## SUPPLEMENTARY MATERIAL

# **CONTENTS:**

- 1. Assessment of heterogeneity according to type of controls
- 2. Sensitivity analysis
- 3. Publication bias

## 1. Assessment of heterogeneity according to type of controls



Supplementary Figure 1: Forest plot showing the effect of varicocele on sperm count according to control group type.



Supplementary Figure 2: Forest plot showing the effect of varicoccele on sperm motility according to the control group type.



Supplementary Figure 3: Forest plot showing the effect of varicocele on sperm morphology according to the control group type.

#### 2. Sensitivity analyses

#### **Sperm Count Meta-Analysis**

Study names		Statistics with study removed									
	Point	Standard error	Variance	Lower Limit	Upper Limit	z-Value	p-Value				
Abd-Elmoaty 2010	-41.593	8.715	75.946	-58.673	-24.512	-4.773	0.000				
Blumer 2011	-46.053	7.988	63.801	-61.708	-30.397	-5.766	0.000				
Camejo 2011	-46.607	8.051	64.813	-62.386	-30.828	-5.789	0.000				
Chan 2013	-46.442	8.022	64.360	-62.166	-30.718	-5.789	0.000				
Mohamed 2011	-40.341	8.600	73.952	-57.196	-23.487	-4.691	0.000				
Mostafa T 2014	-41.972	8.851	78.344	-59.320	-24.624	-4.742	0.000				
Sadek 2011	-44.025	8.686	75.439	-61.048	-27.001	-5.069	0.000				
Tawadrous 2013	-41.549	10.182	103.677	-61.651	-21.637	-4.085	0.000				
Vivas-Acevedo 2010	-53.121	5.183	26.860	-63.279	-42.963	-10.250	0.000				
Vivas-Acevedo 2014	-45.174	7.882	62.128	-63.623	-32.726	-6.112	0.000				
	-44.886	7.704	59.351	-50.986	-29.785	-5.826	0.000				





Supplementary Figure 4: Sensitivity analysis for the effect of varicocele on sperm count.

### Sperm Motility Meta-Analysis

Study names	Statistics with study removed								
	Point	Standard error	Variance	Lower Limit	Upper Limit	z-Value	p-Value	WI	
Abd-Elmoaty 2010	-25.317	5.012	25.120	-35.140	-15.494	-5.051	0.000	_ <b>→</b>	
Blumer 2011	-29.422	4.499	20.242	-38.240	-20.604	-6.540	0.000		
Camejo 2011	-26.242	5.028	25.279	-36.097	-16.388	-5.219	0.000		
Chan 2013	-29.118	4.338	18.815	-37.620	-20.617	-6.713	0.000		
Mohamed 2011	-26.028	4.907	24.046	-35.645	-16.411	-5.304	0.000	_ <b>→</b>	
Mostafa T 2014	-25.586	5.048	25.483	-35.480	-15.692	-5.068	0.000	_ <b>→</b>	
Sadek 2011	-26.327	4.904	24.946	-35.938	-16.716	-5.369	0.000	_ <b>→</b>	
Tawadrous 2013	-24.851	4.121	16.979	-32.927	-16.775	-6.031	0.000	_ <b>→</b>	
Vivas-Acevedo 2010	-27.840	4.635	21.485	-36.925	-18.755	-6.006	0.000		
Vivas-Acevedo 2014	-27.439	4.881	23.828	-37.006	-17.872	-5.621	0.000		
	-26.818	4.533	20.548	-35.702	-17.933	-5.916	0.000		

Difference in means (95% CI) with study removed



Supplementary Figure 5: Sensitivity analysis for the effect of varicocele on sperm motility.

# Sperm Morphology Meta-Analysis

Study names				Statistics	with study re		Difference in means (95% CI)					
	Point	Standard error	Variance	Lower Limit	Upper Limit	z-Value	p-Value			with	study remove	ea
Abd-Elmoaty 2010	-16.631	5.521	30.485	-27.452	-5.809	-3.012	0.003	1	<b>+_</b>	- 1		1
Blumer 2011	-22.309	6.920	35.045	-33.912	-10.706	-3.768	0.000					
Camejo 2011	-20.786	6.110	37.336	-32.762	-8.810	-3.402	0.001			-		
Mostafa T 2014	-18.723	6.691	32.889	-29.877	-7.569	-3.290	0.001			-   -		
Sadek 2011	-20.746	6.189	38.300	-32.876	-8.616	-3.352	0.001			-		
Tawadrous 2013	-14.820	3.945	15.563	-22.553	-7.088	-3.757	0.000			-		
Vivas-Acevedo 2010	-21.770	6.326	40.019	-34.169	-9.371	-3.441	0.001			·		
Vivas-Acevedo 2014	-22.088	6.217	38.645	-34.272	-9.904	-3.553	0.000			·		
	-19.737	6.347	28.595	-30.218	-9.257	-3.691	0.000					
								-50.00	-25.00	0.00	25.00	50.00
									Varicocele		Control	

Supplementary Figure 6: Sensitivity analysis for the effect of varicocele on sperm morphology.

# 3. Publication bias

If the meta-analysis had captured all the relevant studies we would expect the funnel plot to be symmetric. That is, we would expect studies to be dispersed equally on either side of the overall effect. As seen in Supplementary Figure 7, the funnel plot is actually

symmetric, with a similar number of studies falling toward the left and right of the mean effect. The tunnel plot results are confirmed by the 'trim-and-fill' method, which initially trims the asymmetric studies from the left-hand side to locate the unbiased effect (in an iterative procedure) and then fills the plot by re-inserting the trimmed studies on the left as well as their imputed counterparts to the right the mean effect.

The program is looking for missing studies, based on random effects models, only to the right side of the mean effect (these parameters are set by the user). Using these parameters, the method suggests that no studies are missing.

Under the fixed effect models, the point estimate (95% confidence interval) for sperm count in the combined studies is -63.04115 (-64.82480, -61.25751). Using trim-and-fill, these values are unchanged. Under the random effects models, the point estimate (95% confidence interval) for sperm count in the combined studies is -44.88577 (-59.98632, -29.78521). Using trim-and-fill, these values are unchanged (see Supplementary Table 1).



Supplementary Figure 7: Funnel plot for the meta-analysis of varicocele on sperm count.

Supplementary	Table	1:	Duval	and	Tweedie's	trim	and	fill
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		Fixed effe	cts		Q value			
	Studies trimmed	Point estimate	Lower limit	Upper limit	Point estimate	Lower limit	Upper limit	
Observed values		-63.04115	-64.82480	-61.25751	-44.88577	-59.98632	-29.78521	468.63296
Adjusted values	0	-63.04115	-64.82480	-61.25751	-44.88577	-59.98632	-29.78521	468.63296