

Cohort Study
Potential PURL Review Form
PURL Jam Version
Version #12 Sept 20, 2010

It's time to reconsider early-morning testosterone tests.
J Fam Pract. 2015;64:418-419.

PURLs Surveillance System
Family Physicians Inquiries Network

SECTION 1: Identifying Information for Nominated Potential PURL
[to be completed by PURLs Project Manager]

- | | |
|---|---|
| 1. Citation | Welliver RC Jr, Wiser HJ, Brannigan RE, Feia K, Monga M, Köhler TS. Validity of Midday Total Testosterone Levels in Older Men with Erectile Dysfunction. <i>J Urol.</i> 2014 Feb 8. pii: S0022-5347(14)00115-3. doi: 10.1016/j.juro.2014.01.085. [Epub ahead of print] PubMed PMID: 24518771. |
| 2. Hypertext link to PDF of full article | http://www.ncbi.nlm.nih.gov/pubmed/?term=Validity+of+midday+total+testosterone+levels+in+older+men+with+erectile+dysfunction&report=docsum |
| 3. First date published study available to readers | 02/08/14 |
| 4. PubMed ID | 24518771 |
| 5. Nominated By | Jim Stevermer Other: |
| 6. Institutional Affiliation of Nominator | University of Missouri Other: |
| 7. Date Nominated | 07/21/14 |
| 8. Identified Through | Other Other: InfoPoems |
| 9. PURLS Editor Reviewing Nominated Potential PURL | Kate Rowland |
| 10. Nomination Decision Date | 8/28/14 |
| 11. Potential PURL Review Form (PPRF) Type | Cohort Study |
| 12. Other comments, materials or discussion | |
| 13. Assigned Potential PURL Reviewer | Liz Nguyen, MD |
| 14. Reviewer Affiliation | University of Chicago Other: |
| 15. Date Review Due | 09/25/14 |
| 16. Abstract | <p>PURPOSE: Based on studies showing the circadian rhythmicity of testosterone the optimal time of day to draw total testosterone in men has classically been reported as between 8 and 11 a.m. However, further studies demonstrated that the testosterone circadian rhythmicity becomes blunted with age.</p> <p>MATERIALS AND METHODS: We retrospectively reviewed the charts of 2,569 men who presented with erectile dysfunction for total testosterone and draw times. We compared the men by age group, including less than 40 years and 5-year groupings after age 40 years. Total testosterone was analyzed for variability during the most common draw time hours (7 a.m. to 2 p.m.).</p> <p>RESULTS:</p> |

Mean total testosterone at 7 to 9 a.m. and 9 a.m. to 2 p.m. clinically and statistically differed only in men younger than 40 vs 40 to 44 years old (mean difference 207 ng/dl, 95% CI 98-315, p = 0.0004 vs 149 ng/dl, 95% CI 36-262, p = 0.01). No other group showed a clinically and statistically significant difference between those periods.

CONCLUSIONS:

Total testosterone in men with erectile dysfunction who are younger than 45 years should be drawn as close to 7 a.m. as possible because a statistically and clinically relevant decrease in testosterone will occur during the course of the day. Men older than 45 years with erectile dysfunction can have total testosterone drawn at any time before 2 p.m. without misleading results.

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KEYWORDS:

age groups; circadian rhythm; erectile dysfunction; testis; testosterone

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.

- | | |
|--|---|
| <input checked="" type="checkbox"/> Well covered | <input type="checkbox"/> Not addressed |
| <input type="checkbox"/> Adequately addressed | <input type="checkbox"/> Not reported |
| <input type="checkbox"/> Poorly addressed | <input type="checkbox"/> Not applicable |

Comments: 1. Does testosterone level vary by time of day
2. Does the testosterone level diurnal variation differ by patient age

2 The two groups being studied are selected from source populations that are comparable in all respects other than the factor under investigation.

- | | |
|--|---|
| <input type="checkbox"/> Well covered | <input type="checkbox"/> Not addressed |
| <input type="checkbox"/> Adequately addressed | <input type="checkbox"/> Not reported |
| <input checked="" type="checkbox"/> Poorly addressed | <input type="checkbox"/> Not applicable |

Comments: 2,569 males ages 26-84 presenting with CC: ED.No information regarding past medical history, current medications that may represent confounding variables.

3 The study indicates how many of the people asked to take part did so, in each of the groups being studied

- | | |
|---|--|
| <input type="checkbox"/> Well covered | <input type="checkbox"/> Not addressed |
| <input type="checkbox"/> Adequately addressed | <input type="checkbox"/> Not reported |
| <input type="checkbox"/> Poorly addressed | <input checked="" type="checkbox"/> Not applicable |

Comments: Retrospective study

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.

- | | |
|---|--|
| <input type="checkbox"/> Well covered | <input type="checkbox"/> Not addressed |
| <input type="checkbox"/> Adequately addressed | <input type="checkbox"/> Not reported |
| <input type="checkbox"/> Poorly addressed | <input checked="" type="checkbox"/> Not applicable |

Comments: The outcome was testosterone level.

5 What percentage of individuals or clusters recruited into each arm of the study dropped out before the study was completed?

None, this was a retrospective study

6 Comparison is made between full participants and those lost to follow up, by exposure status.

- | | |
|---|--|
| <input type="checkbox"/> Well covered | <input type="checkbox"/> Not addressed |
| <input type="checkbox"/> Adequately addressed | <input type="checkbox"/> Not reported |
| <input type="checkbox"/> Poorly addressed | <input checked="" type="checkbox"/> Not applicable |

Comments: No patients were lost to f/u as the study was retrospective

- 7 The outcomes are clearly defined.
- Well covered
 Adequately addressed
 Poorly addressed
- Not addressed
 Not reported
 Not applicable
- Comments: Variance in testosterone levels by time of day and patient age.
- 8 The assessment of outcome is made blind to exposure status
- Well covered
 Adequately addressed
 Poorly addressed
- Not addressed
 Not reported
 Not applicable
- Comments: Outcome was testosterone level. Blinding unnecessary as the outcome was a lab level (an objective-rather than subjective outcome)
- 9 Where blinding was not possible, there is some recognition that knowledge of exposure status could have influenced the assessment of outcome.
- Well covered
 Adequately addressed
 Poorly addressed
- Not addressed
 Not reported
 Not applicable
- Comments: Testosterone lab value is objective so blinding unnecessary.
- 10 What are the key findings of the study?
- Statistically significant Total Testosterone levels vary as the day progresses for men < 45 years old.
- 11 How was the study funded? Any conflicts of interest? Any reason to believe that the results may be influenced by other interests?
- Funding not documented- possibly through the VA?
One author with ties to several Pharmaceutical companies that provide ED treatments.

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. Hypogonadism in Males Author. None listed In: DynaMed [database online]. Available at: www.DynamicMedical.com Last updated: May 2014. Accessed 9/21/14
3. Bottom line recommendation or summary of evidence from DynaMed (1-2 sentences)
- Morning testosterone levels should be obtained in males presenting with signs of androgen deficiency.

4. UpToDate excerpts

5. UpToDate citation/access date

Always use Basow DS as editor & current year as publication year.
Title. Clinical features and diagnosis of male hypogonadism

6. Bottom line recommendation or summary of evidence from UpToDate (1-2 sentences)

Author. Peter J. Snyder MD In: UpToDate [database online]. Available at: <http://www.uptodate.com>. Last updated: Jan 2013. Accessed 9/21/14
Total testosterone can be measured for most patients. Timing of testosterone testing should be at 8 AM. No distinction made for patient age.

7. PEPID PCP excerpts

www.pepidonline.com
username: fpinauthor
pw: pepidpcp

8. PEPID citation/access data

Author. Title. In: PEPID [database online]. Available at: <http://www.pepidonline.com>. Last updated: . Accessed

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 (E) 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.)

AACE Hypogonadism Guidelines 2002: Total testosterone in the morning, if Total Testosterone abnormal, draw free/bioavailable T levels. No distinction for age.

11. Citations for other excerpts

European Association of Urology: Obtain AM Testosterone levels.

12. Bottom line recommendation or summary of evidence from Other Sources (1-2 sentences)

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

Unclear if confounding variables present- no information re: past medical history, medication lists. Also testosterone levels weren't repeated in any patients(ie- morning -vs-later afternoon testosterone levels in same patient)

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?

4. If 4.3 was coded as 4, 5, 6, or 7, please 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?

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.

7. 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?

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?

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=extremely well; 4=neutral; 7=extremely poorly)

1 2 3 4 5 6 7

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

Unsure if most docs order AM testosterone levels still.

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

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

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

14. Comments on your response in 4.13

Is testosterone difference of 100-200 clinically meaningful since all values were still within normal range? The difference may be detecting normal versus low-normal values.

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

Practice changer would be stop drawing morning Testosterone levels on patients > 45. Whether it's a PURL depends on if docs are ordering AM levels.

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

This is a retrospective cohort study evaluating whether diurnal variations in testosterone level vary with patient age. Inclusion criteria included men presenting to an outpatient VA clinic between 1986-2004 with a chief complaint of erectile dysfunction who had at least one testosterone level drawn. Patients were excluded if their testosterone level wasn't drawn between 7AM and 2PM and if their testosterone level was outside the reference range of 50-1,000 ng/dL.

The testosterone levels of 2,569 patients meeting the study inclusion criteria were analyzed by patient age(<40 and in 5 year intervals if > 40, ie. 40-44, 45-49, etc) and time of blood draw (7-9 AM or 9AM-2PM). Each patient had only one testosterone level drawn during the time period studied. Mean age of patients studied was 63.

Statistically significant diurnal variations in testosterone level were only found in patients <40 years old (mean difference 207, p 0.0004), 40-44 years old(MD 149, p 0.0103) and 70-74 years old(MD 34, p 0.0379).

2.Criteria- note yes or no for those which this study meets

RELEVANT - Yes
VALID - Yes
CHANGE IN PRACTICE- ?
MEDICAL CARE SETTING - Yes
IMMEDIATELY APPLICABLE - Yes
CLINICALLY MEANINGFUL - ?

3. Bottom Line- one –two sentences noting the bottom line recommendation

Evaluating symptoms of androgen deficiency should be performed using morning testosterone levels only in men < 45 years old as diurnal variations in testosterone levels are no longer significant in older men.

4. Title Proposal

Drawing morning testosterone levels is no longer necessary.

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
3. 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:

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

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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