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Keywords: colorectal cancer; diagnostic delays; obesity; body mass index; appraisal interval

The contribution of body mass index to appraisal delay in colorectal cancer diagnosis: a structural equation modelling study

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Background: Appraisal delay (AD) refers to the time interval between onset of symptoms and the date a patient first seeks healthcare. Because studies have shown that individuals who are overweight or obese may delay or avoid seeking healthcare due to stigma, this study aims to investigate the role that weight plays in AD among symptomatic individuals subsequently diagnosed with colorectal cancer (CRC).

Methods: Structural equation modelling tested the relationship between AD, body mass index (BMI), financial barriers, cognitive barriers, and reported symptoms among 179 newly diagnosed CRC patients in two U.S. healthcare systems.

Results: BMI was directly and significantly related to AD ($\beta = 0.10$; P = 0.044) and to cognitive barriers ($\beta = 0.24$; P = 0.005). Cognitive barriers were direct and significant predictors of increased AD ($\beta = 0.32$; P = 0.000). Symptom experience and financial barriers were mediated through cognitive barriers.

Conclusions: Model results support the hypothesis that increased BMI is significantly and directly associated with increased AD and key cognitive barriers relevant to care-seeking behaviour.

Delays in colorectal cancer (CRC) diagnosis pose a continuing challenge to timely treatment efforts worldwide, and may result from a combination of patient, practitioner, and health system factors (Mitchell *et al*, 2008; Butler *et al*, 2013). Obesity is a known CRC risk factor (Renehan *et al*, 2008; Norat *et al*, 2010); however, obesity-related stigma is pervasive (Puhl and Heuer, 2010), and both obesity and its related stigma have been linked to healthcare-seeking delays and avoidance (Merrill and Grassley, 2008; Mold and Forbes, 2013). For example, a medical chart review study

examining receipt of CRC screening found that obese patients had 25% decreased odds of having been screened compared to non-obese patients (Ferrante *et al*, 2006).

Because of the linkages among obesity, CRC risk and healthcare-seeking behaviour, we became interested in the potential role of body mass index (BMI) in CRC diagnostic delays. Delays can be characterised according to intervals between specific time-points: dates of first symptom, first presentation, referral, and diagnosis (Weller *et al*, 2012). Here we consider delays occurring in

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the first interval, often termed appraisal delay (AD) (Mitchell *et al*, 2008; Simon *et al*, 2010). We have shown in a previous study that AD is strongly associated with four avoidant coping behaviours, or 'cognitive barriers,' among symptomatic CRC patients; these behaviours mediate the impact of financial barriers and reported symptoms on AD (Siminoff *et al*, 2011; Siminoff *et al*, 2014). However, it is not well-understood which patients may face these barriers. Because of previously-identified associations between obesity and healthcare avoidance, we tested the role that increased BMI may play in AD in the same sample.

MATERIALS AND METHODS

This was a cross-sectional, mixed-methods study designed to test whether or not BMI contributes to increases in AD among symptomatic patients subsequently diagnosed with CRC. Patients were recruited from academic and community oncology settings in two U.S. states, had been diagnosed with CRC stages I–IV within the previous six months, and were experiencing symptoms before initial healthcare consultation. Data collection methods for the larger study are detailed elsewhere, and included medical chart reviews and two-hour semi-structured interviews with 252 newly diagnosed CRC patients (Siminoff *et al.*, 2011, 2014). A second

chart review was conducted at a later date to extract documented height/weight for BMI calculation. The study was approved by relevant ethics boards and all participants provided informed consent

The primary outcome variable was AD, operationalized as the time elapsed between patient-reported symptom onset and medical record-verified date of first provider consultation. AD was calculated as a continuous measure in months and log-transformed for analysis.

BMI was calculated from medical record-documented height/ weight and used as both a continuous measure and ordinal measure. The variable 'financial barriers' represented the presence/ absence of patient-reported financial difficulties to seeking healthcare. 'Cognitive barriers' was a latent variable representing the presence/absence of four avoidant coping behaviours: patients' fear of tests, embarrassment seeking care, belief that patient is too young to have cancer, and belief that symptoms are not serious. 'Reported symptoms' represented the number of cardinal CRC symptoms participants experienced before seeking healthcare (range = 0–10). Socio-demographic variables were derived from a structured questionnaire.

Statistical analysis. Chi-square tests and independent samples *t*-tests were used to identify differences in the above variables

		BMI Data		BMI category		
Variable	Full sample (N = 252)	Available (n = 179)	Not available (n=73)	Normal weight ^a (BMI \leq 24.9) ($n = 54$)	Overweight (BMI = 25-29.9) (n = 58)	Obese (BMI ≥ 30) (n = 67)
Age	•			<u> </u>		
<50 years 50–75 years >75 years	25.4% (64) 64.3% (162) 10.3% (26)	25.1% (45) 64.8% (116) 10.1% (18)	26.0% (19) 63.0% (46) 11.0% (8)	20.4% (11) 63.0% (34) 16.7% (9)	19.0% (11) 74.1% (43) 6.9% (4)	34.3% (23) 58.2% (39) 7.5% (5)
Race	1					
Caucasian African American Other	52.8% (133) 44.0% (111) 3.2% (8)	54.7% (98) 41.9% (75) 3.4% (6)	47.9% (35) 49.3% (36) 2.7% (2)	64.8% (35) 27.8% (15) 7.4% (4)	48.3% (28) 50.0% (29) 1.7% (1)	52.2% (35) 46.3% (31) 1.5% (1)
Gender	50.40/./400	50.00/ (04)	5 (00 ((44)	11.10/ (0.1)	54 70/ (00)	55.00/ /07/
Male Female	52.4% (132) 47.6% (120)	50.8% (91) 49.2% (88)	56.2% (41) 43.8% (32)	44.4% (24) 55.6% (30)	51.7% (30) 48.3% (28)	55.2% (37) 44.8% (30)
Total household incom	ne					
Less than \$10 000 \$10 000–29 000 \$30 000–49 000 \$50 000–74 000 \$75 000–100 000 > \$100 000 Don't know	16.7% (42) 25.0% (63) 18.3% (46) 10.3% (26) 13.1% (33) 11.9% (30) 4.8% (12)	16.2% (29) 24.6% (44) 16.8% (30) 11.2% (20) 14.5% (26) 14.0% (25) 2.8% (5)	17.8% (13) 26.0% (19) 21.9% (16) 8.2% (6) 9.6% (7) 6.8% (5) 9.6% (7)	20.4% (11) 22.2% (12) 20.4% (11) 3.7% (2) 20.4% (11) 9.3% (5) 3.7% (2)	19.0% (11) 19.0% (11) 13.8% (8) 10.3% (6) 12.1% (7) 22.4% (13) 3.4% (1)	10.4% (7) 31.3% (21) 16.4% (11) 17.9% (12) 11.9% (8) 10.4% (7) 2.8% (1)
Marital status ^b						
Married/Partnered Not married/Partnered	52.4% (132) 47.6% (120)	52.5% (94) 47.5% (85)	52.1% (38) 47.9% (35)	38.9% (21) 61.1% (33)	46.6% (27) 53.4% (31)	68.7% (46) 31.3% (21)
Education						
HS degree or less Some college or higher Missing	47.6% (120) 52.0% (131) 0.4% (1)	45.8% (82) 54.2% (97) 0.0% (0)	52.1% (38) 46.6% (34) 1.4% (1)	50.0% (27) 50.0% (27) 0.0% (0)	43.1% (25) 56.9% (33) 0.0% (0)	44.8% (30) 55.2% (37) 0.0% (0)
Occupation						
Employed Not employed	44.4% (112) 55.6% (140)	44.1% (79) 55.9% (100)	45.2% (33) 54.8% (40)	40.7% (22) 59.3% (32)	50.0% (29) 50.0% (29)	41.8% (28) 58.2% (39)
Study site						
Virginia Ohio	66.7% (168) 33.3% (84)	63.1% (113) 36.9% (66)	75.3% (55) 24.7% (18)	64.8% (35) 35.2% (19)	69.0% (40) 31.0% (18)	56.7% (38) 43.3% (29)

Abbreviation: BMI = body mass index

The underweight category (BMI < 18.5) included only three participants and was collapsed into the normal weight category (BMI = 18.5–24.9) for analysis (BMI \leq 24.9).

^bSignificant difference in marital status among BMI categories (χ 2=11.85, P=0.003, Cramer's V=0.257).

Table 2. Financial barriers, cognitive barriers, and symptoms										
		Available BMI data		BMI category						
Variable	Full sample (N = 252)	Available (n = 179)	Not available (n=73)	Normal weight ^a (BMI ≤ 24.9) (n = 54)	Overweight (BMI = 25-29.9) (n = 58)	Obese (BMI ≥ 30) (n = 67)				
Financial barriers ^b										
Reported	28.6% (72)	24.6% (44)	38.4% (28)	31.5% (17)	22.4% (13)	20.9% (14)				
Cognitive barriers										
Fear of tests ^c Embarrassment seeking care	24.2% (61) 11.9% (30)	20.2% (36) 11.7% (21)	34.2% (25) 12.3% (9)	18.9% (10) 11.1% (6)	13.8% (8) 8.6% (5)	26.9% (18) 14.9% (10)				
Belief too young to have cancer ^d	11.5% (29)	10.7% (19)	13.7% (10)	9.4% (5)	3.4% (2)	17.9% (12)				
Belief symptoms not serious	39.7% (100)	40.8% (73)	37.0% (27)	31.5% (17)	44.8% (26)	44.8% (30)				
Total symptoms										
No cardinal symptoms	6.0% (15)	7.8% (14)	1.4% (1)	1.9% (1)	13.8% (8)	7.5% (5)				
1–2 3–4	44.8% (113) 37.3% (94)	45.8% (82) 35.2% (63)	42.5% (31) 42.5% (31)	50.0% (27) 35.2% (19)	43.1% (25) 29.3% (17)	44.8% (30) 40.3% (27)				
5–6 7–8	7.9% (20) 4.0% (10)	7.8% (14) 3.6% (6)	8.2% (6) 5.5% (4)	13.0% (7) 0.0% (0)	8.6% (5) 5.2% (3)	3.0% (2) 4.5% (3)				
Symptoms										
Stomach pain	57.5% (145)	57.0% (102)	58.9% (43)	55.6% (30)	60.3% (35)	55.2% (37)				
Diarrhoea Constipation	36.5% (92) 37.7% (95)	36.9% (66) 38.0% (68)	35.6% (26) 37.0% (27)	25.9% (14) 40.7% (22)	39.7% (23) 43.1% (25)	43.3% (29) 31.3% (21)				
Indigestion Weight loss ^e	32.9% (83) 34.1% (86)	34.6% (62) 34.1% (61)	28.8% (21) 34.2% (25)	33.3% (18) 48.1% (26)	39.7% (23) 29.3% (17)	31.3% (21) 26.9% (18)				
Blood in stool Fatigue	46.4% (117) 38.5% (97)	44.1% (79) 36.3% (65)	52.1% (38) 43.8% (32)	42.6% (23) 37.0% (20)	39.7% (23) 39.7% (23)	49.3% (33) 32.8% (22)				
Vomiting Rectal bleeding	17.5% (44) 33.7% (85)	16.2% (29) 36.9% (66)	20.5% (15) 26.0% (19)	14.8% (8) 31.5% (17)	10.3% (6) 39.7% (23)	22.4% (15) 38.8% (26)				
Nausea ^f	25.0% (63)	20.7% (37)	35.6% (26)	20.4% (11)	22.4% (13)	19.4% (13)				

fSignificant difference in nausea as a pre-diagnosis symptom between cases with/without BMI data ($\chi 2 = 5.41$, P = 0.020, phi = 0.157).

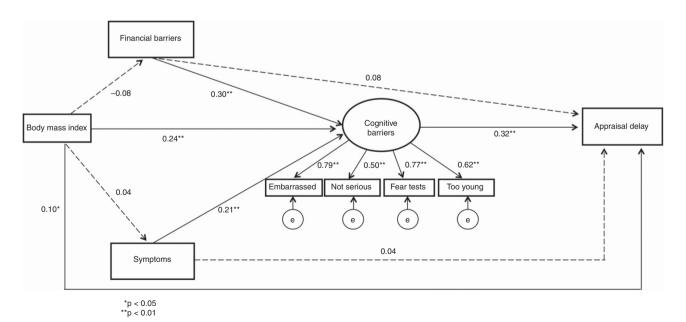


Figure 1. Mediation model with standardised parameter estimates. Final model of factors contributing to AD (outcome variable), including BMI, financial barriers, reported symptoms, and cognitive barriers, with standardised parameter estimates (β) (n = 179).

Abbreviation: BMI = body mass index.

^aThe underweight category (BMI < 18.5) included only three participants and was collapsed into the normal weight category (BMI = 18.5–24.9) for analysis (BMI ≤ 24.9).

 $^{^{\}mathbf{b}}$ Significant difference in financial barriers between cases with/without BMI data ($\chi 2 = 4.17$, P = 0.041, phi = 0.138).

c. Significant difference in fear of tests between cases with/without BMI data ($\chi 2 = 4.80$, P = 0.029, phi = 0.148).

 $^{^{}m d}$ Significant difference in belief too young to have cancer among BMI categories ($\chi 2 = 6.94$, P = 0.031, Cramer's V = 0.197).

eSignificant difference in weight loss as a pre-diagnosis symptom among BMI categories (χ 2=6.90, P=0.032, Cramer's V=0.196).

between cases for whom BMI could and could not be calculated and among BMI categories. ANOVAs were used to identify differences in AD length by BMI category.

Using results from Siminoff and colleagues as a guide (Siminoff et al, 2014), we developed a conceptual framework hypothesising an association between AD and BMI (continuous measure), financial barriers, reported symptoms, and cognitive barriers (Supplementary Figure 1). Because the prior analysis illustrated the importance of considering the direct and indirect effects of predictor variables, and because the cognitive barriers construct available was a latent (or unobserved) variable, we used structural equation modelling to test these relationships. Structural equation modelling represents a flexible approach to estimating several equations simultaneously, with the same variable serving as predictor in one equation and criterion in another. It allows for latent variable estimation simultaneously with other models of interest (Nachtigall et al, 2003). Full information maximum likelihood (FIML) estimation was used to fit the model to handle missing data. Mplus (v7.4) was used for model estimation.

RESULTS

The mean age of the sample was 57.9 years (s.d. \pm 12.2, median = 57.0). See Table 1 for sociodemographic characteristics and Table 2 for information on financial barriers, cognitive barriers, and total and specific symptoms reported. Financial barriers were reported by 28.6% (n=72) of the total sample, cognitive barriers were expressed by 52.0% (n=131), and mean number of symptoms reported was 2.6 (s.d. \pm 1.7, range = 0-8).

A total of 179 patients (71.0%) out of 252 had sufficient medical record documentation to enable BMI calculation. Few differences between the two groups were found, although cases with BMI information were less likely to report financial barriers (24.6% vs 38.4%, P = 0.041), express a fear of tests (20.2% vs 34.2%, P = 0.029), or experience nausea pre-diagnosis (20.7% vs 35.6%, P = 0.020). The sample reflected the U.S. population's age-adjusted weight distribution (CDC, 2015): 30.2% (n = 54) were underweight/normal weight, 32.4% (n = 58) were overweight, and 37.4%(n=67) were obese. Significant differences were found among BMI groups in marital status (38.9%, 46.6%, 68.7% married, P = 0.003), belief that patient is too young to have cancer (9.4%, 3.4%, 17.9%, P = 0.031), and pre-diagnosis weight loss (48.1%, 29.3%, 26.9%, P = 0.032). Mean BMI was 29.2 (s.d. ± 7.2 , range = 13.0-60.8). Mean AD was 4.8 months (s.d. ± 7.0 , range = 0.0-57.2) for all participants, with no significant differences among groups.

The mediation model with standardised parameter estimates is shown in Figure 1. Though prior analyses tested the demographic variables and did not find the covariate effects to be significant, they were adjusted for in this model and were again not significant. The unadjusted mediation model resulted in good fit to the data $(x^2 = 15.45; df = 14; P = 0.349; CFI = 0.99; TLI = 0.98; RMSEA$ (90% CI) = 0.02(0.00-0.07)). The direct effect of BMI on AD was significant ($\beta = 0.10$; P = 0.044). The relationship between BMI and AD was also mediated through the cognitive barriers variable $(\beta = 0.24; P = 0.005)$, which itself had a significant direct effect on AD ($\beta = 0.32$; P = 0.000). The standardised factor loadings for the latent variable supported their use (i.e., they ranged from 0.50 to 0.79 and were all significant (P < 0.01)). As in the initial model, reported symptoms ($\beta = 0.04$; P = 0.470) and financial barriers $(\beta = 0.08; P = 0.215)$ did not have significant direct effects on AD, and were not significantly associated with BMI ($\beta = 0.04$; P = 0.639and $\beta = -0.08$; P = 0.246, respectively). Instead, the effects of symptoms ($\beta = 0.21$; P = 0.010) and financial barriers ($\beta = 0.30$;

 $P\!=\!0.000$) on AD were mediated through the set of cognitive barriers, indicating that patients' subjective experiences of their symptoms and financial situation were not independently related to healthcare-seeking behaviours but instead were governed by their beliefs and emotions surrounding cancer and testing. The variables included in this model explained 15.3% of the variability in AD

DISCUSSION

This study sought to determine the contribution of BMI to AD among symptomatic CRC patients. Model results supported the hypothesis that increased BMI is significantly and directly associated with increased AD, as well as key cognitive barriers involved in care-seeking behaviour. Cognitive barriers were direct and significant predictors of increased AD, and mediated the impact of both symptom experience and financial barriers

Obesity-related stigma has been shown to play a role in healthcare-seeking delays and avoidance (Mold and Forbes, 2013). While we did not directly measure stigma, two cognitive barriers tested here are related: embarrassment seeking care and fear of tests (Simon *et al*, 2010; Forbes *et al*, 2014; May *et al*, 2016). These barriers may be exacerbated for overweight patients given research underscoring the negative impacts of obesity stigma, such as demeaning interactions with providers, embarrassment being weighed, and a need for differently-sized equipment and gowns (Amy *et al*, 2006; Merrill and Grassley, 2008). They may also interact with the non-specificity of many CRC symptoms, such as gastrointestinal distress. Specifically, individuals with high BMI can experience a greater number of co-morbidities or physical discomfort, which may heighten appraisal difficulties.

Findings should be interpreted with limitations in mind. First, a subset of medical records lacked sufficient height/weight documentation for BMI calculation; ideally, weight would be measured anthropometrically at symptom onset. The risk of selectivity bias may limit generalisability, although minimal differences were found between participants with/without BMI data. Our approach to handling missing data using FIML estimation was conservative, and findings remain robust. Second, it is possible that retrospective self-report resulted in recall bias, although we used accepted recall stimulation techniques (Barsky, 2002) and studies have demonstrated the reliability of CRC symptom self-report (Adelstein *et al*, 2008). Finally, this study may not be generalisable to non-U.S. healthcare contexts.

While this study cannot determine causality, it provides a basis for future prospective analyses focused on weight and healthcare-seeking delays. Findings highlight the need to consider the complex interplay between individual perceptions, social norms and health system factors (such as the availability of weight-accommodating equipment) that is likely contributing to the observed relationship between weight and increased AD. Although we studied this relationship among newly diagnosed patients, a similar relationship is likely to exist across the cancer care continuum, from screening to treatment, surveillance and even end-of-life care.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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Supplementary Information accompanies this paper on British Journal of Cancer website (http://www.nature.com/bjc)