Cross-sectional adherence with the multi-target stool DNA test for colorectal cancer screening in a Medicaid population

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ABSTRACT

Colorectal cancer (CRC) is the third leading cause of cancer death in the US. Early detection improves CRC outcomes and multiple options are endorsed for CRC screening; however, adherence remains challenging. Among Medicaid enrollees, the fecal immunochemical test (FIT) is often used for average-risk CRC screening, with suboptimal adherence rates reported (12.3–23.2%). The navigation-supported (personalized outreach by phone, mail, email and text), at home collection, multi-target stool DNA (mt-sDNA) test represents a relatively recent and broadly accessible option for average-risk CRC screening in Medicaid enrollees. We assessed cross-sectional mt-sDNA adherence in a national sample of Medicaid patients. Data from Exact Sciences Laboratories LLC (ESL; Madison, WI) were retrospectively analyzed. Participants included individuals 45+ years covered by Fee-For-Service (FFS)- or Managed-Medicaid. Primary analysis focused on the 50–74 age cohort and included those with valid mt-sDNA orders between January 1–December 31, 2018. Data from 25,794 individuals who received valid orders for mt-sDNA were included in analysis (61.2% women; mean age at order 57.5 years). Overall adherence—completion of an ordered test—was 51.3%. Adherence was 54.6% in Managed-Medicaid and 38.9% in FFS-Medicaid. Adherence by age was: 51.5% for 50–64 years and 47.7% for 65–74 years. Mt-sDNA tests ordered by gastroenterologists had higher adherence (60.5%) compared with primary care clinicians (51.3%). These data from a large, national sample of Medicaid-insured patients substantiate mt-sDNA testing as a viable patient-supported, home-based option to improve average-risk CRC screening participation in Medicaid enrollees.

1. Introduction

Colorectal cancer (CRC) is an important public health concern, ranking as the third most commonly diagnosed cancer and third leading cause of cancer death in the United States (American Cancer Society, 2021), with estimates of 151,030 incident and 52,580 fatal cases in 2022 (Siegel, et al., 2022). Encouragingly, effective early detection has been consistently shown to reduce CRC incidence and mortality rates (Levin, Nov. 2018).

While multiple options are guideline endorsed for average-risk CRC screening, underutilization remains pervasive (Davidson, May 2021). Notably, among Medicaid enrollees, adherence to CRC screening is particularly challenging. In their “Improving Colorectal Cancer Screening Rates” practice guide for state-Medicaid agencies, the National Colorectal Cancer Roundtable (NCCRT) iterates their mission to reduce the incidence and mortality of CRC in the United States through the goal of 80% of adults 50 and over being screened for CRC (Roundtable, 2021). The NCCRT guide summarizes evidence-based practices to improve CRC screening rates, including: providing education and technical support to Managed Care Organizations and providers, working closely with Federally Qualified Health Centers that serve large Medicaid populations, promoting evidence-based strategies and interventions, and promoting test options to overcome compliance barriers, provider shortages, geographic issues, and logistical constraints (Roundtable, 2021).

The multi-target stool DNA test (mt-sDNA; marketed as Cologuard – Exact Sciences, Madison, WI) represents a broadly available, at-home CRC screening option for average-risk individuals, and includes 24 h per day, 7 days per week, and 365 days per year of navigation support for both patients and providers (with translation services for over 240

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languages). Specialized support staff provide personalized outreach to help facilitate screening completion – which includes a welcome call, along with postal mail, email, and/or text reminders. These attributes of the mt-sDNA screening test have considerable potential to overcome CRC screening adherence barriers at multiple levels. Additionally, with overall CRC screening rates declining during the COVID-19 pandemic due at least in part to patient avoidance of medical facilities, the home-based mt-sDNA test represents an accurate and accessible option for improving CRC early detection in Medicaid enrollees. Based on Exact Sciences Laboratory data eligible patients who are actively enrolled in state Medicaid programs have access to mt-sDNA, and nationally, 98% of mt-sDNA Medicaid patients have no out-of-pocket costs.

To assess participation with mt-sDNA screening in the Medicaid population, we examined the cross-sectional adherence with this test in a national sample of patients covered by Medicaid insurance.

2. Methods

2.1. Design

We retrospectively analyzed aggregate mt-sDNA test order and cross-sectional adherence (test completion) data from Exact Sciences Laboratories LLC (ESL; Madison, WI). The primary analyses focused on patients aged 50–74 and included those with a valid mt-sDNA order between January 1 – December 31, 2018. A valid order includes orders with no missing patient information, not canceled for any reason (for example patient ineligibility, duplicate order, or at the provider’s request). Adherence was defined as successful completion of the mt-sDNA test within 365 days of the shipment date (Fig. 1). The data herein were retrospectively reviewed as part of ongoing ESL laboratory quality management processes in compliance with the Health Insurance Portability and Accountability Act, and was deemed exempt from IRB review by the Mayo Clinic Institutional Review Board.

2.2. Study population and data acquisition

Eligible subjects for study analysis included individuals ages 45–85 years who were at average risk for colorectal cancer and were enrolled in Medicaid Fee-For-Service (MFFS) or Managed-Medicaid (MM), with a mt-sDNA test shipped to the order-specified address from ESL. Determination of average-risk status and eligibility for mt-sDNA is made by the prescribing provider.

During the time period of the index data collection (January 1 – December 31, 2018) the United States Preventive Services Task Force (USPSTF) guideline-recommended CRC screening was for patients aged 50 and over. However, these data were also inclusive of patients who were between the ages of 45–49, for whom mt-sDNA was subsequently approved by the FDA in September 2019. Additionally, the USPSTF guidelines for CRC screening were updated in May 2021 to recommend CRC screening begin at age 45 for all average-risk adults. Thus, as a secondary analysis, we examined cross-sectional adherence in this subgroup as well.

Our primary outcome, adherence, was defined as return of a valid mt-sDNA test kit containing all information required to analyze the sample and report a positive or negative test result. Additional variables of interest (time to test completion, patient sex and age, as well as provider specialty and practice location) were retrieved from Exact Sciences Laboratories internal databases. Inclusion and exclusion criteria (including removal of provider/patient cancellations, duplicate orders, missing information, and reasons for ineligibility) were applied to construct the final analysis cohort.

2.3. Statistical analysis

Descriptive statistics were used to summarize the baseline characteristics of the study population, overall and by Medicaid plan type, with counts and percentages for population-level statistics. Given the large size of the study population, p-values did not provide meaningful

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**Fig. 1.** Shipments & mt-sDNA Completion Results Consort Diagram.
insights for the reported comparisons and are therefore not reported, per established convention (Sullivan and Feinn, Sep. 2012).

3. Results

In total, 25,794 participants met the study criteria and were included in the analysis (61.2 % women; mean age 57.5 years). The overall mt-sDNA adherence was 51.3 %. Cohort adherence by plan was 54.6 % in MM, and 38.9 % in Medicaid-FFS. Overall adherence by sex was similar between males (51.9 %) and females (50.9 %), while stratification by participant age revealed varying, but similar, adherence rates: 51.5 % (50–64 years) and 47.7 % (65–74 years) (Table 1). In data not shown (due to the USPSTF CRC screening guidelines to begin CRC screening at age 50 during the study period), a secondary analysis of mt-sDNA completion in a subset of patients ages 45–49 revealed a 50 % adherence rate (n = 40).

Adherence was greater for mt-sDNA tests ordered by gastroenterologists (60.5 %), followed by OB/GYN specialists (55.4 %), and then primary care physicians (51.3 %). For mt-sDNA orders placed by nurse practitioners/physician assistants, the adherence was (50.2 %). (Table 1).

With respect to geography, adherence was revealed to be highest in the Mid-Atlantic (55.7 %), East North Central (51.2 %), and Pacific (51 %) regions, followed closely by the Mountain (50.8 %) and East South Central (50.9 %) regions. The lowest completion rates were seen in the New England (45.7 %) and West South Central (44.5 %) regions (Table 1). Adherence data from Puerto Rico and U.S. Territories is not displayed due to inadequate sample size (<0.1 %).

4. Discussion

Data from this retrospective study of a large, national sample of

Table 1

| Demographics                | Total Cohort (%) | Managed Medicaid-MM (%) | Medicaid Fee-for-Service-FFS (%) |
|-----------------------------|------------------|-------------------------|---------------------------------|
| **Age, years**              |                  |                         |                                 |
| 50 – 64                     | 24,204 (93.8)    | 19,357 (95.0)           | 4,847 (89.3)                    |
| 65 – 74                     | 1,590 (6.2)      | 1,011 (5.0)             | 579 (10.7)                      |
| **Sex**                     |                  |                         |                                 |
| Male                        | 9,996 (38.8)     | 7,882 (38.7)            | 2,114 (39.0)                    |
| Female                      | 15,790 (61.2)    | 12,478 (61.3)           | 3,312 (61.0)                    |
| Unspecified                 | 8 (0.0)          | 8 (0.0)                 | 0 (0.0)                         |
| **Patient/Provider Factors & Adherence (All Eligible Study Patients)** | | | |
| Completed/ % TTA Completed/ |                  |                         |                                 |
| Ordered                     | 13,228/25,794    | 11,116/20,368           | 2,112/5,426                     |
| Age, years                  |                  |                         |                                 |
| 50 – 64                     | 12,470/24,204    | 10,579/19,357           | 1,891/4,847                     |
| 65 – 74                     | 758/1,590        | 537/1,011               | 221/579                         |
| **Sex**                     |                  |                         |                                 |
| Male                        | 5,189/9,996      | 4,347/7,882             | 842/2,114                       |
| Female                      | 8,035/15,790     | 6,765/12,478            | 1,270/3,312                     |
| Unspecified                 | 4/8              | 4/8                     | 0/0                             |
| **Specialty (overall % of cohort)** | | | |
| GI (3.5)                    | 543/897          | 425/653                 | 118/244                         |
| OB/GYN (0.9)                | 124/224          | 114/194                 | 10/30                           |
| NP/PA (30.2)                | 3,913/7,795      | 3,298/6,232             | 615/1,563                       |
| Primary Care (61.7)         | 8,164/15,917     | 6,896/12,565            | 1,268/3,352                     |
| Other (3.7)                 | 484/961          | 383/724                 | 101/237                         |
| Practice Location (Region)  |                  |                         |                                 |
| East North Central          | 4,885/8,953      | 4,156/7,676             | 429/1,277                       |
| East South Central          | 1,270/2,499      | 1,204/2,329             | 66/170                          |
| Mid-Atlantic                | 2,335/4,194      | 2,217/3,877             | 118/317                         |
| Mountain                    | 1,291/2,534      | 1,039/1,872             | 252/662                         |
| New England                 | 482/1,055        | 294/588                 | 188/467                         |
| Pacific                     | 396/777          | 320/602                 | 76/175                          |
| South Atlantic              | 1,117/2,224      | 722/1,298               | 395/926                         |
| West North Central          | 1,180/2,333      | 803/1,416               | 377/917                         |
| West South Central          | 406/912          | 219/453                 | 187/459                         |

Table 1: Study Population Demographics & Cross-sectional Adherence by Medicaid Coverage Type and Patient Factors.

Abbreviations: TTA, time to adherence (Median); GI, gastroenterology; OB/GYN, obstetrician-gynecologist; NP, nurse practitioner; OB, obstetrics; PA, physician assistant; TTA, time to adherence (median); “Puerto Rico and U.S. Territories” location data not shown due to small sample size (<0.1 %)
Medicaid-insured patients demonstrate a relatively high overall adherence rate (51.3 %) with the mt-sDNA test, while stratification by provider and geographical region revealed variation in mt-sDNA test completion amongst the cohort. For context, previous studies of FIT screening in the Medicaid population have reported much lower test completion rates (ranging from 12.3 – 23.2 %) (Brenner, Aug. 2018; Wheeler, Sep. 2020). Moreover, recent reports show favorable mt-sDNA adherence among commercially- and Medicare-insured patients (Miller-Wilson, 2021; Weiser, 2020).

Adherence was highest overall, and by Medicaid type, among patients for whom tests were ordered by a gastroenterologist compared to other healthcare providers. Although not directly evaluated in this study, it seems plausible that the high adherence to gastroenterologist orders is because recommendations by disease specialists may include a more detailed discussion during patient-provider encounters regarding the importance of CRC screening completion.

Geographic differences in adherence were also observed, with the highest completion rates pertaining to practice location being seen in the Mid-Atlantic, East North Central, and Pacific regions in our study. The increased adherence trend aligns with current literature regarding the percentage of adults being up-to-date with CRC screening by state; although, adherence was lower in New England where up-to-date screening hovers around ≥ 70 % (Joseph, et al., 2018). Also, in accordance with available literature, adherence was the lowest in the West South-Central region of the country.

The cohort size in this study of nearly 26,000 patients serves as a valuable contribution to the existing literature regarding CRC screening in the Medicaid population. Interestingly, data not shown in this brief report revealed that mt-sDNA completion in the 45–49 years subgroup of patients was 50 %, although the sample size was very small (n = 40). Considering the recently updated guideline recommendation by the USPSTF (Davidson, May 2021) to begin screening for colorectal cancer in all average-risk adults at age 45, this finding warrants further investigation in a larger cohort.

As aforementioned, the mt-sDNA test is offered in conjunction with patient and provider navigation support. Prior studies have shown that patient navigation provides a beneficial effect on patient health behavior, demonstrating increased CRC screening rates (Weiser, 2020; Rice, Sep. 2017; Dougherty, Dec. 2018). The patient navigation support and at-home convenience of the mt-sDNA stool-based CRC screening test may have great potential to increase screening compliance in patients insured by Medicaid, thereby reducing CRC cancer burden via earlier detection. Adherence to mt-sDNA in the Medicaid population is lower than in Medicare enrollees and commercially insured patients (Wheeler, Sep. 2020); however, low adherence among Medicaid enrollees could reasonably be assumed to be affected by disproportionately low access to healthcare in low income and underserved populations.

Health insurance access plays a critical role in increasing CRC screening completion, although variations could manifest based on patient socioeconomic characteristics (Lin, et al., 2022; Zhao, et al., 2018). As observed in our study, a nominal gap in screening adherence was seen between those insured with MM and those insured with Medicaid-FFS. The Medicaid cohort in our study exhibited significantly greater adherence with mt-sDNA than the adherence that has been reported in the literature for FIT (Brenner, Aug. 2018; Wheeler, Sep. 2020). However, the study designs and populations included in the aforementioned references differ significantly from our study; thus, no head-to-head comparison can be made. Future studies should consider a head-to-head comparison between the two stool-based tests. Moreover, increasing Medicaid enrollee CRC screening adherence may warrant more innovative strategies and approaches to encourage patients to follow the screening process through to completion.

We acknowledge several limitations of our study. First, there was limited reporting of race and ethnicity in this study population, with 85 % of orders not specifying a racial category (this is an optional field). This prohibited the examination of potential correlations of race and ethnicity with screening completion and adherence. Secondly, patient and provider factors were limited to those characteristics that could be captured from the existing ESL laboratory database, and we relied on the ordering clinician to assume CRC average-risk status; thus, it was not confirmed if each provider complied with the test’s FDA-approved label for indication. Therefore, the study population could include some individuals at higher than average-risk for CRC. Thirdly, we did not assess longitudinal adherence. Future evaluations of longitudinal mt-sDNA adherence are anticipated. Moreover, in accordance with the USPSTF, we recognize that in order for screening benefits to be achieved, positive mt-sDNA results require follow-up colonoscopy. This is in the purview of the ordering providers; however, data on rates of referral and completion of follow-up colonoscopy are not available for analysis. Reporting on test results were not included in the scope of this study, and the analysis was limited to assessing adherence.

5. Conclusions

These real-world results demonstrate favorable mt-sDNA adherence among Medicaid enrollees, as compared to results reported in other studies with other commonly utilized, stool-based CRC screening strategies. These data should help to inform clinical decision-making for Medicaid patients. The results reported herein reinforce mt-sDNA as a guideline-endorsed, navigation-supported, home-based option that carries the potential to increase CRC screening participation among Medicaid enrollees.

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Availability of data and material: Study data are available upon reasonable request.

Code availability: Not applicable for this study.

Ethics approval: The data herein were retrospectively reviewed as part of ongoing laboratory (Exact Sciences Laboratories, LLC) quality management processes in compliance with the Health Insurance Portability and Accountability Act (HIPAA). The study was deemed exempt from IRB review by the Mayo Clinic Institutional Review Board.

Consent to participate/publish: Not applicable; this was a retrospective review of deidentified data.

CRediT authorship contribution statement

Lesley-Ann Miller-Wilson: Conceptualization, Formal analysis, Investigation, Methodology, Project administration, Resources, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing, Lila J. Finney Rutten: Conceptualization, Formal analysis, Methodology, Writing – original draft, Writing – review & editing. Jack Van Thomme: Data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Software, Validation, Visualization, Writing – original draft, Writing – review &
Declarations of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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