Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good
	[ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing
	[ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [Y] Accept (General priority)
	[ ] Minor revision [ ] Major revision [ ] Rejection
Re-review	[ ] Yes [Y] No
Peer-reviewer statements	Peer-Review: [ ] Anonymous [Y] Onymous
	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

This study indicated the novel genetic biomarkers, MTNR1B, combined with CDKN2A and MGMT gene methylation statuses, maybe a predictive tool for CRC prognosis. The researchers hypothesised that the influence of MTNR1B gene variation combined with the hypermethylation of CDKN2A and MGMT genes would predict the prognosis and provide clinical recommendations for optimal treatment of CRC. This study offers insights into novel genetic and epigenetic biomarkers for the prediction of CRC prognosis, and the findings could be used to individualise the treatment of patients with CRC. Since CRC is a high-incidence cancer, such a clinical research that investigated the new biomarkers of CRC is helpful. One concern is that adjusting for confounding factors such as obesity, a sedentary lifestyle, and unhealthy dietary habits in Table 4, 5 and 6 would be better for studying the effect of MTNR1B SNPs associated with 5-year OS of CRC patients, as this study mentioned. Secondly, the inclusion and exclusion criteria for this study seem to be unclear. Thirdly, it would be better to review format of the full text carefully, with respect to spaces between text and punctuation in the method.

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [Y] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection
Re-review	[ ] Yes [Y] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

acceptable

PEER-REVIEW REPORT

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection
Re-review	[ ] Yes [Y] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

In general, this is a well-designed and mature retrospective trial. I only have a few comments for authors. 1. The introduction of CDKN2A and MGMT genes is abrupt. Please supplement more information about them and explain why choose these two genes for combination analysis. 2. Authors used Cox proportional-hazards models for to analyze the survival. The adjusted factors included age, sex, stage, adjuvant chemotherapy, tumour location, and the methylation status of the CDKN2A, MLH1 and MGMT genes. What about BMI and combined primary diseases? 3. The sample size is a concern. The wide 95%CI indicated poor stability.