

# Endoscopic Diagnosis of Gastrointestinal Acute Graft-vs-Host Disease After Allogeneic Hematopoietic Stem Cell Transplantation: A Systematic Review and Meta-Analysis of Biopsy Site, Procedure Selection, and CMV Co-Infection



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## INTRODUCTION

Gastrointestinal acute graft-vs-host disease (GI-aGVHD) is a leading cause of non-relapse mortality after allogeneic hematopoietic stem cell transplantation (allo-HSCT). Endoscopic biopsy is required for definitive diagnosis, yet the optimal biopsy site, the diagnostic adequacy of flexible sigmoidoscopy versus full colonoscopy, and the frequency of cytomegalovirus (CMV) co-infection remain unsettled. Resolving these questions is crucial for guiding procedure selection in patients who are often thrombocytopenic, immunocompromised, and hemodynamically fragile.

## AIM

This study set out to clarify how endoscopy should be selected and performed when GI-aGVHD is suspected. Drawing together the published evidence, we asked whether histologic yield differs meaningfully across the stomach, duodenum, terminal ileum, and rectosigmoid, and how much additional disease a full colonoscopy uncovers beyond flexible sigmoidoscopy alone. We also sought to establish how often CMV co-infection is found on immunohistochemistry (IHC) in allo-HSCT recipients undergoing evaluation.

## METHODS

- PRISMA 2020 systematic review
- PubMed and Google Scholar through April 2026
- 18 eligible studies
- DerSimonian-Laird random-effects model
- Freeman-Tukey transformation
- Analyses stratified by patient and specimen
- Heterogeneity quantified by I<sup>2</sup>

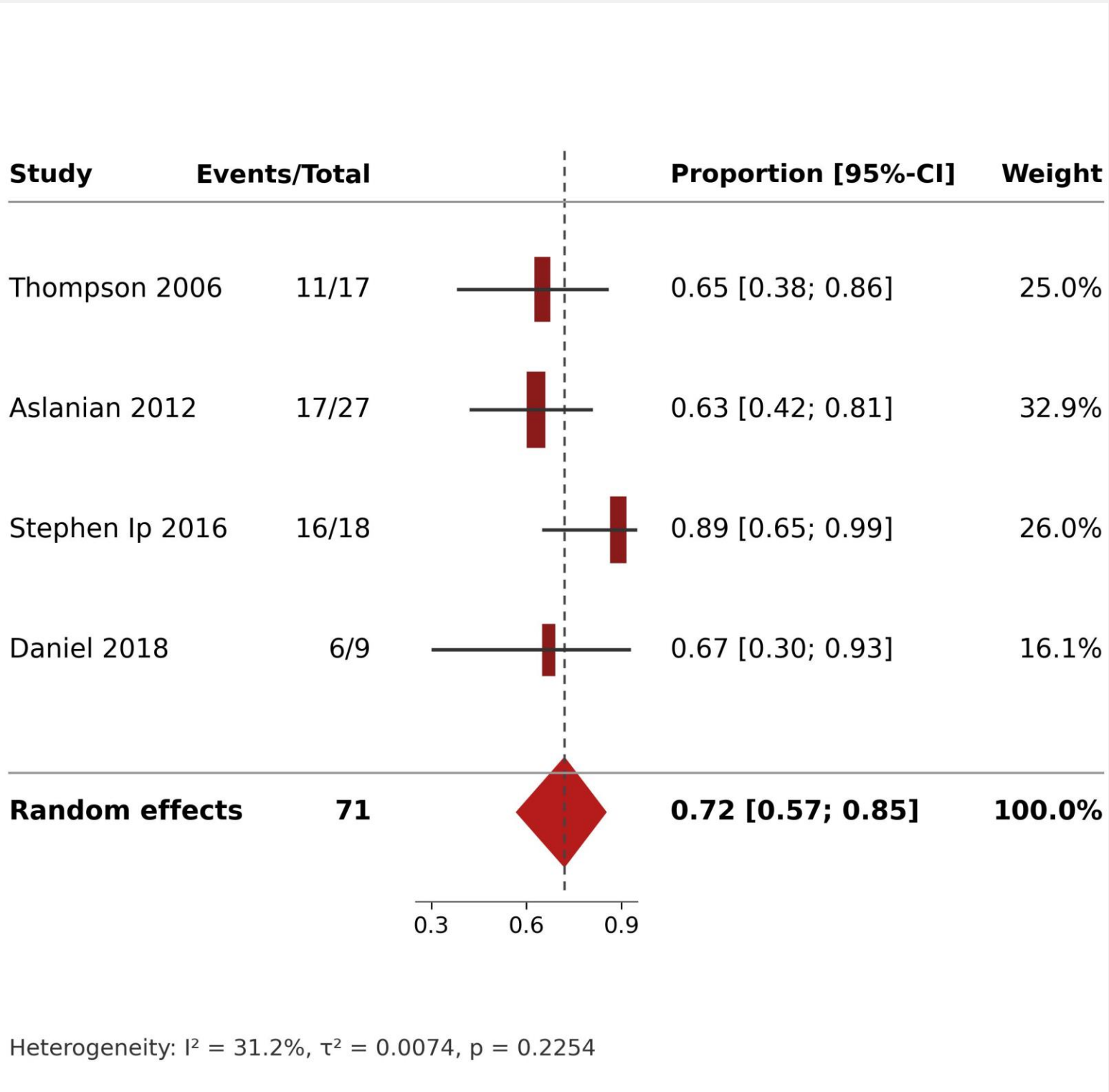
## CONCLUSIONS

Site yields clustered at 60 - 72%, but because these comparisons come from different studies rather than the same cohort of patients, the finding is reassuring while still falling short of proving that the sites are equivalent. CMV co-infection was found by IHC in 5% patients which is uncommon but consequential enough to keep on the differential. A distal-first strategy with routine CMV IHC is reasonable, reserving full colonoscopy for persistent suspicion after negative distal biopsies.

**FIRST-LINE DIAGNOSTIC STRATEGY**  
Flexible sigmoidoscopy with distal biopsies and routine CMV IHC

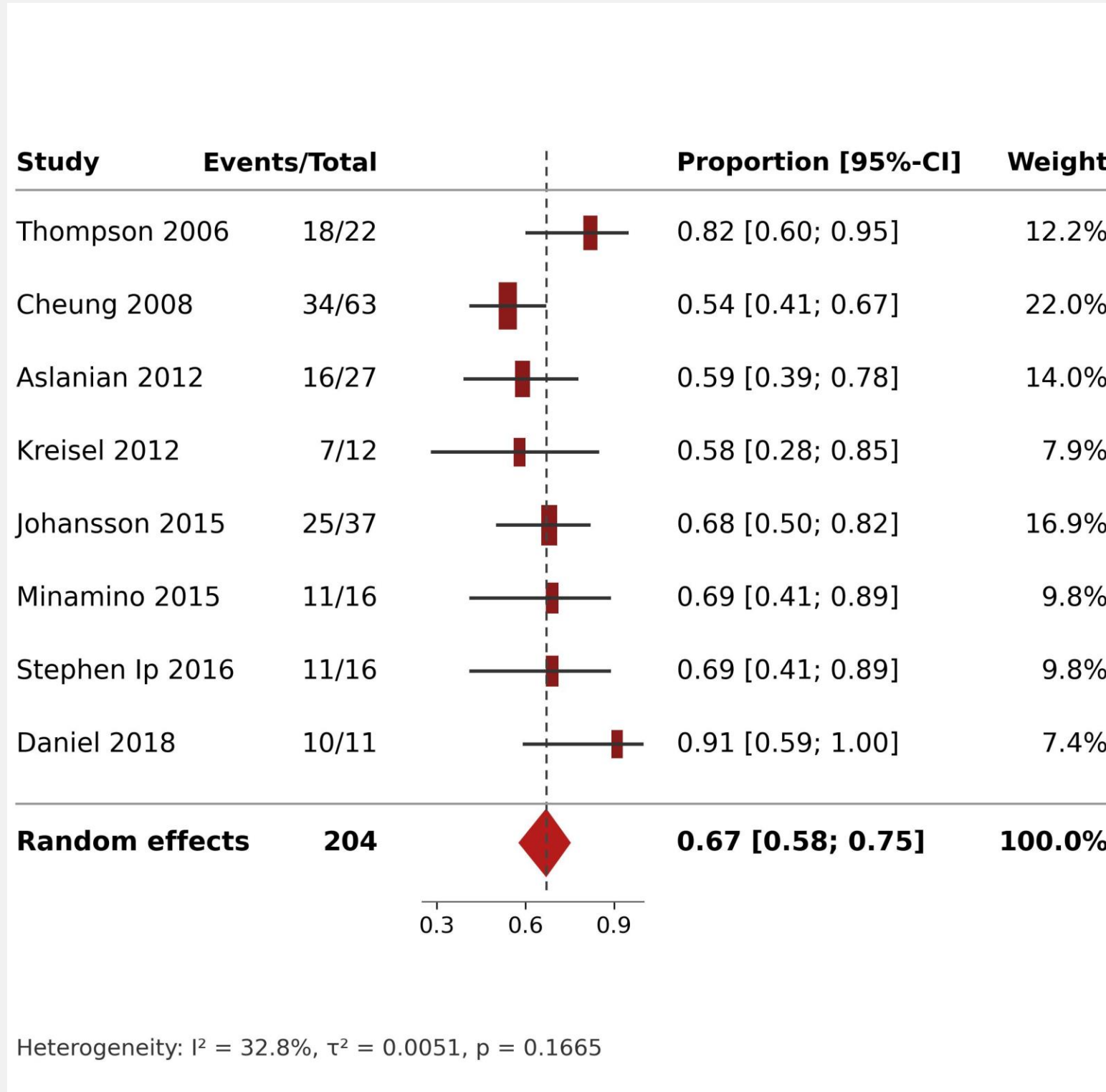
## RESULTS

### Duodenum



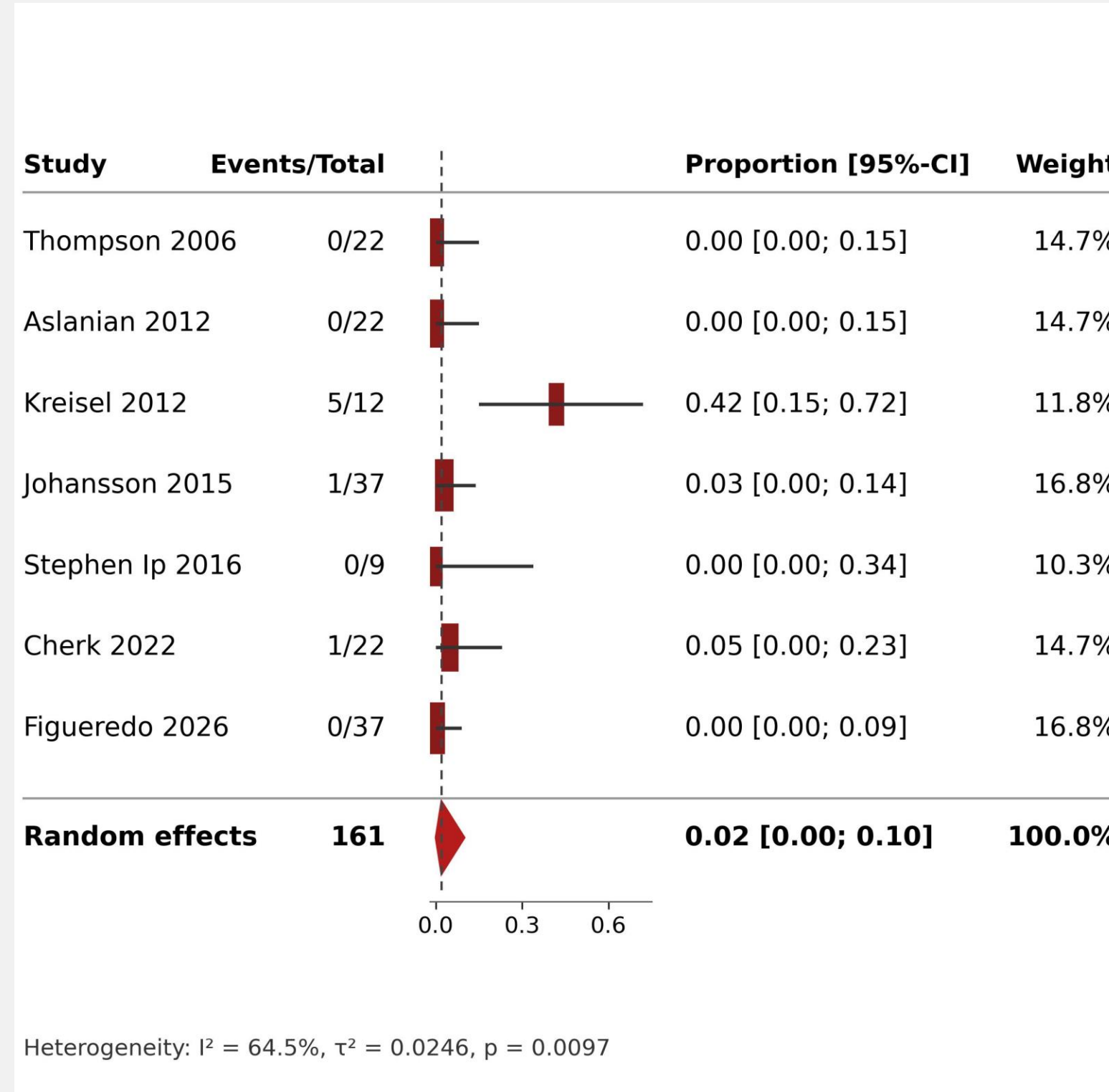
72% (95% CI, 57% - 85%)

### Rectosigmoid



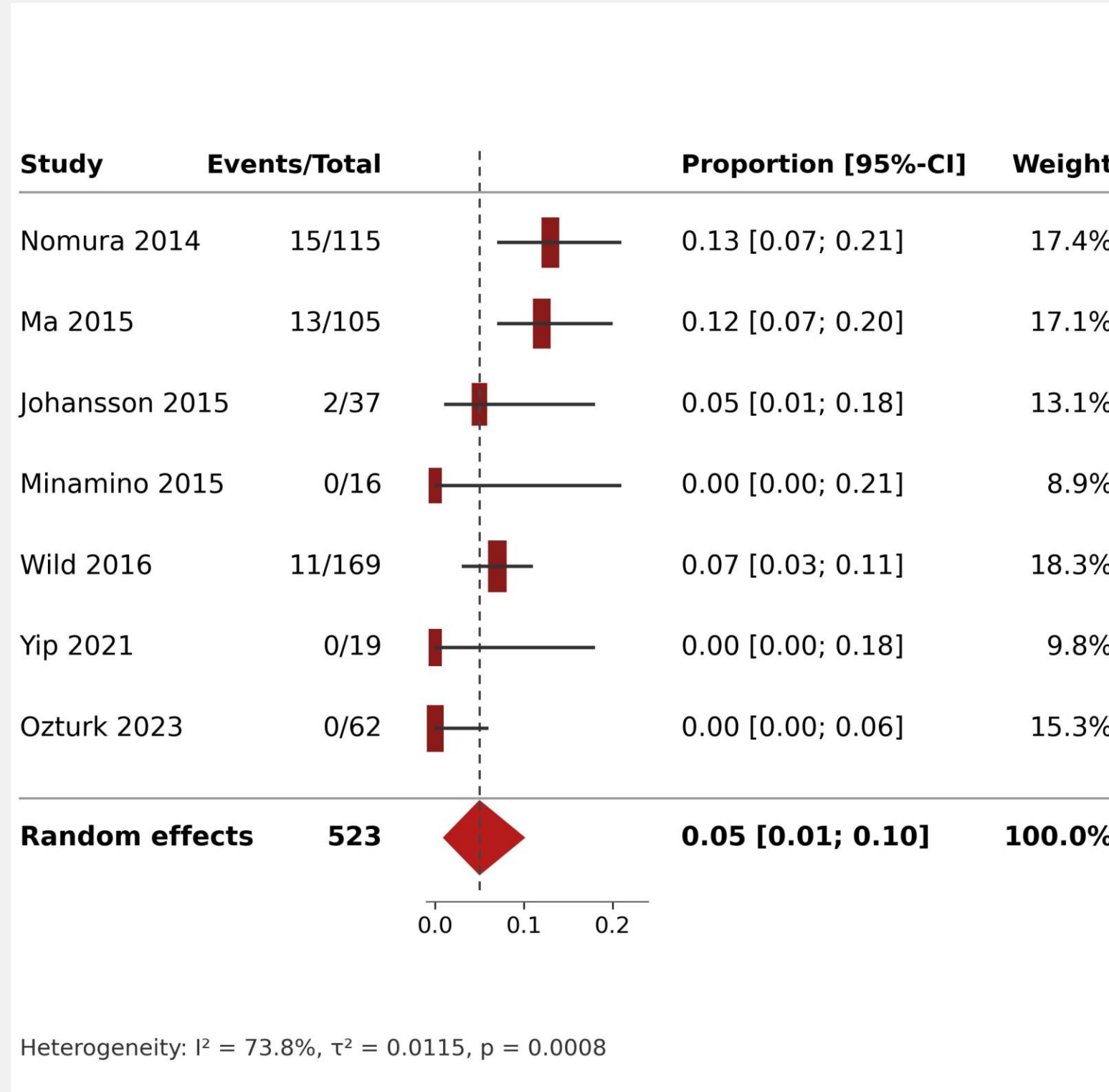
67% (95% CI, 58% - 75%)

### Full colonoscopy



2% incremental detection

### CMV co-infection



5% by IHC (95% CI, 1% - 10%)

## CLINICAL INTERPRETATION

Per-patient estimates overlapped across stomach, duodenum, terminal ileum, and rectosigmoid. Full colonoscopy added 2% detection; after exclusion of one influential outlier, the estimate fell to 0.4% with I<sup>2</sup>=0%.

## REFERENCES

- Cruz-Correa M et al. Endoscopic Diagnosis of GvHD · Endoscopy 2002;
- Schulenburg A, Turetschek K, Wrba F, Vogelsang H, Greinix HT, Keil F, et al. Early and late gastrointestinal complications after myeloablative and nonmyeloablative allogeneic stem cell transplantation. Ann Hematol. 2004;
- Oomori S et al. Colonoscopy in Patients with Intestinal GVHD after Stem Cell Transplantation · Endoscopy 2005;
- Thompson B, Salzman D, Steinhauer J, Lazenby AJ, Wilcox CM. Prospective endoscopic evaluation for gastrointestinal graft-versus-host disease: determination of the best diagnostic approach. Bone Marrow Transplant. 2006;
- Melson J, Jakate S, Fung H, Aral S, Keshavarzian A. Crypt loss is a marker of clinical severity of acute gastrointestinal graft-versus-host disease. Am J Hematol. 2007;
- Cheung DY, Kim JI, Kim SS, Sung HY, Cho SH, Park SH, et al. Endoscopic evaluation in gastrointestinal graft-versus-host disease: comparisons with histological findings. Dig Dis Sci. 2008;
- Nguyen CV, Kastenberger DM, Choudhary C, Katz LC, DiMarino A, Palazzo JP. Is single-cell apoptosis sufficient for the diagnosis of graft-versus-host disease in the colon? Dig Dis Sci. 2008
- Ross WA, Ghosh S, Dekovich AA, Liu S, Ayers GD, Cleary KR, et al. Endoscopic biopsy diagnosis of acute gastrointestinal graft-versus-host disease: rectosigmoid biopsies are more sensitive than upper gastrointestinal biopsies. Am J Gastroenterol. 2008;
- Xu CF, Zhu LX, Xu XM, Chen WC, Wu DP. Endoscopic diagnosis of gastrointestinal graft-versus-host disease. World J Gastroenterol 2008;
- Varadarajan P, Dunford LM, Thomas JA, Brown K, Paplham P, Syta M, et al. Seeing what's out of sight: wireless capsule endoscopy's unique ability to visualize and accurately assess the severity of gastrointestinal graft-versus-host-disease. Biol Blood Marrow Transplant. 2009;
- Aslanian H, Chander B, Robert M, Cooper D, Proctor D, Seropian S, et al. Prospective evaluation of acute graft-versus-host disease. Dig Dis Sci. 2012;
- Kreisel W, Dahlberg M, Bertz H, Harder J, Potthoff K, Deibert P, et al. Endoscopic diagnosis of acute intestinal GVHD following allogeneic hematopoietic SCT: a retrospective analysis in 175 patients. Bone Marrow Transplant. 2012;
- Calabrese E, Zorzi F, Visconti E, De Angelis G, Cerretti R, Del Vecchio Blanco G, et al. Bowel ultrasonography as an aid for diagnosis of intestinal acute graft-versus-host-disease after allogeneic haematopoietic stem cell transplantation. Dig Liver Dis. 2013;
- Liu A, Meyer E, Johnston L, Brown J, Gerson LB. Prevalence of graft versus host disease and cytomegalovirus infection in patients haematopoietic cell transplantation presenting with gastrointestinal symptoms. Aliment Pharmacol Ther. 2013;
- Yamasaki S, Miyagi-Maeshima A, Kakugawa Y, Matsuno Y, Ohara-Waki F, Fuji S, et al. Diagnosis and evaluation of intestinal graft-versus-host disease after allogeneic hematopoietic stem cell transplantation following reduced-intensity and myeloablative conditioning regimens. Int J Hematol. 2013

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## PRACTICAL DIAGNOSTIC PATHWAY

Suspected GI-aGVHD → Flexible sigmoidoscopy → Distal biopsies + routine CMV IHC → If negative and suspicion persists, proceed to full colonoscopy

Sensitivity analysis supports a distal-first strategy while preserving escalation for unresolved cases.