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Article

The Outcome and Impact of Academic Cancer Clinical Trials with Participation from Canadian Sites (2015–2024)

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Simple Summary

Academic-sponsored cancer clinical trials are important for improving care, especially for patients with rare cancers or unique needs. These trials often explore questions that matter most to patients and clinicians. In Canada, the Canadian Cancer Clinical Trial Network (3CTN) supported hundreds of such trials over the past decade through coordinated national infrastructure and public funding. This study looks at the outputs and impact of these trials by assessing publication of results, and incorporation into practice guidelines. In total, completion and publication rates were high and 36% of completed Phase III trials led to changes in clinical practice. These findings highlight how modest sustained investment in academic sponsored trials and trial infrastructure can drive meaningful improvements in cancer outcomes that benefit patients, clinicians, policy makers and funders.

Abstract

Background/Objectives: Academic sponsored cancer clinical trials (ACCTs) are essential for advancing patient-centered care, particularly in areas underserved by commercial research. In Canada, the Canadian Cancer Clinical Trials Network (3CTN) was established to support high-quality multi-centre ACCTs. This study evaluates the outcomes and impact of trials supported by 3CTN between 2015 and 2024. **Methods:** We conducted a descriptive analysis of 350 ACCTs that were closed to recruitment and had primary completion dates within the study period. Trial characteristics, results, publication rates, and incorporation into clinical guidelines were assessed using registry data, peer-reviewed publications, and structured searches of oncology guidelines. **Results:** Among the 350 complete trials, 116 were Phase III studies. Of these, 36% were incorporated into clinical practice guidelines and 7% were likely to be incorporated. Overall, 81% of trials were published in journals, and 45% posted results in public registries. Trials addressed diverse cancer types, with notable contributions in rare cancers and vulnerable populations. **Conclusions:** 3CTN supported ACCTs had high completion and reporting rates, with substantial influence on clinical practice. These findings highlight the importance of sustained infrastructure and funding ACCTs and their role in improving cancer care. The impact achieved with relatively modest investment from public funders underscores the value of sustained investment in investigator-led research and coordinated network support.

Keywords: academic cancer clinical trials; Canadian Cancer Clinical Trials Network (3CTN); Phase III trials; rare cancers; trial outcomes; trial reporting; cancer research impact; evidence-based oncology; clinical practice guidelines; cancer guidelines

1. Introduction

Clinical trials are essential for advancing scientific knowledge, improving cancer care, and providing patients with access to innovative therapies [1]. Among these, cancer clinical trials led by academic investigators (ACCTs), and cooperative clinical trial groups are distinct in their purpose from industry-sponsored trials which are often driven by product development pipelines. Academic led trials often focus on underexplored clinical questions, rare cancers, real-world effectiveness of interventions, unmet clinical needs, or patient-centered outcomes such as quality of life assessments [2, 3].

The influence of ACCTs on clinical practice has been significant, driving advances in screening, prevention and treatment approaches, including combination chemotherapy regimens, multimodality therapies and treatments of rare cancers. In the United States, 45.1% of National Cancer Institute Clinical Trials Network (NCTN) contributed to clinical guidelines or drug approvals [4]. In Canada, 62.8% of Phase III trials sponsored by the Canadian Cancer Trials Group (CCTG), were cited in clinical guidelines [5]. Despite their clinical and scientific value, ACCTs can face added resource constraints due to funding limitations and lower budgets as well as accrual challenges [6-8]. A lack of core funding to support clinical trial unit operations and increased expectations for institutional cost recovery have tended to favour participation in industry sponsored trials [9].

In response to observed year-over-year declines in Canada, in the number of new ACCTs, site participation and accruals to open trials [2], the Canadian Cancer Clinical Trials Network (3CTN, Network) was established in 2014 through public funding. Currently, there are 38 adult and 13 pediatric member cancer centers and hospitals located in 8 Canadian provinces. Member centres, organized into local-regional nodes overseen by the larger tertiary cancer centres, commit to participating in a portfolio of ACCTs (the 3CTN 'Portfolio'). All trials are multicentered, have undergone peer review and some funding to support trial activities. Participating members report their Portfolio ACCT performance on a quarterly basis; members also participate in collaborative initiatives to improve the quality and efficient performance of trials opened locally. A central Coordinating Centre serves as the administrative and communication hub, providing systems support, oversight of data reporting processes, project coordination, and a comprehensive, accessible library of data informatics, best practice tools and resources.

To help ensure a robust Canadian ACCT ecosystem, Portfolio trial candidates are required to be peer-reviewed, academic-sponsored, interventional, and multicentered. The 3CTN governance and operating frameworks enable creation of relevant strategic priorities. Provincial core funding support for member centre trial units in each region creates capacity to achieve aligned objectives while incentive funding from the national funder can be earned by centres for surpassing performance targets aligned with the Network's overall strategic goals for accrual and rapid trial activation. Over the course of ten years, funders provided an average of approximately \$4.3 million annually, primarily from federal and provincial public sources. This represents the largest and most sustained investment in cancer clinical trials conduct in Canada.

Since its inception, there have been over 850 trials included in the 3CTN Portfolio. With member trial performance data, 3CTN holds one of the most comprehensive ACCT datasets in Canada. While Canada contributes strongly to global oncology research, there has not been a systematic assessment of ACCT outcomes and impact at the national level. This study addresses that gap.

This study goals were to assess the outcomes and impact of ACCTs supported by 3CTN between 2015 and 2024. Specifically, we:

- Identified trends and gaps in completed trials, including patterns in evidence dissemination and translation into clinical practice.
- Assessed the contributions of 3CTN-supported trials to peer-reviewed publications and clinical treatment guidelines.

2. Materials and Methods

This exploratory descriptive analysis used data from the 3CTN ACCT Portfolio. Trials that were closed to recruitment and had primary completion dates between 2015 and 2024 were included. This timeframe aligns with the period following the establishment of the 3CTN Portfolio and provides time for trial completion and publication. The data selection process is illustrated in Figure 1. The workflow used to assess practice-changing impact is detailed in Appendix Figure A1.

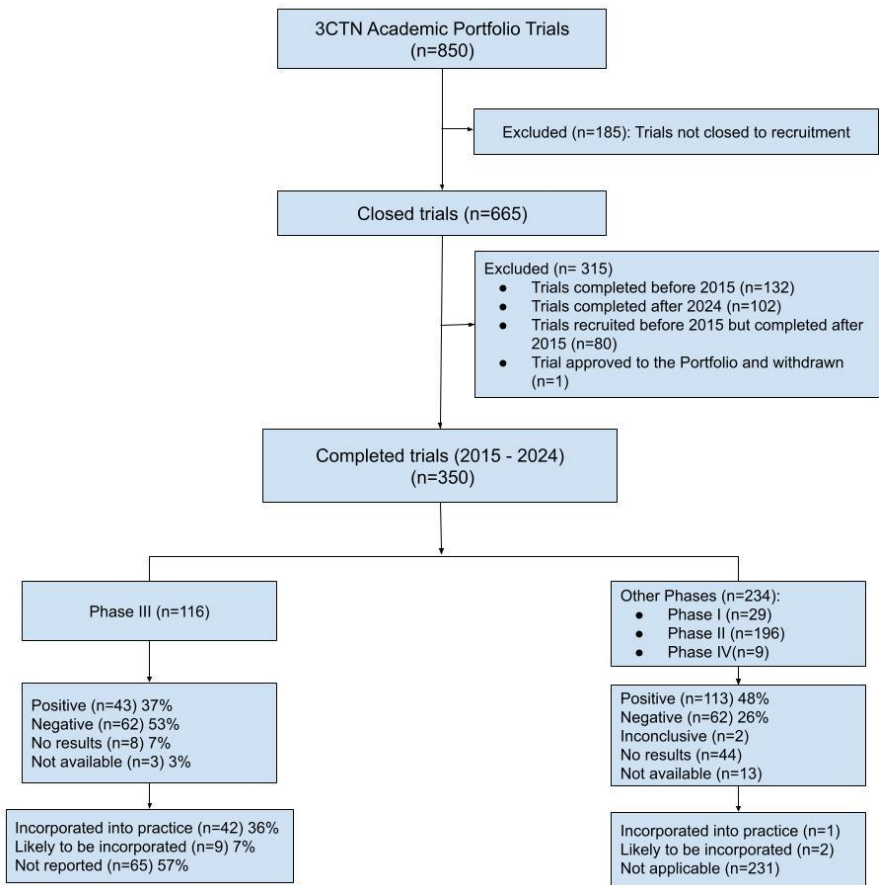


Figure 1. Data selection process for included trials (2015–2024). Data lock: October 9, 2025.

Trial status, design, and results data were extracted from the Portfolio database, ClinicalTrials.gov and PubMed. Manual searches were supplemented by a machine learning tool, which was used intermittently to validate linkages between trials and resulting publications [10]. Although not central to the analysis, these tools supported quality control and may offer future opportunities for automation.

Clinical impacts were assessed primarily for Phase III trials. Structured searches of North American and European oncology guidelines were conducted (see Appendix A2). Trials were considered “incorporated into practice” if cited in the evidence or recommendations sections of guidelines. Additionally, we defined the classification “likely to be incorporated into practice” for cases where a peer-reviewed source explicitly stated that the trial results are informing clinical decisions, are currently influencing practice, or are likely to be incorporated into clinical guidelines in the future. Regulatory impact was captured through FDA and Health Canada drug approval announcements.

Trial results were classified as positive, negative, or inconclusive based on primary outcome reporting. Detailed definitions and classification criteria are provided in Appendix A1. We

summarized trial characteristics, outcomes, and reporting rates using counts and percentages. Where relevant, confidence intervals were calculated to indicate the precision of estimates.

3. Results

3.1. Trial Characteristics

Between 2015-2024, 350 ACCTs (41% of the 3CTN Portfolio) closed to recruitment, including 116 completed Phase III trials and 31 (9%) that closed prematurely with the most often cited reason being poor accrual (Appendix Table A3). Most trials evaluated drug therapies, were randomized and involved diverse cancer types and settings. Trials evaluating precision medicine strategies were common (68%) while 33% addressed rare cancers and 22% involved vulnerable populations (see Appendix Table A4 for the Characteristics of the Completed 3CTN Portfolio Trials 2015-2024).

3.2. Trial Outcomes

Of the 350 completed trials that were reviewed for results of the primary outcomes, 156 (44%) were classified as positive and 124 (35%) were negative and a small portion with inconclusive (1%) and no results reported (20%). Of the 68 trials with no results reported, 39 (57%) were closed between 2021 and 2024. Figure 2 highlights a peak in trial completions in 2020, followed by a decline in subsequent years, which may reflect broader trends such as the impact of the COVID-19 pandemic on trial performance or capacity or changes in research priorities among some sponsors and site institutions.

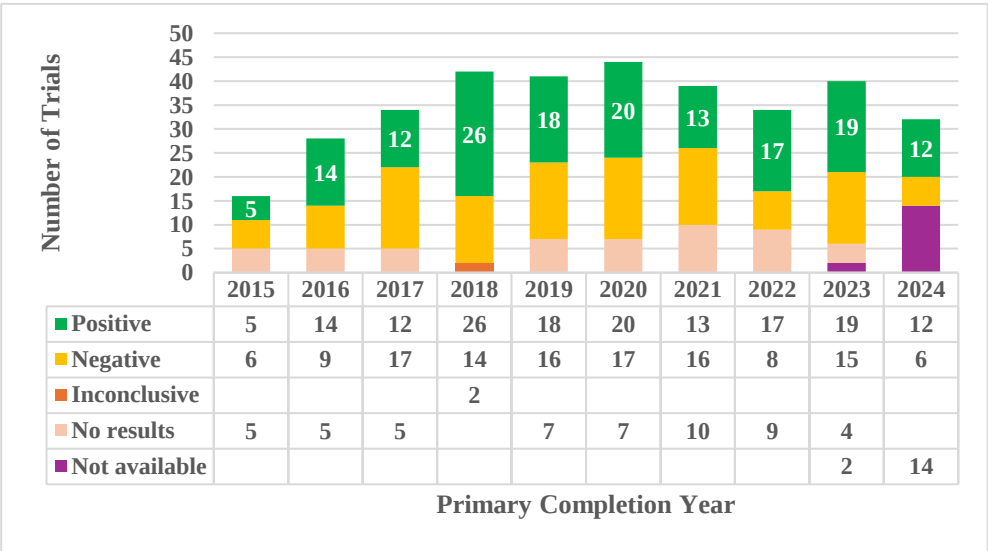


Figure 2. Annual distribution of study results for completed trials (N=350).

3.2.1. Reporting and Publication Rates

Rates for posting of Portfolio trial results in registries as well as publication in scientific journals are summarized in Table 2. Among all trials, 45% had reported results posted in a public registry, primarily on ClinicalTrials.gov. 81% published their findings as abstracts or full articles, with 117 trials being published in high impact journals, defined as those ranked within the top 10% based on 2022 CiteScores. The top three journals were Journal of Clinicl Oncology, JAMA Oncology and New England Journal of Medicine.

Table 2. Completed trial results reporting by phase.

Phase	All trials	Reported in Registry	Journal Publication
Phase I	29	2 (7%)	21 (72%)

Phase II	196	79 (40%)	148 (76%)
Phase III	116	76 (66%)	105 (91%)
Phase IV	9	2 (22%)	8 (89%)
Total	350	159 (45%)	282 (81%)

3.2.2. Practice Guideline Incorporation

Of 116 completed Phase III ACCTs, 36% (42/116) were incorporated into practice guidelines and 7% (9/116) were marked as likely to be incorporated into practice, as they were cited in practice guidelines for future consideration or contributed to new drug approvals. Of 43 positive Phase III clinical trials, 32 (74.4%) were either already, or likely to be incorporated into practice. Both positive and negative results contributed to evidence-based care (see Figure 3 for the distribution of the practice changing trials). Although Phase III trials were our key focus, we also identified a small portion of Phase II and Phase IV trials that have led to changes in practice. For the full review of the completed trials, refer to Figure 1.

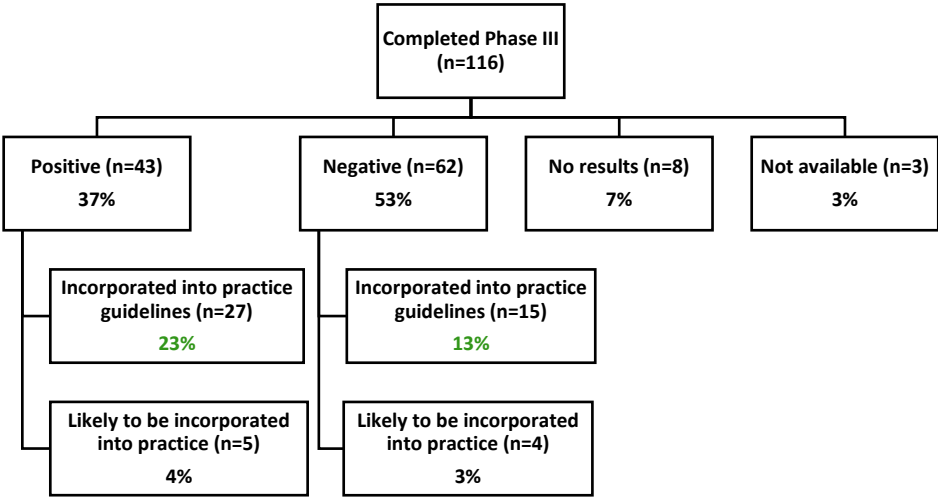


Figure 3. Distribution of Practice-Changing Trials Incorporated into Guidelines.

3.2.3. Sponsorship and Practice-Changing Impact

Among the 116 completed Phase III trials in the 3CTN Portfolio, the two largest academic sponsors were the U.S. National Cancer Institute (NCI) and the Canadian Cancer Trials Group (CCTG). NCI sponsored 67 adult and pediatric trials (58%), while CCTG sponsored 39 trials (33%), reflecting the important role of cooperative groups in supporting academic oncology research. Importantly, 42 trials (36%) led to changes in clinical practice through incorporation into guidelines or contribution to drug approval decisions. Of these, 31 trials (74%) were NCI-funded, highlighting a strong association between NCI sponsorship and practice-changing outcomes.

3.3. Recruitment Contributions from Network Sites

3CTN member sites contributed 17% of overall patient recruitment to completed global clinical trials. Contributions grew over time, climbing to 33% in 2024, highlighting the Network’s role in the accrual success of ACCT trials (Table 3).

Table 3. Annual Patient Recruitment to Completed Portfolio Trials (2015-2024).

Trial Completion Year	# of ACCT Trials	Sample Size	Global Recruitment *	3CTN Sites Recruitment	3CTN Sites Contribution (%)
2015	16	2930	2158	181	8%

2016	28	4406	2894	836	29%
2017	34	8861	7596	859	11%
2018	42	14873	14231	3134	22%
2019	41	14536	16554	2595	16%
2020	44	20217	20458	2962	14%
2021	39	11886	11221	2312	21%
2022	34	25381	18903	2894	15%
2023	40	18777	17821	2521	14%
2024*	32	11553	8223	2681	33%
Total	350	133420	120059	20975	17%
Median	36.5	13211	12726	2558	15%
IQR	8.25	8267	9751.5	1618.5	7%

*Global recruitment data for some trials is not available in clinicaltrials.gov.

For Phase III trials specifically, 3CTN sites contributed 9% to the overall global recruitment (Table 4) and 6.6% of recruitment to practice-changing trials (Table 5).

Table 4. 3CTN member site contribution to Phase III ACCTs completed (2015-2024).

Study Results	Number of Trials	Total Recruitment	3CTN Member Sites Recruitment
Negative	62 (53%)	52999	3763 (7%)
No results	8 (7%)	1500	355 (24%)
Not available	3 (3%)	385	139 (36%)
Positive	43 (37%)	37679	3771 (10%)
Total	116	92563	8028 (9%)

Table 5. Canadian ACCTs in Guidelines and 3CTN Global Recruitment Contribution.

Study Results	Number of Trials*	Total Recruitment	3CTN Sites Recruitment
Negative	15	211518	958 (4.5%)
Positive	28	32826	2593 (7.1%)
Total	43	54007	3551 (6.6%)

*Including phase III and IV practice changing trials of this period.

4. Discussion

This review highlights the significant contributions of 3CTN Portfolio ACCTs to advancing scientific knowledge and evidence-based cancer care. Portfolio trials reflect a broad spectrum of high quality research, with a notable emphasis on rare cancers, supportive care, and vulnerable populations (i.e. pediatric or elderly patients) [11], areas often underserved by industry-sponsored trials. Our finding that 36% of Phase III trials were incorporated into guidelines or contributed to drug approvals compares favorably with existing literature. For example, Elimova et al. reported that 20% of positive Phase III trials published in high-impact journals between 1990–2010 were incorporated into practice guidelines [12]. While not directly comparable due to differences in inclusion criteria and timeframe, our analysis which encompasses both positive and negative trials shows that academic trials supported by 3CTN have had a substantial and diverse impact on clinical practice. Practice-changing contributions were often seen through repurposing, optimization of treatment regimens, or patient management strategies and were most prevalent in studies involving hematologic, breast, genitourinary, and gynecologic cancers. A selection of notable practice-changing trials is listed in Appendix Table A5.

To make these impacts visible and accessible to stakeholders, 3CTN developed an interactive outcome and publication search board for all Portfolio trials closed to recruitment. Built using

Microsoft Power BI, this publicly available tool enhances transparency and enables users to explore trial-related publications, posted results, and impacts on clinical guidelines. It serves as a centralized resource for Network stakeholders. The full dataset and dashboard are available on the 3CTN website [13].

Canadian participation in NCI-sponsored trials has remained consistently high over the past decade, reflecting strong international collaboration and the strategic alignment between Canadian trial units and U.S. cooperative groups. The impact of this collaboration is substantial: of the 42 Phase III trials that led to changes in clinical practice, 74% (31 trials) were NCI-funded. This underscores the pivotal role of NCI sponsorship in generating practice-changing evidence and highlights Canada's meaningful contribution to these global efforts.

Despite persistent challenges and limitations affecting our national trial system [9, 14], the number of Canadian-led trials and recruitment to NCI-funded studies have increased. At the same time, Canadian-led trials have demonstrated leadership in areas often underserved by industry-sponsored research, including rare cancers, supportive care, systemic therapies, and radiotherapy. These contributions reflect the strength of Canada's academic trial ecosystem and the value of sustained support for investigator-led research.

Approximately 280 (80%) completed trials had results reported at the time of review. Of the remainder, nearly 145 (60%) were closed between 2021 and 2024, suggesting that reporting delays may be due to factors such as ongoing analysis, and delays in publication processes including negative decisions. Overall, improvements in recruitment and outcomes reporting rates for completed trials occurred during the 3CTN period suggest a contributing role for the Network. 3CTN's supportive infrastructure and initiatives designed to overcome barriers to ACCT conduct in Canada were aimed to increase participation of clinicians and patients and enable completion of trials and subsequent publication. The substantial impact achieved with a relatively modest annual budget demonstrates the value of a coordinated national program to support academic cancer clinical trials.

Journal publication rates may improve through enhancing recruitment, timeliness of reporting and adoption of innovative trial methods. Over time, the use of adaptive and master protocols for rare cancer histology or molecularly defined subgroups increased, as did decentralized trial conduct and digital tools for data collection. Trials testing precision medicine strategies also became more common. In addition, incenting researchers and journals to publish all trials, including those with negative outcomes. Future opportunities to improve trial accrual and completion include applied use of artificial intelligence to support translation of patient information materials into multiple languages to promote equitable access and improve screening of medical records against complex inclusion criteria.

Our analysis depended on trial performance data reported by 3CTN sites and available registry data, which varied in completeness. Data was reviewed and validated to the extent possible. Publication and guideline searches, while extensive and labor intensive, may have missed citations due to inconsistent and/or delayed referencing in guidelines. Use of natural language processing (NLP) and machine learning tools was incorporated for supplemental data validation activities and illustrated the potential for automating and enhancing these tasks. However, further validation will be required before routine use. In addition, recently completed trials may not yet have been included in practice guidelines, underestimating impact. Our use of publications and citations to assess impact, while important, does not fully capture broader policy or patient-level outcomes. Despite recent efforts to promote publication of negative results [15, 16], further improvements are needed to ensure that all trial outcomes contribute to scientific knowledge and resource optimization [17].

5. Conclusions

3CTN-supported ACCTs have high completion and reporting rates, with substantial influence on practice guidelines and patient care. Their focus on identifying better treatments for patients with rare cancers, supportive care, and treatments for vulnerable populations highlight the value of ACCTs. 3CTN and member cancer centre trial units require long-term infrastructure support to

sustain and expand upon performance improvements and beneficial impacts realized to date. Recognizing the essential role of the Network in supporting these achievements is critical. Coupled with sustained investments in academic cancer trials, system innovation, performance improvement, and strategic priorities for equitable trial access, Canada can leverage its strengths and position itself as a global leader in advancing patient-centered oncology research. Doing so is not only a scientific imperative, but also a strategic opportunity to shape the future of cancer care for all Canadians.

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Abbreviations

The following abbreviations are used in this manuscript:

3CTN	Canadian Cancer Clinical Trials Network
ACCT	Academic Cancer Clinical Trials
ALL	Acute Lymphoblastic Leukemia
ASCO	American Society of Clinical Oncology
ASTRO	American Society for Radiation Oncology
CCO	Cancer Care Ontario
CCTG	Canadian Cancer Trials Group
CNS	Central Nervous System
COG	Children’s Oncology Group
COVID-19	Coronavirus Disease 2019
CMA	Canadian Medical Association
DSMB	Data Safety Monitoring Board
EANM	European Association of Nuclear Medicine
ESMO	European Society for Medical Oncology
GU	Genitourinary
ML-DS	Myeloid Leukemia of Down syndrome
NCCN	National Comprehensive Cancer Network
OICR	Ontario Institute for Cancer Research
SIOPE	European Society for Paediatric Oncology
SNMMI	Society of Nuclear Medicine and Molecular Imaging

Appendix A

Appendix A.1 Definitions and Flow Diagram of Impact Tracking Process for Practice Change Assessment

Definitions of the Study Results:

Positive: Results are reported in the literature and demonstrate a positive primary outcome:

- For phase III trials, a positive primary outcome was defined as a statistically significant ($p < 0.05$, or per the study’s pre specified threshold) and favourable effect for the experimental treatment compared with a placebo or active comparator.
- For earlier phase trials, a positive primary outcome was defined as sufficient efficacy/safety evidence to justify progression to a later phase trial, as stated by the authors.

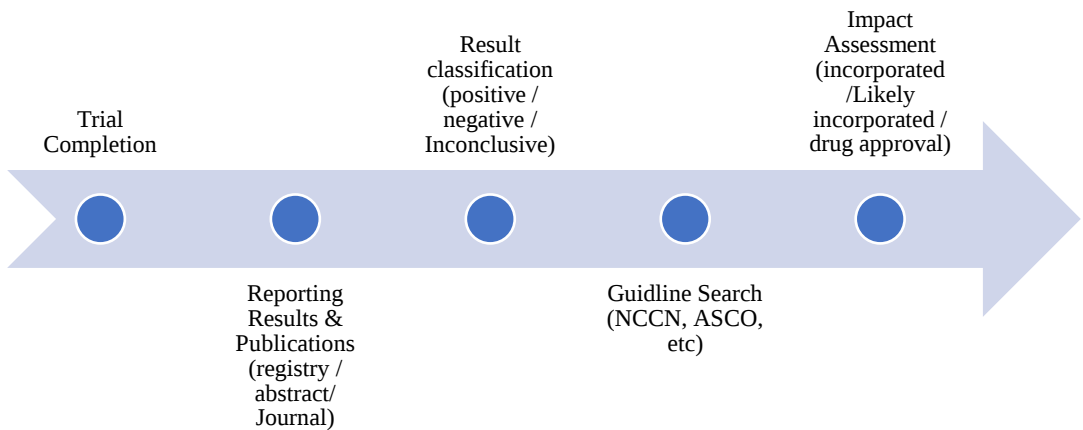
Negative: Results are reported in the literature and demonstrate a negative primary outcome, meaning:

- For phase III trials, a negative primary outcome was defined as an effect that is not statistically significant or is statistically significant but favours the control arm.
- For earlier phase trials, a negative primary outcome was defined as insufficient evidence to justify progression to a later phase trial.

Inconclusive: Results were classified as inconclusive when the direction or significance of the primary outcome could not be determined from the available data, including cases where the study was prematurely terminated prior to reaching target accrual.

No Results Reported including the following:

- Not available: No peer reviewed results found, and the primary study completion date is < 24 months ago.
- No results: No peer reviewed results found, and the primary study completion date is ≥ 24 months ago.
- Pending final publication: No final, peer reviewed results for the entire study population, but interim or subgroup results are available, or a peer reviewed source explicitly states that results are pending or expected.



Appendix A2. Oncology Guidelines Reviewed for Practice Change Assessment

Guideline inclusion was assessed by reviewing recommendations from the following major oncology, general medical, and specialty-specific international bodies:

- National Comprehensive Cancer Network (NCCN)
 - via both the JNCCN journal (<https://jnccn.org>)
 - and the official NCCN guideline PDFs (https://www.nccn.org/professionals/physician_gls).
- American Society of Clinical Oncology (ASCO)

- via <https://asco.org/practice-patients/guidelines>
- and ASCO Publications (<https://ascopubs.org>) for joint or collaborative guidelines updates.
- American Society for Radiation Oncology (ASTRO) Guidelines
- European Society for Paediatric Oncology (SIOP Europe or SIOPE)
- International Childhood Liver Tumors Strategy Group – for pediatric liver cancer
- Cancer Care Ontario (CCO)
- American Urological Association Guidelines
- European Association of Urology – for prostate and bladder cancer.
- European Society for Radiotherapy and Oncology
- European Society for Medical Oncology (ESMO) – for European oncology practice
- European Association of Neuro-Oncology – for neuro-oncology
- Canadian Medical Association (CMA)
- Trip Database- <https://www.tripdatabase.com> – aggregates global guidelines.
- EANM/SNMMI Joint Guidelines for trials involving diagnostic imaging. These guidelines are published by the European Association of Nuclear Medicine and the Society of Nuclear Medicine and Molecular Imaging.
- The American Society for Transplantation and Cellular Therapy Practice Guidelines
- Society of American Gastrointestinal and Endoscopic Surgeons - GI Surgery for all GI Surgeons

Note: Searches will include both full guideline documents and peer-reviewed guideline updates to ensure that trials cited in collaborative or journal-based recommendations (e.g., ASCO–CCO updates, JNCCN articles) are captured. In the case of multiple guidelines are mentioned, we will cite the primary North American guidelines such as NCCN, ASCO and ASTRO.

Table A3. Terminated and Withdrawn Trials by Phase (2015–2024).

Reasons Cited for Termination	Phase I	Phase II	Phase III	Phase IV	Grand Total
Drug company decision		2	1		3
DSMB review			1		1
Lack of funding		1			1
Negative study		2			2
Poor accrual	3	14	1	1	19
Staffing issues				1	1
Unacceptable Toxicity			1		1
Unknown		2			2
COVID-19 pandemic		1			1
Total	3	22	4	2	31

Table A4. Characteristics of completed 3CTN Portfolio trials 2015-2024.

Trial Characteristics	Analysis	Phase III	Overall
Number of trials	N	116	350
	I	-	29(8%)
	II	-	196(56%)
	III	116	116(33%)
	IV	-	9(3%)
Disease Site	Bone	1(1%)	5(1%)
	Brain/CNS	8(7%)	19(5%)
	Breast	16(14%)	49(14%)
	Gastrointestinal	11(9%)	32(9%)
	Genito-Urinary	17(15%)	56(16%)
	Gynecological	12(10%)	25(7%)

Country of Sponsor	Head and neck	3(3%)	11(3%)
	Hematology	23(20%)	55(16%)
	Lung	10(9%)	32(9%)
	Neuroblastoma	1(1%)	7(2%)
	Other	9(8%)	43(12%)
	Sarcoma	4(3%)	9(3%)
	Skin / Melanoma	1(1%)	7(2%)
	Canada	33(28%)	192(55%)
	United States	71(61%)	142(41%)
Sponsor	Other	13(11%)	16(5%)
	NCI(USA)	67(58%)	123 (35%)
	CCTG	39 (33%)	87 (25%)
Special Interest	COG	21 (6%)	41(12%)
	Lifestyle Interventions	4(3%)	10(3%)
	Novel therapy	9(8%)	69(20%)
	Rare cancer setting	39(33%)	109(31%)
	Vulnerable populations	26(22%)	71(20%)
Interventions	Precision medicine	80(68%)	80(23%)
	Behavioral	3(3%)	13(4%)
	Drug	75(64%)	232(66%)
	Device	3(3%)	8(2%)
	Radiation	39(33%)	82(23%)
	Procedure	0(0%)	58(17%)
	Biological	24(21%)	51(15%)
	Basket Trial	0	2
	Platform Trial	1	5
Type of Design	Umbrella Trial	0	1
	Low complexity method	1	5
	Multiple steps	13	22
	Closed to recruitment	60(52%)	129(37%)
Completion status	Completed	52(45%)	190(54%)
	Prematurely completed (terminated or withdrawn)	4(3%)	31(9%)

Table A5. Notable Phase III Trials in the 3CTN Portfolio.

Trial	Practice-defining trial outcome	Disease Site	Active recruitment	NCT Number	Recruitment Contribution (%)	Publication	Practice Guidelines Changed
NRG-CC001	Recommended HA-WBRT plus memantine to reduce neurocognitive decline in patients with brain metastases.	Brain Metastases	2016 - 2018	NCT02360215	8.9% (46/518)	[18]	NCCN [19]
(CCTG) MA.36 / Olympia	Adjuvant Olaparib recommended for HER2-negative,	Breast	2015 - 2019	NCT02032823	1.9% (35/1837)	[20]	NCCN [21]

	BRCA-mutated early breast cancer with residual disease after neoadjuvant chemotherapy, based on Olympia trial results.						
	FDA approves Olaparib for adjuvant treatment of high-risk early breast cancer.						
OCOG-2016-PETABC	PETABC trial supported guideline recommendation for using 18F-FDG PET/CT in staging stage IIB–III breast cancer, showing improved detection of stage IV disease and influencing treatment decisions	Breast	2016 -2022	NCT02751710	100% (369/369)	[22]	EJNMMI [23]
(CCTG) MA.37 / PALLAS	PALLAS trial showed no benefit of adjuvant palbociclib, leading to guideline recommendations against its use in early breast cancer.	Breast	2017-2025	NCT02513394	2.6% (152/5796)	[24]	NCCN [25]
(EORTC) 1333-GUCC/PEACE III	Combining radium-223 with enzalutamide for mCRPC showed improved	GU/Prostate	2018 - 2023	NCT02194842	4.5% (20/446)	[26]	NCCN [27]

	progression-free survival and potential overall survival benefit.						
GOG – 0275	For low-risk gestational trophoblastic neoplasia, supporting methotrexate and actinomycin-D are effective first-line single-agent therapies.	Gyne/Gestational Trophoblastic	2015 - 2017	NCT01535053	3.5% (2/57)	[28]	NCCN [29]
(CCTG) ENC.1 / NRG-GY018 / MK-3475-868	Pembrolizumab plus chemotherapy as a new standard for advanced or recurrent endometrial cancer, regardless of mismatch repair status; led to FDA approval and guideline inclusion.	Gyne/Endometrial	2021 - 2022	NCT03914612	3.7% (30/813)	[30]	NCCN [31]
(CCTG) CLC.2 / Alliance A041202	Ibrutinib was superior to Bendamustine–rituximab for older patients with untreated CLL, supporting guideline recommendations and FDA-approved frontline use.	Chronic Lymphocytic Leukemia (CLL)	2015 – 2016	NCT01886872	7.9% (43/547)	[32]	NCCN [33]
(COG) AHOD1331	Use of brentuximab Vedotin with AVE-PC for high-risk pediatric	Hodgkin lymphoma	2015 - 2019	NCT02166463	6.5% (39/600)	[34]	NCCN [35]

	Hodgkin lymphoma showed superior efficacy and reduced need for radiation.						
(COG) AALL1331	For relapsed pediatric B-ALL, Blinatumomab was as a treatment option despite early trial termination and no significant difference in disease-free survival.	B-ALL	2015 - 2019	NCT02101853	7.9% (53/669)	[36]	NCCN [37]
(COG) AAML1531	For ML-DS, supporting risk-based treatment and use of HD-AraC to improve outcomes in standard-risk patients.	ML-DS	2016 - 2022	NCT02521493	5.4% (15/280)	[38]	SIOP Europe [39]
(CCTG) ALC.4 (ECOG E1910)	Adding Blinatumomab to consolidation chemotherapy for newly diagnosed B-lineage ALL, improving overall survival and establishing a new standard for BCR::ABL1-negative patients;	ALL	2017 - 2019	NCT02003222	1.8% (9/488)	[40]	NCCN [41]
(CCTG) HDC.1/SWG S1826	Nivolumab + AVD as first-line treatment for advanced-stage Hodgkin lymphoma,	Hodgkin Lymphoma	2021 - 2022	NCT03907488	1.8% (18/994)	[42]	NCCN [43]

	showing better progression-free survival than BV + AVD; now a Category 1 recommendation in NCCN guidelines.						
(EORTC) STRASS	No overall benefit of preoperative radiotherapy for retroperitoneal sarcoma, but supported selective use in Liposarcoma.	Sarcoma	2015 – 2017	NCT01344018	4.5% (12/266)	[44]	NCCN [45]
(CCTG) SRC.7 / Alliance A091105	Sorafenib significantly improved progression-free survival in desmoid tumors; now recommended in NCCN guidelines as a systemic therapy option.	Sarcoma	2015 – 2016	NCT02066181	5.7% (5/87)	[46]	NCCN [45]
(CCTG) SC.24	SC.24 trial showed stereotactic body radiotherapy improved pain control over conventional radiotherapy for spinal metastases; cited in Ontario guidelines for spine SBRT planning and delivery.	Spinal Metastases	2015 – 2019	NCT02512965	76.4% (175/229)	[47]	CCO [48]

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