

**MONARCH**  
**FOR THE**  
**ESTABLISHMENT OF CAUSAL**  
**(CAUSE EFFECT) RELATIONSHIP**  
**OF HOMOEOPATHIC INTERVENTION AND**  
**CLINICAL**  
**OUTCOME IN CASE REPORTS**

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# Overview

Introduction

Hierarchy of evidence

Significance and Challenges of case reports

Causality Assessment

MONARCH –History, Development, Validation and Elaboration

# Introduction

Case reports are scientific documentation of a single clinical observation.

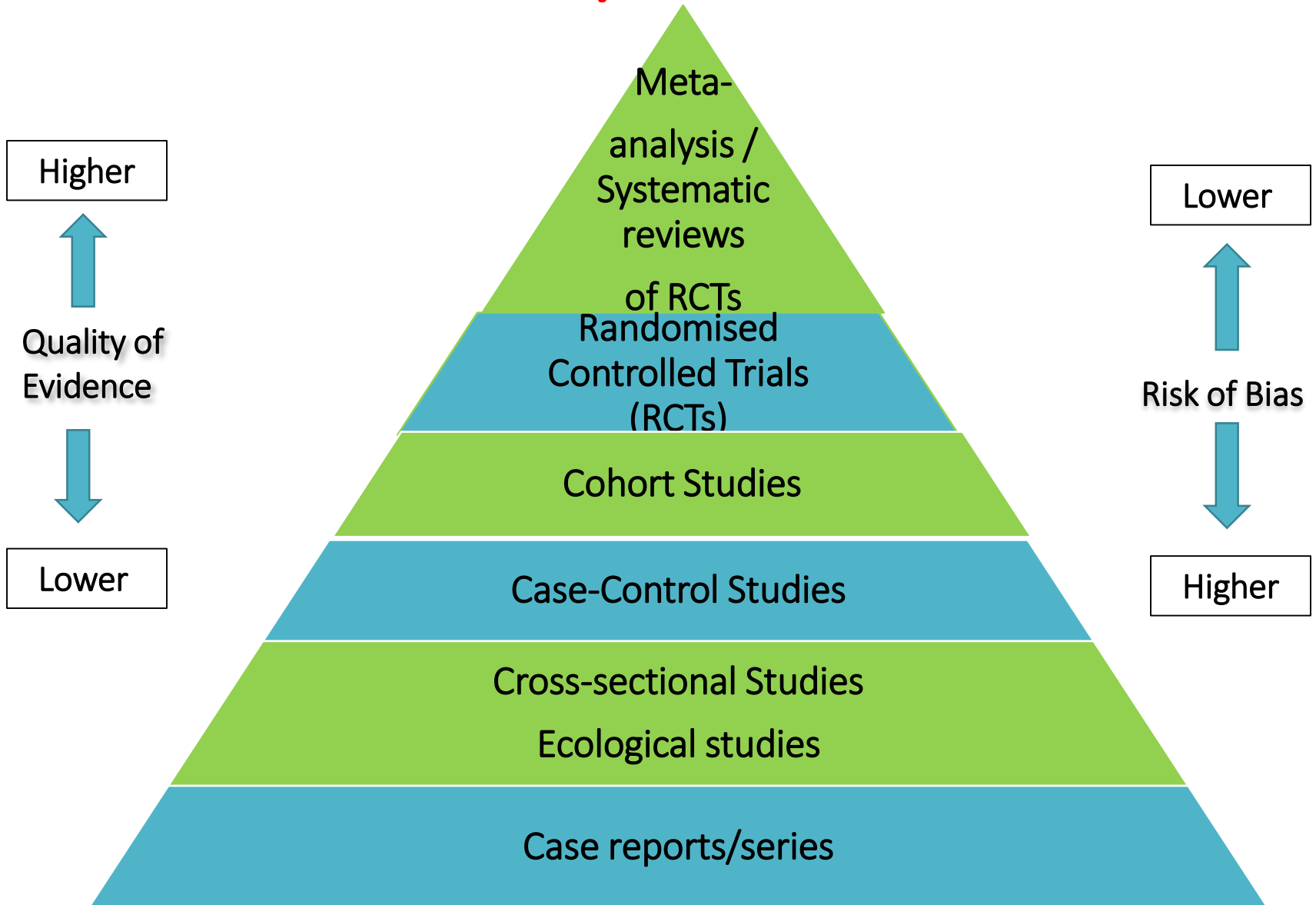
Have a time-honored and rich tradition in medicine and scientific publication.

Probably the oldest example of preserved medical literature containing clinical cases is a text from an Egyptian antiquity papyrus.



Ancient medical writing

# Hierarchy of evidence



# Significance

- It allows an in-depth, multi-faceted exploration of complex issues in their real-life settings.
- It is considered when an experimental design is either inappropriate to answer the research questions posed or impossible to undertake.
- Assessment of safety and the generation of hypotheses.
- Teaching purpose
- Intrinsic freedom for reporting
- Easiest to initiate into Scholarly writing

## THALIDOMIDE AND CONGENITAL ABNORMALITIES

STR.—Congenital abnormalities are present in approximately 1.5% of babies. In recent months I have observed that the incidence of multiple severe abnormalities in babies delivered of women who were given the drug thalidomide ('Distaval') during pregnancy, as an anti-emetic or as a sedative, to be almost 20%.

These abnormalities are present in structures developed from mesenchyme—i.e., the bones and musculature of the gut. Bony development seems to be affected in a very striking manner, resulting in polydactyly, syndactyly, and failure of development of long bones (abnormally short femora and radii).

Have any of your readers seen similar abnormalities in babies delivered of women who have taken this drug during pregnancy?

Hurstville, New South Wales.

W. G. McBRIDE.

# Challenges

**Weakest** level of evidence with regard to establishing cause and effect relationships.

Often **insufficiently rigorous** to be combined for data analysis, inform research design, or guide clinical practice.

If **carefully conceptualized, thoughtfully undertaken and reported**, Case Reports have the potential to offer **evidence from the point of care that can be useful for clinical research, guide clinical practice guidelines, and improve medical education.**

# Improving case reports- From evidence point of view

Development of tools for improving Case Reports

**The CARE Guidelines:** Consensus-based Clinical Case Reporting Guideline Development by Gagnier et al

Homeopathic clinical case reports: Development of a supplement (**HOM-CASE**) to the CARE clinical case reporting guideline by Dr. R A van Haselen

**Modified Naranjo's Criteria for Homeopathy:** Assessment of the likelihood of a causal relationship between the homeopathic medicine and improvement proposed by Dr. Lex Rutten and latter adopted and modified by Clinical working group of HPUS.

**MONARCH:** The validated version of **Modified Naranjo's Criteria for Homeopathy** -The Causal Attribution Inventory



# History of MONARCH

Causality assessment plays a pivotal role in clinical practice as well as in drug development.

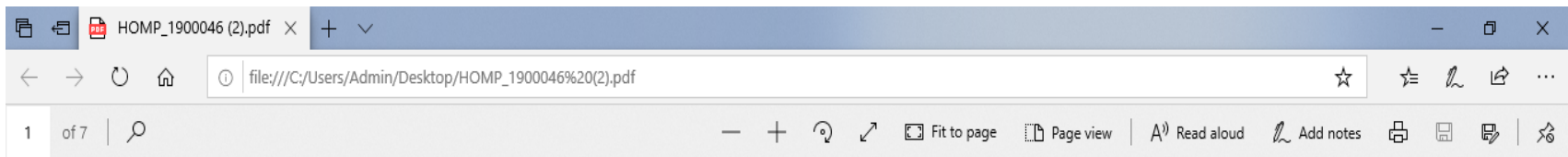
In modern medicine, the Naranjo criteria is one such algorithm that has been utilized to classify the probability that an adverse event is related to drug therapy based on a list of weighted questions, which examine factors such as the temporal association of drug administration and event occurrence, potential alternative causes for the event, drug levels, and previous patient experience with the medication.

# History of MONARCH

Dr. Lex Rutten (2013) was first to propose that for assessing causal relationships in homoeopathic practice, it might be useful to develop an algorithm (like Naranjo Algorithm available for ADR). Such algorithms could be adapted for homeopathy and he proposed a modified version of the same for homeopathy.

Subsequently, HPUS Clinical Data Working group modified the version by Rutten further and proposed the adapted Naranjo Algorithm (version June 2014). Thereafter, the latest version of the same was proposed in 2016 as the reduced modified Naranjo criteria.

Further its validation was undertaken as PhD study from Homoeopathy University, Jaipur, Rajasthan, India, under the supervision of Padmashri Dr. V . K. Gupta and advisorship of Dr. Robbert van Haselen and Dr. Lex Rutten. Dr. Nidhi Mahajan, PhD and Dr. Abdul Martin Molla, MD, were the experts.



Original Research Article

# Evaluation of the Modified Naranjo Criteria for Assessing Causal Attribution of Clinical Outcome to Homeopathic Intervention as Presented in Case Reports

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# Objective

The objective of this study was to establish the reliability and content validity of the “Modified Naranjo Criteria for Homeopathy—Causal Attribution Inventory” as a tool for attributing a causal relationship between the homeopathic intervention and outcome in clinical case reports.

Validity refers to whether or not the test measures what it claims to measure.

Inter-rater reliability (IRR) is a measure of reliability used to assess the degree to which different judges or raters agree in their assessment decisions.

# Case Selection Criteria

The cases were sampled based on the following criteria

## Inclusion criteria

Case reports covering around 9 items out of 30 on the generic CARE checklist (all domains and sub-domains numbered from 1 to 30) and a minimum of 3 out of 6 as per the HOM-CASE extension items (main and the sub-domains numbered from 1 to 6, except domain 10h3, which is the possible causal attribution of changes explicitly assessed/discussed).

## Exclusion criteria

Case reports with poorly described prescribing symptoms, and homeopathic patent medicines or compound formulations or proprietary products or combinations where more than one medicine was administered simultaneously.

The Modified Naranjo Criteria for Homeopathy Inventory consists of 10 Domains	Yes	No	Not sure or N/A
1. Was there an improvement in the main symptom or condition for which the homeopathic medicine was prescribed?	+2	-1	0
2. Did the clinical improvement occur within a plausible timeframe relative to the drug intake?	+1	-2	0
3. Was there an initial aggravation of symptoms?	+1	0	0
4. Did the effect encompass more than the main symptom or condition (i.e., were other symptoms ultimately improved or changed)?	+1	0	0
5. Did overall well-being improve? (suggest using validated scale)	+1	0	0

Domains	Yes	No	Not sure or N/A
6A Direction of cure: did some symptoms improve in the opposite order of the development of symptoms of the disease?	+1	0	0
6B Direction of cure: did at least two of the following aspects apply to the order of improvement of symptoms: –from organs of more importance to those of less importance? –from deeper to more superficial aspects of the individual? –from the top downwards?	+1	0	0
7. Did “old symptoms” (defined as non-seasonal and non-cyclical symptoms that were previously thought to have resolved) reappear temporarily during the course of improvement?	+1	0	0

Domains	Yes	No	Not sure or N/A
8. Are there alternate causes (other than the medicine) that—with a high probability—could have caused the improvement? (Consider known course of disease, other forms of treatment, and other clinically relevant interventions)	-3	+1	0
9. Was the health improvement confirmed by any objective evidence? (e.g., laboratory test, clinical observation, etc.)	+2	0	0
10. Did repeat dosing, if conducted, create similar clinical improvement?	+1	0	0



# Outcome assessment

Inter-rater agreement in the scoring of these domains was determined by calculating the percentage agreement and kappa ( $\kappa$ ) values. Kappa is a commonly used measure that indicates the level of inter-rater agreement.

The range of Kappa is from 0 (chance agreement) to 1 (perfect agreement).

A  $\kappa$  greater than 0.4, indicating fair agreement between raters, in conjunction with the absence of concerns regarding the face validity (is a measure of how representative an instrument or test is 'at face value,' as judged by experts in the field and whether it appears to be a good instrument), was taken to indicate the validity of a given domain. Each domain was assessed by four raters for the selected case reports.

# Results

Sixty case reports met the inclusion criteria and were assessed by 4 raters. The percentage agreement and  $\kappa$  was calculated for each of the domains.

Domain	Agreement (%)	Kappa ( $\kappa$ )	Inference	Valid ( $\kappa > 0.40$ )
1	100	1.00	Perfect agreement	Yes
2	100	1.00	Perfect agreement	Yes
3	96.7	0.80	Substantial agreement	Yes
4	83.3	0.60	Moderate agreement	Yes
5	91.1	0.70	Substantial agreement	Yes
6A	46.7	0.03	Slight agreement	No
6B	50.3	0.18	Slight agreement	No
7	67.8	0.46	Moderate agreement	Yes
8	97.5	0.86	Almost perfect agreement	Yes
9	99.2	0.50	Moderate agreement	Yes
10	56.1	0.38	Fair agreement	Yes

# Conclusion

The Modified Naranjo Criteria for Homeopathy—Causal Attribution Inventory was identified as a valid tool for assessing the likelihood of a causal relationship between a homeopathic intervention and clinical outcome.

Improved wordings for several criteria have been proposed for the assessment tool, under the new acronym “MONARCH”.

Further assessment of two MONARCH domains is required.

# Causality assessment

Cases successfully treated can have different treatment approaches based on the nature of disease, susceptibility and various other factors-

Single medicine- Likelihood of causality attributed to single medicine

Series of medicines based on the changing symptomatology-  
Likelihood of causality to overall homoeopathic treatment

# MONARCH

Elaboration of 10 domains  
(Updated wording as underlined)

Domain 1: Was there an improvement in the main symptom or condition for which the homeopathic medicine was prescribed?

What is main symptom or condition for which the patient reported?

- Diagnosed disease condition
- All symptoms of disease should be assessed

## Domain 2: Did the clinical improvement occur within a plausible timeframe relative to the medicine intake?

The effect of medicine should be within a reasonable time period of intake of medicine so that the causality can be established. It may be difficult to say that a single dose acted after months of taking medicine.

## Domain 3: Was there a homeopathic aggravation of symptoms?

Definition: Homeopathic aggravation is the temporary worsening of pre-existing symptom(s) within a plausible timeframe after the administration of a homeopathic medicine, followed by an improvement in the patient's condition.

Homeopathic aggravation is characteristic of homoeopathic system of medicine. If observed, it can increase the confidence in the likelihood of a causal relation between intervention and effect.



Domain 4: Did the effect encompass more than the main symptom or condition (i.e., were other symptoms, not related to the main presenting complaint, improved or changed)?

The symptoms not related to the disease should be considered for assessing this domain.

Domain 5: Did overall well-being improve?  
(suggest using a validated scale or mention  
about changes in physical, emotional, and  
behavioral elements)

The validated scale (Quality of life –generic/ specific to disease condition) should be used.

Or

A note about improvement in physical, emotional and behavioral sphere should be mentioned to judge the overall well-being.

Domain 6A: *Direction of cure*: did some symptoms improve in the opposite order of the development of symptoms of the disease?

Explicitly mention the chronology of the symptoms in which these developed and improved, drawing a corollary between the two.

Domain 6B: *Direction of cure*: did at least one of the following aspects apply to the order of improvement in symptoms:

–from organs of more importance to those of less importance?

–from deeper to more superficial aspects of the individual?

–from the top downward?

In absence of any clear-cut guidelines defining the 3 parameters (hierarchy of organs, definition of deeper to superficial and top downwards), further work in this direction is required. However, this domain should be precisely reported as far as possible so that the data can be used to define and validate it.

Domain 7: Did “old symptoms” (defined as non-seasonal and non-cyclical symptoms that were previously thought to have resolved) reappear temporarily during the course of improvement?

Summarize the chronological sequence of old symptoms in which these reappear.

Domain 8: Are there alternative causes (i.e. other than the medicine) that—with a high probability—could have produced the improvement? (Consider known course of disease, other forms of treatment, and other clinically relevant interventions)

Mention concurrent treatment, if any.

Lifestyle Management advised and if medicine has any added effect. This is to substantiate the causal relationship between intervention and outcome.

Domain 9: Was the health improvement confirmed by any objective evidence? (e.g., investigations, clinical examination, etc.)

Relevant investigations/ relevant clinical examination/ photographs (for dermatological conditions)/ validated questionnaire (especially for subjective conditions)

## Domain 10: Did repeat dosing, if conducted, create similar clinical improvement?

Repeat dosing implies when the disease has been in abeyance/ under remission for quite a long time and the similar symptoms re-appear and are improved with the previously selected medicine i.e. to ascertain reproducibility.



# The way ahead

The overarching CARE/HOM CASE guidelines should be followed for standardized and therefore more thorough case reporting followed by assessment of the likelihood of a causal relationship between homeopathic intervention and clinical outcome using MONARCH—Causal Attribution Inventory.

# Take home message

We can apply MONARCH to assess the likelihood of a causal relation between the remedy prescribed and outcome in our successfully treated cases.

It helps us to critically consider both homoeopathic and general aspects when assessing the patient's response to the remedy prescribed

In acute (COVID-19) cases, very often domains 3, 6A, 6B, 7 and 10 will not be observed or applicable, but when present, these significantly improve the likelihood of causality

The MONARCH tool is applicable to both Acute and Chronic cases.

A paper which further elaborates on how to work with the MONARCH domains is in preparation, your experiences and suggestions are greatly appreciated!

Thank  
you

