Availability and use of number needed to treat (NNT) based decision aids for pharmaceutical interventions

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ABSTRACT

Background: The number needed to treat (NNT) is a medical statistic used to gauge the efficacy of therapeutic interventions. The versatility of this absolute effect measure has allowed its use in the formulation of many decision aids to support patients and practitioners in making informed healthcare choices. With the rising number of tools available to health professionals, this review synthesizes what is known of the current NNT-based tools which depict the efficacy of pharmaceutical interventions.

Objective(s): To explore the current spectrum of NNT-based decision aids accessible to health professionals with a focus on the potential utility of these devices by pharmacist practitioners.

Methods: A literature review was performed in MEDLINE, CINAHL, Web of Science, PsychINFO and Cochrane Library (CENTRAL, Cochrane Database of Systematic Reviews and the Cochrane Methodology Register) for studies published between January 1st 2000 and August 29th 2019. The language was restricted to English unless an appropriate translation existed. Studies that reported NNT-based decision aids of pharmaceutical or therapeutic interventions were included. One author performed study selection and data extraction.

Results: A total of 365 records were identified, of which 19 NNT-based tools met the eligibility criteria, comprising of 8 tool databases and 11 individual decision aids. Decision aids appeared in multiple forms: databases, pictograms, graphs, interactive applications, calculators and charts. All aids were accessible online with a printer-friendly option, and very few came at a cost (e.g. requiring a subscription or access fee). The main tool innovators were the United Kingdom (UK) and United States (US), with English being the language of choice.

Conclusions: Evidence that NNT-based decision aids can contribute to greater satisfaction and involvement of patients in medical decision making is limited and inconclusive. A case for the utilization of these tools by pharmacists has yet to be fully examined in the medical research. NNT tools may provide a valuable resource to upskill pharmacists in communication of research evidence.

Contents

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Introduction

Risks are routinely reported in the scientific literature as measures of treatment effect or harm. They are crucial in highlighting the benefit of one treatment over another or determining whether treatment at all is a viable option.[1] Proficiency in understanding and relaying these concepts is fundamental in the intersectional model of patient care; integrating evidence-based medicine (EBM), communication skills, and shared decision making (Fig. 1).[2]

The *number needed to treat,* or 'NNT' is a 'simple numerical' measure of risk generally used to assess the efficacy of therapeutic interventions producing binary outcomes.[3] It denotes the number of subjects who would need to be treated with an intervention (e.g., drug, therapy, surgery) over a defined time period for one patient to achieve treatment success.[4] This is compared to a control intervention or placebo.[5,6] A NNT of 9 means that 9 patients need to undergo therapy (e.g., topical antibiotics) over a specific time frame (e.g., 2–5 days) in order for 1 patient to receive the treatment benefit (e.g., cure of bacterial conjunctivitis), as opposed placebo.[7]

Originally described by Laupacis et al. (1988) in the landmark paper addressing clinically applicable measures of treatment consequences, the NNT was formulated to assist clinicians in deciphering the often abstruse clinical results of randomized controlled trials (RCTs) that form the basis of therapeutic comparisons.[8,9] Among other statistical measures it was determined most able to (i) compare the consequences of intervention versus no action; (ii) gauge the potential for harms or adverse events associated with interventions; and (iii) allow a measure or comparison of the treatment methods, where the repercussions of one intervention in the diagnosis, treatment or prevention of the condition(s) may be weighed against other interventions.[8] The NNT better enables clinicians and their patients to discuss treatment options and focus efforts where needed.[8,9]

The effects of new medications or therapies assessed in literature often involve dichotomous outcomes (e.g., survival vs. death). Such outcomes can be refined into NNTs with relative ease instead of continuous measures (e.g., blood glucose levels).[10] NNTs are absolute effect measures and can be used interchangeably with *numbers needed to benefit* (NNTBs).[11] A more contemporary term, the *number unnecessarily treated* (NUT) represents the inverse of the NNT and depicts the number of patients who do not receive any treatment benefit.[12] When extended to toxicity or adverse events, the *number needed to harm* (NNH or NNTH) quantifies the number of patients who need to receive an intervention for one patient to obtain a harmful outcome.[13,14] The *number needed to screen* (NNS or NNTS) is another convention that extends to the number of patients needed to screen in order to prevent one adverse event or death.[15]

Calculating NNT

Often studies reporting NNT are accompanied by other statistical terms (e.g., event rates, absolute risk reductions (ARR), relative risk reductions (RRR), risk ratios (RR), odds ratios (OR), etc.), which are further explained in other sources.[1,10,16,17] It is calculated by the taking the reciprocal of the ARR ($\frac{1}{ARR}$) and by convention is rounded up to the nearest whole number.[1] More detailed guides on calculating NNT have been produced by multiple authors (Appendix A).[1,16,17]

Interpreting NNTs and NNHs

NNT and NNH data can be framed differently according to the author's preference. The metrics are expressed in the literature in a multitude of ways, such as:

- an absolute value or whole number e.g., "NNTB = x"
- a simple frequency e.g., "1 in x", "x in 100" or "x in n"[18]
- a comparative measure, e.g., "x more patients will benefit" or "x fewer patients will benefit"
- pictographic depictions

The value should always be accompanied by a > 95% confidence interval (CI) or *p*-value for statistical significance and a time frame to conclude the short or long term benefits of treatments.[18,19] Confidence intervals are calculated around a point estimate of the result giving a range between which the true value exists.[20] In contrast to *p*-values which can only indicate the strength of the observed result, CIs are markers of precision.[20] A wide CI indicates an imprecise outcome that warrants caution upon interpretation regardless of the statistical significance.[20]

The NNT and NNH should be considered together when evaluating treatment.[21] An ideal intervention treating short-term or symptomatic outcomes would have a single-digit NNT for efficacy (fewer people need intervention for one to reap treatment benefit) and a double-digit or higher NNH for adverse outcomes (more patients need intervention for one to be
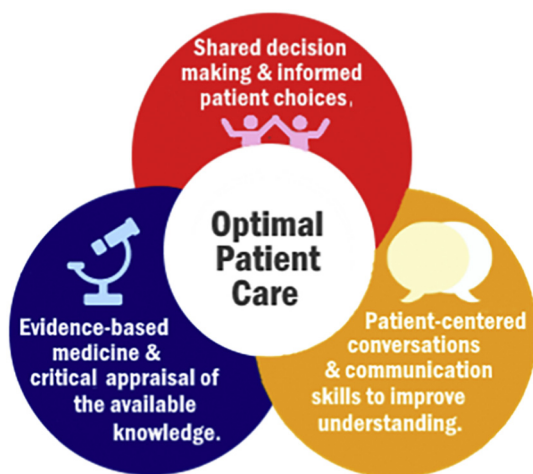

Fig. 1. Intersectional model of patient care. The triad of optimal patient care: EBM, shared decision making, and communication *(Adapted from Hoffman, 2014).*

Table 1

Pros and Cons of NNT.

Pros	Cons
• Arguably basic calculation method.[28] • Useful summary measure for controlled trials and meta-analyses.[28] • Absolute measures are more accurate than relative measures at portraying risk differences.[26] • Clearly demonstrates benefits (NNTs) and risks (NNHs) of treatments.[29] • Can be transformed easily into images/pictograms/graphs or charts.[30] • Expresses benefits/risks with or without treatment. • Facilitates simplistic economic considerations for care in cost-benefit analysis.[31]	• Relies on complete reporting of RCT cohort data (e.g., ratios, confidence intervals, or *p*-values). • Should be adjusted to account for individual patients' treatment duration and baseline characteristics.[28] • Trials must be conducted appropriately with adequate sample sizes.[32] • Deals only with dichotomous outcomes.[10] • Some variances in calculation method across sources.[29] • Clinical meaning of an NNT is subject to interpretation.[28] • The external validity of any trial will also determine whether an NNT is suitable for reflection upon any one patient.[6]

The advantages and disadvantages of statistical analysis using NNT.

harmed); it suggests that the intervention is well tolerated.[22] For example, the NNT with acupuncture for 50% reduction of tension-type headache frequency was 3, and the NNH with acupuncture for patient withdrawal due to adverse events was 416.[23] This implies that acupuncture treatment for 3 months may be more beneficial than routine care (e.g., pharmacological, cognitive, physical interventions or no treatment) in the same time-frame for relieving tension-type headaches.[23] Where the outcome is severe, for example mortality, a higher NNT may be acceptable.[24] The NNTs for antihypertensives range from 1157 in healthy younger women to 17 in high-risk older males to prevent 1 death over 5 years, where the NNT may be lowered further by longer treatment durations.[24] This is the case for many long-term or preventative therapies where clinicians may accept a higher NNT for treatments averting hard outcomes (e.g., cardiovascular death, cancer survival, stroke), which may improve prognosis over greater lengths of time.

Using NNT to describe treatment benefits has several strengths and flaws, which are listed in Table 1. Absolute risk reductions (ARRs) used to generate NNTs measure the difference in risk (i.e., probability of an outcome) between subjects of the control and experimental groups of any controlled trial.[25] They differ from relative risk reductions (RRRs), which express the risk difference between the aforementioned groups as a proportion of the risk in the control group.[25] Most RCTs preferentially report relative risk reductions (RRRs), which are more likely to prompt positive responses to therapy, with values perceived to be much more impressive (Fig. 2).[26] A 4-year trial comparing orlistat 120 mg vs. placebo for prevention of type 2 diabetes in obese patients reported a RRR of 37.3%, corresponding to an ARR of 2.8%.[27] The more remarkable 37.3% rather than the seemingly insignificant 2.8% (NNT 36) is more likely to be quoted in
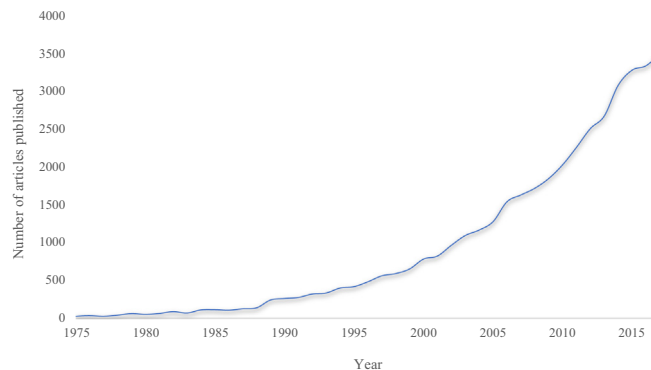

Fig. 3. NNT in MEDLINE. The number of articles quoting 'number needed to treat' in the titles or abstracts of articles in MEDLINE from 1975 to 2016 *(Adapted from Corlan, 2004).*

marketing campaigns to drive pharmaceutical sales for orlistat. Thus, the use of RRRs can be misleading, with NNT presenting a truer depiction of experimental results as a comprehensible whole number.

NNT in the literature

The medical literature has seen an upsurge in the utilization of NNT to describe the results of therapy trials, evident in the near exponential trend in the appearance of 'number needed to treat' in the titles and abstracts of articles in MEDLINE from 1975 to 2016 (Fig. 3).[33] This continual increase of NNT reporting in the literature can be attributed to the increasing need for meta-analyses to pool the best available evidence for therapies and the adoption of NNT into numerous guidelines.[34] The metric is noted in the Consolidated Standards of Reporting Trials (CONSORT) Statement, where the 'NNT' is considered as a valuable indicator of the likelihood of help or harm an intervention entails.[5,35] It also appears in the Cochrane Handbook for Systematic Reviews of Interventions as the preferred method for interpreting dichotomous outcome data.[36] The frequency of its reporting suggests that this measure has become more known to researchers over the last 33 years of its existence as a reliable way of representing therapeutic benefit.

Gaps in NNT understanding

There remains a gap in the understanding of the NNT by both patients and practitioners. A systematic review that quantitatively assessed patients' expectations of the benefits and/or harms of therapeutic interventions found that participants were more inclined to overestimate the benefits and underestimate the harms of medical tests and procedures.[37] To assist
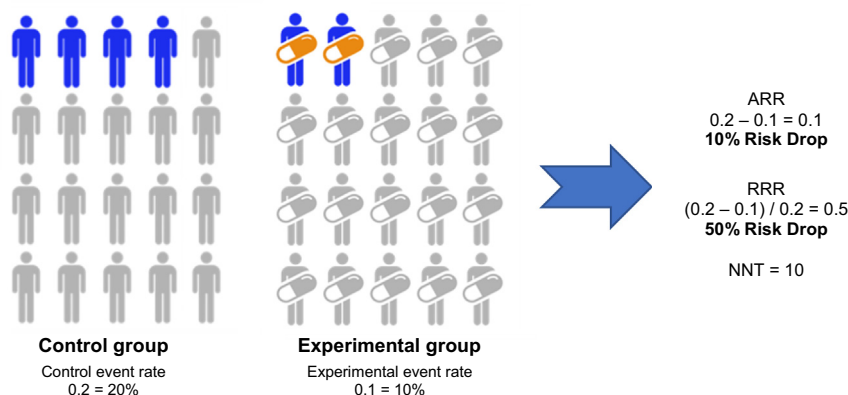

Fig. 2. ARRs vs. RRRs. Hypothetical example of a study including 40 patients: 20 in the control (unexposed) group and 20 in the experimental (exposed) group. The absolute risk reduction (ARR) was 10% compared to a relative risk reduction (RRR) of 50% *(Adapted from Gosall and Gosall, 2015).*

patients in understanding the benefits and harms of therapies, health professionals should first understand risk and communicate it effectively.[38] It is unclear whether pharmacists are proficient in comprehending and delivering quantitative evidence, as most studies utilize medical practitioners.[39,40] A study of physicians' understanding of rates of the benefits and harms of common medical interventions showed that most participants tended to overestimate the benefits (79%) and harms (66%) of treatments.[39] Number sense has been observed to be generally poor among medical trainees[40] where numeracy is rarely addressed even among evidence-based curricula.[41] Furthermore, health professionals may, without continual practice, experience a decline in their number skills and hence their ability to effectively communicate quantitative information.[38] This appears to be the case even when clinicians have a firm grasp of numeracy, where expressing numerical evidence in ways patients or colleagues can comprehend is challenging.[39] In 2 independent studies, only 32.5–33% of physicians were confident in their ability to communicate numerical data to patients.[39,42]

Utilization of up-to-date, accurate, and balanced decision aids created and reviewed regularly by true experts may enhance both clinician and patient understanding of treatment effects.[43] Current evidence sees uncommon utilization of such tools with few incorporated into electronic medical records.[39,44] Krouss et al. found that 93% of physicians indicated they would use a website or app for ARR, RRR, and/or NNT information, indicating positive attitudes towards accessing further resources to advance medical risk understanding.[39]

Decision aids

While the benefit of the NNT being an absolute measure extends to increased accuracy of reiterating treatment effects, the measure is yet to be understood completely.[45] Studies assessing patients' or physicians' understanding of an NNT typically frame the measure as a simple statement; none of which have investigated the use of decision aids or tools to communicate NNTs or NNHs. Decision aids are defined by the International Patient Aids Standards (IPDAS) Collaboration as paper-based (e.g., pictographs) or software (e.g., electronic calculators) tools which assist persons in participating in health care options.[46] They provide evidence-based estimates of the benefits and risks of different options and help patients 'personalize information, appreciate the scientific uncertainties inherent in that choice, and clarify the personal value they associate with different features of the options'.[46] Decision aids have clinically demonstrated the effect of enhancing patient knowledge, feelings of acknowledgment, and inclusivity in making decisions.[47] There is little literature describing methods to improve number sense in health professionals. Thus, the utilization of NNT tools may provide both a learning opportunity and accessory to better relaying NNT to patients regarding treatment options.

To the best of our knowledge, no reviews have been conducted on NNT-based decision aids. Therefore, this review aimed to critically appraise, synthesize and present existing guidelines, tools, and decision aids that utilize NNT to compare pharmaceutical interventions.

Methods

A review was performed to condense, map and summarize the available NNT-based decision aids in a tabular format. This review was conducted following the Preferred Reporting Items for Systematic reviews and Meta-Analyses statement for Searching (PRISMA-S).

Search strategy

The following online databases were searched with validation by a health liaison and a supervising author (MB): Scopus, MEDLINE, CINAHL, Web of Science, PsychINFO, and Cochrane Library (CENTRAL, Cochrane Database of Systematic Reviews, and the Cochrane Methodology Register). Boolean operators and truncations were employed to produce the initial 'search term' that was then systematically inputted into each database,

"('communicate risk' OR 'communicating risk' OR 'shared decision*' OR 'clinical decision*' OR 'health literacy' OR 'risk educat*') AND (patient* OR consumer OR pharmac*) AND ('number needed to treat' OR 'NNT' OR 'number needed to harm' OR 'NNH')." Only English texts published between January 1, 2000, and August 19, 2019, were searched and considered.

Study selection

The author independently screened the titles and abstracts of all studies identified from the search, and those not meeting the inclusion criteria were excluded. The full texts of the remaining articles were then screened and appraised by CN with validation by another author, MB. A computer record of the excluded studies was retained using the EndNote X9 software. Bibliographic mining of selected studies was conducted by scanning the citations of major studies. Any ambiguity regarding study selection was clarified with a supervisory panel.

To be included in this review, studies or articles had to describe or report print or software NNT-based decision aids for pharmaceutical interventions. In addition, studies had to report the use or availability of decision support tools that synthesized evidence relating to medicinal goods or products using the NNT as a treatment benefit perception parameter. There was no restriction on the study design in this review. Studies that did not depict NNT-based decision aids or tools were excluded. A narrative synthesis was conducted due to the heterogeneity of the methods and presentation of results.

Data extraction

A predefined data extraction form was composed to extract and present the study characteristics, which included: first author, year of publication, country of study, name of NNT tool, accessibility of tool (e.g., form, fee, language), framing of the NNT (e.g., 'x in n'), relevant characteristics (e.g., patient or practitioner interface, pictograph inclusion, design features) and limitations (e.g., patient individualization, medical jargon, disease-specificity, requiring clinical parameters). One reviewer extracted the research data, which was checked by a second supervising reviewer independently. Discrepancies were resolved via discussion.

Results

Search results

The electronic search identified 348 potentially relevant articles in addition to 17 studies linked to the reference lists of the included studies. Following duplicate deletion and review of the titles and abstracts, 92 articles were selected for full-text review. Ultimately, 19 articles met the inclusion criteria and were incorporated in the narrative synthesis. A flowchart of the literature search is shown in Fig. 4.

Summary of the results of the included studies

Various NNT decision aids ranging from single disease-specific infographics, generic tool databases, online NNT, and risk/benefit calculators, all presenting research evidence from RCTs and systematic reviews (SRs), were detailed in the literature. Tools that were a constituent of a larger database containing greater than 5 tools were grouped as "NNT Tool Databases" (Table 2). Tools that existed either singularly or as part of a platform providing access to less than or equal to 5 NNT tools were categorized under "NNT Tools" (Table 3). The current NNT tools come in many forms: databases, pictograms, graphs, interactive applications, calculators, and charts.[30] All aids were accessible online with a printer-friendly option, and very few came at a cost (e.g., requiring a subscription or access fee). The majority of NNT tools (n = 17) expressed both the NNT and NNH in the presentation of treatment outcomes: benefits and harms.
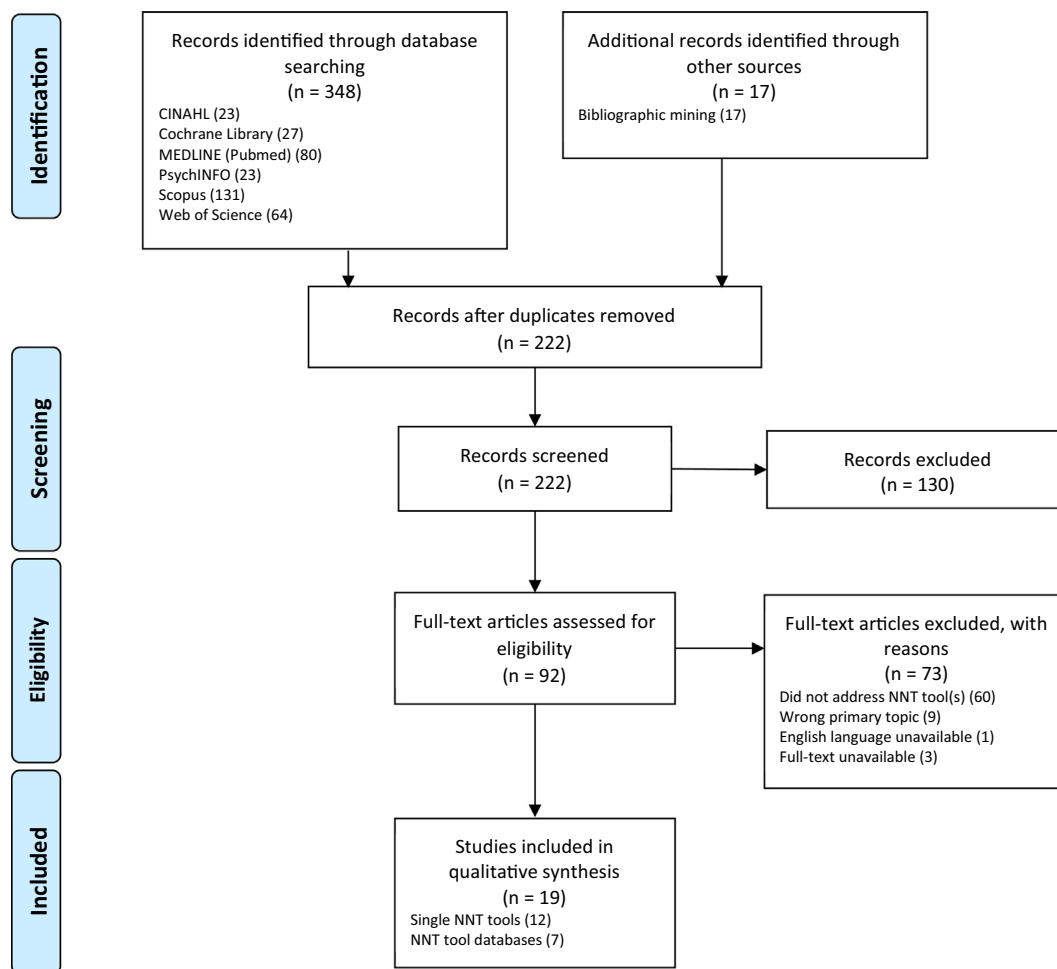
Fig. 4. PRISMA flowchart on the selection strategy of eligible articles.

Many tools (n = 14) also used a shared interface where patients and practitioners were generated the same view. Other aids (n = 5) boasted a separate patient and practitioner view setting with more complex and evidence-centered formatting suited to the more informed clinician. There were also options for 'patient individualization' where users could input individual patient data (i.e., age, sex, gender, smoking status, diabetes status, cholesterol levels, etc.), which would then allow some tools (n = 10) to generate the patient or subject a personalized decision aid specific to the entries made. The primary language captured by the aids was English, with some tools offering translations in Spanish, Arabic, Chinese, French, and Dutch.

Discussion

This review aimed to provide an overview and comparison of the availability of NNT-based decision aids accessible to either health professionals or consumers. Most aids were produced for either an American or European audience; the major innovators of NNT tools being the United States (US) and United Kingdom (UK). The market for NNT decision aids is in its infancy, and thus there is room for growth in territory that has been relatively unexplored. Some tools, including but not limited to the Absolute CVD Risk/Benefit Calculator,[74] COMPASS Decision Aid,[79] and the numerous Mayo Clinic Decision Aids[66,72,73,77,81] (Table 3), allowed for patient individualization. There is potential inaccuracy in applying an NNT to an audience who are unlike the trial participants from which the NNT was derived (differing baseline characteristics).[29] In such cases, NNT tools that take into consideration patients' clinical parameters allow for the selection of the most applicable studies and generation of an aid where individual patients'

potential outcomes are more accurately represented.[18] Other tools which provide no method for patient individualization can still be used effectively, provided that appropriate caution is taken to assess a patient's baseline characteristics against those of the associated study from which the aid is derived.[18]

The development of new NNT tools using clinical research data more generalizable to different populations may present an opportunity to better health outcomes by improving practitioner and patient understanding of the risks and benefits of treatment options. A potential barrier may stem from the general dearth of high-quality reporting of RCT data to facilitate clear communication of treatment outcomes with patients.[84] Despite the availability of guidelines such as the CONSORT statement, a review of a sample of RCTs published within the past two decades in leading surgical and medical journals found only 5 of 88 articles mentioned an NNT or NNH. However, an NNT/NNH could have been calculated based on the absolute figures given for 8 out of 46 reported primary outcomes (NNT) and 2 of the 63 documented primary adverse outcomes (NNH).[84] Similar shortcomings in the reporting of precision measures such as confidence intervals, the generalizability of the results, and statistical uncertainty around effect measures were found in the vast majority of RCTs.[84] Failure to openly disclose the reported benefits and harms of study trials correctly can preclude the development of NNT tools and impede application by practitioners.

Few NNT decision aids were tested in study trials. However, where NNT tools were trialed as an intervention, patients generally favored the use of the tools and experienced less decision conflict.[66] The majority of study participants noted that NNT tools were of "significant value," leading to higher quality clinical decisions and better collaboration between patients and

Table 2
NNT Tool databases.

Year published	Author(s)	Origin	Tool	Framing of NNT/NNH	Access	Language(s)	Features	Limitations
2007	National Institute of Healthcare Excellence (NICE).[106]	United Kingdom (UK) URL: https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-guidelines/shared-decision-making	NICE Patient Decision Aids	NNT = n NNH = n x in 100 x in 1000 Pictogram	Website Print App No fee	English	NNT: n, 1 in x, x in 100, pictogram. NNH: n, 1 in x, x in 100, pictogram. Large database of decision aids available through NICE for various therapies and medications. Some tools account for individual patient baseline risk, which is calculated prior to selecting the appropriate aid o Both shared/separate tools for patients and practitioners. o NNT and NNH are given as numerical values and depicted in a pictogram. o Evidence synthesis of various RCTs and SRs.	o Online access o Some require clinical parameters[a] o Only some have patient individualization[b] o Some complex medical jargon
2007	Schwartz et al.[48]	Germany URL: https://www.harding-center.mpg.de/en/fact-boxes	Fact Boxes	x in 100	Website Print No Fee	English	NNT: x in 100. NNH: x in 100. Expresses the pros and cons of therapies (e.g., vaccines, dietary supplements, antibiotics, cancer screening) in a tabular format that is easily understood. o Shared patient and practitioner tool. o NNT and NNH are given as numerical values. o Developed by the Harding Centre for Risk Literacy; adapted from a balance sheet developed by Eddy in 1990.[49] o Evidence synthesis of various RCTs and SRs.	o Limited no. of tools o No pictorials o No patient individualization[b] o Only some fact boxes employ NNT/NNH
2010	© The NNT Group.[50]	United States (US) URL: http://www.thennt.com/	Thennt.com	1 in x Percent (%)	Website No fee	English	NNT: 1 in x, %. NNH: 1 in x, %. Large database of Therapy (NNT) reviews for many interventions with study populations, endpoints, narratives, and caveats given in textual format. Uses a color-coded system to inform decisions on therapy: green (benefits > harms), yellow (unclear benefits > harms), red (no clear benefits or harms), black (harms > benefits). o Shared patient and practitioner tool. o Numerical NNT/NNH given. o Evidence synthesis of Cochrane Collaboration SRs or RCTs reviewed by DARE or ACP Journal Club[50] o Reviewed by both *TheNNT* Editorial Board and Scientific Advisory Boards.[50]	o Online access o No pictorials o Some complex medical jargon
2011	Cochrane Musculoskeletal Group[51]	Various URL: https://musculoskeletal.cochrane.org/decision-aids	Decision Aids	x in 100 Pictogram	Website Print No fee	English	NNT: x in 100, pictogram. NNH: x in 100, pictogram. Various aids about the benefits, harms, scientific uncertainties, and probabilities of treatment options for osteoarthritis, osteoporosis, and rheumatoid arthritis. o Shared patient and practitioner tool. o Numerical NNT/NNH with an annotated pictogram. o Collaboration with The Patient Decision Aids Research Group.[51] o Evidence synthesis of Cochrane SRs.	o Limited no. of tools o No patient individualisation[b] o Some complex medical jargon

Year	Author	Tool	URL/Country	Format	Access	Languages	Description	Limitations
2012	Elwyn et al.[52]	Option Grid™	United Kingdom (UK) URL: https://health.ebsco.com/products/option-grid	x in 100	Website Print Fee	Spanish English Arabic	NNT: x in 100. NNH: x in 100. Treatment options are displayed in a tabular format with columns (treatment options) and rows (frequently asked questions *FAQs* by patients). Side-effects, costs, and summaries fit to single-sided standard size page. Customized to fit age, gender, and other risk factors. o Separate patient and practitioner tools. o Numerical NNT/NNH given. o Evidence synthesis of high-quality SRs, i.e., National Institute of Health and Care Excellence (NICE) reviews with regular updating[52] o Efficacy has been assessed in GP and psychiatric settings[53-56]	o Limited no. of tools o No pictorials o Fees o Fits only 6–8 *FAQs* o Only US/UK data o Only some option grids employ NNT/NNH
2013	Guyatt and Vandvik.[57]	MAGICapp – SHARE IT Project	Norway URL: https://app.magicapp.org/app#/evidence-summaries	x in 1000 x fewer x more Pictogram	Website Print App No fee	Arabic Dutch Danish English French German Norwegian Spanish Swedish	NNT: x in 1000, x fewer, x more, pictogram. NNH: x in 1000, x fewer, x more, pictogram. MAGICapp (**MA**king GRADE the Irresistible Choice) is a web-based publication platform for guidelines and evidence summaries, requiring no software installation.[58] Uses the GRADE (Grades of Recommendation, Assessment, Development, and Evaluation) approach to determine the strength of recommendations.[58] Can be digitized to show the latest versions of available evidence automatically. o Shared patient and practitioner tool. o NNT and NNH are given as numerical values and depicted in a pictogram. o Evidence synthesis of SRs and clinical guidelines through import data from reference managers and databases.[58] o Researchers, admins, systematic reviewers, and technical teams can collaborate to produce content.	o Some tools are in development; hence no aids available o Authors decide who can access guidelines o Some complex medical jargon o Complex navigation
2016	British Medical Journal (BMJ)[59]	BMJ Rapid Recommendations[59]	Various https://www.bmj.com/rapid-recommendations	x more per 1000 x less per 1000 Diagram	Website Print App No fee	English	NNT: x more per 1000, diagram. NNH: x more per 1000, x less per 1000, diagram. 'Rapid Recommendations' are generated from systematic reviews conducted on the benefits and harms of interventions using the GRADE approach.[59] Consultation decision aids, evidence summaries, and recommendations in a multilayered digital format analyzing the practical issues, values, and preferences of consumers and risks or benefits of interventions.[59] o Shared patient and practitioner tool. o NNT/NNH in annotated diagrams. o Collaboration between MAGIC and the BMJ. o A team of researchers identifies literature that may change practice or be of interest to the medical community to conduct a systematic review. The evidence is then submitted to the BMJ for peer review, and preliminary conclusions will be drawn.[59] Such research is then refined into a 'BMJ Rapid Recommendation.'	o Limited no. of tools o Some patient individualisation[b] o Some complex medical jargon
2017	Health Decision, Inc.[60]	Health Decision® Support Tools	United States (US) URL: https://www.healthdecision.org/tool#/	NNT = n x in n Pictogram	Website Print App No fee	English	NNT: x in n, n, pictogram. NNH: x in n, pictogram. 6 interactive tools developed by Health Decision® for mostly 10 yr risk with:	o Online access o Limited no. of tools o Clinical parameters needed[a] o Some complex medical jargon

Table 2 (*continued*)

Year published	Author(s)	Origin	Tool	Framing of NNT/NNH	Access	Language(s)	Features	Limitations
							▪ Anticoagulants in atrial fibrillation ▪ Statins/smoking cessation in CVD ▪ Bisphosphonates in osteoporosis ▪ Mammograms in cancer screening ▪ CT scans in lung cancer screening ▪ BP lowering in ASCVD risk Each tool is tailored to patient factors with information input (e.g., age, sex, ethnicity, clinical parameters, smoking status) before generating an individualized pictogram and report. ○ Shared patient and practitioner tool. ○ NNT/NNH in annotated graphs and pictograms. ○ Depending on the tool, there are various sources of evidence synthesis such as; ▪ U.S Clinical Guidelines ▪ Risk calculators, e.g., BCSC Risk calculator, FRAX™ Risk assessment tool,[61] ACC/AHA ASCVD (US) 10 yr Risk[62] ▪ Various RCTs and SRs	

Databases that contain greater than 5 tools used to communicate number needed to treat (NNT).

^a Clinical parameters, for example, systolic blood pressure, total cholesterol, and HDL cholesterol need to be measured in a clinical setting for risk calculation. These tools are more likely to be incorporated in routine patient-physician discussions.

^b Tool does not account for other baseline characteristics, including but not limited to ethnicity, physiological parameters, comorbidities, gender, lifestyle factors, or specific age range.

practitioners.[52,55,85] Patient knowledge, confidence, and involvement also saw improvement with the use of decision aids, as opposed to usual care.[52,77,86] Patients, clinicians, and administrators noted that additional training and/or support might be required to integrate the tools into shared-decision making more effectively.[55] The use of sophisticated medical terminology was prominent in most aids, potentially limiting patient understanding.[87] Thus, ideally, NNT tools should be used as part of clinical discussions between the patient and practitioner, where any ambiguity can be resolved on-premises as opposed to a supplementary decision aid provided to the patient outside of a clinical encounter.

Gaps in NNT interpretation

Despite its growing use in the medical literature, understanding of NNT has potential for improvement. Studies on health professionals' interpretation of NNT have mainly focused on medical practitioners with limited sample sizes. Borracci et al. compared Spanish cardiologists' understanding of NNT, ARR, and RRR. When treatment benefits were depicted as RRRs, more than 60% of individuals accepted data that should have been either questioned or rejected; the percentages were much lower when cardiologists were presented with NNT and ARR.[88] Sturmberg and Pond showed that 20.8% of general practitioners (GPs) presented with absolute risk figures were unable to interpret the risk.[89] Yoon et al. investigated the ability of specialist trainee doctors to differentiate risk values where 69% of participants were able to calculate a risk reduction correctly.[90] Halvorsen et al. concluded that medical doctors' recommendations were sensitive to the magnitude of the NNT (i.e., they could interpret the difference between an NNT of 50 and 200), but noted a considerable proportion would advise against intervention because of the "wasted effort" argument (no foreseeable benefit for treated patients).[19]

The effects of using alternative statistical presentations on the understanding, perception, behavior, and persuasiveness of health professionals and consumers were evaluated as part of a 2011 Cochrane analysis.[91] When comparing RRRs, ARRs, and NNTs, relative risk reductions were better understood and more persuasive, followed by absolute risk reductions and numbers needed to treat respectively.[91] Although there is a general favor towards the presentation of treatment benefits in relative terms, these measures can exaggerate the effect size. The benefit of the NNT, being an absolute measure, extends to its increased accuracy in reiterating treatment effects, but the measure is yet to be understood completely.[45] Studies assessing patients' or physicians' understanding of NNT typically frame the measure as a statement or as part of a clinical scenario; none of which have investigated the use of decision aids, tools, or guidelines to communicate NNTs or NNHs. Decision aids have clinically demonstrated the effect of enhancing patient knowledge, feelings of acknowledgment, and inclusivity in making decisions.[47] The utilization of such tools may provide a solution to better relaying NNT, promoting evidence-based discussions with patients regarding treatment options.

The future of NNT – a case for pharmacists

It is evident from the literature that pharmacist intervention in using and explaining NNT is not currently well evaluated. The contexts in which the NNT tools have been clinically trialed have generally been confined only to GP practice, limiting its research scope in other occupations; for example, pharmacists where the NNT could potentially differentiate between medication treatment options.[52,53,73,77,85,86] Where 'surgeons are compelled to seek informed consent; there is no equivalent requirement when a drug is prescribed.'[92] This is a cause for concern, mainly as drug-related problems are relatively common in contexts where there are unknown or marginal risk-benefit ratios.[92] The Pharmaceutical Society of Australia (PSA) noted that medication errors, misadventure, interactions, and misuse were the cause of 250,000 hospitalizations each year, four times the rate of hospitalizations resultant of motor vehicle accidents in Australia.[93] Medication errors account for 1% of the total global health expenditure, totaling US$ 42 billion per annum.[94] With the decreasing

Table 3
NNT tools.

Year of publish	Author(s)	Tool	Origin	Framing of NNT/NNH	Access	Language(s)	Features	Limitations
2003	Cates[63]	*VisualRx*: NNT Calculator	England URL: https://www.nntonline.net/visualrx/	NNTB = n NNTH = n x in 100 x in 1000 Pictogram	Website No fee	English	NNT: NNTB, n, pictogram. NNH: n, pictogram. Free software that converts odds and risk ratios from clinical trials into NNT/NNHs. o Shared patient and practitioner tool. o NNT and NNH are given as numerical values and depicted in a pictogram. o Efficacy has been established.[64,65]	o Online access o Calculator only, inferences to be made by the reader o Some complex medical jargon
2007	Weymiller et al.[66] Mayo Clinic	Statin/Aspirin Choice Aids	United States (US) URL: https://shareddecisions.mayoclinic.org/decision-aid-information/decision-aids-for-chronic-disease/cardiovascular-prevention/	x in 100 1 in x Pictogram	Website Print App No fee	English Chinese French Arabic Spanish	NNT: x in 100, pictogram. NNH: 1 in x. Online interactive statin choice decision aid for 10 yr CVD risk. Generates pictogram from patient information input (e.g., age, sex, lifestyle factors, clinical parameters)—separate version for aspirin in CVD. o Shared patient and practitioner tool. o NNT as pictogram with numerical NNH. o Evidence synthesis of Cochrane SRs[67] and four risk calculators: ■ ACC/AHA ASCVD (US) 10 yr Risk[62] ■ D'Agostino Stroke Risk[68] ■ Framingham (US) 10 yr Risk[69] ■ Reynolds (US) 10 yr Risk Score[70] o Efficacy has been provided in clinical settings.[66,71]	o CVD risk only o 30–85 yrs. only o Clinical parameters needed[a] o Some complex medical jargon
2009	Pencille et al.[72] Mayo Clinic	Osteoporosis Choice Aid	United States (US) URL: https://shareddecisions.mayoclinic.org/decision-aid-information/decision-aids-for-chronic-disease/other-decision-aids/	x in 100 1 in x Pictogram	Website Print App No fee	English	NNT: x in 100, pictogram. NNH: 1 in x. One-page decision aid estimates the benefit of bisphosphonate therapy for 10 yr patient individualized risk of osteoporotic fracture(s). o Shared patient and practitioner tool. o NNT as pictogram with numerical NNH. o Evidence synthesis of one risk calculator: o FRAX™ Risk Assessment Tool[61]	o Osteoporotic fracture risk only o 40–95 yrs. only o Clinical parameters needed[a] o Some complex medical jargon
2012	Coylewright et al.[73] Mayo Clinic	Percutaneous Coronary Intervention (PCI) Choice	United States (US) URL: https://shareddecisions.mayoclinic.org/decision-aid-information/decision-aids-for-chronic-disease/pci-choice/	x in 100 Pictogram	Website Print App No fee	English	NNT: x in 100, pictogram. NNH: x in 100, pictogram. Compares optimal medical therapy (OMT) alone vs. OMT and percutaneous coronary intervention (PCI) for stable coronary artery disease (CAD) patients. 2-sided page with dot diagrams for risk. Two aids for CAD class I/II and CAD class III. o Shared patient and practitioner tool. o Numerical NNT/NNH with an annotated pictogram. o Evidence synthesis of SR conducted by 2 independent cardiologists; reviewed by cardiology fellows and experts.[73]	o CAD risk only o No patient individualization[b]

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Table 3 (*continued*)

Year of publish	Author(s)	Origin	Tool	Framing of NNT/NNH	Access	Language (s)	Features	Limitations
2013	McCormack and Pfiffner.[74]	British Columbia	The Absolute CVD Risk/ Benefit Calculator URL:http://chd. bestsciencemedicine. com/calc2.html#calculator	NNT = n Pictogram	Website Print No fee	English French Russian	NNT: n. NNH: none. Online CVD risk calculator for 5–10 yr risk of CVD based on patient lifestyle and physiological factors.[74] Compares multiple interventions including physical activity, omega-3 supplements, blood pressure medications, statins, fibrates, smoking cessation, and metformin.[74] ○ Shared patient and practitioner tool. ○ Numerical NNT with an annotated pictogram. ○ Evidence synthesis of four risk calculators ▪ Framingham (US) 10 yr Risk[69] ▪ QRISK®2–2014 (UK) 10 yr Risk[75] ▪ ACC/AHA ASCVD (US) 10 yr Risk[62] ▪ PREDICT (NZ) 5 yr Risk[76]	○ CVD risk only ○ 30–80 yrs. only ○ Clinical parameters needed[a] ○ Some complex medical jargon ○ Only UK/US/ NZ data
2014	National Institute for Health and Care Excellence (NICE).[107]	United Kingdom (UK) URL: https://www. nice.org.uk/ guidance/cg181/ resources/patient- decision-aid-188102	Statins for Coronary Heart Disease and Stroke Decision Aid	x in 100 Pictogram	Website Print No fee	English	NNT: x in 100. NNH: none. Designed for patients who are deciding whether or not to take statins to reduce the risk of coronary heart disease or stroke. Accompanied by a separate user guide for health professionals. Baseline risk needs to be accessed using QRISK®2–2014 prior to use of aid. ○ Separate patient and practitioner tools ○ NNT in annotated graphs and pictograms ○ Evidence synthesis of RCTs, *Medicines and Healthcare products Regulatory Agency (MHRA)* drug safety updates and NICE guideline. Cates plot generated using VisualRx.	○ CVD risk only ○ Clinical parameters needed[a] ○ Some complex medical jargon
2015	Brito et al.[77] Mayo Clinic	United States (US) URL: https:// shareddecisions. mayoclinic.org/decision-aid- information/graves- disease-decision-aid/	Graves' Disease Decision Aid	x in 10 x in 100 Pictogram	Website Print App No fee	English	NNT: x in 10. NNH: x in 10, x in 100. Compares three treatment options for Graves' Disease (GD) or hyperthyroidism: radioactive iodine treatment, anti-thyroid drugs, or surgical removal of the thyroid. Accompanied by cost-analysis studies and infographics. ○ Shared patient and practitioner tool. ○ NNT in annotated pictograms and NNH given as numerical value. ○ Evidence synthesis of an SR and network meta-analysis[78]	○ GD risk only ○ No patient individualization[b]

Year	Source	Tool	Graphics	Medium	Language	Description	Limitations
2015	Flynn et al.[79] United Kingdom (UK) URL: http://www.compasstpa.com/	COMPASS Decision Aid	x in 100 x more benefit per 100 Pictogram Bar Chart Flow Chart	Website Print App Fee	English	NNT: x in 100, x more benefits per 100, pictogram, bar chart, flow chart. NNH: x in 100, pictogram, bar chart, flow chart. Computerized decision aid for stroke thrombolysis. Communicates the personalized benefits and harms of thrombolysis using predictive algorithms, decision trees, clear risk descriptions, and timeline data for patients/relatives – requires prior input of clinical parameters for individual risk assessment.[79] ○ Shared patient and practitioner tool. ○ NNT/NNH in annotated graphs and pictograms. ○ Evidence synthesis of decision-analytic models and predictive equations.[79] ○ Efficacy established by stroke physicians, emergency department physicians, stroke nurse practitioners, and patients.[79]	○ Stroke thrombolysis risk only ○ Fees ○ Clinical parameters needed[a] ○ Some complex medical jargon
2016	Australia URL: https://www.safetyandquality.gov.au/our-work/shared-decision-making/patient-decision-aids/ Australian Commission on Safety and Quality in Healthcare (ACSQHC)[80]	Antibiotic Use Decision Aids	x in 100 Pictogram	Website Print No fee	English	NNT: x in 100, pictogram. NNH: x in 100, pictogram. Three decision aids on antibiotic use for: ▪ Sore throat ▪ Acute bronchitis ▪ Middle ear infection Two-sided page detailing NNT/NNH, antibiotic resistance, and symptoms requiring referral. ○ Shared patient and practitioner tool. ○ NNT/NNH in annotated graphs and pictograms. ○ Evidence synthesis of Cochrane SR and other SRs.[80]	○ Limited no. of tools ○ No patient individualization[b] ○ Evaluates children only
2017	Anderson et al.[81] Mayo Clinic United States (US) URL: https://a44kyu.axshare.com/home.html	Acute Otitis Media Decision Aid	1 in x x in n Pictogram	Website Print App No Fee	English	NNT: x in n. NNH: 1 in x. Decision aid comparing three interventions for acute otitis media (AOM) in children: (a) wait and see, (b) wait and see prescription, and (c) immediate antibiotics. ○ Shared patient and practitioner tool. ○ NNT as pictogram with numerical NNH. ○ Evidence synthesis of Cochrane SR[82]	○ AOM risk only ○ Child risk only ○ No patient individualization[b]
2018	Prasad et al.[83] Various URL: https://www.bmj.com/content/363/bmj.k5130/rapid-responses	Dual vs. Single Antiplatelet Therapy	x in 1000 x fewer per 1000	Website Print App No Fee	English	NNT: x in 1000, x fewer per 1000, pictogram. NNH: x in 1000, x fewer per 1000, pictogram. Comparisons of benefits and harms of single-agent vs. dual antiplatelet and short duration vs. long duration of therapy for secondary prevention of stroke, designed for straightforward patient interpretation. ○ Shared patient and practitioner tool. ○ NNT/NNH in an annotated pictogram. ○ Evidence synthesis of major RCTs and SRs.[83]	○ Secondary stroke and transient ischemic attack risk only ○ No patient individualization[b] ○ Some complex medical jargon

Individual guidelines, tools, decision aids, or databases with less than 5 tools communicate the number needed to treat (NNT).

[a] Clinical parameters, for example, systolic blood pressure, total cholesterol, and HDL cholesterol need to be measured in a clinical setting for risk calculation. These tools are more likely to be incorporated in routine patient-physician discussions.

[b] Tool does account for other baseline characteristics, including but not limited to ethnicity, physiological parameters, comorbidities, gender, lifestyle factors, or specific age range.

Table 4

Clinical scenarios.

Scenario	Example
✓ Where the risk changes with factors such as age or comorbidities and the benefit of a specific therapy as was evaluated in the past is no longer apparent	Statins with increasing age
✓ Where polypharmacy exists and interactions are identified, for example, in a pharmacist-led medication review and risk-benefit information can readily assist in deciding therapy	Warfarin/NSAIDs vs. warfarin/paracetamol
✓ Where a multitude of medications are prescribed at once and the patient overwhelmed	Influx of medications post-myocardial infarction
✓ Complementary therapies or medications	Homeopathic remedies vs. Western medications
✓ Patient presents with a private script and is curious as to the risks and benefit of considering a government scheme subsidized drug.	Agomelatine vs. venlafaxine for major depressive disorder
✓ Convincing patients to undergo life-long medication therapy	Blood pressure medications

Scenarios where communication of NNT/NNH risk-benefit analysis may be useful.

thresholds for recommendations of preventative interventions, numbers needed to treat are rising, and many people are now eligible for treatment who were previously deemed too high risk (e.g., side effects).[92] Most therapies are pharmacological and are also initiated in primary care.[92] Pharmacists as primary care providers and experts in medicines sit in a position to lead medication reconciliation conversations and comprehensive reviews to reduce drug-related problems (Table 4).[95] Alongside the wave of modern health consumerism comes the task of actively involving patients in decisions regarding their own therapy options, paving the way for more meaningful patient-practitioner relationships. For pharmacists to more effectively communicate scientifically valid information, an NNT tool would fit well into the evidence-based decision-making process, where pharmacist interventions have already demonstrated improved patient health literacy and medication adherence.[96]

With the influx of research information pertaining to drug substances already made available through the Cochrane Library, major RCTs, or landmark studies, pharmacists can fully utilize their experience with the addition of these tools to communicate risk-benefit ratios to consumers. Moreover, point-of-care decision aids would be rather progressive, particularly with the international EBM movement where the profession is being upskilled to communicate the risks and benefits of treatments better. With EBM having been included in the medical and pharmacy university curriculum since the early 2000s, new generation pharmacists will be well-equipped to use and interpret NNT tools with the aid of many continuing professional development (CPD) programs accessible to them.[16,97,98] A growing number of available NNT tools for clinicians to use have emerged as naturally complementary to this effort. Recent years have also noted the increasing rate of pharmacist integration into general practice (GP) clinics, with significant improvements demonstrated in chronic disease management.[99] Integration of NNT aids has the potential to benefit pharmacists in the multidisciplinary environment as a supplement to medication reviews or consultations. Such tools can guide discussions regarding new and emerging medications, drug-related problems, and decisions as to medication options to aid patient understanding.

The NNT and associated NNH also bear particular significance in the benefit-risk assessment of medicines, particularly in developing, appraisal, and regulating drugs in their respective national markets.[100] Public summary documents released by the Pharmaceutical Benefits Advisory Committee (PBAC) frequently use NNTs as a means of justification for drugs approved under the Pharmaceutical Benefits Scheme (PBS) subsidiary in Australia.[101] For instance, in response to a request in the Senate (2010), PBAC produced a review of statin therapies and reinvestigated the newest evidence on rosuvastatin and atorvastatin (drugs for hypercholesterolemia).[101] NNTB and NNH were reported in tables which clearly illustrated the risk-benefit ratio of the drugs pooled from multiple studies.[101,102] The United States Food and Drug Administration's (FDA)

approved pharmacotherapies for bipolar manic/mixed episodes largely depict single-digit NNTs; a consideration meaning fewer patients have to be treated in order for one person to have a treatment response to said medications.[103,104]

Conveying risk-benefit biostatistics (e.g., NNT and NNH) to patients in a language that they understand may lead to increased medication safety and reduced drug-related problems in the community.[17] The use of NNT tools, in this case, presents an innovative option for clinicians to communicate the otherwise complicated numerical results of therapy trials in ways that are more engaging and clear-cut to the patient. With the oncoming development of new tools and prospects of implementing NNT decision aids in the context of pharmacy practice, it is apparent that inclusion of NNT in healthcare professional training may be required. Future research is needed to evaluate the effectiveness of newer tools and their effects on patient- or clinician-centered outcomes (i.e., understanding, attitude, or health literacy), but necessitates that decision aids be utilized in study trials which at current are few and far between.

Limitations

The present review has some limitations. First, it is possible that some studies were missed due to not being indexed in the relevant databases or being published by scientific institutions or societies. Additionally, grey literature databases were not searched. This study was also limited to tools and decision aids based on pharmaceutical interventions. The inclusion of terms such as 'medical' or 'therapeutic interventions may have captured a greater sample of articles. Finally, this review did not analyze the quality of the studies as the scope of research was to confirm the availability and description of current NNT tools for pharmaceutical interventions.

Conclusion

It has not yet been demonstrated whether NNT tools used in pharmacy practice (e.g., medication reviews, medication reconciliation, transition care, or therapeutic drug monitoring) to disseminate risk-benefit information better can result in positive health outcomes through better decision-making. While the use of NNT tools has shown a demonstrated benefit on improving patient involvement, decision conflict, and understanding of evaluating treatment options, there is a paucity of using and developing these aids. Further research and development of risk communication aids may lead to ameliorating action by pharmacists in tackling issues related to medication misadventure, patient compliance, and/or de-prescribing. Communication of NNT as part of a decision aid or tool provides an opportunity for patients and practitioners to infer the results of clinical trials better and gauge the real risks and benefits of therapies. Adopting NNT tools into pharmacy practice may lead to better promotion of EBM in the profession, with clinical application of scientific advances for more secure, cost-effective, and optimized healthcare.

Conflicts of interest

None.

Appendix A

The effects of new medications or therapies assessed in RCTs and systematic reviews often involves dichotomous outcomes, for example, survival vs. death, stroke vs. no stroke or myocardial infarction (MI) vs. no MI, and are defined in the literature as statistical measures such as absolute risks, relative risks, odds ratios, event rates, and NNTs.[10] Such figures are measures of treatment effect and can differentiate between the efficacy of new treatments compared to placebos, no intervention, or other treatments.[10] Setting up a 2 × 2 contingency table (Box 1) allows for quick extrapolation of trial data and ease of calculating said risk metrics.

Box 1 (*Adapted from Gosall and Gosall, 2015*)

2x2 Contingency Table
Input RCT data as follows. Note that *a, b, c and d* indicate the number of patients who fall under each category.

		OUTCOME e.g. pain, cancer, death, survival		
		YES	**NO**	
INTERVENTION e.g. medication, therapy, diagnostic test or lifestyle changes	**Positive exposure (+)** Intervention Group	a	b	a + b
	Negative exposure (-) Control Group	c	d	c + d
		a + c	b + d	a + b + c + d

Formulas

Measure	Equation
Experimental Event Rate [EER]	$\dfrac{a}{a+b}$
Control Event Rate [CER]	$\dfrac{c}{c+d}$
Absolute Risk Reduction [ARR]	$CER - EER$
Number Needed To Treat [NNT]	$\dfrac{1}{ARR}$

Table A1
Sample trial data.

Duration: 2.6 yrs	Exposure	Outcome		
		Doubling serum concentration, end-stage renal disease, and death		
		YES	NO	Total
Intervention *Irbesartan (medication)*	Positive (+)	189 (a)	390 (b)	579 (a + b)
	Negative (−)	222 (c)	347 (d)	569 (c + d)
	Total	411 (a + c)	737 (b + d)	1148 (a + b + c + d)

Irbesartan vs. placebo in patients with nephropathy due to Type II Diabetes.[105]

Event rates

The experimental and control event rates, *EER* and *CER,* respectively, are probabilities expressing the likelihood of an event or outcome to occur within patients of their respective trial arm.[1] In a comparison of the renoprotective effect of irbesartan against placebo in patients with nephropathy due to Type II Diabetes (T2D), the EER and CER were 0.33 and 0.39, meaning that there was a 33% chance of renal outcomes (elevated serum concentration, end-stage renal disease or death) in patients trialing irbesartan as oppose to a 39% chance in patients taking placebo.[105] The data from the trial can be extrapolated from a 2 × 2 contingency table (Table 1).

$$EER = \frac{a}{a+b} = \frac{189}{579} = 0.33 \ (or\ 33\%)$$

$$CER = \frac{c}{c+d} = \frac{222}{569} = 0.39 \ (or \ 39\%)$$

Absolute risk reduction (ARR)

The absolute risk reduction (ARR), otherwise known as risk difference (RD), is the difference in absolute risk of events between patients of the RCT experimental and control groups.[10] 39% of patients taking irbesartan developed renal outcomes compared to 33% of patients in the control group, meaning there was a 6% drop in the risk of renal outcomes in patients engaging in drug therapy with irbesartan.[105] Where there is a higher chance of outcomes in the control group and a 'negative' probability is generated, the absolute value is taken, and its clinical application can be termed an absolute risk increase; intervention would increase the risk of outcomes compared to control.[10]

$$ARR = CER - EER = 0.39 - 0.33 = 0.06 \ (or \ 6\%)$$

Number needed to treat (NNT)

The NNT denotes the number of patients who must undergo intervention over a defined period of time in order for one patient to receive the treatment benefit.[10] It is calculated by taking the reciprocal of the ARR ($\frac{1}{ARR}$) and by convention is rounded up to the nearest whole number.[1] The NNT for the Irbesartan Diabetic Nephropathy Trial (IDNT) comparing irbesartan to placebo was 17, meaning 17 patients would have to take irbesartan for 2.6 years to prevent renal outcomes for one patient.[105]

$$NNT = \frac{1}{ARR} = \frac{1}{0.06} = 17 \ (rounded \ up \ from \ 16.7).$$

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