the number of micturitions per day</li> </ul> <li>Secondary outcomes <ul> <li>Mean decrease in total incontinence episodes (related or not to urgency)</li> <li>Dry mouth</li> <li>Constipation</li> <li>Withdrawals resulting from drug-related adverse effects</li> </ul> </li>	
Study type	Randomized controlled trials (RCTs)	Non RCTs

<b>Table 1</b> Selection criteria of included studies	(PICOs)	
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Abbreviation: PICOs, population, intervention, comparison and outcomes.

of micturitions per day. The secondary outcomes included the mean decrease in total incontinence episodes (either related or not to urgency), dry mouth, constipation, and withdrawals resulting from drug-related adverse effects. We tried to perform meta-analytic comparisons between each drug (and their different dosages) versus placebo, comparisons between different drugs, and comparisons between different dosages of the same drug.

#### **Risk of Bias Assessment**

We followed the guidance suggested by the Cochrane Collaboration<sup>13</sup> to assess the risk of bias from the included studies. We evaluated sequence generation, allocation concealment, blinding, and incomplete outcome data for each trial included in the review. A low risk of bias was considered when a judgment of "yes" for all domains was obtained, whereas a high risk of bias was considered when a judgment of "no" for one or more domains was obtained. An unclear risk of bias was defined when an "unclear" judgment in any domain was considered. The quality assessment of the included trials is shown in **-Table 2**.

#### Analysis

We pooled the data of the continuous outcomes from the original studies to obtain the mean difference (MD) for the occurrence of an outcome event, and presented their corresponding 95% confidence intervals (CIs). Data for dichotomous outcomes from the original studies were pooled to obtain the relative ratio (RR), and the corresponding 95% CIs were calculated. Statistical significance was set at a *p*-value of < 0.05. In order to quantify the statistical heterogeneity,

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we used the I2 statistic to describe the variations across trials that were due to heterogeneity and not to sampling error. We pooled the outcome data from each study using a Mantel–Haenszel model, and applied the fixed-effects model. When the heterogeneity was greater than 50% (I2 > 50%), we applied the random-effects model.<sup>14</sup> We used the software Review Manager (RevMan, Version 5.3; Copenhagen) to conduct the meta-analysis.

# Results

Our electronic search retrieved 468 articles. After screening the titles and abstracts, we ended up with 37 articles that were considered eligible for inclusion in this review by one or both reviewers, and the full texts were subsequently assessed. The complete article selection process is presented in **~ Fig. 1**.

### **Description of Included Studies**

Fifteen RCTs assessing the pharmacological management (drugs and dosages available in Brazil) of OAB met the inclusion criteria and provided data to perform the metaanalysis. With the available data of the included studies,<sup>15–29</sup> it was only possible to perform comparisons between tolterodine (and its different dosages) versus placebo, solifenacin versus placebo, and oxybutynin versus tolterodine.

#### **Excluded Studies**

Twenty-two articles were excluded because they either did not meet the inclusion criteria<sup>30–35</sup> or they did not provide adequate data to be included in the meta-analysis.<sup>36–51</sup>

Study	Sequence generation	Allocation concealed	Blinding	Incomplete outcome data
Appell et al. <sup>15</sup>	Unclear	Yes	Yes	Yes
Drutz et al. <sup>16</sup>	Unclear	Yes	Yes	Yes
Lee et al. <sup>17</sup>	Yes	Yes	Yes	Yes
Malone-Lee et al. <sup>18</sup>	Unclear	Unclear	Yes	Yes
Chapple et al. <sup>19</sup>	Unclear	Yes	Unclear	Yes
Jacquetin et al. <sup>20</sup>	Unclear	Yes	Unclear	Yes
Khullar et al. <sup>21</sup>	Yes	Yes	Yes	Yes
Millard et al. <sup>22</sup>	Unclear	Unclear	Unclear	Yes
Swift et al. <sup>23</sup>	Yes	Yes	Yes	Yes
Van Kerrebroeck et al. <sup>24</sup>	Unclear	Unclear	Unclear	Yes
Van Kerrebroeck et al. <sup>25</sup>	Yes	Yes	Yes	Yes
Zinner et al. <sup>26</sup>	Yes	Yes	Yes	Yes
Cardozo et al. <sup>27</sup>	Unclear	Unclear	Unclear	Yes
Karram et al. <sup>28</sup>	Unclear	Unclear	Unclear	Yes
But et al. <sup>29</sup>	Yes	Unclear	Unclear	Yes

 Table 2
 Quality assessment of included trials

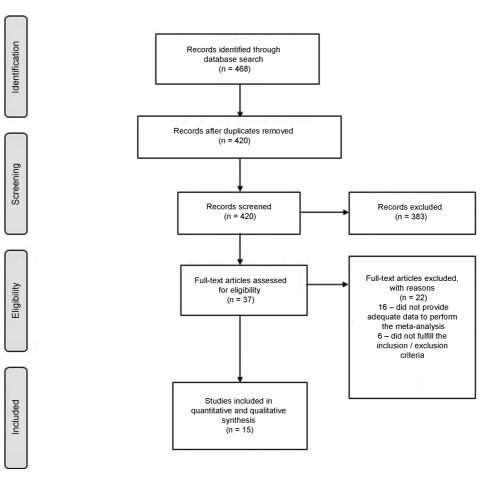


Fig. 1 Flowchart for the trial identification and selection process.

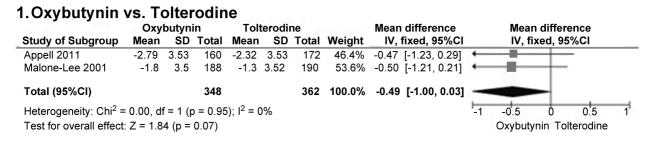


Fig. 2 Forest plot - mean difference in decrease in urge urinary incontinence (UUI) episodes per day.

#### **Primary Outcomes**

Mean decrease in UUI episodes per day

For this outcome, it was only possible to perform a comparison between oxybutynin and tolterodine. The MD in the mean decrease in UUI episodes per day was higher for patients that used oxybutynin than for those that used tolterodine (MD = -0.49; 95% CI: -1.00, 0.03; I2 = 0; p = 0.07); however, this difference was not significant (**Fig. 2**).

· Mean decrease in the number of micturitions per day

We were able to perform the following comparisons: oxybutynin versus tolterodine; tolterodine (and its different doses) versus placebo; different doses of tolterodine; and solifenacin versus placebo. We found significant differences that favored tolterodine 1 mg when compared with placebo (MD = -0.55; 95% CI: -1.08, -0.02; I2 = 0; p = 0.04); tolterodine 2 mg versus placebo (MD = -0.57; 95% CI: -0.82, -0.32; I2 = 0; *p* < 0.001); and tolterodine 4 mg versus placebo (MD = -0.66; 95% CI: -0.85, -0.47; I2 = 0; p < 0.001). Moreover, significant differences favored the use of solifenacin when compared with placebo (MD = -0.77; 95% CI: -1.09, -0.45; I2 = 0; p < 0.001) ( **Fig. 3**). All of these outcome data were pooled from each study using a Mantel-Haenszel model, and a fixed-effects model was applied, as there was no heterogeneity (I2 = 0) among the studies. For all other available comparisons for this outcome (oxybutynin versus tolterodine; tolterodine 2 mg versus tolterodine 1 mg; and tolterodine 4 mg versus tolterodine 2 mg), the MD was not significant, as presented in **Fig. 3**.

#### Secondary Outcomes

Mean decrease in incontinence episodes per day

Significant differences were found that favored tolterodine 2 mg when compared with placebo (MD = -0.45; 95% CI: -0.76, -0.14; I2 = 0; p = 0.005); tolterodine 4 mg versus placebo (MD = -0.46; 95% CI: -0.83, -0.08; I2 = 0; p = 0.02); and solifenacin versus placebo (MD = -0.77; 95% CI: -1.09, -0.45; I2 = 0; p < 0.001) (**Fig. 4**). All of these outcome data were pooled from each study using a Mantel–Haenszel model, and a fixed-effects model was applied, as there was no heterogeneity (I2 = 0) among the studies. We did not find significant differences across any of the other available comparisons (oxybuty-nin versus tolterodine; tolterodine 1 mg versus placebo;

tolterodine 2 mg versus tolterodine 1 mg; and tolterodine 4 mg versus tolterodine 2 mg).

#### • Dry mouth

There were significant differences and higher RRs in patients treated with oxybutynin when compared with tolterodine (RR = 1.49; 95% CI: 1.06, 2.10; I2 = 84%; p = 0.02); tolterodine 1 mg versus placebo (RR = 2.33; 95% CI: 1.26, 4.29; I2 = 84%; p = 0.02); tolterodine 2 mg versus placebo (RR = 3.72; 95% CI: 3.05, 4.54; I2 = 0%; p < 0.001); tolterodine 4 mg versus placebo (RR = 2.88; 95% CI: 2.40, 3.45; I2 = 0%; p < 0.001); tolterodine 2 mg versus placebo (RR = 2.88; 95% CI: 2.40, 3.45; I2 = 0%; p < 0.001); tolterodine 2 mg versus tolterodine 1 mg (RR =1.69; 95% CI: 1.26, 2.28; I2 = 0%; p < 0.001), and solifenacin versus placebo (RR =3.73; 95% CI: 1.80, 7.77; I2 =0%; p < 0.001). The group of patients that used tolterodine 4 mg exhibited a lower risk (RR = 0.79; 95% CI: 0.68, 0.92; I2 = 0%; p = 0.02) when compared with tolterodine 2 mg. All of these results are presented in **~Fig. 5**.

Constipation

The findings indicated that there was a significant difference and a higher RR in patients treated with tolterodine 2 mg versus those treated with placebo (RR = 1.61; 95% CI: 1.11, 2.32; I2 = 0%; p = 0.01), and those treated with tolterodine 4 mg versus placebo (RR = 1.52; 95% CI: 1.11, 2.09; I2 = 0%; p = 0.009). We did not find significant differences across any of the other available comparisons (oxybutynin versus tolterodine; solifenacin versus placebo). All of these results are presented in **- Fig. 6**.

· Withdrawals resulting from drug-related adverse effects

We did not find statistical differences in any of the available comparisons (oxybutynin versus tolterodine, p = 0.18; tolterodine 1 mg versus placebo, p = 0.47; tolterodine 2 mg versus placebo, p = 0.32; tolterodine 4 mg versus placebo, p = 0.13; tolterodine 2 mg versus tolterodine 1 mg, p = 0.59; tolterodine 4 mg versus tolterodine 2 mg, p = 0.92; and solifenacin versus placebo, p = 0.67) when evaluating the risk of withdrawals due to drug-related adverse effects.

#### Discussion

To our knowledge, this is the first comprehensive review featuring a pooled analysis that has addressed the question of efficacy and the main adverse effects of all antimuscarinic drugs available in Brazil for the treatment of OAB.

Obudu at O 1		utynin	F - 4 - F		rodine	<b>T</b> - 4 - 4	141-1-1-1		in difference	Mean difference
Study of Subgroup	Mean	SD 1		Mean	SD		Weight		fixed, 95%Cl	IV, fixed, 95%Cl
Appell 2011	-3.53		160	-2.87	6.44	172	0.0%		[-2.06, 0.74]	
Drutz 1999 Lee 2002	-2 -1.8	2.3 4.2	41 116	-2 -2.6	2.5 2.9	70 112	0.0% 0.0%		[-0.92, 0.92] [-0.13, 1.73]	
Malone-Lee 2001	-1.8 -1.7	4.2 0.07		-2.6 -1.7	2.9 0.07	190	0.0% 99.9%		[-0.13, 1.73] [-0.01, 0.01]	2 C C C C C C C C C C C C C C C C C C C
	-1.7	0.07		-1.7	0.07					
Total (95%CI)			505			544	100.0%	0.00	[-0.01, 0.01]	
Heterogeneity: Chi <sup>2</sup> = 3.6	67, df = 3 (p	o = 0.30	); I <sup>2</sup> = 18	3%						-1 -0.5 0 0.5
Test for overall effect: Z =	= 0.02 (p =	0.99)								Oxybutynin Tolterodine
2. Tolterodine 1m	na vs. I	Place	bo							
		rodine		F	lacebo			Mea	n difference	Mean difference
Study of Subgroup	Mean	and the second			ו SD		Weight		fixed, 95%Cl	IV, fixed, 95%Cl
Jacquetin 2001	-1.4	2.8		-1.2		51	32.6%	-0.20	[-1.13, 0.73]	
Millardi 1999 Van Kerrebroeck 1998	-2.3 -0.4	3 2.1		-1.4 -0.1		64 16	46.9% 20.5%	-0.90 0.30	[-1.67, -0.13]	
	-0.4	Ζ.		-0.1	1				[-1.47, 0.87]	
Total (95%CI)			235			131	100.0%	-0.55	[-1.08, -0.02]	
Heterogeneity: Chi <sup>2</sup> = 1.5	51, df = 2 (p	o = 0.47	); I <sup>2</sup> = 09	%						-1 -0.5 0 0.5
Test for overall effect: Z =	= 2.03 (p =	0.04)								Tolterodine 1mg Placebo
3. Tolterodine 2m	na ve I	Place	ho							
		terodin			Plac	ebo		Mea	n difference	Mean difference
Study of Subgroup	Mean		Total	Mean		Total	Weight		fixed, 95%Cl	IV, fixed, 95%Cl
Chapple 2004	-1.88	3	250	-1.2	3.26	253	20.8%		[-1.23, -0.13]	•==
Drutz 1999	-2	2.5	70	-1.1	2.9	36	5.0%	-0.90	[-2.01, 0.21]	+
Jacquetin 2001	-1.4	4.3	103	-1.2	2.7	51	5.0%	-0.20	[-1.31, 0.91]	
Millardi 1999	-2.3	2.1	129	-1.4	2.3	64	13.9%		[-1.57, -0.23]	•
Swift 2003 Van Kerrebroeck 1998	-1.7 -0.1	2.9 1.8	408 17	-1.2 -0.1	2.9 1	410 16	39.4% 6.4%		[-0.90, -0.10] [-0.99, 0.99]	Not an and a second
Van Kerrebroeck 1996	-0.1 -1.7	1.0 3.3	514	-0.1 -1.2	2.9	57	6.4% 9.6%		[-0.99, 0.99] [-1.31, 0.31]	1000 Con
		2.0			2.0				shi ush da	
Total (95%CI)			1491			887	100.0%	-0.57	[-0.82, -0.32]	
Heterogeneity: Chi <sup>2</sup> = 3.2	28, df = 6 (	p = 0.77	'); I <sup>2</sup> = 0	%						-1 -0.5 0 0.5
Test for overall effect: Z										Tolterodine 2 mg Placebo
1 Taltaradina Am			ha							
4. Tolterodine 4m		rodine		i i i	Placebo			Mer	n difference	Mean difference
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Study of Subaroup	Mean	SD			ו SD	Total	Weight	IV. 1	fixed, 95%Cl	IV, fixed. 95%CI
Study of Subgroup Khullar 2004	Mean -2.1	<b>SD</b> 2.4	Tota	l Mear		Total 258	Weight 30.5%	and the second se	fixed, 95%Cl	IV, fixed, 95%Cl
the last to be a set of the last to be a			<b>Tota</b>	I Mean ∋ -1.3	2.3		30.5%	-0.80 [	fixed, 95%Cl -1.14, -0.46] -1.13, -0.27]	IV, fixed, 95%Cl
Khullar 2004 Swift 2003 Van Kerrebroeck 1998	-2.1 -1.9 -0.3	2.4 3.4 2.2	<b>Tota</b> 569 417	<b>I Mear</b> 9 -1.3 7 -1.2 5 -0.1	2.3 2.9 1	258 410 16	30.5% 19.4% 2.4%	-0.80 [ -0.70 [ -0.20	-1.14, -0.46] -1.13, -0.27] [-1.42, 1.02]	IV, fixed, 95%Cl
Khullar 2004 Swift 2003 Van Kerrebroeck 1998 Van Kerrebroeck 2001	-2.1 -1.9 -0.3 -1.8	2.4 3.4 2.2 3.4	Total 569 417 15 507	Mean           9         -1.3           7         -1.2           5         -0.1           7         -1.2	2.3 2.9 1 2.9	258 410 16 507	30.5% 19.4% 2.4% 23.7%	-0.80 [ -0.70 [ -0.20 -0.60 [	-1.14, -0.46] -1.13, -0.27] [-1.42, 1.02] -0.99, -0.21]	IV, fixed, 95%Cl
Khullar 2004 Swift 2003 Van Kerrebroeck 1998 Van Kerrebroeck 2001 Zinner 2002a	-2.1 -1.9 -0.3 -1.8 -2	2.4 3.4 2.2 3.4 3.1	Tota 569 417 15 507 292	Mean           9         -1.3           7         -1.2           5         -0.1           7         -1.2           5         -0.1           7         -1.2           2         -1.4	2.3 2.9 1 2.9 3.1	258 410 16 507 284	30.5% 19.4% 2.4% 23.7% 14.0%	-0.80 [ -0.70 [ -0.20 -0.60 [ -0.60 [	-1.14, -0.46] -1.13, -0.27] [-1.42, 1.02] -0.99, -0.21] -1.11, -0.09]	IV, fixed, 95%Cl
Khullar 2004 Swift 2003 Van Kerrebroeck 1998 Van Kerrebroeck 2001	-2.1 -1.9 -0.3 -1.8	2.4 3.4 2.2 3.4	Tota 569 417 15 507 292	Mean           9         -1.3           7         -1.2           5         -0.1           7         -1.2           2         -1.4	2.3 2.9 1 2.9 3.1	258 410 16 507	30.5% 19.4% 2.4% 23.7%	-0.80 [ -0.70 [ -0.20 -0.60 [ -0.60 [	-1.14, -0.46] -1.13, -0.27] [-1.42, 1.02] -0.99, -0.21]	IV, fixed, 95%Cl
Khullar 2004 Swift 2003 Van Kerrebroeck 1998 Van Kerrebroeck 2001 Zinner 2002a	-2.1 -1.9 -0.3 -1.8 -2	2.4 3.4 2.2 3.4 3.1	Tota 569 417 15 507 292	Mear           9         -1.3           7         -1.2           5         -0.1           7         -1.2           2         -1.4           4         -0.9	2.3 2.9 1 2.9 3.1	258 410 16 507 284	30.5% 19.4% 2.4% 23.7% 14.0% 9.9%	-0.80 [ -0.70 [ -0.20 -0.60 [ -0.60 [ -0.50	-1.14, -0.46] -1.13, -0.27] [-1.42, 1.02] -0.99, -0.21] -1.11, -0.09]	IV, fixed, 95%Cl
Khullar 2004 Swift 2003 Van Kerrebroeck 1998 Van Kerrebroeck 2001 Zinner 2002a Zinner 2002b Total (95%CI)	-2.1 -1.9 -0.3 -1.8 -2 -1.4	2.4 3.4 2.2 3.4 3.1 3.7	<b>Tota</b> 569 417 2 15 507 292 214 <b>2014</b>	Mear           9         -1.3           7         -1.2           5         -0.1           7         -1.2           2         -1.4           4         -0.9           I         -0.9	2.3 2.9 1 2.9 3.1	258 410 16 507 284 223	30.5% 19.4% 2.4% 23.7% 14.0% 9.9%	-0.80 [ -0.70 [ -0.20 -0.60 [ -0.60 [ -0.50	-1.14, -0.46] -1.13, -0.27] [-1.42, 1.02] -0.99, -0.21] -1.11, -0.09] [-1.10, 0.10]	
Khullar 2004 Swift 2003 Van Kerrebroeck 1998 Van Kerrebroeck 2001 Zinner 2002a Zinner 2002b	-2.1 -1.9 -0.3 -1.8 -2 -1.4	2.4 3.4 2.2 3.4 3.1 3.7 p = 0.90	<b>Tota</b> 569 417 212 202 212 <b>2014</b> 0); I <sup>2</sup> = 0	Mear           9         -1.3           7         -1.2           5         -0.1           7         -1.2           2         -1.4           4         -0.9           I         -0.9	2.3 2.9 1 2.9 3.1	258 410 16 507 284 223	30.5% 19.4% 2.4% 23.7% 14.0% 9.9%	-0.80 [ -0.70 [ -0.20 -0.60 [ -0.60 [ -0.50	-1.14, -0.46] -1.13, -0.27] [-1.42, 1.02] -0.99, -0.21] -1.11, -0.09] [-1.10, 0.10]	IV, fixed, 95%Cl
Khullar 2004 Swift 2003 Van Kerrebroeck 1998 Van Kerrebroeck 2001 Zinner 2002a Zinner 2002b <b>Total (95%CI)</b> Heterogeneity: Chi <sup>2</sup> = 1.6 Test for overall effect: Z	-2.1 -1.9 -0.3 -1.8 -2 -1.4 64, df = 5 ( = 6.83 (p <	2.4 3.4 2.2 3.4 3.1 3.7 p = 0.90 c 0.0000	$\begin{array}{c c} \hline Tota \\ \hline Tota \\ \hline 56\% \\ 417 \\ 216 \\ 507 \\ 292 \\ 214 \\ 2014 \\ 0); \  ^2 = 0 \\ 1) \end{array}$	Mear           9         -1.3           7         -1.2           5         -0.1           7         -1.2           2         -1.4           4         -0.9           4         -0.9           5         -0.1	2.3 2.9 1 2.9 3.1 2.9 3.1 2.6	258 410 16 507 284 223	30.5% 19.4% 2.4% 23.7% 14.0% 9.9%	-0.80 [ -0.70 [ -0.20 -0.60 [ -0.60 [ -0.50	-1.14, -0.46] -1.13, -0.27] [-1.42, 1.02] -0.99, -0.21] -1.11, -0.09] [-1.10, 0.10]	
Khullar 2004 Swift 2003 Van Kerrebroeck 1998 Van Kerrebroeck 2001 Zinner 2002a Zinner 2002b <b>Total (95%CI)</b> Heterogeneity: Chi <sup>2</sup> = 1.6 Test for overall effect: Z	-2.1 -1.9 -0.3 -1.8 -2 -1.4 64, df = 5 ( = 6.83 (p <	2.4 3.4 2.2 3.4 3.1 3.7 p = 0.90 < 0.0000 <b>Folter</b>	Total           569           417           517           417           507           292           214           2014           2); 1 <sup>2</sup> = 0           1);           1);           rodin	Mear           9         -1.3           7         -1.2           5         -0.1           7         -1.2           2         -1.4           4         -0.9           %         Part of the second se	2.3 2.9 2.9 2.9 3.1 2.6	258 410 16 507 284 223 <b>1698</b>	30.5% 19.4% 2.4% 23.7% 14.0% 9.9%	-0.80 [ -0.70 [ -0.20 - 0.60 [ -0.60 [ -0.50 -	-1.14, -0.46] -1.13, -0.27] [-1.42, 1.02] -0.99, -0.21] -1.11, -0.09] [-1.10, 0.10] <b>-0.85, -0.47]</b>	-1 -0.5 0.5 Tolterodine 4mg Placebo
Khullar 2004 Swift 2003 Van Kerrebroeck 1998 Van Kerrebroeck 2001 Zinner 2002a Zinner 2002b <b>Total (95%CI)</b> Heterogeneity: Chi <sup>2</sup> = 1.6 Test for overall effect: Z	-2.1 -1.9 -0.3 -1.8 -2 -1.4 64, df = 5 ( = 6.83 (p <	2.4 3.4 2.2 3.4 3.1 3.7 p = 0.90 c 0.0000	Total           569           417           507           292           2014           0); I <sup>2</sup> = 0           1)           rodin           2mg           Total	Mear           9         -1.3           7         -1.2           5         -0.1           7         -1.2           2         -1.4           4         -0.9           %         Market	2.3 2.9 2.9 2.9 3.1 2.6 <b>g</b>	258 410 16 507 284 223 1698	30.5% 19.4% 2.4% 23.7% 14.0% 9.9% <b>100.0%</b>	-0.80 [ -0.70 [ -0.20 - -0.60 [ -0.60 [ -0.50 -	-1.14, -0.46] -1.13, -0.27] [-1.42, 1.02] -0.99, -0.21] -1.11, -0.09] [-1.10, 0.10]	
Khullar 2004 Swift 2003 Van Kerrebroeck 1998 Van Kerrebroeck 2001 Zinner 2002a Zinner 2002b <b>Total (95%CI)</b> Heterogeneity: Chi <sup>2</sup> = 1.6 Test for overall effect: Z <b>5. Tolterodine 2m</b> <b>Study of Subgroup</b> Jacquetin 2001	-2.1 -1.9 -0.3 -1.8 -2 -1.4 54, df = 5 ( = 6.83 (p < 54, df = 5 ( = 6.83 (p < 10 VS. Tolter Mean -1.4	2.4 3.4 2.2 3.4 3.1 3.7 \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$	Total           569           417           507           292           2014           2014           2015           1); 12 = 0           1); 12 = 0           1); 12 = 0           1); 12 = 0           1); 12 = 0           10           Total           103	Mean           9         -1.3           7         -1.2           5         -0.1           7         -1.2           2         -1.4           %         Understand           Wean         Tolter           Mean         -1.4	<b>g</b> 2.3 2.9 1 2.9 3.1 2.6 <b>g</b> rodine 2.8	258 410 16 507 284 223 1698 1mg Tota 97	30.5% 19.4% 2.4% 23.7% 14.0% 9.9% 100.0%	-0.80 [ -0.70 [ -0.20 -0.60 [ -0.60 [ -0.50 -0.66 [ -0.66 [ -0.66 [ -0.66 [ -0.66 [ -0.66 [ -0.66 [	-1.14, -0.46] -1.13, -0.27] [-1.42, 1.02] -0.99, -0.21] -1.11, -0.09] [-1.10, 0.10] -0.85, -0.47] an difference fixed, 95%Cl [-1.00, 1.00]	1 -0.5 0 0.5 Tolterodine 4mg Placebo
Khullar 2004 Swift 2003 Van Kerrebroeck 1998 Van Kerrebroeck 2001 Zinner 2002a Zinner 2002b <b>Total (95%CI)</b> Heterogeneity: Chi <sup>2</sup> = 1.6 Test for overall effect: Z <b>5. TOLterodine 2m</b> <b>Study of Subgroup</b> Jacquetin 2001 Millardi 1999	-2.1 -1.9 -0.3 -1.8 -2 -1.4 54, df = 5 ( = 6.83 (p < 19 VS. Tolter Mean -1.4 -2.3	2.4 3.4 2.2 3.4 3.1 3.7 \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$	Total           569           417           507           212           2014           2015           2014           2015 <td>Mear           9         -1.3           7         -1.2           5         -0.1           7         -1.2           2         -1.4           4         -0.9           N         Tolter           Mean         -1.4           -1.4         -2.3</td> <td>2.3 2.9 1 2.9 3.1 2.6 <b>g</b> odine 2.6</td> <td>258 410 16 507 284 223 <b>1698</b> <b>1mg</b> <b>Tota</b> 97 123</td> <td>30.5% 19.4% 2.4% 23.7% 14.0% 9.9% 100.0%</td> <td>-0.80 [ -0.70 [ -0.20 -0.60 [ -0.60 [ -0.50 - -0.66 [ -0.50 - -0.66 [ -0.50 - -0.66 [</td> <td>-1.14, -0.46] -1.13, -0.27] [-1.42, 1.02] -0.99, -0.21] -1.11, -0.09] [-1.10, 0.10] <b>-0.85, -0.47]</b> <b>-0.85, -0.47]</b> <b>-0.85, -0.47]</b></td> <td>1 -0.5 0 0.5 Tolterodine 4mg Placebo</td>	Mear           9         -1.3           7         -1.2           5         -0.1           7         -1.2           2         -1.4           4         -0.9           N         Tolter           Mean         -1.4           -1.4         -2.3	2.3 2.9 1 2.9 3.1 2.6 <b>g</b> odine 2.6	258 410 16 507 284 223 <b>1698</b> <b>1mg</b> <b>Tota</b> 97 123	30.5% 19.4% 2.4% 23.7% 14.0% 9.9% 100.0%	-0.80 [ -0.70 [ -0.20 -0.60 [ -0.60 [ -0.50 - -0.66 [ -0.50 - -0.66 [ -0.50 - -0.66 [	-1.14, -0.46] -1.13, -0.27] [-1.42, 1.02] -0.99, -0.21] -1.11, -0.09] [-1.10, 0.10] <b>-0.85, -0.47]</b> <b>-0.85, -0.47]</b> <b>-0.85, -0.47]</b>	1 -0.5 0 0.5 Tolterodine 4mg Placebo
Khullar 2004 Swift 2003 Van Kerrebroeck 1998 Van Kerrebroeck 2001 Zinner 2002a Zinner 2002b <b>Total (95%CI)</b> Heterogeneity: Chi <sup>2</sup> = 1.6 Test for overall effect: Z <b>5. Tolterodine 2m</b> <b>Study of Subgroup</b> Jacquetin 2001	-2.1 -1.9 -0.3 -1.8 -2 -1.4 54, df = 5 ( = 6.83 (p < 54, df = 5 ( = 6.83 (p < 10 VS. Tolter Mean -1.4	2.4 3.4 2.2 3.4 3.1 3.7 \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$	Total           569           417           507           292           2014           2014           2015           1); 12 = 0           1); 12 = 0           1); 12 = 0           1); 12 = 0           1); 12 = 0           10           Total           103	Mean           9         -1.3           7         -1.2           5         -0.1           7         -1.2           2         -1.4           %         Understand           Wean         Tolter           Mean         -1.4	<b>g</b> 2.3 2.9 1 2.9 3.1 2.6 <b>g</b> rodine 2.8	258 410 16 507 284 223 <b>1698</b> <b>1mg</b> <b>Tota</b> 97 123	30.5% 19.4% 2.4% 23.7% 14.0% 9.9% 100.0%	-0.80 [ -0.70 [ -0.20 -0.60 [ -0.60 [ -0.50 - -0.66 [ -0.50 - -0.66 [ -0.50 - -0.66 [	-1.14, -0.46] -1.13, -0.27] [-1.42, 1.02] -0.99, -0.21] -1.11, -0.09] [-1.10, 0.10] -0.85, -0.47] an difference fixed, 95%Cl [-1.00, 1.00]	1 -0.5 0 0.5 Tolterodine 4mg Placebo
Khullar 2004 Swift 2003 Van Kerrebroeck 1998 Van Kerrebroeck 2001 Zinner 2002a Zinner 2002b <b>Total (95%CI)</b> Heterogeneity: Chi <sup>2</sup> = 1.6 Test for overall effect: Z <b>5. TOLterodine 2m</b> <b>Study of Subgroup</b> Jacquetin 2001 Millardi 1999	-2.1 -1.9 -0.3 -1.8 -2 -1.4 54, df = 5 ( = 6.83 (p < 19 VS. Tolter Mean -1.4 -2.3	2.4 3.4 2.2 3.4 3.1 3.7 \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$	Total           569           417           507           212           2014           2015           2014           2015 <td>Mear           9         -1.3           7         -1.2           5         -0.1           7         -1.2           2         -1.4           4         -0.9           N         Tolter           Mean         -1.4           -1.4         -2.3</td> <td>2.3 2.9 1 2.9 3.1 2.6 <b>g</b> odine 2.6</td> <td>258 410 16 507 284 223 <b>1698</b> <b>1mg</b> <b>Tota</b> 97 123</td> <td>30.5% 19.4% 2.4% 23.7% 14.0% 9.9% 100.0%</td> <td>-0.80 [ -0.70 [ -0.20 - 0.60 [ -0.60 [ -0.50 - -0.66 [ -0.66 [ .0.66 [ .0.60 - .0.00 0.00 0.30</td> <td>-1.14, -0.46] -1.13, -0.27] [-1.42, 1.02] -0.99, -0.21] -1.11, -0.09] [-1.10, 0.10] <b>-0.85, -0.47]</b> <b>-0.85, -0.47]</b> <b>-0.85, -0.47]</b></td> <td>1 -0.5 0 0.5 Tolterodine 4mg Placebo</td>	Mear           9         -1.3           7         -1.2           5         -0.1           7         -1.2           2         -1.4           4         -0.9           N         Tolter           Mean         -1.4           -1.4         -2.3	2.3 2.9 1 2.9 3.1 2.6 <b>g</b> odine 2.6	258 410 16 507 284 223 <b>1698</b> <b>1mg</b> <b>Tota</b> 97 123	30.5% 19.4% 2.4% 23.7% 14.0% 9.9% 100.0%	-0.80 [ -0.70 [ -0.20 - 0.60 [ -0.60 [ -0.50 - -0.66 [ -0.66 [ .0.66 [ .0.60 - .0.00 0.00 0.30	-1.14, -0.46] -1.13, -0.27] [-1.42, 1.02] -0.99, -0.21] -1.11, -0.09] [-1.10, 0.10] <b>-0.85, -0.47]</b> <b>-0.85, -0.47]</b> <b>-0.85, -0.47]</b>	1 -0.5 0 0.5 Tolterodine 4mg Placebo
Khullar 2004 Swift 2003 Van Kerrebroeck 1998 Van Kerrebroeck 2001 Zinner 2002a Zinner 2002b <b>Total (95%CI)</b> Heterogeneity: Chi <sup>2</sup> = 1.6 Test for overall effect: Z <b>5. TOIterodine 2m</b> <b>Study of Subgroup</b> Jacquetin 2001 Millardi 1999 Van Kerrebroeck 1998 <b>Total (95%CI)</b>	-2.1 -1.9 -0.3 -1.8 -2 -1.4 64, df = 5 ( = 6.83 (p < 19 VS. Tolter Mean -1.4 -2.3 -0.1	2.4 3.4 2.2 3.4 3.1 3.7 • 0.900 • 0.0000 <b>Tolte:</b> <b>rodine 2</b> <b>SD</b> 4.3 2.1 1.8	Total           569           417           569           417           507           2014           2014           2011           2014           2011           2012           2014           2014           2014           2011           2014 <td>Mear           9         -1.3           7         -1.2           5         -0.1           7         -1.2           2         -1.4           %         Tolter           Mean         -1.4           -2.3         -0.4</td> <td>2.3 2.9 1 2.9 3.1 2.6 <b>g</b> odine 2.6</td> <td>258 410 16 507 284 223 1698 1698 1698 97 123 15</td> <td>30.5% 19.4% 2.4% 23.7% 14.0% 9.9% 100.0%</td> <td>-0.80 [ -0.70 [ -0.20 - 0.60 [ -0.60 [ -0.50 - -0.66 [ -0.66 [ .0.66 [ .0.60 - .0.00 0.00 0.30</td> <td>-1.14, -0.46] -1.13, -0.27] [-1.42, 1.02] -0.99, -0.21] -1.11, -0.09] [-1.10, 0.10] <b>-0.85, -0.47]</b> <b>-0.85, -0.47]</b> <b>-1.00</b>, 1.00] [-0.64, 0.64] [-1.06, 1.66]</td> <td>-1 -0.5 0 0.5 Tolterodine 4mg Placebo Mean difference IV, fixed, 95%CI</td>	Mear           9         -1.3           7         -1.2           5         -0.1           7         -1.2           2         -1.4           %         Tolter           Mean         -1.4           -2.3         -0.4	2.3 2.9 1 2.9 3.1 2.6 <b>g</b> odine 2.6	258 410 16 507 284 223 1698 1698 1698 97 123 15	30.5% 19.4% 2.4% 23.7% 14.0% 9.9% 100.0%	-0.80 [ -0.70 [ -0.20 - 0.60 [ -0.60 [ -0.50 - -0.66 [ -0.66 [ .0.66 [ .0.60 - .0.00 0.00 0.30	-1.14, -0.46] -1.13, -0.27] [-1.42, 1.02] -0.99, -0.21] -1.11, -0.09] [-1.10, 0.10] <b>-0.85, -0.47]</b> <b>-0.85, -0.47]</b> <b>-1.00</b> , 1.00] [-0.64, 0.64] [-1.06, 1.66]	-1 -0.5 0 0.5 Tolterodine 4mg Placebo Mean difference IV, fixed, 95%CI
Khullar 2004           Swift 2003           Van Kerrebroeck 1998           Van Kerrebroeck 2001           Zinner 2002a           Zinner 2002b           Total (95%CI)           Heterogeneity: Chi <sup>2</sup> = 1.6           Test for overall effect: Z           5. Tolterodine 2m           Study of Subgroup           Jacquetin 2001           Millardi 1999           Van Kerrebroeck 1998           Total (95%CI)           Heterogeneity: Chi <sup>2</sup> = 0.	-2.1 -1.9 -0.3 -1.8 -2 -1.4 54, df = 5 ( = 6.83 (p < Tolter Mean -1.4 -2.3 -0.1 16, df = 2 (	2.4 3.4 2.2 3.4 3.1 3.7 p = 0.90 c 0.0000 <b>Folter</b> rodine 2 <b>SD</b> 4.3 2.1 1.8 (p = 0.92	Total           569           417           569           417           507           2014           2014           2011           2014           2011           2012           2014           2014           2014           2011           2014 <td>Mear           9         -1.3           7         -1.2           5         -0.1           7         -1.2           2         -1.4           %         Tolter           Mean         -1.4           -2.3         -0.4</td> <td>2.3 2.9 1 2.9 3.1 2.6 <b>g</b> odine 2.6</td> <td>258 410 16 507 284 223 1698 1698 1698 97 123 15</td> <td>30.5% 19.4% 2.4% 23.7% 14.0% 9.9% 100.0%</td> <td>-0.80 [ -0.70 [ -0.20 - 0.60 [ -0.60 [ -0.50 - -0.66 [ -0.66 [ .0.66 [ .0.60 - .0.00 0.00 0.30</td> <td>-1.14, -0.46] -1.13, -0.27] [-1.42, 1.02] -0.99, -0.21] -1.11, -0.09] [-1.10, 0.10] <b>-0.85, -0.47]</b> <b>-0.85, -0.47]</b> <b>-1.00, 1.00</b> [-1.00, 1.00] [-1.06, 1.66]</td> <td>-1 -0.5 0 0.5 Tolterodine 4mg Placebo Mean difference IV, fixed, 95%CI</td>	Mear           9         -1.3           7         -1.2           5         -0.1           7         -1.2           2         -1.4           %         Tolter           Mean         -1.4           -2.3         -0.4	2.3 2.9 1 2.9 3.1 2.6 <b>g</b> odine 2.6	258 410 16 507 284 223 1698 1698 1698 97 123 15	30.5% 19.4% 2.4% 23.7% 14.0% 9.9% 100.0%	-0.80 [ -0.70 [ -0.20 - 0.60 [ -0.60 [ -0.50 - -0.66 [ -0.66 [ .0.66 [ .0.60 - .0.00 0.00 0.30	-1.14, -0.46] -1.13, -0.27] [-1.42, 1.02] -0.99, -0.21] -1.11, -0.09] [-1.10, 0.10] <b>-0.85, -0.47]</b> <b>-0.85, -0.47]</b> <b>-1.00, 1.00</b> [-1.00, 1.00] [-1.06, 1.66]	-1 -0.5 0 0.5 Tolterodine 4mg Placebo Mean difference IV, fixed, 95%CI
Khullar 2004 Swift 2003 Van Kerrebroeck 1998 Van Kerrebroeck 2001 Zinner 2002a Zinner 2002b <b>Total (95%CI)</b> Heterogeneity: $Chi^2 = 1.6$ Test for overall effect: Z <b>5. Tolterodine 2m</b> <b>Study of Subgroup</b> Jacquetin 2001 Millardi 1999 Van Kerrebroeck 1998 <b>Total (95%CI)</b> Heterogeneity: $Chi^2 = 0.$ Test for overall effect: Z	-2.1 -1.9 -0.3 -1.8 -2 -1.4 64, df = 5 ( = 6.83 (p < <b>1G VS.</b> <b>Tolter</b> <b>Mean</b> -1.4 -2.3 -0.1 16, df = 2 ( = 0.16 (p =	2.4 3.4 3.4 3.1 3.7 p = 0.90 c 0.0000 <b>Tolte:</b> rodine 2 <u>SD</u> 4.3 2.1 1.8 (p = 0.92 = 0.87)	$\begin{array}{c} {\bf Total} \\ {\bf 569} \\ {\bf 417} \\ {\bf 569} \\ {\bf 500} \\ {\bf 292} \\ {\bf 2014} \\ {\bf 2014} \\ {\bf 0); \ l^2 = 0 \\ {\bf 10} \\ {\bf rodin} \\ {\bf rodin} \\ {\bf 103} \\ {\bf 129} \\ {\bf 17} \\ {\bf 249} \\ {\bf 2); \ l^2 = 0 \end{array}$	Mean           9         -1.3           7         -1.2           5         -0.1           7         -1.2           2         -1.4           -0.9           -1.4           -0.4           -0.4           -0.4           -0.4	2.3 2.9 1 2.9 3.1 2.9 2.9 2.6 <b>SE</b> 2.6 3 2.1	258 410 16 507 284 223 1698 1698 1698 97 123 15	30.5% 19.4% 2.4% 23.7% 14.0% 9.9% 100.0%	-0.80 [ -0.70 [ -0.20 - 0.60 [ -0.60 [ -0.50 - -0.66 [ -0.66 [ .0.66 [ .0.60 - .0.00 0.00 0.30	-1.14, -0.46] -1.13, -0.27] [-1.42, 1.02] -0.99, -0.21] -1.11, -0.09] [-1.10, 0.10] <b>-0.85, -0.47]</b> <b>-0.85, -0.47]</b> <b>-1.00, 1.00</b> [-1.00, 1.00] [-1.06, 1.66]	-1 -0.5 0 0.5 Tolterodine 4mg Placebo Mean difference IV, fixed, 95%CI
Khullar 2004 Swift 2003 Van Kerrebroeck 1998 Van Kerrebroeck 2001 Zinner 2002a Zinner 2002b Total (95%CI) Heterogeneity: $Chi^2 = 1.6$ Test for overall effect: Z 5. Tolterodine 2m Study of Subgroup Jacquetin 2001 Millardi 1999 Van Kerrebroeck 1998 Total (95%CI) Heterogeneity: $Chi^2 = 0.$ Test for overall effect: Z	-2.1 -1.9 -0.3 -1.8 -2 -1.4 54, df = 5 ( = 6.83 (p < 10 VS. Tolter Mean -1.4 -2.3 -0.1 16, df = 2 ( = 0.16 (p = 10 VS.	2.4 3.4 2.2 3.4 3.1 3.7 <b>p</b> = 0.90 c 0.0000 <b>Tolter</b> rodine 2 <u>SD</u> 4.3 2.1 1.8 ( <i>p</i> = 0.92 = 0.87) <b>Tolter</b>	Total           566           417           568           417           18           507           292           2014           2017           2018           2019           1003           103           129           17           249           22); 1 <sup>2</sup> = 0           rodin	Mean           9         -1.3           7         -1.2           5         -0.1           7         -1.2           2         -1.4           %         Image: Comparison of the second	2.3 2.9 1 2.9 3.1 2.9 2.9 2.6 <b>SE</b> 2.6 3 2.1	258 410 16 507 284 223 <b>1698</b> <b>1mg</b> <b>Tota</b> 97 123 15 <b>235</b>	30.5% 19.4% 2.4% 23.7% 14.0% 9.9% 100.0%	-0.80 [ -0.70 [ -0.20 - -0.60 [ -0.60 [ -0.50 - -0.66 [ -0.66 [ -0.66 [ 0.00 0.00 0.30 0.00 6 0.04	-1.14, -0.46] -1.13, -0.27] [-1.42, 1.02] -0.99, -0.21] -1.11, -0.09] [-1.10, 0.10] -0.85, -0.47] -0.85, -0.47] -0.85, -0.47] [-1.00, 1.00] [-0.64, 0.64] [-0.46, 0.54]	-1 -0.5 0 0.5 Tolterodine 4mg Placebo Mean difference IV, fixed, 95%CI
Khullar 2004 Swift 2003 Van Kerrebroeck 1998 Van Kerrebroeck 2001 Zinner 2002a Zinner 2002b <b>Total (95%CI)</b> Heterogeneity: Chi <sup>2</sup> = 1.6 <b>Test</b> for overall effect: Z <b>5. Tolterodine 2m</b> <b>Study of Subgroup</b> Jacquetin 2001 Millardi 1999 Van Kerrebroeck 1998 <b>Total (95%CI)</b> Heterogeneity: Chi <sup>2</sup> = 0. Test for overall effect: Z <b>6. Tolterodine 4m</b>	-2.1 -1.9 -0.3 -1.8 -2 -1.4 54, df = 5 ( = 6.83 (p < 10 VS. Tolter Mean -1.4 -2.3 -0.1 16, df = 2 ( = 0.16 (p = 10 VS.	2.4 3.4 3.4 3.1 3.7 p = 0.90 c 0.0000 <b>Tolte:</b> rodine 2 <u>SD</u> 4.3 2.1 1.8 (p = 0.92 = 0.87)	Total           4         566           4         16           507         18           202         214           2014         292           211         2014           2011         101           rodin         rodin           2011         103           103         129           17         249           20; 1 <sup>2</sup> = 0         rodin           rodin         rodin	Mean           9         -1.3           9         -1.2           5         -0.1           7         -1.2           7         -1.2           2         -1.4           %         Market	2.3 2.9 1 2.9 3.1 2.6 3.1 2.6 <b>9</b> <b>odine</b> 2.8 2.1 <b>9</b> 2.1	258 410 16 507 284 223 1698 1698 1698 97 123 15 235	30.5% 19.4% 2.4% 32.7% 14.0% 9.9% 100.0%	-0.80 [ -0.70 ] -0.20 - -0.60 [ -0.60 ] -0.50 - -0.66 [ .0.00 0.00 0.30 6 0.04	-1.14, -0.46] -1.13, -0.27] [-1.42, 1.02] -0.99, -0.21] -1.11, -0.09] [-1.10, 0.10] <b>-0.85, -0.47]</b> <b>-0.85, -0.47]</b> <b>-0.85, -0.47]</b> <b>-1.100, 1.00]</b> [-1.00, 1.00] [-1.00, 1.66] [-1.06, 1.66] <b>[-0.46, 0.54]</b>	Mean difference IV, fixed, 95%CI
Khullar 2004 Swift 2003 Van Kerrebroeck 1998 Van Kerrebroeck 2001 Zinner 2002a Zinner 2002b Total (95%CI) Heterogeneity: $Chi^2 = 1.6$ Test for overall effect: Z 5. Tolterodine 2m Study of Subgroup Jacquetin 2001 Millardi 1999 Van Kerrebroeck 1998 Total (95%CI) Heterogeneity: $Chi^2 = 0.$ Test for overall effect: Z	-2.1 -1.9 -0.3 -1.8 -2 -1.4 64, df = 5 ( = 6.83 (p < 19 VS. Tolter Mean -1.4 -2.3 -0.1 16, df = 2 ( = 0.16 (p = 19 VS. TolterOf	2.4 3.4 2.2 3.4 3.1 3.7 c 0.0000 <b>Folter</b> rodine 2 <b>SD</b> 4.3 2.1 1.8 (p = 0.92 5.0 (0.0000 <b>Folter</b> 1.8 (p = 0.92 5.0 (0.0000 <b>Folter</b> 1.8 (0.9000 <b>Folter</b> 5.0 (0.9000 <b>Folter</b> 5.0 (0.9000 <b>Folter</b> 5.0 (0.9000 <b>Folter</b> 5.0 (0.9000 <b>Folter</b> 5.0 (0.9000 <b>Folter</b> 5.0 (0.9000 <b>Folter</b> 5.0 (0.9000 <b>Folter</b> 5.0 (0.9000 <b>Folter</b> 5.0 (0.9000 <b>Folter</b> 5.0 (0.9000 <b>Folter</b> 5.0 (0.9000 <b>Folter</b> 5.0 (0.9000 <b>Folter</b> 5.0 (0.9000 <b>Folter</b> 5.0 (0.9000 <b>Folter</b> 5.0 (0.9000 <b>Folter</b> 5.0 (0.9000 <b>Folter</b> 5.0 (0.9000 <b>Folter</b> 5.0 (0.9000 <b>Folter</b> 5.0 (0.9000 <b>Folter</b> 5.0 (0.9000 <b>Folter</b> 5.0 (0.9000 <b>Folter</b> 5.0 (0.9000 <b>Folter</b> 5.0 (0.9000 <b>Folter</b> 5.0 (0.9000 <b>Folter</b> 5.0 (0.9000 <b>Folter</b> 5.0 (0.9000 <b>Folter</b> 5.0 (0.9000 (0.9000) (	Total           566           417           568           417           18           507           292           2014           2017           2018           2019           1003           103           129           17           249           22); 1 <sup>2</sup> = 0           rodin	Mean           9         -1.3           7         -1.2           5         -0.1           7         -1.2           2         -1.4           %         Image: Comparison of the second	2.3 2.9 1 2.9 3.1 2.9 2.9 2.6 <b>SE</b> 2.6 3 2.1	258 410 16 507 284 223 1698 1698 1698 97 123 15 235	30.5% 19.4% 2.4% 23.7% 14.0% 9.9% 100.0%	-0.80 [ -0.70 [ -0.20 [ -0.60 [ -0.50 - -0.66 [ -0.66 [ .0.00 0.00 0.30 0.30 6 0.04	-1.14, -0.46] -1.13, -0.27] [-1.42, 1.02] -0.99, -0.21] -1.11, -0.09] [-1.10, 0.10] -0.85, -0.47] -0.85, -0.47] -0.85, -0.47] [-1.00, 1.00] [-0.64, 0.64] [-0.46, 0.54]	-1 -0.5 0 0.5 Tolterodine 4mg Placebo Mean difference IV, fixed, 95%CI
Khullar 2004           Swift 2003           Van Kerrebroeck 1998           Van Kerrebroeck 2001           Zinner 2002a           Zinner 2002b           Total (95%Cl)           Heterogeneity: Chi <sup>2</sup> = 1.6           Test for overall effect: Z           5. Tolterodine 2m           Study of Subgroup           Jacquetin 2001           Millardi 1999           Van Kerrebroeck 1998           Total (95%Cl)           Heterogeneity: Chi <sup>2</sup> = 0.7           Test for overall effect: Z           5. Tolterodine 4m           Study of Subgroup           Van Kerrebroeck 1998           Yan Kerrebroeck 1998           Yan Kerrebroeck 1998	-2.1 -1.9 -0.3 -1.8 -2 -1.4 64, df = 5 ( = 6.83 (p < 19 VS. Tolter Mean -1.4 -2.3 -0.1 16, df = 2 ( = 0.16 (p = 19 VS. Tolter Mean	2.4 3.4 2.2 3.4 3.1 3.7 <b>p</b> = 0.90 0.0000 <b>Folter</b> <b>rodine 2</b> <b>SD</b> 4.3 2.1 1.8 (p = 0.92 = 0.87) <b>Folter</b> 0.87) <b>Folter</b> 0.87) <b>Folter</b>	Total           +         566           +         567           +         567           +         11           +         507           292         214           2014         2014           2017         2014           101         103           102         17           249         17           249         201           rodin         17           rodin         17           7         749           10         17           Total         17	Mean           9         -1.3           9         -1.2           5         -0.1           7         -1.2           7         -1.2           4         -0.9           We         Mean           -0.13         -0.9           Mean         -1.4           -0.4         -0.4           9%         Tolter           Mean         -0.4	2.3 2.9 1 2.9 3.1 2.6 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	258 410 16 507 284 223 1698 1698 1698 1701 235 235	30.5% 19.4% 2.4% 23.7% 14.0% 9.9% 100.0% 100.0% 100.0% 100.0% 100.0% 39.2% 21.2%	-0.80 [ -0.70] -0.60 [ -0.60 [ -0.66 [ -0.50] -0.66 [ -0.50] -0.66 [ -0.50] -0.66 [ -0.50] -0.66 [ -0.50] -0.66 [ -0.50] -0.66 [ -0.50] -0.60 [ -0.50] -0.50 [ -0.50] -0.50] -0.50 [ -0.50] -0.50] -0.50 [ -0.50] -0.50] -0.50 [ -0.50]	-1.14, -0.46] -1.13, -0.27] [-1.42, 1.02] -0.99, -0.21] -1.11, -0.09] [-1.10, 0.10] -0.85, -0.47] -0.85, -0.47] -0.64, 0.64] [-1.00, 1.00] [-0.64, 0.64] [-1.06, 1.66] [-0.46, 0.54] an difference fixed, 95%Cl	Mean difference IV, fixed, 95%CI
Khullar 2004 Swift 2003 Van Kerrebroeck 1998 Van Kerrebroeck 2001 Zinner 2002a Zinner 2002b <b>Total (95%CI)</b> Heterogeneity: Chi <sup>2</sup> = 1.6 Test for overall effect: Z <b>5. TOIterodine 2m</b> <b>Study of Subgroup</b> Jacquetin 2001 Millardi 1999 Van Kerrebroeck 1998 <b>Total (95%CI)</b> Heterogeneity: Chi <sup>2</sup> = 0.7 Test for overall effect: Z <b>5. TOIterodine 4m</b> <b>Study of Subgroup</b> Swift 2003	-2.1 -1.9 -0.3 -1.8 -2 -1.4 54, df = 5 ( = 6.83 (p < 19 VS. Tolter Mean -1.4 -2.3 -0.1 16, df = 2 ( = 0.16 (p = 19 VS. Tolterc Mean -1.9	2.4 3.4 2.2 3.4 3.1 3.7 <b>p</b> = 0.90 0.0000 <b>Folter</b> <b>rodine 2</b> <b>SD</b> 4.3 2.1 1.8 ( <b>p</b> = 0.92 = 0.87) <b>Folter</b> <b>SD</b> 3.4	Total           +         566           +         567           +         567           +         129           -         214           2014         2014           101         101           103         129           17         249           22); 1 <sup>2</sup> = 0         10           roddin         mg           rotal         417	Mean           9         -1.3           9         -1.2           5         -0.1           7         -1.2           7         -1.2           2         -1.4           %         •           Mean         -1.4           -2.3         -0.4           %         •           Tolter         Mean           -1.7         •	2.3 2.9 2.9 3.1 2.9 3.1 2.9 3.1 2.9 3.1 2.6 <b>SD</b> 2.9 2.9 2.9	258 410 16 507 284 223 1698 Total 97 123 15 235 235	30.5% 19.4% 2.4% 23.7% 14.0% 9.9% 100.0% 100.0% 100.0% 100.0% Weight 39.2%	-0.80 [ -0.70 ] -0.60 [ -0.60 ] -0.66 <b>[</b> -0.50 -0.66 <b>[</b> -0.50 -0.66 <b>[</b> 0.00 0.30 0.30 0.30 0.30 0.30 0.30 0.3	-1.14, -0.46] -1.13, -0.27] [-1.42, 1.02] -0.99, -0.21] -1.11, -0.09] [-1.10, 0.10] -0.85, -0.47] -0.85, -0.47] -0.85, -0.47] [-1.00, 1.00] [-0.64, 0.64] [-1.06, 1.66] [-0.46, 0.54] -0.46, 0.54]	-1 -0.5 0 0.5 Tolterodine 4mg Placebo Mean difference IV, fixed, 95%CI
Khullar 2004 Swift 2003 Van Kerrebroeck 1998 Van Kerrebroeck 2001 Zinner 2002a Zinner 2002b <b>Total (95%CI)</b> Heterogeneity: Chi <sup>2</sup> = 1.6 Test for overall effect: Z <b>5. TOIterodine 2m</b> <b>Study of Subgroup</b> Jacquetin 2001 Millardi 1999 Van Kerrebroeck 1998 <b>Total (95%CI)</b> Heterogeneity: Chi <sup>2</sup> = 0. Test for overall effect: Z <b>6. TOIterodine 4m</b> <b>Study of Subgroup</b> Swift 2003 Van Kerrebroeck 1998 Van Kerrebroeck 1998 Van Kerrebroeck 1998	-2.1 -1.9 -0.3 -1.8 -2 -1.4 64, df = 5 ( = 6.83 (p < 10 VS. Tolter Mean -1.4 -2.3 -0.1 16, df = 2 ( = 0.16 (p = 10 VS. Tolterc Mean -1.9 -3	2.4 3.4 2.2 3.4 3.1 3.7 p = 0.90 c 0.0000 <b>Tolter</b> rodine 2 <u>SD</u> 4.3 2.1 1.8 (p = 0.92 = 0.87) <b>Tolter</b> <b>Dolter</b> 0.87) <b>Tolter</b> 0.87) <b>SD</b> 3.4 2.2	$\begin{array}{c c c c c c c c c c c c c c c c c c c $	Mean           -1.3           -1.3           -1.2           -0.12           -0.12           -1.2           -1.2           -1.2           -1.2           -1.2           -1.2           -1.2           -1.4           -2.3           -0.4           %           E 2mm           Tolter           Mean           -1.7           -0.4	2.3 2.9 2.9 3.1 2.9 3.1 2.9 2.9 2.9 2.6 <b>Odine</b> 2.6 <b>SD</b> 2.9 1.8	258 410 16 507 284 223 1698 Total 123 15 235 235 235	30.5% 19.4% 2.4% 23.7% 14.0% 9.9% 100.0% 100.0% 100.0% 100.0% Weight 39.2% 21.2% 39.5%	-0.80 [ -0.70] -0.60 [ -0.60 [ -0.50] -0.66 [ -0.50] -0.66 [ -0.50] -0.66 [ -0.50] -0.66 [ -0.50] -0.66 [ -0.50] -0.66 [ -0.50] -0.60 [ -0.50] -0.50] -0.60 [ -0.50] -0.50] -0.50 [ -0.50] -0.50] -0.50 [ -0.50] -0.50] -0.50 [ -0.50] -0.50] -0.50 [ -0.50] -0.50] -0.50 [ -0.50] -0.50] -0.50 [ -0.50] -0.50] -0.50 [ -0.50] -0.	-1.14, -0.46] -1.13, -0.27] [-1.42, 1.02] -0.99, -0.21] -1.11, -0.09] [-1.10, 0.10] -0.85, -0.47] -0.85, -0.47] -0.85, -0.47] -0.64, 0.64] [-0.64, 0.64] [-0.46, 0.54] -0.46, 0.54] -0.63, 0.23] [-4.30, -1.50] [-0.51, 0.31]	-1 -0.5 0 0.5 Tolterodine 4mg Placebo Mean difference IV, fixed, 95%CI
Khullar 2004 Swift 2003 Van Kerrebroeck 1998 Van Kerrebroeck 2001 Zinner 2002a Zinner 2002b <b>Total (95%CI)</b> Heterogeneity: Chi <sup>2</sup> = 1.6 Test for overall effect: Z <b>5. TOIterodine 2m</b> <b>Study of Subgroup</b> Jacquetin 2001 Millardi 1999 Van Kerrebroeck 1998 <b>Total (95%CI)</b> Heterogeneity: Chi <sup>2</sup> = 0. Test for overall effect: Z <b>6. TOIterodine 4m</b> <b>Study of Subgroup</b> Swift 2003 Van Kerrebroeck 1998 Van Kerrebroeck 1998 Van Kerrebroeck 2001 <b>Total (95%CI)</b>	-2.1 -1.9 -0.3 -1.8 -2 -1.4 54, df = 5 ( = 6.83 (p < 10 VS. Tolter Mean -1.4 -2.3 -0.1 16, df = 2 ( = 0.16 (p = 10 VS. Tolter Mean -1.9 -3 -1.8	2.4 3.4 2.2 3.4 3.1 3.7 <b>P</b> = 0.90 0.0000 <b>Tolter</b> rodine 2 <b>SD</b> 4.3 2.1 1.8 (p = 0.92 = 0.87) <b>Tolter</b> <b>Dolter</b> 50 3.4 2.2 3.4	$\begin{array}{c c c c c c c c c c c c c c c c c c c $	Mean           -1.3           -1.3           -1.3           -1.2           -0.12           -1.2           -1.2           -1.2           -1.2           -1.2           -1.2           -1.2           -1.4           -0.4           -0.4           -0.4           -0.4           -0.4           -0.4           -0.4           -0.4           -0.4	2.3 2.9 2.9 3.1 2.9 3.1 2.9 3.1 2.9 2.9 2.6 <b>9</b> <b>00ine</b> 2.8 <b>9</b> 2.1 <b>9</b> <b>00ine</b> 3.2 2.1	258 410 16 507 284 223 1698 Total 123 15 235 235 235 235	30.5% 19.4% 2.4% 23.7% 14.0% 9.9% 100.0% 100.0% 100.0% 100.0% 100.0% 39.2% 21.2%	-0.80 [ -0.70] -0.60 [ -0.60 [ -0.50] -0.66 [ -0.50] -0.66 [ -0.50] -0.66 [ -0.50] -0.66 [ -0.50] -0.66 [ -0.50] -0.66 [ -0.50] -0.60 [ -0.50] -0.50] -0.60 [ -0.50] -0.50] -0.50 [ -0.50] -0.50] -0.50 [ -0.50] -0.50] -0.50 [ -0.50] -0.50] -0.50 [ -0.50] -0.50] -0.50 [ -0.50] -0.50] -0.50 [ -0.50] -0.50] -0.50 [ -0.50] -0.	-1.14, -0.46] -1.13, -0.27] [-1.42, 1.02] -0.99, -0.21] -1.11, -0.09] [-1.10, 0.10] -0.85, -0.47] -0.85, -0.47] -0.85, -0.47] -1.00, 1.00] [-0.64, 0.64] [-0.64, 0.54] -0.46, 0.54] -0.63, 0.23] [-0.30, 2.33] [-4.30, -1.50]	-1 -0.5 0 0.5 Tolterodine 4mg Placebo Mean difference IV, fixed, 95%CI
Khullar 2004 Swift 2003 Van Kerrebroeck 1998 Van Kerrebroeck 1998 Van Kerrebroeck 2001 Zinner 2002a Zinner 2002b Total (95%CI) Heterogeneity: Chi <sup>2</sup> = 1.6 Test for overall effect: Z 5. Tolterodine 2m Study of Subgroup Jacquetin 2001 Millardi 1999 Van Kerrebroeck 1998 Total (95%CI) Heterogeneity: Chi <sup>2</sup> = 0. Test for overall effect: Z 6. Tolterodine 4m Study of Subgroup Swift 2003 Van Kerrebroeck 1998 Van Kerrebroeck 1998 Van Kerrebroeck 1998 Van Kerrebroeck 1998 Van Kerrebroeck 2001 Total (95%CI) Heterogeneity: Tau <sup>2</sup> = 0.	-2.1 -1.9 -0.3 -1.8 -2 -1.4 64, df = 5 ( = 6.83 (p < 19 VS. Tolter Mean -1.4 -2.3 -0.1 16, df = 2 ( = 0.16 (p = 10 VS. Tolter Mean -1.9 -1.8 50; Chi <sup>2</sup> =	2.4 3.4 2.2 3.4 3.1 3.7 coline 2 colono0 <b>Folter</b> codine 2 <b>SD</b> 4.3 2.1 1.8 <b>Colone 2</b> <b>SD</b> 3.4 2.2 3.4 2.2 3.4 2.2 3.4	$\begin{array}{c c c c c c c c c c c c c c c c c c c $	Mean           -1.3           -1.3           -1.3           -1.2           -0.12           -1.2           -1.2           -1.2           -1.2           -1.2           -1.2           -1.2           -1.4           -0.4           -0.4           -0.4           -0.4           -0.4           -0.4           -0.4           -0.4           -0.4	2.3 2.9 2.9 3.1 2.9 3.1 2.9 3.1 2.9 2.9 2.6 <b>9</b> <b>00ine</b> 2.8 <b>9</b> 2.1 <b>9</b> <b>00ine</b> 3.2 2.1	258 410 16 507 284 223 1698 Total 123 15 235 235 235 235	30.5% 19.4% 2.4% 23.7% 14.0% 9.9% 100.0% 100.0% 100.0% 100.0% Weight 39.2% 21.2% 39.5%	-0.80 [ -0.70] -0.60 [ -0.60 [ -0.50] -0.66 [ -0.50] -0.66 [ -0.50] -0.66 [ -0.50] -0.66 [ -0.50] -0.66 [ -0.50] -0.66 [ -0.50] -0.60 [ -0.50] -0.50] -0.60 [ -0.50] -0.50] -0.50 [ -0.50] -0.50] -0.50 [ -0.50] -0.50] -0.50 [ -0.50] -0.50] -0.50 [ -0.50] -0.50] -0.50 [ -0.50] -0.50] -0.50 [ -0.50] -0.50] -0.50 [ -0.50] -0.	-1.14, -0.46] -1.13, -0.27] [-1.42, 1.02] -0.99, -0.21] -1.11, -0.09] [-1.10, 0.10] -0.85, -0.47] -0.85, -0.47] -0.85, -0.47] -0.64, 0.64] [-0.64, 0.64] [-0.46, 0.54] -0.46, 0.54] -0.63, 0.23] [-4.30, -1.50] [-0.51, 0.31]	Mean difference IV, fixed, 95%CI
Khullar 2004 Swift 2003 Van Kerrebroeck 1998 Van Kerrebroeck 1998 Van Kerrebroeck 2001 Zinner 2002a Zinner 2002b <b>Total (95%CI)</b> Heterogeneity: Chi <sup>2</sup> = 1.6 <b>5. Tolterodine 2m</b> <b>Study of Subgroup</b> Jacquetin 2001 Millardi 1999 Van Kerrebroeck 1998 <b>Total (95%CI)</b> Heterogeneity: Chi <sup>2</sup> = 0. <b>Test for overall effect:</b> Z <b>5. Tolterodine 4m</b> <b>Study of Subgroup</b> Swift 2003 Van Kerrebroeck 1998 Van Kerrebroeck 1998 Van Kerrebroeck 1998 Van Kerrebroeck 2001 <b>Total (95%CI)</b> Heterogeneity: Tau <sup>2</sup> = 0. Test for overall effect: Z	-2.1 -1.9 -0.3 -1.8 -2 -1.4 64, df = 5 ( = 6.83 (p < <b>19 VS.</b> <b>Tolter</b> <b>Mean</b> -1.4 -2.3 -0.1 (p <b>vS.</b> <b>Tolter</b> <b>Mean</b> -1.9 -3 -1.8 50; Chi <sup>2</sup> = = 1.58 (p =	2.4 3.4 2.2 3.4 3.1 3.7 <b>p</b> = 0.90 c 0.0000 <b>Folter</b> <b>rodine 2</b> <b>SD</b> 4.3 2.1 1.8 ( <b>p</b> = 0.92 = 0.87) <b>Folter</b> <b>odine 4</b> <b>SD</b> 3.4 14.23, d = 0.11)	$\begin{array}{c c c c c c c c c c c c c c c c c c c $	Mean           -1.3           -1.3           -1.3           -1.2           -0.12           -1.2           -1.2           -1.2           -1.2           -1.2           -1.2           -1.2           -1.4           -0.4           -0.4           -0.4           -0.4           -0.4           -0.4           -0.4           -0.4           -0.4	2.3 2.9 2.9 3.1 2.9 3.1 2.9 3.1 2.9 2.9 2.6 <b>9</b> <b>00ine</b> 2.8 <b>9</b> 2.1 <b>9</b> <b>00ine</b> 3.2 2.1	258 410 16 507 284 223 1698 Total 123 15 235 235 235 235	30.5% 19.4% 2.4% 23.7% 14.0% 9.9% 100.0% 100.0% 100.0% 100.0% Weight 39.2% 21.2% 39.5%	-0.80 [ -0.70] -0.60 [ -0.60 [ -0.50] -0.66 [ -0.50] -0.66 [ -0.50] -0.66 [ -0.50] -0.66 [ -0.50] -0.66 [ -0.50] -0.66 [ -0.50] -0.60 [ -0.50] -0.50] -0.60 [ -0.50] -0.50] -0.50 [ -0.50] -0.50] -0.50 [ -0.50] -0.50] -0.50 [ -0.50] -0.50] -0.50 [ -0.50] -0.50] -0.50 [ -0.50] -0.50] -0.50 [ -0.50] -0.50] -0.50 [ -0.50] -0.	-1.14, -0.46] -1.13, -0.27] [-1.42, 1.02] -0.99, -0.21] -1.11, -0.09] [-1.10, 0.10] -0.85, -0.47] -0.85, -0.47] -0.85, -0.47] -0.64, 0.64] [-0.64, 0.64] [-0.46, 0.54] -0.46, 0.54] -0.63, 0.23] [-4.30, -1.50] [-0.51, 0.31]	-1 -0.5 0 0.5 Tolterodine 4mg Placebo Mean difference IV, fixed, 95%CI
Khullar 2004 Swift 2003 Van Kerrebroeck 1998 Van Kerrebroeck 1998 Van Kerrebroeck 2001 Zinner 2002a Zinner 2002b <b>Total (95%CI)</b> Heterogeneity: Chi <sup>2</sup> = 1.6 <b>5. Tolterodine 2m</b> <b>Study of Subgroup</b> Jacquetin 2001 Millardi 1999 Van Kerrebroeck 1998 <b>Total (95%CI)</b> Heterogeneity: Chi <sup>2</sup> = 0. <b>Test for overall effect:</b> Z <b>5. Tolterodine 4m</b> <b>Study of Subgroup</b> Swift 2003 Van Kerrebroeck 1998 Van Kerrebroeck 1998 Van Kerrebroeck 1998 Van Kerrebroeck 2001 <b>Total (95%CI)</b> Heterogeneity: Tau <sup>2</sup> = 0. Test for overall effect: Z	-2.1 -1.9 -0.3 -1.8 -2 -1.4 64, df = 5 ( = 6.83 (p < <b>19 VS.</b> <b>Tolter</b> <b>Mean</b> -1.4 -2.3 -0.1 (p <b>vS.</b> <b>Tolter</b> <b>Mean</b> -1.9 -3 -1.8 50; Chi <sup>2</sup> = = 1.58 (p =	2.4 3.4 2.2 3.4 3.1 3.7 <b>p</b> = 0.90 c 0.0000 <b>Folter</b> <b>rodine 2</b> <b>SD</b> 4.3 2.1 1.8 ( <b>p</b> = 0.92 = 0.87) <b>Folter</b> <b>odine 4</b> <b>SD</b> 3.4 14.23, d = 0.11)	$\begin{array}{c c c c c c c c c c c c c c c c c c c $	Mean           -1.3           -1.3           -1.3           -1.2           -0.12           -1.2           -1.2           -1.2           -1.2           -1.2           -1.2           -1.2           -1.4           -0.4           -0.4           -0.4           -0.4           -0.4           -0.4           -0.4           -0.4           -0.4	2.3 2.9 2.9 3.1 2.9 3.1 2.9 3.1 2.9 2.9 2.6 <b>9</b> <b>00ine</b> 2.8 <b>9</b> 2.1 <b>9</b> <b>00ine</b> 3.2 2.1	258 410 16 507 284 223 1698 Total 123 15 235 235 235 235	30.5% 19.4% 2.4% 23.7% 14.0% 9.9% 100.0% 100.0% 100.0% 100.0% Weight 39.2% 21.2% 39.5%	-0.80 [ -0.70] -0.60 [ -0.60 [ -0.50] -0.66 [ -0.50] -0.66 [ -0.50] -0.66 [ -0.50] -0.66 [ -0.50] -0.66 [ -0.50] -0.66 [ -0.50] -0.60 [ -0.50] -0.50] -0.60 [ -0.50] -0.50] -0.50 [ -0.50] -0.50] -0.50 [ -0.50] -0.50] -0.50 [ -0.50] -0.50] -0.50 [ -0.50] -0.50] -0.50 [ -0.50] -0.50] -0.50 [ -0.50] -0.50] -0.50 [ -0.50] -0.	-1.14, -0.46] -1.13, -0.27] [-1.42, 1.02] -0.99, -0.21] -1.11, -0.09] [-1.10, 0.10] -0.85, -0.47] -0.85, -0.47] -0.85, -0.47] -0.64, 0.64] [-0.64, 0.64] [-0.46, 0.54] -0.46, 0.54] -0.63, 0.23] [-4.30, -1.50] [-0.51, 0.31]	Mean difference IV, fixed, 95%CI
Khullar 2004 Swift 2003 Van Kerrebroeck 1998 Van Kerrebroeck 1998 Zinner 2002a Zinner 2002b <b>Total (95%CI)</b> Heterogeneity: Chi <sup>2</sup> = 1.6 Test for overall effect: Z <b>5. TOIterodine 2m</b> <b>Study of Subgroup</b> Jacquetin 2001 Millardi 1999 Van Kerrebroeck 1998 <b>Total (95%CI)</b> Heterogeneity: Chi <sup>2</sup> = 0. Test for overall effect: Z <b>6. TOIterodine 4m</b> <b>Study of Subgroup</b> Swift 2003 Van Kerrebroeck 1998 Van Kerrebroeck 2001 <b>Total (95%CI)</b> Heterogeneity: Tau <sup>2</sup> = 0. Total (95%CI) Heterogeneity: Tau <sup>2</sup> = 0. Total (95%CI)	-2.1 -1.9 -0.3 -1.8 -2 -1.4 64, df = 5 ( = 6.83 (p < 19 VS. Tolter Mean -1.4 -2.3 -0.1 16, df = 2 ( = 0.16 (p = 19 VS. Tolter Mean -1.9 -3 -1.8 50; Chi <sup>2</sup> = = 1.58 (p =	$\begin{array}{c} 2.4\\ 3.4\\ 3.4\\ 2.2\\ 3.4\\ 3.1\\ 3.7\\ p = 0.90\\ 0.0000\\ \hline \textbf{Folter}\\ \textbf{rodine 2}\\ \textbf{sp}\\ \textbf{a}.3\\ 2.1\\ 1.8\\ p = 0.92\\ \textbf{s}.0\\ \textbf{s}.3\\ 2.1\\ 1.8\\ \textbf{s}.3\\ 2.1\\ 1.8\\ \textbf{s}.3\\ 2.1\\ 3.4\\ 2.2\\ 3.4\\ 3.4\\ 3.4\\ 3.4\\ 3.4\\ 3.4\\ 3.4\\ 3.4$	Total           +         566           +         567           +         567           +         11           +         500           202         21           2014         2012           2011         103           103         129           107         103           129         17           107         249           202); I <sup>2</sup> = 0         0           roddin         129           107         249           507         507           939         if = 2 (p	Mean           9         -1.3           9         -1.2           5         -0.1           7         -1.2           7         -1.2           2         -1.4           %         •           H         Mean           -1.4         -2.3           -0.4         •           9%         E         Email           1.1.7         -0.1           -1.7         -0.4           9%         •           1.1.7         = 0.0000	2.3 2.9 2.9 3.1 2.9 3.1 2.9 3.1 2.6 <b>SD</b> 2.9 1.8 3.3 3.3 8);   <sup>2</sup> = {	258 410 16 507 284 223 1698 1698 704 123 15 235 235 235 235 235 235 235 235 235 23	30.5% 19.4% 2.4% 23.7% 14.0% 9.9% 100.0% 100.0%	-0.80 [ -0.70] -0.60 [ -0.60 [ -0.66 <b>[</b> -0.50 -0.66 <b>[</b> -0.50 -0.66 <b>[</b> -0.50 -0.66 <b>[</b> -0.50 -0.66 <b>[</b> -0.50 -0.66 <b>[</b> -0.50 -0.66 <b>[</b> -0.50 -0.60 -0.50 -0.60 -0.50 -0.60 -0.50 -0.60 -0.50 -0.60 -0.50 -0.60 -0.50 -0.60 -0.50 -0.60 -0.50 -0.50 -0.60 -0.50 -	-1.14, -0.46] -1.13, -0.27] [-1.42, 1.02] -0.99, -0.21] -1.11, -0.09] [-1.10, 0.10] -0.85, -0.47] -0.85, -0.47] -0.85, -0.47] -0.85, -0.47] [-1.00, 1.00] [-0.64, 0.64] [-1.00, 1.66] [-0.46, 0.54] -0.46, 0.54] -1.00, 1.03] [-0.46, 0.54] -1.00, 1.03] [-0.51, 0.31] [-1.64, 0.18] -1.64, 0.18]	Mean difference IV, fixed, 95%Cl Mean difference IV, fixed, 95%Cl
Khullar 2004 Swift 2003 Van Kerrebroeck 1998 Van Kerrebroeck 2001 Zinner 2002a Zinner 2002b <b>Total (95%CI)</b> Heterogeneity: Chi <sup>2</sup> = 1.6 Test for overall effect: Z <b>5. TOIterodine 2m</b> <b>Study of Subgroup</b> Jacquetin 2001 Millardi 1999 Van Kerrebroeck 1998 <b>Total (95%CI)</b> Heterogeneity: Chi <sup>2</sup> = 0.7 Test for overall effect: Z <b>6. TOIterodine 4m</b> <b>Study of Subgroup</b> Swift 2003 Van Kerrebroeck 1998 Van Kerrebroeck 1998	-2.1 -1.9 -0.3 -1.8 -2 -1.4 64, df = 5 ( = 6.83 (p < 19 VS. Tolter Mean -1.4 -2.3 -0.1 16, df = 2 ( = 0.16 (p = 19 VS. Tolter Mean -1.9 -3 -1.8 50; Chi <sup>2</sup> = = 1.58 (p = Solift Mean	2.4 3.4 2.2 3.4 3.1 3.7 <b>P</b> = 0.90 <b>Colter</b> <b>rodine 2</b> <b>SD</b> 4.3 2.1 1.8 <b>P</b> = 0.92 = 0.87) <b>Tolter</b> <b>solution</b> 3.4 2.2 3.4 3.4 2.2 3.4 3.4 3.4 3.4 3.4 3.4 3.4 3.4 3.4 3.4	Total           Form           - Total           - Total           - Total           - Total           - Total	Mean           -1.3           -1.13           -1.2           -0.11           7           -1.2           -0.12           -1.2           -1.2           -1.2           -1.2           -1.2           -1.2           -1.4           -0.9           Mean           -1.7           -0.1           -1.7           = 0.0000           Pla           Mean	2.3 2.3 2.9 1.2 2.9 1.2 2.9 1.2 2.9 1.2 2.9 1.2 2.9 1.2 2.9 1.2 2.9 1.2 2.9 1.2 2.9 1.2 2.9 1.2 2.9 1.2 2.9 1.2 2.9 1.8 3.3 3.3 8); 1 <sup>2</sup> = 4 cebo SD T	258 410 16 507 284 223 1698 Total 408 17 514 939 36%	30.5% 19.4% 2.4% 23.7% 14.0% 9.9% 100.0% 100.0% 100.0% Weight 39.2% 21.2% 39.5% 100.0% Veight	-0.80 [ -0.70] -0.60 [ -0.60 [ -0.50] -0.66 [ -0.50] -0.60 [ -0.50] -0.50] -0.60 [ -0.50] -0.50] -0.50 [ -0.50] -0.50 [ -0.50] -0.73 [ -0.73] -0.73 [ -0.73]	-1.14, -0.46] -1.13, -0.27] [-1.42, 1.02] -0.99, -0.21] -1.11, -0.09] [-1.10, 0.10] <b>-0.85, -0.47]</b> <b>-0.85, -0.47]</b> <b>-0.64, 0.64]</b> [-1.00, 1.00] [-0.64, 0.64] [-1.06, 1.66] <b>[-0.46, 0.54]</b> <b>-0.46, 0.54]</b> <b>-0.46, 0.54]</b> <b>-0.46, 0.54]</b> <b>-1.64, 0.18]</b> <b>-1.64, 0.18]</b>	Mean difference IV, fixed, 95%CI
Khullar 2004 Swift 2003 Van Kerrebroeck 1998 Van Kerrebroeck 2001 Zinner 2002a Zinner 2002b Total (95%CI) Heterogeneity: Chi <sup>2</sup> = 1.6 Test for overall effect: Z 5. Tolterodine 2m Study of Subgroup Jacquetin 2001 Millardi 1999 Van Kerrebroeck 1998 Total (95%CI) Heterogeneity: Chi <sup>2</sup> = 0.: Test for overall effect: Z 6. Tolterodine 4m Study of Subgroup Swift 2003 Van Kerrebroeck 1998 Van Kerrebroeck 1998 Van Kerrebroeck 1998 Van Kerrebroeck 2001 Total (95%CI) Heterogeneity: Tau <sup>2</sup> = 0.: Test for overall effect: Z 7. Solifenacin vs. Study of Subgroup Cardozo 2008	-2.1 -1.9 -0.3 -1.8 -2 -1.4 54, df = 5 ( = 6.83 (p < <b>19 VS.</b> <b>Tolter</b> <b>Mean</b> -1.4 -2.3 -0.1 16, df = 2 ( = 0.16 (p = <b>19 VS.</b> <b>Tolter</b> <b>Mean</b> -1.9 -3 -1.8 50; Chi <sup>2</sup> = = 1.58 (p = <b>Solif</b> <b>Mean</b> -2.1	2.4 3.4 2.2 3.4 3.1 3.7 p = 0.90 0.0000 <b>Folter</b> <b>rodine 2</b> <b>SD</b> 3.4 2.2 3.4 14.23, d 14.23, d 14.23, d 2.6	$\begin{array}{c c c c c c c c c c c c c c c c c c c $	Mean           -1.3           -1.3           -1.3           -1.2           -0.12           -0.12           -1.2           -1.2           -1.2           -1.2           -1.2           -1.2           -1.2           -1.2           -1.2           -1.4           -2.3           -0.4           %           E 2mm           Tolter           Mean           -1.7           -0.1           -1.7           = 0.0000           Pla           Mean           -1.3	2.3 2.9 2.9 3.1 2.9 3.1 2.9 3.1 2.9 2.9 3.1 2.6 2.6 2.6 2.6 2.1 2.7 2.9 1.8 3.3 8); l <sup>2</sup> = { 8 5D 2.9 1.8 3.3 2.9 2.9 2.9 2.9 1.2 2.9 2.9 1.2 2.9 2.9 1.2 2.9 2.9 1.2 2.9 2.9 1.2 2.9 2.6 1.2 2.9 2.6 1.2 2.9 2.6 1.2 2.9 2.6 1.2 2.9 2.6 1.2 2.9 2.6 1.2 2.6 2.6 2.6 2.6 2.6 2.6 2.6 2.6 2.6 2	258 410 507 284 223 1698 1698 97 123 15 235 235 235 235 235 235 235 235 235 23	30.5% 19.4% 2.4% 23.7% 14.0% 9.9% 100.0% 100.0% 100.0% 100.0% Weight 39.2% 21.2% 39.5% 100.0% Veight 57.5%	-0.80 [ -0.70] -0.60 [ -0.60 [ -0.66 [ -0.50 -0.66 [ -0.50 -0.66 [ -0.50 -0.66 [ -0.50 -0.66 [ -0.73 -0.20 -0.20 -0.20 -0.20 -0.20 -0.20 -0.20 -0.20 -0.20 -0.20 -0.20 -0.20 -0.20 -0.20 -0.20 -0.20 -0.20 -0.60 [ -0.50 -0.60 [ -0.50 -0.	-1.14, -0.46] -1.13, -0.27] -1.42, 1.02] -0.99, -0.21] -1.11, -0.09] -1.11, -0.09] -1.11, -0.09] -1.11, -0.09] -1.10, 0.10] -0.85, -0.47] -0.85, -0.47] -0.85, -0.47] -1.00, 1.00] -0.64, 0.64] -1.00, 1.00] -0.64, 0.64] -1.00, 1.00] -0.64, 0.54] -1.00, 1.00] -0.63, 0.23] -4.30, -1.50] -0.51, 0.31] -1.64, 0.18] -1.64, 0.18] -1.64, 0.73]	Mean difference IV, fixed, 95%Cl Mean difference IV, fixed, 95%Cl
Khullar 2004 Swift 2003 Van Kerrebroeck 1998 Van Kerrebroeck 2001 Zinner 2002a Zinner 2002b <b>Total (95%CI)</b> Heterogeneity: Chi <sup>2</sup> = 1.6 Test for overall effect: Z <b>5. TOIterodine 2m</b> <b>Study of Subgroup</b> Jacquetin 2001 Millardi 1999 Van Kerrebroeck 1998 <b>Total (95%CI)</b> Heterogeneity: Chi <sup>2</sup> = 0.7 Test for overall effect: Z <b>6. TOIterodine 4m</b> <b>Study of Subgroup</b> Swift 2003 Van Kerrebroeck 1998 Van Kerrebroeck 2001 <b>Total (95%CI)</b> Heterogeneity: Tau <sup>2</sup> = 0.7 <b>Test for overall effect: Z</b> <b>7. SOIifenacin vs.</b> <b>Study of Subgroup</b>	-2.1 -1.9 -0.3 -1.8 -2 -1.4 54, df = 5 ( = 6.83 (p < <b>19 VS.</b> <b>Tolter</b> <b>Mean</b> -1.4 -2.3 -0.1 16, df = 2 ( = 0.16 (p = <b>19 VS.</b> <b>Tolter</b> <b>Mean</b> -1.9 -3 -1.8 50; Chi <sup>2</sup> = = 1.58 (p = <b>Solif</b> <b>Mean</b> -2.1	2.4 3.4 2.2 3.4 3.1 3.7 <b>P</b> = 0.90 <b>Colter</b> <b>rodine 2</b> <b>SD</b> 4.3 2.1 1.8 <b>P</b> = 0.92 = 0.87) <b>Tolter</b> <b>solution</b> 3.4 2.2 3.4 3.4 2.2 3.4 3.4 3.4 3.4 3.4 3.4 3.4 3.4 3.4 3.4	Total           Form           - Total           - Total           - Total           - Total           - Total	Mean           -1.3           -1.3           -1.3           -1.2           -0.12           -0.12           -1.2           -1.2           -1.2           -1.2           -1.2           -1.2           -1.2           -1.2           -1.2           -1.4           -2.3           -0.4           -%           E 2mm           Tolter           Mean           -1.7           -0.1           -1.7           = 0.0000           Pla           Mean           -1.3	2.3 2.9 2.9 3.1 2.9 3.1 2.9 3.1 2.9 2.9 3.1 2.6 2.6 2.6 2.6 2.1 2.7 2.9 1.8 3.3 8); l <sup>2</sup> = { 8 5D 2.9 1.8 3.3 2.9 2.9 2.9 2.9 1.2 2.9 2.9 1.2 2.9 2.9 1.2 2.9 2.9 1.2 2.9 2.9 1.2 2.9 2.6 1.2 2.9 2.6 1.2 2.9 2.6 1.2 2.9 2.6 1.2 2.9 2.6 1.2 2.9 2.6 1.2 2.6 2.6 2.6 2.6 2.6 2.6 2.6 2.6 2.6 2	258 410 507 284 223 1698 1698 97 123 15 235 235 235 235 235 235 235 235 235 23	30.5% 19.4% 2.4% 23.7% 14.0% 9.9% 100.0% 100.0% 100.0% Weight 39.2% 21.2% 39.5% 100.0% Veight	-0.80 [ -0.70] -0.60 [ -0.60 [ -0.66 [ -0.50 -0.66 [ -0.50 -0.66 [ -0.50 -0.66 [ -0.50 -0.66 [ -0.73 -0.20 -0.20 -0.20 -0.20 -0.20 -0.20 -0.20 -0.20 -0.20 -0.20 -0.20 -0.20 -0.20 -0.20 -0.20 -0.20 -0.20 -0.60 [ -0.50 -0.60 [ -0.50 -0.	-1.14, -0.46] -1.13, -0.27] [-1.42, 1.02] -0.99, -0.21] -1.11, -0.09] [-1.10, 0.10] <b>-0.85, -0.47]</b> <b>-0.85, -0.47]</b> <b>-0.64, 0.64]</b> [-1.00, 1.00] [-0.64, 0.64] [-1.06, 1.66] <b>[-0.46, 0.54]</b> <b>-0.46, 0.54]</b> <b>-0.46, 0.54]</b> <b>-0.46, 0.54]</b> <b>-1.64, 0.18]</b> <b>-1.64, 0.18]</b>	Mean difference IV, fixed, 95%Cl Mean difference IV, fixed, 95%Cl
Khullar 2004 Swift 2003 Van Kerrebroeck 1998 Van Kerrebroeck 2001 Zinner 2002a Zinner 2002b <b>Total (95%CI)</b> Heterogeneity: Chi <sup>2</sup> = 1.6 Test for overall effect: Z <b>5. TOIterodine 2m</b> <b>Study of Subgroup</b> Jacquetin 2001 Millardi 1999 Van Kerrebroeck 1998 <b>Total (95%CI)</b> Heterogeneity: Chi <sup>2</sup> = 0. Test for overall effect: Z <b>6. TOIterodine 4m</b> <b>Study of Subgroup</b> Swift 2003 Van Kerrebroeck 1998 Van Kerrebroeck 1998 Van Kerrebroeck 1998 Van Kerrebroeck 1998 Van Kerrebroeck 2001 Total (95%CI) Heterogeneity: Tau <sup>2</sup> = 0. Test for overall effect: Z = <b>7. SOIifenacin vs.</b> <b>Study of Subgroup</b> Cardozo 2008 Karram 2009	-2.1 -1.9 -0.3 -1.8 -2 -1.4 54, df = 5 ( = 6.83 (p < <b>19 VS.</b> <b>Tolter</b> <b>Mean</b> -1.4 -2.3 -0.1 16, df = 2 ( = 0.16 (p = <b>19 VS.</b> <b>Tolter</b> <b>Mean</b> -1.9 -3 -1.8 50; Chi <sup>2</sup> = = 1.58 (p = <b>Solif</b> <b>Mean</b> -2.1	2.4 3.4 2.2 3.4 3.1 3.7 p = 0.90 0.0000 <b>Folter</b> <b>rodine 2</b> <b>SD</b> 3.4 2.2 3.4 14.23, d 14.23, d 14.23, d 2.6	Total           +         566           +         567           +         567           +         11           +         507           2292         212           2014         2014           2017         2011           rodin         103           103         129           17         249           2012         229           121         249           rotal         417           507         939           91f = 2 (p         704           502         348	Mean           -1.3           -1.3           -1.3           -1.2           -0.12           -0.12           -1.2           -1.2           -1.2           -1.2           -1.2           -1.2           -1.2           -1.2           -1.2           -1.4           -2.3           -0.4           %           E 2mm           Tolter           Mean           -1.7           -0.1           -1.7           = 0.0000           Pla           Mean           -1.3	2.3 2.9 2.9 3.1 2.9 3.1 2.9 3.1 2.9 3.1 2.9 2.9 1.8 3.3 3.3 8); 1 <sup>2</sup> = 8 <b>Cebo</b> <b>SD</b> T 2.7 3.3	258 410 16 507 284 223 1698 Total 408 17 514 408 17 514 939 939 36%	30.5% 19.4% 2.4% 23.7% 14.0% 9.9% 100.0% 100.0% 100.0% Weight 39.2% 21.2% 39.5% 100.0% Veight 57.5% 42.5%	-0.80 [ -0.70] -0.60 [ -0.66 [ -0.50] -0.66 [ -0.50] -0.66 [ -0.50] -0.66 [ -0.50] -0.66 [ -0.50] -0.66 [ -0.73] -0.80 -0.73	-1.14, -0.46] -1.13, -0.27] [-1.42, 1.02] -0.99, -0.21] -1.11, -0.09] [-1.10, 0.10] -0.85, -0.47] -0.85, -0.47] -0.64, 0.64] [-1.00, 1.00] [-0.64, 0.64] [-1.00, 1.66] [-0.46, 0.54] -0.63, 0.23] [-4.30, -1.50] [-0.51, 0.31] [-1.64, 0.18] -1.64, 0.18] -1.64, 0.18]	Mean difference IV, fixed, 95%Cl Mean difference IV, fixed, 95%Cl
Khullar 2004 Swift 2003 Van Kerrebroeck 1998 Van Kerrebroeck 2001 Zinner 2002a Zinner 2002b Total (95%CI) Heterogeneity: Chi <sup>2</sup> = 1.6 Test for overall effect: Z 5. Tolterodine 2m Study of Subgroup Jacquetin 2001 Millardi 1999 Van Kerrebroeck 1998 Total (95%CI) Heterogeneity: Chi <sup>2</sup> = 0.: Test for overall effect: Z 6. Tolterodine 4m Study of Subgroup Swift 2003 Van Kerrebroeck 1998 Van Kerrebroeck 1998 Van Kerrebroeck 1998 Van Kerrebroeck 2001 Total (95%CI) Heterogeneity: Tau <sup>2</sup> = 0.: Test for overall effect: Z 7. Solifenacin vs. Study of Subgroup Cardozo 2008	-2.1 -1.9 -0.3 -1.8 -2 -1.4 64, df = 5 ( = 6.83 (p < 19 VS. Tolter Mean -1.4 -2.3 -0.1 16, df = 2 ( = 0.16 (p = 10 VS. Tolter Mean -1.9 -3 -1.8 50; Chi <sup>2</sup> = = 1.58 (p = <b>Place</b> Soliff Mean -2.1 -2.67	2.4 3.4 2.2 3.4 3.1 3.7 <b>P</b> = 0.90 <b>Colter</b> <b>rodine 2</b> <b>SD</b> 4.3 2.1 1.8 <b>P</b> = 0.92 = 0.87) <b>Folter</b> <b>odine 4</b> <b>SD</b> 3.4 2.2 3.4 2.2 3.4 2.2 3.4 2.2 3.4 2.2 3.4 2.2 3.4 2.2 3.4 2.2 3.4 2.2 3.4 2.2 3.4 2.2 3.4 2.2 3.4 2.2 3.4 2.2 3.4 2.2 3.4 2.2 3.4 2.2 3.4 2.2 3.4 2.1 5 <b>D</b> <b>D</b> <b>D</b> <b>D</b> <b>D</b> <b>D</b> <b>D</b> <b>D</b> <b>D</b> <b>D</b>	$\begin{tabular}{ c c c c c } \hline Total \\ \hline Tot$	Mean           -1.3           -1.2           -1.2           -0.1           7           -1.2           -0.1           7           -1.2           -0.1           %           %           model           Mean           -1.3           -1.3           -1.3	2.3 2.9 2.9 3.1 2.9 3.1 2.9 3.1 2.9 3.1 2.9 2.9 1.8 3.3 3.3 8); 1 <sup>2</sup> = 8 <b>Cebo</b> <b>SD</b> T 2.7 3.3	258 410 16 507 284 223 1698 Total 408 17 514 939 939 36% total V 2216 3337	30.5% 19.4% 2.4% 23.7% 14.0% 9.9% 100.0% 100.0% 100.0% 100.0% Weight 39.2% 21.2% 39.5% 100.0% Veight 57.5%	-0.80 [ -0.70] -0.60 [ -0.66 [ -0.50] -0.66 [ -0.50] -0.66 [ -0.50] -0.66 [ -0.50] -0.66 [ -0.50] -0.66 [ -0.50] -0.20 -2.90 -0.10 -0.73 Mea IV, 1 -0.80 -0.73	-1.14, -0.46] -1.13, -0.27] -1.42, 1.02] -0.99, -0.21] -1.11, -0.09] -1.11, -0.09] -1.11, -0.09] -1.11, -0.09] -1.10, 0.10] -0.85, -0.47] -0.85, -0.47] -0.85, -0.47] -1.00, 1.00] -0.64, 0.64] -1.00, 1.00] -0.64, 0.64] -1.00, 1.00] -0.64, 0.54] -1.00, 1.00] -0.63, 0.23] -4.30, -1.50] -0.51, 0.31] -1.64, 0.18] -1.64, 0.18] -1.64, 0.73]	Mean difference IV, fixed, 95%Cl Mean difference IV, fixed, 95%Cl

Fig. 3 Forest plot – mean difference in decrease in the number of micturitions per day.

# 1. Oxybutynin vs. Tolterodine

	Favo	urs Oxyt	outyni	Tolter	odine			Mean difference		Mean dif	ference	
Study of Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, fixed, 95%CI		IV, rando	m, 95%Cl	
Appell 2011	-3.07	4.14	160	-2.53	4.17	172	29.0%	-0.54 [-1.43, 0.35]	+	-		1.1
Drutz 1999	-1.7	1.7	39	-1.7	2	60	33.0%	0.00 [-0.74, 0.74]			÷	
Lee 2002	-1.4	1.8	116	-2.2	2.3	112	38.1%	0.80 [0.26, 1.34]				$\rightarrow$
Total (95%CI)			315			344	100.0%	0.15 [-0.64, 0.94]				-
Heterogeneity: Tau <sup>2</sup> = 0.	.35; Chi <sup>2</sup> =	7.34, df =	= 2 (p =	0.03); I <sup>2</sup>	= 73%				-			-
Test for overall effect: Z	= 0.37 (p =	0.71)	u.						-1	-0.5 Oxybutyn	0 0.5 in Tolterodine	1

# 2. Tolterodine 1mg vs. Placebo

	Toltero	odine 1r	ng	P	acebo	<b>)</b>		Mean difference	Mean difference
Study of Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, fixed, 95%CI	IV, fixed, 95%Cl
Millardi 1999	-1.7	2.8	109	-1.3	2.5	55	87.6%	-0.40 [-1.24, 0.44]	+
Van Kerrebroeck 1998	-1.2	3.9	15	-1.9	2.2	16	12.4%	0.70 [-1.55, 2.95]	• <u> </u>
Total (95%CI)			124			71	100.0%	-0.26 [-1.05, 0.53]	
Heterogeneity: Chi <sup>2</sup> = 0.	81, df = 1 (p	= 0.37);	$I^2 = 0\%$						
Test for overall effect: Z	= 0.65 (p = 0	0.51)							-1 -0.5 0 0.5 Tolterodine 1mg Placebo

#### 3. Tolterodine 2mg vs. Placebo

	,	1000							
	Tolt	erodin	e 2mg	Р	lacebo			Mean difference	Mean difference
Study of Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, fixed, 95%CI	IV, fixed, 95%Cl
Chapple 2004	-1.14	2.15	157	-0.76	2.26	153	40.0%	-0.38 [-0.87, 0.11]	
Drutz 1999	-1.7	2	39	-1	2.2	33	10.1%	-0.70 [-1.68, 0.28]	• <u> </u>
Mllardi 1999	-1.7	2.5	117	-1.3	2.5	55	15.0%	-0.40 [-1.20, 0.40]	+
Swift 2003	-1.44	5.89	408	-1.03	5.74	410	15.2%	-0.41 [-1.21, 0.39]	• • • • • • • • • • • • • • • • • • •
Van Kerrebroeck 1998	-2.4	3.5	17	-1.9	2.2	16	2.5%	-0.50 [-2.48, 1.48]	+
Van Kerrebroeck 2001	-1.51	6.38	514	-0.99	5.81	507	17.2%	-0.52 [-1.27, 0.23]	· · · · · · · · · · · · · · · · · · ·
Total (95%CI)			1252			1174	100.0%	-045 [-0.76, -0.14]	-
Heterogeneity: Chi <sup>2</sup> = 0.39,	df = 5 (r)	b = 1.00	$1^{2} = 1^{2}$	0%					
Test for overall effect: $Z = 2$				0,0					-1 -0.5 0 0.5 Tolterodine 2mg Placebo

#### 4. Tolterodine 4mg vs. Placebo

	Tolter	odine 4	mg	Р	lacebo			Mean difference	Mean difference
Study of Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, fixed, 95%Cl	IV, fixed, 95%Cl
Khullar 2004	-0.68	4.72	569	-0.57	5.21	258	25.6%	-0.11 [-0.85, 0.63]	
Swift 2003	-1.69	6.79	417	-1.03	5.74	410	19.4%	-0.66 [-1.52, 0.20]	• • • • • • • • • • • • • • • • • • •
Van Kerrebroeck 1998	-1.5	1.7	15	-1.9	2.2	16	7.5%	0.40 [-0.98, 1.78]	
Van Kerrebroeck 2001	-1.69	6.72	507	-0.99	5.81	507	23.8%	-0.70 [-1.47, 0.07]	• <del>•</del>
Zinner 2002a	-1.71	6.64	292	-1.06	5.89	284	13.6%	-0.65 [-1.67, 0.37]	+
Zinner 2002b	-1.64	6.87	214	-0.9	5.66	223	10.2%	-0.74 [-1.92, 0.44]	•
Total (95%CI)			2014			1698	100.0%	-0.46 [-0.83, 0.08]	-
Heterogeneity: Chi <sup>2</sup> = 3.2	7. df = 5 (c	= 0.66	$  ^2 = 0$	%					
Test for overall effect: Z =									-1 -0.5 0 Tolterodine 4mg Placel

# 5. Tolterodine 2mg vs. Tolterodine 1mg

	Toltero	dine 2	mg	Toltero	dine 1	mg		Mean difference	Mean difference
Study of Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, fixed, 95%CI	IV, fixed, 95%CI
Millardi 1999	-1.7	2.5	117	-1.7	2.8	109	93.3%	0.00 [-0.69, 0.69]	
Van Kerrebroeck 1998	-2.4	3.5	17	-1.2	3.9	15	6.7%	-1.20 [-3.78, 1.38]	$\leftarrow$ $\rightarrow$
Total (95%CI)			134			124	100.0%	-0.08 [-0.75, 0.59]	
Heterogeneity: Chi <sup>2</sup> = 0.7			8); I <sup>2</sup> = C	)%					-1 -0.5 0 0.5
Test for overall effect: Z	= 0.24 (p =	0.81)							Tolterodine 2mg Tolterodine 1mg

# 6. Tolterodine 4mg vs. Tolterodine 2mg

	Tolter	odine 4	mg	Tolter	odine 2	mg		Mean difference	Mean difference
Study of Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, fixed, 95%Cl	IV, fixed, 95%CI
Swift 2003	-1.69	6.79	417	-1.44	5.89	408	42.1%	-0.25 [-1.12, 0.62]	·
Van Kerrebroeck 1998	-1.5	1.7	15	-2.4	3.5	17	9.0%	0.90 [-0.97, 2.77]	· · · · · · · · · · · · · · · · · · ·
Van Kerrebroeck 2001	-1.69	6.72	507	-1.51	6.38	514	48.9%	-0.18 [-0.98, 0.62]	· · · · · · · · · · · · · · · · · · ·
Total (95%CI)			939			939	100.0%	-0.11 [-0.67, 0.45]	
Heterogeneity: Chi <sup>2</sup> = 1.2	25. df = 2 (	(p = 0.5)	4); $I^2 = C$	)%					
Test for overall effect: Z			,,						-0.5 -0.25 0 0.25 0.5 Tolterodine 4mg Tolterodine 2mg

#### 7. Solifenacin vs. Placebo

	Soli	fenaciı	ı	Pla	cebo			Mean difference	Mean difference
Study of Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, fixed, 95%Cl	IV, fixed, 95%Cl
Cardozo 2008	-2.1	2.6	502	-1.3	2.7	216	57.5%	-0.80 [-1.23, -0.37]	+ <u>-</u>
Karram 2009	-2.67	3.31	348	-1.94	3.3	337	42.5%	-0.73 [-1.23, -0.23]	
Total (95%CI)			850			553	100.0%	-0.77 [-1.09, -0.45]	•
Heterogeneity: Chi <sup>2</sup> = 0			83); I <sup>2</sup> =	0%		555	100.070	-0.77 [-1.00, -0.40]	-1 -0.5 0 0.5
Test for overall effect: Z	<u>z</u> = 4.68 (p	< 0.00	001)						Solifenacin Placebo



Study of Subgroup	Tolterodi Oxybutynin Events To		rodine s Tota	l Weig	aht N		sk ratio Idom, 95%Cl	Risk M-H, rando	
Appell 2011		185 6				0.80	[0.62, 1.15]		
Drutz 1999		112 3				1.97	[1.49, 2.62]	22	-
Lee 2002		112 3				1.80	[1.35, 2.40]		-
Malone-Lee 2001		188 7				1.60	[1.31, 2.02]		•
Maj0110-L00 2001	114	55 1	190	, 20.0		1.02	[1.01, 2.02]		
Total (95%CI) Total events	315	<b>500</b> 21:	<b>607</b> 3	7 100.0	0%	1.49	[1.06, 2.10]		<u> </u>
Heterogeneity: Tau <sup>2</sup> = 0.1				<sup>2</sup> = 84%				0.01 0.1	1 10 1
Test for overall effect: Z =								Tolterodine	Oxybutynin
2. Tolterodine 1mg	g vs. Plac		Placebo			Ri	sk ratio	Risk	ratio
Study of Subgroup	Events	Total E	vents T			M-H, f	ixed, 95%Cl	M-H, fixe	
Jacquetin 2001	20	97			27.2%		[1.09, 11.24]		
Millardi 1999	29	123	8	64	72.8%	1.89	[0.92, 3.88]		-
Total (95%CI)		220		115	100.0%	2.33	[1.26, 4.29]		-
	49	220	11	. 13	100.070	2.33	[1.20, 4.23]		
Total events		07) 12 001	H 68					0.01 0.1 1	10 1
Heterogeneity: Chi <sup>2</sup> = 0.8								Placebo	Tolterodine 1m
Test for overall effect: Z =	: 2.70 (p = 0.00	7)							
3. Tolterodine 2mg	g vs. Plac	ebo							
	Tolterodi	ne 2mg	Placet				Risk ratio		ratio
Study of Subgroup	Events	Total	the second s	and the second se	Weight		fixed, 95%Cl	M-H, fix	ed, 95%Cl
Chapple 2004	49	263	13	267	11.6%	3.83	[2.13, 6.88]		
Drutz 1999	33	109	8	56	9.5%	2.12	[1.05, 4.28]		
Jacquetin 2001	35	103	3	51	3.6%	5.78	[1.87, 17.89]		
Millardi 1999	50	129	8	64	9.6%	3.10			
			-				[1.57, 6.14]		-
Swift 2003	127	407	33	410	29.6%	3.88	[2.71, 5.54]	· · · · ·	
Van Kerrebroeck 1998	3	18	1	19	0.9%	3.17	[0.36, 27.72]		-
Van Kerrebroeck 2001	156	512	39	507	35.2%	3.96	[2.85, 5.50]		
				· • - ·					•
Total (95%CI)		1541		1374	100.0%	3.72	[3.05, 4.54]		
Total events	453		105					H +	<u> </u>
Heterogeneity: Chi <sup>2</sup> = 3.54	4. $df = 6 (n = 0)$	(74): $I^2 = 0\%$						0.01 0.1	1 10 1
Test for overall effect: Z =								Placebo	Tolterodine 2n
Study of Subgroup Khullar 2004	Events 112	Total 569	Events 23	Total 258	Weight 22.0%	<u>м-н,</u> 2.21	fixed, 95%Cl [1.45, 3.37]	M-H, fix	ed, 95%Cl
Swift 2003	105	415	33	410	23.1%	3.14	[2.18, 4.54]		-
Van Kerrebroeck 1998	3	17	1	19	0.7%	3.35	[0.38, 29.26]		
Van Kerrebroeck 2001	118	505	39	507	27.1%	3.04	[2.16, 4.27]		
Zinner 2002a	66	291	23	285	16.2%	2.81	[1.80, 4.39]		
Zinner 2002b	52	214	16	200	10.2%	3.37	[1.99, 5.72]		7.00
	52	214	10	222	10.370	5.57	[1.55, 5.72]		•
Total (95%CI)		2011		1701	100.0%	2.88	[2.40, 3.45]	<u> </u>	
Total events	,456	aa) 1 <sup>2</sup> aay	135					0.01 0.1	1 10 1
Heterogeneity: Chi <sup>2</sup> = 2.20	0, af = 5 (p = 0	.82); 1 = 0%							
	11 17 (0 - 0 0							Placebo	Tolterodine 4m
Test for overall effect: Z =		0001)						Placebo	l olterodine 4m
Test for overall effect: Z = 5. Tolterodine 2mg	g vs. Tolt	0001) erodine 2mg T	1mg				Risk ratio	Risk	ratio
Test for overall effect: Z = 5. Tolterodine 2mg Study of Subgroup	g vs. Tolt Tolterodine Events	0001) erodine 2mg T Total	1mg olterodine Events	Tota	al Weigh	t M-H	l, fixed, 95%Cl	Risk	
Test for overall effect: Z = <b>5. Tolterodine 2m</b> <b>Study of Subgroup</b> Jacquetin 2001	g vs. Tolt Tolterodine Events 35	0001) erodine 2mg T Total 103	1mg Tolteroding Events 20	Tota 9	7 40.5%	t M-H %	<ol> <li>fixed, 95%Cl</li> <li>1.65 [1.03, 2.65]</li> </ol>	Risk	ratio
Test for overall effect: Z = <b>5. Tolterodine 2m</b> <b>Study of Subgroup</b> Jacquetin 2001 Millardi 1999	g vs. Tolt Tolterodine Events 35 50	0001) erodine 2mg T Total 103 129	1mg folterodine Events 20 29	<b>Tota</b> 91 123	7 40.5% 3 58.4%	t M-H % %	<b>H, fixed, 95%Cl</b> 1.65 [1.03, 2.65] 1.64 [1.12, 2.42]	Risk	ratio ted, 95%Cl
Test for overall effect: Z = <b>5. Tolterodine 2m</b> <b>Study of Subgroup</b> Jacquetin 2001	g vs. Tolt Tolterodine Events 35	0001) erodine 2mg T Total 103	1mg Tolteroding Events 20	Tota 9	7 40.5% 3 58.4%	t M-H % %	<ol> <li>fixed, 95%Cl</li> <li>1.65 [1.03, 2.65]</li> </ol>	Risk	ratio ted, 95%Cl
Test for overall effect: Z = <b>5. Tolterodine 2m</b> <b>5. Study of Subgroup</b> Jacquetin 2001 Millardi 1999 Van Kerrebroeck 1998	g vs. Tolt Tolterodine Events 35 50	0001) erodine 2mg T Total 103 129 18	1mg folterodine Events 20 29	<b>Tota</b> 97 123 16	7 40.5% 3 58.4% 6 1.0%	t M-H % % % 6.2	<b>H, fixed, 95%Cl</b> 1.65 [1.03, 2.65] 1.64 [1.12, 2.42] 6 [0.35, 112.70]	Risk	ratio ted, 95%Cl
Test for overall effect: Z = <b>5. Tolterodine 2mg</b> <b>Study of Subgroup</b> Jacquetin 2001 Millardi 1999 Van Kerrebroeck 1998 <b>Total (95%CI)</b>	g vs. Tolt Tolterodine Events 35 50 3	0001) erodine 2mg T Total 103 129	1mg folterodine Events 20 29 0	<b>Tota</b> 91 123	7 40.5% 3 58.4% 6 1.0%	t M-H % % % 6.2	<b>H, fixed, 95%Cl</b> 1.65 [1.03, 2.65] 1.64 [1.12, 2.42]	Risk	ratio ted, 95%Cl
Test for overall effect: Z = 5. Tolterodine 2mg Study of Subgroup Jacquetin 2001 Millardi 1999 Van Kerrebroeck 1998 Total (95%CI) Total events	g vs. Tolt Tolterodine Events 35 50 3 88	0001) erodine 2mg T Total 103 129 18 250	1mg folterodine Events 20 29	Tota 97 123 16	7 40.5% 3 58.4% 6 1.0%	t M-H % % % 6.2	<b>H, fixed, 95%Cl</b> 1.65 [1.03, 2.65] 1.64 [1.12, 2.42] 6 [0.35, 112.70]	Risk M-H, fix	ratio red, 95%Cl
Test for overall effect: Z = 5. Tolterodine 2mg Study of Subgroup Jacquetin 2001 Millardi 1999 Van Kerrebroeck 1998 Total (95%CI) Total events Heterogeneity: Chi <sup>2</sup> = 0.83	g vs. Tolt <u>Tolterodine</u> <u>Events</u> 35 50 3 88 2, df = 2 (p = 0.	0001) erodine 2mg T Total 103 129 18 250 66); l <sup>2</sup> = 0%	1mg folterodine Events 20 29 0	Tota 97 123 16	7 40.5% 3 58.4% 6 1.0%	t M-H % % % 6.2	<b>H, fixed, 95%Cl</b> 1.65 [1.03, 2.65] 1.64 [1.12, 2.42] 6 [0.35, 112.70]	Risk M-H, fix	ratio red, 95%CI
Test for overall effect: Z = 5. Tolterodine 2mg Study of Subgroup Jacquetin 2001 Millardi 1999 Van Kerrebroeck 1998 Total (95%CI) Total events	g vs. Tolt <u>Tolterodine</u> <u>Events</u> 35 50 3 88 2, df = 2 (p = 0.	0001) erodine 2mg T Total 103 129 18 250 66); l <sup>2</sup> = 0%	1mg Folterodine Events 20 29 0	Tota 97 123 16	7 40.5% 3 58.4% 6 1.0%	t M-H % % % 6.2	<b>H, fixed, 95%Cl</b> 1.65 [1.03, 2.65] 1.64 [1.12, 2.42] 6 [0.35, 112.70]	Risk M-H, fix	ratio red, 95%Cl
Test for overall effect: Z = 5. Tolterodine 2mg Study of Subgroup Jacquetin 2001 Millardi 1999 Van Kerrebroeck 1998 Total (95%CI) Total events Heterogeneity: Chi <sup>2</sup> = 0.8; Test for overall effect: Z =	g vs. Tolt Tolterodine Events 35 50 3 8 8 2, df = 2 (p = 0 3.47 (p = 0.00	0001) erodine 2mg T Total 103 129 18 250 66); I <sup>2</sup> = 0% 05)	1mg folteroding Events 20 29 0 49	Tota 97 123 16	7 40.5% 3 58.4% 6 1.0%	t M-H % % % 6.2	<b>H, fixed, 95%Cl</b> 1.65 [1.03, 2.65] 1.64 [1.12, 2.42] 6 [0.35, 112.70]	Risk M-H, fix	ratio red, 95%CI
Test for overall effect: Z = 5. Tolterodine 2mg Study of Subgroup Jacquetin 2001 Millardi 1999 Van Kerrebroeck 1998 Total (95%CI) Total events Heterogeneity: Chi <sup>2</sup> = 0.8; Test for overall effect: Z =	g vs. Tolt Tolterodine <u>Events</u> 35 50 3 2, df = 2 (p = 0. 347 (p = 0.00 g vs. Tolt	0001) erodine 2 2mg T Total 103 129 18 250 66); I <sup>2</sup> = 0% 05) erodine	1mg olterodine 20 29 0 49 2mg	97 123 16 230	7 40.5% 3 58.4% 6 1.0%	t <u>M-</u> H % % 6.2 % ·	<b>H, fixed, 95%Cl</b> 1.65 [1.03, 2.65] 1.64 [1.12, 2.42] 6 [0.35, 112.70]	Risk M-H, fix 0.01 0.1 Tolterodine 1mg	ratio ted, 95%Cl
Test for overall effect: Z = 5. Tolterodine 2mg Study of Subgroup Jacquetin 2001 Millardi 1999 Van Kerrebroeck 1998 Total (95%CI) Total events Heterogeneity: Chi <sup>2</sup> = 0.8; Test for overall effect: Z =	g vs. Tolt Tolterodine Events 35 50 3 88 2, df = 2 (p = 0 : 3.47 (p = 0.00 g vs. Tolt Tolterodine	0001) erodine 2mg T Total 103 129 18 250 66); I <sup>2</sup> = 0% 05) erodine 4mg T	1mg ioiterodine 20 29 0 49 29g 0 49	Tota 9 123 16 230	7 40.59 3 58.49 6 1.09 6 100.09	t <u>M-H</u> % % 6.2 % ·	H, fixed, 95%Cl 1.65 [1.03, 2.65] 1.64 [1.12, 2.42] 16 [0.35, 112.70] 1.69 [1.26, 2.28] 1.69 xatio	Risk M-H, fix 0.01 0.1 Tolterodine 1mg Risk	ratio red, 95%Cl
Test for overall effect: Z = <b>5. Tolterodine 2mg</b> <b>Study of Subgroup</b> Jacquetin 2001 Millardi 1999 Van Kerrebroeck 1998 <b>Total (95%CI)</b> Total events Heterogeneity: Chi <sup>2</sup> = 0.8: Test for overall effect: Z = <b>5. Tolterodine 4mg</b> <b>Study of Subgroup</b>	g vs. Tolt Tolterodine Events 35 50 3 88 2, df = 2 (p = 0 3.47 (p = 0.00) g vs. Tolt Tolterodine Events	0001) erodine Total 103 129 18 250 66); l <sup>2</sup> = 0% 05) erodine 4mg T Total	1mg folterodine 20 29 0 49 29g 0 49	Tota 9 12: 16 23 23 e 2mg Total	7 40.59 3 58.49 6 1.09 6 100.09 Weight	t <u>M-H</u> % 6.2 % ·	<ol> <li>fixed, 95%Cl</li> <li>fixed, 1.03, 2.65]</li> <li>fi.64 [1.12, 2.42]</li> <li>f6 [0.35, 112.70]</li> <li>f.69 [1.26, 2.28]</li> <li>fi.69 [1.26, 2.68]</li> <li>fixed, 95%Cl</li> </ol>	Risk M-H, fix 0.01 0.1 Tolterodine 1mg	ratio red, 95%Cl
Test for overall effect: Z = 5. Tolterodine 2mg Study of Subgroup Jacquetin 2001 Millardi 1999 Van Kerrebroeck 1998 Total (95%CI) Total events Heterogeneity: Chi <sup>2</sup> = 0.8: Test for overall effect: Z = 5. Tolterodine 4mg Study of Subgroup Swift 2003	g vs. Tolt Tolterodine <u>Events</u> 35 50 3 88 2, df = 2 (p = 0, : 3.47 (p = 0.00 g vs. Tolt <u>Tolterodine</u> <u>Events</u> 105	0001) erodine 2 2mg T Total 103 129 18 250 66); l <sup>2</sup> = 0% 05) erodine 4mg T Total 415	1mg folterodinu Events 20 29 0 49 49 2mg olterodine Events 127	Tota 97 123 18 230 230 230 230 230 230 230 230 230 230	7 40.59 3 58.49 6 1.09 6 100.09 Weight 44.8%	t M-H % % 6.2 % • F M-H, 0.8	<ul> <li>fixed, 95%Cl</li> <li>1.65 [1.03, 2.65]</li> <li>1.64 [1.12, 2.42]</li> <li>66 [0.35, 112.70]</li> <li>1.69 [1.26, 2.28]</li> <li>1.69 [1.26, 2.28]</li> <li>1.69 [5, 20, 20, 20, 20, 20, 20, 20, 20, 20, 20</li></ul>	Risk M-H, fix 0.01 0.1 Tolterodine 1mg Risk	ratio red, 95%Cl
Test for overall effect: Z = 5. Tolterodine 2mg Study of Subgroup Jacquetin 2001 Millardi 1999 Van Kerrebroeck 1998 Total (95%CI) Total events Heterogeneity: Chi <sup>2</sup> = 0.8; Test for overall effect: Z = 5. Tolterodine 4mg Study of Subgroup Swift 2003 Van Kerrebroeck 1998	g vs. Tolt Tolterodine Events 35 50 3 2, df = 2 (p = 0. 3.47 (p = 0.00 g vs. Tolt Tolterodine Events 105 3	0001) erodine 2 mg T Total 129 18 250 66); I <sup>2</sup> = 0% 05) erodine 4mg T Total 415 17	1mg folteroding Events 20 29 0 49 49 2mg olteroding Events 20 29 0 49	Tota 97 123 18 230 e 2mg Total 407 18	7 40.59 3 58.49 6 1.09 6 100.09 Weight 44.8% 1.0%	t M-H % % 6.2 % • F M-H, 0.8 1.00	H, fixed, 95%Cl 1.65 [1.03, 2.65] 1.64 [1.12, 2.42] 6 [0.35, 112.70] 1.69 [1.26, 2.28] Risk ratio fixed, 95%Cl [0.65, 1.01] 6 [0.25, 4.54]	Risk M-H, fix 0.01 0.1 Tolterodine 1mg Risk	ratio red, 95%Cl
Test for overall effect: Z = 5. Tolterodine 2mg Study of Subgroup Jacquetin 2001 Millardi 1999 Van Kerrebroeck 1998 Total (95%CI) Total events Heterogeneity: Chi <sup>2</sup> = 0.8: Test for overall effect: Z = 5. Tolterodine 4mg Study of Subgroup Swift 2003	g vs. Tolt Tolterodine <u>Events</u> 35 50 3 88 2, df = 2 (p = 0, : 3.47 (p = 0.00 g vs. Tolt <u>Tolterodine</u> <u>Events</u> 105	0001) erodine 2 2mg T Total 103 129 18 250 66); l <sup>2</sup> = 0% 05) erodine 4mg T Total 415	1mg folterodinu Events 20 29 0 49 49 2mg olterodine Events 127	Tota 97 123 18 230 230 230 230 230 230 230 230 230 230	7 40.59 3 58.49 6 1.09 6 100.09 Weight 44.8%	t M-H % % 6.2 % • F M-H, 0.8 1.00	<ul> <li>fixed, 95%Cl</li> <li>1.65 [1.03, 2.65]</li> <li>1.64 [1.12, 2.42]</li> <li>66 [0.35, 112.70]</li> <li>1.69 [1.26, 2.28]</li> <li>1.69 [1.26, 2.28]</li> <li>1.69 [5, 20, 20, 20, 20, 20, 20, 20, 20, 20, 20</li></ul>	Risk M-H, fix 0.01 0.1 Tolterodine 1mg Risk	ratio red, 95%Cl
Test for overall effect: Z = 5. Tolterodine 2mg Study of Subgroup Jacquetin 2001 Millardi 1999 Van Kerrebroeck 1998 Total (95%CI) Total events Heterogeneity: Chi <sup>2</sup> = 0.8: Test for overall effect: Z = 5. Tolterodine 4mg Study of Subgroup Swift 2003 Van Kerrebroeck 1998 Van Kerrebroeck 2001	g vs. Tolt Tolterodine Events 35 50 3 2, df = 2 (p = 0. 3.47 (p = 0.00 g vs. Tolt Tolterodine Events 105 3	0001) erodine 2 2mg T Total 103 129 18 250 666); I <sup>2</sup> = 0% 05) erodine 4mg T Total 415 17 505	1mg folteroding Events 20 29 0 49 49 2mg olteroding Events 20 29 0 49	Tota 9; 122 12 230 230 e 2mg Total 407 18 512	7 40.5% 3 58.4% 6 1.0% 6 100.0% Weight 44.8% 1.0% 54.2%	t M-H % % % 6.2 % ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~	<ul> <li>H, fixed, 95%Cl</li> <li>1.65 [1.03, 2.65]</li> <li>1.64 [1.12, 2.42]</li> <li>166 [0.35, 112.70]</li> <li>1.69 [1.26, 2.28]</li> <li>1.69 [1.26, 2.28]</li> <li>1.69 [1.26, 2.28]</li> <li>1.65 [1.26, 2</li></ul>	Risk M-H, fix 0.01 0.1 Tolterodine 1mg Risk	ratio red, 95%Cl
Test for overall effect: Z = 5. Tolterodine 2mg Study of Subgroup Jacquetin 2001 Millardi 1999 Van Kerrebroeck 1998 Total (95%CI) Total events Heterogeneity: Chi <sup>2</sup> = 0.8; Test for overall effect: Z = 5. Tolterodine 4mg Study of Subgroup Swift 2003 Van Kerrebroeck 1998 Van Kerrebroeck 1998 Van Kerrebroeck 2001 Total (95%CI)	g vs. Tolt Tolterodine Events 35 50 3 2, df = 2 (p = 0. 3.47 (p = 0.00 g vs. Tolt Tolterodine Events 105 3 118	0001) erodine 2 mg T Total 129 18 250 66); I <sup>2</sup> = 0% 05) erodine 4mg T Total 415 17	1mg folteroding Events 20 29 0 49 49 2mg olteroding Events 20 29 0 49	Tota 97 123 18 230 e 2mg Total 407 18	7 40.59 3 58.49 6 1.09 6 100.09 Weight 44.8% 1.0%	t M-H % % % 6.2 % ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~	H, fixed, 95%Cl 1.65 [1.03, 2.65] 1.64 [1.12, 2.42] 6 [0.35, 112.70] 1.69 [1.26, 2.28] Risk ratio fixed, 95%Cl [0.65, 1.01] 6 [0.25, 4.54]	Risk M-H, fix 0.01 0.1 Tolterodine 1mg Risk	ratio red, 95%Cl
Test for overall effect: Z = 5. Tolterodine 2mg Study of Subgroup Jacquetin 2001 Millardi 1999 Van Kerrebroeck 1998 Total (95%CI) Total events Heterogeneity: Chi <sup>2</sup> = 0.8 Test for overall effect: Z = 5. Tolterodine 4mg Study of Subgroup Swift 2003 Van Kerrebroeck 1998 Van Kerrebroeck 1998 Van Kerrebroeck 2001 Total (95%CI) Total events	g vs. Tolt Tolterodine Events 35 50 3 8 2, df = 2 (p = 0 3.47 (p = 0.00 g vs. Tolt Tolterodine Events 105 3 118 226	$\begin{array}{c} \text{0001} \\ \text{erodine} \\ \text{rod} \\ $	1mg folteroding Events 20 29 0 49 49 2mg olteroding Events 20 29 0 49	Tota 9; 122 12 230 230 e 2mg Total 407 18 512	7 40.5% 3 58.4% 6 1.0% 6 100.0% Weight 44.8% 1.0% 54.2%	t M-H % % % 6.2 % ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~	<ul> <li>H, fixed, 95%Cl</li> <li>1.65 [1.03, 2.65]</li> <li>1.64 [1.12, 2.42]</li> <li>166 [0.35, 112.70]</li> <li>1.69 [1.26, 2.28]</li> <li>1.69 [1.26, 2.28]</li> <li>1.69 [1.26, 2.28]</li> <li>1.65 [1.26, 2</li></ul>	Risk M-H, fix	ratio (ed, 95%Cl
Test for overall effect: Z = 5. Tolterodine 2mg Study of Subgroup Jacquetin 2001 Millardi 1999 Van Kerrebroeck 1998 Total (95%CI) Total events Heterogeneity: Chi <sup>2</sup> = 0.8; Test for overall effect: Z = 5. Tolterodine 4mg Study of Subgroup Swift 2003 Van Kerrebroeck 1998 Van Kerrebroeck 2001 Total (95%CI)	g vs. Tolt Tolterodine Events 35 50 3 8 2, df = 2 (p = 0 3.47 (p = 0.00 g vs. Tolt Tolterodine Events 105 3 118 226	$\begin{array}{c} \text{0001} \\ \text{erodine} \\ \text{rod} \\ $	1mg olterodine 29 0 49 2mg olterodine Events 127 3 156	Tota 9; 122 12 230 230 e 2mg Total 407 18 512	7 40.5% 3 58.4% 6 1.0% 6 100.0% Weight 44.8% 1.0% 54.2%	t M-H % % % 6.2 % ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~	<ul> <li>H, fixed, 95%Cl</li> <li>1.65 [1.03, 2.65]</li> <li>1.64 [1.12, 2.42]</li> <li>166 [0.35, 112.70]</li> <li>1.69 [1.26, 2.28]</li> <li>1.69 [1.26, 2.28]</li> <li>1.69 [1.26, 2.28]</li> <li>1.65 [1.26, 2</li></ul>	Risk M-H, fix 0.01 0.1 Tolterodine 1mg Risk M-H, fixe	ratio ratio 1 10 1 Tolterodine 2n d, 95%Cl
Test for overall effect: Z = 5. Tolterodine 2mg Study of Subgroup Jacquetin 2001 Millardi 1999 Van Kerrebroeck 1998 Total (95%CI) Total events Heterogeneity: Chi <sup>2</sup> = 0.8 Test for overall effect: Z = 5. Tolterodine 4mg Study of Subgroup Swift 2003 Van Kerrebroeck 1998 Van Kerrebroeck 1998 Van Kerrebroeck 2001 Total (95%CI) Total events	g vs. Tolt Tolterodine Events 35 50 3 88 2, df = 2 (p = 0, 3.47 (p = 0.00 g vs. Tolt Tolterodine Events 105 3 118 9, df = 2 (p = 0, 226 9, df = 2 (p = 0, 105 3 118	0001) erodine Total 103 129 18 250 66); l <sup>2</sup> = 0% 05) erodine 4mg T. Total 415 17 505 937 87); l <sup>2</sup> = 0%	1mg olterodine 29 0 49 2mg olterodine Events 127 3 156	Tota 9; 122 12 230 230 e 2mg Total 407 18 512	7 40.5% 3 58.4% 6 1.0% 6 100.0% Weight 44.8% 1.0% 54.2%	t M-H % % % 6.2 % ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~	<ul> <li>H, fixed, 95%Cl</li> <li>1.65 [1.03, 2.65]</li> <li>1.64 [1.12, 2.42]</li> <li>166 [0.35, 112.70]</li> <li>1.69 [1.26, 2.28]</li> <li>1.69 [1.26, 2.28]</li> <li>1.69 [1.26, 2.28]</li> <li>1.65 [1.26, 2</li></ul>	Risk M-H, fix	ratio (ed, 95%Cl
Test for overall effect: Z = 5. Tolterodine 2mg Jacquetin 2001 Millardi 1999 Van Kerrebroeck 1998 Total (95%CI) Total events Heterogeneity: Chi <sup>2</sup> = 0.8 Totterodine 4mg Study of Subgroup Swift 2003 Van Kerrebroeck 1998 Van Kerrebroeck 1998 Van Kerrebroeck 1998 Van Kerrebroeck 2001 Total (95%CI) Total events Heterogeneity: Chi <sup>2</sup> = 0.2 Total or verall effect: Z =	g vs. Tolt Tolterodine Events 35 50 3 8 2, df = 2 (p = 0 3.47 (p = 0.00 g vs. Tolt Tolterodine Events 105 3 118 9, df = 2 (p = 0 3.47 (p = 0.00 g vs. Tolt 108 108 108 108 108 108 108 108	0001) erodine Total 103 129 18 250 66); l <sup>2</sup> = 0% 05) erodine 4mg T. Total 415 17 505 937 87); l <sup>2</sup> = 0%	1mg olterodine 29 0 49 2mg olterodine Events 127 3 156	Tota 9; 122 12 230 230 e 2mg Total 407 18 512	7 40.5% 3 58.4% 6 1.0% 6 100.0% Weight 44.8% 1.0% 54.2%	t M-H % % % 6.2 % ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~	<ul> <li>H, fixed, 95%Cl</li> <li>1.65 [1.03, 2.65]</li> <li>1.64 [1.12, 2.42]</li> <li>166 [0.35, 112.70]</li> <li>1.69 [1.26, 2.28]</li> <li>1.69 [1.26, 2.28]</li> <li>1.69 [1.26, 2.28]</li> <li>1.65 [1.26, 2</li></ul>	Risk M-H, fix 0.01 0.1 Tolterodine 1mg Risk M-H, fixe	ratio ratio 1 10 1 Tolterodine 2n d, 95%Cl
Test for overall effect: Z = <b>5. Tolterodine 2mg</b> Jacquetin 2001 Millardi 1999 Van Kerrebroeck 1998 <b>Total (95%CI)</b> Total events Heterogeneity: Chi <sup>2</sup> = 0.8 <b>Tolterodine 4mg</b> <b>Study of Subgroup</b> Swift 2003 Van Kerrebroeck 1998 Van Kerrebroeck 1998 Van Kerrebroeck 1998 Van Kerrebroeck 2001 <b>Total (95%CI)</b> Total events Heterogeneity: Chi <sup>2</sup> = 0.2 Total events Heterogeneity: Chi <sup>2</sup> = 0.2 Test for overall effect: Z =	g vs. Tolt Tolterodine Events 35 50 3 88 2, df = 2 (p = 0. 3.47 (p = 0.00 g vs. Tolt Tolterodine Events 105 3 118 9, df = 2 (p = 0. 3.41 (p = 0.00 9, df = 2 (p = 0. 3.11 (p = 0.00 Placebo	$\begin{array}{c} \text{0001} \\ \text{erodine} \\ \text{rod} \\ $	1mg olterodine 20 29 0 49 2mg olterodine 20 29 0 127 3 156 286	Tota 9; 122 12 230 230 e 2mg Total 407 18 512	7 40.5% 3 58.4% 6 1.0% 6 100.0% Weight 44.8% 1.0% 54.2%	t M-H % % 6.2 % 6.2 % 6.2 % 6.2 % 6.2 % 6.2 % % 6.2 % % % 6.2 % % % % % % % % % % % % % % % % % % %	<ul> <li>4, fixed, 95%Cl</li> <li>1.65 [1.03, 2.65]</li> <li>1.64 [1.12, 2.42]</li> <li>16 [0.35, 112.70]</li> <li>1.69 [1.26, 2.28]</li> </ul>	Risk M-H, fix	ratio red, 95% CI
Test for overall effect: Z = 5. Tolterodine 2mg Study of Subgroup Jacquetin 2001 Millardi 1999 Van Kerrebroeck 1998 Total (95%CI) Total events Heterogeneity: Chi <sup>2</sup> = 0.8: Test for overall effect: Z = 5. Tolterodine 4mg Study of Subgroup Swift 2003 Van Kerrebroeck 1998 Van Kerrebroeck 1998 Van Kerrebroeck 2001 Total events Heterogeneity: Chi <sup>2</sup> = 0.22 Total (95%CI) Total events Heterogeneity: Chi <sup>2</sup> = 0.22 Test for overall effect: Z = 7. Solifenacin vs.	g vs. Tolt Tolterodine Events 35 50 3 2, df = 2 (p = 0, 3.47 (p = 0.00 g vs. Tolt Tolterodine Events 105 3 118 9, df = 2 (p = 0, -3.47 (p = 0.00 g vs. Tolt Tolterodine Events 105 3 118 9, df = 2 (p = 0, -3.11 (p = 0.00 Placebo Solifenacin	0001) erodine Total 103 129 18 250 66); l <sup>2</sup> = 0% 05) erodine 4mg T. Total 415 17 505 937 87); l <sup>2</sup> = 0% 2) Place	1mg olterodinc 20 29 0 49 2mg olterodinc Events 127 3 156 286	Tota 97 123 124 230 230 230 407 18 512 937	7 40.5% 3 58.4% 6 1.0% 6 100.0% Weight 44.8% 1.0% 54.2% 100.0%	t M-H % % 6.2 % - % M-H, 0.8 1.00 0.7 1.07 9.7 9.7 9.7 9.7 9.7 9.7 9.7 9.7 9.7 9.	<ul> <li>4, fixed, 95%Cl</li> <li>1.65 [1.03, 2.65]</li> <li>1.64 [1.12, 2.42]</li> <li>16 [0.35, 112.70]</li> <li>1.69 [1.26, 2.28]</li> </ul>	Risk M-H, fix 0.01 0.1 Tolterodine 1mg Risk M-H, fixe 0.1 0.2 0.5 Tolterodine 2mg Risk	ratio ratio 1 10 1 Tolterodine 2n d, 95%Cl
Test for overall effect: Z = 5. Tolterodine 2mg Study of Subgroup Jacquetin 2001 Millardi 1999 Van Kerrebroeck 1998 Total (95%CI) Total events Heterogeneity: Chi <sup>2</sup> = 0.8; Test for overall effect: Z = 5. Tolterodine 4mg Study of Subgroup Swift 2003 Van Kerrebroeck 1998 Van Kerrebroeck 1998 Van Kerrebroeck 2001 Total (95%CI) Total events Heterogeneity: Chi <sup>2</sup> = 0.2; Test for overall effect: Z = 7. Solifenacin vs. Study of Subgroup	g vs. Tolt Tolterodine Events 35 50 3 2, df = 2 (p = 0, 0) g vs. Tolt Tolterodine Events 105 3 118 9, df = 2 (p = 0, 0) 9, df = 2 (p = 0, 0) 3, 118 226 9, df = 2 (p = 0, 0) Solifenacin Events To	0001) erodine 2 mg T Total 129 18 250 66); l <sup>2</sup> = 0% 05) erodine 4mg T Total 415 17 505 937 87); l <sup>2</sup> = 0% 2) Play paid Event	1mg otterodine Events 20 29 0 49 2mg otterodine Events 126 286 286 286	Tota 97 123 16 230 e 2mg Total 407 18 512 937 937	7 40.5% 3 58.4% 6 1.0% 6 100.0% Weight 44.8% 1.0% 54.2% 100.0% ht M-I	nt M-H % % % 6.2 % - FI, 0.8 1.00 0.7 1.00 0.00 0	<ul> <li>fixed, 95%Cl</li> <li>1.65 [1.03, 2.65]</li> <li>1.64 [1.12, 2.42]</li> <li>66 [0.35, 112.70]</li> <li>1.69 [1.26, 2.28]</li> <li>1.69 [1.26, 2.28]</li> <li>1.69 [1.26, 2.28]</li> <li>1.69 [1.26, 2.28]</li> <li>1.69 [0.25, 4.54]</li> <li>7 [0.62, 0.94]</li> <li>2 [0.68, 0.92]</li> <li>ratio</li> <li>om, 95%Cl</li> </ul>	Risk M-H, fix	ratio ratio 1 10 1 Tolterodine 2n d, 95%Cl
Test for overall effect: Z = 5. Tolterodine 2mg Study of Subgroup Jacquetin 2001 Millardi 1999 Van Kerrebroeck 1998 Total (95%CI) Total events Heterogeneity: Chi <sup>2</sup> = 0.8: Test for overall effect: Z = 5. Tolterodine 4mg Study of Subgroup Swift 2003 Van Kerrebroeck 1998 Van Kerrebroeck 2001 Total (95%CI) Total events Heterogeneity: Chi <sup>2</sup> = 0.22 Total (95%CI) Total events Heterogeneity: Chi <sup>2</sup> = 0.22 Test for overall effect: Z = 7. Solifenacin vs.	g vs. Tolt Tolterodine Events 35 50 3 2, df = 2 (p = 0, 0) g vs. Tolt Tolterodine Events 105 3 118 9, df = 2 (p = 0, 0) 9, df = 2 (p = 0, 0) 3, 118 226 9, df = 2 (p = 0, 0) Solifenacin Events To	0001) erodine 2 mg T Total 129 18 250 66); l <sup>2</sup> = 0% 05) erodine 4mg T Total 415 17 505 937 87); l <sup>2</sup> = 0% 2) Play paid Event	1mg olterodinc 20 29 0 49 2mg olterodinc Events 127 3 156 286	Tota 97 123 16 230 e 2mg Total 407 18 512 937 937	7 40.5% 3 58.4% 6 1.0% 6 100.0% Weight 44.8% 1.0% 54.2% 100.0% ht M-I	nt M-H % % % 6.2 % - FI, 0.8 1.00 0.7 1.00 0.00 0	<ul> <li>4, fixed, 95%Cl</li> <li>1.65 [1.03, 2.65]</li> <li>1.64 [1.12, 2.42]</li> <li>16 [0.35, 112.70]</li> <li>1.69 [1.26, 2.28]</li> </ul>	Risk M-H, fix 0.01 0.1 Tolterodine 1mg Risk M-H, fixe 0.1 0.2 0.5 Tolterodine 2mg Risk	ratio ratio 1 10 1 Tolterodine 2n d, 95%Cl
Test for overall effect: Z = 5. Tolterodine 2mg Study of Subgroup Jacquetin 2001 Millardi 1999 Van Kerrebroeck 1998 Total (95%CI) Total events Heterogeneity: Chi <sup>2</sup> = 0.8; Test for overall effect: Z = 5. Tolterodine 4mg Study of Subgroup Swift 2003 Van Kerrebroeck 1998 Van Kerrebroeck 2001 Total (95%CI) Total events Heterogeneity: Chi <sup>2</sup> = 0.2; Test for overall effect: Z = 7. Solifenacin vs. Study of Subgroup	g vs. Tolt Tolterodine Events 35 50 3 2, df = 2 (p = 0.0) g vs. Tolt Tolterodine Events 105 3 118 9, df = 2 (p = 0.0) Placebo Solifenacin Events To 80 50 50 50 3 118 11	0001) erodine 2 mg T 103 129 18 250 66); l <sup>2</sup> = 0% 05) erodine 4mg T Total 415 17 505 937 87); l <sup>2</sup> = 0% 937 87); l <sup>2</sup> = 0% 2) Plat 505	1mg otterodine Events 20 29 0 49 2mg otterodine Events 126 286 286 286	Tota 9 122 16 230 e 2mg Total 407 18 512 937 Weigl 38.3	7 40.5% 3 58.4% 6 1.0% 6 100.0% Weight 44.8% 1.0% 54.2% 100.0% ht M-I 3%	t M-H % % % 6.2 % % 6.2 % % % % % % % % % % % % % % % % % % %	<ul> <li>fixed, 95%Cl</li> <li>1.65 [1.03, 2.65]</li> <li>1.64 [1.12, 2.42]</li> <li>66 [0.35, 112.70]</li> <li>1.69 [1.26, 2.28]</li> <li>1.69 [1.26, 2.28]</li> <li>1.69 [1.26, 2.28]</li> <li>1.69 [1.26, 2.28]</li> <li>1.69 [0.25, 4.54]</li> <li>7 [0.62, 0.94]</li> <li>2 [0.68, 0.92]</li> <li>ratio</li> <li>om, 95%Cl</li> </ul>	Risk M-H, fix 0.01 0.1 Tolterodine 1mg Risk M-H, fixe 0.1 0.2 0.5 Tolterodine 2mg Risk	ratio ratio 1 10 1 Tolterodine 2n d, 95%Cl

	Solifena	acin	Placel	bo		Risk ratio	Risk ratio
Study of Subgroup	Events	Total	Events	Total	Weight	M-H, random, 95%Cl	M-H, random, 95%Cl
Cardozo 2008	80	505	6	223	38.3%	5.89 [2.61, 13.30]	
Karram 2009	94	372	33	367	61.7%	2.81 [1.94, 4.07]	=
Total (95%CI)		877		590	100.0%	3.73 [1.80, 7.72]	+
Total events	174		39				
Heterogeneity: Tau <sup>2</sup> = 0	0.19, Chi <sup>2</sup> = 2	2.80, df =	1 (p = 0.0)	9); I <sup>2</sup> = 6	4%		
Test for overall effect: Z	z = 3.54 (p =	0.01 0.1 1 10 100 Placebo Solifenacin					

Fig. 5 Forest plot – Risk Ratio (RR) of dry mouth.

#### 1. Oxybutynin vs. Tolterodine

	Oxybuty	nin	Toltero	dine		Risk ratio	Risk ratio
Study of Subgroup	Events	Total	Events	Total	Weight	M-H, fixed, 95%Cl	M-H, fixed, 95%Cl
Appell 2011	13	185	12	193	42.5%	1.13 [0.53, 2.41]	
Malone-Lee 2001	11	188	16	190	57.5%		
Total (95%CI)		373		383	100.0%	0.88 [0.52, 1.49]	+
Total events	24		28				
Heterogeneity: Chi <sup>2</sup> = 0.8 Test for overall effect: Z			0%				0.01 0.1 1 10 100 Oxybutynin Tolterodine

# 2. Tolterodine 2mg vs. Placebo

	Tolterodine	Placebo			Risk ratio	Risk ratio			
Study of Subgroup	Events	Total	Events	Total	Weight	M-H, fixed, 95%Cl	M-H, fixed, 95%Cl		
Chapple 2004 Jacquetin 2001	7	263 103	5 2	267 51	11.4% 6.1%	1.42 [0.46, 4.42] 0.50 [0.07, 3.41]			
Swift 2003	27	407	14	410	31.9%	1.94 [1.03, 3.65]			
Van Kerrebroeck 2001	35	512	22	507	50.6%	1.58 [0.94, 2.65]	-		
Total (95%CI)		1285		1235	100.0%	1.61 [1.11, 2.32]	•		
Total events	71		43						
Heterogeneity: $Chi^2 = 1.83$ , Test for overall effect: Z = 2	0.01 0.1 1 10 10 Placebo Tolterodine 2mg								
	T lacebo Tollerodine zing								

#### 3. Tolterodine 4mg vs. Placebo

Tolterodine 4	Place	00		Risk ratio	Risk ratio			
Events	Total	Events	Total	Weight	M-H, fixed, 95%Cl	M-H, fixed, 95%Cl		
9	569	2	258	4.5%	2.04 [0.44, 9.38]			
27	415	14	410	23.2%	1.91 [1.01, 3.58]			
30	505	22	507	36.2%	1.37 [0.80, 2.34]			
17	291	12	285	20.0%	1.39 [0.67, 2.85]			
13	214	10	222	16.2%	1.35 [0.60, 3.01]	-		
	1994		1682	100.0%	1.52 [1.11, 2.09]	•		
96		60						
Heterogeneity: $Chi^2 = 0.93$ , df = 4 (p = 0.92); $i^2 = 0\%$								
60 (p = 0.009)						0.01 0.1 1 10 Placebo Tolterodine 4mg		
	<b>Events</b> 9 27 30 17 13 96	$9 569  27 415  30 505  17 291  13 214  1994  96  df = 4 (p = 0.92); l^2 = 0\%$	Events         Total         Events           9         569         2           27         415         14           30         505         22           17         291         12           13         214         10           IP94           96         60           df = 4 (p = 0.92); l <sup>2</sup> = 0%         50%	Events         Total         Events         Total           9         569         2         258           27         415         14         410           30         505         22         507           17         291         12         285           13         214         10         222           1994         1682           96         60         60           aff = 4 (p = 0.92); l <sup>2</sup> = 0%         50%         50%	Events         Total         Events         Total         Weight           9         569         2         258         4.5%           27         415         14         410         23.2%           30         505         22         507         36.2%           17         291         12         285         20.0%           13         214         10         222         16.2%           1994         1682         100.0%           96         60         60         df = 4 (p = 0.92); l <sup>2</sup> = 0%         10         225         100.0%         10	Events         Total         Events         Total         Weight         M-H, fixed, 95%CI           9         569         2         258         4.5%         2.04 [0.44, 9.38]           27         415         14         410         23.2%         1.91 [1.01, 3.58]           30         505         22         507         36.2%         1.37 [0.80, 2.34]           17         291         12         285         2.0.0%         1.35 [0.60, 3.01]           13         214         10         222         16.2%         1.35 [0.60, 3.01]           994         1682         100.0%         1.52 [1.11, 2.09]           96         60         40         40         40         40		

#### 4. Solifenacin vs. Placebo

	Solifena	Solifenacin				Risk ratio	Risk ratio
Study of Subgroup	Events	Total	Events	Total	Weight	M-H, random, 95%Cl	M-H, random, 95%Cl
Cardozo 2008	35	505	2	223	41.3%	7.73 [1.87, 31.85]	
Karram 2009	55	372	34	367	58.7%	1.60 [1.07, 2.39]	
Total (95%CI)		877		590	100.0%	3.06 [0.62, 15.17]	
Total events	90		36				20. ISBN 01. ISBN 01.
Heterogeneity: Tau <sup>2</sup> = 1	.09, Chi <sup>2</sup> = 4.88	0.05 0.2 1 5 20					
Test for overall effect: Z	= 1.37 (p = 0.1	Placebo Solifenacin					

Fig. 6 Forest plot – Risk Ratio (RR) of constipation.

This systematic review showed that there is no significant difference in the mean decrease in UUI episodes per day between oxybutynin and tolterodine. Although there was a trend of a higher reduction in UUI episodes with the use of oxybutynin, the difference was not statistically significant. It was not possible to perform comparisons between oxybutynin versus solifenacin, oxybutynin versus darifenacin, tolterodine versus solifenacin, tolterodine versus darifenacin, and solifenacin versus darifenacin due to limitations in data reporting (that is, studies without a measure of variation) and the lack of similarity in measures.

Regarding the decrease in the number of micturitions per day, which was another important primary outcome, the results favored tolterodine in its various dosages and solifenacin when compared with placebo. The comparison between oxybutynin and tolterodine showed no significant difference in treatment efficacy across any of the outcomes; the same was found for the comparisons of tolterodine in its various dosages. As result of the relative paucity of data that qualified for inclusion in the meta-analysis – and that directly compared pharmacological agents –, it is impossible to report definitively whether any specific agent is superior to another in terms of efficacy.

Antimuscarinic agents may be associated with adverse effects. The human bladder tissue contains M2 and M3 muscarinic receptors. The M3 subtype has been identified as the primary mediator of detrusor contraction in response to cholinergic activation.<sup>52,53</sup> Different subtypes of muscarinic receptors are widely distributed in the body. M1 receptors in the brain and salivary glands are involved in cognition and in the

production of mucous saliva;<sup>54,55</sup> M2 receptors in the cardiovascular system play a role in mediating heart rate and cardiac output;<sup>56</sup> and M5 receptors in the eye are involved in ciliary muscle contraction.<sup>57–59</sup> As a result, antimuscarinic agents, which bind to some or all of these receptors, are effective in treating OAB symptoms, but they may also be associated with adverse effects such as dry mouth, constipation, cognitive impairment, tachycardia, and blurred vision.<sup>57</sup> This systematic review showed that oxybutynin was associated with significantly higher rates of dry mouth when compared with tolterodine. When compared with placebo, tolterodine, in its various dosages, and solifenacin were associated with significantly higher rates of dry mouth. The group of patients that used tolterodine 4 mg presented lower risk when compared with the group treated with tolterodine 2 mg. This can be explained by the fact that tolterodine 4 mg is an extended-release (ER) presentation. Compared with the immediate-release drug, tolterodine ER releases the drug in a steady and constant manner, thus lowering peaks. This translates into more constant serum concentrations and theoretically improves patient tolerability.<sup>60</sup> Concerning constipation, differences were not found between oxybutynin and tolterodine. Significantly high rates of constipation were found in patients treated with tolterodine 2 mg and 4 mg when compared with placebo.

The current data demonstrate that a substantial proportion of patients discontinue anticholinergic drugs, with 75–90% of patients discontinuing therapy within 12 months. Among those studies that provided information about the reasons for the discontinuation of the therapy, the most frequently cited reasons were that the medication did not work as expected, and that the medication's side effects were not desirable.<sup>7</sup> We did not find a statistical difference associated with withdrawals resulting from drug-related adverse effects.

New drugs for the treatment of OAB are emerging, such as imidafenacin and tarafenacin, but they are not available in Brazil yet. Mirabegron, a  $\beta$ 3-adrenoreceptor agonist, has just recently been released into the Brazilian market with some promising results, especially when associated with regular antimuscarinic drugs.<sup>61,62</sup>

The quality of the available evidence that supports these results is moderate. The main limitation of the available evidence concerning OAB treatment is that although there is a large amount of RCTs, it is not possible to combine all of the data in a meta-analysis due to their heterogeneity. If the goal of a meta-analysis is to estimate the MD between two treatments, then the means, sample sizes, and a measure of variation (standard deviation, standard error, or a confidence interval) are required. Thus, many of the available RCTs on OAB treatment did not contribute to the meta-analysis, and were excluded from our study. Unfortunately, we discovered a lack of high-quality evidence pertaining to the available drugs and dosages for the treatment of OAB in Brazil that can inform clinical decision making for patients and care providers.

In summary, the results of this meta-analysis suggest that there is a moderate to high quality of evidence supporting the benefits of using anticholinergic drugs in alleviating OAB symptoms when compared with placebo. Despite its lower improvement in primary and secondary outcomes when compared with anticholinergics, the use of placebo contributed to many of the improvements in OAB symptoms. It is still not clear if any one specific drug available in Brazil has any advantage over the others. The use of these drugs is associated with adverse effects (mainly dry mouth and constipation), although the use of these agents is not related to an increase in the number of withdrawals.

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