## Efficacy and safety of Adipose-derived Stem Cell Therapy for the Treatment of Complex Perianal Fistula Not Associated with Crohn's Disease: A Systematic Review and Meta-Analysis

# Indiana University

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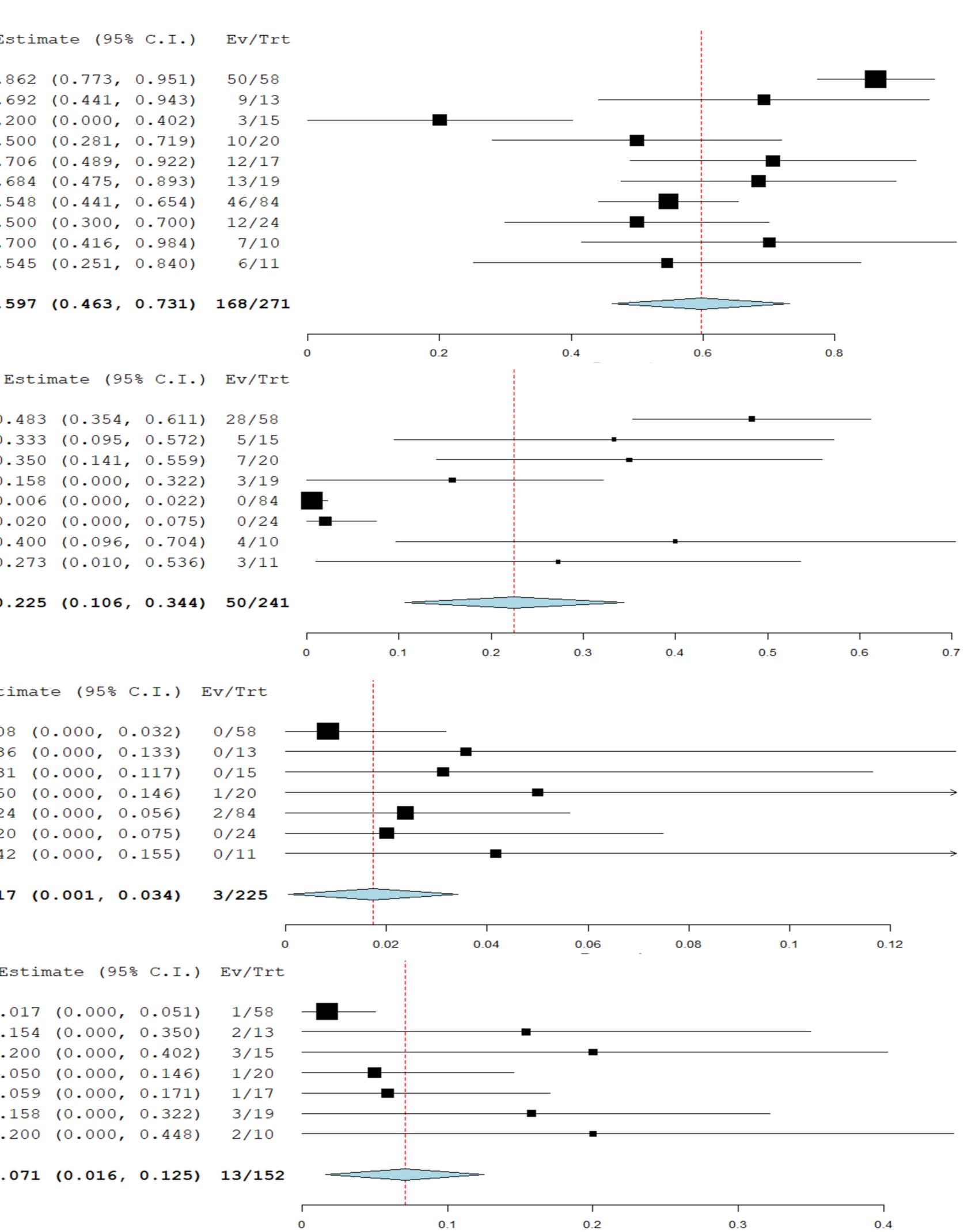
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A)	Studies	Estin	nate (95	€ C.I.)	Ev/Trt
	Ascanelli, 2021	0.862	(0.773,	0.951)	50/58
	Choi, 2017	0.692	(0.441,	0.943)	9/13
	Dozois, 2019	0.200	(0.000,	0.402)	3/15
	Garcia-Arranz 2020	0.500	(0.281,	0.719)	10/20
	Garcia-Olmo 2009	0.706	(0.489,	0.922)	12/17
	Gutierrez, 2021	0.684	(0.475,	0.893)	13/19
	Herreros, 2012	0.548	(0.441,	0.654)	46/84
	Herreros, 2019	0.500	(0.300,	0.700)	12/24
	Topal, 2019	0.700	(0.416,	0.984)	7/10
	Zhang, 2020	0.545	(0.251,	0.840)	6/11
	Overall (I^2=81.8 % , P< 0.001)	0.597	(0.463,	0.731)	168/271
B)	B) Studies Estimate (95% C.I.)				Ev/Trt

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Ascanelli, 2021	0.483	(0.354,	0.611)	28/58
Dozois, 2019	0.333	(0.095,	0.572)	5/15
Garcia-Arranz 2020	0.350	(0.141,	0.559)	7/20
Gutierrez, 2021	0.158	(0.000,	0.322)	3/19
Herreros, 2012	0.006	(0.000,	0.022)	0/84
Herreros, 2019	0.020	(0.000,	0.075)	0/24
Topal, 2019	0.400	(0.096,	0.704)	4/10
Zhang, 2020	0.273	(0.010,	0.536)	3/11

Overall (I^2=91.37 %, P< 0.001) 0.225 (0.106, 0.344) 50/241

C) s	Studies	Estin	nate (95	% C.I.)	Ev/Trt	
A	scanelli, 2021	0.008	(0.000,	0.032)	0/58	
C	Choi, 2017	0.036	(0.000,	0.133)	0/13	
D	Dozois, 2019	0.031	(0.000,	0.117)	0/15	
G	Sarcia-Arranz 2020	0.050	(0.000,	0.146)	1/20	
Н	lerreros, 2012	0.024	(0.000,	0.056)	2/84	
Н	lerreros, 2019	0.020	(0.000,	0.075)	0/24	
Z	Zhang, 2020	0.042	(0.000,	0.155)	0/11	
c	Overall (I^2=0 % , P=0.954)	0.017	(0.001,	0.034)	3/225	
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))	Studies	Estin	Ev/Trt		
	Ascanelli, 2021	0.017	(0.000,	0.051)	1/58
	Choi, 2017	0.154	(0.000,	0.350)	2/13
	Dozois, 2019	0.200	(0.000,	0.402)	3/15
	Garcia-Arranz 2020	0.050	(0.000,	0.146)	1/20
	Garcia-Olmo 2009	0.059	(0.000,	0.171)	1/17
	Gutierrez, 2021	0.158	(0.000,	0.322)	3/19
	Topal, 2019	0.200	(0.000,	0.448)	2/10
	Overall (I^2=34.48 % , P=0.165)	0.071	(0.016,	0.125)	13/152



### Introduction

- Given the high recurrence rate and the risk of fecal incontinence with surgical options, Injection of adipose tissue-derived stem cells (ASC) has been arising as a novel method for treating complex perianal fistulas (CPAF).
- Therefore, we conducted a meta-analysis to evaluate the efficacy and safety of ASC in the management of CPAF not associated with Crohn's disease.

#### Methods

- We systematically searched Medline and Embase databases through April 20, 2022, for all studies that assessed the efficacy and safety of ASC for the treatment of CPAF not associated with Crohn's disease.
- We excluded patients with rectovaginal fistulas and perianal fistulas associated with Crohn's disease.
- Our primary outcome was the complete closure.
- The secondary outcomes included overall nonserious adverse events (NSAE), serious adverse events (SAE), and perianal abscess rate.
- All meta-analyses were conducted using a random-effect model.



### Results

- Ten studies (eight clinical trials and two observational studies) with 271 patients were included in the pooled analysis.
- The pooled complete closure rate was 59.7% (95% confidence interval (CI): 0.46-0.73, Figure 1A).
- On subgroup analysis based on country of origin, six studies with 213 patients were conducted in European countries, and four studies with 58 patients were conducted in non-European countries.
- The complete closure rate was higher in European countries than non-European countries, 64.1% vs. 52.6%.
- Eight studies reported overall NSAEs with the pooled NSAE rate of 22.5% (95% CI: 0.11-0.34, Figure 1B).
- Seven studies reported SAEs with the pooled SAE rate of 1.7% (95% CI: 0.001-0.034, Figure 1C).
- Seven studies reported the perianal abscess rate with a pooled perianal abscess rate of 7.1% (95% CI: 0.016-0.125, Figure 1D).

#### Conclusions

• Our meta-analysis demonstrated that ASC is a promising therapeutic option for CPAF not associated with Crohn's disease with a clinically adequate efficacy and low rate of adverse events.