

genetic loci (via look up-GWAS) in the histological NLP cohort

**METHODS/STUDY POPULATION:** We will utilize the Million Veteran Program Biobank where a total of 10,959 subjects have been identified using liver biopsy reports in the EMR via CPT codes. Cases will be based on i) steatosis, steatohepatitis, inflammation or fibrosis in liver biopsy reports with ii) exclusion of other causes of liver disease. Controls will be comprised of the general VA population. In collaboration with the Applied NLP and Precision Medicine groups at the VA Informatics and Computing Infrastructure(VINCI); we will attempt to create and validate a histological cohort of NAFLD in the MVP database by: 1)Annotation of biopsy reports for the NLP algorithm 2)Automation/training of the NLP algorithm We will then perform a multi-ancestry genetic lookup of previously established genetic loci among the cases identified.

**RESULTS/ANTICIPATED RESULTS:** Recently published data: the MVP NAFLD research led by Dr. Chang and Dr. Vujkovic had first validated a proxy NAFLD phenotype based on chronic alanine aminotransferase elevation (cALT). A GWAS was then performed using this phenotype which revealed 77 loci of genome-wide significance including 10 established NAFLD- and 52 ALT-associated SNPs were identified. Replication in external Liver Biopsy and Imaging Cohorts validated 17 SNPs of which 9 were novel. Preliminary data on Liver Biopsy reports: Using CPT codes for Liver Biopsy we estimated a total of 10,959 unique patients and 18,812 notes in the MVP biobank. We anticipate 2,000-3,000 NAFLD cases (based on the prevalence of NAFLD in the general population). Initial review reveals 90% concordance between analysts for the purposes of developing an NLP.

**DISCUSSION/SIGNIFICANCE:** NAFLD is a major cause for morbidity and mortality in liver disease. Gold standard for diagnosis is based on biopsy. GWAS studies with biopsy proven phenotypes are limited. The study will aim to isolate a histologically defined NAFLD cohort in MVP to conduct further GWAS that can provide new clinically relevant knowledge for future research.

## Contemporary Research Challenges

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### Development and content validation of a tool to assess quality of primary care practice

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**OBJECTIVES/GOALS:** Primary care practices struggle to identify which combination of care structures and processes need to be implemented to improve practice performance and subsequently, patient outcomes. The goal of this study is to develop and validate a tool to assess care structures and processes that are associated with better quality and patient outcomes.

**METHODS/STUDY POPULATION:** Data from a scoping review, Delphi study, and qualitative interviews with high-performing primary care practices contributed to the development and content validation of the Tool for Advancing Practice Performance (TAPP). From these sources we identified 314 items representing care structures (e.g., care team makeup, use of electronic health records) and processes (e.g., care coordination, panel management). We developed criteria

for deleting and rescuing items and received input from our expert panel to refine the pool of items. We eliminated items that were redundant and lacked clarity/specificity. The tool was further modified based on feedback from cognitive interviewing and pilot testing with practice managers, quality improvement leaders, and physicians from primary care practices.

**RESULTS/ANTICIPATED RESULTS:** The pool of 314 items was winnowed to 188 after applying criteria for deleting and rescuing items. During the expert review, 70 items were eliminated and 8 new items were added, resulting in a working tool of 126 items. We conducted eight cognitive interviews with the 126-item tool and received feedback on the content, item structure, and language, which led to the elimination of 13 items that were poorly or incorrectly understood by respondents. We also modified the language of 23 items for clarity. After cognitive interviewing, the resulting tool comprised 113 items. Fifteen practices piloted the tool and no additional items were eliminated. We modified the instructions for completing the tool and resolved technical issues related to online administration.

**DISCUSSION/SIGNIFICANCE:** TAPP is a novel tool for assessing care structures and processes that are associated with better quality and patient outcomes in primary care settings. The tool can be used by researchers and primary care clinicians to identify areas for improvement in practice performance and patient outcomes related to chronic disease prevention and management.

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### Effect of probiotic supplementation on intestinal permeability in subjects with overweight and obesity: A systematic review of randomized controlled trials

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**OBJECTIVES/GOALS:** Obesity is associated with gut dysbiosis, inflammation, and increased intestinal permeability. Probiotic consumption may reverse these outcomes. The goal of this study is to evaluate the evidence linking probiotic consumption to changes in intestinal permeability in subjects with overweight or obesity.

**METHODS/STUDY POPULATION:** Articles were searched in Pubmed, Web of Science, and CAB Direct through February 2022 using search terms: intestinal permeability, overweight or obesity, and probiotic supplementation. 694 articles were exported, and 289 duplicates were identified. Titles and abstract were screened in the 405 remaining references by two investigators to determine eligibility. Eligible studies had data extracted on study participant characteristics, probiotic strain used, probiotic dosage, length of intervention, and intestinal barrier outcomes. Results were summarized in tabular form based on intestinal permeability response to probiotics. Quality of the studies was assessed based on Cochrane-Risk of Bias' tool (RoB2).

**RESULTS/ANTICIPATED RESULTS:** Thirteen eligible studies were identified. Probiotic genera included Akkermansia, Bifidobacterium, Lactobacillus, Streptococcus, Lactococcus, and Bacillus. Single strain probiotics were used in 3 studies, while the other 10 used multi-strain formulas. Dosage and length of probiotic supplementation ranged from 2.4 x 10<sup>7</sup> to 5 x 10<sup>10</sup> CFU/person/day and 3 to 26 weeks, respectively. The most widely used gut permeability outcomes were serum lipopolysaccharide (LPS) (n=10) and mixed sugar solution consumption with urine analysis (n=6). Five of the 10 studies reported decreases in serum LPS following probiotic consumption, while the other 5