nature portfolio

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Reporting Summary

Nature Portfolio wishes to improve the reproducibility of the work that we publish. This form provides structure for consistency and transparency in reporting. For further information on Nature Portfolio policies, see our Editorial Policies and the Editorial Policy Checklist.

Statistics

For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.

n/a	Confirmed
☐	☒ The exact sample size (*n*) for each experimental group/condition, given as a discrete number and unit of measurement
☐	☒ A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
☐	☒ The statistical test(s) used AND whether they are one- or two-sided *Only common tests should be described solely by name; describe more complex techniques in the Methods section.*
☐	☒ A description of all covariates tested
☒	☐ A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
☐	☒ A full description of the statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
☐	☒ For null hypothesis testing, the test statistic (e.g. *F*, *t*, *r*) with confidence intervals, effect sizes, degrees of freedom and *P* value noted *Give P values as exact values whenever suitable.*
☒	☐ For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
☐	☒ For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
☒	☐ Estimates of effect sizes (e.g. Cohen's *d*, Pearson's *r*), indicating how they were calculated

Our web collection on statistics for biologists contains articles on many of the points above.

Software and code

Policy information about availability of computer code

Data collection

Database search: PubMed-Medline, EMBASE, Scopus, Google Scholar, the Cochrane Central Registry of Controlled Trials and ClinicalTrial.gov.

Efficacity & safety: "Heterozygous familial hypercholesterolemia" OR "HeFH" OR "FH phenotype" AND "Pediatric familial hypercholesterolemia" OR "children" AND "Treatment" OR "Lipid lowering therapy" OR "LLT" OR "Statins") OR "PCSK9 inhibitors" OR "Dietary regimens" OR "Dietary interventions" AND "Outcome"

Occurrence term: "Outcome" OR "Efficacity" OR "Safety" OR "Adverse events"

Data analysis

We used RevMan and RStudio using the packages 'meta' and 'metafor'. A random-effects model (Der Simonian and Laird method) was applied to estimate the pooled prevalence of adverse events across the studies:

```
Study <- c("Study1", "Study2", "Study3", "Study4", "Study5")
events <- c(30, 45, 20, 50, 10)  # Number of adverse events in each study
total <- c(100, 150, 80, 120, 60)  # Total participants in each study

# Meta-analysis of proportions (adverse events in this case)
meta_analysis <- metaprop
  event = events,          # Number of adverse events
  n = total,             # Total participants per study
  sm = "PLOGIT",           # Logit transformation (for proportions)
  method = "DL",           # Use DerSimonian-Laird method for random effects
  studlab = study,         # Study labels
```

```
comb.random = TRUE,         # Perform random-effects model
hakn = TRUE                 # Apply Hartung-Knapp adjustment for better precision)
```

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors and reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Portfolio guidelines for submitting code & software for further information.

Data

Policy information about availability of data

All manuscripts must include a data availability statement. This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A description of any restrictions on data availability
- For clinical datasets or third party data, please ensure that the statement adheres to our policy

The data were collected from electronic databases.

Research involving human participants, their data, or biological material

Policy information about studies with human participants or human data. See also policy information about sex, gender (identity/presentation), and sexual orientation and race, ethnicity and racism.

Reporting on sex and gender	We reported the mean/SD of age and the gender percentage (F, M) of the patients in the study, but we did not have data on sexual orientation, race, or racism.
Reporting on race, ethnicity, or other socially relevant groupings	We reported the countries the patients belonged to, but we did not have enough data to test for race or religion, etc.
Population characteristics	Participants were included in the studies based on genetic criteria (heterozygous HeFH), treatment, and outcomes.
Recruitment	Articles were eligible if they reported the treatment with LLT in paediatric patients with HeFH and met the following inclusion criteria: i) trials or cohorts reporting treatment with LLT compared to control or comparison before-after treatment in the same group, ii) available mean change of lipidic profile and/or adverse events, and iii) genetically confirmed diagnosis of heFH.
Ethics oversight	Every paper included in the studies had reported the ethical issue.

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Field-specific reporting

Please select the one below that is the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

☒ Life sciences ☐ Behavioural & social sciences ☐ Ecological, evolutionary & environmental sciences

For a reference copy of the document with all sections, see nature.com/documents/nr-reporting-summary-flat.pdf

Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

Sample size	The sample size (41 studies with 4,667 pediatric patients) is sufficient to draw conclusions about the efficacy and safety of LLT and various types of LLT in children with HeFH.
Data exclusions	Exclusion criteria were as follows: i) studies with unclear methodologies to obtain the estimates of the LLT efficacy and safety, ii) ongoing trials (unless they reported relevant interim results), iii) studies only investigating diet regiments without LLT treatment, and iv) articles not published in English.
Replication	The assessment of risk of bias in the included studies using RoB2 for RCTs and NOS for cohort studies showed that most studies had moderate to high quality level in defining objectives and the main outcomes.
Randomization	Out of the 41 articles, 22 were randomized controlled trials (RCTs), and 19 were cohort studies.
Blinding	All included randomized trials were either single-blind or double-blind.

Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

Materials & experimental systems

n/a	Involved in the study
☒	☐ Antibodies
☒	☐ Eukaryotic cell lines
☒	☐ Palaeontology and archaeology
☒	☐ Animals and other organisms
☐	☒ Clinical data
☒	☐ Dual use research of concern
☒	☐ Plants

Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☒	☐ Flow cytometry
☒	☐ MRI-based neuroimaging

Clinical data

Policy information about clinical studies

All manuscripts should comply with the ICMJE guidelines for publication of clinical research and a completed CONSORT checklist must be included with all submissions.

Clinical trial registration	All included randomized trials reported their registration number.
Study protocol	All included randomized trials reported their study protocols.
Data collection	All included papers reported the locations and centers where the patients were recruited.
Outcomes	The main endpoint was efficacy of goal achievement for LDL-C and other lipid parameters: total cholesterol [TC], triglycerides [TG], high density lipoprotein cholesterol [HDL-C], apolipoprotein B [apo B] and lipoprotein(a) [Lp(a)]), and the LLT safety (adverse events [AEs], including endocrine function, and growth indices). The secondary endpoint was an effect of LLT on attainment of LDL-C goal treatment (<3.5 mmol/L/130 mg/dL).

Plants

Seed stocks	They were not part of our study
Novel plant genotypes	They were not part of our study
Authentication	They were not part of our study