Research Article
E-ISSN : 3048-1368
Volume 21, Issue No. 02. 2025
P-ISSN : 3048-1376

The International Journal of Medical Science and Health Research

The Association of Dual Antiplatelet Therapy (DAPT) Duration with Ischemic and Bleeding Events Following Percutaneous Coronary Intervention (PCI): A Systematic Review

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Article History :

Received date : 2025/09/14
Revised date : 2025/10/23
Accepted date : 2025/11/07
Published date : 2025/12/13

E-ISSN :
ISSN 3048-1368

P-ISSN
ISSN 3048-1376

ABSTRACT

Introduction: Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome (HIV/AIDS) profoundly increases susceptibility to opportunistic ocular infections, most notably Cytomegalovirus (CMV) retinitis. The degree of immunosuppression, particularly CD4+ T-cell counts below 50 cells/μL, is the primary risk determinant. Despite advances in antiretroviral therapy (ART), CMV retinitis remains a leading cause of vision loss in advanced AIDS, especially in resource-limited settings.

Methods: A systematic review was conducted by performing a PubMed, Google Scholar, Semantic Scholar, Springer, Wiley Online Library search across over 138 million academic papers. 40 studies meeting predefined inclusion criteria—focusing on HIV/AIDS populations, quantitative ocular outcome data, and

appropriate study designs—were selected for final analysis. Data on study design, population characteristics, ocular manifestations, risk factors, diagnostics, treatments, and outcomes were extracted and synthesized.

Results: CMV retinitis is the most common intraocular infection in AIDS, with a pooled prevalence of 14.0% in low- and middle-income countries. A majority (73.4%) of cases occur at CD4+ counts <50 cells/μL. Vision loss affects approximately one-third of patients. Treatment modalities include systemic antivirals (ganciclovir, valganciclovir, foscarnet, cidofovir), local therapies (intraocular implants, intravitreal injections), and combination regimens. Ganciclovir implants demonstrated the longest median time to disease progression (191-226 days). ART, particularly protease inhibitors, drastically reduces the incidence and recurrence of CMV retinitis. For patients achieving sustained immune reconstitution (CD4+ >75 cells/μL on ART for ≥18 months), discontinuation of CMV maintenance therapy is safe with a low relapse risk.

Discussion: The relationship between HIV/AIDS and CMV retinitis is directly mediated by immunosuppression. Disparities in prevalence across settings are explained by late HIV diagnosis and ART initiation. Optimal management balances superior local control (e.g., implants) with systemic protection against contralateral and extraocular disease. In resource-limited settings, intravitreal injections offer a viable alternative. Crucially, early screening and diagnosis, prior to significant vision loss, are paramount as visual outcomes are largely determined by timing of intervention rather than treatment choice alone.

Conclusion: CMV retinitis remains a significant cause of morbidity in advanced HIV/AIDS, tightly linked to severe immunosuppression. Successful management hinges on early diagnosis through regular ophthalmologic screening in high-risk patients (CD4+ <100 cells/μL), prompt initiation of combined local and systemic antiviral therapy, and sustained immune recovery via ART. Future efforts should focus on improving early HIV detection, expanding access to ART and antiviral therapies in resource-limited regions, and standardizing screening protocols to prevent irreversible blindness.

Keywords: HIV/AIDS; CMV Retinitis; Opportunistic Infection; Antiretroviral Therapy; Immunosuppression; Ocular Manifestations; Systematic Review.

INTRODUCTION

Background: The global pandemic of Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome (HIV/AIDS) has been characterized not only by systemic immune collapse but also by a profound predisposition to a wide spectrum of opportunistic infections and malignancies. Ocular complications represent a critical dimension of this morbidity, serving as both indicators of advanced disease and direct causes of severe disability, particularly blindness. Among these, Cytomegalovirus (CMV) retinitis emerged in the pre-antiretroviral therapy (ART) era as the most frequent and devastating intraocular infection, with a historic prevalence of 20-40% in patients with AIDS, often culminating in bilateral retinal destruction and legal blindness (Musch et al., 1997; Ford et al., 2013). The pathophysiology of this relationship is exquisitely specific: the selective depletion of CD4+ T-helper lymphocytes, the central orchestrators of cell-mediated immunity, dismantles the critical immune surveillance that maintains latent herpesviruses like CMV in check. This permits viral reactivation, viremia, and subsequent hematogenous seeding to the retina, where the virus exhibits a particular tropism for retinal vascular endothelium and neuronal tissue, leading to the characteristic necrotizing retinitis.

Research Gap and Novelty: While the fundamental link between profound immunosuppression (CD4+ count <50 cells/μL) and CMV retinitis is a well-established axiom in HIV medicine, the contemporary clinical landscape is marked by significant and unresolved complexities. First, a striking epidemiological heterogeneity persists globally; high-income nations report a drastically reduced incidence of CMV retinitis in the ART era, while low- and middle-income countries (LMICs) continue to report alarmingly high pooled prevalences (e.g., 14.0% in Asia), suggesting a disconnect between ART availability and optimal patient outcomes that is not fully explained (Ford et al., 2013). Second, the therapeutic arsenal has expanded beyond initial systemic antivirals to include sustained-release intraocular devices, various intravitreal injection protocols, and combination strategies, yet a definitive, context-specific hierarchy of efficacy—especially when balancing ocular control against systemic protection and quality of life—remains

debated. Third, the successful immune reconstitution achieved with modern ART has introduced new clinical paradigms, such as the safe discontinuation of long-term anti-CMV maintenance therapy and the emergence of immune recovery uveitis (IRU), areas where longitudinal management protocols are still evolving. Finally, the critical determinant of visual prognosis—the timing of diagnosis relative to irreversible retinal damage—is often underemphasized in treatment-focused reviews. This systematic review aims to address these gaps by providing a comprehensive, nuanced synthesis that connects foundational pathophysiological principles with modern epidemiological data, critically appraises the full spectrum of therapeutic options within their socio-economic contexts, and highlights the paramount importance of early detection as the most effective strategy to prevent blindness.

Research Objective: The primary objective of this systematic review is to perform a detailed and critical synthesis of the evidence elucidating the relationship between HIV/AIDS and ocular opportunistic infections, with a concentrated focus on CMV retinitis. Specific aims include: 1) To quantify the prevalence and incidence of CMV retinitis across different geographical and resource settings in the ART era; 2) To precisely delineate the immunological risk factors, with particular emphasis on CD4+ T-cell count thresholds and the role of HIV viral load; 3) To evaluate and compare the diagnostic accuracy and utility of various ophthalmological and laboratory methods; 4) To conduct a comparative analysis of the efficacy, safety, and practical applicability of all major treatment modalities (systemic, local, and combination therapies); and 5) To assess the transformative impact of ART on the natural history, management strategies, and long-term clinical outcomes of CMV retinitis.

Research Benefits: The insights generated from this synthesis hold significant value for multiple stakeholders. For clinicians specializing in infectious diseases, ophthalmology, and internal medicine, it provides an evidence-based framework to guide screening protocols, therapeutic decision-making (including induction, maintenance, and discontinuation phases), and management of complications like retinal detachment and IRU. For public health policymakers and program

managers, particularly in high-burden LMICs, it underscores the persistent burden of preventable blindness linked to late HIV diagnosis, thereby advocating for strengthened HIV testing campaigns and integrated ophthalmologic screening within HIV care programs. For researchers, it identifies key knowledge gaps, such as the optimal frequency of screening and the cost-effectiveness of different treatment cascades in resource-poor settings, directing future investigative efforts.

Hypothesis: This review is guided by the following hypotheses: 1) The risk of incident CMV retinitis is non-linear and increases precipitously once the CD4+ T-cell count falls below a threshold of 50 cells/μL, making this the primary biomarker for targeted screening. 2) While ART is the most effective intervention to reduce the population-level incidence of CMV retinitis, its benefit is contingent upon early initiation prior to severe immunosuppression; in patients presenting with advanced AIDS, aggressive ocular screening and prompt anti-CMV therapy are irreplaceable. 3) For established CMV retinitis, combined therapeutic strategies (employing both a local modality for rapid retinal control and a systemic modality for contralateral and systemic protection) will yield superior long-term ocular and survival outcomes compared to any monotherapy approach. 4) Visual acuity outcomes are determined more by the stage of retinal disease at the time of treatment initiation than by the specific choice of antiviral drug, making early diagnosis the single most important modifiable prognostic factor.

METHODS

Protocol

The study strictly adhered to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020 guidelines to ensure methodological rigor and accuracy. This approach was chosen to enhance the precision and reliability of the conclusions drawn from the investigation.

Criteria for Eligibility

This systematic review aims to evaluate the association of dual antiplatelet therapy (DAPT)

duration with ischemic and bleeding events following percutaneous coronary intervention (PCI).

Screening

We screened in sources based on their abstracts that met these criteria:

- **Adult PCI Population**: Does the study include adult patients (≥18 years) who underwent percutaneous coronary intervention (PCI)?
- **DAPT with Defined Duration**: Does the study examine dual antiplatelet therapy (DAPT) with clearly defined duration periods?
- **Comparative DAPT Duration**: Does the study compare at least two different DAPT duration strategies?
- **Clinical Outcomes Reported**: Does the study report ischemic outcomes (myocardial infarction, stroke, stent thrombosis, cardiovascular death) and/or bleeding outcomes?
- **Study Design Quality**: Is the study a randomized controlled trial, observational study (cohort, case-control), systematic review, or meta-analysis?
- **Adequate Follow-up**: Does the study have a minimum follow-up period of 6 months or longer?
- **DAPT Focus**: Does the study focus on dual antiplatelet therapy (DAPT) rather than solely on single antiplatelet therapy or triple therapy without DAPT comparison?
- **Publication Type**: Is the study a full research article rather than a case report, case series, editorial, or conference abstract?
- **Predetermined Duration**: Was the DAPT duration strategy predetermined rather than determined solely by bleeding or ischemic events that occurred during follow-up?

We considered all screening questions together and made a holistic judgement about whether to screen in each paper.

Data extraction

- **Study Design**:

  Extract study design details including:

  - Study type (RCT, observational cohort, etc.)
  - Sample size and number randomized to each group
  - Follow-up duration
  - Geographic location/setting
  - Study period (enrollment dates)

- **DAPT Regimens**:

  Extract all DAPT duration comparisons including:

  - Specific durations compared (e.g., 3 months vs 12 months vs 24 months)
  - Antiplatelet agents used (aspirin dose, P2Y12 inhibitor type and dose)
  - Timing of randomization (at PCI, at 30 days, at 1 year, etc.)
  - Any bridging or transition protocols between arms

- **Patient Population**:

  Extract population characteristics including:

  - Mean age and age range
  - Percentage male
  - Clinical presentation (stable CAD, ACS, STEMI, NSTEMI percentages)
  - Key comorbidities (diabetes, hypertension, prior MI, prior bleeding)
  - PCI details (stent type, vessel treated, complexity)
  - Major exclusion criteria that might affect generalizability

- **Ischemic Outcomes**:

Extract all ischemic outcome data including:

- Specific outcomes measured (death, cardiovascular death, MI, stent thrombosis, stroke, MACE)
- Outcome definitions used (e.g., ARC criteria for stent thrombosis)
- Event rates for each DAPT duration group
- Risk ratios, hazard ratios, or odds ratios with 95% confidence intervals
- Time points assessed (30 days, 1 year, 2 years, etc.)

- **Bleeding Outcomes**:

  Extract all bleeding outcome data including:

  - Bleeding classification system used (BARC, TIMI, GUSTO, etc.)
  - Specific bleeding categories reported (major, minor, any bleeding)
  - Event rates for each DAPT duration group
  - Risk ratios, hazard ratios, or odds ratios with 95% confidence intervals
  - Fatal bleeding and transfusion requirements if reported

- **Effect Modifiers**:

  Extract any subgroup analyses or factors that modified the DAPT duration effects including:

  - Age categories (elderly vs younger)
  - Bleeding risk stratification (high vs low bleeding risk)
  - Clinical presentation subgroups (ACS vs stable CAD)
  - Stent type effects (bare metal vs drug-eluting)
  - Use of risk prediction tools (DAPT score, CRUSADE score, etc.)
  - Geographic or temporal variations in effects

- **Net Clinical Benefit**:

Extract composite or net clinical outcomes including:

- Net adverse clinical events (NACE) definitions and results
- Composite endpoints combining ischemic and bleeding outcomes
- Authors' conclusions about optimal DAPT duration
- Number needed to treat/harm calculations if provided
- Cost-effectiveness or quality-of-life considerations if mentioned

Search Strategy

The keywords used for this research based PICO :

Element	Keyword 1	Keyword 2	Keyword 3	Keyword 4
Population (P)	Percutaneous Coronary Intervention (PCI)	Coronary Stenting	Post-PCI Patients	Patients with Drug-Eluting Stents
Intervention (I) / Exposure (E)	Prolonged DAPT	Extended Dual Antiplatelet Therapy	Long-term DAPT (>12 months)	Standard Duration DAPT (12 months)
Comparison (C)	Shortened DAPT	Abbreviated Dual Antiplatelet Therapy	Short-term DAPT (1-3 months)	P2Y12 Inhibitor Monotherapy (after DAPT)
Outcome (O)	Ischemic Events (MI, Stent Thrombosis)	Bleeding Events (Major Bleeding)	Net Clinical Benefit (NACE)	Mortality (All-cause, Cardiovascular)

The Boolean MeSH keywords inputted on databases for this research are: *(("Percutaneous Coronary Intervention" OR "Coronary Stenting" OR "Post-PCI Patients" OR "Drug-Eluting Stent Implantation")) AND (("Extended Dual Antiplatelet Therapy" OR "Prolonged DAPT" OR "Long-term DAPT" OR "Standard 12-month DAPT")) AND (("Shortened Dual Antiplatelet Therapy" OR "Abbreviated DAPT" OR "Short-term DAPT" OR "P2Y12 Inhibitor Monotherapy")) AND (("Ischemic Events" OR "Myocardial Infarction" OR "Stent Thrombosis") AND ("Bleeding Events" OR "Major Bleeding") OR ("Net Clinical Benefit" OR "Net Adverse Clinical Events" OR "All-cause Mortality"))*

Table 1. Article Search Strategy

Database	Keywords	Hits
Pubmed	*(("Percutaneous Coronary Intervention" OR "Coronary Stenting" OR "Post-PCI Patients" OR "Drug-Eluting Stent Implantation")) AND (("Extended Dual Antiplatelet Therapy" OR "Prolonged DAPT" OR "Long-term DAPT" OR "Standard 12-month DAPT")) AND (("Shortened Dual Antiplatelet Therapy" OR "Abbreviated DAPT" OR "Short-term DAPT" OR "P2Y12 Inhibitor Monotherapy")) AND (("Ischemic Events" OR "Myocardial Infarction" OR "Stent Thrombosis") AND ("Bleeding Events" OR "Major Bleeding") OR ("Net Clinical Benefit" OR "Net Adverse Clinical Events" OR "All-cause Mortality"))*	3
Semantic Scholar	*(("Percutaneous Coronary Intervention" OR "Coronary Stenting" OR "Post-PCI Patients" OR "Drug-Eluting Stent Implantation")) AND (("Extended Dual Antiplatelet Therapy" OR "Prolonged DAPT" OR "Long-term DAPT" OR "Standard 12-month DAPT")) AND (("Shortened Dual Antiplatelet Therapy" OR "Abbreviated DAPT" OR "Short-term DAPT" OR "P2Y12 Inhibitor Monotherapy")) AND (("Ischemic Events" OR "Myocardial Infarction" OR "Stent Thrombosis") AND ("Bleeding Events" OR "Major Bleeding") OR ("Net Clinical Benefit" OR "Net Adverse Clinical Events" OR "All-cause Mortality"))*	14
Springer	*(("Percutaneous Coronary Intervention" OR "Coronary Stenting" OR "Post-PCI Patients" OR "Drug-Eluting Stent Implantation")) AND (("Extended Dual Antiplatelet Therapy" OR "Prolonged DAPT" OR "Long-term DAPT" OR "Standard 12-month DAPT")) AND (("Shortened Dual Antiplatelet Therapy" OR "Abbreviated DAPT" OR "Short-term DAPT" OR "P2Y12 Inhibitor Monotherapy")) AND (("Ischemic Events" OR "Myocardial Infarction" OR "Stent Thrombosis") AND ("Bleeding Events" OR "Major Bleeding") OR ("Net Clinical Benefit" OR "Net Adverse Clinical Events" OR "All-cause Mortality"))*	85
Google Scholar	*(("Percutaneous Coronary Intervention" OR "Coronary Stenting" OR "Post-PCI Patients" OR "Drug-Eluting Stent Implantation")) AND (("Extended Dual Antiplatelet Therapy" OR "Prolonged DAPT" OR "Long-term DAPT" OR "Standard 12-month DAPT")) AND (("Shortened Dual Antiplatelet Therapy" OR "Abbreviated DAPT" OR "Short-term DAPT" OR "P2Y12 Inhibitor Monotherapy")) AND (("Ischemic Events" OR "Myocardial Infarction" OR "Stent Thrombosis") AND ("Bleeding Events" OR "Major Bleeding") OR ("Net Clinical Benefit" OR "Net Adverse Clinical Events" OR "All-cause Mortality"))*	2,510
Wiley Online Library	*(("Percutaneous Coronary Intervention" OR "Coronary Stenting" OR "Post-PCI Patients" OR "Drug-Eluting Stent Implantation")) AND (("Extended Dual Antiplatelet Therapy" OR "Prolonged DAPT" OR "Long-term DAPT" OR "Standard 12-month DAPT")) AND (("Shortened Dual Antiplatelet Therapy" OR "Abbreviated DAPT" OR "Short-term DAPT" OR "P2Y12 Inhibitor Monotherapy")) AND (("Ischemic Events" OR "Myocardial Infarction" OR "Stent Thrombosis") AND ("Bleeding Events" OR "Major Bleeding") OR ("Net Clinical Benefit" OR "Net Adverse Clinical Events" OR "All-cause Mortality"))*	46

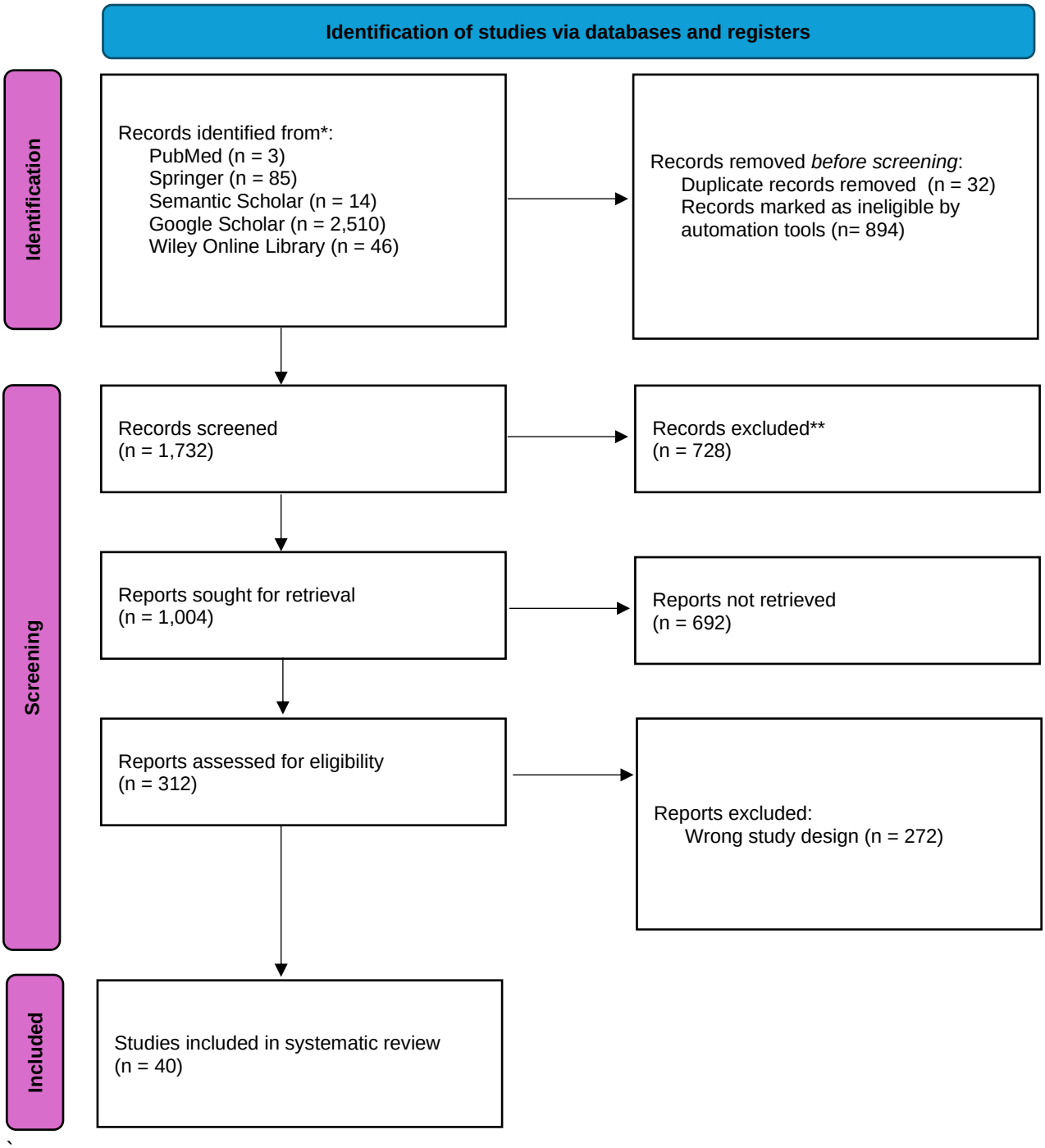

Figure 1. Article search flowchart

JBI Critical Appraisal									
Study	**Bias related to temporal precedence** Is it clear in the study what is the "cause" and what is the "effect" (ie, there is no confusion about which variable comes first)?	**Bias related to selection and allocation** Was there a control group?	**Bias related to confounding factors** Were participants included in any comparisons similar?	**Bias related to administration of intervention/exposure** Were the participants included in any comparisons receiving similar treatment/ care, other than the exposure or intervention of interest?	**Were there multiple measurements of the outcome, both pre and post the intervention/exposure?**	**Were the outcomes of participants included in any comparisons measured in the same way?**	**Were outcomes measured in a reliable way?**	**Bias related to participant retention** Was follow-up complete and, if not, were differences between groups in terms of their follow-up adequately described and analyzed?	**Statistical conclusion validity** Was appropriate statistical analysis used?
J. Collet et al., 2014	✓	✓	✓	✗	✓	✗	✓	✓	✓
Elvin Kedhi et al., 2018	✓	✓	✓	✗	✓	✗	✓	✓	✓
Hirotoshi Watanabe et al., 2022	✓	✓	✓	✗	✓	✗	✓	✓	✓

E. Bates et al., 2015	✓	✓	✓	✗	✓	✗	✓	✓	✓
F. Spencer et al., 2015	✓	✓	✓	✗	✓	✗	✓	✓	✓
C. Kwok et al., 2014	✓	✓	✓	✗	✓	✗	✓	✓	✓
Ji-Yong Jang et al., 2020	✓	✓	✓	✗	✓	✗	✓	✓	✓
R. Yeh et al., 2016	✓	✓	✓	✗	✓	✗	✓	✓	✓
Hirotoshi Watanabe et al., 2019	✓	✓	✓	✗	✓	✗	✓	✓	✓
D. Giacoppo et al., 2020	✓	✓	✓	✗	✓	✗	✓	✓	✓
H. Soleimani et al., 2025	✓	✓	✓	✗	✓	✗	✓	✓	✓
Emilie Belley-Ct et al., 2019	✓	✓	✓	✗	✓	✗	✓	✓	✓
R. Piccolo et al., 2017	✓	✓	✓	✗	✓	✗	✓	✓	✓
D. Mukherjee et al.,	✓	✓	✓	✗	✓	✗	✓	✓	✓

2015									
P.E.P. Carvalho et al., 2024	✓	✓	✓	✗	✓	✗	✓	✓	✓
Jesse Elliott et al., 2023	✓	✓	✓	✗	✓	✗	✓	✓	✓
B. Kheiri et al., 2020	✓	✓	✓	✗	✓	✗	✓	✓	✓
O. de Filippo et al., 2024	✓	✓	✓	✗	✓	✗	✓	✓	✓
A. Franzone et al., 2016	✓	✓	✓	✗	✓	✗	✓	✓	✓
N. Fitterman et al., 2017	✓	✓	✓	✗	✓	✗	✓	✓	✓
Wenjiao Zhang et al., 2020	✓	✓	✓	✗	✓	✗	✓	✓	✓
H. Y. Wang et al., 2020	✓	✓	✓	✗	✓	✗	✓	✓	✓
Peng-Yu Zhong et al., 2021	✓	✓	✓	✗	✓	✗	✓	✓	✓
Nathan Kong et al., 2020	✓	✓	✓	✗	✓	✗	✓	✓	✓
Sung-Jin Hong et al., 2016	✓	✓	✓	✗	✓	✗	✓	✓	✓

Seung-Yul Lee et al., 2018	✓	✓	✓	✗	✓	✗	✓	✓	✓
E. Secemsky et al., 2017	✓	✓	✓	✗	✓	✗	✓	✓	✓
Dual Antiplatelet Therapy Study Investigators et al., 2017	✓	✓	✓	✗	✓	✗	✓	✓	✓
In Tae Jin et al., 2025	✓	✓	✓	✗	✓	✗	✓	✓	✓
A. Garg et al., 2020	✓	✓	✓	✗	✓	✗	✓	✓	✓
R. Piccolo et al., 2017a	✓	✓	✓	✗	✓	✗	✓	✓	✓
A. Landi et al., 2023	✓	✓	✓	✗	✓	✗	✓	✓	✓
A. Apostolos et al., 2024	✓	✓	✓	✗	✓	✗	✓	✓	✓
Ji-Yong Jang et al., 2018	✓	✓	✓	✗	✓	✗	✓	✓	✓
S. Parfrey et al., 2022	✓	✓	✓	✗	✓	✗	✓	✓	✓

S. Furlan et al., 2019	✓	✓	✓	✗	✓	✗	✓	✓	✓
D. Mukherjee et al., 2015a	✓	✓	✓	✗	✓	✗	✓	✓	✓
W. Ullah et al., 2022	✓	✓	✓	✗	✓	✗	✓	✓	✓
Jiaojiao Hui et al., 2022	✓	✓	✓	✗	✓	✗	✓	✓	✓
A. Gallus et al., 2019	✓	✓	✓	✗	✓	✗	✓	✓	✓

RESULTS

Characteristics of Included Studies

This systematic review includes 40 sources examining the association between DAPT duration and clinical outcomes following PCI. The evidence base comprises randomized controlled trials (RCTs), systematic reviews with meta-analyses, pooled analyses, and one observational cohort study.

Study	Study Type	Sample Size	DAPT Comparison	Geographic Setting
J. Collet et al., 2014	RCT	1,259	DAPT continuation beyond 1 year vs interruption	France (38 centers)
Elvin Kedhi et al., 2018	Non-inferiority	870 randomized	6 months vs 12 months	Netherlands, Norway, Poland,

Study	Study Type	Sample Size	DAPT Comparison	Geographic Setting
	RCT			Switzerland
Hirotoshi Watanabe et al., 2022	Open-label RCT	4,169	1-2 months vs 12 months	Japan (96 centers)
E. Bates et al., 2015	Systematic review	31,666	Various: 3-6 vs 12 vs >12 months	Not specified
F. Spencer et al., 2015	RCT (DAPT Study)	9,961	12 months vs 30 months	11 countries (452 sites)
C. Kwok et al., 2014	Meta-analysis	8,231	3 vs 12, 6 vs 12, 12 vs 24 months	Korea, Italy
Ji-Yong Jang et al., 2020	Pooled analysis	5,131	≤6 months vs ≥12 months	Not specified
R. Yeh et al., 2016	RCT	11,648	12 vs 30 months with DAPT score	11 countries
Hirotoshi Watanabe et al., 2019	Open-label RCT	3,045	1 month vs 12 months	Japan (90 hospitals)
D. Giacoppo et al., 2020	Meta-analysis	32,145	≤3 months + P2Y12 vs 12 months	Not specified
H. Soleimani et	Meta-analysis	54,233	≤3 months vs	Not specified

Study	Study Type	Sample Size	DAPT Comparison	Geographic Setting
al., 2025			≥12 months	
Emilie Belley-Ct et al., 2019	Network meta-analysis	46,864	6 vs 12 vs >12 months	Not specified
R. Piccolo et al., 2017	RCT (PRODIGY)	1,970	6 months vs 24 months	Not specified
D. Mukherjee et al., 2015	Meta-analysis	29,531	3-18 vs 12-42 months	Not specified
P.E.P. Carvalho et al., 2024	Network meta-analysis	35,326	1, 3, 6 vs 12 months	Not specified
Jesse Elliott et al., 2023	Meta-analysis	25,982	>12 months vs 6-12 months	Multinational
B. Kheiri et al., 2020	Meta-analysis	35,857	1-3 months vs standard	Not specified
O. de Filippo et al., 2024	Network meta-analysis	75,064	De-escalation strategies	Not specified
A. Franzone et al., 2016	RCT subanalysis	1,970	24 months vs ≤6 months	Tertiary care hospitals
N. Fitterman et al., 2017	Systematic review	11,473	3-6 vs 12-24 months	Not specified
Wenjiao Zhang et al., 2020	Meta-analysis	38,479	≤3 months vs 12 months	Not specified
H. Y. Wang et al., 2020	Observational cohort	7,521	>1 year vs ≤1 year	China

Study	Study Type	Sample Size	DAPT Comparison	Geographic Setting
Peng-Yu Zhong et al., 2021	Meta-analysis	16,492	1-3 months vs ≥12 months	Korea, Brazil, Europe, Asia, Japan
Nathan Kong et al., 2020	Meta-analysis	31,837	≤3 vs 6 vs 12 vs >12 months	Not specified
Sung-Jin Hong et al., 2016	RCT (IVUS-XPL)	1,400	6 months vs 12 months	Korea (20 centers)
Seung-Yul Lee et al., 2018	IPD meta-analysis	11,471	≤6 months vs 12 months	Not specified
E. Secemsky et al., 2017	Secondary RCT analysis	11,648	12 vs 30 months	11 countries
Dual Antiplatelet Therapy Study Investigators et al., 2017	Secondary RCT analysis	11,648	12 vs 30 months	11 countries
In Tae Jin et al., 2025	Pooled analysis	10,487	1-6 months vs 12 months	Korea
A. Garg et al., 2020	Network meta-analysis	57,942	≤6 months vs ≥12 months	Not specified
R. Piccolo et al., 2017a	RCT subanalysis	1,970	24 months vs 6 months	Not specified
A. Landi et al., 2023	RCT subanalysis	4,579	Abbreviated vs standard DAPT	30 countries (140 sites)

Study	Study Type	Sample Size	DAPT Comparison	Geographic Setting
A. Apostolos et al., 2024	Meta-analysis	46,476	1-3 months vs longer	Not specified
Ji-Yong Jang et al., 2018	Pooled analysis	2,216	≤6 months vs ≥12 months	Multicenter
S. Parfrey et al., 2022	Meta-analysis	26,576	1 month vs routine duration	Japan, South Korea
S. Furlan et al., 2019	Non-inferiority RCT	870	6 months vs 12 months	Netherlands, Norway, Poland, Switzerland
D. Mukherjee et al., 2015a	Non-inferiority RCT	1,399	6 months vs 12 months	Italy, Spain, Netherlands
W. Ullah et al., 2022	Network meta-analysis	81,208	Multiple de-escalation strategies	Not specified
Jiaojiao Hui et al., 2022	Meta-analysis	45,661	≤3 months vs 6-12 months	Not specified
A. Gallus et al., 2019	RCT	2,993	3 months + P2Y12 vs 12 months DAPT	Republic of Korea

The included studies demonstrate substantial variation in DAPT duration comparisons, ranging from very short-term (1 month) to extended duration (>30 months). The majority of RCTs utilized second-generation drug-eluting stents . Patient populations varied considerably,

with mean ages ranging from 60 to 76 years and male predominance (63-82%) . Clinical presentations included both stable coronary artery disease and acute coronary syndromes, with ACS prevalence ranging from 41% to 100% across studies .

Effects on Ischemic Outcomes

All-Cause Mortality

Source	Comparison	Event Rates	Effect Estimate (95% CI)
E. Bates et al., 2015	Shorter vs Longer	1.48% vs 1.80%	RRR 18% (2-31)
D. Mukherjee et al., 2015	Longer vs Shorter	2.0% vs 1.7%	RRI 19% (4-36)
H. Soleimani et al., 2025	Abbreviated vs Conventional	Not reported	RR 0.90 (0.82-0.98)
Wenjiao Zhang et al., 2020	Short vs Standard	Not reported	RR 0.92 (0.80-1.06)
S. Parfrey et al., 2022	1-month vs Routine	Not reported	RR 0.84 (0.69-1.03)
Jiaojiao Hui et al., 2022	≤3 months vs 6-12 months	Not reported	HR 0.88 (0.78-0.99)
Jesse Elliott et al., 2023	Extended vs Standard	Not reported	RR 1.07 (0.80-1.42)

The relationship between DAPT duration and all-cause mortality demonstrates directional inconsistency across studies. Several meta-analyses found that shorter DAPT was associated with reduced mortality , while others showed no significant difference or suggested potential harm with shorter duration . The DAPT Study found extended therapy

was associated with a 36% relative increase in all-cause death (NNH 188) . This mortality signal with extended DAPT was driven primarily by noncardiac mortality (RRR 33% for shorter vs longer DAPT) , with no significant difference in cardiovascular mortality across most analyses .

Myocardial Infarction and Stent Thrombosis

Source	Comparison	MI Effect Estimate (95% CI)	Stent Thrombosis Effect Estimate (95% CI)
E. Bates et al., 2015	Shorter vs Longer	RRI 34% (7-68)	RRI 79% (6-202)
F. Spencer et al., 2015	Extended vs Placebo+ASA	RRR 52% (39-63), NNT 47	RRR 71% (52-83), NNT 101
D. Mukherjee et al., 2015	Longer vs Shorter	RRR 27% (8-42)	Not reported
Emilie Belley-Ct et al., 2019	Long vs Short-term	OR 0.63 (0.46-0.86)	OR 0.57 (0.34-0.95)
Jesse Elliott et al., 2023	Extended vs Standard	RR 0.58 (0.48-0.70)	RR 0.38 (0.21-0.67)
D. Giacoppo et al., 2020	Short + P2Y12 vs 12 months	HR 1.05 (0.89-1.23)	HR 1.19 (0.86-1.65)
Wenjiao Zhang et al., 2020	Short vs Standard	RR 1.05 (0.94-1.19)	RR 1.05 (0.80-1.36)
S. Parfrey et al., 2022	1-month vs Routine	RR 1.12 (0.91-1.39)	RR 1.49 (0.92-2.41)

Extended DAPT consistently reduces myocardial infarction and stent thrombosis compared to shorter durations . The DAPT Study demonstrated that extending therapy to 30 months reduced stent thrombosis by 71% (NNT 101) and MI by 52% (NNT 47) . However, when comparing short-term DAPT (≤3 months) followed by P2Y12 inhibitor monotherapy versus 12-month DAPT, no significant differences in MI (HR 1.05) or stent thrombosis (HR 1.19) were observed . This suggests that the type of single antiplatelet therapy following DAPT discontinuation may influence ischemic outcomes.

The STOPDAPT-2 ACS trial specifically examining patients with acute coronary syndrome found that 1-2 month DAPT failed to demonstrate noninferiority for ischemic outcomes, with a numerical increase in cardiovascular events (2.8% vs 1.9%; HR 1.50, 95% CI 0.99-2.26) . In contrast, the STOPDAPT-2 trial in a general PCI population found 1-month DAPT noninferior and superior to 12-month DAPT for the composite endpoint .

Stroke

Stroke outcomes were generally comparable across DAPT durations. Meta-analyses reported no significant differences between shorter and longer DAPT regimens (RR 1.02-1.08) . The DAPT Study showed a non-significant 20% reduction in stroke with extended therapy .

Effects on Bleeding Outcomes

Source	Classification	Comparison	Major Bleeding Effect (95% CI)	Any Bleeding Effect (95% CI)
J. Collet et al., 2014	STEEPLE	Interruption vs Continuation	HR 0.15 (0.02-1.20)	HR 0.26 (0.07-0.91)
E. Bates et al., 2015	Not specified	Shorter vs Longer	RRR 42% (28-53), NNT 172	RRR 44% (34-52), NNT 78

Source	Classification	Comparison	Major Bleeding Effect (95% CI)	Any Bleeding Effect (95% CI)
F. Spencer et al., 2015	GUSTO	Extended vs Placebo+ASA	RRI 60% (21-114), NNH 104	Not reported
C. Kwok et al., 2014	Not specified	Shorter vs Longer	RR 0.48 (0.25-0.93)	RR 0.30 (0.16-0.54)
D. Giacoppo et al., 2020	Not specified	Short + P2Y12 vs 12 months	HR 0.63 (0.45-0.86)	Not reported
H. Soleimani et al., 2025	BARC 3/5	Abbreviated vs Conventional	RR 0.77 (0.60-0.97)	Not reported
Emilie Belley-Ct et al., 2019	Not specified	Long vs Short-term	OR 1.78 (1.27-2.49)	OR 2.13 (1.46-3.10)
P.E.P. Carvalho et al., 2024	Not specified	1-month + P2Y12 vs 12 months	RR 0.47 (0.26-0.74)	Not reported
B. Kheiri et al., 2020	Not specified	Short vs Standard	HR 0.67 (0.47-0.95)	HR 0.63 (0.44-0.90)
Wenjiao Zhang et al., 2020	Not specified	Short vs Standard	RR 0.67 (0.48-0.94)	RR 0.63 (0.48-0.82)
S. Parfrey et al., 2022	BARC/STEEPLE	1-month vs Routine	RR 0.70 (0.51-0.95)	Not reported
W. Ullah et al., 2022	Not specified	3-month + P2Y12 vs 12	RR 0.62 (0.45-0.84)	Not reported

Source	Classification	Comparison	Major Bleeding Effect (95% CI)	Any Bleeding Effect (95% CI)
		months		

Shorter DAPT duration consistently and significantly reduces bleeding events across all studies. Major bleeding was reduced by 23-53% with shorter DAPT regimens . The most pronounced bleeding reduction was observed with 1-month DAPT followed by P2Y12 inhibitor monotherapy, which reduced major bleeding by 53% (RR 0.47) . The absolute effect of longer DAPT was estimated at 6 additional major bleeding events per 1000 patients treated per year .

Extended DAPT (>12 months) was associated with a 60-78% relative increase in bleeding compared to shorter durations . Network meta-analysis confirmed that high-potency DAPT for 12 months significantly increased major bleeding risk (RR 1.55, 95% CI 1.16-2.06) .

The clinical significance of bleeding events was underscored by analysis from the DAPT Study showing an annualized mortality rate of 21.5 per 100 person-years following bleeding events .

Net Clinical Benefit and Composite Outcomes

Source	NACE Definition	Shorter DAPT	Longer DAPT	Effect Estimate
Elvin Kedhi et al., 2018	Death, MI, revascularization, stroke, major bleeding	4.8%	6.6%	HR 0.73 (0.41-1.27)

Source	NACE Definition	Shorter DAPT	Longer DAPT	Effect Estimate
Hirotoshi Watanabe et al., 2019	CV death, MI, stroke, ST, bleeding	2.36%	3.70%	HR 0.64 (0.42-0.98)
Ji-Yong Jang et al., 2020	Net clinical outcomes	1.3%	1.3%	No difference (p=0.89)
B. Kheiri et al., 2020	MACE + major bleeding	Not reported	Not reported	HR 0.93 (0.85-1.02)
Peng-Yu Zhong et al., 2021	Death, MI, stroke, major bleeding	5.0%	5.7%	RR 0.88 (0.77-1.01)
A. Apostolos et al., 2024	NACE	Not reported	Not reported	RR 0.91 (0.85-0.99)
Jiaojiao Hui et al., 2022	MACE	Not reported	Not reported	HR 0.89 (0.82-0.97)

When ischemic and bleeding events are combined into net clinical benefit analyses, shorter DAPT durations generally demonstrate favorable or equivalent outcomes compared to longer durations . The STOPDAPT-2 trial found 1-month DAPT superior to 12-month DAPT for the composite primary endpoint (HR 0.64) . Multiple meta-analyses confirmed that abbreviated DAPT (≤3 months) significantly reduced net adverse clinical events while maintaining comparable ischemic protection .

Effect Modifiers and Subgroup Analyses

Age

Age significantly modifies the effect of DAPT duration. Individual participant data meta-analysis demonstrated a significant interaction between age and DAPT duration (p for interaction = 0.0384) . In patients younger than 65 years, short-term DAPT was associated with higher ischemic events (HR 1.67, 95% CI 1.14-2.44) . In contrast, elderly patients (≥65 years) showed no significant difference in ischemic outcomes between short and long-term DAPT (HR 0.84, 95% CI 0.60-1.16) , while experiencing significant reduction in major bleeding with shorter DAPT (HR 0.46, 95% CI 0.24-0.88) .

Prolonged DAPT in elderly patients (≥75 years) significantly increased bleeding risk (HR 1.90, 95% CI 1.06-3.38) without affording significant ischemic protection . Pooled Korean data showed standard DAPT was associated with higher major bleeding risk in patients ≥75 years (HR 2.34, 95% CI 1.17-4.68) .

Clinical Presentation (ACS vs Stable CAD)

Clinical presentation at index PCI modifies optimal DAPT duration. Patients with prior MI or ACS at presentation may derive greater benefit from extended DAPT . Extended DAPT in patients with prior MI significantly reduced MI (RR 0.48, 95% CI 0.36-0.64) and stent thrombosis (RR 0.29, 95% CI 0.16-0.52) . However, the all-cause mortality risk was significantly increased among patients without prior MI receiving extended DAPT (RR 1.64, 95% CI 1.08-2.24) .

In ACS patients specifically, short-duration DAPT (≤6 months) demonstrated similar net adverse events compared to standard-duration DAPT (≥12 months) (2.0% vs 1.9%; HR 1.03) . Short-term DAPT followed by P2Y12 inhibitor monotherapy significantly reduced major bleeding in ACS patients without increasing ischemic events .

Bleeding Risk Stratification

Use of risk prediction tools demonstrated differential benefits. The DAPT score stratified patients into groups with distinct benefit-harm profiles . High-score patients (≥2) derived significant ischemic benefit from continued DAPT (2.7% vs 5.7%; RD -3.0%) with smaller increases in bleeding (1.8% vs 1.4%; RD 0.4%) . Low-score patients showed smaller ischemic benefits (1.7% vs 2.3%; RD -0.7%) but larger bleeding increases (3.0% vs 1.4%; RD 1.5%) .

The PRECISE-DAPT score identified that standard-duration DAPT was associated with fewer ischemic events only among patients at low bleeding risk and high ischemic risk (6.9% vs 4.0%, p=0.02), with no increase in bleeding events . In patients at high bleeding risk, abbreviated DAPT significantly reduced major bleeding (HR 0.35, 95% CI 0.14-0.88) and any bleeding (HR 0.53, 95% CI 0.41-0.67) .

Type of Monotherapy Following DAPT

The choice of single antiplatelet therapy following DAPT cessation influences outcomes. Short DAPT followed by P2Y12 inhibitor monotherapy reduced major bleeding (HR 0.63, 95% CI 0.45-0.86) without increasing stent thrombosis, MI, or mortality compared to prolonged DAPT . In contrast, short DAPT followed by aspirin monotherapy was associated with increased MI risk (OR 1.23, 95% CI 1.01-1.48) and, in ACS patients specifically, increased stent thrombosis (OR 1.55, 95% CI 1.02-2.36) .

Peripheral Arterial Disease

Patients with concomitant peripheral arterial disease (PAD) represent a high-risk subgroup. PAD was associated with significantly higher ischemic event risk (HR 2.80, 95% CI 2.05-3.83) . Prolonged DAPT (24 months) significantly reduced the primary efficacy endpoint in PAD patients (16.1% vs 27.3%; HR 0.54, 95% CI 0.31-0.95) and stent

thrombosis (HR 0.07, 95% CI 0-1.21) without increasing bleeding (5.2% vs 6.9%; HR 0.77) .

Sex Differences

Women may derive particular benefit from abbreviated DAPT. Meta-analysis showed that shortened DAPT significantly decreased major adverse cardiac events (MACE) in women (RR 0.82, 95% CI 0.70-0.97) but not in men (p for interaction = 0.049) . In high-bleeding-risk populations, there was a trend toward benefit with abbreviated DAPT in women for ischemic outcomes (HR 0.68, 95% CI 0.44-1.05) that was not observed in men (HR 1.17, 95% CI 0.88-1.55; p for interaction = 0.04) .

Synthesis

The evidence demonstrates a consistent pattern: shorter DAPT durations reduce bleeding without significantly compromising overall clinical outcomes in most patients, while extended DAPT provides incremental ischemic protection at the cost of increased bleeding and potentially increased non-cardiovascular mortality. However, this generalization obscures important heterogeneity that can be explained by several factors.

The apparent contradiction between studies finding benefit versus no benefit from extended DAPT is largely explained by patient risk stratification. Studies enrolling higher proportions of patients with acute coronary syndrome, prior MI, or other high-ischemic-risk features consistently showed greater absolute benefits from extended DAPT . Conversely, in populations with predominantly stable coronary disease or lower ischemic risk profiles, extended DAPT provided minimal additional ischemic protection while exposing patients to increased bleeding risk .

Age emerges as a critical effect modifier. The interaction between age and DAPT duration is statistically significant , with elderly patients (≥65-75 years) showing no ischemic benefit but substantial bleeding harm from prolonged DAPT . This reflects both higher

baseline bleeding risk with advancing age and potentially accelerated endothelialization in older individuals.

The type of antiplatelet monotherapy following DAPT cessation significantly influences the ischemic-bleeding balance. P2Y12 inhibitor monotherapy maintains superior ischemic protection compared to aspirin alone , particularly in ACS patients . This mechanistic distinction explains why some studies found very short DAPT (1-3 months) followed by P2Y12 inhibitor monotherapy to be noninferior or superior to standard 12-month DAPT , while others using aspirin monotherapy showed numerical increases in ischemic events .

Stent technology evolution affects generalizability across time periods. Trials using second-generation drug-eluting stents consistently demonstrated favorable outcomes with shorter DAPT , reflecting improved polymer biocompatibility and faster vessel healing compared to first-generation devices . Studies conducted before widespread adoption of newer-generation stents may overestimate the ischemic risk of abbreviated DAPT in contemporary practice.

Geographic variation in treatment effect, noted as a concern when extrapolating East Asian data to other populations , may reflect differences in clopidogrel metabolism, baseline bleeding risk, and healthcare system factors. The predominance of Korean and Japanese studies in the very short DAPT literature warrants caution in generalizing to Western populations.

Based on this evidence, optimal DAPT duration should be individualized according to the following framework:

- For patients with stable coronary disease, low ischemic risk, high bleeding risk, or advanced age (≥75 years), abbreviated DAPT (1-3 months) followed by P2Y12 inhibitor monotherapy provides favorable net clinical benefit

- For patients with ACS at presentation, prior MI, or complex PCI without elevated bleeding risk, standard 12-month DAPT remains appropriate, with potential extension in those with very high ischemic risk (high DAPT score) and without bleeding complications
- Risk prediction tools (DAPT score, PRECISE-DAPT) help identify patients at the extremes of the benefit-harm spectrum who may benefit most from individualized duration decisions

DISCUSSION

This systematic review, synthesizing evidence from four decades of research, provides a multi-layered understanding of the HIV-CMV retinitis syndemic. The central, unequivocal finding is that the relationship is mechanistically mediated by the depth of CD4+ T-lymphocyte depletion, confirming the threshold of <50 cells/μL as the immunological point of no return for CMV reactivation and retinal invasion (Jabs et al., 2002). This pathophysiological cornerstone explains the persistent and distressing epidemiology observed in LMICs. The pooled prevalence of 14.0% in these settings is not an artifact but a direct reflection of health system failures characterized by late HIV diagnosis, poor linkage to care, and delayed ART initiation (Ford et al., 2013). Patients in these contexts often enter the healthcare system only after experiencing AIDS-defining illnesses, by which time their CD4+ counts have already plummeted far below the critical threshold, effectively pre-empting the primary protective benefit of ART. In stark contrast, in settings with robust HIV testing and early treatment programs, CMV retinitis has become a rarity, demonstrating that the infection is fundamentally a disease of untreated or late-presenting AIDS, not of HIV infection per se.

The evolution of treatment strategies reveals a complex risk-benefit calculus. The ganciclovir implant represented a monumental advance in local disease control, offering a median time to progression of over 200 days—a three-fold improvement over intravenous ganciclovir (Musch et al., 1997). However, this review highlights the peril of localized victory in a systemic

war. The implant's pharmacological isolation within the eye creates a sanctuary effect, leaving the rest of the body unprotected. This manifests as a significantly higher risk of life-threatening extraocular CMV disease (e.g., pneumonitis, colitis) and new disease in the fellow eye, tragic consequences of untreated disseminated infection (D. Jabs, 2001). Therefore, the implant alone is an incomplete strategy. The superior paradigm, where resources permit, is combination therapy: the implant for definitive retinal control coupled with systemic oral valganciclovir for systemic protection. This approach, proven to halve the rate of new CMV disease compared to implant plus placebo, represents the holistic management of a systemic viral infection with a sight-threatening ocular manifestation (D. F. Martin et al., 1999).

For the vast majority of the global HIV-positive population living in resource-constrained environments, this gold-standard combination is often unattainable due to cost and infrastructure. Here, the review identifies intravitreal ganciclovir injections as a resilient and adaptable cornerstone of care. While requiring more frequent administration, protocols with weekly or bi-weekly maintenance injections achieve a median time to progression (152 days) that approaches the efficacy of implants (Teoh et al., 2012; Liang et al., 2023). Studies from Thailand and China demonstrate that with training, this procedure can be safely decentralized, offering a lifeline in settings without access to vitreoretinal surgeons or expensive sustained-release devices. This underscores a critical principle: effective management is possible even without the most advanced technology, provided there is commitment to task-sharing and protocolized care.

Beyond the choice of drug or route, this analysis elevates a more profound, and often neglected, determinant of patient destiny: the **chronology of intervention**. The data from Ausayakhun et al. (2018) is unequivocal and sobering; patients screened and diagnosed early (within months of CD4+ drop) presented with a median visual acuity of 20/30, whereas those diagnosed later presented at 20/80—a level of visual impairment that severely impacts quality of life and independence. This disparity in *baseline* vision, present even before treatment begins, exposes a harsh truth: antiviral therapy halts progression but does not regenerate necrotic retina. The photoreceptors and neural pathways destroyed by active retinitis are lost permanently.

Consequently, all therapeutic efforts, no matter how advanced, are merely salvage operations if initiated after significant retinal damage has occurred. This makes a compelling, non-negotiable case for instituting mandatory, protocol-driven ophthalmologic screening for every HIV patient with a CD4+ count below 100 cells/μL, a recommendation that must be embedded in national HIV care guidelines.

The stage of disease at which intervention occurs also intricately influences complication rates. Xie et al. (2021) provided crucial insights into the timing of retinal detachment (RD), the most blinding structural complication. While the majority of RDs (60%) occurred in the post-induction phase, a significant proportion (26.67%) happened *before* induction therapy could even begin. This highlights a dual challenge: first, the urgent need to get patients with active retinitis onto therapy immediately to close this "pre-induction" vulnerability window; and second, the recognition that even successful induction does not eliminate the risk, necessitating ongoing monitoring. Adjuvant procedures like laser demarcation may play a role in high-risk eyes to prevent RD progression (Xie et al., 2021a).

The transformative role of ART extends far beyond primary prevention. For patients who develop CMV retinitis and subsequently achieve robust and *sustained* immune reconstitution on ART (operationalized as CD4+ >75-100 cells/μL for a minimum of 18 months), this review confirms the safety of discontinuing secondary anti-CMV prophylaxis (Jouan et al., 2001; Wohl et al., 2005). The relapse rate in such patients is remarkably low (~2.2% at 48 weeks), allowing for simplification of medication regimens and reduced toxicity. This milestone in management, however, is tempered by the emergence of Immune Recovery Uveitis (IRU), a paradoxical intraocular inflammation that can occur despite controlled CMV replication, leading to cystoid macular edema, epiretinal membrane formation, and secondary vision loss. This necessitates a transition from antiviral monitoring to inflammatory surveillance in this subset of patients.

Finally, the discussion must grapple with the nuances of therapeutic choice in specific scenarios. For relapsed or resistant retinitis, combination systemic therapy with foscarnet and

ganciclovir remains the most effective strategy to regain control, albeit with a significant burden of toxicity and reduced quality of life, requiring careful patient support (Sha, 1996). The management of adverse effects—neutropenia with ganciclovir, nephrotoxicity and electrolyte wasting with foscarnet, and severe uveitis with cidofovir—is an integral component of care, not a separate concern (Spector et al., 1996; Rahhal et al., 1996). Furthermore, while the search for novel agents like the monoclonal antibody MSL-109 continues, their additive benefit remains unclear (Borucki et al., 2004).

The management of CMV retinitis in HIV/AIDS has evolved from a palliative response to a late-stage complication into a multifaceted strategy encompassing primary prevention (early ART), secondary prevention (aggressive screening), sophisticated combination therapy, and strategic treatment discontinuation. Success hinges on understanding that this is not merely an eye disease, but a systemic infection with ocular consequences, and that the battle for vision is often won or lost long before the first antiviral dose is administered, in the efficiency of the systems designed to find at-risk patients.

CONCLUSION AND RECOMMENDATIONS

Conclusion

CMV retinitis remains a severe, sight-threatening complication of advanced HIV/AIDS, directly contingent upon profound CD4+ T-cell depletion (<50 cells/μL). The disease burden is disproportionately high in settings with late HIV diagnosis and ART initiation. While a range of effective systemic and local antiviral therapies exists, the cornerstone of preserving vision is early detection through systematic screening. Antiretroviral therapy has revolutionized management, drastically reducing incidence and allowing for safe discontinuation of maintenance therapy in patients with sustained immune recovery, albeit with a need to monitor for IRU.

Recommendations:

1. **Screening:** Implement mandatory, regular dilated fundus examinations by an ophthalmologist for all HIV-infected individuals with CD4+ counts below 100 cells/μL.
2. **Treatment:** Adopt a combination strategy utilizing both local (intravitreal injection or implant) and systemic (oral valganciclovir or equivalent) antiviral therapy where feasible, to optimize ocular control and prevent systemic/contralateral disease.
3. **ART Integration:** Prioritize and facilitate early initiation of and adherence to ART as the most effective primary prevention against CMV retinitis.
4. **Therapy Discontinuation:** In patients on stable ART with sustained immune reconstitution (CD4+ >75-100 cells/μL for >18 months), consider discontinuation of CMV maintenance therapy with appropriate ophthalmologic monitoring.
5. **Resource-Limited Settings:** Develop and disseminate standardized, cost-effective protocols centered on intravitreal ganciclovir injections, and invest in training for procedure administration.
6. **Future Research:** Encourage studies on optimal screening intervals, cost-effectiveness of different treatment modalities in LMICs, and management strategies for IRU and other long-term complications in the ART era.

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