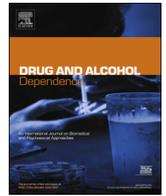




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Utility of routine alcohol screening for monitoring changes in alcohol consumption



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ABSTRACT

Background: Routine alcohol screening scores are increasingly available in electronic health records (EHRs). Changes in such scores could be useful for monitoring response to brief intervention or treatment of alcohol use disorder. However, it is unclear whether changes in clinically-documented AUDIT-C alcohol screening scores reflect true changes in drinking. This study evaluated associations between changes in EHR AUDIT-C scores and changes in high density lipoprotein cholesterol (HDL), a laboratory test that reflects average alcohol consumption.

Methods: National U.S. Veterans Affairs EHR data (2004–2007) were used to identify patients screened with the AUDIT-C (0–12 points), on two occasions at least a year apart, who had HDL measured in the year after each screen. First differencing linear regression estimated associations between changes in AUDIT-C score (-12 to 12 points; modeled categorically to allow for non-linear associations) and subsequent changes in HDL (mg/dL), adjusting for baseline HDL. Additional analyses evaluated whether associations between changes in AUDIT-C and changes in HDL were modified by baseline AUDIT-C.

Results: Among 316,712 patients, increases—but not decreases—in AUDIT-C scores were associated with commensurate changes in HDL. However, a significant interaction was observed with baseline AUDIT-C score ($p < 0.00001$), which revealed that decreases in AUDIT-C scores were also associated with commensurate decreases in HDL (p -values < 0.05) except among the 1.5% of patients with the highest baseline AUDIT-C scores (10–12).

Conclusions: Findings suggest that changes in EHR AUDIT-C scores reflect changes in drinking. These results support the use of clinically-documented alcohol screening scores for monitoring patients' alcohol use over time.

1. Introduction

Over a decade ago, experts recommended that high quality care for unhealthy alcohol use requires monitoring changes in alcohol use over

time (Institute of Medicine (US) Committee on Crossing the Quality Chasm: Adaptation to Mental Health and Addictive Disorders, 2006). With increasing implementation of routine screening for unhealthy alcohol use, the need for simple and effective methods of monitoring

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alcohol use has only become more pressing (Bradley and Kivlahan, 2014; National Council for Behavioral Health, 2018). Such monitoring would be appropriate for all patients identified to have unhealthy alcohol use and particularly important for assessing response to interventions, whether counseling, behavioral therapy, or medication.

Some have suggested that scaled screening questionnaires for unhealthy alcohol use may be useful for monitoring changes in drinking over time (National Council for Behavioral Health, 2018), much the same way scores on the PHQ-9 screen for depression can also be used to monitor changes in depression severity (Kroenke and Spitzer, 2002; Unutzer et al., 2006). Brief alcohol screening questionnaires, such as the 3-item Alcohol Use Disorders Identification Test – Consumption (AUDIT-C) questionnaire, have been implemented in routine clinical care across diverse settings through the use of electronic health records (EHRs) (Johnson et al., 2013a, 2013b; Rose et al., 2008; Ornstein et al., 2013; Bradley et al., 2006; Bobb et al., 2017). Because AUDIT-C scores are strongly associated with average alcohol consumption based on confidential in-depth interviews (Rubinsky et al., 2013), they may be useful for monitoring changes in drinking over time. However, it is unknown whether within-person changes in AUDIT-C scores documented in EHRs as part of routine care reflect changes in alcohol consumption. Specifically, clinically-documented AUDIT-C scores can be biased (Bradley et al., 2011; Hawkins et al., 2007; Davis et al., 2010; Williams et al., 2015; McGinnis et al., 2016), and changes in scores could reflect measurement error due to inconsistent administration of the questionnaire by clinicians (e.g., skipping and altering items) and/or patient social desirability bias (Williams et al., 2015).

The primary aim of this study was to determine whether changes in AUDIT-C scores documented as part of routine medical care are associated with commensurate changes in a laboratory test known to reflect average alcohol consumption—high density lipoprotein cholesterol (HDL) (Brien et al., 2011). HDL is commonly measured in routine primary care (Helfand and Carson, 2008) and has been shown to increase in response to increased drinking in numerous experimental interventional studies (Brien et al., 2011). Prior studies have demonstrated a strong association between cross-sectional EHR AUDIT-C scores and HDL (Berger et al., 2013) and between changes in EHR AUDIT-C score groups and subsequent HDL (Bradley et al., 2016), but no study has evaluated whether within-person changes in AUDIT-C scores reflect changes in drinking. The present study examines the within-person association between changes in EHR AUDIT-C scores and changes in HDL using analytic methods that implicitly control for unobserved confounding by time-invariant factors. Additionally, to understand whether EHR AUDIT-C scores could be used for monitoring within-person changes in drinking equally across subgroups of patients, this study planned *a priori* to evaluate whether the association between changes in AUDIT-C score and changes in HDL was modified by baseline AUDIT-C groups as well as demographic or clinical factors known to be associated with alcohol use.

2. Methods

2.1. Study sample and data sources

This longitudinal cohort study included patients from 24 VA medical centers in the Northern and Western U.S. (VA Networks 18–22) who had (1) documented alcohol screening with the AUDIT-C on two occasions at least a year apart (1/1/04–12/31/07) and (2) HDL laboratory results within a year after each screen. Alcohol screening scores, HDL levels, diagnoses, addictions treatment utilization, and demographic characteristics documented in the EHR were obtained from the VA Informatics and Computing Infrastructure (VINCI), which includes a national warehouse of VA clinical and administrative data. VA Medicare claims were used to supplement information on demographic characteristics and diagnoses. Approval of this study and waivers of informed consent and Health Insurance Portability and Accountability

Act (HIPAA) authorization were granted by the VA Puget Sound Health Care System Institutional Review Board (IRB).

2.2. Measures

2.2.1. AUDIT-C alcohol screening scores

The VA has required annual alcohol screening with the AUDIT-C since 2003 and screened over 90% of primary care outpatients during the study period (Bradley et al., 2006). The AUDIT-C is a validated screen for past-year unhealthy alcohol use scored 0–12 points (Johnson et al., 2013a, 2013b; Bradley et al., 2007), with a score of 0 indicating no past-year alcohol use and increasing scores indicative of greater consumption (Rubinsky et al., 2013; Berger et al., 2013). Patients' first AUDIT-C during the study period is referred to as their baseline AUDIT-C, and their first subsequent AUDIT-C at least 12 months later is referred to as their follow-up AUDIT-C. Change in AUDIT-C was computed as the difference in scores from the patient's baseline AUDIT-C to follow-up AUDIT-C (range: –12 to 12 points; 0 indicates no change, positive values indicate an increase in AUDIT-C score, and negative values indicate a decrease in AUDIT-C score).

2.2.2. HDL cholesterol

HDL was selected as the outcome for this study because it is commonly measured in primary care as part of routine cardiovascular risk assessment (U.S. Preventive Services Task Force et al., 2016), it reflects average daily alcohol consumption and changes rapidly in response to experimentally manipulated changes in drinking (Rimm et al., 1999; Brien et al., 2011), and is therefore amenable to studying within-person change. Experimental trials of alcohol administration have shown that HDL increases with consumption in a dose-response manner: drinking 1–2, 2–4 or ≥ 4 drinks per day for a period of at least two weeks was associated with increases in HDL of 2.8, 3.9, and 5.4 milligrams (mg) of cholesterol per deciliter (dL) of blood, respectively (Brien et al., 2011). Because HDL is typically ordered for reasons unrelated to drinking, it is available on a sample of medical outpatients relatively unbiased by level of alcohol use.

The first HDL measurement on the day of or within the 365 days following the patient's baseline and follow-up AUDIT-Cs were used as the baseline HDL and follow-up HDL, respectively. When there was more than one HDL recorded on the same day, the mean was used. Change in HDL was computed as the difference in mg/dL from the patient's baseline HDL to their follow-up HDL (such that 0 indicates no change, positive values indicate an increase in HDL, and negative values indicate a decrease in HDL).

2.2.3. Other measures

Demographic characteristics included gender (male, female), race/ethnicity (white, non-white), age at the time of baseline AUDIT-C (21–29, 30–44, 55–64, 65+ years), and marital status (married, divorced/separated/widowed, never married) at the time of each AUDIT-C. VA service coverage, based on multiple factors including military service history, service-connected disability rating, and income level, was determined at the time of each AUDIT-C and categorized into no copay (indicating higher service-connected medical need and/or lower socioeconomic status), partial copay, or full copay. Clinical measures included 1) past-year smoking (yes, no) determined at the time of each AUDIT-C using EHR text data elements (McGinnis et al., 2011), 2) medical comorbidity measured using the Deyo-Charlson comorbidity index computed based on International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnosis codes in the year prior to each AUDIT-C and dichotomized at a threshold of ≥ 3 points (Deyo et al., 1992), and 3) any recognized substance use disorder (yes, no) measured based on any documented VA addictions treatment or any ICD-9-CM diagnosis indicating a substance use disorder or an alcohol-related medical condition in the year prior to the baseline AUDIT-C. Time from AUDIT-C to HDL was calculated based on the number of

days between each AUDIT-C and the subsequent HDL, and a single indicator of whether both intervals (days from baseline AUDIT-C to baseline HDL and days from follow-up AUDIT-C to follow-up HDL) were ≤ 90 days was calculated.

2.3. Analyses

Initial analyses describe demographic and clinical characteristics overall and across groups of patients defined by their change in AUDIT-C score. Differences in patient characteristics across groups were tested based on Pearson chi-squared statistics for categorical variables and non-parametric Kruskal-Wallis tests for continuous variables.

Main analyses estimated the change in HDL associated with each possible change in AUDIT-C score (-12 to 12) based on a linear regression model that adjusted for baseline HDL using the best fitting fractional polynomial (powers -2 and 3) and estimated robust standard errors using the sandwich estimator to account for correlated data among patients from the same medical center. By design, such “change-in-change” or first-differencing analyses implicitly control for all patient-specific factors, whether measured or unmeasured, that do not vary over the study period (e.g., clinical and/or social factors that may be associated with propensity to change drinking and/or HDL) because they are present on both sides of the equation and subtract out in these differencing models (Liker et al., 1985). To allow for a non-linear association between change in AUDIT-C score and change in HDL, each possible change in AUDIT-C score was modeled as a separate categorical variable, with 0 points (no change in AUDIT-C) as the referent. A linear trend was evaluated based on a linear contrast test.

To understand whether the association between change in AUDIT-C and change in HDL held across subgroups of patients, additional analyses evaluated interactions between AUDIT-C change and baseline AUDIT-C score as well as demographic and clinical characteristics hypothesized *a priori* to potentially modify the association. Specifically, we repeated main analyses adding baseline AUDIT-C score and the interaction between baseline AUDIT-C score and change in AUDIT-C at follow-up screening. Baseline AUDIT-C scores (0, 1–4, 5–9, 10–12) and changes in AUDIT-C scores ($\pm 0, 1, 2, 3-4, 5-9, 10-12$ points) were grouped to facilitate interpretability and increase precision of the estimates. Average change in HDL was estimated across categories of change in AUDIT-C score for each baseline AUDIT-C group based on recycled prediction methods that hold the covariate distribution constant (Basu and Rathouz, 2005). Wald tests were used to evaluate an overall interaction and to compare the average change in HDL associated with each category of change in AUDIT-C versus no change in AUDIT-C (the referent). We similarly evaluated interactions between the above AUDIT-C change groups and gender, age, and any recognized substance use disorder.

Sensitivity analyses, planned *a priori*, evaluated the association between change in AUDIT-C score and change in HDL in the subset of patients who had HDLs within the 90 days following each AUDIT-C, a timeframe that reduces the likelihood patients may have changed their drinking after an AUDIT-C. We also assessed whether the inclusion of covariates measured at the time of each AUDIT-C, that could possibly (but were unlikely to) vary with time, meaningfully changed results; these covariates included marital status, VA service coverage, past-year smoking status, and Deyo-Charlson comorbidity.

3. Results

Overall 549,563 patients had a documented pair of AUDIT-Cs at least a year apart during the study period. Of those, 316,712 (58%) had HDLs documented in the year after each AUDIT-C and were included in the study. Most eligible patients were male (96%), White (67%), 65 years and older (60%), and married (56%) (Table 1). Over half (51%) of eligible veterans reported no past-year alcohol use (AUDIT-C score 0) on their baseline AUDIT-C, while another 40% had low-level drinking

Table 1
Characteristics of the Study Sample at the time of Baseline Alcohol Screening.

	N	(Column %)
Total	316,712	(100%)
Female	13,582	(4.3%)
Age*		
21-29	928	(0.3%)
30-44	9,474	(3.1%)
45-64	117,830	(37%)
65+	188,480	(60%)
Race*		
Non-white	49,316	(16%)
White	212,353	(67%)
Marital Status*		
Single/Never Married	40,305	(13%)
Divorced/Separated/Widowed	97,538	(31%)
Married	178,501	(56%)
VA Service Coverage		
No Copay (Full Coverage)	59,390	(19%)
Partial Copay	64,592	(20%)
Full Copay	192,730	(61%)
Deyo Comorbidity ≥ 3	39,002	(12%)
Past-year Smoker	85,592	(27%)
Baseline AUDIT-C		
0 points	162,574	(51%)
1-4 points	126,550	(40%)
5-9 points	22,983	(7.3%)
10-12 points	4,605	(1.5%)
Days between:	Median	(Interquartile range)
Baseline and Follow-up AUDIT-C	489	(407, 658)
Baseline AUDIT-C and HDL	47	(0, 170)
Follow-up AUDIT-C and HDL	67	(0, 181)

* Total may not sum to 100% due to missing values.

(scores 1–4), and only 7.3% and 1.5% had AUDIT-C scores 5–9 and 10–12, respectively.

Most (83%) patients with non-drinking (AUDIT-C score 0) at baseline had no change in AUDIT-C score at follow-up, and most (72%) with low-level drinking (AUDIT-C score 1–4) at baseline changed their AUDIT-C score 0–1 points (Appendix A*). Changes in AUDIT-C score were more common among men vs. women, younger vs. older age groups, unmarried vs. married patients, patients reporting past-year smoking vs. not, patients with vs. without VA service copays, and patients with less vs. more comorbidity.

Main analyses based on first-differenced regression adjusting for baseline HDL revealed an overall dose-response association between change in AUDIT-C score and change in HDL with a significant linear trend ($p < 0.0005$). Among patients with no change in AUDIT-C score, HDL decreased by 0.05 mg/dL on average. Compared to no change in AUDIT-C score, increases in AUDIT-C score of every magnitude were associated with statistically significant increases in HDL (p -values < 0.05), whereas significant decreases in HDL were observed only if AUDIT-C scores decreased by at least 9 points. Fig. 1 depicts the estimated change in HDL associated with each possible change in AUDIT-C at follow-up screening (Appendix B*). Increases in AUDIT-C score of 1, 2, 3 and 4 points were associated with progressively larger increases in HDL: 0.5, 1.0, 1.3 and 2.0 mg/dL, respectively. Mean change in HDL stayed relatively stable across changes in AUDIT-C scores of 5–9 points (~2.0 mg/dL) but increased to approximately 3.0 mg/dL for those with changes in AUDIT-C scores of 10 or more points. A decrease in AUDIT-C score of 9 points was associated with a decrease in HDL of 1.3 mg/dL, whereas decreases in AUDIT-C score of 10–12 points were associated with decreases in HDL up to 3.4 mg/dL.

In analyses assessing differences in the association across subgroups, baseline AUDIT-C statistically significantly modified the association between changes in AUDIT-C and changes in HDL (Fig. 2). Increases in AUDIT-C score were most strongly associated with increases in HDL in the large group of patients who reported no past-year drinking (AUDIT-C 0) at baseline. Decreases in AUDIT-C score of every magnitude were

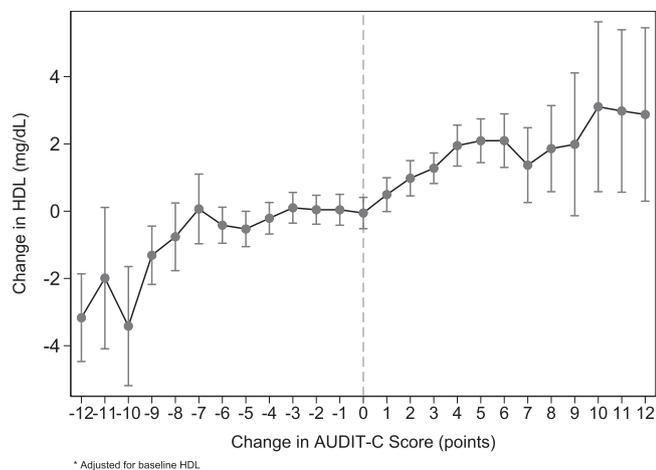


Fig. 1. Change in AUDIT-C score and change in HDL.

associated with significant decreases in HDL except in the small group (1.5%) of patients with the highest baseline AUDIT-C scores (AUDIT-C 10–12). Age and the presence of a substance use disorder diagnosis statistically significantly modified the association between changes in AUDIT-C and changes in HDL (interaction p-values < 0.00001), but gender did not (p = 0.06). Nonetheless, in stratified analyses, associations appeared similar across subgroups (Appendices C–D*).

The median number of days between AUDIT-C screening and HDL was 54 (IQR 0, 171) at baseline and 68 (IQR 0, 180) at follow-up (Table 1). Analyses restricted to the subset of patients with HDL measured within 90 days following both AUDIT-Cs (n = 115,481; 36%) revealed a stronger association between change in AUDIT-C and change in HDL, with extreme changes in AUDIT-C score in either direction associated with larger changes in HDL compared to overall findings (Appendix E*) As expected, adjusting for covariates at the time of each AUDIT-C did not appreciably change results (not shown).

4. Discussion

In this large study of over 300,000 outpatients, changes in AUDIT-C scores were associated with changes in HDL, a laboratory test known to reflect recent average alcohol consumption. Moreover, the association was stronger when the AUDIT-C and HDL were obtained closer together

temporally, as would be expected if there was a causal association. Findings suggest that changes in AUDIT-C scores reflect changes in drinking and support the use of clinically-documented alcohol screening scores for monitoring patients’ alcohol use over time.

Although AUDIT-C scores are strongly associated with average alcohol consumption based on confidential interviews (Rubinsky et al., 2013), few studies have evaluated implications of changes in clinically-documented AUDIT-C scores over time, which may be subject to quality issues related to non-standard verbal administration of the questionnaire and/or patient response bias (Bradley et al., 2011; Hawkins et al., 2007; Davis et al., 2010; Williams et al., 2015; McGinnis et al., 2016). One study, restricted to patients with HIV, evaluated the association between within-person changes in clinically-documented AUDIT-C scores and changes in HIV outcomes and found that those with relatively stable drinking had the greatest improvements in HIV severity (Williams et al., 2018). Another study included HDL as one of three outcomes and evaluated the association between changes in alcohol risk group based on routine AUDIT-C screening and subsequent HDL measured at a single timepoint (Bradley et al., 2016). In line with the present study, that study found that compared to patients who had no change in their alcohol risk group at follow-up screening, those who increased to a higher alcohol risk group had higher HDL, and those who decreased to a lower alcohol risk group had a lower HDL on average.

Measurement-based care is increasingly recommended to improve the quality of care for patients with unhealthy substance use in primary care as well as specialty treatment settings (Institute of Medicine (US) Committee on Crossing the Quality Chasm: Adaptation to Mental Health and Addictive Disorders, 2006; National Council for Behavioral Health, 2018; Marsden et al., 2019). Moreover, systematic measurement of substance use is a core dimension of such measurement-based care (Marsden et al., 2019), and AUDIT-C scores have been recommended as a practical tool for monitoring alcohol use over time in those with unhealthy alcohol use (National Council for Behavioral Health 2018). Our study findings therefore have key implications for clinical care and research. This study suggests that such an approach would be valid for monitoring whether patients decrease drinking after brief interventions or treatment for AUD in most patients. Specifically, findings suggest that clinically-documented AUDIT-C scores reflect “real” decreases in drinking, with the possible exception of the relatively few patients with the highest AUDIT-C scores (10–12). Results also suggest that AUDIT-Cs can be useful for monitoring changes in drinking among patients who report no alcohol use, most of whom have

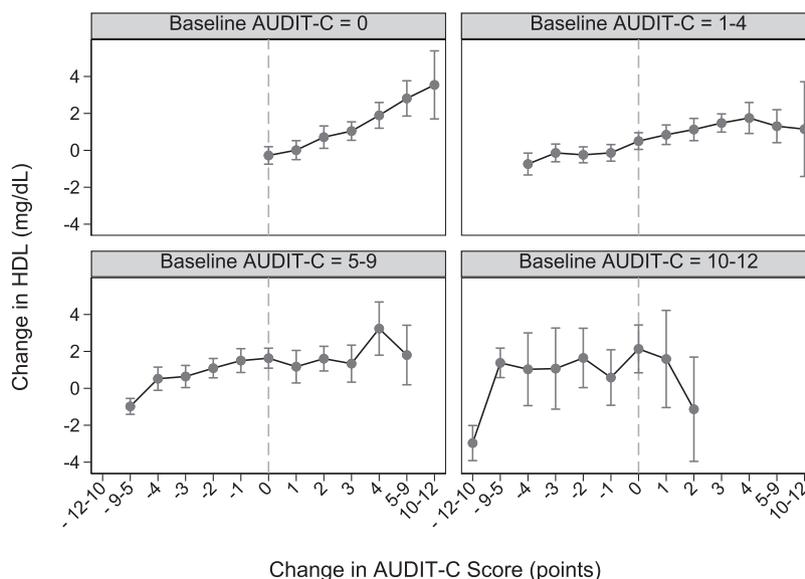


Fig. 2. Change in AUDIT-C score and change in HDL, by baseline AUDIT-C score group.

stable (non-)drinking over time. In the minority of patients with non-drinking who increase alcohol use—perhaps after relapse of an AUD—this study suggests that AUDIT-C scores are an effective indicator of increased consumption. Changes in AUDIT-C scores could also be used as an outcome for comparative effectiveness research (Williams et al., 2010, 2014; Williams et al., 2017) or future pragmatic trials comparing interventions aiming to decrease drinking in patients with unhealthy alcohol use. Study findings also suggest a potential role for HDL in alcohol intervention research as an objective measure of changes in drinking over time.

This study has important limitations. First, HDL levels tend to be affected by other changeable behaviors such as diet, exercise, conditions such as diabetes and hypothyroidism, and medication use. Second, HDL changes rapidly with changes in alcohol consumption and is thus a shorter-term marker of alcohol use than the AUDIT-C score, which asks about drinking over the past year. Third, the utility of HDL at high levels of alcohol consumption is unclear; studies of the effect of experimentally manipulated alcohol consumption on HDL have evaluated levels of consumption below those associated with AUDIT-C scores 10–12 (Brien et al., 2011; Rubinsky et al., 2013). Finally, the study sample was drawn from patients in VA outpatient care and included relatively few women, racial/ethnic minorities, younger patients, and patients with the highest AUDIT-C scores. Findings warrant replication and further exploration, including in healthcare systems with higher representation of these groups. Further, if used for routine alcohol screening, other instruments (e.g., the full 10-item AUDIT) may similarly serve as practical tools for monitoring changes in drinking and could be evaluated in future studies. At the same time, the study has unique strengths. We used data from a national sample of outpatients screened with the AUDIT-C without recruitment bias, an objective reference standard (HDL) that reflects average alcohol consumption (avoiding biases associated with self-report), and a novel analytic approach to account for differences in all observed and unobserved time-invariant patient characteristics.

5. Conclusion

This study is the first to evaluate the utility of within-person changes in AUDIT-C scores as an indicator of changes in alcohol use based on an objective laboratory test that changes with changes in consumption. Findings provide empirical support for use of the AUDIT-C to monitor drinking and treatment outcomes in clinical care and research. Clinicians and researchers need practical measures of alcohol consumption, and findings suggest the AUDIT-C as a candidate tool.

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Contributors

Anna D. Rubinsky: design, interpretation of analyses, drafting the manuscript, manuscript editing.

Laura J. Chavez: interpretation of analyses, drafting the manuscript, manuscript editing.

Douglas Berger: manuscript editing.

Gwen T. Lapham: interpretation of analyses, manuscript editing.
Eric J. Hawkins: interpretation of analyses, manuscript editing.
Emily C. Williams: design, interpretation of analyses, manuscript editing.

Katherine A. Bradley: funding, design, interpretation of analyses, manuscript editing.

We confirm that the manuscript has been read and approved by all named authors and that there are no other persons who satisfied the criteria for authorship but are not listed. We further confirm that the order of authors listed in the manuscript has been approved by all of us.

We confirm that we have given due consideration to the protection of intellectual property associated with this work and that there are no impediments to publication, including the timing of publication, with respect to intellectual property. In so doing we confirm that we have followed the regulations of our institutions concerning intellectual property.

We understand that the Corresponding Author is the sole contact for the Editorial process (including Editorial Manager and direct communications with the office). He/she is responsible for communicating with the other authors about progress, submissions of revisions and final approval of proofs. We confirm that we have provided a current, correct email address which is accessible by the Corresponding Author and which has been configured to accept email from Anna D. Rubinsky.

Conflict of interest

We wish to confirm that there are no known conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome.

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Appendix A. Supplementary data

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