Economic Benefits of Cangrelor in Patients With Coronary Artery Disease Undergoing Percutaneous Coronary Intervention: A Systematic Literature Review

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INTRODUCTION

- **Acute coronary syndrome (ACS)** is a subcategory of **coronary artery disease (CAD)**, a leading causes of death worldwide that places a substantial economic burden on healthcare systems[1]
- The current management of ACS includes **percutaneous coronary intervention (PCI)**, a procedure that restores myocardial blood supply in blocked vessels through the insertion of a stent[2,3]
- Although being a highly effective therapy, PCI may be associated with complications such as **stent thrombosis (ST)**, which can lead to **myocardial infarction (MI)** and **death**, and may require **additional revascularization**, **longer hospital stays** and **hospital re-admissions**[4]
- Clinical guidelines recommend **dual antiplatelet therapy (DAPT)**, consisting of aspirin and a $P2Y_{12}$ inhibitor or glycoprotein IIb/IIIa inhibitor (GPI) as bail-out therapy, to reduce the risk of adverse events during PCI[2,3]
- However, commonly available $P2Y_{12}$ inhibitors have limitations linked to their **oral administration route** and slow onset/offset of action, making them **unsuitable for patients at high risk** of experiencing PCI-induced complications, or patients that are unconscious, intubated, or vomiting[5]
- Moreover, while GPIs are administered intravenously, they present an **increased risk of serious bleeding** and need for transfusions[6]
- **Cangrelor is the only intravenous $P2Y_{12}$ inhibitor** with rapid onset and offset proven to significantly reduce the risks of PCI-related complications[7]
- Previous systematic literature reviews (SLRs) have assessed cangrelor safety and efficacy, while the humanistic and economic burden associated with the management of PCI with cangrelor has not been systematically reviewed[8,9]

OBJECTIVES

- The SLR aims to identify and summarise recently published evidence on the **clinical, humanistic, and economic outcomes of cangrelor** in patients with ACS undergoing PCI
- **We present here a summary of the economic evidence only**

METHODS

Data collection and extraction

- The SLR was conducted following the **standard systematic review methodology** endorsed by Cochrane. The process included:
  - **Screening of all abstracts and selected full texts** by two reviewers with discrepancies resolved by a third reviewer; linking multiple reports of the same study together before data extraction and determining the primary publication for each study
  - **Extraction of data from primary references** conducted by a single reviewer using a standardized data extraction form and validated by a second reviewer with discrepancies resolved by a third reviewer, as needed
  - **Quality-check** using Cochrane Risk of Bias 2.0 (RCTs only), Newcastle-Ottawa Scale (for observational studies) and CHEERS checklist (for economic evaluations)

Search methods

- The search was conducted on the **29th of April 2022**
- The following electronic databases were queried:
  - **MEDLINE®**, **EMBASE®**, and **Cochrane** Database of Systematic Reviews
  - Relevant **conference proceedings** for the last 3 years (2019-2022)
  - **ClinicalTrials.gov**
- Bibliographies of the included studies were reviewed to obtain further relevant references
- Only publications in English were retrieved

Eligibility criteria

- **Inclusion criteria** related to population, intervention, comparator, outcomes, study design and timeframe (**PICOS-T**) are presented in **Table 1**

Table 1. SLR inclusion criteria

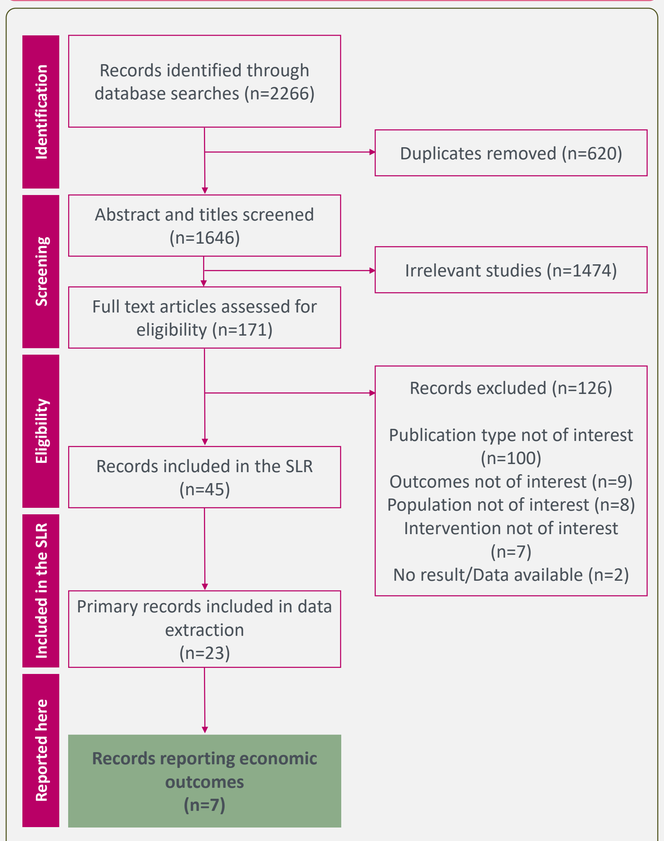
Criteria	Inclusion Criteria
Population	Adult (≥18 years) Treatment-naïve (not received $P2Y_{12}$ inhibitor in the previous 5 days) Diagnosis of CAD/ACS undergoing PCI In the European Union, the United Kingdom, Turkey, Mexico, Russia, and the United States
Intervention	Cangrelor
Comparator	With or without a comparator
Outcomes	Economic outcomes (e.g., cost-effectiveness, cost-consequence, budget impact) Clinical outcomes (e.g., death, MI, ST, bleedings) Humanistic outcomes (e.g., quality-adjusted life years (QALY), disability-adjusted life years (DALY))
Study design	Randomized and non-randomized controlled trials Observational studies Health economic evaluations Systematic reviews and/or meta-analyses*
Timeframe	Peer reviewed full-text from 2009 to 2022† Conference abstract from 2019 to 2022‡

*Included and flagged for bibliography searches; †Up to September 2022; ‡Up to May 2022
ACS, acute coronary syndrome; CAD, coronary artery disease; DALY, disability-adjusted life years; MI, myocardial infarction; PCI, percutaneous coronary intervention; QALY, quality-adjusted life years; ST, stent thrombosis

RESULTS

- In total, 45 publications met the SLR inclusion criteria, referring to **23 studies** (**Figure 1**)
- Data was extracted from the 23 primary references based on the criteria listed in the methods section
- **Seven studies reported economic outcomes: four budget impact models (BIMs), one cost-consequence model, a study on the cost implications of the CHAMPION PHOENIX, and one observational study**

Figure 1. PRISMA flow diagram



PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; SLR, systematic literature review

Budget-impact models

- One BIM published in 2020 and three BIMs published in 2021 assessed the **impact of introducing cangrelor into hospital formularies** in four European countries (**Table 2**)[10-13]
- The models calculated the cost difference between two scenarios (**without and with cangrelor** in hospital formularies) to treat CAD patients undergoing PCI in whom oral $P2Y_{12}$ inhibitors were not feasible or desirable, over 3 years
- Results demonstrated that the economic effort needed to incorporate cangrelor into the hospital pharmacy formulary from the National Health System perspective falls within **reasonable margins**

Cost-implications study

- A US economic sub-study of the CHAMPION PHEONIX randomized trial evaluated the costs of **intraprocedural thrombotic events (IPTE) and bleeding complications** during PCI[14]
- Although IPTE and bleeding complications were infrequent, these were associated with **substantially increased costs and higher healthcare resource use** (**Figures 2,3**)

Cost-consequences model

- A US decision analytic model published in 2022 evaluated **hospital cost implications** of cangrelor use in PCI patients with two or more **angiographic high-risk features (HRFs)**[15]
- The model assumed an increase in cangrelor use over 3-years in two scenarios (50% or 100% reduction in oral $P2Y_{12}$ pre-treatment) (**Figure 4**)

RESULTS (continued)

Cost-consequence model (continued)

- Results showed that increasing cangrelor use in high-risk PCI patients provided a **reduction in hospital annual costs** with savings attributed to a **reduction in ischemic events**, **decrease in GPI use** and **shortened $P2Y_{12}$ inhibitor washout period** (**Figure 4**)

Observational study

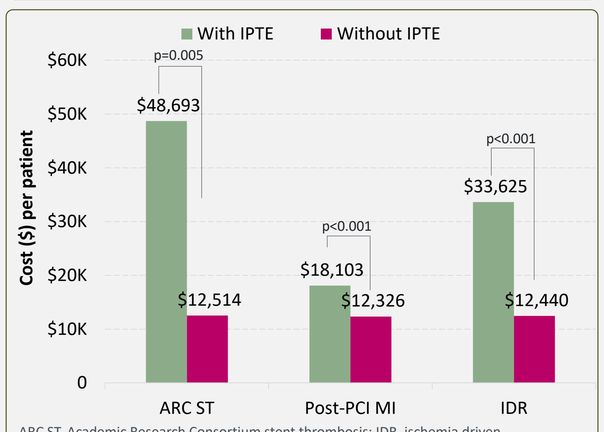
- A US retrospective, single-centre study evaluated the safety and effectiveness of cangrelor compared to GPIs as an adjunctive antiplatelet therapy during PCI (from 2005 to 2018)[6]
- Results indicated that **hospital length of stay (LOS)**, including **intensive care**, was **significantly reduced** when patients were treated with cangrelor compared to GPIs (**Figure 5**)

Table 2. Budget impact models evaluating cangrelor introduction in hospital formularies over 3 years[10-13]

Author, year	Abstract/ Full text	Country	Timeframe	Current scenario	Alternative scenario	N. of cangrelor patients in alternative scenario	Budget impact
Lizano-Diez 2021a[10]	Abstract	Belgium	2019-2021	Without cangrelor in the hospital formulary	With cangrelor in the hospital formulary, cangrelor uptake rises from 20.60% to 38.30% over 3 years	From 730 in year 1 to 1,399 in year 3	EUR (€2019) 1,100,000
Lizano-Diez 2021b[11]	Abstract	Portugal	2019-2021	Without cangrelor in the hospital formulary	With cangrelor in the hospital formulary, cangrelor uptake rises from 0.80% to 1.40% over 3 years	From 79 in year 1 to 149 in year 3	EUR (€2019) 115,000
Lizano-Diez 2021c[12]	Full-text	Spain	2019-2021	Without cangrelor in the hospital formulary and receiving oral $P2Y_{12}$ (pre-treatment) or GPIs (bail-out)	With cangrelor in the hospital formulary and receiving $P2Y_{12}$ (pre-treatment) or GPIs (bail-out)	5,769 patients over 3 years	EUR (€2019) 1,021,717
Lizano-Diez 2020[13]	Abstract	Germany	2019-2021	Without cangrelor in the hospital formulary	With cangrelor in the hospital formulary, cangrelor uptake rises from 0.40% to 0.90% over 3 years	NA	EUR (€2019) 500,000

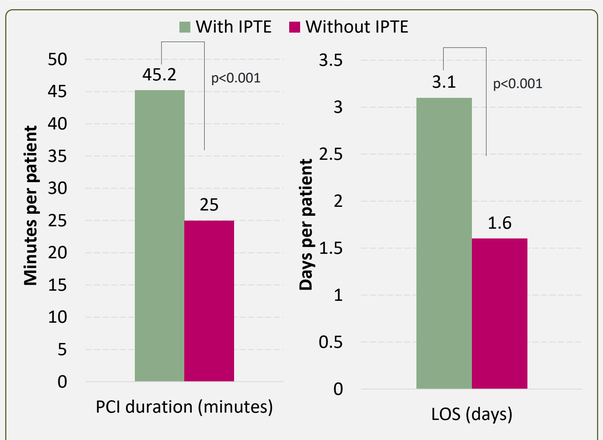
DAPT, dual antiplatelet therapy; GPI, glycoprotein IIb / IIIa inhibitor; NA, not available; PCI, percutaneous coronary intervention

Figure 2. Mean hospitalization cost associated with PCI-associated complications[14]



ARC ST, Academic Research Consortium stent thrombosis; IDR, ischemia driven revascularization; IPTE, intraprocedural thrombotic events; MI, myocardial infarction; PCI, percutaneous coronary intervention

Figure 3. Healthcare resource use associated with PCI-associated complications[14]



IPTE, intraprocedural thrombotic events LOS, length of stay; PCI, percutaneous coronary intervention

Figure 4. Hospital costs with increased use of cangrelor over 3 years[15]

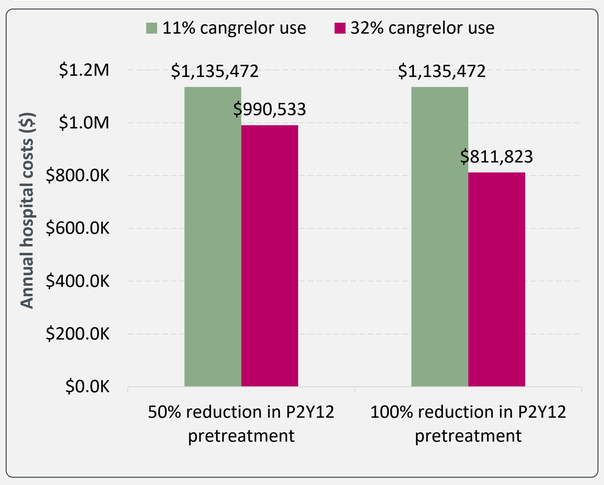
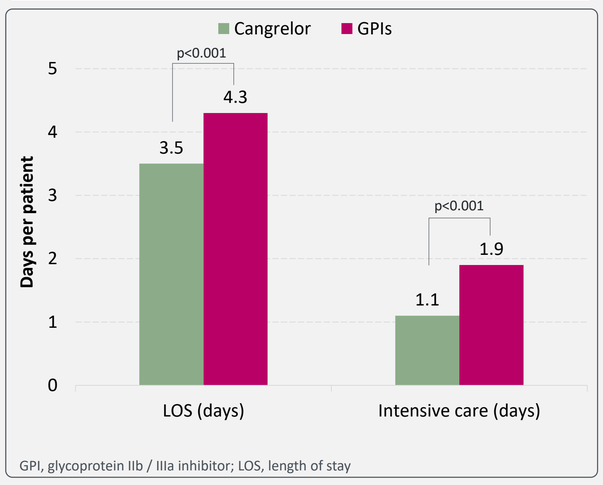


Figure 5. Hospital LOS associated with cangrelor vs GPIs[6]



GPI, glycoprotein IIb / IIIa inhibitor; LOS, length of stay

DISCUSSION

- **This SLR found evidence from the US and Europe demonstrating that cangrelor is an economically viable option and can reduce avoidable costs for healthcare systems**[6,10-15]
- **Increasing cangrelor adoption in the US for CAD patients undergoing PCI is associated with positive economic outcomes at the hospital level**, assuming that cangrelor use either avoids or reduces oral $P2Y_{12}$ use. The largest cost savings were attributable to a reduction in oral $P2Y_{12}$ washout costs and a reduction in ischemic event-related costs[15]
- **Budget impact analysis of introducing cangrelor into hospital formularies** in Belgium, Portugal, Spain and Germany **demonstrated a reasonable budget impact** of EUR 1,100,000, EUR 115,000, EUR 1,021,717, and EUR 500,000, respectively. The variability in budget impact between countries could be attributable to the estimated growth of the PCI population and cangrelor uptake in each country. For example, in Portugal, the PCI population was assumed to grow from 13,422 to 14,370 over 3 years, and cangrelor uptake increase by 0.6%. Oppositely, the PCI population in Spain was predicted to grow from 74,217 to 77,768 and cangrelor uptake increase by 27.6%. Despite these differences, all BIMs concluded that cangrelor represents an affordable option[10-13]
- Three out of seven publications were conference abstracts, specifically BIMs, that presented a low level of detail.[10,11,13] Corresponding full-text articles should be assessed in the future, once available

CONCLUSIONS

Economic evidence sourced through the present SLR demonstrates that:

- Cangrelor appears to be a **safe and affordable option** when introduced to **hospital formularies** in Europe [10-13]
- Cangrelor can **provide savings at the hospital level** by reducing costs associated with periprocedural ischemic events, decreasing the use of GPIs, and reducing delays in further surgeries in the US[15]
- Cangrelor has been reported to **reduce hospital length of stay** and **days spent in intensive care** in the US[6]

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Disclosures
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