

The economic burden of preterm labor (PTL): A systematic literature review

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Background

- PTL is a contributing factor in nearly 50% of preterm births (PTB).^{1,2}
- While the clinical consequences of PTL are known, the economic consequences associated with PTL are less clear.^{3,4}
- A synthesis of the contemporary evidence on the economic burden associated with PTL would advance understanding of unmet patient need and inform priority areas of maternal health research.

Objective

- To synthesize contemporary real-world estimates of economic burden among mothers diagnosed with PTL or infants born following a PTL diagnosis (whether born at term or preterm).

Methods

- A systematic review was conducted using MEDLINE and EMBASE.
- Observational studies reporting PTL-related costs or healthcare resource use (HCRU) from high-income countries, identified *a priori*, were of interest:
 - United States (US), Canada, Italy, France, Spain, Germany, United Kingdom (UK), Australia, and Japan.
- Articles published in English between 01/2012 and 07/2022 of interest.
- Abstracts and full-texts were reviewed for eligibility according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines⁶ and Population, Exposure/Comparator, Outcomes and Study Design (PECOS) criteria (Figure 1).
- Direct and indirect cost estimates and HCRU were tabulated and synthesized by country and, if available, by important predictors of PTB (gestational age, birth plurality, and race/ethnicity).⁷⁻⁹

Figure 1: PECOS (Population, Exposure/Comparator, Outcomes, Study Design) criteria

Population		Women diagnosed with spontaneous PTL in one or more pregnancies and infants born after PTL (either preterm [<37 weeks] or term [≥ 37 weeks])
Exposure		Standard of care or no treatment
Outcomes		Costs (direct and indirect) and HCRU for mother with PTL and their infants*
Study design		<ul style="list-style-type: none"> Retrospective or prospective observational studies Economic or burden of illness studies Mixed methods research publications on the maternal experience with PTL and PTB

*Estimates tabulated and synthesized by country and, if available, by gestational age, birth plurality, and race/ethnicity. Articles published in English between 01/2012 and 07/2022 were considered for inclusion.

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Results

- Of 662 records identified, 7 studies included (Figure 2).
 - 1 described direct costs and HCRU;¹⁰ 6 solely described HCRU;¹¹⁻¹⁶ 0 studies reported indirect costs. All studies are shown in Table 1.
 - Sample sizes ranged: 22 to 29,553.
 - Mean maternal age at PTL ranged: 24.5 to 29.3 years.
 - The 1 study¹⁰ reporting direct costs analyzed Texas Medicaid-related HCRU claims from 8,196 women with PTL. Mean total all-cause costs in the 5 months before delivery were \$14,112 per woman with PTL (2015 US\$).
- Of the 6 studies on HCRU, 3 studies^{12,14,16} reported on HCRU among infants born preterm after maternal diagnosis of PTL. These studies primarily reported on neonatal intensive care unit (NICU) stays and need for ventilation.
 - 13.3%¹² of infants who were born preterm as a result of PTL went to the NICU; mean (standard deviation [SD]) length-of-stay (LOS) was 9 (7.3) days.¹⁴
 - Compared to term births, a higher proportion of PTB following PTL are transferred to the NICU.¹²
 - >25% of infants born preterm following PTL required respiratory support and cardiac procedures directly following birth^{14,16} and had an average of 1.1 (1.76) respiratory-related hospitalizations in year one of life.¹⁶

Figure 2: PRISMA flow diagram

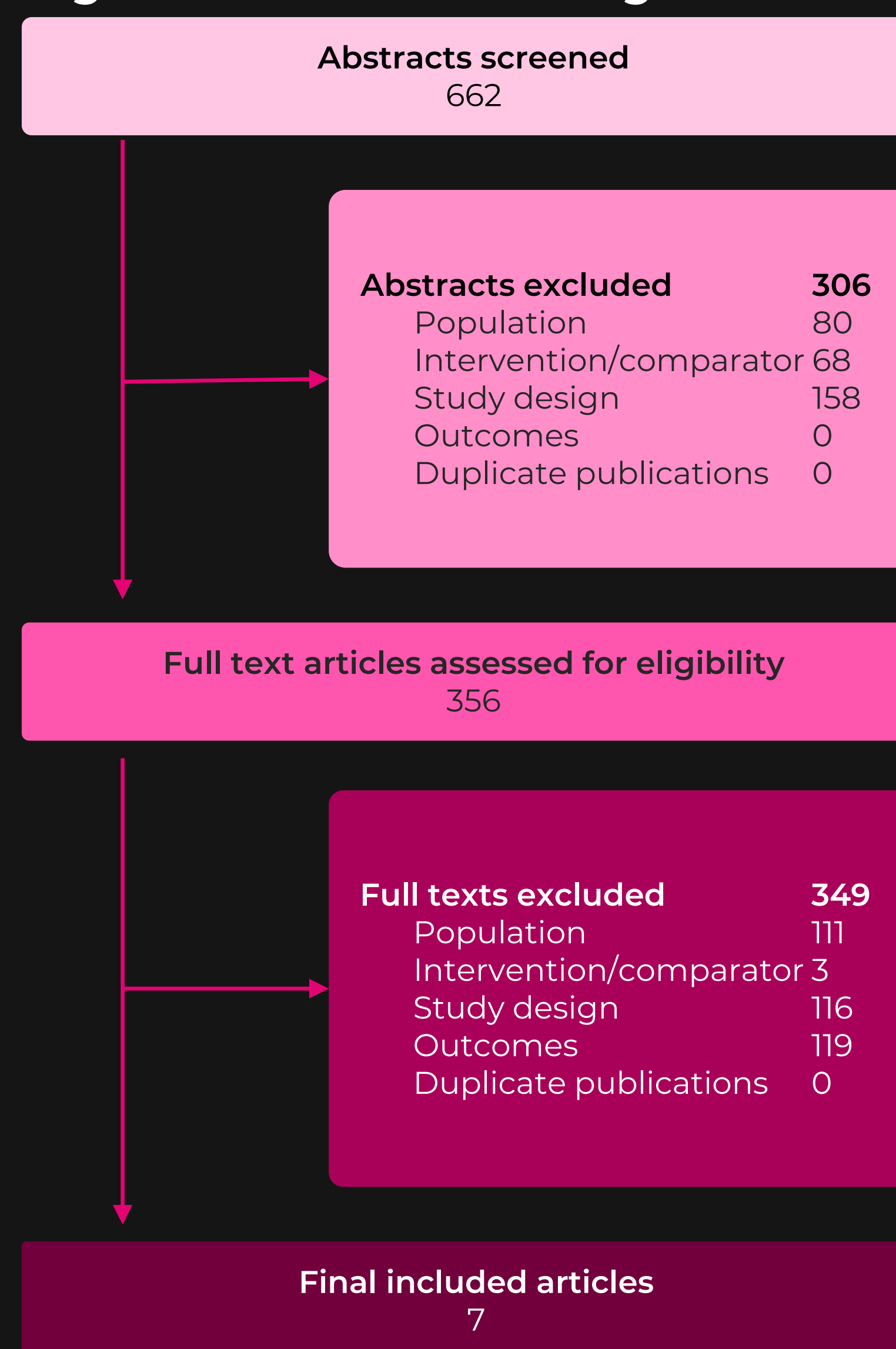


Table 1: Study characteristics and availability of economic outcomes

Study details	Study period	Study population	Population characteristics			Study exposure/comparator	Short-term economic outcomes*				
			PTL definition	PTL maternal sample size	Number of gestations		Maternal cost	Infant cost	Maternal HCRU	Infant HCRU	Key stratifications
Medicaid database study, USA ¹⁰	2012 - 2015	Women ED/ hospital encounters for PTL	PTL	29,553	Any	fFN testing vs. without testing†	✓	-	✓	-	-
Single center chart review, Canada ¹⁴	2015 - 2017	Late preterm infants (34-36 weeks)	PTB from PTL	63 sPTL infants	Any	PTL vs. PPROM vs. medically indicated PTBs†	-	-	-	✓	-
Multicenter chart review, Australia ¹¹	2001 - 2008	Women hospitalized at 20-36 WG with multiples and delivered at ≥ 24 weeks	PTL	7,023	Multiples	Cohorts defined by outcome of preterm admission (discharge, transfer, delivery)	-	-	✓	-	-
Single center chart review, UK ¹⁵	2009 - 2010	Women presenting with tPTL	tPTL	29	Any	fFN testing vs. without testing†	-	-	✓	-	-
Single center prospective cohort, France ¹³	2015 - 2016	Women with twins and PTL at 24-33 WG	PTL	40	Twins	Short vs. normal cervical length and/or positive vs. negative fFN testing†	-	-	✓	-	-
Single center chart review, France ¹⁶	2003 - 2007	Women with PPROM at 15-24 WG (matched PTL cohort)	PTL	22	Singletons	PPROM vs. spontaneous PTL†	-	-	-	✓	-
Single center prospective cohort, France ¹²	2014 - 2016	Women with singletons and PTL at 24-36 WG	tPTL	124	Singletons	Term vs. PTB†	-	-	✓	✓	(term vs. PTB)

fFN, fetal fibronectin; HCRU, healthcare resource use; PPROM, preterm premature rupture of membranes; PTB, preterm birth; PTL, preterm labor; RU, resource use; sPTB, spontaneous preterm birth; tPTL, threatened preterm labor; UK, United Kingdom; US, United States; vs. versus; WG, weeks gestation; y, years.

*No long-term economic outcomes beyond 1 year following birth were identified.

†Study reported economic outcomes, but aimed to estimate effects of specific testing on causes or outcomes associated with PTB. In that way, study populations were recruited based on specific risk factors and might not be representative of the larger PTL population.

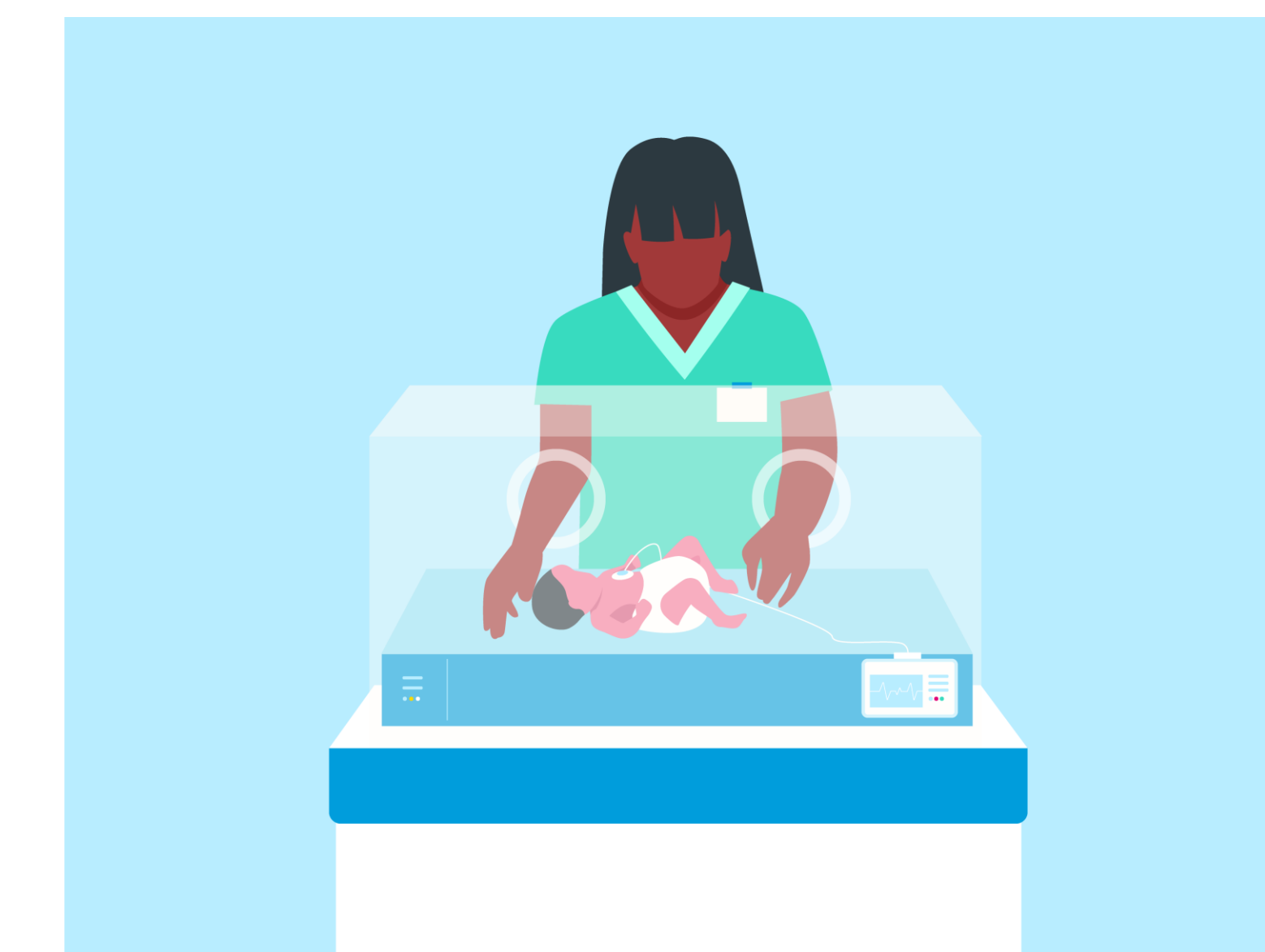
Conclusions



- Few studies have examined the economic burden of PTL and available estimates are variable.
- Contemporary estimates of short- and long-term maternal and infant costs and HCRU associated with PTL are needed. These studies need to account for key baseline risk factors and include a generalizable population with PTL.

Discussion

- The clinical management required for PTL and PTB can be extensive. For example, while only 8.7% of pregnant women overall are hospitalized during pregnancy,¹⁷ all women with PTL are hospitalized at diagnosis and average at least one re-hospitalization during their pregnancy.¹⁰
- The required level of clinical management can be costly. Women with PTL have almost three times higher costs than the average pregnant woman (\$14,112, 2015 USD¹⁰ vs. \$4,840, 2011 USD).¹⁸
- This review documented the varied and more intensive HCRU required to care for infants born preterm following PTL in their first year of life, compared to infants not born preterm.^{19,20}



- Understanding the economic burden associated with PTL is important but based on this synthesis, contemporary evidence is lacking.
- Important knowledge gaps were identified:
 - Data specific to subgroups of interest were limited.
 - Results from studies were difficult to compare due to differences in outcomes, populations, and PTL management.
 - No studies of long-term HCRU or costs were identified.
- Strengths include the use of rigorous systematic review methods; but as with all evidence syntheses, this review was limited by the validity and reporting accuracy of the included studies.
- Most studies reviewed presenting estimates of costs/HCRU did so based on highly selected populations (and thus may have limited generalizability).

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