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What you see depends on where you sit: the effect of geographical location on web-searching for systematic reviews: A case study.

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Background

There is limited guidance on how to web-search in systematic reviews and concern relates to the reproducibility of searches using search engines such as Google. The aim of this paper is to address one potential source of variation in Google searches: does the geographical location of a researcher affect Google search returns?

Methods

Using a virtual private network, we ran the same web-search for the medical technology Dasatinib in twelve different countries. Two researchers independently extracted the search returns by country organised by page rank.

We compared:

C1. any difference in the items returned by Google searches between countries; and C2. any difference in the page rank of items returned between countries.

Findings

Searches were undertaken on Monday September 28th 2020. From 12 countries, 43 items were identified.

For C1: 19 items were common to all 12 countries. Twenty-four items were missed by searches in some countries. This means that there were differences in search returns between countries.

For C2: a randomised trial reported by Raddich *et al.* was the first search return for all countries. All other items, common to all countries, varied in their page-rank.

Conclusions

We find that geographic location would appear to influence Google search returns based on the findings of this case study.

The findings suggest that recording the location of the researcher undertaking web-searching may now be an important factor to report alongside detail on steps taken to minimise personalisation of web-searches covered by recent guidance. This finding also has implications for stopping-rules.

Background

Guidance indicates that web-searching should form part of a composite search for studies and study data when undertaking a systematic review.¹ There is limited guidance on how to web-search in systematic reviews, compared with the guidance available on how to search bibliographic databases, and conducting and documenting web searches presents specific challenges.¹⁻⁹

One potential concern relates to the reproducibility of searches using search engines such as Google.⁹⁻¹¹ That is, unlike database searches, web searches may return different results depending on the user, such that the search process is not fully reproducible.^{1,9-13} While this issue is widely recognised in theory, and some studies indicate it is a real concern,¹⁴ detailed data on the extent of the variation are lacking.^{9,12,13}

The aim of this paper is to address one potential source of variation in Google searches, namely geographical location. If running searches in different locations returns different results, this could have implications not only for searching, but also on the processing and reporting of web-searches in systematic reviews.

The lens we use to examine the hypothesis is that of a web-search for a single medical technology. This is not because we anticipate web-searching to be a key search method in reviews of medical technologies.¹⁵ Rather, the focus on a medical technology is pragmatic. To test the hypothesis, we need a well-defined intervention which is consistently described and reported, and used globally, such that we could expect to identify search returns in different countries.

Research question

Does the geographical location of a researcher affect Google search returns when undertaking a web-search for a medical technology?

Methods

Searches

As a case study, we utilised a review of Dasatinib for patients with chronic myeloid leukemia.¹⁶ A search strategy based on the searches undertaken for that review (written by the lead author of this paper) was developed, taking the following form:^{7,16,17}

((Dasatinib OR DasatinibTM OR Sprycel OR SprycelTM OR "X78UG0A0RN" OR "302962-49-8")) "(RANDOM)"

Searches were undertaken using Google.Com on a PC (Windows 10, 64-bit) using the Chrome browser (version 85.0.4183.121). As with the original review, we attempted to limit our searches to studies reporting randomised trials or systematic reviews including randomised trials.¹⁸ This was done by using the Royle and Waugh brief RCT search strategy (the BRSS), specifically the term "Random".¹⁹⁻²¹ A Virtual Private Network (VPN) was used to mimic the effect of geographic location. The VPN was SurfShark²² with an extension for Google Chrome (version 2.1.4). No restrictions were placed on the searches (e.g. date or language). Cookies were cleared before each search and the same computer was used each time. The searcher (TL) was not logged into a Google account at the time of the searches.

Selecting countries

We selected countries pragmatically using the Nature Index (2019) list of countries by research output.²³ The sampling frame comprised the 12 highest countries in the Nature list for which a server was available in SurfShark, viz.:

- 1. Australia;
- 2. Canada;
- 3. France;
- 4. Germany;
- 5. India;
- 6. Italy;
- 7. Japan;
- 8. South Korea;
- 9. Spain;
- 10. Sweden;
- 11. the USA; and
- 12. UK;

Data extraction

The following data were extracted from all items returned by each of the 12 countries searched:

- Item type (i.e. study, systematic review etc.); and
- Item identifier (citation detail) and description (description of the item).

Data extraction was undertaken by one researcher and checked by another. Data were extracted into Microsoft Excel, organised by country and by page rank.

Analysis

To determine if the geographic location of a researcher influences Google search returns, we compared:

1. Any difference in the items returned by Google searches between countries. This comparison allows us to asses if a researcher's location influences search returns.

2. Any difference in the page rank of items returned between countries. This may be relevant as some guidance suggests that only the first few pages of search returns need be assessed for inclusion,^{24,25} so page rank may influence whether items are included or not.

Findings

Results of the searches

Searches were undertaken on Monday September 28th 2020. From 12 countries, 43 items were identified in total across the searches (see Table 1: characteristics of items). The number of search returns varied between countries with the highest number of search returns being 22 (Canada) and the lowest being 19 (France/Japan). Eleven categories of items were identified

by the searches, namely: study reports, systematic reviews, protocols for systematic reviews, guidelines, reports, theses, wikis, web-pages, R Coding sheets, Web-hosted databases, and books.

Results of the analysis

Comparison 1: any difference in the items returned by Google searches between countries

Figure 1 summarises the search returns by country with their associated page rank. 19 items were common to all 12 countries, namely:

- two study reports (Raddich *et al.* reported as two items^{26,27} and Cortes *et al.* DASISION reported as two items);^{28,29}
- three systematic reviews (Douxfils *et al.* reported as two items;^{30,31} Pavey *et al.* reported as three items;^{16,18,32} and Tang *et al.* reported as one item);³³
- one protocol for a systematic review (Balakumaran *et al.*);³⁴
- one guideline (De Souza *et al.* reported as four items);³⁵⁻³⁸
- the Wikipedia page for Dasatinib;³⁹ and
- three books (Gunderson LL and Tepper JE;⁴⁰ Hehlmann R;⁴¹ and Weissleder *et al*.:⁴² all reported as single items).

Twenty-four items were missed by searches in some countries. This means that there were differences in search returns between countries.

Comparison 2: any difference in the page rank of items returned between countries Figure 1 also details the difference between items in page rank between countries. The randomised trial reported by Raddich *et al.* was consistently the first search return for all 12 countries.²⁶ All other items, common to all countries, varied in their page rank. This means that, aside from Raddich *et al.*, there was variation in the reporting of items by page rank between countries.

Discussion

The findings indicate that the geographical location of a researcher influenced Google search returns when undertaking a web-search for a systematic review of a medical technology in this case study. We also found the distribution of search returns varied by country. This aligns with and confirms previous work which has raised concerns about the role of web-searching in systematic reviews.¹⁰ That is, whilst it is possible to be systematic in searching (i.e. you can search using a search strategy defined *a priori* and transparently report your searches), it is not possible to replicate exactly search findings since these would appear to vary between countries.

Further research may examine other sources of variation, such as different users in the same location, the effect of non-English language search terms prioritising or excluding search returns by country, or the use of other search engines. We also see a space for further research to explore the influence of our findings in reviews which do utilise web-searching to identify studies, evidence or data, not available in bibliographic databases.^{2,43-45} This is likely where the value of web-searching is to be found and where a problem may arise. Further work could examine if the effect we have identified here applies in other types of systematic review and if the effect we identify could be turned to be an advantage in study identification.^{2,15}

We see two implications for practice:

1. Stopping-rules: 'the first 100 search returns were screened'⁴⁶

Stopping-rules, that is when to stop searching or – in the case of web-searches – when to stop scrolling through search returns, are sometimes used by researchers to describe their approach to processing web-searches.⁴⁷⁻⁴⁹ Our findings might suggest a problem. Using the example above, there is no guarantee that the first 100 search returns seen in one country are the same as in another and the order of search returns may vary such that eligible results may be within 100 results in one country but not in another. There is no obvious solution beyond reporting the geographic location of the researcher (see below). Reporting stopping rules may still be useful (even if arbitrary) since, at the very least, it explains how the researchers conducted their web-search.

2. Search reporting

It may be desirable to record the geographic location of the researcher undertaking websearches (alongside other search data and steps to reduce personalisation of data).^{9,50} Researcher location is not currently a requirement of relevant search reporting and, as we find in this case-study, it may be an influencing factor in study identification.^{5,50,51}

Conclusions

Based on the findings of this case study, we find that geographic location would appear to influence Google search returns when searching for a single medical technology.

The implications for practice appear to focus on stopping rules and search reporting. Researchers should be aware that search results appear to vary by country and this may affect the use of informal stopping rules. Our findings also suggest that recording the location of the researcher undertaking web-searching may now be an important factor to report alongside detail on steps taken to minimise personalisation of web-searches covered by recent guidance.

Highlights

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• What is already known

Web-searching is recommended as a non-database search method in systematic reviews but there is concern as to the reproducibility of searches using web-search engines.

What is new

We critique the method of web-searching, finding that geographical location can affect search returns using the web-browser Google. We also found that the number of search returns and the order of search returns varies by country which may impact stopping rules.

Potential impact for *Research Synthesis Methods* readers outside the authors' field

- Researchers undertaking or reading systematic reviews which utilise websearching should be aware that the search returns and page rank appear to vary by country. This could impact identification of relevant items and inform stopping rules.
- Researchers undertaking web-searches should report their geographical location, alongside other search data.

Data sharing statement

All data relied upon is reported in the paper.

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82YzsAhXJUhUIHRe0A2IQ6AEwAHoECAEQAQ#v=onepage&q=%22CASE%20STUDY %205%20(Continued)%20the%20saturated%20concentration%20of%20dasatinib%20at%20 pH%204.0%20was%203.6%20%22&f=false. [Accessed October 7th 2020.]

Table 1: Characteristics of items

Item type	Item identifier/ description	Version(s) identified	In which countries $(X^2 = page rank)$	Overall, was the item missed in any countries?
Study	 Radich JP, Kopecky KJ, Appelbaum FR, et al. A randomized trial of dasatinib 100 mg versus imatinib 400 mg in newly diagnosed chronic-phase chronic myeloid leukemia. Study report of the phase IIb trial (NCT00070499) comparing Dasatinib v Imatinib. 	 PubMed Abstract of the study reported in the journal, <i>Blood</i>.²⁶ ResearchGate profile for the published study.²⁷ 	AU:1 CA:1 FR:1 GE:1 I:1 IN:1 JA:1 S:1 SK:1 SP:1 UK:1 USA:1 AU:7 CA:7 FR:2 GE:2 I:2 IN:3 JA:2 S:2 SK:2 SP:2	No
Study	Cortes JE, Jiang Q, Wang J, et al. Dasatinib vs. imatinib in patients with chronic myeloid leukemia in chronic phase (CML-CP) who have not achieved an optimal response to 3 months of imatinib therapy: the DASCERN randomized study	3. ResearchGate profile for the published study. ⁵²	UK:11 USA:9 AU:19 FR:3 GE:3 I:3 IN:4 JA:3 S:3 SK:3 SP:3 UK:12	Canada USA
Study	Cortes JE, Saglio G, Kantarjian HM, et al. Final 5-Year Study Results of DASISION: The Dasatinib Versus Imatinib Study in Treatment-Naïve Chronic Myeloid Leukemia Patients Trial. Study report of the phase 3 DASISION study (NCT00481247)	 4. Study reported on journal web- page (<i>Journal of</i> <i>Clinical</i> <i>Oncology</i>).²⁹ 5. Bibliographic record from PubMed ²⁸ 	AU:26 FR:16 GE:21 I:18 IN:19 JA:19 S:17 SK:19 SP:18 UK:16 CA:2 USA:2	No
Study	Adam Olshen, Min Tang, Jorge Cortes, et al. Dynamics of chronic myeloid leukemia response to dasatinib, nilotinib, and high-dose imatinib.	6. Study reported on journal web- page (<i>Haematologica</i>). ⁵³	GE:22 I:19 S:18 USA:20	Australia Canada France India Japan South Korea Sweden UK
Study	Karaman MW, Herrgard S, Treiber DK, et al. A quantitative analysis of kinase inhibitor selectivity.	7. Link to the PDF version of the published study reported in <i>Nature</i>	AU:15 GE:16 UK:13 USA:7	Canada France India Italy

Item type	Item identifier/ description	Version(s) identified	In which countries $(X^2 = page rank)$	Overall, was the item missed in any countries?
	Study explores how Kinase inhibitors (e.g. Dasatinib) interact with the human kinome.	<i>Biotechnology</i> via Friends of Cancer.org web- site. ⁵⁴		Japan South Korea Spain Sweden
Study	 Krijanovski Y, Donato N, Sun H, et al. Dasatinib Resistance in Patients with Chronic Myelogenous Leukemia: Identification of a Novel bcr-abl Kinase Domain Mutation. Study re-analyses bcr-abl kinase domain from 22 CML patients who demonstrated clinical evidence of dasatinib failure to assess the potential mechanisms of Dasatinib resistance. 	8. Study reported on journal web- page (<i>Clinical</i> <i>Leukemia</i>). ⁵⁵	FR:17 GE:20 I:21 JA:17 SK:18 SP:19	Australia Canada India Sweden UK USA
Study	Shah NP, Guilhot F, Cortes JE, et al. Long-term outcome with dasatinib after imatinib failure in chronic-phase chronic myeloid leukemia: follow-up of a phase 3 study. Long-term follow-up of a Dasatinib patients with imatinib- resistant/-intolerant chronic myeloid leukemia (CML).	9. Study reported on journal web- page (<i>Blood</i>). ⁵⁶	CA:17 USA:17	Australia France Germany India Italy Japan South Korea Spain Sweden UK
Study	 Fornier MN, Morris PG, Abbruzzi A, et al. A phase I study of dasatinib and weekly paclitaxel for metastatic breast cancer. A phase I study of Dasatinib and weekly paclitaxel for metastatic breast cancer. 	10. Study reported on journal web- page (Annals of Oncology). ⁵⁷	FR:18 JA:16 SK:16 SP:20	Australia Canada Germany India Italy Sweden UK USA
Study	Hausner et al (2016) Search appendix to Prospective comparison of search strategies for systematic reviews: an objective approach yielded higher sensitivity than a conceptual one	11. Appendix of study. ⁵⁸	S:12	Australia Canada France Germany India Italy

Item type	Item identifier/ description	Version(s) identified	In which countries $(X^2 = page rank)$	Overall, was the item missed in any countries?
				Japan South Korea Spain UK USA
Systematic Review	Douxfils J, Haguet H, Mullier F, Chatelain C, Graux C, Dogné J-M. Association Between BCR-ABL Tyrosine Kinase Inhibitors for Chronic Myeloid Leukemia and Cardiovascular Events, Major Molecular Response, and Overall Survival: A Systematic Review and Meta-analysis Systematic review and meta-analysis to assess the risk of vascular occlusive events in patients with CML treated by new generations of TKIs and provide an overall assessment of the clinical benefit.	12. Review reported on journal web-page (<i>JAMA</i> <i>Oncology</i>). ³⁰ 13. web-page linking to the PDF annex of the review. ³¹	AU:10 CA:8 FR:5 GE:6 I:6 IN:9 JA:5 S:5 SK:7 SP:5 AU:4 CA:3 FR:4 GE:5 I:5 IN:5 JA:4 S:4 SK:4 SP:4 UK:5 USA:3	No
Systematic Review	Pavey T, Hoyle M, Ciani O, et al. Dasatinib, nilotinib and standard-dose imatinib for the first-line treatment of chronic myeloid leukaemia: systematic reviews and economic analyses.	14. Link to PDF download of the NIHR library version of the review. ¹⁶	UK:7	No
	PenIAG Health Technology Assessment Report	15. University of Queensland repository version. ¹⁸	AU:3 CA:12 FR:10 GE:12 I:14 IN:11 JA:10 S:10 SK:11 SP:15 UK:10 USA:8	
		16. Link to PDF download of the technical annex to item 14. ³²	AU:8 CA:9 FR:9 GE:9 I:9 IN:10 JA:8 S:7 SK:10 SP:11 UK:4 USA:10	
Systematic Review	Tang L, Zhang H, Peng YZ, et al. Comparative efficacy and tolerability of front-line treatments for newly diagnosed chronic-phase chronic myeloid leukemia: an update network meta-analysis.	17. Link to the PDF version of the published review reported in <i>BMC</i> <i>Cancer</i> . ³³	AU:25 CA:20 FR:19 I:20 IN:20 JA:18 S:19 SK:5 SP:21 UK:15 USA:19	Germany

Item type	Item identifier/ description	Version(s) identified	In which countries $(X^2 = page rank)$	Overall, was the item missed in any countries?
	Systematic review and meta-analyses of multiple treatments for direct and indirect evidence of efficacy and tolerability for patients with newly diagnosed CML.			
Protocol	Rossi RE, Pozzi R, Gonzalez-Lorenzo M, et al. Tyrosine kinase inhibitors for unresectable hepatocellular carcinoma in adults. <i>Cochrane systematic review of tyrosine kinase inhibitors</i> <i>for unresectable hepatocellular carcinoma in adults.</i>	18. Appendix (searches) to the protocol. ⁵⁹	CA:22 IN:22 UK:20 USA:21	Australia France Germany Italy Japan South Korea Spain Sweden
Protocol	 Balakumaran J, Birk T, Golemiec B, et al. Evaluating the endometabolic and bone health effects of Tyrosine Kinase Inhibitors in Chronic Myeloid Leukaemia: a systematic review protocol. Protocol for a systematic review to investigate the endometabolic and bone health effects of TKI therapy in CML 	19. PDF of the protocol reported in BMJ Open. ³⁴	AU:6 CA:5 FR:6 GE:7 I:7 IN:6 JA:6 S:6 SK:6 SP:7 UK:3 USA:5	No
Guideline	De Souza <i>et al.</i> Brazilian Medical Association Guideline Guideline for diagnosis and treatment of Chronic myeloid leukemia (CML).	20. repository copy. ³⁶ 21. copy from SciELO. ³⁵ 22. PDF of page 67 of the technical annex to item 11. ³⁸	FR:7 SP:6 UK:8 AU:12 FR:11 GE:11 I:8 IN:8 JA:9 S:8 SK:9 SP:10 AU:13 I:11 IN:12 JA:7 SK:8 SP:8 USA:11	No
		23. PDF of page 68 of the technical annex to item 11. ³⁷	AU:14 CA:10 GE:8 I:10 IN:14 USA:12	
Report	Canadian Agency for Drugs and Technologies in Health. Pruning Emtree: Does Focusing Embase Subject Headings Impact Search Strategy Precision and Sensitivity?	24. PDF of main report. ⁶⁰	CA:11	Australia France Germany India Italy

Item type	Item identifier/ description	Version(s) identified	In which countries $(X^2 = page rank)$	Overall, was the item missed in any countries?
	Report which examines the impact of focusing controlled indexing headings in Emtree (Embase)			Japan South Korea Spain Sweden UK USA
Report	Gemeinsamer Bundesausschuss (GbA). Kriterien zur Bestimmung der zweckmäßigen Vergleichstherapie undRecherche und Synopse der Evidenz zur Bestimmung der zweckmäßigen Vergleichstherapie nach § 35a SGB VVorgang: 2017-B-226 Bosutinib. 2017. Federal Joint Committee (GbA). Document describes which drugs are approved for CML in Germany and reports a search to identify potential comparators and a summary of identified literature.	25. PDF report. ⁶¹	GE:4	Australia Canada France India Italy Japan South Korea Spain Sweden UK USA
Report	European Medicines Agency. Sprycel: EPAR - Product Information. European Medicines Agency EPAR for Dasatinib (Sprycel)	26. Annex 1 (Summary of product characteristics). ⁶²	FR:8 GE:18 I:16 IN:17 JA:11 S:11 SK:20 SP:9 UK:14	Australia Canada USA
Theses	Benjamin Gregory Carlisle: Appendices to The moral efficiency of clinical trials in anti-cancer drug development Appendices to P.hD thesis of Benjamin Gregory Carlisle (2019)	27. Appendices to the thesis. ⁶³	AU:21 CA:16 GE:19 I:17 IN:18 SK:17 SP:17 USA:13	Australia Canada Germany India Italy South Korea Spain USA
Theses	Liu Lu: in Vitro Investigation Of Intracellular Ponatinib Transport And Modeling Ponatinib Resistance In BCR,ABL1+ Cell Lines: Implications For Therapeutic Strategies <i>P.hD thesis of Liu Lu (2015)</i>	28. PDF copy of thesis from University of Adelaide Repository. ⁶⁴	AU:11	Canada France Germany India Italy Japan South Korea

Item type	Item identifier/ description	Version(s) identified	In which countries (X^2 = page rank)	Overall, was the item missed in any countries? Spain Sweden UK USA
Wiki	Dasatinib (Better Known as: Sprycel) Wiki for detail on and mechanism of action for Dasatinib.	29. wiki. Last updated 2017. ⁶⁵	CA:19	Australia France Germany India Italy Japan South Korea Spain Sweden UK USA
Wiki	Dasatinib (Sprycel): Wiki A wiki for Dasatinib (Sprycel) by Hemonc.org	30. wiki. Last updated Feb 2020. ⁶⁶	CA:21 USA:18	Australia France Germany India Italy Japan South Korea Spain Sweden UK
Web-page	MEDSAFE (New Zealand Medicines and Medical Devises Safety Authority) Data Sheet (Sprycel) (2019) Data sheet for the drug Dasatinib (Sprycel). Lists doses and clinical particulars.	31.67	AU:23	Canada France Germany India Italy Japan South Korea Spain Sweden UK USA

Accepted Article

Item type	Item identifier/ description	Version(s) identified	In which countries $(X^2 = page rank)$	Overall, was the item missed in any countries?
Web-page	Dasatinib Wikipedia page	32. Updated 2020. ³⁹	AU:5 CA:4 FR:15 GE:10 I:4 IN:2 JA:15 S:13 SK:15 SP:16 UK:6 USA:4	No
Web-page	Sprycel 20mg, 50mg, 80mg, 100mg and 140mg Film Coated Tablets <i>The electronic medicines compendium (emc) page for</i> <i>Sprycel</i>	33. main item. ⁶⁸	S:20 UK:2	Australia Canada France Germany India Italy Japan South Korea Spain USA
Web-page	Sprycel 50mg Film Coated Tablets The electronic medicines compendium (emc) Page for Sprycel 50mg film coated	34. main item. ⁶⁹	IN:21	Australia Canada France Germany Italy Japan South Korea Spain Sweden UK USA
R Coding sheets	NPARC_workflow.Rmd for Dorothee Childs Coding sheet for analysis for Non-Parametric Analysis of Thermal Proteome Profiles Reveals Novel Drug-Binding Proteins	35.70	GE:17	Australia Canada France India Italy Japan South Korea Spain Sweden UK USA

Item type	Item identifier/ description	Version(s) identified	In which countries $(X^2 = page rank)$	Overall, was the item missed in any countries?
R Coding sheets	Coding sheet for R analyses (R/pRRophetic.R) Coding sheet for R analyses Multi-Omics integration and VIsualization in Cancer Subtyping	36.71	AU:22 CA:18	France Germany India Italy Japan South Korea Spain Sweden UK USA
Web-page	AUSTRALIAN PRODUCT INFORMATION– SPRYCEL®(DASATINIB) Web-page of clinical data for Sprycel from meidcines.gov.au	37.72	AU:2	Canada France Germany India Italy Japan South Korea Spain Sweden UK USA
Web-page	PBS: Dasatinib, tablets, 20 mg, 50 mg, 70 mg and 100 mg, Sprycel® - July 2011 The Pharmacutical Benefits Scheme guidance for Dasatinib (2011)	38.73	AU:20	Canada France Germany India Italy Japan South Korea Spain Sweden UK USA
Web- hosted database	Science.gov Gateway to U.S. Federal Science Search returns for the Cortes study from the Science.gov database.	39. Main database search returns for the Cortes study. ⁷⁴	AU:9 CA:6 IN:7 S:9 UK:9 USA:6	France Germany Italy Japan South Korea

Item type	Item identifier/ description	Version(s) identified	In which countries $(X^2 = page rank)$	Overall, was the item missed in any countries?
				Spain
Book	Clinical Radiation Oncology: Expert Consult Gunderson LL, Tepper JE. Clinical Radiation Oncology: Expert Consult. (2011)	40. Main. ⁴⁰	AU:24	Canada France Germany India Italy Japan South Korea Spain Sweden UK USA
Book	Chronic Myeloid Leukemia (Hematologic Malignancies) Hehlmann R. Chronic Myeloid Leukemia (Hematologic Malignancies) (2016)	41. Main. ⁴¹	AU:18 CA:15 FR:14 GE:15 I:15 IN:16 JA:14 S:16 SK:14 SP:14 UK:19 USA:16	No
Book	Water-Insoluble Drug Formulation Liu R. Water-Insoluble Drug Formulation. 3rd ed (2018)	42. Main. ⁷⁵	AU:16 CA:13 FR:12 GE:13 I:12 IN:13 JA:12 S:14 SK:12 SP:12 UK:17 USA:14	No
Book	Molecular Imaging: Principles and Practice Ralph Weissleder, Brian D. Ross, Alnawaz Rehemtulla, Sanjiv S. Gambhir. Molecular Imaging: Principles and Practice. (2010)	43. Main. ⁴²	AU:17 CA:14 FR:13 GE:14 I:13 IN:15 JA:13 S:15 SK:13 SP:13 UK:18 USA:15	No

Key: Australia = AU; Canada CA; France FR; Germany = GE; Italy = I; India = IN; Japan = JA; Sweden = S; South Korea = SK; Spain = SP; United Kingdom = UK; and United Stated of America = USA. X2 = page rank of the item returned, for example GE9 indicated the item was the 9th returned from the searches in Germany.

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SPA	17	10	8	4	32	15	41	43	42	16	21	26	22	19	20	12	13	3	2	1
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SWED		33	17	4	41	43	42	32	11	26	15	39	21	16	19	12	13	3	2	1
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18 IND	34	17	4	20	41	43	23	42	22	15	16	12	21	39	19	13	3	2	32	1
ITA	8	17	6	27	26	41	15	43	42	22	23	16	21	19	12	13	32	3	2	1
• GERMA	4	8	27	35 26	7 25	41	43	42	15	21	32	16	23	19	12	13	25	3	2	1
FRAN			17	0 10	4	32	41	43	42	21	15	16	26	20	19	12	13	3	2	1
¹⁸ CANA	30	17	29	36	27	41	43	42	15	24	23	16	12	2	39	19	32	13	5	1
36 31 40 17 4	27	38	3	22 41	42	7	23	22	21	28	12	39	16	2	19	32	13	15	37	1

FIGURE 1 a) Search returns by country and page rank

Figure 1a search returns by country and page rank

b) Key: items and identified versions

17

1 2

Radich JP, Kopecky KJ, Appelbaum FR, et al. A randomized trial of dasatinib 100 mg versus imatinib 400 mg in newly diagnosed chronic-phase chronic myeloid leukemia.

3

Cortes JE, Jiang Q, Wang J, et al. Dasatinib vs. imatinib in patients with chronic myeloid leukemia in chronic phase (CML-CP) who have not achieved an optimal response to 3 months of imatinib therapy: the DASCERN randomized study

4 5

Cortes JE, Saglio G, Kantarijan HM, et al. Final 5-Year Study Results of DASISION: The Dasatinib Versus Imatinib Study in Treatment-Naïve Chronic Myeloid Leukemia Patients Trial.

6

Adam Olshen, Min Tang, Jorge Cortes, et al. Dynamics of chronic myeloid leukemia response to dasatinib, nilotinib, and high-dose imatinib.

7

Karaman MW, Herrgard S, Treiber DK, et al. A quantitative analysis of kinase inhibitor selectivity.

8

Krijanovski Y, Donato N, Sun H, et al. Dasatinib Resistance in Patients with Chronic Myelogenous Leutkemia: Identification of a Novel bcr-abl Kinase Domain Mutation.

9

Shah NP, Guilhot F, Cortes JE, et al. Long-term outcome with dasatinib after imatinib failure in chronic-phase chronic myeloid leukemia: follow-up of a phase 3 study.

10

Fornier MN, Morris PG, Abbruzzi A, et al. A phase I study of dasatinib and weekly paclitaxel for metastatic breast cancer.

11

Hausner et al (2016) Search appendix to Prospective comparison of search strategies for systematic reviews: an objective approach yielded higher sensitivity than a conceptual one

12 13

Downfis J. Haguet H, Mullier F, Chatelain C, Graux C, Dogné J-M. Association Between BCR-ABL Tyrosine Kinase Inhibitors for Chronic Myeloid Leukemia and Cardiovascular Events, Major Molecular Response, and Overall Survival: A systematic Review and Meta-analysis

14 15 16

Pavey T, Hoyle M, Ciani O, et al. Dasatinib, nilotinib and standard-dose imatinib for the first-line treatment of chronic myeloid leukaemia: systematic reviews and economic analyses.

Tang L, Zhang H, Peng YZ, et al. Comparative efficacy and tolerability of front-line treatments for newly diagnosed chronic-phase chronic myeloid leukemia: an update network meta-analysis. 18

Rossi RE, Pozzi R, Gonzalez-Lorenzo M, et al. Tyrosine kinase inhibitors for unresectable hepatocellular carcinoma in adults. 19

Balakumaran J. Birk T, Golemiec B, et al. Evaluating the endometabolic and bone health effects of Tyrosine Kinase Inhibitors in Chronic Myeloid Leukaemia: a systematic review protocol.

20 21 23

De Souza et al. Brazilian Medical Association Guideline

24

Canadian Agency for Drugs and Technologies in Health. Pruning Emtree: Does Focusing Embase Subject Headings Impact Search Strategy Precision and Sensitivity?

25

Gemeinsamer Bundesausschuss (GbA). Kriterien zur Bestimmung der zweckmäßigen Vergleichstherapie und Recherche und Synopse der Evidenz zur Bestimmung der zweckmäßigen Vergleichstherapie nach § 35a SGB V Vorgang: 2017-B-226 Bosutinib. 2017. 26

European Medicines Agency. Sprycel: EPAR - Product Information. 27

Benjamin Gregory Carlisle: Appendices to the moral efficiency of clinical trials in anti-cancer drug development

28

Liu Lu: in Vitro Investigation Of Intracellular Ponatinib Transport And Modeling Ponatinib Resistance In BCR,ABL1+ Cell Lines: Implications For Therapeutic Strategies

29

Dasatinib (Better Known as: Sprycel) 30 Dasatinib (Sprycel): Wiki

31

MEDSAFE (New Zealand Medicines and Medical Devices Safety Authority) Data Sheet (Sprycel) (2019)

32 Dasatinib Wikipedia page

33

Sprycel 20mg, 50mg, 80mg, 100mg and 140mg Film Coated Tablets

34

Sprycel 50mg Film Coated Tablets

35 NPARC_workflow.Rmd for Dorothee Childs

36 Coding sheet for R analyses (R/pRRophetic.R)

37 AUSTRALIAN PRODUCT INFORMATION-SPRYCEL® (DASATINIB)

38

PBS: Dasatinib, tablets, 20 mg, 50 mg, 70 mg and 100 mg, Sprycel® - July 2011

39 Science.gov Gateway to U.S. Federal Science

40 Clinical Radiation Oncology: Expert Consult

41 Chronic Myeloid Leukemia (Hematologic Malignancies

42 Water-Insoluble Drug Formulation

43 Molecular Imaging: Principles and Practice

Figure 1b key: items and identifed versions

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