Supplemental Online Content

van der Vaart LR, Vollebregt A, Milani AL, et al. Effect of pessary vs surgery on patient-reported improvement in patients with symptomatic pelvic organ prolapse: a randomized clinical trial. *JAMA*. doi:10.1001/jama.2022.22385

This supplemental material has been provided by the authors to give readers additional information about their work.

eAppendix. Method for Multiple Imputation

Imputation of missing data for the primary endpoint, was done after rejecting the alternative hypothesis of non-inferiority. In light of this finding, imputation was exploratory to assess the impact of missing data on the effect estimates, though results after imputation could not contribute towards an overall claim of non-inferiority.

Missing data of the primary endpoint was imputated using multiple imputation under the missing at random assumption.

Sixteen percent (71 / 439) of all patients in the population as randomized had missing data for the primary endpoint at 24 months follow-up. For the per-protocol population, this was 17% (47 / 271).

Treatment allocated, age, smoking, BMI (categorised using dummy variables as <18.5, 18.5 to 25, and > 25), parity, highest level of perineal tear in obstetric history, family history of prolapse, history of uterine surgery, menopausal status, diabetes vaginal atrophy, positive stress test, prolapse stage, and the duration of complaints were baseline variables included in the imputation model. Discontinuation or additional surgery and reported severity of complaints at 12 months follow-up were also included as predictors.

Some predictive variables had missing observations. This data was imputed first.

Patterns of missingness were suggestive of missingness at random. Imputation was done using SAS 9.4, with fully conditional specification creating 25 imputation datasets.

Model convergence was observed for all models. Observed values after imputation were plausible for the variables concerned. Weighing of results was done using Rubin's rules.

eTable 1. Treatment Details at Initiation		
	Surgery group (*n*=221)	**Pessary group (*n*=218)**
Initiated treatment as randomised [a]	199 (90%)	218 (100%)
Pessary type:	n/a	
Ring	6 (2.7%)	92 (42.2%)
Ring with support	4 (1.8%)	119 (54.6%)
Cube	0 (0%)	4 (1.8%)
Donut	0 (0%)	1 (0.5%)
Gellhorn	0 (0%)	1 (0.5%)
Unknown	2 (0.9%)	1 (0.5%)
Pessary self-managed	5 (2.3%)	154 (71.0%)
If not:	7 (3.2%)	62 (28.4%)
Unable to	0 (0%)	8 (12.9%)
Preference	1 (14.3%)	54 (87.1%)
Unknown	6 (85.7%)	0 (0%)
Topical oestrogens		
Starting	23 (10.4%)	21 (9.6%)
Continuation	79 (35.7%)	79 (36.2%)
Surgery type [b]		n/a
Anterior compartment	15 (6.8%)	
Posterior compartment	18 (8.1%)	
Apical compartment	11 (4.9%)	
Anterior + posterior compartment	10 (4.5%)	
Anterior + posterior + apical compartment	9 (4.0%)	
Anterior + apical compartment	135 (61.1%)	
Posterior + apical compartment	1 (0.5%)	

a. Surgery group: 12 women decided not to undergo surgery but start with a pessary, 4 did not have surgery because of another disease with higher priority, 5 withdrew informed consent before start study and 1 woman died (unrelated to the study).
b. Anterior compartment includes anterior colporrhaphy, posterior compartment includes posterior colporrhaphy, apical compartment includes either sacrospinous hysteropexy, Modified Manchester-Fothergill, vaginal hysterectomy or laparoscopic sacrocolpopexy.

eTable 2. Main Outcomes at 24 Months After Multiple Imputation in the Population as Randomized

			Population as randomized analysis
	Surgery group (n=221)	Pessary group (n=218)	Risk difference (90% CI)
PGI-I: improvement – no./total no. [a]	132/162 (81.5%)	132/173 (76.3%)	-4.90% (-12.94 to 3.14)

CI is confidence interval.
a. no. of patients with primary outcome reported before imputation. No. imputations: 25.
Non-inferiority margin: -10%.

eTable 3. Main Outcomes at 24 Months After Multiple Imputation in Per-Protocol Analysis			
			Per-protocol analysis
	Surgery group (n=190)	Pessary group (n=81)	Risk difference (90% CI)
PGI-I: improvement – no./total no. [a]	125/150 (83.3%)	52/74 (70.3%)	-10.61% (-20.89 to -0.33)

CI is confidence interval.
a. no. of patients with primary outcome reported before imputation. No. imputations: 25.
Non-inferiority margin: -10%.

eTable 4. Change of Sexual Status Within 24 Months			
	Surgery group (*n*=160)	**Pessary group (*n*=167)**	**Relative risk (95% CI), *p*-value**
NSA at baseline	73	66	
Remained NSA	62 (84.9%)	56 (84.8%)	
Change from NSA to SA	11 (15.1%)	10 (15.2%)	1.00 (0.4 – 2.2), 0.99
SA at baseline	87	101	
Remained SA	73 (83.9%)	83 (82.2%)	
Change from SA to NSA	14 (16.1%)	18 (17.8%)	0.90 (0.5 – 1.7), 0.75
Change in sexual status could be calculated for 167 women in the pessary group and 160 women in the surgery group.			

eTable 5. Details About Women Who Had Additional Visit Due to a Change in Size/Shape of Pessary			
Type of continued treatment after change in size/shape of pessary	**No attempt to change size/shape of pessary**	**One attempt to change size/shape of pessary**	**Two attempts to change/size shape of pessary**
Continued with pessary therapy (n = 30)	n/a	26	4
Switched from pessary to surgery due to pessary expulsion (n = 38)	28	8	2
Switched from pessary to surgery due to other reason than pessary expulsion (n = 32)	n/a	29	3
Stopped with any type of treatment (n = 1)	n/a	1	n/a
This table includes information on all women who changed their size/shape of pessary, regardless of whether they continued with a pessary, switched to surgery (for any reason) or discontinued any type of treatment.			