**Cohort Study**

**Potential PURL Review Form**

**PURL Jam Version**

**Version #12 Sept 20, 2010**

**Skip this step when checking lipid levels**

***J Fam Pract*. 2015;64:113-115.**

**PURLs Surveillance System**

**Family Physicians Inquiries Network**

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| **SECTION 1: Identifying Information for Nominated Potential PURL**  **[to be completed by PURLs Project Manager]** | | | | |
| **1.** Citation | Prognostic Value of Fasting vs. Non-Fasting Low Density Lipoprotein Cholesterol Levels on Long-term Mortality: Insight from the National Health and Nutrition Survey III (NHANES-III).  Doran B, Guo Y, Xu J, Weintraub H, Mora S, Maron DJ, Bangalore S.  Circulation. 2014 Jul 11. pii: CIRCULATIONAHA.114.010001. [Epub ahead of print]  PMID: 25015340 | | | |
| **2.** Hypertext link to PDF of full article | http://www.ncbi.nlm.nih.gov/pubmed/?term=Prognostic+Value+of+Fasting+vs.+Non-Fasting+Low+Density+Lipoprotein+Cholesterol+Levels+on+Long-term+Mortality%3A+Insight+from+the+National+Health+and+Nutrition+Survey+III+%28NHANES-III%29. | | | |
| **3.** First date published study available to readers | 7/11/14 | | | |
| **4.** PubMed ID | 25015340 | | | |
| **5.** Nominated By | Other Other: David Beckmann | | | |
| **6.** Institutional Affiliation of Nominator | University of Chicago Other: | | | |
| **7.** Date Nominated | 7/14/14 | | | |
| **8.** Identified Through | Other Other: Medscape | | | |
| **9.** PURLS Editor Reviewing Nominated Potential PURL | Kate Rowland | | | |
| **10.** Nomination Decision Date | 7/31/14 | | | |
| **11.** Potential PURL Review Form (PPRF) Type | Cohort Study | | | |
| **12.** Other comments, materials or discussion |  | | | |
| **13.** Assigned Potential PURL Reviewer | Debbie Stulberg, MD | | | |
| **14.** Reviewer Affiliation | University of Chicago Other: | | | |
| **15.** Date Review Due | 8/28/14 | | | |
| **16.** Abstract | BACKGROUND:  -National and international guidelines recommend fasting lipid panel measurement for risk stratification of patients for prevention of cardiovascular (CV) events. Yet, the prognostic value of fasting vs. non-fasting low density lipoprotein cholesterol (LDL-C) is uncertain.  METHODS AND RESULTS:  -Patients enrolled in the National Health and Nutrition Survey III (NHANES-III), a nationally representative cross-sectional survey performed between 1988 to 1994, were stratified based on fasting status (≥8 hrs or <8 hrs) and followed for a mean of 14.0 (± 0.22) years. Propensity score matching was used to assemble fasting and non-fasting cohorts with similar baseline characteristics. The risk of outcomes as a function of LDL-C and fasting status was assessed using receiver operating characteristic (ROC) curves and bootstrapping methods. The interaction between fasting status and LDL-C was assessed using Cox proportional hazards modeling. Primary outcome was all-cause mortality. Secondary outcome was CV mortality. One-to-one matching based on propensity score yielded 4299 pairs of fasting and non-fasting individuals. For the primary outcome, fasting LDL-C yielded similar prognostic value as non-fasting LDL-C (C-statistics=0.59 [95% confidence interval [CI] 0.57-0.61] vs. 0.58 [95% CI 0.56-0.60; P=0.73]), and LDL-C by fasting status interaction term in the Cox proportional hazard model was not significant (Pinteraction=0.11). Similar results were seen for the secondary outcome (fasting vs. non-fasting C-statistics=0.62 [95% CI 0.60-0.66] vs. 0.62 [95% CI 0.60-0.66]; P=0.96; and Pinteraction=0.34).  CONCLUSIONS:  -Non-fasting LDL-C has similar prognostic value as that of fasting LDL-C. National and international agencies should consider reevaluating the recommendation that patients fast before obtaining a lipid panel. | | | |
| **17.** Pending PURL Review Date |  | | | |
| **sECTION 2: Critical Appraisal of Validity**  **[to be completed by the Potential PURL Reviewer]** | | | | |
| **1** The study addresses an appropriate and clearly focused question. | | Well covered  Not addressed  Adequately addressed  Not reported  Poorly addressed  Not applicable  Comments: | | |
| **2** The two groups being studied are selected from source populations that are comparable in all respects other than the factor under investigation. | | Well covered  Not addressed  Adequately addressed  Not reported  Poorly addressed  Not applicable  Comments: | | |
| **3** The study indicates how many of the people asked to take part did so, in each of the groups being studied | | Well covered  Not addressed  Adequately addressed  Not reported  Poorly addressed  Not applicable  Comments: | | |
| **4** The likelihood that some eligible subjects might have the outcome at the time of enrolment is assessed and taken into account in the analysis. | | Well covered  Not addressed  Adequately addressed  Not reported  Poorly addressed  Not applicable  Comments: | | |
| **5** What percentage of individuals or clusters recruited into each arm of the study dropped out before the study was completed? | | N/A | | |
| **6** Comparison is made between full participants and those lost to follow up, by exposure status. | | Well covered  Not addressed  Adequately addressed  Not reported  Poorly addressed  Not applicable  Comments: | | |
| **7** The outcomes are clearly defined. | | Well covered  Not addressed  Adequately addressed  Not reported  Poorly addressed  Not applicable  Comments: | | |
| **8** The assessment of outcome is made blind to exposure status | | Well covered  Not addressed  Adequately addressed  Not reported  Poorly addressed  Not applicable  Comments: | | |
| **9** Where blinding was not possible, there is some recognition that knowledge of exposure status could have influenced the assessment of outcome. | | Well covered  Not addressed  Adequately addressed  Not reported  Poorly addressed  Not applicable  Comments: | | |
| **10** What are the key findings of the study? | | LDL levels had similar prognostic value in fasting (C-statistic=0.59, 95% CI 0.57-0.61) vs. non-fasting (C-statistic=0.58, 95% CI 0.56-0.60, p=0.73) subjects. The same was true for CV-specific mortality (fasting C-statistic=0.62, 95% CI 0.60-0.66 vs. non-fasting C-statistic=0.62, 95% CI 0.60-0.66, p=0.96). LDL was predictive of death, controlling for confounders, with no significant interaction between LDL and fasting status (all-cause mortality p[interaction]=0.11, CV mortality p[interaction]=0.34). Prognostic power (C-statistic) of fasting vs. non-fasting levels of triglycerides and total cholesterol also showed no significant differences for either all-cause or CV-specific mortality. | | |
| **11** How was the study funded? Any conflicts of interest? Any reason to believe that the results may be influenced by other interests? | | Study funding is not explicitly stated, but they acknowledge support from NYU School of Medicine Cardiovascular Outcomes Group so I get the sense this was internally funded. Two (of the 7) authors have grants or serve on advisory boards of industry groups, including drug companies (Pfizer, maker of Lipitor, AstraZeneca, maker of Crestor) and diagnostic testing companies (Quest, Atherotech diagnostics), both of which could theoretically stand to benefit from more lipid testing. | | |
| **SECTION 3: Review of Secondary Literature**  **[to be completed by the Potential PURL Reviewer]** | | | | |
| **Citation Instructions** | For UpTo Date citations, use style modified from <http://www.uptodate.com/home/help/faq/using_UTD/index.html#cite> & AMA style. Always use Basow DS as editor & current year as publication year.  EXAMPLE: Auth I. Title of article. {insert author name if given, & search terms or title.} In: Basow DS, ed. UpToDate [database online]. Waltham, Mass: UpToDate; 2009. Available at: <http://www.uptodate.com>. {Insert dated modified if given.} Accessed February 12, 2009. {whatever date PPRF reviewer did their search.}  For DynaMed, use the following style: Depression: treatment {insert search terms or title}. In: DynaMed [database online]. Available at: <http://www.DynamicMedical.com>. Last updated February 4, 2009. {Insert dated modified if given.}  Accessed June 5, 2009.{search date} | | | |
| **1.** DynaMed excerpts |  | | | |
| **2.** DynaMed citation/access date | Title. hypercholesterolemia Author. In: DynaMed [database online]. Available at: [www.DynamicMedical.com](http://www.DynamicMedical.com) Last updated: 8/9/14. Accessed 8/28/14 | | | |
| **3.**  Bottom line recommendation or summary of evidence from DynaMed  (1-2 sentences) | Fasting is the standard test but it may not be better | | | |
| **4.** UpToDate excerpts |  | | | |
| **5.** UpToDate citation/access date | Always use Basow DS as editor& current year as publication year.  Title. Screening for lipid disorders Author. Sandeep Vijan In: UpToDate [database online]. Available at: <http://www.uptodate.com>. Last updated: 8/12/14. Accessed: 8/28/14 | | | |
| **6.**  Bottom line recommendation or summary of evidence from UpToDate  (1-2 sentences) | Fasting is not needed for most patients, but if you want a calculated LDL and a triglyceride level, ask patients to fast. | | | |
| **7.** PEPID PCP excerpts  [www.pepidonline.com](http://www.pepidonline.com)  username: fpinauthor  pw: pepidpcp | Main screening tests: lipid profile and glucose (fasting, random, or 2 hr pp), or HgA1C  • Initial random or fasting lipid profile (with total, LDL, and HDL cholesterol, and TGs)  • Random lipid profile increases compliance with screening and give useful information about post-meal TG surge (serious atherogenic factor)  • If high risk for CAD and random LDL even slightly elevated fasting lipid profile to categorize degree of elevated LDL and assess fasting TG | | | |
| **8.** PEPID citation/access data | Author. Title. Dyslipidemias: diagnostics In: PEPID [database online]. Available at: <http://www.pepidonline.com>. Last updated:. Accessed: 8/28/2014 | | | |
| **9.** PEPID content updating | 1. Do you recommend that PEPID get updated on this topic?  Yes, there is important evidence or recommendations that are missing  No, this topic is current, accurate and up to date.  If yes, which PEPID Topic, Title(s):  2. Is there an EBM Inquiry (HelpDesk Answers and Clinical Inquiries) as indicated by the EB icon () that should be updated on the basis of the review?  Yes, there is important evidence or recommendations that are missing  No, this topic is current, accurate and up to date.  If yes, which Evidence Based Inquiry(HelpDesk Answer or Clinical Inquiry), Title(s): | | | |
| **10.** Other excerpts (USPSTF; other guidelines; etc.) | • The preferred screening tests for dyslipidemia are total cholesterol and HDL-C on non-fasting or fasting samples. There is currently insufficient evidence of the benefit of including TG as a part of the initial tests used to screen routinely for dyslipidemia. Abnormal screening test results should be confirmed by a repeated sample on a separate occasion, and the average of both results should be used for risk assessment.  • Measuring total cholesterol alone is acceptable for screening if available laboratory services cannot provide reliable measurements of HDL-C; measuring both total cholesterol and HDL-C is more sensitive and specific for assessing coronary heart disease risk than measuring total cholesterol alone. In conjunction with HDL-C, the addition of either LDL-C or total cholesterol would provide comparable information, but measuring LDL-C requires a fasting sample and is more expensive. Direct LDL-C testing, which does not require a fasting sample measurement, is now available; however, calculated LDL (total cholesterol minus HDL minus TG/5) is the validated measurement used in trials for risk assessment and treatment decisions. In patients with dyslipidemia identified by screening, complete lipoprotein analysis is useful. | | | |
| **11.** Citations for other excerpts | USPSTF 2008 recommendation on screening for lipid disorders (update is currently in progress). See http://www.uspreventiveservicestaskforce.org/uspstf08/lipid/lipidrs.htm accessed 8/28/2014 | | | |
| **12.**  Bottom line recommendation or summary of evidence from Other Sources (1-2 sentences) | If you want a reliable LDL level, you most likely need a fasting blood test. | | | |
|  | | | | |
| **SECTION 4: Conclusions**  **[to be completed by the Potential PURL Reviewer; Revised by the Pending PURL Reviewer as needed]** | | | | |
| **1.** **Validity:** How well does the study minimize sources of internal bias and maximize internal validity? | | | | Give one number on a scale of 1 to 7  (1=extremely well; 4=neutral; 7=extremely poorly)  1 2 3 4 5 6 7 |
| **2.** If 4.1 was coded as 4, 5, 6, or 7, please describe the potential bias and how it could affect the study results. Specifically, what is the likely direction in which potential sources of internal bias might affect the results? | | | |  |
| **3. Relevance:** Are the results of this study generalizable to and relevant to the health care needs of patients cared for by “full scope” family physicians? | | | | Give one number on a scale of 1 to 7  (1=extremely well; 4=neutral; 7=extremely poorly)  1 2 3 4 5 6 7 |
| **4.** If 4.3 was coded as 4, 5, 6, or 7,lease provide an explanation. | | | |  |
| **5. Practice changing potential:** If the findings of the study are both valid and relevant, does the practice that would be based on these findings represent a change from current practice? | | | | Give one number on a scale of 1 to 7  (1=definitely a change from current practice; 4=uncertain; 7=definitely not a change from current practice)  1 2 3 4 5 6 7 |
| **6.** If 4.5 was coded as 1, 2, 3, or 4, please describe the potential new practice recommendation. Please be specific about what should be done, the target patient population and the expected benefit. | | | |  |
| 1. **Applicability to a Family Medical Care Setting:**   Is the change in practice recommendation something that could be done in a medical care setting by a family physician (office, hospital, nursing home, etc), such as a prescribing a medication, vitamin or herbal remedy; performing or ordering a diagnostic test; performing or referring for a procedure; advising, educating or counseling a patient; or creating a system for implementing an intervention? | | | | Give one number on a scale of 1 to 7  (1=definitely could be done in a medical care setting; 4=uncertain; 7=definitely could not be done in a medical care setting)  1 2 3 4 5 6 7 |
| **8.** If you coded 4.7 as a 4, 5, 6 or 7, please explain. . | | | |  |
| **9. Immediacy of Implementation:**  Are there major barriers to immediate implementation? Would the cost or the potential for reimbursement prohibit implementation in most family medicine practices? Are there regulatory issues that prohibit implementation? Is the service, device, drug or other essentials available on the market? | | | | Give one number on a scale of 1 to 7  (1=definitely could be immediately applied; 4=uncertain; 7=definitely could not be immediately applied)  1 2 3 4 5 6 7 |
| **10.** If you coded 4.9 as 4, 5, 6, or 7, please explain why. | | | |  |
| **11. Clinical meaningful outcomes or patient oriented outcomes:**  Are the outcomes measured in the study clinically meaningful or patient oriented? | | | | Give one number on a scale of 1 to 7  (1=definitely clinically meaningful or patient oriented; 4=uncertain; 7=definitely not clinically meaningful or patient oriented)  1 2 3 4 5 6 7 |
| **12.** If you coded 4.11 as a 4, 5, 6, or 7, please explain why. | | | |  |
| **13.** In your opinion, is this a Pending PURL?  Criteria for a Pending PURL:   * Valid: Strong internal scientific validity; the findings appears to be true. * Relevant: Relevant to the practice of family medicine * Practice changing: There is a specific identifiable new practice recommendation that is applicable to what family physicians do in medical care settings and seems different than current practice. * Applicability in medical setting: * Immediacy of implementation | | | | Give one number on a scale of 1 to 7  (1=definitely a Pending PURL; 4=uncertain; 7=definitely not a Pending PURL)  1 2 3 4 5 6 7 |
| **14.** Comments on your response in 4.13 | | | | My sense is that most clinicians are ordering fasting lipid panels as their main or only cholesterol testing and basing treatment largely on LDL levels (despite USPSTF and other guidelines that say only total and HDL are needed for many patients and for these it is well established that fasting doesn't matter). The latest ATP4 guidelines are based on LDL (e.g. risk stratification by LDL> or <190) and on Pooled Cohort Equation which uses LDL, HDL, and total cholesterol. If we believe this study’s conclusion that LDL levels are equally effective predictors whether they are drawn fasting or not, then we should be able to follow the guidelines without every ordering a fasting lipid panel.  My only hesitation is that I haven't reviewed all the RCTs on which treatment guidelines are based. From what this study (and Dynamed) says, it seems treatment can very effectively be based on non-fasting cholesterol levels. But if we are following guidelines based largely on studies done with fasting levels, maybe we need to use caution before recommending a different testing strategy. |
| **SECTION 4.1: Diving for PURLs**  **[optional for the potential PURL reviewer -if you wish to be the author on the summary]** | | | | |
| **1.** Study Summary- Please summarize the study in 5-7 sentences | | | A nationally representative sample of US community-dwelling adults was surveyed and examined in 1988 through 1994 as part of NHANES III. This study followed those subjects for an average of 14 (+/- 0.22) years to assess the prognostic value of fasting vs. non-fasting LDL cholesterol levels in predicting all-cause and cardiovascular-specific mortality. They also assessed fasting vs. non-fasting total cholesterol and triglyceride levels. They defined fasting as not eating for 8 hours or more, and conducted sensitivity analyses to see if 4- or 12-hour definitions would change the outcome. They analyzed all adults for whom LDL could be calculated and fasting time was known. Those with triglyceride levels >400 were initially excluded from analysis. Authors reported both unmatched and matched comparisons. In the matched LDL analysis, fasting and non-fasting participants were paired using a multivariable propensity score to reflect baseline risk of CV disease (including race, smoking, prior CVD, cholesterol medication use, diabetes, hypertension, waist circumference, socioeconomic status, HDL, and total cholesterol). The discriminatory power of fasting and non-fasting LDL was evaluated using the area under the receiver operating curve and comparing Hosmer-Lemeshow C-statistics in fasting vs. non-fasting groups. Cox proportional hazard modeling was also used to assess the association between LDL and death controlling for potential confounders, with a test for significance of the interaction between fasting status and LDL. In all analyses, there was no significant difference between fasting vs. non-fasting lipid levels. Specifically, in the matched cohorts assessing all cause mortality (primary outcome), LDL levels had similar prognostic value in fasting (C-statistic=0.59, 95% CI 0.57-0.61) vs. non-fasting (C-statistic=0.58, 95% CI 0.56-0.60, p=0.73) subjects. The same was true for CV-specific mortality (fasting C-statistic= 0.62, 95% CI 0.60-0.66 vs. non-fasting C-statistic=0.62, 95% CI 0.60-0.66, p=0.96). LDL was predictive of death, controlling for confounders, with no significant interaction between LDL and fasting status (all-cause mortality p[interaction]=0.11, CV mortality p[interaction]=0.34). Prognostic power (C-statistic) of fasting vs. non-fasting levels of triglycerides and total cholesterol also showed no significant differences for either all-cause or CV-specific mortality. Conclusions about the relevance of fasting for LDL levels held true regardless of the definition of fasting (4 vs. 8 vs. 12 hrs), in diabetics and non-diabetics, in shorter and longer term follow-up (5, 10, and 15 yrs), in matched and unmatched analysis, and even in subjects with triglyceride levels >400. | | |
| 1. Criteria- note yes or no for those which this study meets | | | RELEVANT - YES VALID - YES CHANGE IN PRACTICE- YES  MEDICAL CARE SETTING - YES IMMEDIATELY APPLICABLE - YES CLINICALLY MEANINGFUL - YES | | |
| **3.** Bottom Line- one –two sentences noting the bottom line recommendation | | | The prognostic value of lipid testing is not significantly different in fasting vs. non-fasting adults. When ordering cholesterol panels, don't worry about when your patient last ate. | | |
| **4.** Title Proposal | | | Testing your patients’ cholesterol? Let them eat! | | |
| **SECTION 5: Editorial Decisions**  **[to be completed by the FPIN PURLs Editor or Deputy Editor]** | | | | |
| **1.** FPIN PURLs editorial decision  (select one) | | | | 1 Pending PURL Review—Schedule for Review  2 Drop  3 Pending PURL |
| 1. Follow up issues for Pending PURL Reviewer | | | |  |
| **3.** FPIN PURLS Editor making decision | | | | 1 Bernard Ewigman  2 John Hickner  3 Sarah-Anne Schumann  4 Kate Rowland |
| **4.** Date of decision | | | |  |
| **5.** Brief summary of decision | | | |  |
| **SECTION 6: Survey Questions for SERMO, PURLs Instant Polls and Other Surveys**  **[To be completed by the PURLs Survey Coordinator and PURLs Editor]** | | | | |
| **1.** Current Practice Question for Surveys | | | |  |
| **2.** Barriers to Implementation Question for Surveys | | | |  |
| **3.** Likelihood of Change Question for Surveys | | | |  |
| **4.** Other Questions for Surveys | | | |  |
| **SECTION 7: Variables for Secondary Database Analyses** | | | | |
| **1.** Population: Age, gender, race, ethnicity | | | |  |
| **2.** Diagnoses | | | |  |
| **3.** Drugs or procedures | | | |  |
| **SECTION 8: Pending PURL Review Assignment**  **[to be completed by PURLs Project Manager** | | | | |
| **1.** Person Assigned for  Pending PURL Review | | | |  |
| **2.** Date Pending PURL Review is due | | | |  |
| **SECTION 9: Pending PURL Review**  **[to be completed by the Pending PURL Reviewer]** | | | | |
| **1.** Did you address the follow up issues identified at the PURL Jam (Section 5.2). Add comments as needed. | | | | Yes  No  Not applicable  Comments: |
| **2.** Did you review the Sermo poll & Instant Poll results (if available)? Add comments as needed. | | | | Yes  No  Not applicable  Comments: |
| **3.** Did you modify Sections 2, 3, or 4? Add comments as needed. | | | | Yes  No  Not applicable  Comments: |

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| **SECTION 10: PURL Authoring Template**  **[to be completed by the assigned PURL Author]** | |
| **Author Citation Information** (Name, Degrees, Affiliation) |  |
| **1.** Practice Changer |  |
| **2.** Illustrative Case |  |
| **3.** Background/  Clinical Context/Introduction/Current Practice/ |  |
| **4.** Study Summary |  |
| **5.** What’s New |  |
| **6.** Caveats |  |
| **7.** Challenges to Implementation |  |
| **8.**  Acknowledgment Sentence | The PURLs Surveillance System is supported in part by Grant Number UL1RR024999 from the National Center For Research Resources, a Clinical Translational Science Award to the University of Chicago. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Center For Research Resources or the National Institutes of Health.  **If using UHC data:**  We acknowledge Sofia Medvedev of University HealthSystem Consortium (UHC) in Oak Brook, IL for analysis of the National Ambulatory Medical Care Survey data. |
| **9.** References |  |