

# Disease burden of chronic myeloid leukemia (CML) treatment failure in mainland China: a systematic literature review

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## INTRODUCTION

- Since the launch of imatinib in China in 2002, tyrosine kinase inhibitors (TKIs) have become the mainstay of treatment for CML; their use can significantly delay disease progression.
- The emergence of drug resistance and intolerance or treatment failure after long-term TKI treatment has become a major challenge in the management of CML.
- Existing evidence associated with TKI treatment failure should be reviewed to identify and address the unmet medical needs in Chinese CML patients (pts) under current treatment care.

## OBJECTIVES

- To identify existing literature on the disease burden of CML TKI treatment failure in mainland China.

## METHODS

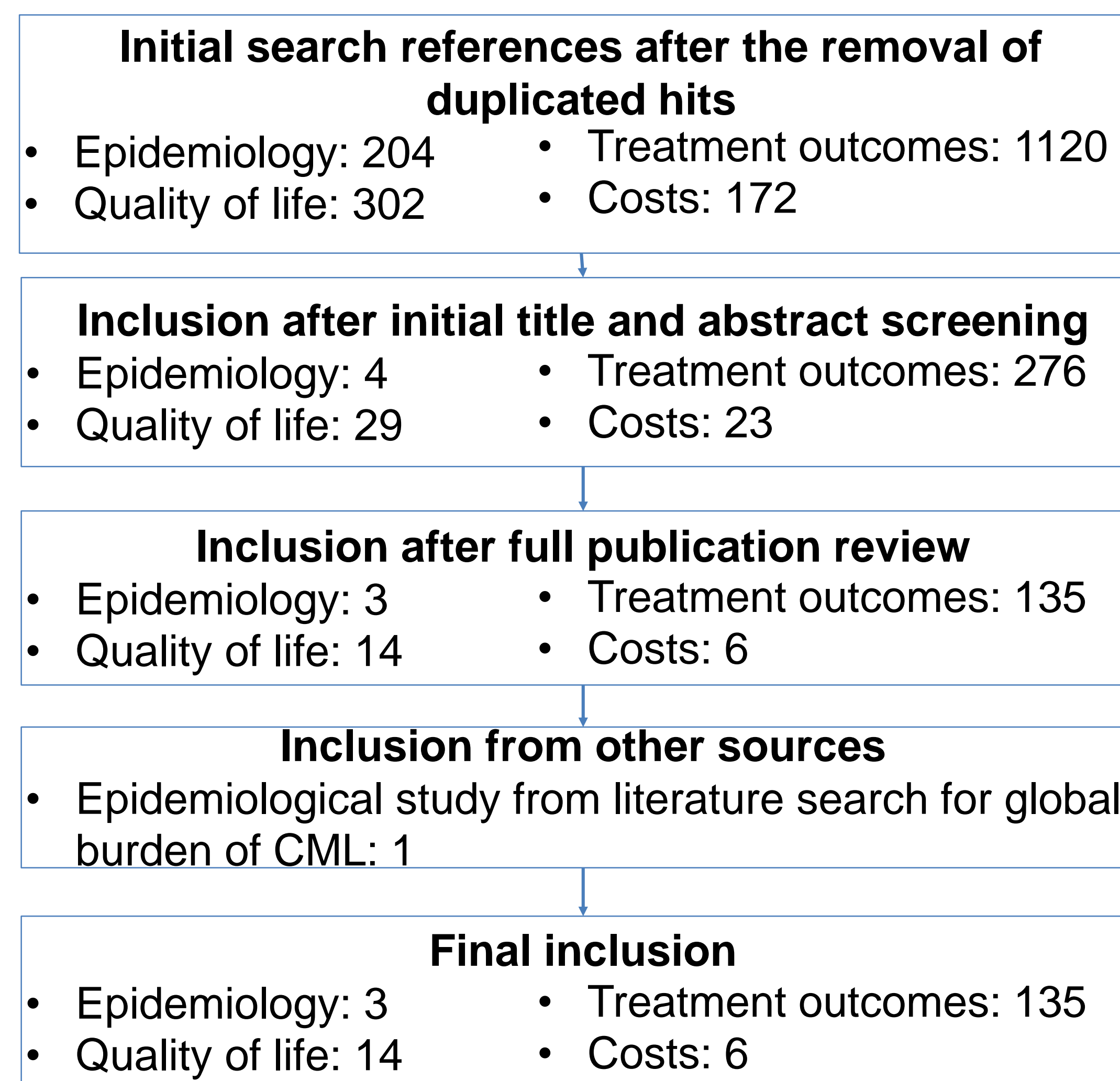
<b>Bibliographic databases</b>	<ul style="list-style-type: none"> <li>• English: MEDLINE, EMBASE, Web of Science, and The Cochrane Library</li> <li>• Chinese: WANFANG, VIP, and CNKI</li> </ul>
<b>Literature search strategies</b>	<ul style="list-style-type: none"> <li>• Publication dates: 2001 to 2021</li> <li>• Keywords: disease, epidemiology, TKI, HSCT, treatment failure, quality of life, health resource utilization and costs</li> </ul>
<b>Study eligibility assessment</b>	<ul style="list-style-type: none"> <li>• PICOS criteria: population, intervention, comparator, outcomes, study type</li> </ul>
<b>Evidence synthesis</b>	<ul style="list-style-type: none"> <li>• Single-arm meta-analysis with a random-effects model</li> <li>• Weighted mean or median method</li> </ul>

## RESULTS

### Study selection

After screening the titles and abstracts and reviewing full publications, a total of 155 references were selected for data extraction and evidence synthesis. The literature search process is illustrated in Figure 1.

**Figure 1. Literature search process for real-world studies exclusively from mainland China**



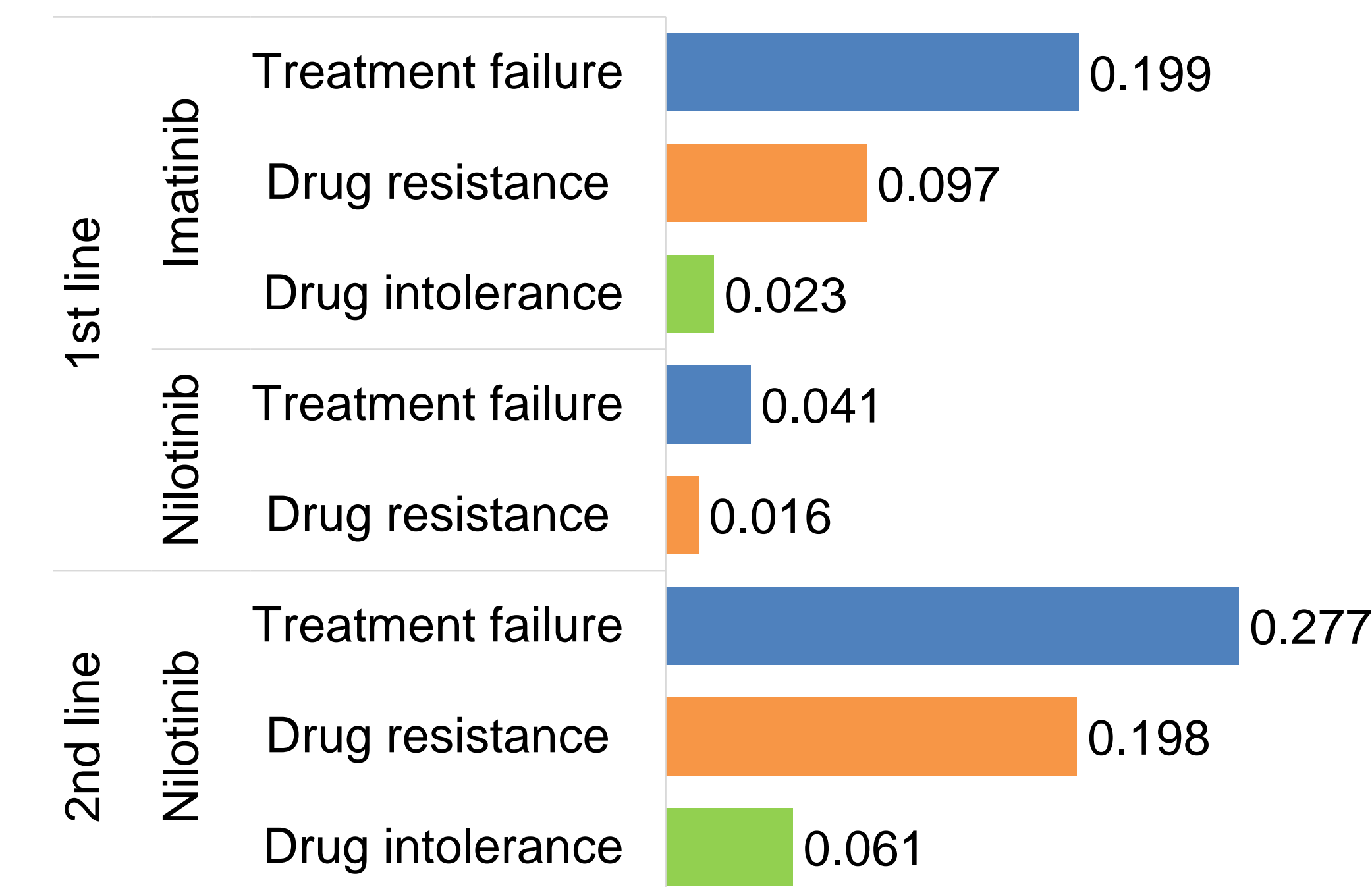
### Epidemiology of CML

- The age-standardized incidence rates of CML in 1990 and in 2017 were highly comparable (0.19 vs. 0.16 per 100,000).
- The age-standardized mortality rate in 2017 (0.06/100,000) was reduced by about half when compared to that in 1990 (0.13/100,000).

### Risk of TKI treatment failure

- Drug resistance was the predominant reason for treatment failure for imatinib in the first-line treatment setting (90.8%) and nilotinib in the second-line setting (85.3%). Annual risk of TKI failure is shown in Figure 2.
- Nilotinib in the second-line treatment setting was associated with the highest annual risk of T315i mutation (0.068).

**Figure 2. Pooled annual risks of treatment failure in pts with CML receiving TKI treatment**



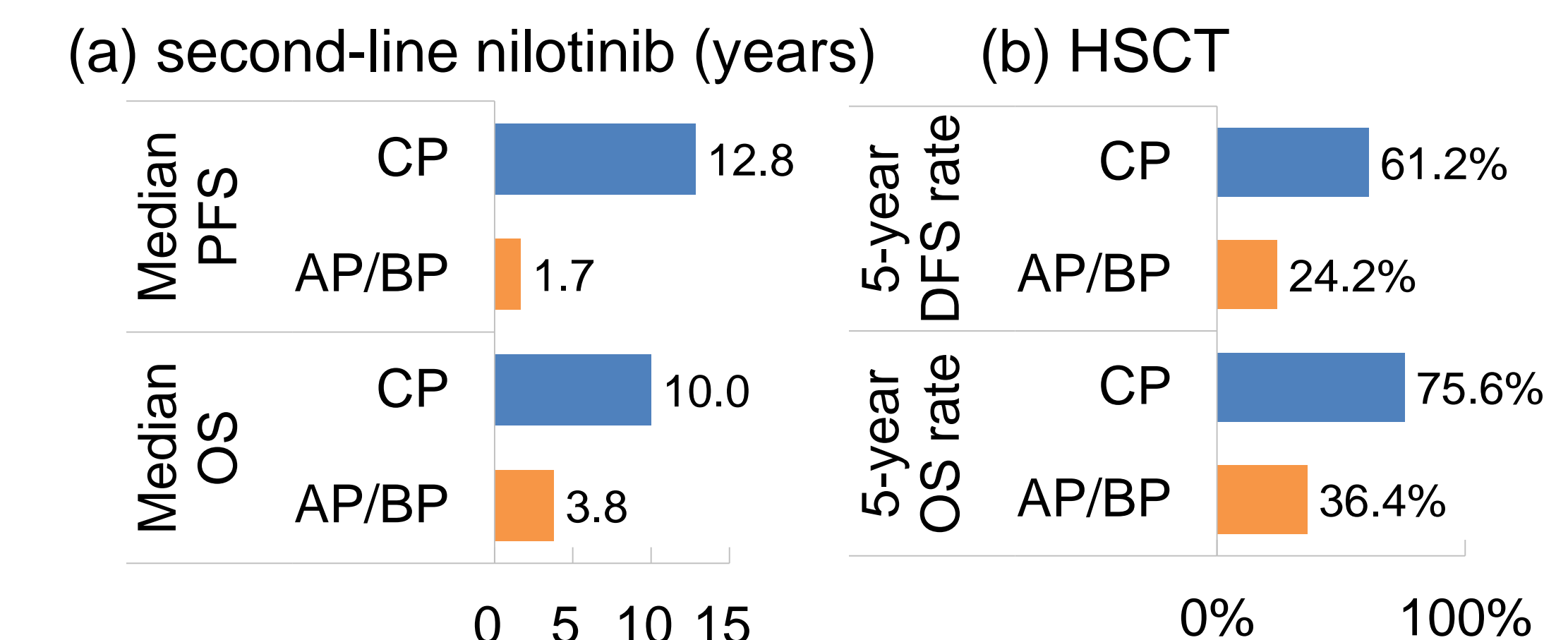
### Patient characteristics and disease progression

- Chinese pts with CML who had TKI treatment failure were characterized by young age (median: 38.6 years); male sex (64.3%); at least one comorbidity (37.1%); and T315i mutation (10.6%).
- The annual risk of disease progression from chronic phase to accelerated/blast-phase (AP/BP) in pts with TKI failure was 0.102. The median overall survival (OS) of pts in AP/BP was 2.5 years.

### Treatment outcomes in pts with TKI treatment failure

- Pts who had TKI failure (78.6%) were switched to a second-generation TKI. Survival outcomes of switched treatment are shown in Figure 3.

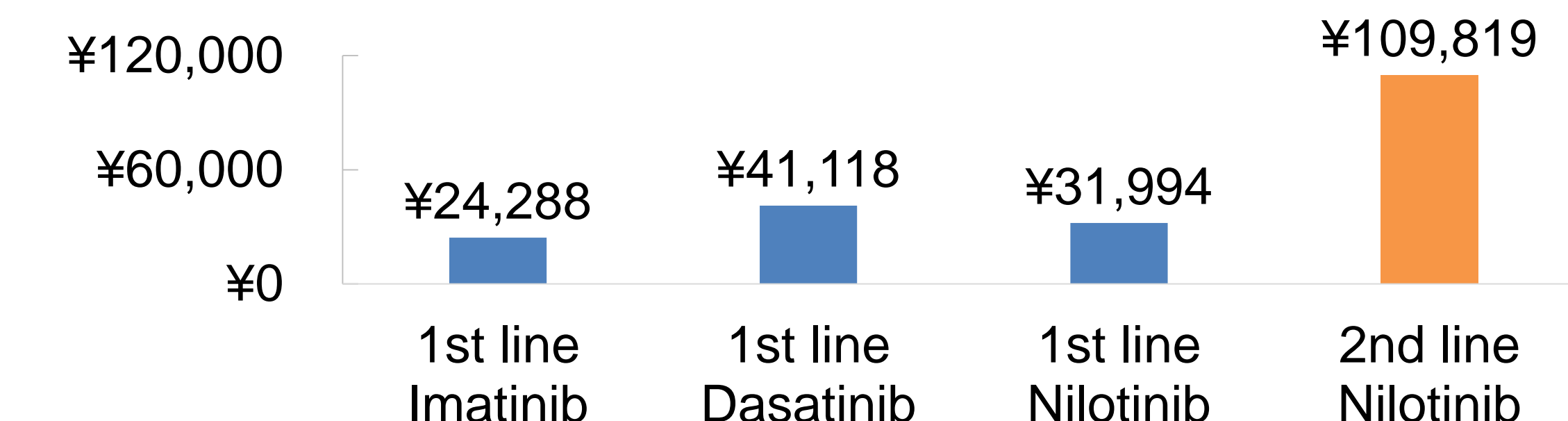
**Figure 3. Survival outcomes of pts with CML who had treatment failures**



### Medical costs

- Annual non-drug medical costs of nilotinib used in the second-line treatment setting were more than twice that used in the first line (Figure 4). Costs were adjusted to 2020 Chinese yuan.

**Figure 4. Annual non-drug medical costs**



## CONCLUSIONS

- The disease burden of CML treatment failure in China is substantial and fast-growing.
- Limited access to HSCT and high costs of HSCT indicate an urgent need for effective and affordable treatments to address the unmet medical needs in Chinese pts with CML who experience TKI treatment failure.