

Association of *FLT3*-internal tandem duplication length with overall survival in acute myeloid leukemia: a systematic review and meta-analysis

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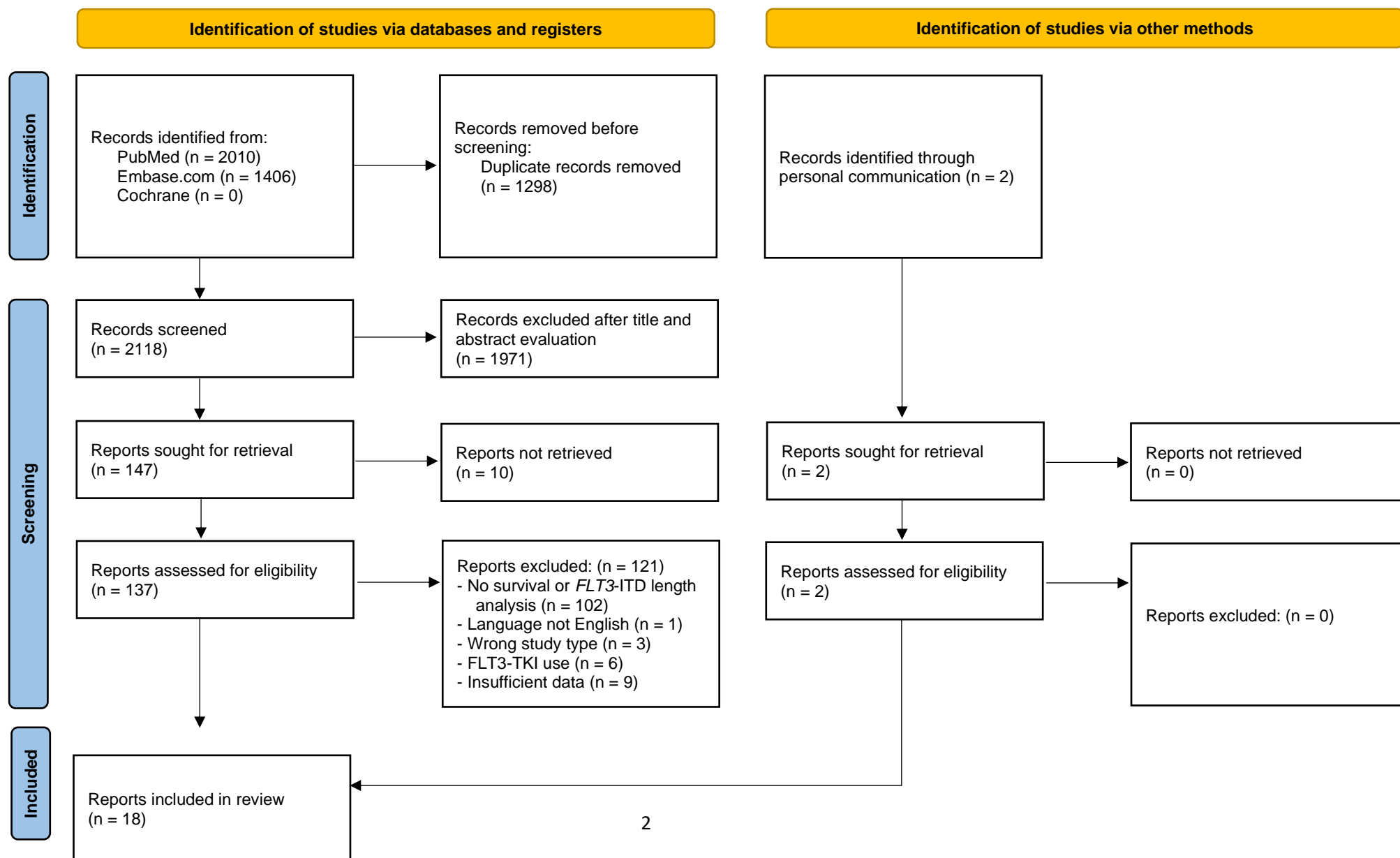
Supplementary data

Association of *FLT3*-ITD length with overall survival in acute myeloid leukemia: a systematic review and meta-analysis

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Supplementary Figure S1: Prisma-diagram.



Supplementary Table S1. Risk of bias according to QUIPS for all individual studies included in this meta-analysis.

<i>Author and reference</i>	<i>Year</i>	<i>Study participation</i>	<i>Study attrition</i>	<i>Prognostic factor measurement</i>	<i>Outcome measurement</i>	<i>Study confounding</i>	<i>Statistical analysis and Reporting</i>
Adult							
Stirewalt et al ¹	2006	Moderate	Moderate	Low	Low	Moderate	Low
Kusec et al ²	2006	High	Moderate	Moderate	Moderate	Low	Moderate
Gale et al ³	2007	Low	Moderate	Moderate	Low	Low	Moderate
Schiller et al ⁴	2012	Low	Moderate	Moderate	Moderate	Low	Moderate
Blau et al ⁵	2012	Low	Moderate	Moderate	Low	Moderate	Low
Schlenk et al ⁶	2014	Low	Moderate	Low	Low	Moderate	Low
Koszarska et al ⁷	2014	Low	Moderate	Low	Low	Low	Low
Kim et al ⁸	2015	Moderate	Moderate	High	Low	Low	Low
Liu et al ⁹	2019	Low	High	Moderate	Low	Low	Low
Zhang et al ¹⁰	2020	Low	Moderate	High	Low	Moderate	Low
Schlenk et al ¹¹	2020	Low	Moderate	Low	Low	Moderate	Low
Cucchi et al ^{12a}	2021	Low	Moderate	Low	Low	Low	Low
Cucchi et al ^{12b}	2021	Low	Moderate	Low	Low	Low	Low
Engen et al ¹³	2021	Low	Moderate	High	Moderate	Moderate	Low
Castaño-Bonilla et al ¹⁴	2021	Low	Moderate	Low	Low	Low	Low
Pediatric							
Meshinchi et al ¹⁵	2008	Low	Moderate	High	Low	High	Low
Gamis et al ¹⁶	2014	Low	Moderate	Low	Low	Moderate	Low
Manara et al ¹⁷	2017	Low	Moderate	Low	Low	Moderate	Low
Cucchi et al ¹⁸	2018	Low	Moderate	High	Moderate	Low	Low

The risk of bias was assessed according to QUIPS¹⁹ by scoring each study using a standardized scoring list, investigating potential bias on six domains. A low risk of bias indicates that there were no factors or one factor in one domain potentially introducing bias. A moderate risk of bias indicates that several

factors were present potentially introducing bias. A high risk of bias indicates that several factors were present that likely introduce bias, such as the use of a 'lowest *p*-value' approach to determine a cut-off value for short and long *FLT3*-ITD length. Factors scored per domain were as follows:

Study participation: source of target population, method used to identify population, recruitment period, place of recruitment, inclusion and exclusion criteria, adequate study participation, baseline characteristics

Study attrition: proportion of baseline sample available for analysis, attempts to collect information on participants who dropped out, reasons and potential impact of subjects lost to follow-up, outcome and prognostic factor information on those lost to follow-up

Prognostic factor measurement: definition of the prognostic factor, valid and reliable measurement of prognostic factor, method and setting of prognostic factor measurement, proportion of data on prognostic factor available for analysis, method used for missing data

Outcome measurement: definition of the outcome, valid and reliable measurement of outcome, method and setting of outcome measurement

Study confounding: important confounders measured, definition of the confounding factor, valid and reliable measurement of confounders, method and setting of confounding measurement, method used for missing data, appropriate accounting for confounding

Statistical analysis and reporting: presentation of analytical strategy, model development strategy, reporting of results

For Cucchi et al¹² results are provided separately for the Dutch-Belgian Cooperative Trial Group for Hematology-Oncology (HOVON)/Swiss Group for Clinical Cancer Research (SAKK) (a) HOVON 102 AML/SAKK 30/09 trial and (b) (SAKK) HOVON 132 AML/SAKK 30/13 trial.

Supplementary Table S2. Median and range of absolute differences of age, percentage of patients with *NPM1* and *DNMT3A* mutations and white blood cell count of *FLT3*-ITD short vs *FLT3*-ITD long AML patients. “Short” and “long” groups are defined as reported in each unique study.

<i>Parameter</i>	<i>Median of absolute difference</i>	<i>Range of absolute difference</i>	<i>Total patients analyzed (N)</i>	<i>References</i>
Age, years	0.75	-4 – 4.5	704	1,7–9,12–14
<i>NPM1</i> mutant, percentage point	-4.6	-20.9 – 11.7	775	7–9,12,13,16
<i>DNMT3A</i> mutant, percentage point	0	-1.5 – 2.9	345	9,12,13
White blood cell count, x 10 ⁹ / L	11	4.4 – 25.5	720	1,7,9,12–14

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