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### A systematic review

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# Rates of adherence to cancer treatment guidelines in Australia and the factors associated with adherence: A systematic review

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## Abstract

Adherence to cancer treatment clinical practice guidelines (CPGs) varies enormously across Australia, despite being associated with improved patient outcomes. This systematic review aims to characterize adherence rates to active-cancer treatment CPGs in Australia and related factors to inform future implementation strategies. Five databases were systematically searched, abstracts were screened for eligibility, a full-text review and critical appraisal of eligible studies performed, and data extracted. A narrative synthesis of factors associated with adherence was conducted, and the median adherence rates within cancer streams calculated. A total of 21,031 abstracts were identified. After duplicates were removed, abstracts screened, and full texts reviewed, 20 studies focused on adherence to active-cancer treatment CPGs were included. Overall adherence rates ranged from 29% to 100%. Receipt of guideline recommended treatments was higher for patients who were younger (diffuse large B-cell lymphoma [DLBCL], colorectal, lung, and breast cancer); female (breast and lung cancer), and male (DLBCL and colorectal cancer); never smokers (DLBCL and lung cancer); non-Indigenous Australians (cervical and lung cancer); with less advanced stage disease (colorectal, lung, and cervical cancer), without comorbidities (DLBCL, colorectal, and lung cancer); with good-excellent Eastern Cooperative Oncology Group performance status (lung cancer); living in moderately accessible places (colon cancer); and treated in metropolitan facilities (DLBCL, breast and colon cancer). This review characterized active-cancer treatment CPG adherence rates and associated factors in Australia. Future targeted CPG implementation strategies should account for these factors, to redress unwarranted variation particularly in vulnerable populations, and improve patient outcomes (Prospero number: CRD42020222962).

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## KEYWORDS

guideline adherence, medical oncology, practice guideline, radiation oncology, surgical oncology

## 1 | INTRODUCTION

Adherence to clinical practice guideline (CPG) recommendations for cancer treatment has been associated with improved patient survival outcomes. This has previously been demonstrated across various cancers including sarcoma,<sup>1</sup> multiple myeloma<sup>2</sup> and cancers of the breast,<sup>3–6</sup> cervix,<sup>7</sup> lung,<sup>8</sup> head and neck,<sup>9</sup> and colon.<sup>10</sup> Despite this, wide variation in practice patterns persist across cancer streams internationally, with adherence rates ranging from 54% to 77% in breast cancer,<sup>11,12</sup> 35% to 56% in lung cancer,<sup>13–16</sup> 42% to 54% in cervical cancer,<sup>7</sup> 22% to 85% in non-muscle invasive bladder cancer,<sup>17,18</sup> 24% to 85% in ovarian cancer,<sup>19,20</sup> 67% to 81% in prostate cancer,<sup>21,22</sup> and 36% to 96% in colon cancer.<sup>23,24</sup> CPG nonadherence, specifically underutilization of guideline recommended treatment (GRT) has been identified as an issue in Australia, including radiotherapy (RT) treatment,<sup>25–28</sup> brachytherapy (BT),<sup>29–31</sup> chemotherapy (CTx),<sup>27,32–35</sup> and endocrine therapy<sup>27,36</sup> for a broad range of cancers. Similarly, overutilization of treatments that are unnecessary or associated with harm leads to wasteful healthcare spending and increased burden on the healthcare system.<sup>37</sup>

A plethora of variables influences adherence to cancer treatment CPGs, including factors related to CPG development. These include content and format, agreement with the underlying evidence, the applicability of GRT to individual patients, CPG currency, and prescriptiveness of the recommendations.<sup>38,39</sup> Similarly, organizational and clinician factors, such as disciplinary preferences and biases, access to treatment options, clinical culture of peer review and multidisciplinary care coordination, and patient specific factors influence adherence.<sup>38,39</sup>

Patient and health specific factors, such as older patient age and comorbidities, also influence adherence to CPGs across a variety of cancers,<sup>40,41</sup> including cancers of the breast,<sup>3,12</sup> lung,<sup>42</sup> colon,<sup>10</sup> and head and neck.<sup>9</sup> Older and less healthy patients are underrepresented in clinical trials, which may reduce clinician confidence in the evidence underpinning some CPG recommendations and contribute to low rates of adherence.<sup>3,38</sup> Eastern Cooperative Oncology Group (ECOG) Performance status,<sup>12,14</sup> cancer stage,<sup>7,9,16</sup> patient race,<sup>13,43</sup> and socioeconomic status (SES)<sup>43</sup> have also been associated with low rates of CPG adherence within specific cancer groups.

Barriers to effective CPG implementation are context specific,<sup>44</sup> and it is unknown whether the factors associated with cancer treatment CPG adherence are common across different cancers in the Australian setting. A better understanding of the impact of poor adherence across cancer streams in Australia, and the patterns of factors associated with CPG adherence (receipt of GRT), is needed to guide the implementation of tailored interventions. This knowledge will address the care gaps and distally contribute to reducing variation in treatment and patient outcomes across the cancer healthcare system. This review aims to (i) determine the rates of receipt of cancer GRT in Australia across various cancer streams, (ii) identify factors associated

with cancer GRT in Australian studies, highlighting factors common across cancer streams, and (iii) examine whether receipt of cancer GRT impacts on patient outcomes.

## 2 | METHODOLOGY

The review<sup>45</sup> was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-analysis (27 item checklist)<sup>46</sup> (see Additional file 1).

### 2.1 | Search strategy, abstract, and full-text review

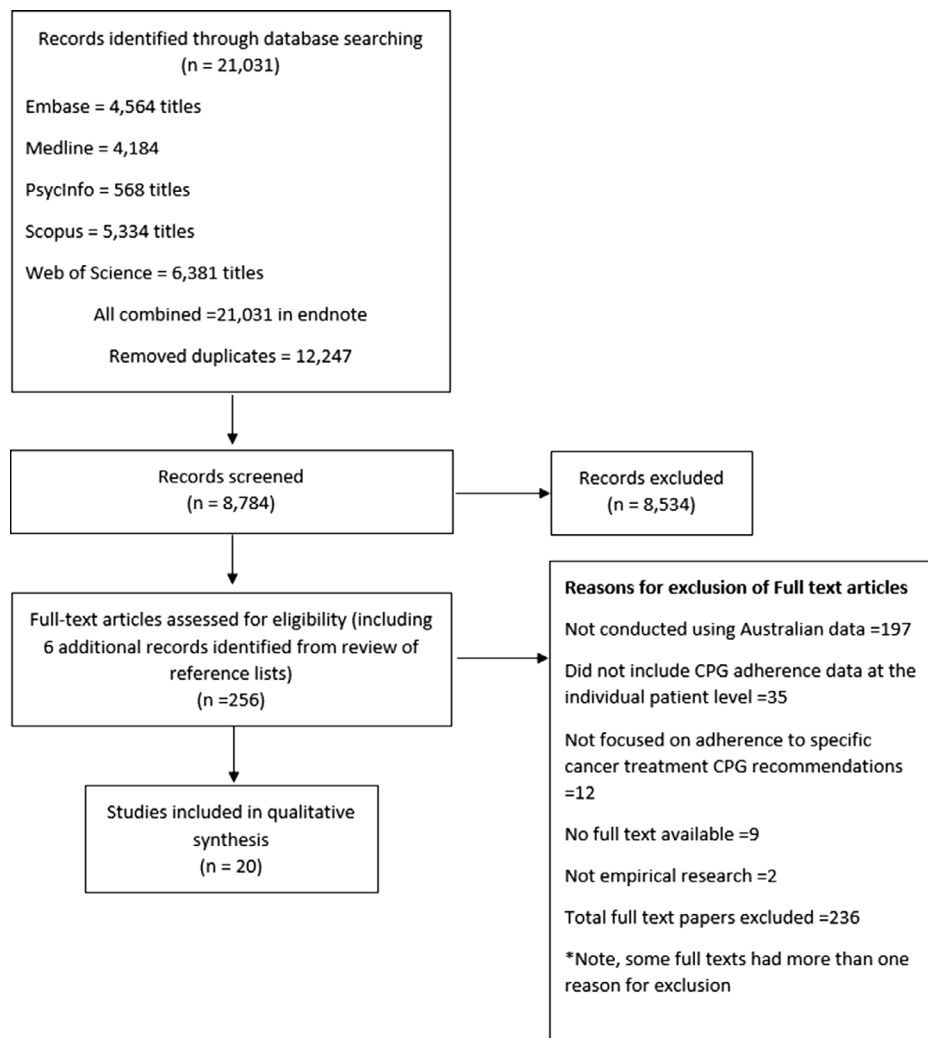
The search strategy was developed in consultation with a research librarian to search literature across five online databases (Medline, Embase, PsycInfo, Scopus, Web of Science core collection). The initial search was conducted by the lead author in August 2021 and updated in June 2022. Search terms are presented in Additional file 2. Abstracts identified by the search were collated in EndNote X9, and duplicates removed. Unique abstracts were then exported to Microsoft Excel V2208 and assessed for eligibility (see criteria below). All titles and abstracts were reviewed in pairs, by the lead author (MB) and a second reviewer (FR, GA, YT, BNGE, KL, RCW, EA, BL, CYL, KC, DFP, LvB, KH, RC, SSO, RN, or PH). Titles and abstracts were assessed for eligibility against predefined criteria, and eligible publications were then selected for full review. The lead author reviewed all full texts, paired with the 17 other reviewers. The acceptability of the interrater reliability scores of reviewing pairs was calculated using Cohen's Kappa score.<sup>47</sup> Disagreements on full texts were resolved through discussions with MB and GA. Reasons why publications were excluded at the full text stage are described in Figure 1. The reference lists of included studies were also searched for additional eligible studies.

### 2.2 | Eligibility criteria for abstracts and full-text review

Studies were eligible for inclusion if they reported adherence rates to cancer treatment CPGs, using Australian data. For the purpose of this review, 'Guideline adherence' includes terms such as *receipt of GRT or compliance, concordance, or adherence* with a recommendation in a cancer CPG, protocol, or CPG-based quality indicator. All treatment types reported in studies were included. The review had no publication year limits.

Studies were excluded if they *did not*

1. include active-cancer treatment CPG adherence as a reported measure (e.g., studies focusing on adherence to CPGs for cancer



**FIGURE 1** Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) Study selection process.

prevention, or the treatment of side effects such as pain management antiemetic prophylaxis, or palliation);

- clearly report Australian patient care data (i.e., independently to data from other countries);
- clearly define which CPG was being adhered to;
- publish in English;
- report quantitative and qualitative data separately;
- report empirical research;
- include full texts (e.g., conference abstracts); and
- publish in peer-reviewed journals (no gray literature was reviewed).

If more than one publication described results from an eligible study, the publication which reported results most relevant to the review was included, or both were included if they reported separate treatments or different results.

### 2.3 | Data extraction

Information on study characteristics (demographics including cancer type, number of participants, proportion of males/females, mean

participant age, as well as study location, study length/year, study type/cohort design, eligibility criteria, data source/s, CPG/s cited, origin of CPG/s), and key findings such as adherence rates, factors associated with adherence and patient outcomes such as survival rates, were extracted by MB using a data collection template specifically developed for this study.

### 2.4 | Study quality assessment

The Joanna Briggs Institute (JBI) checklist for prevalence studies<sup>48</sup> was used to appraise the quality of each study. The tool comprises nine items. Each study was independently assessed by two authors (MB and SS), with any discrepancies resolved through discussion with GA.

### 2.5 | Data analysis

A narrative synthesis approach<sup>49</sup> was used to analyze CPG adherence rates and associated factors. The World Health Organization's (WHO) five dimensions of adherence framework (which includes patient factors, health condition factors, health care system and team factors,

socioeconomic factors, as well as factors related to medical therapy)<sup>50</sup> guided the categorization of factors identified in this study. This framework has also been applied to CPG adherence in other health areas.<sup>51,52</sup> Given the variety of cancers, subgroups, and treatment types and changes in CPGs over time, meta-analysis was not conducted.<sup>53</sup>

### 3 | RESULTS

#### 3.1 | Included studies

After abstracts were downloaded, titles that did not meet the eligibility criteria were excluded, and the full texts of eligible studies (and their reference lists) were reviewed, identifying 20 eligible studies<sup>54–72,118</sup> (Figure 1). Data from included studies was extracted using a predefined template.

#### 3.2 | Interrater reliability scores

The 17 pairs of reviewers who reviewed title and abstracts had acceptable interrater reliability scores, with 3/17 achieving *near perfect agreement* (.81–.99), 9/17 pairs achieving *substantial agreement* (.61–.80), 4/17 achieving *moderate agreement* (.41–.60), and one pair achieved *fair agreement* (.21–.40).<sup>47</sup> The lead author (MB) reviewed all title abstracts and full texts. Disagreements were resolved by consensus with GA, minimizing the significance of any low Kappa scores.

#### 3.3 | Characteristics of included studies, quality assessment, and risk of bias assessments

Of the 20 studies included in the final analysis, the majority of studies assessed adherence to lung cancer treatment CPGs ( $n = 6^{54–58,118}$ ), cervical cancer ( $n = 4^{58–61}$ ), colorectal cancer (CRC) ( $n = 4^{62–65}$ ), and breast cancer ( $n = 3^{66–68}$ ). Two studies assessed adherence to lymphoma CPGs,<sup>69,70</sup> another assessed melanoma CPGs,<sup>71</sup> and another one assessed prostate cancer CPGs.<sup>72</sup> One study assessed adherence to both cervical and lung cancer<sup>58</sup> (Table 1).

This review included various study designs: population-based cohort studies that typically used registry data ( $n = 12^{57–59,62–65,67–69,71,118}$ ), multicenter cohort studies ( $n = 4^{54,56,61,66}$ ), and case-series which followed patients from a single institution ( $n = 4^{55,60,70,72}$ ) (Table 1). The studies were conducted in New South Wales (NSW) and the Australian Capital Territory (ACT) ( $n = 10^{54–56,59,61,65–67,71,118}$ ), South Australia (SA) ( $n = 4^{62,63,70,72}$ ), Victoria (VIC) ( $n = 3^{57,60,69}$ ), Australia-wide ( $n = 2^{64,68}$ ), and Queensland (QLD) ( $n = 1^{58}$ ). The Australia Cancer Network (ACN) CPGs (which were developed in partnership with the National Health and Medical Research Council (NHMRC)) ( $n = 7$ ), National Comprehensive Cancer Network (NCCN) CPGs ( $n = 7$ ), and NHMRC CPGs ( $n = 5$ ) were the most commonly used CPGs across the 20 included studies (with 7 studies referring to more than 1 CPG) (Table 1). The data included in each study spanned the years from 1997 to 2018, with half of the

studies reporting data from a time period that included 2006 (see Additional file 3). Three quarters of the studies were published after 2014 (see Additional file 4). Assessment using the JBI prevalence study critical appraisal tool demonstrated that the included studies were of high quality (see Additional file 5).

#### 3.4 | Rates of receipt of cancer guideline recommended treatment (GRT)

All studies reported CPG adherence (receipt of cancer GRT) as a measure, with varying rates of adherence reported across the different cancer streams. The most notable feature is that the studies differed considerably in whether they examined adherence to a few indicators or many, and whether they stratified by subgroup or not. Adherence rates were also variable (Table 2). As a result of this heterogeneity, meta-analysis was not possible. This was the case even for the four of the lung cancer studies that looked at one CPG, because they looked at different patient subgroups. The CPGs referred to by each study are presented in Table 1, whereas the CPG recommendations are outlined in Table 2.

The median cancer treatment CPG adherence rate was 57% (29% to 66%<sup>54,56–58,118</sup>) across the lung cancer studies, and 83% (54%<sup>59</sup> to 86%<sup>58</sup>) across the cervical cancer studies. Only one study in each of the breast,<sup>67</sup> colon,<sup>63</sup> rectum, melanoma,<sup>71</sup> prostate,<sup>72</sup> diffuse large B-cell lymphoma (DLBCL),<sup>69</sup> and early-stage Hodgkin lymphoma (ESHL)<sup>70</sup> cancer streams reported overall adherence rates, and so a median adherence rate was not calculated (Table 3, Figure 2). CPG adherence varied widely across subgroups within different cancer sites, ranging from 0% to 100% for subgroups within breast cancer,<sup>66–68</sup> 74% to 100% for prostate cancer subgroups,<sup>72</sup> 58% for DLBCL subgroups,<sup>69</sup> 83% to 100% for ESHL subgroups,<sup>70</sup> 35% for melanoma subgroups,<sup>71</sup> 23% to 98% for lung cancer subgroups,<sup>54,56–58,118</sup> 0% to 100% for cervical cancer subgroups,<sup>58–60</sup> 29% to 98% for colon cancer subgroups,<sup>63,65</sup> and 7% to 94% for rectal cancer subgroups<sup>62–65</sup> (Table 2).

#### 3.5 | Factors significantly associated with receipt of GRT

Of the 20 included studies, 16 assessed factors associated with receipt of GRT,<sup>54,56–65,67–69,71,118</sup> whereas 4 studies did not<sup>55,66,70,72</sup> (Table 4). Factors associated with receipt of GRT have been categorized according to the WHO's five dimensions of adherence framework: patient factors, health condition factors, healthcare system and team factors, socioeconomic factors, and medical therapy factors<sup>73</sup> (Table 4 and Figure 3).

The most commonly reported factor significantly associated with receipt of GRT was patient age, reported in 12 studies (across breast cancer,<sup>66,67</sup> DLBCL,<sup>69</sup> lung cancer,<sup>54,56–58,118</sup> cervical cancer,<sup>59</sup> and CRC<sup>62,63,65</sup>), followed by cancer stage in 7 studies (across lung cancer,<sup>54,56,57,118</sup> cervical cancer,<sup>59</sup> and CRC<sup>62,63</sup>), patient comorbidities in 5 studies (across DLBCL,<sup>69</sup> CRC,<sup>63</sup> and lung cancer<sup>56–58</sup>),

**TABLE 1** Characteristics of 20 included studies

Study	Cancer type and stage	N of participants	Study location	Data year/study length	Participant age and gender	Study type	Eligibility criteria	Data source	CPG	CPG origin
Craft 2010 <sup>66</sup>	Breast Early stage	n = 2081	ACT and SE NSW	July 1997–June 2006	Mean age 57.2 ± 11.9 years (ACT), 60.3 ± 12.3 years (SENSW); F: 100%	Prospective cohort study	Women with unilateral invasive EBC undergoing potentially curative surgical resection for breast cancer within the ACT and SE NSW regions were included	An audit study of women treated in metropolitan Canberra and rural settings in the region	Quality indicators from ANBC Audit	Aust
Jung 2019 <sup>67</sup>	Breast TNM stages I or II, early stage	n = 604	ACT	2008–2016	50–69 years (n = 767; F: 65.5%); <50 years (n = 211), <70 years (n = 193); F: 100%	Cohort study (medical record review)	Female cases with histologically proven nonmetastatic early-stage breast cancer who received adjuvant whole breast RT at the Department of Radiation Oncology, Canberra Health Services	ACT and SE-NSW BCTG prospective cohort Quality Assurance study and electronic medical records	ASTRO 2010 <sup>92</sup> ; Cancer Australia 2011 <sup>93</sup> and 2015 <sup>94</sup>	USA, Aust
Lomma 2020 <sup>68</sup>	Breast Stages I–III	n = 99,768	Aust	1 October 2006–30 September 2016	Mean age of males 67.5 years (range: 24.6–94.3) and females 60.8 years (range: 15.4–102.4); F: 99.4%	Retrospective population-based cohort study	Breast cancer cases in BQA dataset. Excluded: cases with de novo metastatic disease or non-recorded gender	BQA	NCCN 2018 <sup>95</sup>	USA
Wong Doo 2019 <sup>69</sup>	DLBCL Limited stages I and II, extensive III and IV	n = 1442, 624 (2008–2009), 818 (2012–2013)	VIC	1 January 2008–31 December 2009 and 1 January 2012–31 December 2013	<60 years 26% (n = 379), 60–79 years 52% (n = 751), >80 years 22% (n = 312); M: 58%	Retrospective population-based cohort study	All new pathologically confirmed DLBCL cases, aged ≥ 18 years	VCR Victorian Cancer registry ESMO 2015 <sup>96</sup> ; NCCN Euro, USA 2017 <sup>97</sup>		
Roos 2017 <sup>70</sup>	ESHL Stages IA, IB, IIA, IIB	n = 60	SA	July 2009–July 2014	Median age 39 years (range 18–79 years); M: 48%	Retrospective case-series (medical record review)	All ESHL cases receiving RT	Electronic medical records database at the Royal Adelaide Hospital	eviQ 2015 <sup>98</sup>	Aust
Freeman 2015 <sup>72</sup>	Prostate Stages T1–T2a, T2b, and T2c, T3 and T4, Tx	n = 215/1089 eligible cases	SA	1 October 2011–30 September 2012	Median age 71 years (range: 46–91 years); gender not reported	Retrospective case-series (medical record review)	All carcinoma of the lung and bronchus cases	Electronic medical records database at the Royal Adelaide Hospital	NCCN 2014 <sup>99</sup> ; eviQ 2009 <sup>100</sup>	Aust, USA

(Continues)

TABLE 1 (Continued)

Study	Cancer type and stage	N of participants	Study location	Data year/study length	Participant age and gender	Study type	Eligibility criteria	Data source	CPG	CPG origin
Varey 2017 <sup>71</sup>	Melanoma Primary in situ or invasive cutaneous	n = 1754/2590 lesions (67% with complete margin data)	NSW	23 October 2006–22 October 2007	Not reported	Retrospective population-based cohort study	Histopathologically confirmed Melanoma cases (primary in situ, invasive cutaneous, unknown primary site)	NSW Cancer Registry	NHMRC 1999 <sup>101</sup>	Aust
Boxer 2016 <sup>54</sup>	Lung Stages I, II, IIIA, IIIB, IV NSCLC; limited and extensive stage SCLC	n = 791/808 (newly diagnosed lung cancer patients discussed at MDM)	NSW	1 December 2005–31 December 2010	Median age 68 years (range: 35–93 years); M: n = 503, F: n = 288	Retrospective multicenter cohort study (medical record review)	All lung cancer cases (primary; NSCLC, SCLC), newly diagnosed, who were discussed at the MDM. Recurrent disease excluded	Lung cancer MDM Liverpool and Macarthur Cancer Therapy Centres in SWS	ACN 2004 <sup>102</sup>	Aust
Conron 2007 <sup>55</sup>	Lung Stages I–IIIA, IIb, IV NSCLC; limited SCLC	n = 257	NSW	September 2002– September 2004	Mean age 68.0 ± 11.2 years (range 22–92 years); M: 70.1%	Retrospective case-series (medical record review)	All cases with known or suspected lung, pleural, or mediastinal malignancies discussed by lung cancer MDC	St Vincent's Hospital lung cancer MDC	ACN 2004 <sup>102</sup>	Aust
Duggan 2016 <sup>118</sup>	Lung Stages I–IIIA, and IIIB NSCLC	n = 592	NSW	January 2006– December 2011	>70 years, 51%; median age 70 years, M: 61%	Retrospective population-based cohort study	All newly diagnosed NSCLC cases	SWS and Sydney LHD Clinical Cancer Registry	ACN 2004 <sup>102</sup>	Aust
Vinod 2010 <sup>56</sup>	Lung Stages I–IV NSCLC, limited, extensive SCLC	n = 335	NSW	1 December 2005–31 December 2007	Median age 69 years; M: 65%	Retrospective multicenter cohort study (MDM medical record review)	All newly diagnosed lung cancer cases presented to the MDM	MDM at Liverpool and Macarthur Cancer Therapy Centres (SWS, NSW)	NCCAC nd <sup>103</sup> ; RRCOIN 1999 <sup>104</sup> ; ACCPHSPC 2003 <sup>105</sup> ; ACN 2004 <sup>102</sup> ; NCCN 2006 V1 <sup>106</sup> ; NCCN 2006 V2 <sup>107</sup>	Aust, USA, UK
Wah 2020 <sup>57</sup>	Lung Stages I–IV, NSCLC; limited SCLC stages I–III, extensive SCLC stage IV	n = 4854	VIC	2011–2018	<60 years n = 951; 60–69 years n = 1492; 70–79 years n = 1659; 80 years n = 752; M: n = 2780/4854	Retrospective population-based cohort study	All NSCLC and SCLC cases. Excluded cases with unknown clinical stages or invalid residential addresses	Victorian Lung Cancer Registry	NCCN 2017 <sup>77,108</sup>	USA
Whop 2017 <sup>58</sup>	Lung/cervical Localized, regional stages	n = 199 NSCLC; n = 105 cervical	QLD	January 1998– December 2004	56.4% of Indigenous and 61.4% of non-Indigenous NSCLC cases were >60 years, 17.9% of Indigenous and 12.2% non-Indigenous cervical cancer cases were >60 years; F: 100%	Retrospective population-based cohort study	All Indigenous cases diagnosed with NSCLC or cervical cancer and a matched comparison group of non-Indigenous cases	QLD Cancer Registry	GMCT 2009 <sup>109</sup> ; ACN 2004 <sup>102</sup>	Aust

(Continues)

TABLE 1 (Continued)

Study	Cancer type and stage	N of participants	Study location	Data year/study length	Participant age and gender	Study type	Eligibility criteria	Data source	CPG	CPG origin
Chiew 2017 <sup>59</sup>	Cervical Stages IA, IB1, IIA, IB2, IIB-IVA	n = 208	NSW	1 July 2005–31 December 2011	Mean and median age was 53 and 50 years; F: 100%	Retrospective population-based cohort study	All newly diagnosed cervical cancer cases	SWSLHD and SLHD Clinical Cancer Registry	NCCN 2015 <sup>110</sup> ; ESMO 2010 <sup>111</sup> ; JSGO 2007 <sup>112</sup> ; SIGN 2008 <sup>113</sup>	Various
Thompson 2015 <sup>61</sup>	Cervical cancer + uterine malignancies FIGO stage IA1, IB, IC, IIA, IIB, IIA, IIB, IIC, IVA, and IVB	n = 163	NSW	Treated in 2003	Mean age 65 years (range: 42–88 years); F: 100%	Retrospective multicentered observational cross-sectional cohort study	All diagnosed cases of malignancy of the uterine corpus (in NSW residents) treated with BT. Excluded: cases with cancer of the uterine cervix	Electronic medical records from nine radiation oncology departments in NSW that deliver BT	NSW GOSG 2004 <sup>114</sup>	NSW
Kang 2015 <sup>60</sup>	Cervical cancer FIGO stages IA1, IA2, IB and IIA, IIB and IVA, IVB	n = 385	VIC	1999–2008	All female; age-distribution not reported	Case-series (medical record review)	All patients who received their first cervical cancer treatment at the Royal Women's Hospital, Melbourne in the study period (approx. 25% of Victorian incident cases in the period)	Royal Women's Hospital in Melbourne	GMCT 2009 <sup>109</sup>	Aust
Adelson 2018 <sup>62</sup>	CRC Stage C Colon; Stage B, C Rectal	n = 738 colon stage C cases eligible for GRT; n = 792 rectal stages B and C cases eligible for GRT; n = 4273 CRC cases treated	SA	2000–2010	<40 years n = 14 colon, 17 rectal; 40–49 years n = 35 colon, 45 rectal; 50–59 years n = 97 colon, 132 rectal; 60–69 years n = 170 colon, 217 rectal; 70–79 years n = 258 colon, 244 rectal; 80 years n = 164 colon, 134 rectal; M: n = 366; F: n = 372 colon cancer; M: n = 480; F: n = 312 rectal cancer	Retrospective population-based cohort study	Patients treated for CRC at four tertiary SA referral hospitals with cancer centers	SACCR	NHMRC 1999 <sup>115</sup> ; ACN 2005 <sup>116</sup>	Aust
Beckmann 2014 <sup>63</sup>	CRC Stages A, B, C, D rectal and colon	n = 4641	SA	January 2003– December 2008	50–79 years (50–59 years 20.7%, 60–69 years 34.5%, 70–79 years 44.8%); M: 57.5%	Retrospective population-based cohort study with data linkage	SA residents aged 50 and 79 years diagnosed with CRC	South Australian Cancer Registry (SACR)	ACN 2005 <sup>116</sup>	Aust

(Continues)



TABLE 1 (Continued)

Study	Cancer type and stage	N of participants	Study location	Data year/study length	Participant age and gender	Study type	Eligibility criteria	Data source	CPG	CPG origin
Young 2007 <sup>65</sup>	CRC	n = 560	NSW	November 2012–May 2013	Mean age 68 years (SD = 12); M: 60%	Retrospective population-based cohort study	All adult cases residing in NSW diagnosed with incident primary CRC. Excluded: cases with a life expectancy <6 months, past CRC malignancy, or hospital or nursing home residents (long term)	NSW Bowel Cancer Care Survey; NSW Cancer Registry	NHMRC 1999 <sup>15</sup>	Aust
McGrath 2004 <sup>64</sup>	CRC	n = 1911	Aust	February–April 2000	80% aged over 60 years; M: 57.4% (1097/1911)	Retrospective population-based cohort study	New CRC cases reported across Australia between February and April 2000, post operation	State based registries and survey to surgeons	NHMRC 1999 <sup>15</sup>	Aust

Abbreviations: ACCPHSPC, American College of Chest Physicians, Health and Science Policy Committee; ACN, Australian Cancer Network; ACT, Australian Capital Territory; ANBCA, Australian National Breast Cancer Audit; ASTRO, American Society for Radiation Oncology; Aust, Australia; BCTG, Breast Cancer Treatment Group; BQA, BreastSurgANZ Quality Audit; BT, brachytherapy; CPG, clinical practice guideline; CRC, colorectal cancer; DLBCL, diffuse large B-cell lymphoma; EBC, early breast cancer; ESHL, early-stage Hodgkin lymphoma; ESMO, European Society of Medical Oncology; F, female; FIGO, International Federation of Obstetrics and Gynecology (Federation Internationale de Gynecologie et d'Obstetrique); GMCT, Greater Melbourne Clinical Taskforce; GOSG, NSW Gynecological Oncology Study Group; GRT, guideline recommended treatment; JSGO, Japan Society of Gynecologic Oncology; M, male; MDC, Multidisciplinary Committee; MDM, Multidisciplinary Meeting; NCCAC, National Collaborating Centre for Acute Care; NCCN, National Comprehensive Cancer Network; ND, no date; NHMRC, National Health and Medical Research Council; NSCLC, non-small cell lung cancer; NSW, New South Wales; QLD, Queensland; RCRCOIN, The Royal College of Radiologists Clinical Oncology Information Network; RT, radiotherapy; SA, South Australia; SACC, South Australian Cancer Registry; SACR, South Australian Cancer Registry; SCLC, non-small cell lung cancer; SE, South Eastern; SIGN, Scottish Intercollegiate Guidelines Network; SLHD, Sydney Local Health District; SWS, South Western Sydney; TNM, Tumor Node Metastasis staging system; VIC, Victoria.

**TABLE 2** Overall reported adherence rates to active cancer clinical practice guideline (CPG) recommendations

Cancer stream	Study	Overall adherence rate reported	Subgroup adherence rates	Predictors of GRT	CPG	CPG recommendations	Treatment types			
							CTx	RT	Sx	ET
Breast	Craft 2010 <sup>66</sup>	93.5% GRT (axillary Sx or SLNB), 6.5% (137/2102) non-GRT	93.5% GRT (axillary Sx or SLNB), 6.5% (137/2102) non-GRT	Age, tumor size, tumor grade, HR status, axillary node	QIs from an Australian National Breast Cancer audit	1. SLNB, axillary lymph node sampling or clearance,	x	x	x	x
		97.6% GRT (attainment of clear surgical margins), 2.4% (51/2094) non-GRT	97.6% GRT (attainment of clear surgical margins), 2.4% (51/2094) non-GRT	HR status, axillary node status, year of diagnosis, treatment in metropolitan hospital	National Breast Cancer audit	2. RT following breast-conserving Sx,	x			
		95.6% GRT (RT after breast-conserving Sx), 4.4% (45/1022) non-GRT	95.6% GRT (RT after breast-conserving Sx), 4.4% (45/1022) non-GRT			3. Attainment of clear margins at final Sx,				
		91.2% GRT (ET for ER or PR +ve tumors), 8.8% (152/1723) non-GRT	91.2% GRT (ET for ER or PR +ve tumors), 8.8% (152/1723) non-GRT			4. ET for estrogen receptor (ER) or PR positive cases, and				
		93.9% GRT (CTx for node +ve, age < 65 years), 6.1% (37/608) non-GRT	93.9% GRT (CTx for node +ve, age < 65 years), 6.1% (37/608) non-GRT			5. CTx for node-positive patients aged less than 65 years				
	Jung 2019 <sup>67</sup>	46.2% GRT (HF-WBRT) (279/604); 17.2% (21/122) in 2008	46.2% GRT (HF-WBRT) (279/604); 17.2% (21/122) in 2008	Age, tumor size, grade, node status, remoteness	ASTRO 2010, Cancer Australia 2011, 2015	CPG criteria for HF-WBRT (HF-WBRT (>50 years NO tumor, no CTx indicated) defined as external beam RT, dose delivery of >2.0 Gy per fraction per day to the whole breast		HF-WBRT		
		56.3% GRT (36/64) in 2010	56.3% GRT (36/64) in 2010							
		31.8% GRT (42/132) in 2011	31.8% GRT (42/132) in 2011							
		53.0% GRT (80/151) in 2013	53.0% GRT (80/151) in 2013							
		74.1% GRT (100/135) in 2015	74.1% GRT (100/135) in 2015							
	Lomma 2020 <sup>68</sup>	HR-, HER2+, size > 10 mm or node positive: 100% GRT, males, 79% GRT, females (CTx, trastuzumab)	HR-, HER2+, size > 10 mm or node positive: 100% GRT, males, 79% GRT, females (CTx, trastuzumab)	Gender	NCCN 2018	NCCN 6 various treatment recommendations:	x		x	x
		HR+, HER2+, size 6–10 mm, node negative: 100% GRT, males, 81% GRT, females (ET ± CTx/trastuzumab)	HR+, HER2+, size 6–10 mm, node negative: 100% GRT, males, 81% GRT, females (ET ± CTx/trastuzumab)			1. HR negative (HR-), HER2+, size > 10 mm or node positive: CTx and trastuzumab				
		HR+, HER2+, size > 10 mm or node positive: 53% GRT, males, 62% (p = .296) GRT, females (CTx, trastuzumab + ET)	HR+, HER2+, size > 10 mm or node positive: 53% GRT, males, 62% (p = .296) GRT, females (CTx, trastuzumab + ET)			2. HR+, HER2+, size 6–10 mm, node negative: ET and/or CTx/trastuzumab				
		HR+, HER2-, node positive: 56% GRT, males, 64% (p = .021) GRT, females (CTx + hormonal)	HR+, HER2-, node positive: 56% GRT, males, 64% (p = .021) GRT, females (CTx + hormonal)			3. HR+, HER2+, size > 10 mm or node positive:				
		Triple negative, tumor ≤ 5 mm and node negative: 0% GRT, males, 36% GRT, females (no treatment)	Triple negative, tumor ≤ 5 mm and node negative: 0% GRT, males, 36% GRT, females (no treatment)			node positive:				
		Triple negative, > 10 mm or node positive: 50% GRT, males, 85% (p = .006) GRT, females (CTx)	Triple negative, > 10 mm or node positive: 50% GRT, males, 85% (p = .006) GRT, females (CTx)			CTx + trastuzumab + ET				
						4. HR+, HER2-, node positive: CTx + ET				
						5. Triple negative, tumor ≤ 5 mm and node negative: no treatment				
						6. Triple negative, > 10 mm or node positive: CTx				

(Continues)

TABLE 2 (Continued)

Cancer stream	Study	Overall adherence rate reported	Subgroup adherence rates	Predictors of GRT	CPG	CPG recommendations	Treatment types				
							CTx	RT	Sx	IMT	
DLBCL	Wong Doo 2019 <sup>69</sup>	58% GRT (830/1442) 35% GRT (323/624) in 2008 62% GRT (507/818) in 2012		Age, gender, smoking status, comorbidities, year of diagnosis, SES, treatment in a public hospital, metropolitan hospital	ESMO, NCCN	'R-CHOP 6–8 cycles ± RT, R-CHOP-like 68 cycles (including R-mini CHOP consisting of reduced doses of cyclophosphamide doxorubicin and prednisone as well as capping of vincristine, rituximab, cyclophosphamide, etoposide, vincristine, prednisone [R-CEOP] in which etoposide replaces doxorubicin and rituximab, cyclophosphamide, doxorubicin, etoposide, prednisone [R-CHEP] in which etoposide replaces vincristine), rituximab, hyper-fractionated cyclophosphamide, vincristine, doxorubicin, dexamethasone (R-hyperCVAD) 6 cycles, rituximab-dose adjusted etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin (R-DA-EPOCH) 6 cycles, rituximab, methotrexate, doxorubicin, cyclophosphamide, vincristine, prednisone, bleomycin (R-MACOPB) and rituximab, cyclophosphamide, doxorubicin, methotrexate alternating with ifosfamide, etoposide, cytarabine (R-CODOX-M/IVAC). If disease stage was I–II, optimal treatment could also include R-CHOP <sub>≥3</sub> cycles with RT.	x			x	
						Suboptimal treatment: R-CHOP or R-CHOP variants <9 cycles (other than stages I–II as described before), or any other CTx-immunotherapy regimen. <sup>69</sup>					

(Continues)

TABLE 2 (Continued)

Cancer stream	Study	Overall adherence rate reported	Subgroup adherence rates	Predictors of GRT	CPG	CPG recommendations	Treatment types			
							CTx	RT	Sx	IMT
ESHL	Roos 2017 <sup>70</sup>	100% GRT (54/54) (type of CTx)	NR	NR	eviQ protocol treatment	RT dose: favorable 20 Gy; unfavorable 30 Gy	x			
		87% GRT (47/54) (number of cycles of CTx)				RT volume: involved site				
		83% GRT (50/60) (RT dose)				Timing of RT: RT should commence between 3 and 6 weeks after the last dose of CTx				
		98% GRT (59/60) (RT volume)				CTx: favorable ABVDx2; unfavorable ABVDx4				
		100% GRT (54/54) (RT timing)								
Melanoma	Varey 2017 <sup>71</sup>	35% GRT (margin excision) Of the 65% non-GRT (margin excision); 45% were overtreated, 21% undertreated	Breslow thickness, caseload	NHMRC 1999		Initial performance of an excision biopsy with 2 mm clinical margins (to confirm the diagnosis) followed by a WLE at a second operation. Clinical surgical excision margins for the WLE (Breslow thickness, mm and CPG surgical margin, mm); in situ: 5 mm; >0–1.5; 10 mm; >1.5–4.0; 10–20 mm; >4.0; 20–30 mm <sup>71</sup>				x
Prostate	Freeman 2015 <sup>72</sup>	85% (176/207) GRT (guideline concordant treatment modality) 100% GRT (EBRT monotherapy and EBRT + HDR boost) 100% GRT (37/37)(WPRT) 94% GRT (98/104) of eligible high-risk cases (ADT) 56% GRT (5/9) of eligible high or intermediate risk cases (EBRT < 73.8 Gy + ADT) 95% GRT (58/61) high-risk monotherapy cases (long-term ADT) 96% GRT (198/207) (ADT): 91% GRT (87/96) high-risk 100% GRT (84/84) interm-risk 100% GRT (27/27) low risk	By risk group 100% GRT (27/27) low-risk cases (EBRT alone or LDR BT alone without ADT and without WPRT) 74% GRT (62/84) intermediate-risk cases 91% GRT (87/96) high-risk cases (EBRT alone or combined with HDR boost) RT dose guideline concordance 92% GRT (125/136) (EBRT monotherapy dose (73.8–81 Gy) alone; 95% high-risk, 91% intermediate-risk and 50% low-risk patients) 94% GRT (32/34) (EBRT dose of 40–50 Gy + HDR boost) 100% GRT (45/45) (LDR monotherapy; iodine-125 implants 145 Gy)	NR	NCCN 2014, eviQ 2009	Appropriate treatment modality option by risk group: High risk, EBRT with long term (2–3 years) concurrent ADT (or 4–6 months in presence of single high risk adverse feature) or EBRT + BT ± concurrent long term ADT and consider use of WPRT Intermediate risk: EBRT alone or EBRT + BT or EBRT + short term (3–8 months) concurrent ADT consider use of WPRT (NCCN only) Low risk: EBRT alone or BT alone Appropriate RT doses: EMBRT ± ADT: 73.8–81 Gy at 1.8–2.0 Gy/fraction (eviQ) if the EBRT monotherapy dose prescribed was <73.8 Gy, for high and intermediate risk patients, concurrent ADT was used (eviQ) EBRT + HDR boost: 40–50 Gy EBRT dose (NCCN)	x			x

(Continues)



TABLE 2 (Continued)

Lung cancer	Overall adherence rate reported	NSCLC treatment CPG adherence rate	SCLC treatment CPG adherence rate	Predictors of GRT	CPG	CPG recommendations	CTx	RT	Sx	ET	IMT
Conron 2007 <sup>65</sup>	NR	Stage I-IIIa NSCLC: 98% GRT (Macroscopically complete surgical resection) Stage IIIB NSCLC: 84% GRT (Completion of 60-Gy RT)	85% GRT (Thoracic RT with CTx)	NR	A.C.N. 2004	(A.C.N. 2004 continued) ECOG 3-4 NSCLC stage 1 best supportive care NSCLC stage II best supportive care with or without palliative RT to symptomatic sites ECOG 4 SCLC limited stage best supportive care SCLC extensive stage palliative RT to symptomatic sites <sup>54,56,58,65,102</sup>	x	x	x		X
Duggan 2016 <sup>118</sup>	66% GRT (389/592)	Stage I: 81% GRT (152/187) Stage II: 79% GRT (87/110) Stage IIIA: 60% GRT (102/171) Stage IIIB: 39% GRT (48/124)	NR	Age, birthplace, stage, ECOG, discussed by an MDT, SES	A.C.N. 2004		x	x	x		X
Whop 2017 <sup>58</sup>	28.6% GRT (57/199) 22.7% GRT of Indigenous cases; 36.4% GRT of non-Indigenous cases, $p = .04$	Localized NSCLC (stage I and II): 44.4% GRT Regional/distant NSCLC (stage IIIA and IIIB/IV): 24.2% GRT, $p < .01$	NR	Age, regional/distant, comorbidities	A.C.N. 2004		x	x	x		X
Vinod 2010 <sup>26</sup>	68% GRT (228/335) (RT); 60% (201/335) MDM Recommended 78% GRT (260/335) (CTx); 60% (200/335) MDM Recommended 9% GRT (29/335) MDM Recommended (Sx)	NR	NR	Age, stage, comorbidities	A.C.N. 2004; NCCAC nd; RRCOIN 1999; ACCPHSPC 2003; NCCN 2006		x	x	x		X
Wah 2020 <sup>57</sup>	60.36% GRT (2930/4854) NSCLC: GRT (2630/4467) SCLC: GRT (300/387)	Stage I-II: 74.41% GRT (756/1016); Sx only (49.7%) Sx + CTx (12.8%) SBRT only (7.68%) Sx + Conv RT + CTx (2.46%) Sx + Conv RT (1.77%) Stage III locally advanced NSCLC: 47.48% GRT (583/1228); Sx + CTx (7.82%) Conv RT + CTx (36.24%) Sx + Conv RT + CTx (3.42%) Stage IV NSCLC: 58.07% GRT (1291/2223); Conv RT + CTx (28.43%) CTx only (27.49%) Conv RT + CTx + Sx (.67%) CTx + Sx (1.48%)	Limited stage SCLC stage I-II: 63.12% GRT (89/141); Sx + CTx (1.42%) Conv RT + CTx (58.16%) Sx + Conv RT + CTx (3.55%) Extensive SCLC stage IV: 85.77% GRT (211/246); Conv RT + CTx (28.46%) CTx (57.32%)	Smoking status, stage, comorbidities, cancer site, ECOG, physician caseload, year of diagnosis, SES, treatment in private hospital	NCCN 2017	NSCLC: 1. Localized (stages I-II): Sx ± additional treatments and/or SBRT ± additional treatments 2. Locally advanced (stage III): Sx + CTx ± additional treatments and/or RT (any regimen) + CTx ± additional treatments 3. Advanced (stage IV): SCLC ± additional treatments 1. Limited (stages I-III): Sx + CTx ± additional treatments and/or RT (any regimen) + CTx ± additional treatments 2. Extensive (stage IV): Sx ± additional treatments <sup>57</sup>	x	x	x		X

(Continues)

TABLE 2 (Continued)

Cervical cancer	Overall adherence rate reported	Localized cervical cancer treatment CPG adherence rate	Regional/distant cervical cancer treatment CPG adherence rate	Predictors of GRT	CPG	CPG recommendations	CTx	RT	Sx	ET	IMT
Cervical cancer Whop2017 <sup>58</sup>	85.7% GRT (90/105)	93.3% GRT	75.6% GRT	Regional/distant tumor, race	GMCT 2009, NHMRC 2004	GMCT 2009 FIGO stage IA1: total hysterectomy, or conization, or modified radical hysterectomy + PL, or BT (depending on clinical indications) IA2: Modified radical hysterectomy + PL, or total hysterectomy + PL, or radical trachelectomy + PL, or radical RT (depending on clinical indications) IB1–IIA: modified Radical hysterectomy + PL, or Radical RT, or Radical hysterectomy + PL + Adj CTxRT, or pelvic RT, or Radical hysterectomy + PL + Adj CTxRT, or RT, or primary CTxRT, or Radical hysterectomy + PL ± Adj RT, or neo-Adj CT + radical hysterectomy + PL ± Adj RT/CTxRT, OR RT (depending on clinical indications) IIB1–IVA: CTxRT, or RT (depending on clinical indications) IVB: CTx, or RT or CTxRT (depending on clinical indications) <sup>60</sup>	X	X	X		
Cervical cancer By Indigenous Status	76.8% GRT, of eligible Indigenous cases; 95.9% GRT, of eligible non-Indigenous cases; $p < .01$										
Kang 2015 <sup>60</sup>	Adherence rates of GRT by FIGO stage	FIGO IA1: 74.0% GRT (.64–.83) FIGO IA2: 69.0% GRT (.41–.89) FIGO IB–IIA, non-bulky, not HR IB1: 68.0% GRT (.58–.77); FIGO subgroups: IB2: 100.0% GRT (.29–1.00); IIA: .0% GRT (.00–.00) FIGO IB–IIA, non-bulky, HR, good PS IB1: 69.0% GRT (.41–.89); FIGO subgroups: IB2: 0% GRT (.00–.00); IIA: .0% GRT (.00–.00) FIGO IB–IIA, non-bulky, HR, poor PS IB1: 69.0% GRT (.32–.84); FIGO subgroups: IB2: 0% GRT (.00–.00); IIA: .0% GRT (.00–.00)	FIGO IIB–IVA, good PS IIB: 63.0% GRT (.49–.76); FIGO subgroups: IIA: 50.0% GRT (.19–.81); IIB: 54.0% GRT (.34–.72) FIGO IVA: 33.0% GRT (.10–.65) FIGO IIB–IVA, poor PS IIB: 85.0% GRT (.72–.93); FIGO subgroups: IIA: 100.0% GRT (.69–1.00); IIB: 71.0% GRT (.51–.87); IVA: 67.0% GRT (.35–.90); FIGO IVB: 80.0% GRT (.28–.99)	NR	GMCT 2009		X	X	X		

(Continues)

TABLE 2 (Continued)

Cervical cancer	Overall adherence rate reported	Localized cervical cancer treatment CPG adherence rate	Regional/distant cervical cancer treatment CPG adherence rate	Predictors of GRT	CPG	CPG recommendations	CTx	RT	Sx	ET	IMT	
		FIGO IB- IIA, bulky, good PS IB1: 100.0% GRT (.29-1.00); FIGO subgroups: IB2: 74.0% GRT (.56-87); IIA: 43.0% GRT (.10-.82) FIGO IB- IIA, bulky, poor PS IB1: 100.0% GRT (.29-1.00); FIGO subgroups: IB2: 82.0% GRT (.65-.93); IIA: 57.0% GRT (.18-.90)		Age, stage, remoteness	NCCN 2015, ESMO 2010, JSGO 2007, SIGN 2008	FIGO stage IA1, IA2, conization, radical trachelectomy, or hysterectomy depending on pathological features IB1, IIA: Radical hysterectomy and pelvic lymph node dissection (radical trachelectomy acceptable if tumor <2 cm and no LVSI) IB1, IIA: RT if not receiving Sx I, IIA, and 2 lymph nodes positive IB2, IIB-IVA: Adj CTxRT IIB-IVA: CTxRT IB2, IIB-IVA: CTxRT with cisplatin IB2, IIB-IVA: CTxRT with OTT for RT <56 days IB2, IIB-IVA: CTxRT with EBRT and BT IB2, IIB-IVA: CTxRT with total RT dose and 80 Gy IA-IVB: Discussion of management by an MDI <sup>59</sup>	x	x	x	x	x	
Chiew 2017 <sup>59</sup>	54.1% GRT (72/133)	NR	NR	Caseload	NSW GOSG 2004	Adj monotherapy doses: LDR BT 50-60 Gy, HDR BT 30-40 Gy in 4-6 fractions. Combined modality treatment doses: 45-54 Gy EBRT in 1.8-2.0 Gy fractions with BT boost by LDR 20 Gy, or by HDR 15-18 Gy/2-4 fractions, EQD2 ( $\alpha/\beta = 10$ ) = 67-76 Gy <sup>61</sup>						
Thompson 2015 <sup>61</sup>	83% GRT (55/66) (Adj RT dose)	NR	NR									

(Continues)



TABLE 2 (Continued)

Colorectal cancer	Overall adherence rates	Colon cancer, stages A, B, C, and D treatment CPG adherence rate	Rectal cancer stages A, B, C, and D treatment CPG adherence rate	Predictors of GRT	CPG	CPG recommendations	CTx	RT	Sx	ET	IMT
CRC	Adelson 2018 <sup>62</sup>	NR	NR								
		60% GRT (n = 443/738) of eligible stage C (Dukes stage C) cases	Stage A: 45.8% GRT (363/792) Stage B: 7.3% GRT (131/351) Stage C: 52.6% GRT (232/441)	Age, stage, cancer site, remoteness	NHMRC 1999; ACN 2005	Postoperative CTx (colon cancer cases) Combined CTxRT Adj therapy (rectal cancer cases) or Adj or neo-Adj RT alone (rectal cancer cases)	x				
	Beckmann 2014 <sup>63</sup>	NR	NR								
		83.3% (2370/2979) of eligible cases received GRT ACP Stage A: 98.1% (524/526) Stage B: 97.0% (989/1011) Stage C: 59.8% (525/872) Stage D: 80.4% (352/438) cases	55.8% GRT (847/1662) Stage A: 94.4% (384/407) Stage B: 27.9% (119/427) Stage C: 37.4% (177/473) Stage D: 79.2% (167/211)	Age, gender, tumor grade and stage, comorbidities, cancer site, year of diagnosis, SES, area of residence	ACN 2005	Sx for stages A–C CRC (or local excision for low-grade stage A CRC) CTx for stage C colon, CTxRT for stages B and C rectal cancers Sx or CTx provided any time after diagnosis for stage D colon cancers Sx or RT provided at any time after diagnosis for stage D rectal cancers. Includes CTxRT for all Dukes' B including low risk <sup>63</sup>	x	x	x		
	Young 2007 <sup>65</sup>	NR	NR								
		Cases with low anterior resection or ultralow anterior resection: 29.1% GRT (169/581; 23.4%–35.5%) (colonic pouch reconstruction) Dukes' C cases who had Sx with curative intent: 76.0% offered GRT (367/483; 69.4%–81.6%) (Adj CTx or combined modality therapy)	T3 and T4 high-risk rectal cancer cases: 59.8% offered GRT (208/348); 52.4%–66.7% (Adj RT alone or as combined modality therapy) Fixed or tethered rectal cancer cases: 59.3% GRT (67/113; 47.4%–70.3%) (preoperative RT)	Age, gender, caseload, treated in a metropolitan hospital	NHMRC 1999	1. Colonic pouch reconstruction is recommended following resection of low rectal cancer 2. Patients with resected node-positive colon cancer should be offered Adj therapy 3. Combined modality therapy or RT is indicated for patients with high-risk rectal cancer 4. Preoperative RT is indicated for patients with fixed or tethered rectal cancer if it is felt that down-staging will enable successful resection Referral of a patient for Adj therapy (CTx or RT), or declined referral was also considered GRT. Other recommendations needed to be followed to be considered GRT					

(Continues)

**TABLE 2** (Continued)

Colorectal cancer	Overall adherence rates	Colon cancer, stages A, B, C, and D treatment CPG adherence rate	Rectal cancer stages A, B, C, and D treatment CPG adherence rate	CPG recommendations	CTx	RT	Sx	ET	IMT
McGrath 2004 <sup>64</sup>	NR	Node-positive (Dukes C/Stage III) 35.4% GRT (64.6%, n = 338 non-GRT) (TME)	35.4% GRT (64.6%, n = 338 non-GRT) (TME)	CPG NHMRC 1999	x		x		
		80.1% GRT (346/432)(CTx) cases:		CPG Predictors of GRT					

Abbreviations: ACCPHSPC, American College of Chest Physicians, Health and Science Policy Committee; ACN, Australian Cancer Network; Adj, adjuvant; ADT, androgen deprivation therapy; ASTRO, American Society for Radiation Oncology; BT, brachytherapy; Conv, conventional; CRC, colorectal cancer; CTx, chemotherapy; DLBCL, diffuse large B cell lymphoma; EBRT, external beam radiation therapy; EOG, Eastern Cooperative Oncology Group; ER, endocrine receptor status; ESHL, early-stage Hodgkin lymphoma; ESMO, European Society of Medical Oncology; ET, endocrine therapy or hormonal therapy; FIGO, International Federation of Obstetrics and Gynecology (Federation Internationale de Gynecologie et d'Obstetrique; GMCT, Greater Melbourne Clinical Taskforce; GOSG, NSW Gynecological Oncology Study Group; Gy, gray unit; HDR, high dose-rate; HER2, human epidermal growth factor receptor 2; HF-WBRT, hypofractionated whole-breast radiation therapy; HR, hormone receptor; IMT, immunotherapy or immune targeted therapy; Interm, intermediate; JSGO, Japan Society of Gynecologic Oncology; LDR, low-dose-rate; MIDM, multidisciplinary team meeting; MDT, multidisciplinary team; MRI, magnetic resonance imaging; NCCAC, National Collaborating Centre for Acute Care; NCCN, National Comprehensive Cancer Network; NHMRC, National Health and Medical Research Council; NSCLC, non-small cell lung cancer; OTT, overall treatment time; PL, pelvic lymphadenectomy; PR, progesterone receptor; RCRCOIN, The Royal College of Radiologists Clinical Oncology Information Network; RT, radiotherapy; SCLC, small cell lung cancer; SES, socioeconomic status; SIGN, Scottish Intercollegiate Guidelines Network; SLNB, sentinel lymph node biopsy; Sx, surgery; TME, total mesorectal excision; WLE, wide local excision; WPRT, whole pelvic RT.

patient gender in 5 studies (across breast cancer,<sup>68</sup> DLBCL,<sup>69</sup> lung cancer,<sup>57</sup> and CRC<sup>63,65</sup>), caseload in 4 studies (across melanoma,<sup>71</sup> lung cancer,<sup>57</sup> cervical cancer,<sup>61</sup> and CRC<sup>65</sup>), year of diagnosis in 4 studies (across breast cancer,<sup>66</sup> DLBCL,<sup>69</sup> lung cancer,<sup>57</sup> and CRC<sup>63</sup>), and SES reported in 4 studies (across DLBCL,<sup>69</sup> lung cancer,<sup>54,57,118</sup> and CRC<sup>63</sup>) (Table 4, Figure 3).

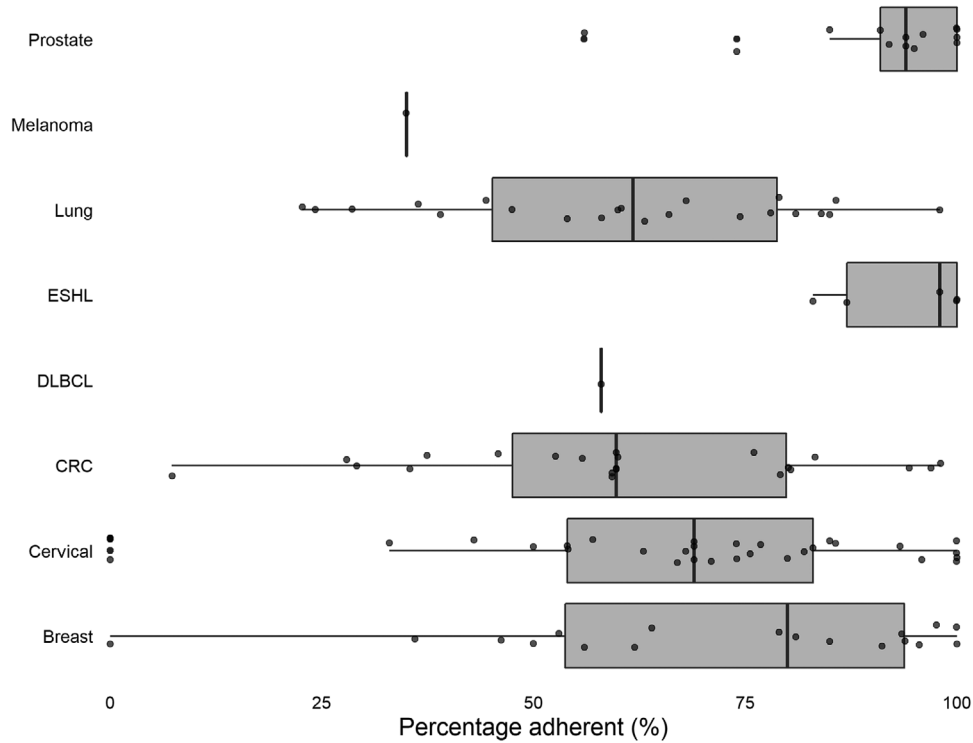
### 3.5.1 | Patient factors

Patient factors (age, gender, smoking status, birthplace, and Indigenous status) were significantly associated with DLBCL, CRC, breast, lung, and cervical cancer GRT (Figure 3, Additional file 6).

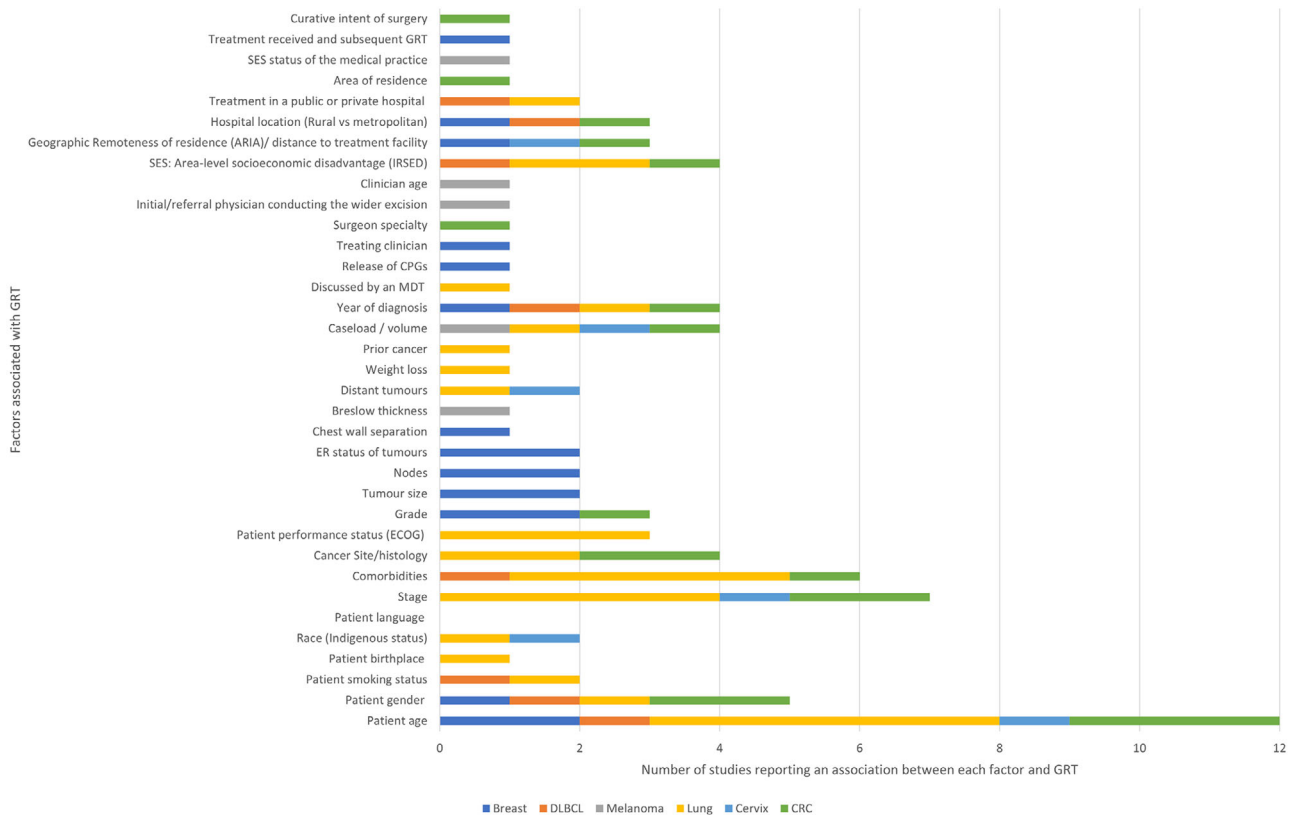
Patient age was associated with GRT across 12 studies, with younger patients more likely to receive GRT in 1 breast cancer study,<sup>66</sup> 1 DLBCL study,<sup>69</sup> 4 lung cancer studies,<sup>54,56,58</sup> and 3 CRC studies.<sup>62,63,65</sup> Patient gender was significantly associated with GRT in five studies. Female cases were significantly more likely to receive GRT in one breast cancer study,<sup>68</sup> and one lung cancer study,<sup>57</sup> whereas male DLBCL cases were more likely to receive GRT,<sup>69</sup> as were male stage C CRC cases,<sup>63</sup> and male high-risk rectal cancer cases GRT.<sup>65</sup> Ex-smokers, compared to people who never smoked, were less likely to receive GRT in one DLBCL study<sup>69</sup> and one lung cancer study.<sup>57</sup> Non-small cell lung cancer and cervical cancer cases who identified as Indigenous were significantly less likely to receive GRT in one study.<sup>58</sup>

### 3.5.2 | Health condition factors

Health condition factors (cancer stage, cancer site/histology, tumor size, node status, histologic grade, endocrine receptor [ER] status and Progesterone Receptor status, Chest Wall Separation Distance, Breslow thickness, distant tumors, comorbidities, ECOG status, weight loss, and prior cancer) were significantly associated with CRC, DLBCL, melanoma, breast, lung, and cervical cancer GRT (Figure 3, Additional file 6). More advanced stage cancer cases were significantly less likely to receive GRT in three lung cancer studies,<sup>54,57,118</sup> one cervical cancer study,<sup>59</sup> and one CRC study.<sup>63</sup> Cases with comorbidities were significantly less likely to receive GRT in one DLBCL study,<sup>69</sup> two lung cancer studies,<sup>57,58</sup> and one CRC study.<sup>63</sup> ECOG performance was significantly associated with GRT in three lung cancer studies. In two studies, cases with good-excellent ECOG performance status (0–1) were more likely to receive GRT than cases with borderline ECOG status (2), but less likely than cases with poor ECOG status (3–4).<sup>54,118</sup> In another study, cases with excellent ECOG (0) status were more likely to receive GRT than cases with a poorer ECOG status of ≥1 (good, borderline, or poor).<sup>57</sup>



**FIGURE 2** Overall and subgroup cancer treatment clinical practice guideline (CPG) adherence rates by cancer stream in Australia.



**FIGURE 3** Factors associated with guideline recommended treatment (GRT) across six cancer streams. [Colour figure can be viewed at wileyonlinelibrary.com]

**TABLE 3** Median clinical practice guideline (CPG) adherence rates across cancer streams

Cancer	No. studies <sup>a</sup>	No. with overall adherence estimate	Median overall adherence estimate	Range of overall adherence estimates	Ranges of subgroup adherence estimates
Breast	3	1	46.2% (HF-WBRT)	N/A	Male: 0%–100% Female: 36%–85%
Lung	6	4	57.18%	29%–66%	Localized NSCLC: 44%–98% Regional/distant NSCLC: 24%–84%
Cervical	4	3	83%	54%–86%	Localized: 0%–100% Regional/distant: 33%–100%
CRC	4	1	83% (colon) 56% (rectal)	N/A	Colon Stage C (Dukes' C): 60%–80% Rectal cancer Stage A: 46%–94% Stage B: 7%–28% Stage C: 37%–53%
Melanoma	1	1	35%	N/A	N/A
Prostate	1	1	85%	N/A	N/A
Lymphoma	2	1	58% (DLBCL)	58%; 83%–100%	DLBCL: 58% ESHL: 83%–100%

Abbreviations: CRC, colorectal cancer; ESHL, early-stage Hodgkin lymphoma; HF-WBRT, hypofractionated whole-breast radiation therapy; NSCLC, non-small cell lung cancer.

<sup>a</sup>One study reports adherence to lung and cervical cancer CPGs.

### 3.5.3 | Healthcare system and team factors

Healthcare system and team factors (caseload, year of diagnosis, being discussed by a multidisciplinary team meeting [MDM], release of CPGs, treating clinician, surgeon specialty, referral physician conducting the excision, and clinician age) were associated with CRC, breast, melanoma, lung, and cervical cancer GRT (Figure 3, Additional file 6).

Caseload was significantly associated with GRT in four studies, although there was no clear trend across cancers. In one melanoma study, cases treated by clinicians with lower caseload were significantly less likely to receive GRT,<sup>71</sup> and cervical cancer cases treated by gynecological BT departments with higher caseloads were more likely to receive GRT.<sup>61</sup> Lung cancer cases who were notified at higher volume hospitals were less likely to receive GRT,<sup>57</sup> and high-risk rectal cancer cases treated by surgeons with lower caseloads were more likely to receive GRT.<sup>65</sup> Rates of GRT increased over time in one breast cancer study,<sup>66</sup> one DLBCL,<sup>69</sup> and one lung cancer study.<sup>57</sup> Rates of GRT (CTx) for stage C colon cancer cases decreased overtime in one CRC study.<sup>63</sup>

### 3.5.4 | Socioeconomic factors and Medical factors

Socioeconomic factors (area-level socioeconomic disadvantage as measured by the Index of Relative Socioeconomic Disadvantage [IRSD], geographic remoteness of residence as measured by the Accessibility/Remoteness Index of Australia score [ARIA]/distance to treatment facility, treatment in a public or private hospital, hospital location [rural vs. metropolitan], area of residence and SES of the medical practice) were found to be significantly associated with CRC, melanoma, DLBCL, breast, lung, and cervical cancer GRT (Figure 3, Additional file 6). Medical Factors (treatment received, and curative intent of surgery [Sx]) were found to be associated with GRT in one breast cancer study<sup>67</sup> and one CRC study.<sup>65</sup>

Lung cancer cases from the fifth SES quintile group (the least disadvantaged) were more likely to receive GRT than cases from more disadvantaged areas.<sup>57,118</sup> This trend was not seen in other cancer streams; DLBCL cases from SES quintile 4 were more likely to receive GRT than those from fifth quintile group,<sup>69</sup> whereas cases with stages B and C rectal cancers from lower SES quintile groups (first, second, and third quintile groups) were more likely to receive GRT than the least disadvantaged group (fifth quintile).<sup>63</sup>

Stage C colon cancer patients who lived in areas of moderate accessibility (where access to services is significantly limited) were more likely to receive GRT than those in highly accessible areas.<sup>62</sup> Breast cancer cases who traveled greater distances to access treatment services (more than 50 km) were also more likely to receive GRT.<sup>67</sup> Conversely, cervical cancer cases who lived 5–10 km from their treatment facility were less likely to receive GRT than those living closer.<sup>59</sup>

The location of hospitals was significantly associated with GRT in three studies, with cases treated in rural facilities for breast cancer,<sup>66</sup> DLBCL,<sup>69</sup> or node-positive colon cancer,<sup>65</sup> being less likely to receive GRT (compared to those treated in metropolitan areas).

## 3.6 | Cancer GRT and patient survival rates

Of the 20 included studies, only six reported survival rates in relation to GRT; survival benefits were found for GRT in patients with DLBCL,<sup>69</sup> breast,<sup>66</sup> lung,<sup>54</sup> cervical,<sup>59</sup> and colon<sup>62</sup> cancer. Patients who received GRT had longer median survival times (lung<sup>118</sup> cancer) and improved 1- and 2-year survival rates (lung<sup>54</sup> cancer), 5-year survival rates (cervical<sup>59</sup> and colon<sup>62</sup> cancer), and 10-year survival rates (colon<sup>62</sup> cancer) (see Additional file 7).

**TABLE 4** Factors associated with guideline recommended treatment (GRT)

WHO five factors framework	Cancer stream	Cervical cancer															
		No. studies	Craft 2010 <sup>66</sup>	Breast Jung 2019 <sup>67</sup>	Breast Lomma 2020 <sup>68</sup>	DLBCL Wong Doo 2019 <sup>69</sup>	Melanoma Varey 2017 <sup>71</sup>	Lung Boxer 2016 <sup>54</sup>	Lung Duggan 2016 <sup>118</sup>	Lung Vlodavich 2010 <sup>56</sup>	Lung Wah 2020 <sup>57</sup>	Lung Whop 2017 <sup>58</sup>	Lung/cervical Chiew 2017 <sup>59</sup>	Thompson 2015 <sup>61</sup>	Adelson 2018 <sup>62</sup>	Beckmann 2014 <sup>63</sup>	CRC Young 2007 <sup>65</sup>
Patient factors	Patient age	12	Y	Y	-	Y	Y	Y	Y	Y	Y(L), NS(C)	Y	-	Y	Y	Y	Y
	Patient gender	5	-	-	Y	Y	NS	NS	-	Y	NS	-	-	NS	Y	Y	Y
	Patient smoking status	2	-	-	-	Y	-	-	-	Y	-	-	-	-	-	-	-
	Patient birthplace	1	-	-	-	NS	-	NS	-	-	-	NS	-	-	-	-	-
	Race (Indigenous status)	1	-	-	-	-	-	-	-	-	Y, Y	-	-	-	-	-	-
	Patient language	0	-	-	-	-	-	NS	-	-	-	-	-	-	-	-	-
Health condition factors	Stage	7	-	-	-	NS	-	Y	Y	Y	-	Y	-	Y	Y	Y	-
	Comorbidities	6	-	-	-	Y	-	Y	Y	Y	Y(L), NS(C)	-	-	-	-	Y	-
	Cancer Site/histology	4	-	-	-	-	-	NS	-	Y	-	-	-	-	Y	Y	-
	Patient performance status (ECOG)	3	-	-	-	-	-	Y	Y	Y	-	-	-	-	-	-	-
	Grade	3	Y	Y	-	-	-	-	-	-	-	-	-	-	-	Y	-
	Tumor size	2	Y	Y	-	-	-	-	-	-	-	-	-	-	-	-	-
	Nodes	2	Y	Y	-	-	-	-	-	-	-	-	-	-	-	-	-
	ER status of tumors	2	Y	Y	-	-	-	-	-	-	-	-	-	-	-	-	-
	Chest wall separation distance	1	-	Y	-	-	-	-	-	-	-	-	-	-	-	-	-
	Breslow thickness	1	-	-	-	-	-	Y	-	-	-	-	-	-	-	-	-
	Distant tumors	1	-	-	-	-	-	-	-	-	Y, Y	-	-	-	-	-	-
	Weight loss	1	-	-	-	-	-	-	Y	-	-	-	-	-	-	-	-
	Prior cancer	1	-	-	-	-	-	-	Y	Y	-	-	-	-	-	-	-
Healthcare system and team factors	Caseload/volume	4	-	-	-	-	-	Y	-	Y	-	-	Y	-	-	-	Y
	Year of diagnosis	4	Y	-	-	Y	-	NS	-	Y	-	-	-	NS	Y	-	-
	Discussed by an MDT	1	-	-	-	-	-	-	-	NS	-	-	-	-	-	-	-
	Release of CPGs	1	-	Y	-	-	-	-	-	-	-	-	-	-	-	-	-
	Treating clinician	1	-	Y	-	-	-	-	-	-	-	-	-	-	-	-	-
	Surgeon specialty	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	Y
	Initial/referral physician conducting the wider excision	1	-	-	-	-	-	Y	-	-	-	-	-	-	-	-	-
	Clinician age	1	-	-	-	-	Y	-	-	-	-	-	-	-	-	-	-

(Continues)

TABLE 4 (Continued)

WHO five factors framework	Cancer stream	Cervical cancer															
		No. studies	Craft	Breast Jung 2019 <sup>67</sup>	Breast Lomma 2020 <sup>68</sup>	DLBCL Wong Doo 2019 <sup>69</sup>	Melanoma Varey 2017 <sup>71</sup>	Lung Boxer 2016 <sup>54</sup>	Lung Duggan 2016 <sup>118</sup>	Lung V/inod 2010 <sup>56</sup>	Lung Wah 2020 <sup>57</sup>	Lung/cervical/Whop 2017 <sup>58</sup>	Chiew 2017 <sup>59</sup>	Thompson 2015 <sup>61</sup>	Adelson 2018 <sup>62</sup>	Beckmann 2014 <sup>63</sup>	CRC Young 2007 <sup>65</sup>
Socioeconomic factors	Area-level socioeconomic disadvantage (IRSED)	4	-	-	Y	-	-	Y	-	Y	NS	NS	-	-	Y	-	-
	Geographic remoteness of residence (ARIA)/distance to treatment facility	3	-	Y	-	-	-	-	-	NS	NS	Y	-	Y	-	-	-
	Hospital location (rural vs. metropolitan)	3	Y	-	-	Y	-	-	-	-	-	-	-	-	-	-	Y
	Treatment in a public or private hospital	2	-	-	-	Y	-	-	-	Y	-	-	-	-	-	-	-
	Area of residence	1	-	-	-	NS	-	-	-	-	-	-	-	-	NS	Y	-
	SES status of the medical practice	1	-	-	-	-	Y	-	-	-	-	-	-	-	-	-	-
Medical therapy factors	Treatment received and subsequent GRT	1	-	Y	-	-	-	-	-	-	-	-	-	-	-	-	-
	Curative intent of surgery	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	Y
	Cancer stream		Breast	Breast	Breast	DLBCL	Melanoma	Lung	Lung	Lung	Lung/cerv	Cervical	Cervical	CRC	CRC	CRC	CRC

Note: NS: not significantly associated with GRT; -: association between factor and GRT not reported.

Abbreviations: ARIA, Accessibility/Remoteness Index of Australia; CPG, clinical practice guideline; CRC, colorectal cancer; DLBCL, diffuse large B-cell lymphoma; ECOG, Eastern Cooperative Oncology Group; ER, endocrine receptor status; IRSED, Index of Relative Socioeconomic Disadvantage; MDT, multidisciplinary team; SES, socioeconomic status; WHO, World Health Organization.

## 4 | DISCUSSION

The implementation of evidence into practice is fundamental to enhance patient outcomes and efficiency of healthcare and research expenditure. This review demonstrates the large degree of adherence variability across active-cancer treatment CPG recommendations in Australia and characterizes the factors associated with GRT. GRT was associated with increased survival rates for patients with breast cancer,<sup>66</sup> DLBCL,<sup>69</sup> lung cancer,<sup>54,118</sup> cervical cancer,<sup>59</sup> and colon cancer.<sup>62</sup>

Of the 20 studies included in this review, 15 reported factors associated with CPG adherence across 6 cancer streams (breast, melanoma, DLBCL, lung, cervical, and CRC). GRT was higher for some characteristics (e.g., younger age, non-Indigenous status, never smoked, lower stage disease, no comorbidities, good-excellent compared to poor ECOG performance status, and treatment in metropolitan hospitals compared to rural hospitals). Some characteristics that were examined in two or more studies showed different patterns depending on the cancer. For example, female patients had higher GRT for breast and lung cancer, but lower for DLBCL and CRC; other characteristics that had mixed results included clinical caseload, patient SES, and distance traveled to access treatment.

Recent research has identified perceived barriers (such as outdated recommendations) and facilitators (such as multidisciplinary peer review) to cancer treatment CPG adherence in Australia,<sup>39</sup> and internationally,<sup>38</sup> and demonstrated that clinician adherence to CPGs is influenced by a multitude of factors, including the quality of CPG development, frequency of updates, patient, clinician and organizational factors, as well as dissemination, and implementation strategies.<sup>38,39,74</sup> These findings add texture by highlighting CPG adherence factors specific to various cancer streams, and in combination, these local contextual factors will inform cancer treatment CPG implementation strategies to address the barriers specific to CPG adherence in Australia, as guided by the Knowledge to Action framework<sup>75</sup> or other implementation frameworks.

Various factors associated with CPG adherence rates in this review are interrelated: patient age, cancer stage, presence of comorbidities, ECOG performance status, SES status, and geographical location of hospitals, and are discussed later in combination, due to the confounding nature of the variables. For example, the association between poorer rates of GRT and older age, advanced disease stage, comorbidities, and borderline ECOG status is supported by recent qualitative findings, which identified the clinician perception that patient age, frailty, and comorbidities were significant considerations when making treatment decisions.<sup>39</sup> This supports the need for further generation of real-world data<sup>76</sup> to build the evidence base to guide cancer treatments for older patients, those with later stage disease and comorbidities, in addition to the healthier and younger patients typically included in clinical trials.<sup>38</sup>

Low SES was associated with poor GRT in lung cancer<sup>57,118</sup>; however, the opposite was true for stages B and C rectal cancer patients, potentially as a result of patient preference, or clinical factors that influence treatment decisions.<sup>63</sup> The association between low SES and

poorer GRT for lung cancer is unsurprising given lower SES has been previously associated with limited access to curative Sx<sup>77</sup> and reduced cancer survival in Australia, despite universal healthcare coverage.<sup>77,78</sup> Patients with low SES also tend to have more comorbidities,<sup>77</sup> potentially limiting treatment options and CPG adherence. Poorer health literacy and education amongst lower SES groups also impact patient understanding of, and adherence to, cancer treatment.<sup>79</sup>

GRT was poorer for breast cancer cases,<sup>66</sup> DLBCL cases,<sup>69</sup> and CRC cases<sup>65</sup> treated in rural centers. Limited access to RT facilities as well as inadequate numbers of resident medical oncologists, radiation oncologists, and surgical oncologists may influence CPG adherence in non-metropolitan centers.<sup>80</sup> Patients with low SES are disproportionately located in rural areas in Australia,<sup>77</sup> resulting in increased distance to travel (and associated time and costs) to access healthcare.<sup>81</sup> Patient nonadherence as a result of travel burdens<sup>39</sup> may be addressed with further adoption of shared-care and telehealth technologies.<sup>82,83</sup> GRT was higher for colon cancer patients who lived in moderately accessible compared to highly accessible areas,<sup>62</sup> and for breast cancer patients who traveled more than 50 km to access treatment,<sup>67</sup> possibly as a result of subsidized travel programs supporting such patients to travel to major referral hospitals for treatment.<sup>62</sup> Given over a quarter of the Australian population (7 million people) live in rural and remote areas,<sup>84</sup> factors contributing to geographic variation in treatment and CPG adherence are important to consider.

Systematic considerations of equity during the development of CPGs will contribute to ensuring treatments are equitably provided to disadvantaged groups,<sup>85</sup> reducing the variation in adherence rates identified across low SES, rural, and older populations. In addition, multifaceted implementation and dissemination strategies that target clinicians treating disadvantaged populations may reduce barriers to CPG adoption and adherence and enhance delivery of evidence-based practice across these groups.

Use of patient navigators<sup>86</sup> may encourage tailored treatment plans to support patients' individualized needs and have previously been identified as a facilitator of cancer CPG adherence in Australia.<sup>39</sup> Other strategies that enhance CPG implementation by increasing clinician awareness and CPG uptake include education and opinion leaders,<sup>87</sup> CPG reminders, and audit and feedback of adherence rates,<sup>88,89</sup> particularly via Computerized Clinical Decision Support Systems (CDSSs) such as cancer therapy prescribing systems. In addition to enabling systematic audit and feedback processes, CDSSs are useful tools to support treatment decision-making and improve care and have been shown to improve adherence to cancer CPGs.<sup>90</sup> Further integration of CDSSs into local Australian systems would better enable systematic audits to provide feedback to hospitals and clinicians. These tailored CPG implementation strategies need to be feasible, and acceptable for use in the target populations, to increase uptake of CPGs.

The findings from this review advocate for the collection and inclusion of real-world evidence that reflect the patient population<sup>91</sup> to support CPG recommendations that cater for a broader range of patient complexities. Implementation strategies should be tailored to specific populations that experience high rates of CPG nonadherence such as older, rural, and low SES populations and incorporate the

wealth of implementation science knowledge as well as patient representation when developing, implementing, and disseminating cancer treatment CPGs.

#### 4.1 | Strengths and limitations

A strength of this review is the use of multiple reviewers to screen and assess studies, with generally strong interrater reliability scores. The main challenge of such reviews is the inconsistent definition of CPG adherence across the Australian studies included, with studies reporting CPG adherence rates, nonadherence rates, compliance with quality indicators, and receipt of GRT. Multiple cancer streams were included in this review, with a small number of studies in each stream. This provides an overview of trends in adherence rates and factors associated with adherence, across streams; however, the heterogeneity of results across studies indicated that it was inappropriate to conduct a meta-analysis. It should be noted that the factors reported to be adherent with GRT are limited by the factors investigated in the included Australian studies and are not an exhaustive list of factors associated with GRT. While only studies published in English were included, this is to be expected when assessing Australian data. This study contributes to the literature by characterizing the rates of adherence to cancer treatment CPGs across Australia, and mapping the factors associated with adherence across a variety of cancer streams, enabling more tailored approaches to CPG implementation that will help to overcome barriers to uptake.

#### AUTHOR CONTRIBUTIONS

Mia Bierbaum conceptualized the study and produced the first draft of the manuscript. Frances Rapport, Gaston Arnolda, Brona Nic Giolla Easpaig, Kristiana Ludlow, Yvonne Tran, and Jeffrey Braithwaite reviewed the study design and provided feedback, whereas Renuka Chittajallu provided clinical advice regarding the study findings. Mia Bierbaum and Gaston Arnolda devised the search strategy, which was carried out by Mia Bierbaum. Mia Bierbaum, in pairs with Frances Rapport, Gaston Arnolda, Brona Nic Giolla Easpaig, Kristiana Ludlow, Yvonne Tran, Robyn Clay-Williams, Elizabeth Austin, Bela Laginha, Chi Yhun Lo, Kate Churruca, Lieke van Baar, Karen Hutchinson, Renuka Chittajallu, Syeda Somyah Owais, Ruqaiya Nullwala, Diana Fajardo Pulido, and Peter Hibbert completed the review of abstracts. Mia Bierbaum carried out the full-text review, in pairs with Gaston Arnolda, Brona Nic Giolla Easpaig, Kristiana Ludlow, Yvonne Tran, Robyn Clay-Williams, Elizabeth Austin, Bela Laginha, Chi Yhun Lo, Kate Churruca, Lieke van Baar, Karen Hutchinson, Renuka Chittajallu, Syeda Somyah Owais, Ruqaiya Nullwala, Diana Fajardo Pulido, and Peter Hibbert. Mia Bierbaum designed the data extraction template and completed data extraction, with data extraction from a five study sample validated by Syeda Somyah Owais. Mia Bierbaum and Syeda Somyah Owais completed the quality assessment of included articles. All authors contributed to revisions of subsequent drafts of the manuscript and approved the final submission.

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#### CONFLICT OF INTEREST STATEMENT

The authors declare that they have no conflict of interests.

#### DATA AVAILABILITY STATEMENT

All data is presented in the tables and additional files.

#### ETHICS STATEMENT

No ethics approval was sought for this systematic review.

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### SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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