

Supplementary online material

Colorectal Cancer among Veterans in Urban and Rural areas: Characteristics and Mortality

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- **Propensity score matching details**

We created a propensity score to match statin-users and active comparators (nonusers) at a ratio of 1:1 using variables chosen *a priori* (Table 1 in the manuscript). We used the routine by Leuven and Sianesi to perform nearest number matching using the logit model with no replacement. We explored a caliper width of 0.01, which approximately represented 0.2 times the standard deviation of the logit of the propensity scores, as suggested in prior publications (Austin PC, *Pharm Stat.* Mar-Apr 2011;10(2):150-161). We subsequently decreased caliper by a decrement of 10% and checked standardized differences on all covariates. Using smaller caliper, we improved balance with < 10% decrease in sample size. A caliper of 0.01 was found to offer best balance in differences, without residual statistically significant differences between treatment groups. After propensity score creation, pseudo R2 decreased to 0.001, indicating that successful balance has been achieved (Staffa et al. *Anesth Analg.* Oct 2018;127(4):1066-1073).

Table S1. Definition of administrative codes used in the study outcomes	
Definition of colorectal cancer ICD-10-CM:	<p>C18.0 Malignant neoplasm of Cecum</p> <p>C18.2 Malignant neoplasm of ascending colon</p> <p>C18.3 Malignant neoplasm of hepatic flexure</p> <p>C18.4 Malignant neoplasm of transverse colon</p> <p>C18.5 Malignant neoplasm of splenic flexure</p> <p>C18.6 Malignant neoplasm of descending colon</p> <p>C18.7 Malignant neoplasm of sigmoid colon Malignant neoplasm of sigmoid (flexure)</p> <p>C18.8 Malignant neoplasm of overlapping sites of colon</p> <p>C18.9 Malignant neoplasm of colon, unspecified- Malignant neoplasm of large intestine NOS</p> <p>C19 and C19.9 Malignant neoplasm of rectosigmoid junction</p> <p>C20 and C20.9 Malignant neoplasm of rectum</p>
Definition of colorectal cancer ICD-9 codes	<p>153.0 hepatic flexure</p> <p>153.1 transverse colon</p> <p>153.2 descending colon</p> <p>153.3 sigmoid colon</p> <p>153.4 cecum</p> <p>153.6 ascending colon</p> <p>153.7 splenic flexure</p> <p>153.8 other specified sites of the large intestine</p> <p>153.9 colon, unspecified</p> <p>154.0 rectosigmoid junction</p> <p>154.1 rectum</p> <p>154.8 other</p>

Colonoscopy ⁴⁻⁶	<ul style="list-style-type: none"> ○ CPT: 44388, 44389, 44390, 44391, 44392, 44393, 44394, 44397, 45378, 45379, 45380, 45381, 45382, 45383, 45384, 45385, 45386 ○ HCPCS: G0105, G0121 ○ ICD-9: 45.22, 45.23, 45.25, 45.41, 45.42, 45.43
Flexible sigmoidoscopy ⁵	<ul style="list-style-type: none"> - CPT: 45300, 45303, 45305, 45308-9, 45315, 45320, 45330-4, 45337-9 - HCPCS: G0104
FOBT/FIT or FIT-DNA	<ul style="list-style-type: none"> ○ CPT⁷: 82270, 82271a, 82272a, 82273a, 82274 ○ HCPCS: G0107, G0328, G0464 ○ LOINC codes^{4, 5}: 2335-8, 12503-9, 12504-7, 14563-1, 14564-9, 14565-6, 27396-1, 27401-9, 27925-7, 27926-5, 29771-3, 56490-6, 56491-4, 57905-2, 58453-2 <p>CPT: 81528 HCPCS: G0464</p>
Barium enema ⁶	<p>CPT: 74270, 74280 HCPCS: G0106, G0120, G0122 ICD-9: 87.64</p>
CT colonography	CPT: 74261, 74262, 74263

Table S2. Categories of colonoscopy indication

Indications	ICD-9	ICD-10
IBD	555.x, 556.x	<p>K50.011 Crohn's disease of small intestine with rectal bleeding</p> <p>K50.112 Crohn's disease of large intestine with intestinal obstruction</p> <p>K50.812 Crohn's disease of both small and large intestine with intestinal obstruction</p> <p>K50.914 Crohn's disease, unspecified, with abscess</p> <p>K50.919 Crohn's disease, unspecified, with unspecified complications</p> <p>K51.311 Ulcerative (chronic) rectosigmoiditis with rectal bleeding</p> <p>K51.313 Ulcerative (chronic) rectosigmoiditis with fistula</p> <p>K51.318 Ulcerative (chronic) rectosigmoiditis with other complication</p> <p>K51.319 Ulcerative (chronic) rectosigmoiditis with unspecified complications</p> <p>K51.514 Left sided colitis with abscess</p>

		K51.813 Other ulcerative colitis with fistula K51.90 Ulcerative colitis, unspecified, without complications K52.839 Microscopic colitis, unspecified K50.119 Crohn's disease of large intestine with unspecified complications K50.911 Crohn's disease, unspecified, with rectal bleeding K51.019 Ulcerative (chronic) pancolitis with unspecified complications K51.212 Ulcerative (chronic) proctitis with intestinal obstruction K51.811 Other ulcerative colitis with rectal bleeding K51.911 Ulcerative colitis, unspecified with rectal bleeding K51.918 Ulcerative colitis, unspecified with other complication K50.013 Crohn's disease of small intestine with fistula K50.912 Crohn's disease, unspecified, with intestinal obstruction K51.00 Ulcerative (chronic) pancolitis without complications K51.014 Ulcerative (chronic) pancolitis with abscess K51.211 Ulcerative (chronic) proctitis with rectal bleeding K51.214 Ulcerative (chronic) proctitis with abscess K51.814 Other ulcerative colitis with abscess K51.914 Ulcerative colitis, unspecified with abscess K50.019 Crohn's disease of small intestine with unspecified complications K50.10 Crohn's disease of large intestine without complications K50.114 Crohn's disease of large intestine with abscess K50.118 Crohn's disease of large intestine with other complication K50.819 Crohn's disease of both small and large intestine with unspecified complications K51.011 Ulcerative (chronic) pancolitis with rectal bleeding K51.013 Ulcerative (chronic) pancolitis with fistula K51.213 Ulcerative (chronic) proctitis with fistula K51.219 Ulcerative (chronic) proctitis with unspecified complications K51.312 Ulcerative (chronic) rectosigmoiditis with intestinal obstruction K50.014 Crohn's disease of small intestine with abscess
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		K51.218 Ulcerative (chronic) proctitis with other complication K51.314 Ulcerative (chronic) rectosigmoiditis with abscess K51.513 Left sided colitis with fistula K51.518 Left sided colitis with other complication K51.812 Other ulcerative colitis with intestinal obstruction K52.3 Indeterminate colitis K51.418 Inflammatory polyps of colon with other complication K51.412 Inflammatory polyps of colon with intestinal obstruction K51.40 Inflammatory polyps of colon without complications K51.419 Inflammatory polyps of colon with unspecified complications K51.411 Inflammatory polyps of colon with rectal bleeding K51.414 Inflammatory polyps of colon with abscess K51.413 Inflammatory polyps of colon with fistula K50.00, K50.10, K50.80, K50.90, K51.80, K51.20, K51.30, K51.40, K51.50, K51.00, K51.90
Symptoms – GI	Gastrointestinal bleeding 286.5 459.0 562.02 562.03 562.12 562.13 569.3 569.84 569.85 569.86 578.1 578.9 792.1 998.11 Constipation 564.0 564.00 564.09 564.01 564.02 Diarrhea 008.42 008.43 008.45 008.5 008.8 009.0–009.3 558.2 558.3 558.9 564.4 564.5 564.8 564.9 787.91 abdominal pain 789.0 787.3 789.4 789.6 ischemic bowel disease 557.0 557.1 557.9 irritated bowel syndrome 564.1 bowel habits change 787.99 Hemorrhoid 455 Diverticulitis 562.11 558.1 560.2 560.30 560.39	K56.0 Paralytic ileus K57.41 Diverticulitis of both small and large intestine with perforation and abscess with bleeding K92.2 Gastrointestinal hemorrhage, unspecified R19.5 Other fecal abnormalities K52.0 Gastroenteritis and colitis due to radiation K52.89 Other specified noninfective gastroenteritis and colitis K59.09 Other constipation K62.89 Other specified diseases of anus and rectum R15.0 Incomplete defecation R15.2 Fecal urgency K56.60 Unspecified Intestinal Obstruction K57.53 Diverticulitis of both small and large intestine without perforation or abscess with bleeding K59.01 Slow transit constipation K59.1 Functional diarrhea R19.4 Change in bowel habit K57.33 Diverticulitis of large intestine without perforation or abscess with bleeding K59.03 Drug induced constipation K59.04 Chronic idiopathic constipation K62.5 Hemorrhage of anus and rectum R15.9 Full incontinence of feces R19.7 Diarrhea, unspecified K52.9 Noninfective gastroenteritis and colitis, unspecified K55.21 Angiodysplasia of colon with hemorrhage K57.21 Diverticulitis of large intestine with perforation and abscess with bleeding

	558.1 569.2 569.41 569.61 569.62 569.69 569.81 569.82 596.1 793.4 863.44 863.45 936 997.4	K59.39 Other megacolon K57.93 Diverticulitis of intestine, part unspecified, without perforation or abscess with bleeding K59.00 Constipation, unspecified K59.02 Outlet dysfunction constipation R19.8 Other specified symptoms and signs involving the digestive system and abdomen R63.0 Anorexia K56.7 Ileus, unspecified K57.31 Diverticulosis of large intestine without perforation or abscess with bleeding K57.91 Diverticulosis of intestine, part unspecified, without perforation or abscess with bleeding K92.1 Melena
Symptoms – Constitutional	Anemia 280.0 280.1 280.8 280.9 281.0 281.8 281.9 285.1 285.2 285.9 Weight loss 783.2 783.7 783.21 260–263 710.3	D50.0 Iron deficiency anemia secondary to blood loss (chronic) R63.6 Underweight D50.8 Other iron deficiency anemias R63.4 Abnormal weight loss D50.9 Iron deficiency anemia, unspecified R15. Fecal smearing D50.1 Sideropenic dysphagia K56.1 Intussusception K57.51 Diverticulosis of both small and large intestine without perforation or abscess with bleeding K57.81 Diverticulitis of intestine, part unspecified, with perforation and abscess with bleeding K92.0 Hematemesis
Prior Colectomy	44150 - 44153, 44155, 44156, 44210 – 44212 (CPT) V44.3 V45.3 V55.3 V58.42 V58.49 V58.75 V67.0 V67.1 V67.9	44150 - 44153, 44155, 44156, 44210 – 44212 (CPT)
History of CRC	153.×, 154.0, 154.1, 154.8, V10.0, V10.05, V10.06 G0105, G0213, G0214, G0215, G0231 (HCPCS)	C18.0, C18.1, C18.2, C18.3, C18.4, C18.5, C18.6, C18.7, C18.8, C18.9, C19., C20., C21.2, C21.8, Z85.00, Z85.01, Z85.028, Z85.038, Z85.048, Z85.05, Z85.068, Z85.07, Z85.09, Z85.810, Z85.818, Z85.819 G0105, G0213, G0214, G0215, G0231 (HCPCS)
History of polyps	211.3, 211.4, 230.3, 230.4, V12.72	D01.0, D01.1, D01.2, D12.0, D12.1, D12.2, D12.3, D12.4, D12.5, D12.6, D12.7, D12.8, D12.9, K63.5, Z86.010
Family history of CRC	V16.0, V18.51	Z80.0, Z83.71

S1-Figure. Study design and cohort assembly

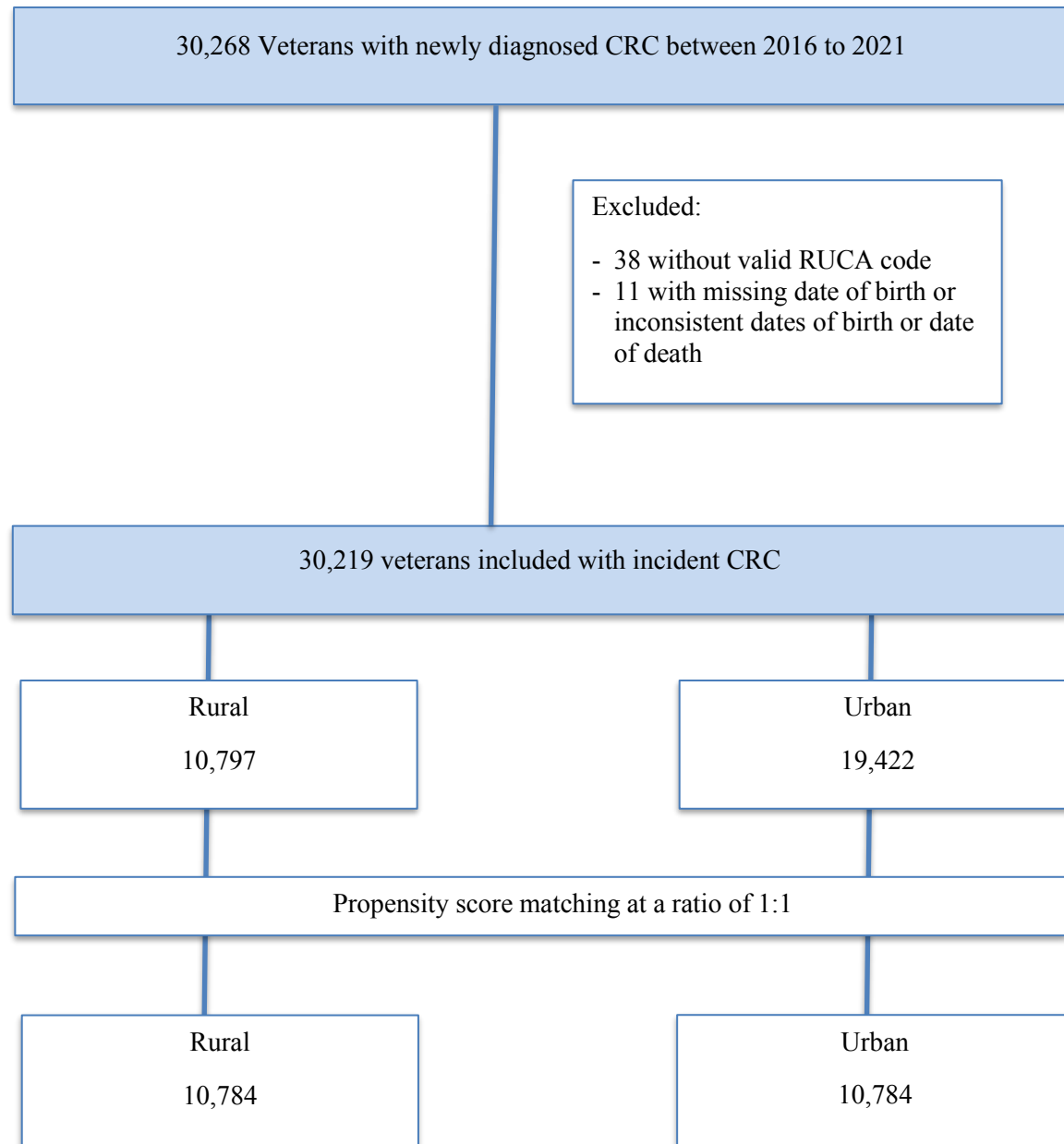


Table S3. Comparison Between Baseline characteristics of veterans with recently diagnosed colorectal cancer of those > 45-year-old vs those ≤45-year-old

Characteristics (n, %)	Rural Cohort			Urban Cohort		
	> 45-year-old	≤45-year-old		> 45-year-old	≤45-year-old	
	N=10,637	N=160		N=19,031	N=391	
CRC diagnosis age, mean (SD)	71.7 (10.1)	39.3 (4.5)	<0.001	72.4 (10.7)	38.8 (11.6)	<0.001
Gender (male)	10,311 (96.9)	132 (82.5)	<0.001	18,260 (96.0)	324 (82.9)	<0.001
Race						
Caucasian	8,896 (83.6)	130 (81.3)	0.419	12,936 (68.0)	229 (58.6)	<0.001
African American	834 (7.8)	16 (10.0)	0.314	4355 (22.9)	106 (27.1)	0.049
Other races	182 (1.7)	2 (1.3)	0.655	433 (2.3)	19 (4.9)	0.001
Unknown/missing	725 (6.8)	12 (7.5)	0.733	1,307 (6.9)	37 (9.5)	0.045
Ethnicity						
Hispanic/Latino	276 (2.6)	9 (5.6)	0.056	942 (5.0)	17 (4.4)	<0.001
Non-Hispanic/Latino	9,809 (92.2)	144 (90.0)		16,660 (87.5)	324 (82.9)	
Unknown/missing	552 (5.2)	7 (4.4)		1,429 (7.5)	50 (12.8)	
Body mass index						
<25 kg/m ²	1,974 (18.6)	28 (17.5)	0.733	4,122 (21.6)	67 (17.1)	0.033
25-30 kg/m ²	3,845 (36.2)	48 (30.0)	0.108	7,094 (37.3)	143 (36.6)	0.776
30-35 kg/m ²	2,932 (27.6)	43 (26.9)	0.846	4,804 (25.2)	102 (26.1)	0.704
35-40 kg/m ²	1,217 (11.4)	27 (16.9)	0.033	1,908 (10.0)	49 (12.5)	0.103
40-45 kg/m ²	407 (3.8)	7 (4.4)	0.720	658 (3.5)	23 (5.9)	0.010
≥45 kg/m ²	175 (1.7)	3 (1.9)	0.821	289 (1.5)	4 (1.0)	0.426
Missing	87 (0.8)	4 (2.5)	0.021	166 (0.9)	3 (0.8)	0.825
Comorbidities						
Charlson comorbidity Index ¹	5.69 (3.43)	3.59 (2.21)	<0.001	5.95 (3.57)	3.54 (2.29)	<0.001
Acute myocardial infarction	1,188 (11.2)	0 (0.0)	<0.001	2,020 (10.6)	4 (1.0)	<0.001
Congestive heart failure	1,717 (16.1)	4 (2.5)	<0.001	3,290 (17.3)	5 (1.3)	<0.001

Peripheral visceral diseases	2,104 (19.8)	4 (2.5)	<0.001	3,917 (20.6)	6 (1.5)	<0.001
Cerebrovascular diseases	1,966 (18.5)	4 (2.5)	<0.001	3,651 (19.2)	4 (0.1)	<0.001
Dementia	478 (4.5)	0 (0.0)	0.006	1,220 (6.4)	0 (0.0)	<0.001
COPD/bronchiectasis	4,050 (38.1)	31 (19.4)	<0.001	6,819 (35.8)	64 (16.4)	<0.001
Rheumatoid diseases	342 (3.2)	3 (1.9)	0.339	571 (3.0)	8 (2.1)	0.272
Peptic ulcer diseases	608 (5.7)	6 (3.8)	0.287	1,150 (6.0)	6 (1.5)	<0.001
Diabetes	4,332 (40.7)	23 (14.4)	<0.001	7,781 (40.9)	34 (8.7)	<0.001
Diabetes with complications	3,231 (30.4)	18 (11.3)	<0.001	5,682 (29.9)	28 (7.2)	<0.001
Hemiplegia	179 (1.7)	2 (1.3)	0.672	393 (2.1)	2 (0.5)	0.031
Kidney diseases	1,753 (16.5)	3 (1.9)	<0.001	3,479 (18.3)	8 (2.1)	<0.001
Mild liver diseases	1,042 (9.8)	16 (10.0)	0.931	2,477 (13.0)	49 (12.5)	0.778
Severe liver diseases	160 (1.5)	2 (1.3)	0.793	356 (1.9)	5 (1.3)	0.391
AIDS	21 (0.2)	3 (1.9)	<0.001	133 (0.7)	9 (2.3)	<0.001
Prior CRC Screening						
FOBT/FIT ²	6,620 (62.2)	31 (19.4)	<0.001	11,040 (58.0)	71 (18.2)	<0.001
Barium enema ²	312 (2.9)	3 (1.9)	0.430	573 (3.0)	5 (1.3)	0.046
Colonography ²	48 (0.45)	0 (0.0)	0.394	142 (0.8)	1 (0.3)	0.262
High risk factors						
Family history of CRC ³	883 (8.3)	21 (13.1)	0.029	1,501 (7.9)	72 (18.4)	<0.001
Inflammatory bowel disease ⁴	412 (3.9)	16 (10.0)	<0.001	777 (4.1)	43 (5.2)	<0.001
Gastrointestinal symptoms & signs ^{4,5}	5,771 (54.3)	97 (61.3)	0.078	10,901 (57.3)	256 (65.5)	0.001
Systemic symptoms & signs ^{4,5}	3,994 (37.6)	51 (31.9)	0.141	8,037 (42.2)	112 (28.6)	<0.001
CRC characteristics						
Proximal CRC	2,304 (21.7)	25 (15.6)	0.065	4,312 (22.7)	75 (19.2)	0.104
Transverse colon CRC	980 (9.2)	14 (8.8)	0.841	1,729 (9.1)	26 (6.7)	0.096
Distal CRC	2,838 (26.7)	63 (39.4)	<0.001	5,333 (28.0)	170 (43.5)	<0.001
Metastatic at time of first diagnosis ⁶	935 (8.8)	17 (10.6)	0.417	1,401 (7.4)	391 (2.0)	0.685

Total mortality during follow up period	3,736 (35.1)	30 (18.8)	<0.001	6,883 (36.2)	76 (19.4)	<0.001
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1 The weighted Charlson comorbidity index was calculated using the method described by Schneeweiss et al.¹⁹

2 Anytime before the date of CRC diagnosis

3 Anytime throughout the study period

4 Within 1 year before date of CRC diagnosis

5 Gastrointestinal symptoms & signs and Systemic symptoms & signs definitions are in Appendix

6 Metastases to liver, bone, lung, or central nervous system

Reference

1. Rogers CR, Blackburn BE, Huntington M, et al. Rural-urban disparities in colorectal cancer survival and risk among men in Utah: a statewide population-based study. *Cancer Causes Control* 2020;31:241-253.
2. Luhn P, Kuk D, Carrigan G, et al. Validation of diagnosis codes to identify side of colon in an electronic health record registry. *BMC Med Res Methodol* 2019;19:177.
3. Abraha I, Serraino D, Giovannini G, et al. Validity of ICD-9-CM codes for breast, lung and colorectal cancers in three Italian administrative healthcare databases: a diagnostic accuracy study protocol. *BMJ Open* 2016;6:e010547.
4. Adams MA, Kerr EA, Dominitz JA, et al. Development and validation of a new ICD-10-based screening colonoscopy overuse measure in a large integrated healthcare system: a retrospective observational study. *BMJ Qual Saf* 2022.
5. Saini SD, Vijan S, Schoenfeld P, et al. Role of quality measurement in inappropriate use of screening for colorectal cancer: retrospective cohort study. *BMJ* 2014;348:g1247.
6. Mittal S, Lin YL, Tan A, et al. Limited life expectancy among a subgroup of medicare beneficiaries receiving screening colonoscopies. *Clin Gastroenterol Hepatol* 2014;12:443-450 e1.
7. Mojica CM, Bradley SM, Lind BK, et al. Initiation of Colorectal Cancer Screening Among Medicaid Enrollees. *Am J Prev Med* 2020;58:224-231.
8. Charlson ME, Pompei P, Ales KL, et al. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987;40:373-83.
9. Cheng D, DuMontier C, Yildirim C, et al. Updating and Validating the U.S. Veterans Affairs Frailty Index: Transitioning From ICD-9 to ICD-10. *J Gerontol A Biol Sci Med Sci* 2021;76:1318-1325.