

Prognostic value of pretreatment serum lactate dehydrogenase level in patients with solid tumors: a systematic review and meta-analysis

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## **Supplements:**

### **Figure:**

S1. Flow diagram showing the selection process for the systematic review.

S2. Publication Bias (Funnel plot of hazard ratio for overall survival for Lactate dehydrogenase (LDH) (horizontal axis) and the standard error (SE) for the hazard ratio (vertical axis). Each study is represented by one circle. The vertical line represents the pooled effect estimate.)

S3. Forest plots showing hazard ratio for progression-free survival for Lactate dehydrogenase (LDH) greater than or less than the cutoff.

S4. Forest plots showing hazard ratio for disease-free survival/recurrence-free survival for Lactate dehydrogenase (LDH) greater than or less than the cutoff.

S5. Forest plots showing hazard ratio for overall survival for LDH as a continuous variable.

### **Figure: Risk of bias summary**

### **Other supplements material:**

S1-Documentation of the Searches

S2-Excluded References

### **Results of Meta-regression**

PubMed search strategy run on  
July 28th, 2014, n=1055

Manuscripts excluded:  
Non-neoplastic disease, n=97  
Non solid tumors, n=792  
Total, n=889

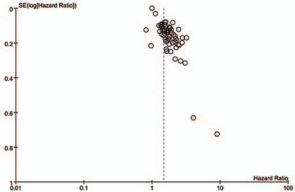
Manuscripts pulled following  
titles/abstracts screened, n=166

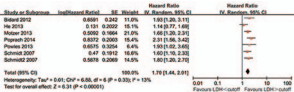
Manuscripts excluded:  
Other topics (eg.LDH expression), n=12  
Sample size less than 200, n=51  
Reviews, system review, n=9  
Total, n=72

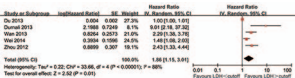
Full paper search, n=94

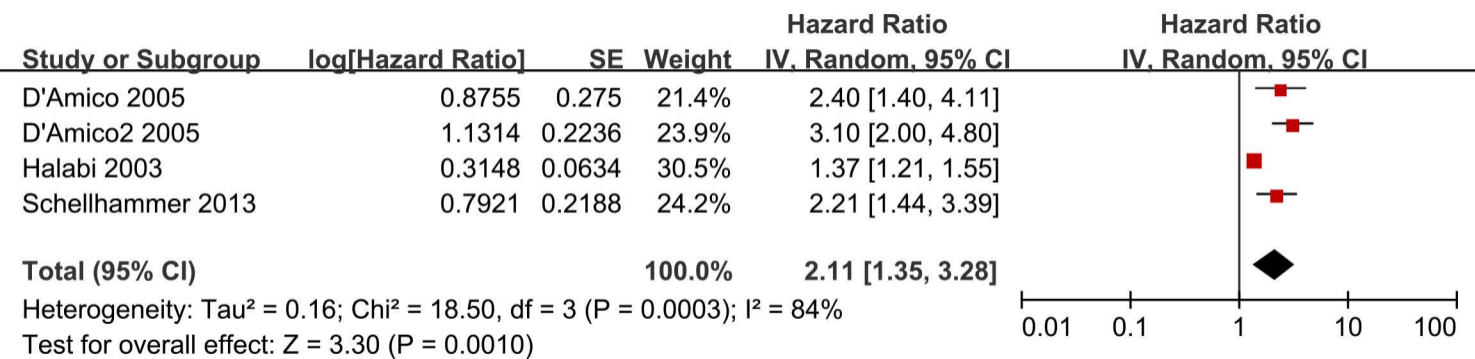
Manuscripts excluded:  
No HR and 95%CI or P value provided,  
n=26  
Total, n=26

Included in final analysis, n=68









|                   | Were adequate eligibility criteria developed and applied? | Was the measurement of both exposure and outcome adequate? | Was confounding adequately controlled for? | Was the follow-up complete and adequate in duration? | Are study reports free of suggestion of selective outcome reporting? | Was the study free of other problems that put it at a high risk of bias? | Risk of bias |
|-------------------|---|--|--|--|--|--|--------------|
| Ace 2004          | +   | +  | +  | +  | +  | -  | -            |
| Ace 2005          | +   | +  | +  | +  | +  | -  | -            |
| Armstrong 2012    | +   | +  | +  | +  | +  | -  | -            |
| Atzpodien 2003    | +   | +  | +  | +  | +  | +  | +            |
| Bacci 2000        | +   | +  | +  | +  | +  | +  | +            |
| Bacci 2004        | +   | +  | +  | +  | +  | +  | +            |
| Bacci 2007        | +   | +  | +  | +  | +  | +  | +            |
| Bedikian 2008     | +   | +  | +  | +  | +  | +  | +            |
| Bedikian 2011     | +   | +  | +  | +  | +  | +  | +            |
| Bidard 2012       | +   | +  | +  | +  | +  | +  | +            |
| Chibaudel 2011    | +   | +  | +  | +  | +  | +  | +            |
| Cook 2006         | +   | +  | +  | +  | +  | +  | +            |
| Culp 2010         | +   | +  | +  | +  | +  | +  | +            |
| D'Amico 2005      | +   | +  | +  | +  | +  | +  | +            |
| Du 2013           | +   | +  | +  | +  | +  | +  | +            |
| Durnali 2013      | +   | +  | +  | +  | +  | +  | +            |
| Escudier 2007     | +   | +  | +  | +  | +  | +  | +            |
| Eton 1998         | +   | +  | +  | +  | +  | -  | -            |
| Feliu 2011        | +   | +  | +  | +  | +  | -  | -            |
| Giaccone 2005     | +   | +  | +  | +  | +  | -  | -            |
| Giessen 2013      | +   | +  | +  | +  | +  | +  | +            |
| Giroux 2012       | +   | +  | +  | +  | +  | -  | -            |
| Gripp 2007        | +   | +  | +  | +  | +  | +  | +            |
| Halabi 2003       | +   | +  | +  | +  | +  | -  | -            |
| Halabi 2014       | +   | +  | +  | +  | +  | +  | +            |
| Han 2003          | +   | +  | +  | +  | +  | -  | -            |
| Hannisdal 1993    | +   | +  | +  | +  | +  | -  | -            |
| Hashimoto 2009    | +   | +  | +  | +  | +  | -  | -            |
| He 2013           | +   | +  | +  | +  | +  | -  | -            |
| Jakob 2012        | +   | +  | +  | +  | +  | +  | +            |
| Jin 2013          | +   | +  | +  | +  | +  | +  | +            |
| Kawahara 1997     | +   | +  | +  | +  | +  | -  | -            |
| Kim 2010          | +   | +  | +  | +  | +  | -  | -            |
| Lagerwaard 1999   | +   | +  | +  | +  | +  | +  | +            |
| Laurie 2007       | +   | +  | +  | +  | +  | +  | +            |
| Li 2012           | +   | +  | +  | +  | +  | +  | +            |
| Meckbach 2014     | +   | +  | +  | +  | +  | +  | +            |
| Mekenkamp 2012    | +   | +  | +  | +  | +  | +  | +            |
| Motzer 1999       | +   | +  | +  | +  | +  | +  | +            |
| Motzer 2002       | +   | +  | +  | +  | +  | +  | +            |
| Motzer 2013       | +   | +  | +  | +  | +  | +  | +            |
| Neuman 2008       | +   | +  | +  | +  | +  | +  | +            |
| Piarga 2001       | +   | +  | +  | +  | +  | +  | +            |
| Polee 2003        | +   | +  | +  | +  | +  | +  | +            |
| Poprach 2014      | +   | +  | +  | +  | +  | +  | +            |
| Powles 2013       | +   | +  | +  | +  | +  | -  | -            |
| Saito 2007        | +   | +  | +  | +  | +  | +  | +            |
| Sau 2013          | +   | +  | +  | +  | +  | +  | +            |
| Schellhammer 2013 | +   | +  | +  | +  | +  | +  | +            |
| Scher 1999        | +   | +  | +  | +  | +  | -  | -            |
| Schmidt 2007      | +   | +  | +  | +  | +  | +  | +            |
| Shinohara 2012    | +   | +  | +  | +  | +  | +  | +            |
| Shinohara 2013    | +   | +  | +  | +  | +  | +  | +            |
| Sougioultzis 2011 | +   | +  | +  | +  | +  | +  | +            |
| Suh 2010          | +   | +  | +  | +  | +  | -  | -            |
| Tamura 1998       | +   | +  | +  | +  | +  | -  | -            |
| Tanrikulu 2010    | +   | +  | +  | +  | +  | -  | -            |
| Templeton 2014    | +   | +  | +  | +  | +  | -  | -            |
| Tonini 1997       | +   | +  | +  | +  | +  | +  | +            |
| van Kessel 2013   | +   | +  | +  | +  | +  | +  | +            |
| Viganó 2000       | +   | +  | +  | +  | +  | +  | +            |
| Wan 2013          | +   | +  | +  | +  | +  | +  | +            |
| Wang 2014         | +   | +  | +  | +  | +  | +  | +            |
| Wei 2014          | +   | +  | +  | +  | +  | +  | +            |
| Weide 2012        | +   | +  | +  | +  | +  | +  | +            |
| Weide 2013        | +   | +  | +  | +  | +  | +  | +            |
| Yamaguchi 2014    | +   | +  | +  | +  | +  | -  | -            |
| Zhou 2012         | +   | +  | +  | +  | +  | +  | +            |



Pubmed 检索式:

(((((l-lactate dehydrogenase[MeSH Terms]) OR lactate dehydrogenase[Title/Abstract]) OR LDH[Title/Abstract])) AND (((prognosis[MeSH Terms]) OR prognosis[Title/Abstract]) OR prognoses[Title/Abstract]) OR prognostic[Title/Abstract])) AND (((((multivariate analysis[MeSH Terms]) OR multivariate analysis[Title/Abstract]) OR proportional hazard model[MeSH Terms]) OR proportional hazard model[Title/Abstract]) OR COX proportional hazard model[Title/Abstract]) OR COX Models[Title/Abstract]))

**Run on: 2014-7-28**

Part 1:

[MeSH Terms]: "l-lactate dehydrogenase"

Title/Abstract: "lactate dehydrogenase"

Title/Abstract: "LDH"

Part 2:

[MeSH Terms]: "prognosis"

Title/Abstract: "prognosis"

Title/Abstract: "prognoses"

Title/Abstract: "prognostic"

Part 3:

[MeSH Terms]: “multivariate analysis”

Title/Abstract: “multivariate analysis”

[MeSH Terms]: “proportional hazard model”

Title/Abstract: “proportional hazard model”

Title/Abstract: “COX proportional hazard model”

Title/Abstract: “Cox Models”

**Title/abstracts:**

Other topics: n=889

Other topics: n=12

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Reviews: n=9

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Sample size less than 200: n=51

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No HR and 95%CI or Pvalues or univariate analysis : n=26

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Meta-regression

Number of obs = 65

REML estimate of between-study variance      tau2      = .05335

% residual variation due to heterogeneity      I-squared\_res = 93.58%

Proportion of between-study variance explained      Adj R-squared = -1.72%

With Knapp-Hartung modification

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|        | loghr       | exp(b) | Std. Err. | t    | P> t  | [95% Conf. Interval] |          |
|--------|-------------|--------|-----------|------|-------|----------------------|----------|
|        | -----+----- |        |           |      |       |                      |          |
| cutoff | 1.000138    |        | .0002724  | 0.51 | 0.614 | .999594              | 1.000683 |
| _cons  | 1.602006    |        | .1513549  | 4.99 | 0.000 | 1.326385             | 1.934902 |

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