의학논문작성의 원칙

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Table 1.1 Time management[4].

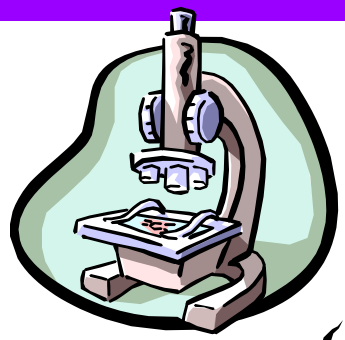
	Urgent	Not urgent
Important	**Quadrant I** Crises, deadlines, patient care, teaching, some meetings, preparation	**Quadrant II** Research, writing, reading, professional development, physical health, and family
Not Important	**Quadrant III** Some phone calls, emails, mail, meetings, and popular activities, for example morning and afternoon teas	**Quadrant IV** Junk mail, some phone calls and emails, time wasters, and escape activities, for example internet browsing, playing computer games, reading magazines, watching TV

Jennifer Peat. Scientific writing. BMJ books. 2002

Research Paper?

Academic writing
Systematic
publish

Research paper ?



Scientific writing

- Void for vagueness (明確性 原則)
- communication

Science *Vs.* Magic

- Study results should be published
- Replication

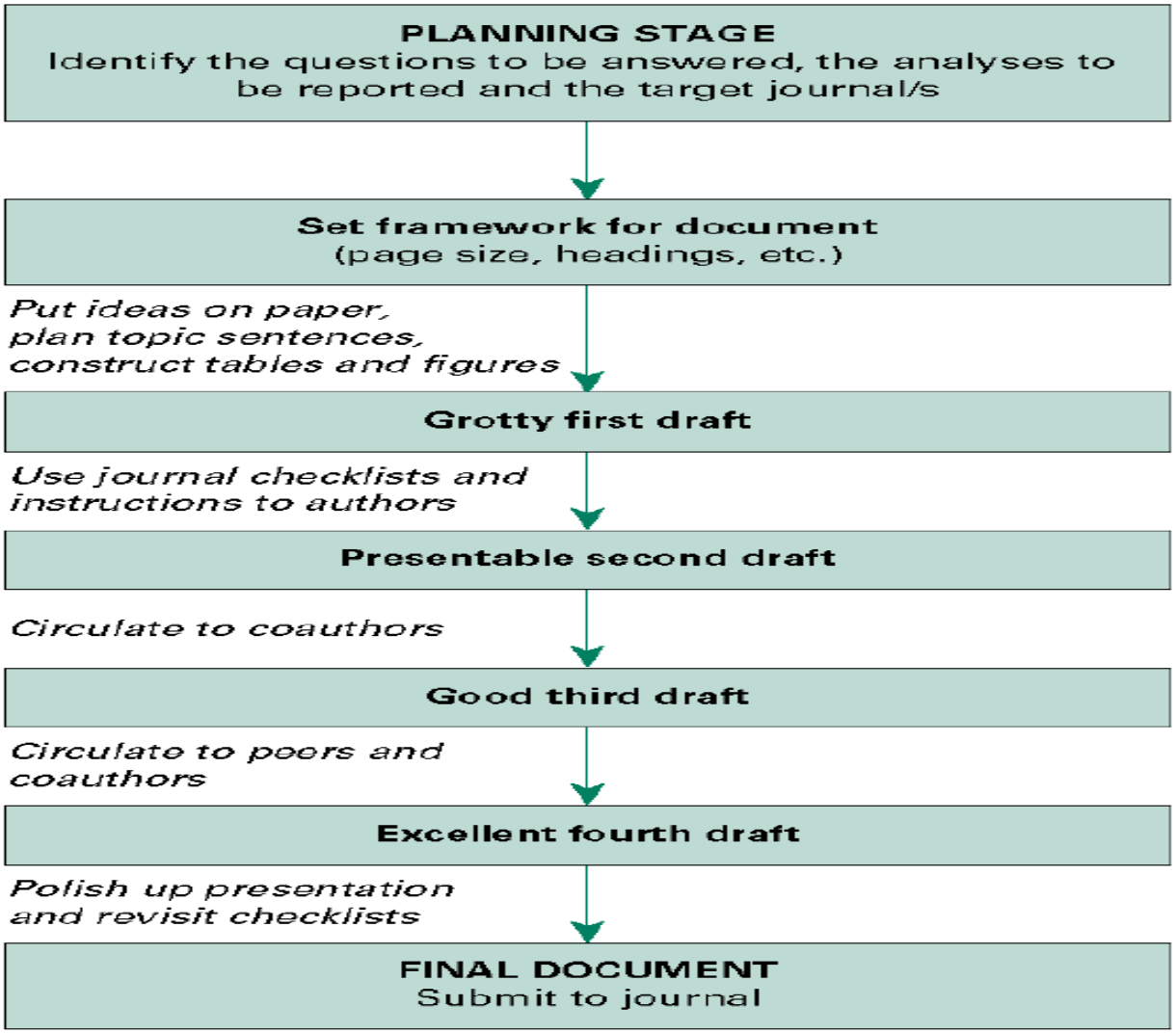
Purpose of scientific research

- **'publication'**

Definition of scientific paper

- Originality, write/publish
- An acceptable primary scientific publication (Council of Biology Editors)
  - first disclosure
  - Sufficient information
    - to assess observations
    - to repeat experiments
    - to evaluate intellectual processes

Plan for wirting a paper



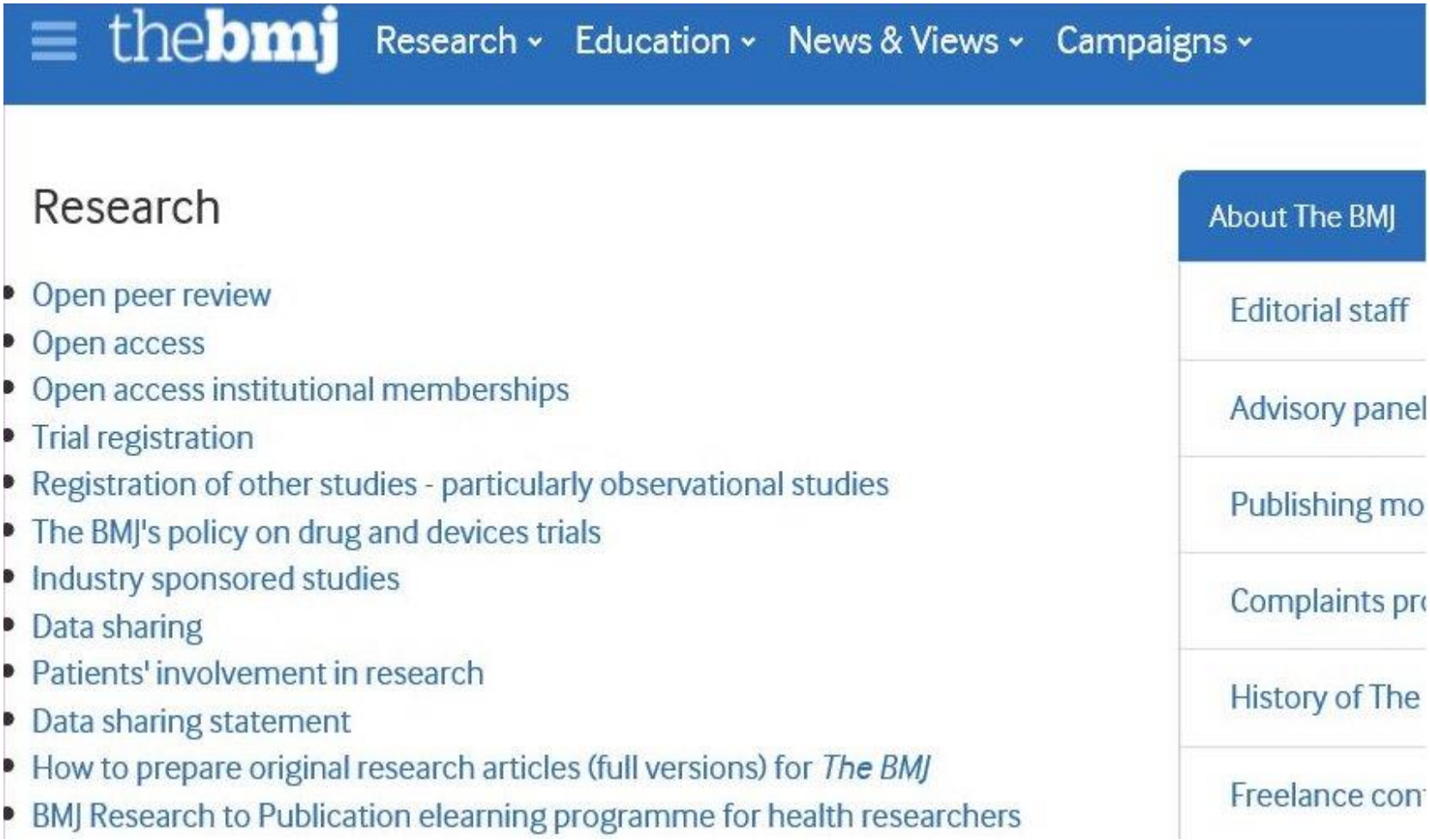
Planning a draft paper

Section	Question to be answered	Purpose	Expected length with A4 paper, font size 10–12 and 1-5 line spacing
Introduction	Why did you start?	Summarise the context of your study and state the aims clearly	1 page
Methods	What did you do?	Give enough detail for the study to be repeated	2–3 pages
Results	What did you find?	Describe the study sample and use the data analyses to answer the aims	2–3 pages
Tables and figures	What do the results show?	Clarify the results	3–6 tables or figures
Discussion	What does it mean?	Interpret your findings in context of other literature and describe their potential impact on health care	2–3 pages
References	Who else has done important work in your field?	Cite the most relevant and most recent literature	20–35 references
Total document			**12–20 pages**

How to write a paper, BMJ books

Journal format

- Cover paper
- Manuscript
- Author agreement
- Copyright transfer agreement
- etc.,
  - ✓ STROBE Statement
  - ✓ Clinical trial registration
  - ✓ Consort statement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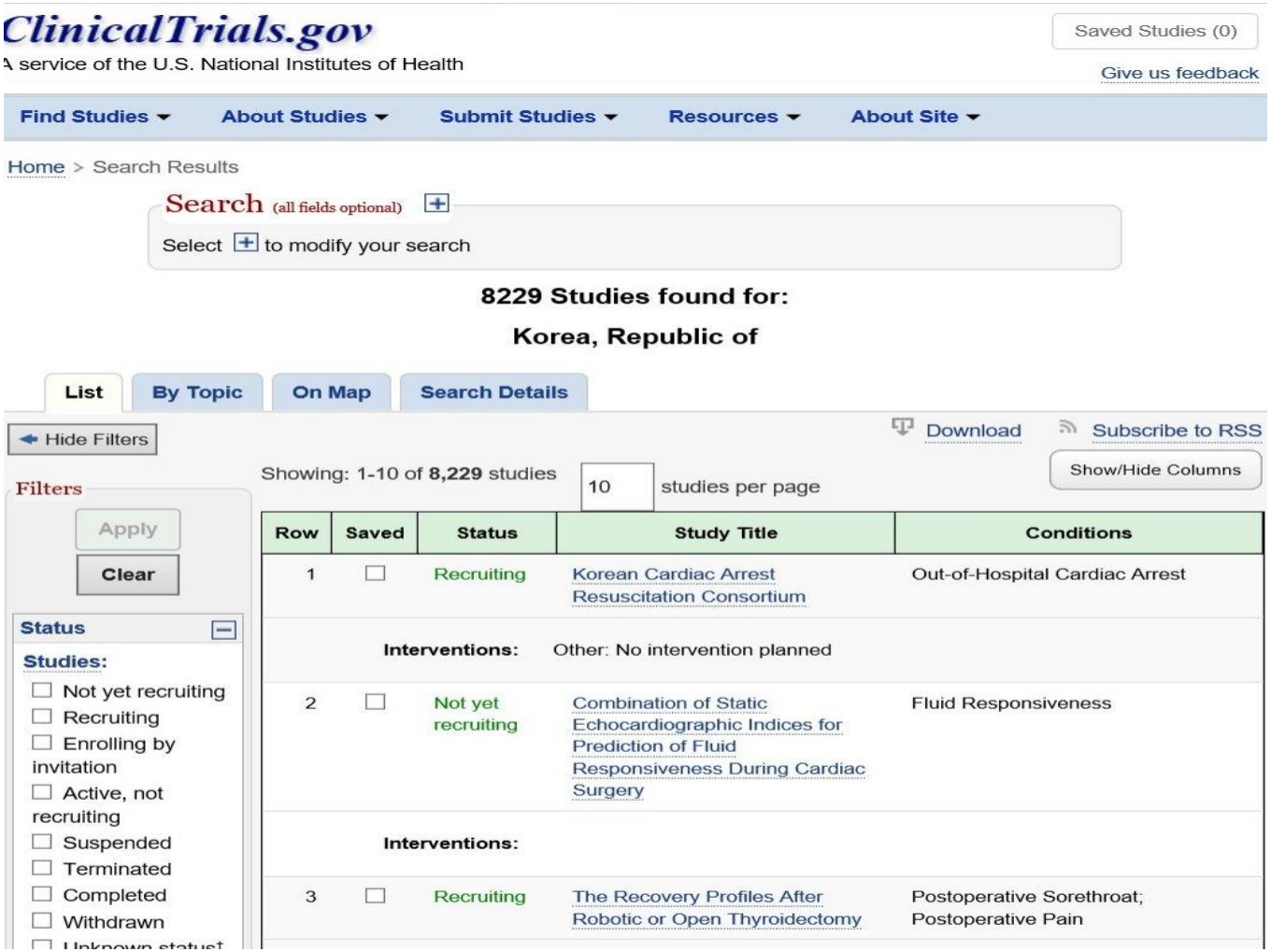
Research
Education
News & Views
Campaigns
Research
Open peer review
Open access
Open access institutional memberships
Trial registration
Registration of other studies - particularly observational studies
The BMJ's policy on drug and devices trials
Industry sponsored studies
Data sharing
Patients' involvement in research
Data sharing statement
How to prepare original research articles (full versions) for The BMJ
BMJ Research to Publication elearning programme for health researchers
About The BMJ
Editorial staff
Advisory panel
Publishing mo
Complaints pr
History of The
Freelance con

Clinical trial registration



논문의 구조
Structure of a scientific paper

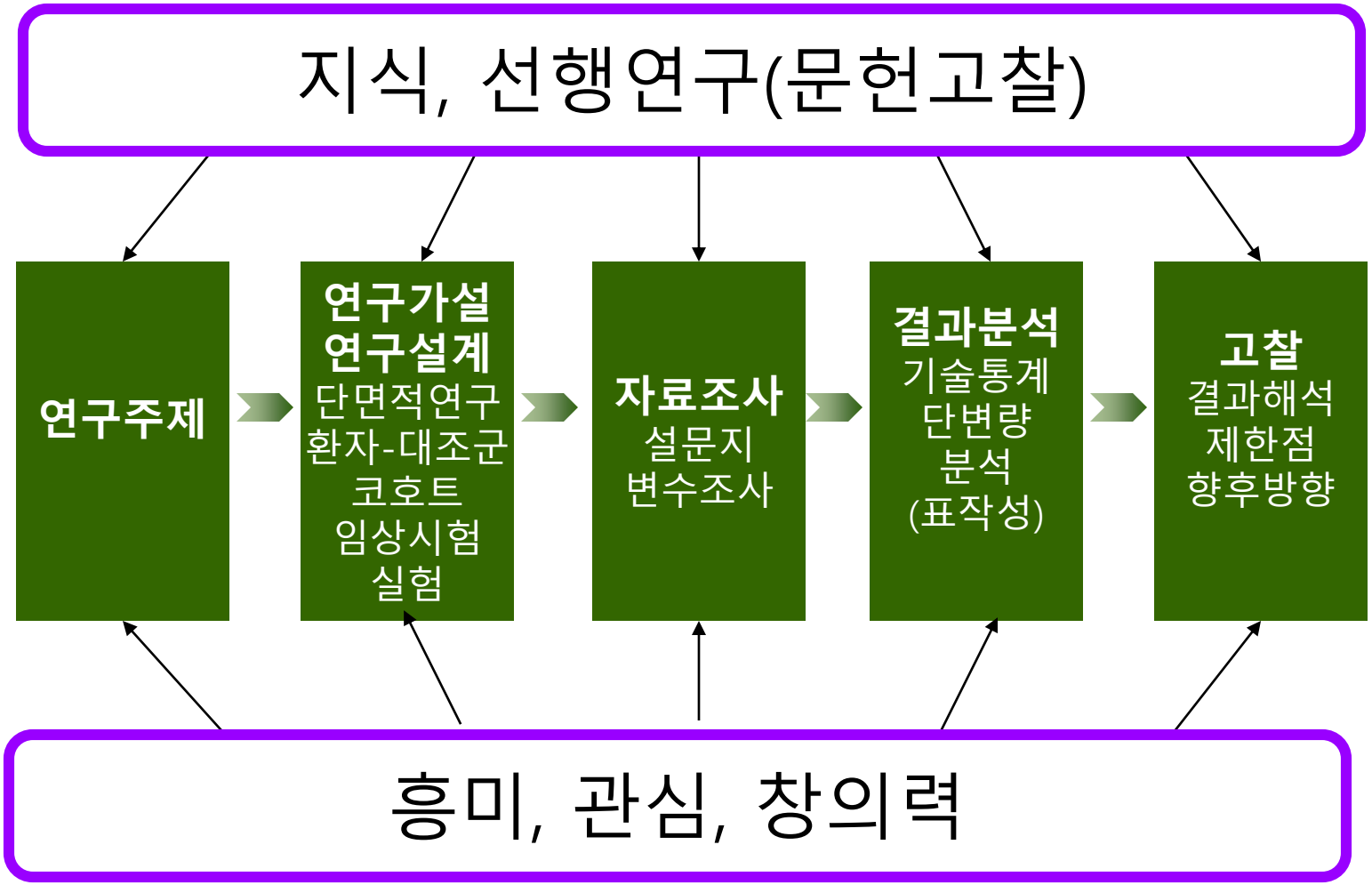
IMRAD format

- The object of publishing a scientific paper;
  - ✓ to provide a document that contains sufficient information to enable readers to:

    - assess the observations you made;
    - repeat the experiment if they wish;
    - determine whether the conclusions drawn are justified by the data.

  - ✓ I - introduction (What question was asked?)
  - ✓ M - methods (How was it studied?)
  - ✓ R – results (What was found?)
  - ✓ A - and
  - ✓ D - discussion (What do the findings mean?)

논문 작성의 순서


지식, 선행연구(문헌고찰)
연구주제
연구가설
연구설계
단면적연구
환자-대조군
코호트
임상시험
실험
자료조사
설문지
변수조사
결과분석
기술통계
단변량
분석
(표작성)
고찰
결과해석
제한점
향후방향
흥미, 관심, 창의력

Principles of Causality:
Sir Austin Bradford Hill

1. There should be evidence of a strong association between the risk factor and the disease. Weak relationships may be due to chance occurrence and are more likely to be explainable by confounding.
2. There should be evidence that exposure to the risk factor preceded the onset of disease.
3. There should be a plausible biological explanation.
4. The association should be supported by other investigations in different study settings. This is to protect against chance findings and bias caused by a particular choice of study population or study design.
5. There should be evidence of reversibility of the effect. That is, if the 'cause' is removed the 'effect' should also disappear, or at least be less likely.
6. There should be evidence of a dose–response effect. That is, the greater the amount of exposure to the risk factor, the greater the chance of disease.
7. There should be no convincing alternative explanation. For instance, the association should not be explainable by confounding.

Cover letter

- Communication : Editor - author
- Originality
- Strength of study: results, **Clinical or Public health interest**
- Author agreement
- Conflict of interest (COI)

Abstract: Editor's perspective

- Structured or unstructured format
- Quality check
- Study importance / reliability
- Result : impact ?
- Screening stage -> reject without peer review

A population-based case-control study was conducted in Connecticut in 1996–2002 to test the hypothesis that lifetime hair-coloring product use increases non-Hodgkin's lymphoma risk. A total of 601 histologically confirmed incident female cases and 717 population-based controls were included in the study. An increased risk of non-Hodgkin's lymphoma was observed among women who reported use of hair-coloring products before 1980 (odds ratio = 1.3, 95% confidence interval (CI): 1.0, 1.8). The odds ratios were 2.1 (95% CI: 1.0, 4.0) for those using darker permanent hair-coloring products for more than 25 years and 1.7 (95% CI: 1.0, 2.8) for those who had more than 200 applications. Follicular type, B-cell, and low-grade lymphoma generally showed an increased risk. On the other hand, the authors found no increased risk of non-Hodgkin's lymphoma overall and by subtype of exposure and disease among women who started using hair-coloring products in 1980 or later. It is currently unknown why an increased risk of non-Hodgkin's lymphoma was found only among women who started using hair-coloring products before 1980. Further studies are warranted to show whether the observed association reflects the change in hair dye formula contents during the past two decades or indicates that recent users are still in their induction and latent periods.

case-control studies; Connecticut; hair dyes; lymphoma, non-Hodgkin; risk factors; women

<American Journal of Epidemiology>

Context Associations have been found between day-to-day particulate air pollution and incre adverse health outcomes, including cardiopulmonary mortality. However, studies of health ef particulate air pollution have been less conclusive.

Objective To assess the relationship between long-term exposure to fine particulate air pollu lung cancer, and cardiopulmonary mortality.

Design, Setting, and Participants Vital status and cause of death data were collected by the A Society as part of the Cancer Prevention II study, an ongoing prospective mortality study, whi approximately 1.2 million adults in 1982. Participants completed a questionnaire detailing ind data (age, sex, race, weight, height, smoking history, education, marital status, diet, alcohol c occupational exposures). The risk factor data for approximately 500 000 adults were linked v data for metropolitan areas throughout the United States and combined with vital status and data through December 31, 1998.

Main Outcome Measure All-cause, lung cancer, and cardiopulmonary mortality.

Results Fine particulate and sulfur oxide–related pollution were associated with all-cause, lur cardiopulmonary mortality. Each 10-μg/m^3 elevation in fine particulate air pollution was assoc approximately a 4%, 6%, and 8% increased risk of all-cause, cardiopulmonary, and lung canc respectively. Measures of coarse particle fraction and total suspended particles were not cons with mortality.

Conclusion Long-term exposure to combustion-related fine particulate air pollution is an imp environmental risk factor for cardiopulmonary and lung cancer mortality.

<JAMA>

제목 (Title)

- 논문의 제목만으로도 논문의 내용을 알 수 있어야 한다

- 제목 작성시에는

  연구주제를 정확하게,

  함축적으로,

  구체적으로,

  간결하게 표현해야 한다.

- 독립변수, 종속변수, 대상인구의 명시가 있어야 한다.

제목 (Title)

American Journal of Epidemiology

Vol. 159, No. 2
Printed in U.S.A.
DOI: 10.1093/aje/kwh033

Hair-coloring Product Use and Risk of Non-Hodgkin's Lymphoma: A Population-based Case-Control Study in Connecticut

Yawei Zhang[1], Theodore R. Holford[1], Brian Leaderer[1], Peter Boyle[2], Shelia Hoar Zahm[3], Stuart Flynn[4], Geovanni Tallini[4], Patricia H. Owens[1], and Tongzhang Zheng[1]

[1] Department of Epidemiology and Public Health, Yale School of Medicine, New Haven, CT.
[2] Department of Epidemiology and Biostatistics, Europe Institute of Oncology, Milan, Italy.
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Received for publication April 24, 2003; accepted for publication July 31, 2003.

Introduction (IMRAD)

Induction

or

inductive reasoning（歸納推論）

“ Tell readers why you have undertaken the study”

And “Clarify what your work adds”

Introduction (IMRAD)

- The introduction should be brief and must state clearly the question that you tried to answer in the study

- The introduction must not include a review of the literature.

  - ✓ Only cite those references that are essential to justify your proposed study.
  - ✓ Three citations from different groups usually are enough to convince most assessors that some fact is ‘ well known ’ or ‘ well recognized’, particularly if the studies are from different countries.
  - ✓ Many research groups write the introduction to a paper before the work is started, but you must never ignore pertinent literature published while the study is in progress.

Introduction (IMRAD)

An example introduction might be:

"It is well known that middle - aged male runners have diffuse brain damage,[1-3] but whether this is present before they begin running or arises as a result of repeated cerebral contusions during exercise has not been established. In the present study, we examined cerebral function in a group of sedentary middle - aged men before and after a six month exercise program. Cerebral function was assessed by . . ."

Example

There have been consistent reports of increases in incidence and mortality due to non-Hodgkin's lymphoma in many parts of the world, and Connecticut is one of the areas in the world with a confirmed increase in incidence (1). Although considerable efforts have been made, little is known about the etiology and the risk factors responsible for the increasing incidence of the disease. Epidemiologic studies of non-Hodgkin's lymphoma have provided contradictory results with respect to even major suspected risk factors.

Epidemiologic studies have linked hair-coloring product use to non-Hodgkin's lymphoma risk, but the results have been inconclusive. Two population-based case-control studies (2, 3) suggested that the use of hair dye increases the risk of non-Hodgkin's lymphoma. Using these results, Pearce and Bethwaite concluded in 1992 that "the environmental exposure which seems most likely to have contributed to the increase in non-Hodgkin's lymphoma is that of hair dyes" (4, p. 5498s).

Two prospective follow-up studies, however, have reached different conclusions. A study by Grodstein et al. (5) found no overall association between hair dye use and risk of non-Hodgkin's lymphoma among participants in the Nurses' Health Study. Another study by Thun et al. (6) reported that permanent hair dye use in general was not associated with the risk of non-Hodgkin's lymphoma, and while prolonged use of black hair dyes may increase the risk, the proportion of the disease that could be explained by dark dye use is small. A population-based case-control study by Holly et al. (7) in the San Francisco Bay Area also found no association between hair-coloring product use and the risk of non-Hodgkin's lymphoma.

Reprint requests to Dr. Tongzhang Zheng, 129 Church Street, Suite 700, New Haven, CT 06510 (e-mail: tongzhang.zheng@yale.edu).

Example

Perhaps more importantly, the risk of non-Hodgkin's lymphoma associated with hair-coloring product use may need to be examined by time period of use since the formulations of hair-coloring products have undergone tremendous change over the past 20 years. As recently reviewed by Corbett (8), after the publication in 1975 by Ames et al. (9) of their finding that a number of hair dye ingredients were mutagenic, the experimental studies by the US National Cancer Institute also showed a carcinogenic effect of some hair dye intermediates in rats and mice (10). In 1979, the US Food and Drug Administration, prompted by the positive National Cancer Institute findings, proposed to require a cancer-warning label on hair dyes containing potential carcinogenic material. According to Corbett, "The resulting concern, under the prevailing opinion that there was no safe dose for a carcinogen, caused manufacturers to reformulate all oxidative dye products during 1978–1982" (8, p. 132). This reformulation involved the replacement or elimination of some of the dyes that had been reported to produce tumors in National Cancer Institute bioassays (8). Thus, the significant changes in hair dye formulation have resulted in the discontinuation of some hair-coloring product formulations over the past 20 years (7).

This population-based case-control study conducted among Connecticut women was designed to further investigate the issue of hair-coloring product use and the risk of non-Hodgkin's lymphoma by type of product used, by subtype of the disease, and by time period of use.

Method (IMRAD)

- The main purposes of the methods section: Replication !!

  - ✓ To describe, and sometimes defend, the experimental design
  - ✓ To provide enough detail that a competent worker could repeat the study.

- To ensure reproducible data,

  - ✓ Give complete details of any new methods used;
  - ✓ Give the precision of the measurements undertaken;
  - ✓ Sensibly use statistical analysis.

Method (IMRAD)

How the study was designed

- Keep the description brief
- Say how randomization was done
- Use names to identify groups or sections of a study

How the study was carried out

- Describe how the participants were recruited and chosen
- Give reasons for excluding participants
- Consider mentioning ethical features
- Give accurate details of materials used
- Give exact drug dosages
- Give the exact form of treatment and accessible details of unusual apparatus

How the data were analyzed

- Use a P-value to disprove the null hypothesis
- Give an estimate of the power of the study (the likelihood of a false negative – the β error)
- Give the exact tests used for statistical analysis (chosen a priori)

Method (IMRAD)

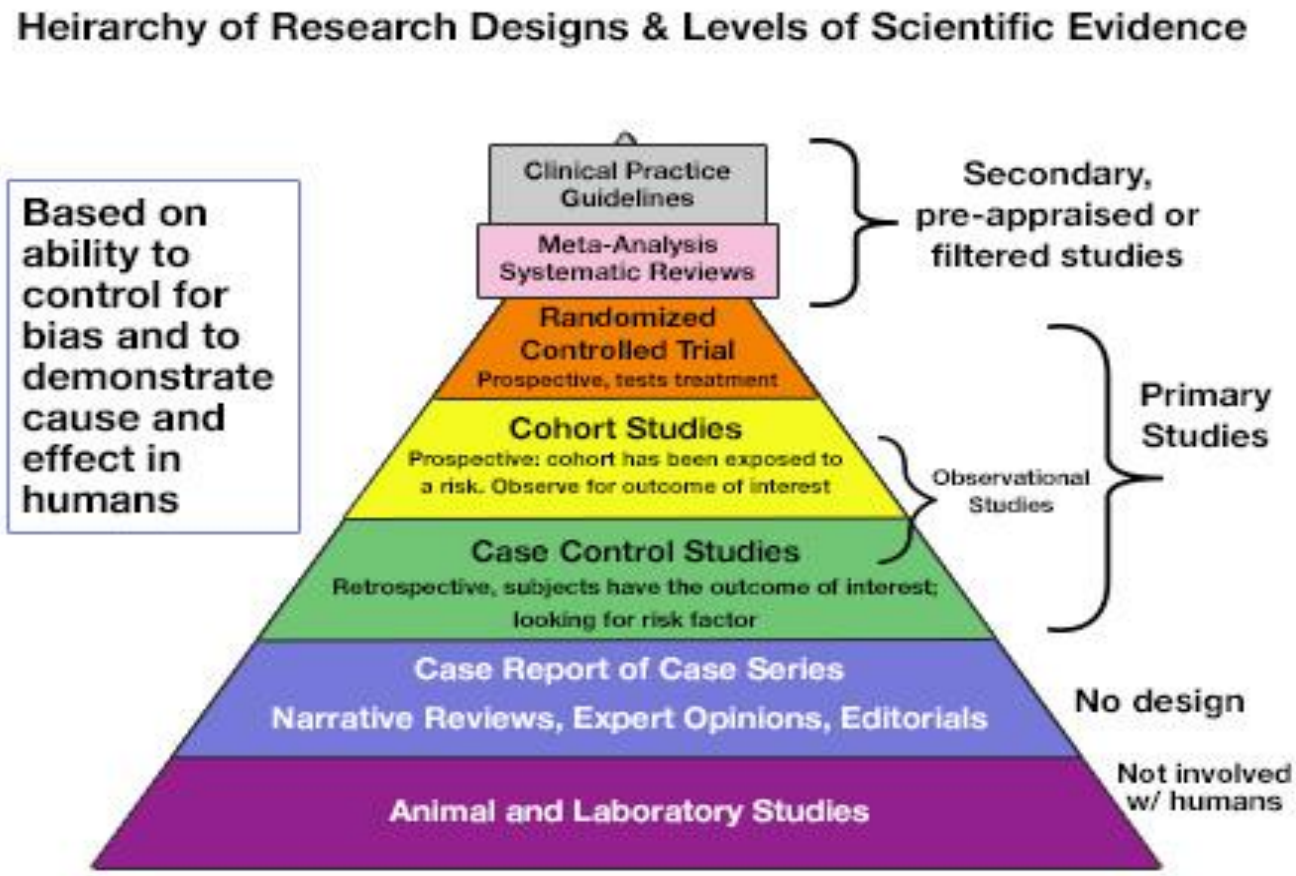
A good methods section; Editor's perspective

- Does the text describe
  - ✓ what question was being asked
  - ✓ what was being tested
  - ✓ how trustworthy are the measurements?

- Were the measurements recorded, analyzed and interpreted correctly?

- Would a suitably qualified reader be able to repeat the experiment in the same way?

Method (IMRAD)



Guidelines addressed in the Method

- Specify the minimum difference between the groups
- Specify the alpha level : statistically significant
- Power calculation
- Identify the statistical test used for each comparison
- Reference for complex or uncommon statistical tests used to analyze the data
- Specify whether the test is one or two tailed
- Reference the statistical packages or program used

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JUNE 16, 2005 VOL. 352 NO. 24

Effect of Treatment of Gestational Diabetes Mellitus on Pregnancy Outcomes

Caroline A. Crowther, F.R.A.N.Z.C.O.G., Janet E. Hiller, Ph.D., John R. Moss, F.C.H.S.E., Andrew J. McPhee, F.R.A.C.P., William S. Jeffries, F.R.A.C.P., and Jeffrey S. Robinson, F.R.A.N.Z.C.O.G., for the Australian Carbohydrate Intolerance Study in Pregnant Women (ACHOIS) Trial Group*

ABSTRACT

BACKGROUND

We conducted a randomized clinical trial to determine whether treatment of women with gestational diabetes mellitus reduced the risk of perinatal complications.

METHODS

We randomly assigned women between 24 and 34 weeks' gestation who had gestational diabetes to receive dietary advice, blood glucose monitoring, and insulin therapy as needed (the intervention group) or routine care. Primary outcomes included serious perinatal complications (defined as death, shoulder dystocia, bone fracture, and nerve palsy), admission to the neonatal nursery, jaundice requiring phototherapy, induction of labor, cesarean birth, and maternal anxiety, depression, and health status.

RESULTS

The rate of serious perinatal complications was significantly lower among the infants of the 490 women in the intervention group than among the infants of the 510 women in the routine-care group (1 percent vs. 4 percent; relative risk adjusted for maternal age, race or ethnic group, and parity, 0.33; 95 percent confidence interval, 0.14 to 0.75; P=0.01). However, more infants of women in the intervention group were admitted to the neonatal nursery (71 percent vs. 61 percent; adjusted relative risk, 1.13; 95 percent confidence interval, 1.03 to 1.23; P=0.01). Women in the intervention group had a higher rate of induction of labor than the women in the routine-care group (39 percent vs. 29 percent; adjusted relative risk, 1.36; 95 percent confidence interval, 1.15 to 1.62; P<0.001), although the rates of cesarean delivery were similar (31 percent and 32 percent, respectively; adjusted relative risk, 0.97; 95 percent confidence interval, 0.81 to 1.16; P=0.73). At three months post partum, data on the women's mood and quality of life, available for 573 women, revealed lower rates of depression and higher scores, consistent with improved health status, in the intervention group.

CONCLUSIONS

Treatment of gestational diabetes reduces serious perinatal morbidity and may also improve the woman's health-related quality of life.

From the Departments of Obstetrics and Gynaecology (C.A.C., J.S.R.) and Public Health (J.E.H., J.R.M.), University of Adelaide; the Department of Perinatal Medicine, Women's and Children's Hospital (A.J.M.); and the Department of Medicine, Lyell McEwin Health Service (W.S.J.) — all in Adelaide, Australia.

*Members of the ACHOIS Trial Group are listed in the Appendix.

N Engl J Med 2005;352:2477-86.

STATISTICAL ANALYSIS

Statistical analyses were based on the intention to treat and used SAS software, version 8.2 (SAS Institute). Analyses were adjusted for maternal age, race or ethnic group, and parity. Binary outcomes are presented as relative risks, with 95 percent confidence intervals; the number needed to treat to benefit (i.e., the number of patients who would need to be treated for a benefit in one patient) and the number needed to treat to harm (i.e., the number of patients who would need to be treated for harm to occur in one patient), with their 95 percent confidence intervals,[26] are presented for primary clinical outcomes. Relative risks were calculated with the use of log binomial regression. Continuous variables were analyzed by means of analysis of variance if they were normally distributed and by means of nonparametric tests if their distribution was not normal. The health state utility was calculated from the SF-36 according to the method of Brazier et al.[27] With no evidence of increased variance owing to the small number of twins in the study, no adjustment was made for clustering of babies with the same mothers. A P value of 0.05 was considered to indicate statistical significance; all P values were two-sided. A step-down Sidak adjustment was made for analyses involving multiple primary clinical end points.[28]

We estimated that we would need to enroll 1000 women for the study to have a statistical power of 80 percent (two-sided alpha value of 0.05) to detect a reduction in the risk of a serious perinatal outcome from 5.2 percent to 2.0 percent, using outcomes reported for all South Australian births[29] and data from Women's and Children's Hospital in Adelaide. Data were reviewed once in January 1999 by our independent data-monitoring committee, whose members were unaware of the treatment assignments, after the enrollment of 460 women. The study protocol included a prespecified stopping rule for a difference in a major end point of at least 3 SD between the groups.

STATISTICAL ANALYSIS

Discrete data are presented as frequencies and percentages, and continuous variables as means and standard deviations or as medians and interquartile ranges if the distributions were skewed. Spearman's correlation coefficient was used to measure the linear associations between the rank values of the oxidized phospholipid:apo B-100 ratio and Lp(a) lipoprotein levels as well as lipid levels and other clinical risk factors. The association of the oxidized phospholipid:apo B-100 ratio and Lp(a) lipoprotein levels with the extent of coronary artery disease was tested by one-way analysis of variance of the log-transformed values followed by a one-degree-of-freedom test for trend. The percentages of patients with obstructive coronary artery disease and the odds ratios were calculated for quartiles of the oxidized phospholipid:apo B-100 ratio and Lp(a) lipoprotein levels for all patients, according to age (≤60 years or >60 years), and according to the presence or absence of hypercholesterolemia.

Logistic-regression models were used to estimate the associations between patients' characteristics and lipid measurements and obstructive coronary artery disease. Multiple logistic-regression analysis was used to estimate the partial associations between the oxidized phospholipid:apo B-100 ratio and Lp(a) lipoprotein levels and obstructive coronary artery disease, with adjustment for age, sex, smoking status, the presence or absence of hypertension, and levels of LDL cholesterol, HDL cholesterol, triglycerides, and CRP. The base-2 logarithms ($\log_2$) of the oxidized phospholipid:apo B-100 ratio and the levels of Lp(a) lipoprotein, triglycerides, and CRP were used in all the logistic-regression models to account for skewness in the distributions. Thus, odds ratios for these variables reflect the change in odds for an increase of 1 $\log_2$ (the equivalent of a doubling of the value) in the measure.

1. Descriptive statistics

2. Univariate analysis

3. Multivariate analysis

결 과 (IMRAD)

Statistic inference

- Objectivity

결 과 (IMRAD)

A well-written results section; Editor's perspective

- Account for all subjects in the study and double check that the number of subjects is consistent in the abstract, text, tables and figures.
- Be concise and emphasise the important findings.
- Do not repeat information provided in the tables.
- Minimise abbreviations.
- Describe the results from each table or figure in a separate paragraph.
- Begin each paragraph with a topic sentence but do not simply repeat the table or figure legend.
- Importantly, the results should be interpreted in the discussion, not in the results section.

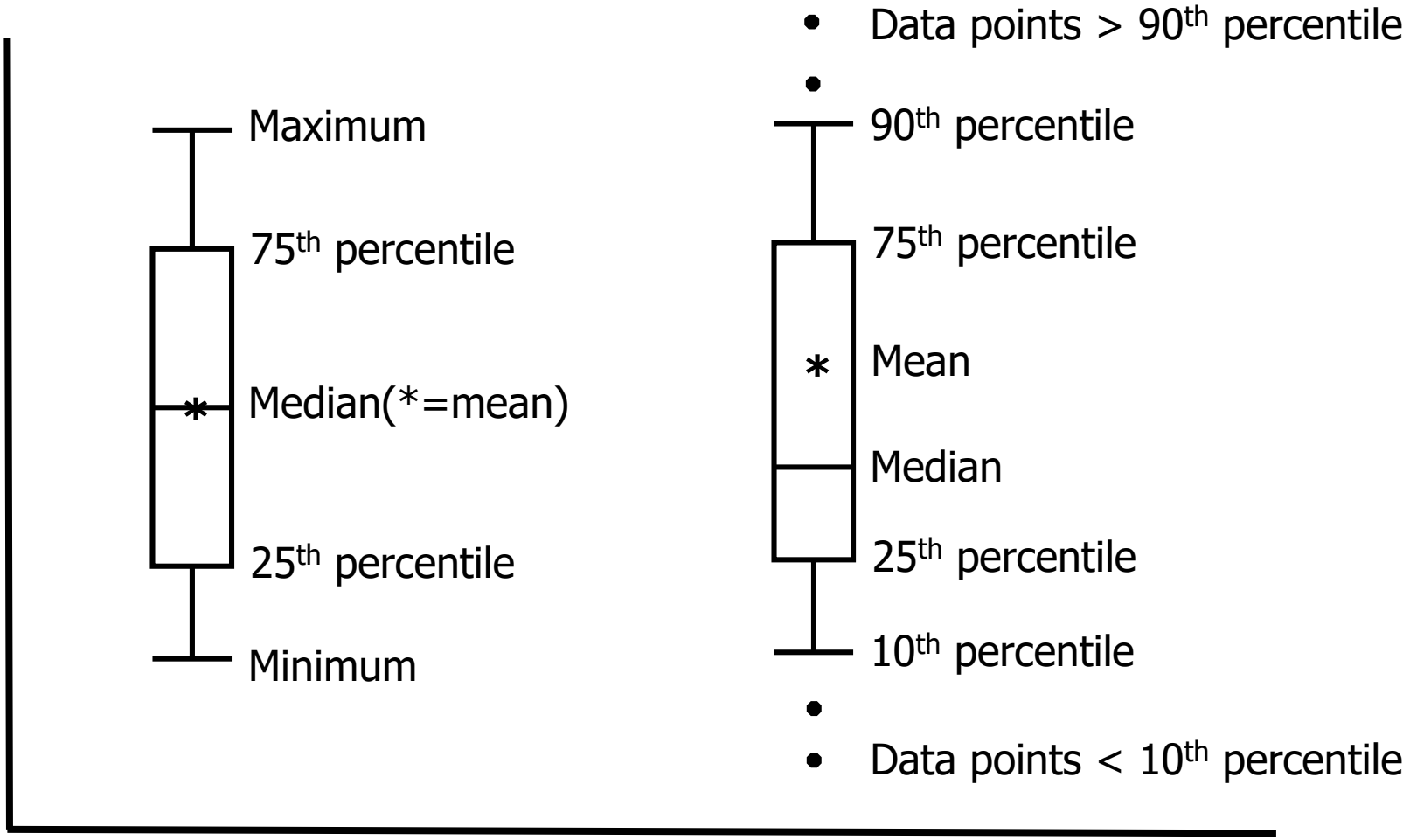
Example

Table 1. Selected baseline characteristics of non-Hodgkin's lymphoma cases and controls,Connecticut, 1996-2002

	Cases		Controls	
	No.	%	No.	%
Age (years)				
<50	119	19.8	155	21.6
50–70	277	46.1	317	44.2
>70	205	34.1	245	34.2
Race				
White	571	95.0	667	93.0
Black	18	3.0	25	3.5
Others	12	2.0	25	3.5
Family history of NHL*				
No	592	98.5	713	99.4
Yes	9	1.5	4	0.6
Tobacco smoking				
No	270	44.9	323	45.0
Yes	331	55.1	394	55.0
Alcohol drinking				
No	228	37.9	231	32.2
Yes	371	61.8	484	67.5
Missing	2	0.3	2	0.3
Educational level				
High school or less	261	43.4	265	37.0
College or higher	340	56.6	452	63.0

* NHL, non-Hodgkin's lymphoma.

Sample presentations



Normally distributed **Non-normally distributed**

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Oxidized Phospholipids, Lp(a) Lipoprotein, and Coronary Artery Disease

Sotirios Tsimikas, M.D., Emmanouil S. Brilakis, M.D., Elizabeth R. Miller, B.S., Joseph P. McConnell, Ph.D., Ryan J. Lennon, M.S., Kenneth S. Kornman, Ph.D., Joseph L. Witztum, M.D., and Peter B. Berger, M.D.

ABSTRACT

BACKGROUND

Lp(a) lipoprotein binds proinflammatory oxidized phospholipids. We investigated whether levels of oxidized low-density lipoprotein (LDL) measured with use of monoclonal antibody E06 reflect the presence and extent of obstructive coronary artery disease, defined as a stenosis of more than 50 percent of the luminal diameter.

METHODS

Levels of oxidized LDL and Lp(a) lipoprotein were measured in a total of 504 patients immediately before coronary angiography. Levels of oxidized LDL are reported as the oxidized phospholipid content per particle of apolipoprotein B-100 (oxidized phospholipid:apo B-100 ratio).

RESULTS

Measurements of the oxidized phospholipid:apo B-100 ratio and Lp(a) lipoprotein levels were skewed toward lower values, and the values for the oxidized phospholipid:apo B-100 ratio correlated strongly with those for Lp(a) lipoprotein ($r=0.83$, $P<0.001$). In the entire cohort, the oxidized phospholipid:apo B-100 ratio and Lp(a) lipoprotein levels showed a strong and graded association with the presence and extent of coronary artery disease (i.e., the number of vessels with a stenosis of more than 50 percent of the luminal diameter) ($P<0.001$). Among patients 60 years of age or younger, those in the highest quartiles for the oxidized phospholipid:apo B-100 ratio and Lp(a) lipoprotein levels had odds ratios for coronary artery disease of 3.12 ($P<0.001$) and 3.64 ($P<0.001$), respectively, as compared with patients in the lowest quartile. The combined effect of hypercholesterolemia and being in the highest quartiles of the oxidized phospholipid:apo B-100 ratio (odds ratio, 16.8; $P<0.001$) and Lp(a) lipoprotein levels (odds ratio, 14.2; $P<0.001$) significantly increased the probability of coronary artery disease among patients 60 years of age or younger. In the entire study group, the association of the oxidized phospholipid:apo B-100 ratio with obstructive coronary artery disease was independent of all clinical and lipid measures except one, Lp(a) lipoprotein. However, among patients 60 years of age or younger, the oxidized phospholipid:apo B-100 ratio remained an independent predictor of coronary artery disease.

CONCLUSIONS

Circulating levels of oxidized LDL are strongly associated with angiographically documented coronary artery disease, particularly in patients 60 years of age or younger. These data suggest that the atherogenicity of Lp(a) lipoprotein may be mediated in part by associated proinflammatory oxidized phospholipids.

From the Divisions of Cardiovascular Diseases (S.T.) and Endocrinology and Metabolism (E.R.M., J.L.W.), University of California, San Diego; the Division of Cardiovascular Diseases (E.S.B.), the Department of Laboratory Medicine and Pathology (J.P.M.), and the Division of Biostatistics (R.J.L.), Mayo Clinic, Rochester, Minn.; Interleukin Genetics, Waltham, Mass. (K.S.K.); and the Division of Cardiovascular Diseases, Duke Clinical Research Institute, Durham, N.C. (P.B.B.). Address reprint requests to Dr. Tsimikas at the Vascular Medicine Program, University of California, San Diego, 9500 Gilman Dr., Basic Sciences Bldg., Rm. 1080, La Jolla, CA 92093-0682, or at stsimikas@ucsd.edu.

N Engl J Med 2005;353:46-57.

Table 1. Baseline Characteristics and Lipid Levels in the Study Group.*

Variable	Value
Age — yr	60.1±10.9
Female sex — no. (%)	193 (38)
White race — no. (%)†	490 (97)
Hypertension — no. (%)	232 (46)
Current smoker — no. (%)	40 (8)
Previous myocardial infarction — no. (%)	77 (15)
Congestive heart failure — no. (%)	59 (12)
Family history of coronary artery disease — no. (%)	128 (25)
Hypercholesterolemia — no. (%)	286 (57)
Statin therapy — no. (%)	142 (28)
Serum creatinine level — mg/dl	
Median	1.1
Interquartile range	1.0–1.3
Indications for angiography — no. (%)‡	
Myocardial infarction within 6 wk before enrollment	41 (8)
Unstable angina	147 (29)
Dyspnea on exertion	137 (27)
Ischemia on nuclear stress test	125 (25)
Other	166 (33)
Lipid levels — mg/dl	
Total cholesterol	207±45
LDL cholesterol	124±37
HDL cholesterol	48±15
Triglycerides	
Median	153
Interquartile range	112–207
Apolipoprotein B-100	98±21
Lp(a) lipoprotein	
Median	21.1
Interquartile range	8.8–39.6
C-reactive protein — mg/liter	
Median	2.9
Interquartile range	1.2–6.7

* The study group was made up of 504 patients. Plus–minus values are means ±SD. LDL denotes low-density lipoprotein, and HDL high-density lipoprotein.
† Race was self-reported.
‡ Patients could have more than one indication for angiography.

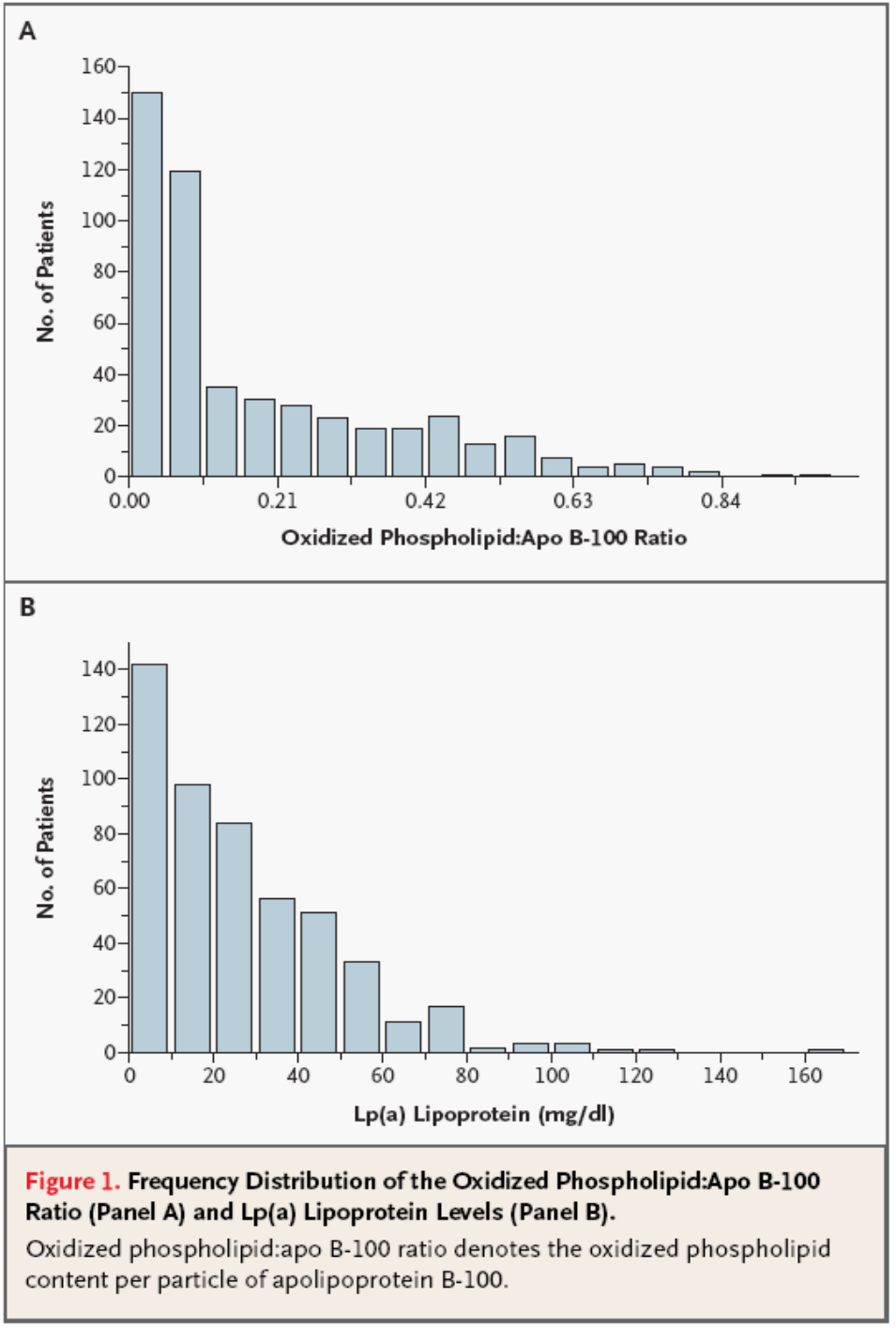
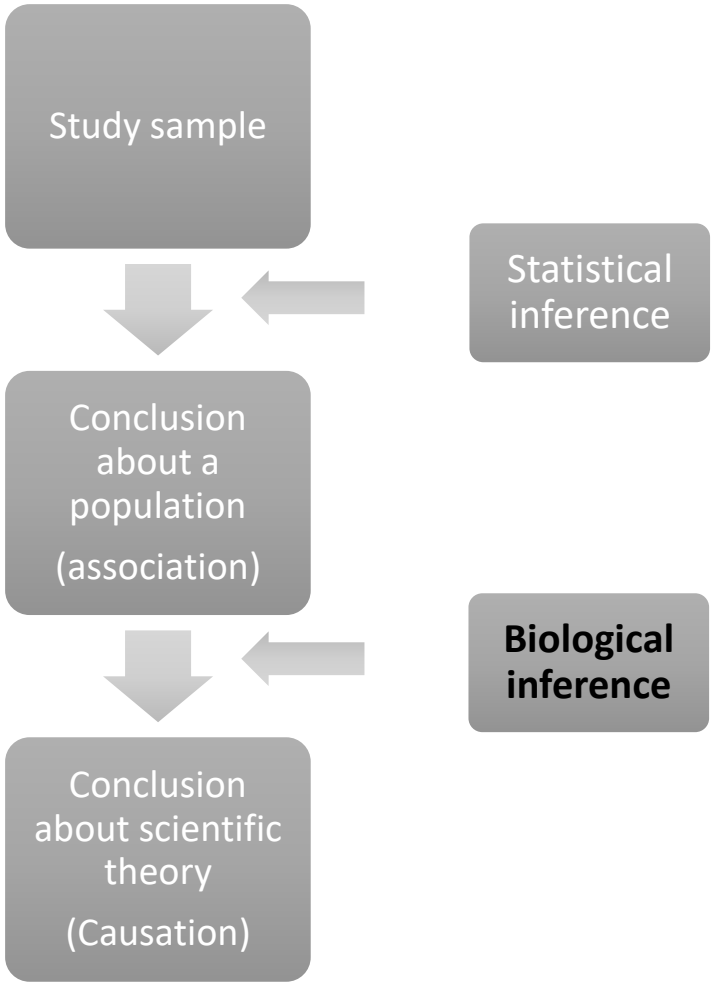


Figure 1. Frequency Distribution of the Oxidized Phospholipid:Apo B-100 Ratio (Panel A) and Lp(a) Lipoprotein Levels (Panel B).

Oxidized phospholipid:apo B-100 ratio denotes the oxidized phospholipid content per particle of apolipoprotein B-100.

고 찰(IMRAD)

- Causality
  - ✓ Biological inference
  - ✓ Replication
- Confounding or Bias



고 찰(IMRAD)

- Summarize the major findings
- Discuss possible problems with the methods used
- Compare your results with previous work
- Discuss the clinical and scientific implications of your findings
- Suggest further work
- Produce a succinct conclusion

Principles of Causality:
Sir Austin Bradford Hill

1. There should be evidence of a strong association between the risk factor and the disease. Weak relationships may be due to chance occurrence and are more likely to be explainable by confounding.
2. There should be evidence that exposure to the risk factor preceded the onset of disease.
3. There should be a plausible biological explanation.
4. The association should be supported by other investigations in different study settings. This is to protect against chance findings and bias caused by a particular choice of study population or study design.
5. There should be evidence of reversibility of the effect. That is, if the 'cause' is removed the 'effect' should also disappear, or at least be less likely.
6. There should be evidence of a dose–response effect. That is, the greater the amount of exposure to the risk factor, the greater the chance of disease.
7. There should be no convincing alternative explanation. For instance, the association should not be explainable by confounding.

Example

Several strengths and potential limitations of the study design must be considered in interpreting our findings. First, in this relatively large population-based case-control study, we assessed hair dye use at the time of diagnosis of the disease, not years before the diagnosis when young women may not have begun their hair dye use; second, we asked detailed questions and used a long list of names of hair-coloring processes to capture all hair dye uses; third, we collected detailed information on the duration, frequency, and type and color of hair-coloring products used for each period of use, which allowed us to quantitatively evaluate the risk by the major characteristics of hair-coloring product uses. Information regarding the year of first use allowed evaluation of the effect of changes in the contents of hair-coloring products during the past 20 years. Finally, the standardized, structured questionnaires used in this study were administered through face-to-face interviews with the subjects; no surrogate interviewing was used, which minimized the potential for misclassification of exposure.

One limitation for this case-control study is the potential for recall bias resulting from self-report of lifetime hair-coloring product use. In a reliability study, Shore et al. (16) reported a correlation coefficient (r) of 0.86 for duration of hair dye use from two interviews 1 year apart, with virtually no difference for cases and controls. The correlation coefficient for frequency of use was 0.92. However, although the results may indicate that the hair-coloring product information collected through self-report was reliable, differential overreporting of hair-coloring product use among non-Hodgkin's lymphoma patients may still occur if patients believe that hair-coloring product use or specific type (or color) of hair-coloring product may increase a person's non-Hodgkin's lymphoma risk. The lack of association between overall hair-coloring product use or hair color products used after 1980 and non-Hodgkin's lymphoma argues against recall bias as having a major role for the results of our study.

Another potential limitation of the study is the relatively low response rate from potentially eligible subjects. Selection bias, however, is unlikely to have played a major role in the observed associations since we found no overall association between hair-coloring product use and non-Hodgkin's lymphoma risk when all cases and controls were considered. The observed association also differs by duration of use and total number of applications and varies by type, color of products used, and period of use.

The role of chance should also be considered when interpreting our findings. Although a sample size of 601 cases and more than 700 age-matched controls gives us sufficient power to examine the overall relation between hair-coloring product use and non-Hodgkin's lymphoma risk, the statistical power to examine the relation by non-Hodgkin's lymphoma subtype, by color and type of hair-coloring products used, and by time period of use may be still limited.

Thanks for your attention