# Introduction

Colorectal liver metastatic cancer (CRLM))…..

# Methods

## Objective

The present study aims to determine the prognostic value of primary tumour location (left versus right) in patients with stage four KRAS mutated colorectal liver metastatic tumours that underwent colorectal surgery. The reporting of this systematic review follows the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) statement [cit].

Data Sources and Search Strategies

We performed a comprehensive literature search in PubMed database for full-text articles published in print or online from inception until May 2020. The detailed search strategy is as described in the Supplementary material. The search strategy was designed and conducted by an experienced librarian (A.T.) with input from the study investigators. Two of us (M.B and A.M.) identified and reviewed full-text articles that were deemed relevant by screening their titles and abstracts. Disagreements between the 2 reviewers were resolved with consensus. Outcomes of interests included OS and progression-free survival (PFS). We also included manually studies after contact with experts in Surgical Oncology.

## Inclusion Criteria

Consistent to our goal mentioned above we included studies that reported the mortality on patients with stage 4 colorectal liver metastasis that underwent resection, reported KRAS mutation and location of the primary tumour. We excluded studies not written in English, Dutch, Greek or German.

Data Extraction

For the studies gathered through the literature search we extracted prespecified data elements including baseline characteristics, sample size, and location of the primary tumour and KRAS mutation (yes/no). One of us extracted the data from the included studies (M.B.). Initial analysis was performed on September 20, 2021. An updated search was performed in February 2021. For the studies suggested by experts, we contacted the authors via e-mail requesting access on individual participant data (partially or as a whole). If IPD sharing was not possible we requested the authors to perform the analysis on their data and share their results.

## IPD definitions

Rectum (location)  
Death (any type of death)

Time to event (for non-events)

Excluded 1 month

## Statistical Analysis

We pooled the extracted hazard ratios (HRs) from the included studies random-effects meta-analysis method with empirical Bayes τ2. We used the I2 statistic to assess for heterogeneity across studies. Two-sided P < .05 was deemed statistically significant. We didn’t perform a risk of bias assessment as the quality of the studies was expected to be similar across studies.

# Results

## Study Selection

A total of 1169 titles and abstracts were identified by the screening electronic search strategy. After title and abstract screening 5 articles met the eligibility criteria (eFigure 1 in the Supplement). After full text inspection all 5 were considered relevant and included in the meta-analysis. Three studies [cit] were suggested by experts and included in the meta-analysis. Although, the objective of these three studies was different than the current analysis, they were considered relevant since they gathered KRAS mutation, surgery information and primary tumour location.

# Study Characteristics

The 5 studies comprised xxx patients.