Journal of Clinical Oncology

Dear Author,

Your article from *Journal of Clinical Oncology* (*JCO*) is available for download. Refer to the accompanying e-mail notification for Web address, article number, login, and password to retrieve your proof.

For all communication regarding this proof, PLEASE REPLY TO SENDER:
JCOcorrections@asco.org

This letter describes how to review your manuscript scheduled for an upcoming issue of *JCO*. Send your response via fax or e-mail within 48 hours. Failure to do so may affect the publication date of your manuscript.

AS AUTHOR, YOU ARE RESPONSIBLE FOR DETECTING ERRORS. REVIEW ALL PORTIONS OF THE ARTICLE CAREFULLY AND COMPLETELY.

Journal Style

Your manuscript and figures have been edited to conform to *JCO* style. Our expert copy editors have prepared your manuscript with the intent of communicating your scientific discovery in the clearest, most concise manner possible. Therefore, understand that *only changes essential to the content can be made at this point*. Significant changes to data or wording may result in the article being removed from production and routed through editorial review once again.

Proof Retrieval and Corrections

The proof retrieval site indicated in the notification e-mail contains one file. You will need to use Adobe Acrobat Reader software to read the file. This free software is available at http://get.adobe.com/reader/.

The file you will download contains the following:

- E-mail notification and proofing instructions
- Reprint order form (please note that the corresponding author will receive 10 gratis e-mail prints of the article
- Proofreading marks
- Page proofs of your article and author queries

Communicate any corrections and answers to author queries by e-mail or by fax. Alternatively, we encourage you to input corrections directly into the comment-enabled PDF file (see Adobe Acrobat Reader Instructions). If you choose to send corrections by e-mail, you may type the corrections within the body of an e-mail message itself. If you choose to return proof corrections by fax, print the PDF file and mark your corrections clearly, directly on the hard copy.

Regardless of how you wish to submit your corrections, read the page proofs carefully:

- Indicate changes or corrections in the margins of the page proofs, on a separate sheet, or within the comment-enabled PDF.
- Answer all author queries (indicated as AQ:A, AQ:B, AQ:C, etc) in the margins of the proof pages or on the last page of the PDF proof.
- Proofread tables, figures, legends, and equations carefully.
- Ensure that figures are described accurately in associated legend text.
- Confirm that Greek symbols, especially mu, have translated correctly.

Figures

Figures in your article have been edited and redrawn to conform to *JCO* style. **As author, it is your responsibility to review *all* figure content carefully and completely for accuracy.** *JCO* will accept changes to figures to correct data/factual errors, or errors that severely compromise clarity or meaning. If any figure requires corrections, provide specific details describing the changes needed.

No Corrections Needed

If you are not making changes to the article, indicate "No corrections" on the first page of the proof, sign and date it, and return it by fax to the number provided below. You may also return your message of "No corrections" by e-mail. **Remember to review the author queries page, answer any questions, and transmit the answers accordingly, even if you do not wish to make any changes to your article.**

Adobe Acrobat Reader Instructions

The proof PDF has been comment enabled, which allows you to use the Comments and Notes features in Adobe Acrobat Reader. We encourage you to use these features when making corrections to your PDF because doing so will allow us to process the corrections for your article efficiently. As with hand-annotated proof corrections, the important points are to communicate changes clearly and thoroughly, to answer all queries, and to provide complete information.

When you open your PDF, the Comments, Notes, and Edit tools are shown clearly on the tool bar. You may use the following features to correct the PDF of your article:

Sticky Note Tool

- Click Sticky Note tool.
- Click where you would like to insert new text, such as a comment, correction, or note for your Journal Production contact.

Text Edits Tool

- Click Text Edits Tool.
- Click where you would like to insert new text.
- Type text to be inserted.

Highlight Text Tool

- Click Highlight Text Tool.
- Click and drag the cursor over text to be highlighted.
- Highlight Text is useful when paired with a note about global changes (for example, "All highlighted text should be set in italics").

Cross-Out Text Tool

- Click Cross-Out Text Tool.
- Click and drag the cursor over text to be deleted.

Text Box Tool

- Click Text Box Tool.
- Click where you wish a text box to open.
- Type correction within the text box.

Adobe Acrobat Reader's Help menu provides additional details on the Comments and Notes tools. To use the Comments and Notes features on this PDF, download Adobe Acrobat Reader version 7 or higher for free at http://get.adobe.com/reader/.

NIH Public Access

For all manuscripts accepted on or after April 7, 2008, that report research supported by any funds or grants from the National Institutes of Health (NIH), *JCO* will assume responsibility for depositing the final published version of the manuscript into PubMed Central, as a service to ASCO members and to *JCO* authors. Authors should NOT submit their unedited accepted manuscripts to the PubMed Central archive as instructed by the NIH Public Access Policy (NOT-OD-08-033); instead, *JCO* will provide a copy of the published article to the NIH to be made available for public access by PubMed Central 12 months after the date of publication. In so doing, *JCO* will fulfill the authors' obligation and meet the NIH deposit requirement. More information from the NIH can be found at http://publicaccess.nih.gov/FAQ.htm.

Reprints

If you wish to order reprints, please use the Publication Fees Worksheet/Reprint Order Form. Direct all inquiries about reprints and invoices to the Reprint Department (1-866-487-5625, ext. 3736) or Tracy.Harding@cenveo.com

Sincerely,

Heather Poirier
Senior Production Editor
Journal of Clinical Oncology
American Society of Clinical Oncology
2318 Mill Road, Ste 800
Alexandria, VA 22314
e-mail: JCOcorrections@asco.org
Phone: 571-483-1740
FAX: 571-366-9566

Journal of Clinical Oncology 2014

This is your reprint order form or pro forma invoice

(Please keep a copy of this document for your records.)

Reprint order forms and purchase orders or prepayments must be received 72 hours after receipt of form either by mail or by fax at 877-705-1373. It is the policy of Cadmus Reprints to issue one invoice per order. **Please print clearly**.

Author Name _____
Title of Article _____
Issue of Journal_____ Reprint # 3869840 Manuscript # C8213 Publication Date_____
Number of Pages 2 Color in Article? Yes / No (Please Circle) Symbol JCO

Please include the journal name and reprint number or manuscript number on your purchase order or other correspondence.

Order and Shipping Information

Reprint Costs **(Please see page 2 of 2 for reprint costs/fees.)**

_____ Number of color reprints ordered $_____
Articles more than 90 days from publication:
_____ Pages @ $6.22/page –
late order fee $_____

Subtotal $_____

Taxes $_____

(*Add appropriate sales tax for Virginia, Maryland, Pennsylvania, and the District of Columbia or Canadian GST to the reprints if your order is to be shipped to these locations.*)

First address included, add $32 for
each additional shipping address $_____

Total Amount Due $_____

Shipping Address **(cannot ship to a P.O. Box) Please Print Clearly**

Name_____
Institution_____
Street_____
City _____ State _____ Zip _____
Country_____
Quantity_____ Fax _____
Phone: Day _____ Evening _____
E-mail Address _____

Additional Shipping Address* **(cannot ship to a P.O. Box)**

Name_____
Institution_____
Street_____
City _____ State _____ Zip _____
Country_____
Quantity_____ Fax _____
Phone: Day _____ Evening _____
E-mail Address _____

** Add $32 for each additional shipping address*

Payment and Credit Card Details

Enclosed: Personal Check _____
Institutional Purchase Order _____
Credit Card Payment Details _____
Checks must be paid in U.S. dollars and drawn on a U.S. Bank.

Credit Card: __ VISA __ Am. Exp. __ MasterCard
Card Number _____
Expiration Date_____
Signature: _____

Please send your order form and purchase order or prepayment made payable to:

Cadmus Reprints
P.O. Box 822942
Philadelphia, PA 19182-2942

Note: Do not send express packages to this location, PO Box.
FEIN #:540157890

Invoice or Credit Card Information

Invoice Address Please Print Clearly
Please complete Invoice address as it appears on credit card statement

Name _____
Institution _____
Department _____
Street _____
City _____ State _____ Zip _____
Country _____
Phone _____ Fax _____
E-mail Address _____
Purchase Order No._____

Cadmus will process credit cards and *Cadmus Journal Services* will appear on the credit card statement.

If you do not mail your order form, you may fax it to 877-705-1373 with your credit card information.

Signature _____ Date _____
Signature is required. By signing this form, the author agrees to accept the responsibility for the payment of reprints and/or all charges described in this document.

8-23-13

Journal of Clinical Oncology 2014

Color Reprint Prices

Domestic (USA only)						
# of Pages	50	100	200	300	400	500
1-4	$261	$390	$451	$518	$581	$619
5-8	$604	$746	$832	$1,007	$1,090	$1,159
9-12	$888	$1,099	$1,229	$1,491	$1,625	$1,726
13-16	$1,166	$1,460	$1,628	$1,978	$2,154	$2,289
17-20	$1,404	$1,722	$1,930	$2,311	$2,511	$2,632

International (includes Canada and Mexico)						
# of Pages	50	100	200	300	400	500
1-4	$290	$408	$480	$564	$640	$694
5-8	$656	$780	$892	$1,096	$1,207	$1,302
9-12	$972	$1,156	$1,321	$1,631	$1,797	$1,943
13-16	$1,293	$1,540	$1,754	$2,163	$2,393	$2,579
17-20	$1,564	$1,823	$2,088	$2,544	$2,806	$2,986

Minimum order is 50 copies. For orders larger than 500 copies or longer than 20 pages, please consult Cadmus Reprints at 410-943-0629.

Shipping

Shipping costs are included in the reprint prices. Domestic orders are shipped via UPS Ground service. Foreign orders are shipped via an expedited proof of delivery air service. The shipping address printed on an institutional purchase order always supercedes.

Multiple Shipments

Orders can be shipped to more than one location. Please be aware that it will cost $32 for each additional location.

Delivery

Your order will be shipped within 2 weeks of the journal print date. Allow extra time for delivery.

Late Order Charges

Articles more than 90 days from publication date will carry an additional charge of $6.22 per page for file retrieval.

Tax Due

Residents of Virginia, Maryland, Pennsylvania, and the District of Columbia are required to add the appropriate sales tax to each reprint order. For orders shipped to Canada, please add 5% Canadian GST unless exemption is claimed.

Ordering

Prepayment or a signed institutional purchase order is required to process your order. Please reference journal name and reprint number or manuscript number on your purchase order or other correspondence. You may use the reverse side of this form as a proforma invoice. Please return your order form and purchase order or prepayment to:

Cadmus Reprints
P.O. Box 822942
Philadelphia, PA 19182-2942

Note: Do not send express packages to this location, PO Box.
FEIN #:540157890

Please direct all inquiries to:

Reprints
866-487-5625 (toll free number)
410-943-0629 (direct number)
877-705-1373 (FAX number)
cjsreprints@cadmus.com

Reprint Order Forms and Purchase Orders or prepayments must be received 72 hours after receipt of form.

PROOFREADERS' MARKS

Symbol	Meaning	Example
	delete	take it out
	close up	print as one word
	delete and close up	close up
^ or > or	caret	insert here (something
#	insert a space	put onehere
eq#	space evenly	space evenly where indicated
stet	let stand	let marked text stand as set
tr	transpose	change order the
/	used to separate two or more marks and often as a concluding stroke at the end of an insertion	
[	set farther to the left	too far to the right
]	set farther to the right	too far to the left
	set as ligature (such as)	encyclopaedia
	align horizontally	alignment
||	align vertically	align with surrounding text
x	broken character	imperfect
	indent or insert em quad space	
¶	begin a new paragraph	
sp	spell out	set 5 lbs. as five pounds
cap	set in CAPITALS	set nato as NATO
sm cap or s.c.	set in SMALL CAPITALS	set signal as SIGNAL
lc	set in lowercase	set South as south
ital	set in *italic*	set oeuvre as *oeuvre*
rom	set in roman	set *mensch* as mensch
bf	set in **boldface**	set important as **important**
= or -/ or or /H/	hyphen	multi-colored
1/N or en or /N/	en dash	1965–72
1/M or em or /M/	em (or long) dash	Now—at last!—we know.
∨	superscript or superior	as in πr^2
∧	subscript or inferior	as in $H_2 0$
	centered	for a centered dot in $p \cdot q$
	comma	
	apostrophe	
⊙	period	
; or ;/	semicolon	
: or	colon	
	quotation marks	
(/)	parentheses	
[/]	brackets	

JOURNAL OF CLINICAL ONCOLOGY

CORRESPONDENCE

Reply to J. Moline et al

Moline and Eng[1] have raised important points regarding universal versus age-restricted screening of endometrial cancer for features of mismatch repair (MMR) deficiency, and the debate over what should happen ideally versus what can happen in the public health arena. The scheme we propose for identification of germline MMR mutation carriers in our article[2] suggests that all women younger than age 60 years at diagnosis should undergo tumor MMR immunohistochemistry (IHC) testing as primary triage for MMR mutation testing. Although we and others have shown that universal screening is more sensitive for the identification of MMR gene mutation carriers, implementation of universal MMR screening is largely dependent on testing facilities and financial resources. This is likely why universal screening is still not widely adopted internationally, or even in the United States.[3]

Previous publications in the endometrial cancer arena have suggested an age cutoff of 50 years,[4,5] and this is the age cutoff that is currently suggested for patients with endometrial cancer by the National Comprehensive Cancer Network[6,7] and Comprehensive Cancer Centre of the Netherlands[8] guidelines for hereditary cancer. The diagnostic yield of MMR gene mutation carriers among patients with endometrial cancer (and also colorectal cancer) decreases with increasing age. In our study, approximately 60% of the MMR IHC tests (n = 408) were performed in patients 60 years of age or older for the identification of three carriers. The age-limited scheme we propose as optimal was selected, from the public health perspective, to substantially reduce burden on the health care system while detecting the vast majority of mutation carriers. We note also that the recently published article by Moline et al states that "screening in patients diagnosed ≤ 60 . . . [years] would have identified all patients with Lynch syndrome in ~~their~~ cohort."[9(pXXXX)]

Compared with other guidelines (such as the National Comprehensive Cancer Network and Comprehensive Cancer Centre of the Netherlands guidelines) that suggest screening/clinical action for only patients with endometrial cancer diagnosed at or before age 50 years, our proposed scheme will greatly improve carrier detection while nevertheless considering resource limitations that are frequently encountered in the international clinical setting. We acknowledge openly that some mutation carriers will be missed by an age-restricted scheme. However, universal screening with MMR IHC is itself not without limitations because of suboptimal MMR IHC testing[10,11] or an IHC-normal profile of protein-stable mutations (mutations that will remain undetected by universal screening)—both of which would lead to so-called missing of MMR gene mutation carriers. We recommended additional IHC and/or microsatellite instability testing as a secondary screen or direct MMR gene testing when there is a high clinical suggestion of Lynch syndrome, irrespective of age, that can assist in detecting so-called missed MMR gene mutation carriers. It is worthwhile to note that a parallel colorectal cancer screening program would identify some families missed by implementing age-limited endometrial cancer screening programs. In our study, all three mutation carriers older than age 60 years reported colorectal cancer in at least one first-degree relative (age 38 to 63 years).

Moline and Eng[1] have noted the following specific issues regarding the use of age at diagnosis of endometrial cancer as a screening criterion in the clinical setting. First, they pointed out that the frequency of MMR gene mutation carriers older than age 60 years at diagnosis is lower in our study[2] than in two other ~~reports~~,[12-14] highlight in Table 1 that such estimates from any unselected cohort will be based on relatively small numbers. The frequency of MMR gene mutation carriers in women age 60 years or older at diagnosis did not differ significantly between all studies of unselected endometrial cancer cohorts identified from the literature[2,12-16] (Table 1). Furthermore, the range in point estimates across studies does not seem to be explained by differences in the upper age limits between studies, which ranged from age 70 years[14] to 94 years.[12]

Moline and Eng[1] next assert that placing any age cutoff on tumor screening allows an opportunity for pathologist errors. It is inevitable

Table 1. Comparison of MMR IHC Results and MMR Gene Mutation Frequency in Studies of Unselected Endometrial Cancer*

Characteristic	Australia[2] (N = 702)	US[12,13] (N = 543)	The Netherlands[14] (N = 179)	Korea[15] (N = 113)	Spain[16] (N = 173)
Cohort age range, years	18-79	17-94	≤ 70	NA	29-90
IHC loss, %	24.2	23.3	23.5	23.0	33.5
MMR mutation carriers, %†	3.1	2.3	3.9	4.4	4.6
MLH1	0.4	0.2	0	0.9	0.6
MSH2	1.1	0.6	0	1.8	1.7
MSH6	1.4	1.5	3.4	1.8	1.7
PMS2	0.1	0	0.6	0	0.6
Mutation carriers, total	22	13	7	5	8
No. of carriers age ≥ 60 years	3	5	3	1	2
% of carriers age ≥ 60 years	14	38	43	20	25
95% CI, %	4 to 36	15 to 68	12 to 80	1 to 70	5 to 64

Abbreviations: IHC, immunohistochemistry; MMR, mismatch repair; NA, not available; US, United States.
*Study design was as follows: Australia was an Australian population–based case-control study; US was an Ohio population–based study, Netherlands was a Dutch multicenter study, and Korea and Spain were both single-center studies.
†Total may not add up to 100% because of rounding.

Corresponding author: Amanda B. Spurdle, PhD, Molecular Cancer Epidemiology Laboratory, Genetics and Computational Biology Division, Queensland Institute of Medical Research, 300 Herston Rd, Herston, Brisbane, 4006, Australia; e-mail: Amanda.Spurdle@qimr.edu.au.

<zdoi;10.1200/JCO.2014.55.8213> • <zjs;Correspondence> • <zjss;Correspondence>

that cases will be overlooked. However, a computer decision-support system (eg, GRAIDS software or electronic health record reminders) may assist in flagging patients for tumor testing, and furthermore, as demonstrated previously, in flagging patients for appropriate referral to clinical genetics services.[17,18]

Moline and Eng[1] also state that having an age cutoff for endometrial and not colorectal cancer constitutes unequal treatment of endometrial versus colorectal cancer for Lynch syndrome screening. From a public health perspective, decisions about screening will be implemented in the context of available resources, and it is in the best interests of the research and clinical community internationally that all relevant information be provided to develop tailored local/national guidelines that can be feasibly implemented.

Further research will almost certainly refine recommendations for the testing of patients with endometrial cancer for suspected Lynch syndrome, but the immediate need is to encourage systematic MMR IHC testing over other family history–based criteria.

Daniel D. Buchanan
Queensland Institute of Medical Research Berghofer Medical Research Institute, Brisbane, Queensland, Australia

Yen Y. Tan
Queensland Institute of Medical Research Berghofer Medical Research Institute; The University of Queensland School of Medicine, Brisbane, Queensland, Australia

Michael D. Walsh, Mark Clendenning, Alexander M. Metcalf, Kaltin Ferguson, Sven T. Arnold, Bryony A. Thompson, Felicity A. Lose, Michael T. Parsons, Rhiannon J. Walters, and Sally-Ann Pearson
Queensland Institute of Medical Research Berghofer Medical Research Institute, Brisbane, Queensland, Australia

Margaret Cummings
University of Queensland Centre for Clinical Research, Herston, Queensland, Australia

Martin K. Oehler
Royal Adelaide Hospital, Adelaide, South Australia, Australia

Penelope B. Blomfield
Royal Hobart Hospital, Hobart, Tasmania, Australia

Michael A. Quinn
Royal Women's Hospital, Melbourne, Victoria, Australia

Judy A. Kirk
Westmead Institute for Cancer Research, Westmead Millennium Institute, University of Sydney, New South Wales, Australia

Colin J. Stewart
PathWest, King Edward Memorial Hospital, Perth, Western Australia, Australia

Andreas Obermair
Queensland Centre for Gynaecological Oncology, University of Queensland, Brisbane, Queensland, Australia

Joanne P. Young, Penelope M. Webb, and Amanda B. Spurdle
Queensland Institute of Medical Research Berghofer Medical Research Institute, Brisbane, Queensland, Australia

ACKNOWLEDGMENT

A.B.S. and P.M.W. are supported by National Health and Medical Research Council Senior Research Fellowships. Y.Y.T. is supported by an International Postgraduate Research Scholarship, the University of Queensland Centennial Scholarship, and Advantage Top-Up Scholarship. D.D.B. was supported by the Australasian Colorectal Cancer Family Registry (Grant No. U01 CA097735).

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The author(s) indicated no potential conflicts of interest.

REFERENCES

1. Moline J, Eng C: Equality in Lynch syndrome screening: Why should we hold patients with endometrial cancer to a different standard? J Clin Oncol doi: 10.1200/JCO.2014.55.3602
2. Buchanan DD, Tan YY, Walsh MD, et al: Tumor mismatch repair immunohistochemistry and DNA MLH1 methylation testing of patients with endometrial cancer diagnosed at age younger than 60 years optimizes triage for population-level germline mismatch repair gene mutation testing. J Clin Oncol 32:90-100, 2014
3. Beamer LC, Grant ML, Espenschied CR, et al: Reflex immunohistochemistry and microsatellite instability testing of colorectal tumors for Lynch syndrome among US cancer programs and follow-up of abnormal results. J Clin Oncol 30:1058-1063, 2012
4. Lu KH, Schorge JO, Rodabaugh KJ, et al: Prospective determination of prevalence of Lynch syndrome in young women with endometrial cancer. J Clin Oncol 25:5158-5164, 2007
5. Berends MJ, Wu Y, Sijmons RH, et al: Toward new strategies to select young endometrial cancer patients for mismatch repair gene mutation analysis. J Clin Oncol 21:4364-4370, 2003
6. National Comprehensive Cancer Network (NCCN). NCCN Guidelines: Uterine neoplasms. Ver 1.2014, 2014. http://www.nccn.org/
7. National Comprehensive Cancer Network (NCCN). NCCN Guidelines: Colorectal cancer screening. Ver 1.2014, 2014. http://www.nccn.org/
8. Comprehensive Cancer Centre the Netherlands: Hereditary colorectal cancer. Ver 1.0, 2009. http://www.oncoline.nl/hereditary-colorectal-cancer
9. Moline J, Mahdi H, Yang B, et al: Implementation of tumor testing for lynch syndrome in endometrial cancers at a large academic medical center. Gynecol Oncol 130:121-126, 2013
10. Klarskov L, Ladelund S, Holck S, et al: Interobserver variability in the evaluation of mismatch repair protein immunostaining. Hum Pathol 41:1387-1396, 2010
11. Overbeek LI, Ligtenberg MJ, Willems RW, et al: Interpretation of immunohistochemistry for mismatch repair proteins is only reliable in a specialized setting. Am J Surg Pathol 32:1246-1251, 2008
12. Hampel H, Frankel W, Panescu J, et al: Screening for Lynch syndrome (hereditary nonpolyposis colorectal cancer) among endometrial cancer patients. Cancer Res 66:7810-7817, 2006
13. Hampel H, Panescu J, Lockman J, et al: Comment on: Screening for Lynch syndrome (hereditary nonpolyposis colorectal cancer) among endometrial cancer patients. Cancer Res 67:9603, 2007
14. Leenen CH, van Lier MG, van Doorn HC, et al: Prospective evaluation of molecular screening for Lynch syndrome in patients with endometrial cancer ≤ 70 years. Gynecol Oncol 125:414-4202, 2012
15. Yoon SN, Ku JL, Shin YK, et al: Hereditary nonpolyposis colorectal cancer in endometrial cancer patients. Int J Cancer 122:1077-1081, 2008
16. Egoavil C, Alenda C, Castillejo A, et al: Prevalence of Lynch syndrome among patients with newly diagnosed endometrial cancers. PLoS One 8:e79737, 2013
17. Emery J, Morris H, Goodchild R, et al: The GRAIDS Trial: A cluster randomised controlled trial of computer decision support for the management of familial cancer risk in primary care. Br J Cancer 97:486-493, 2007
18. Scheuner MT, Hamilton AB, Peredo J, et al: A cancer genetics toolkit improves access to genetic services through documentation and use of the family history by primary-care clinicians. Genet Med 16:60-69, 2014

DOI: 10.1200/JCO.2014.55.8213; published online ahead of print at www.jco.org on Month XX, 2014

AUTHOR QUERIES

AUTHOR PLEASE ANSWER ALL QUERIES 1

A—**AUTHOR: You are responsible for detecting any errors in this proof.** Confirm that all dosing information and treatment regimens are complete and accurate in text, tables, and figures, if applicable to article content.

B—AUTHOR: Per JCO style, all genes, oncogenes, and proto-oncogenes must be italicized. Please confirm throughout text that all genes have been correctly italicized and capitalized, and mark corrections as needed on your page proofs. Proteins, antigens, and receptors are not italicized.

C—AUTHOR: The letter by Moline and Eng was added as reference 1, and your own article needed to be renumbered as reference 2, as it is mentioned in the first paragraph. Other references were renumbered accordingly; please confirm accuracy.

D—AUTHOR: Please confirm that "Comprehensive Cancer Centre of the Netherlands" is correct name.

E—AUTHOR: Sentence beginning "The diagnostic yield of MMR gene…" edited for clarity.

F—AUTHOR: Please provide page number of direct quote from article by Moline et al.

G—AUTHOR: Cross references within text such as "see above" or "see below" are not permitted, per JCO style.

H—AUTHOR: Please confirm that MSI has been correctly defined as microsatellite instability.

I—AUTHOR: Please clarify: you mention three references following the phrase "two other reports." Please confirm that references 12, 13, and 14 should all be cited here.

J—AUTHOR: If GRAIDS is an acronym, please indicate what it stands for. Please confirm that sentence beginning "However, a computer decision-support system…" is accurate as edited.

K—AUTHOR: Sentence beginning "From a public health perspective…" edited for clarity.

L—AUTHOR: Please confirm that statement of support pertains to this correspondence piece; if it pertains only to original study, it should be removed.

M—**AUTHOR:** Please verify conflicts of interest information is complete and accurate as of acceptance date.