# Medical Publishing and How to Get Published Insights From an Editor

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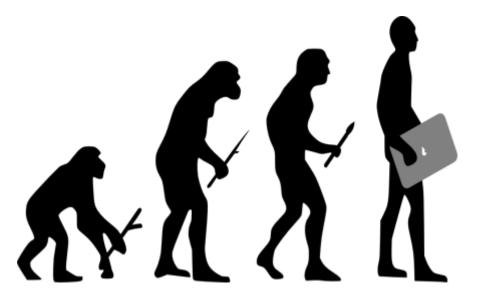
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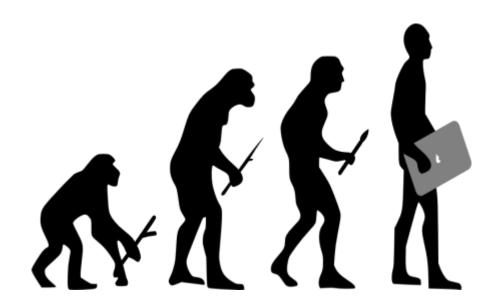
The Lancet through the ages and drivers of change

Getting published successfully (what Editors look for)





# The Lancet through the ages and drivers of change

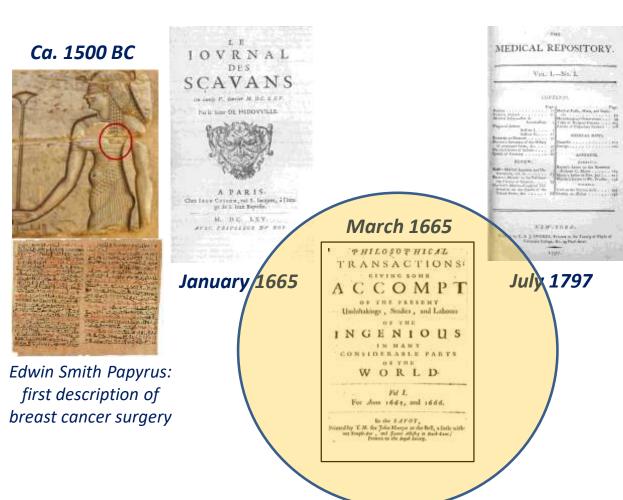


### Numbers of journals increasing rapidly



Growth in peer-reviewed journals, 1900-2013. Source: Researcher Academy, Elsevier

### Science and medical publishing through the ages



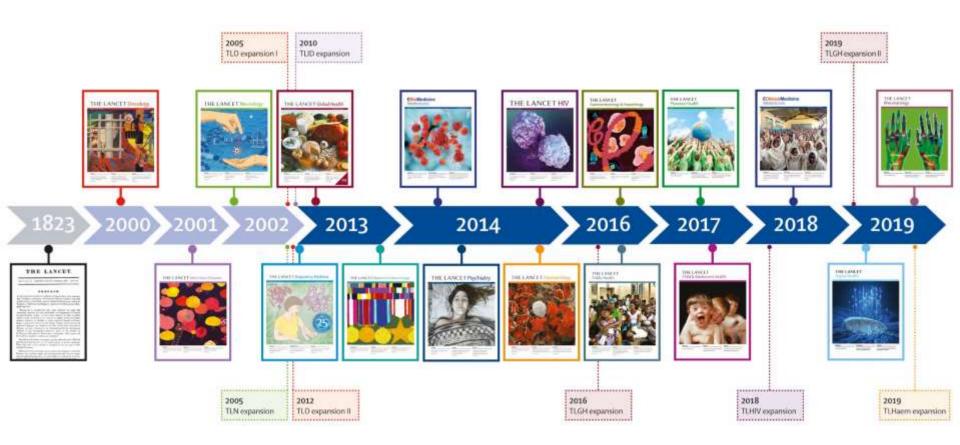
January 1812



THE LANCET.

October 1823

### The Lancet Portfolio



Who are we, what motivates us?

We are a family of medical science journals committed to:

# THE BEST SCIENCE FOR BETTER LIVES

- We stand for high quality and reliable medical science
- We are vigilant, responsive, and fast
- We are more than a collection of journals
- We are annoyed about the health disparities in our world
- We campaign for health equity and the right to health
- We are political
- We hold those in power accountable for their promises
- We are advocates and activists for health justice

### Founding of The Lancet

October 5, 1823

Thomas Wakley, founding Editor of The Lancet, member of Parliament, and coroner was a radical reformer of the Victorian age

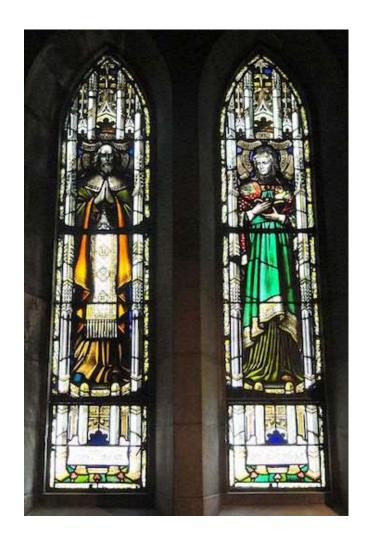
He founded The Lancet to root out corruption and quackery, and to challenge the medical establishment

The Lancet was, and still is, registered as a 'newspaper'; as a journalistic endeavour, we have a duty to hold institutions, people, science, and medicine accountable for their actions





### Founding of The Lancet



A Lancet "can be an arched window to let in the light, or it can be a sharp surgical instrument to cut out the dross, and I intend to use it in both senses."

Thomas Wakley, 1823



### Some Lancet 'firsts'

- First successful blood transfusion (1829)
- First description of chloroform an anaesthetic (1847)
- Artificial respiration (1856)
- Lister's theory of antisepsis (1867)
- Letter from Florence Nightingale on poor sanitation in India (1870)
- Nitro-glycerine for angina (1879)
- First use of x-rays (1896)
- Use of new 'hypnotic': heroin (1898)
- First publication from China (1911)
- Description of shell shock (aka, PTSD)
   (1918)
- Importance of medical statistics (1936)
- First test for tuberculosis (1951)

- Blood typing (1956)
- Thalidomide and birth defects (1961)
- Foetal alcohol syndrome (1973)
- Introduction of Glasgow Coma Scale, still in use today (1974)
- First "test tube baby" (1978)
- First use of MRI (1981)
- Discovery of Helicobacter pylori (1983)
- Use of statins for prevention of heart disease (1994)
- Creutzfeldt-Jakob syndrome (1996)
- Intensive blood glucose control for diabetes (1998)
- Causative agent of SARS (2003)
- Ebola vaccine (2015)

#### Organised science can provide a strong platform for health (and political) advocacy

#### **Mission statement**

The Lancet Oncology's global advocacy programme maps out the inequalities and inequities in health systems worldwide, and highlights deficiencies in all aspects of cancer care, health policy, structural organisation, and leadership.

The programme offers a neutral platform to bring together thought-leaders from across different disciplines and organisations to offer solutions to those barriers that hinder provision of high quality cancer control, irrespective of socioeconomic status or country of residence.

We aim to use the journal's international and influential voice to deliver the *best* science for better lives.

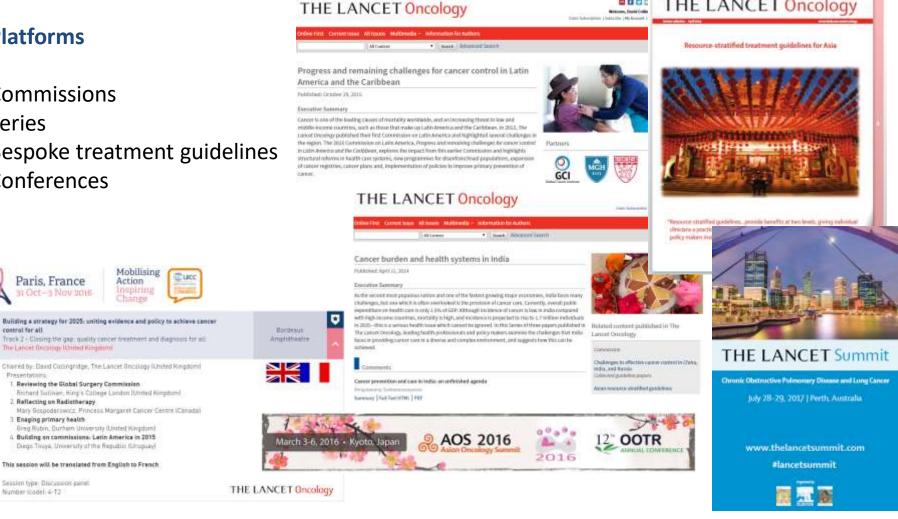
THE LANCET Oncology

#### **Platforms**

Presentations

Number (codel: 4-12

Commissions Series Bespoke treatment guidelines Conferences



#### More than a journal: Commissions

THE LANCET, REPORT ON THE OVERCHOWDING OF LONDON WORKHOUSES. STAY, 4, 1879. 27

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The two ellers mobile for modeling given by the Rayal seturns its each, Pop-Academy of Arts, at the recent distribution of prime to the act students at Burlington House, were unused to Mr. Artfor G. Atkinson, the san of Dr. Atkinson, of Kew green. The medals were given respectively for distinguished meets to neededing from life and for the restoration of an untique

#### REPORT

#### Che Tancet Special Commission

#### OVERCROWDING OF THE LONDON WORKHOUSES.

Two announces has gone forth, with all the publishy that the Charity Organisation Society sen give it, that at present there is no extra or special distress in London, no aced for special subscriptions, and that nothing is warned, accept, of course, money and mon, to strongthen the limitary is question. This optimiss stew is, however, evidently con-mitted without any knowledge of a special plane of the partition which is not only menacing to the pase thermelros, but may endanger the general health of the metropolis. We at once recognized that the number of persons receiving parton relief has not, on the whole, harmont; and, tedeol, in some partitles we have found that official postporten has the here reduced, though we dealt if poverty and distress be taught the certified may the less keen. But if the assessment of our-four relief has in only 760. This or my the less keen. Het if the ansents of out-door reief has been addened, the number of in-door paymes who people have nothing the number of in-door paymes who people may envisionmen has numbly increased, while the accommunication has not been improved to reset the certa cracks. The conversariality of the property of

The present condition of the parish of Maryletone will forcibly (Hasteste our successing. The grand total of in- and est-door poor for the week ending Doc. 21st, 1678, accounted to 4725; wherean at the end of the same week of the talked 476 present partition year the total was 4815; then showing a decrease, as owing all searches, a commonwed with \$877, of 1816. Yet this partial is at personal Newtynton Anylone recipions with \$577, of £26. Yet the partid is at person: 470 persons in the in a roost serious prelimentation, and it will require mean 470 persons in the roose arrives prelimentation. special and nanopolic effort to prevent the continuance of a next continuance state of affairs. During the above relief to maxificed weak the mythesitian had be given in-door relief to mentioned work the nethestitude had be give below that S. Sarlaur's, a sortioned work the nethestic had be give below reflect the sorty 1900 persons in 1971; while this year the number becreased in 2011. In reader nextens were, it as happens that the workbosses is in a state of traustion. It has been detormized to thild a separate infrastry, and for this pear, the state of the pear of the state of the pear of t

Ten profession will regret to heart that the medical officer ougable of hobling siz, perhaps night, hundred patients,

to cases in which there are strong or clear grounds of suspicion.) the Coroner's Court. The inquest, if it is to be of any value, gations concerning the outbreak in East London. should in all cases determine the actual cause of death; and when it fails to do so it is not only unsatisfactory, but a useless, and, it may be, a mischievous inquiry. The fact of so large a number of deaths being "uncertified" points to the vast amount of illegal practice which is carried on in this country, not only by quacks and impostors, but by druggists, and calls

A SANIYARY handbill is in circulation, drawn up at the suggestion of Dr. Aldis, and with his assistance, by Mr. Edward Hall, for the Working Men's Club. We noticed in The LANCET some little time back a movement by this Club is a sanitary direction, but were not aware that it originated with Dr. Aldis. He had, however, written a letter, which appeared in two or three newspapers, recommending the establishment of a Working Men's Sanitary Club. The result was that one of the council of the existing Club invited him to a conference with its agents, when he suggested that sanitary measures should form a prominent part of their operations, that the working man might be informed as to what was detrimental to health, and that he might have some channel through which he could make complaints, if he feared the responsibility of doing so himself. The handbill is a very useful one, and affords a great deal of should have, and even more so while the present epidemic is prevalent than at other times. It ought to be widely circulated amongst the poorer classes.

Junging from the number of letters which we receive on the subject, the question of assurance against sickness engages the attention of many members of the profession. It is certainly remarkable, in a calling so precarious and beset with so many dangers to health as ours, that no society exists in which a medical practitioner can assure against the time of sickness, of accident, or of incapacity for practice by advanced age or infirmity. A large proportion of the members of the me profession, however laborious their occupation and thrifty their habits, die poor, from being unable to lay by for any future calamity or necessity. The knowledge of this fact embitters the life of many a worthy man, and its causes, if possible, should be removed. Few are so straitened that they could not pay a moderate annual premium to be assured against the day of sorrow. Why should we not in this respect follow the example set us by the benefit clubs which are everywhere established by the working classes? Now that the system of life assurance has become so extended, why is the assurance against sickness-in our profession at leastall but impossible! One life assurance office, if not more, has, we know, entertained the question. It is high time that some definite step should be taken in the matter,

Mr. Staton is preparing to carry out for the Privy Council an investigation concerning the present outbreak of cholers. The arrangements are still incomplete; but the following appointments have been mads: — Treatment Committee: Dr. Wilks, Dr. Martin, Dr. Bristowe, and Dr. Hughlings Jackson. Pathological Committee: Dr. Thudichum (chemical pathology); Dr. Burdon Sanderson (contagion experiments); other men hers not yet appointed. Water-stand Conditions: Mr. Glaisher.

• Since writing the above, we have precived the report of the British Modella Association, containing an account of the career of the British Provident Society, which has, we ergent to observe, yeared a fablar, and is about to be wound up. Only thirty-two members had Johnel, although great effects have been made to extend its uperations.

In addition, it is known that the medical inspectors of the that the death has not been natural. The Medical Witnesses Privy Council-Dr. Scaton, Dr. Euchanan, and Dr. Hunter, Act, if properly carried out, would remove this scandal from | together with Mr. Rawlinson - have been making investi-

THE CHOLERA IN EAST LONDON.

#### Report

THE LANCET SANITARY COMMISSION

#### EPIDEMIC OF CHOLERA IN THE EAST END OF LONDON.

THE outbreak of cholera in London has now become so extensive as to furnish material for profitable investigation into some of the circumstances which are influencing its progress. In the fortnight ending July 28th, 1820 deaths from cholera and diarrhora have been recorded as having occurred in the registration districts of London. Although there have been eases in most of these districts, the vast majority have occurred in those of East London. The inquiry therefore immediately suggests itself why cholera is prevailing so extensively in these as compared with the other districts of London. That it should first appear about the ports of London was to be expected, Information which it is always important that working men should have, and even more so while the present epidemia is by ahips which have come in. The initial cases will require the property of the present epidemia is a supersymmetric transfer or the present epidemia is a supersymmetric transfer investigation. In any case, however, the fact of its rapid spread through Poplar, Bow, and Whitechapel, and not over other localities, where at least one case has occurred which might have formed a centre, would not be thus explained. The general absence of sunitary conditions in these places is only in part sufficient to account for it, for there are other districts, such as those south of the Thames, in which this is at least equalled. The one great difference in the circumstances which may influence the sanitary condition of East London, as compared with other parts of the metropolis in most respects similarly circumstanced, is its supply of drinking-water. The present purpose of this Commission is to make inquiry how far there is ground for supposing that the water supply is a cause of the spread of the cholera in London, Before proceeding with this investigation, it is very necessary to set forth in a general way the evidence we already have that the spread of cholera among a population may be influ-enced by the nature of the drinking-water, though few readers will be altogether unfamiliar with the facts we are going to

> 41 An experiment, at which mankind would have shuddered if its full meaning could have been prefigured to them, has been conducted during two epidemics of cholera on 500,000 human beings. One half of this multitude was doomed in both epidemics [1848-49 and 1853-54] to drink the same fecalized water, and on both occasions to illustrate its fatal results; while another section, freed in the second epidemic from that influence which had so aggravated the first, was happily enabled to evince by a double contrast the comparative im munity which a cleanlier beverage could give."\*

> The unfortunate people who were experimented upon were the inhabitants of nine districts of London, south of the Thames - namely, of St. Saviour's, St. Olave's, and St. George's, Southwark; of Bermondsey, Newington, Lambeth, Wandsworth, Camberwell, and Rotherhithe. One part of this people were sopplied by the Southwark and Vauxhall Company with water from the Thames at Battersea during

Mr. Sisson's Report on the last two Cholers Epidemies of Landon as affacted by the Consumption of Impure Waser, Addressed to the Hight Hon, the Frestdeet of the Board of Health.

#### **Health Policy**



#### (1) Health workers and the weaponisation of health care in Syria: a preliminary inquiry for The Lancet-American University of Beirut Commission on Syria

Fored M Found\*, Annie Spamow\*, Ahmad Tarakij, Mohamed Alameddine, Fadi El-Jardall, Adam P Coults, Nour El Amaout, Lama Bou Karrouni, Mohammed Jawad, Sophie Robergh, Auta Abbara, Fadi Albakahi, Mrahim AlMasri, Samer Jabbour

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(mmx/202/390-2516-26) The conflict in Syrta presents new and unprecedented challenges that undermine the principles and practice of health workers, health facilities, and Num 14, 2017 ambulances. Syria has become the most dangerous place on earth for health-care providers. The weaponisation of nno,(recoccupro.tinic)
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them of nt—has translated into hundreds of health workers killed, hundreds more incarcerated or tortured, and hundreds of health facilities deliberately and systematically attacked. Evidence shows use of this strategy on an unprecedented scale by the Syrian Covernment and allied forces, in what human rights organisations described as a worker NATO waterine strategy, although all parties seem to have committed volations. Attacks on health care laws synthetic at techniques all parties of eaching of the properties of the and with no health care a major factor in the flight of refugees, the effect extends well beyond Syria. The international community has left these violations of international humanitarian and human rights law largely unanswered, despite their enormous consequences. There have been repudiated denunciations, but little action on bringing the perpetrators to justice. This inadequate response challenges the foundation of medical neutrality needed to sustain the operations of global health and humanitarian agencies in situations of armed conflict. In this Health Policy, we analyse the situation of health workers facing such systematic and serious violations of international humanitarian PROFIT LIMITATION. Law. We describe the tremendous pressures that health workers have been under and continue to endure, and the NIJARANGEMEN. remarkable resilience and resourcefulness they have displayed in response to this crists. We propose policy imperatives to protect and support health workers working in armed conflict zones.

This Health Policy presents preliminary results from an inquiry of The Lancet-American University of Betrut Commission on Syria: Health in Conflict, V Health workers 1 Box Euroses MPH, American affected by the Syria conflict face serious short-term and long-term threats. In this paper, we examine the experiences of health workers tostde Syrta, and the hazardous situation School of Modern at Mount and precarrious conditions these workers face. The origins or evolution of the Syrta conflict are not described in this (A Spanner MERCLE System paper, nor the associated impact on populations and health Ametica Method Southy

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Act systematic violations of international humanitarian law the attrition of health workers, the challenges facing health S noon MS Literary of workers in different areas, and the evolving roles of health workers. Examples include the expansion in health-care tender, UK provision of single-speciality to multiple specialities, (AAbbus, Missed; Methad whether in medicine, surgery, public health, or all three, as well as role expansion beyond direct health care into newsy, and administration of hospitals or health directorates, SAMS, Added, Litheron

development of non-governmental organisations for aid delivery, coordination of vaccine campaigns, cooperation Same labour tandy of with UN and other international aid organisations, and Health Sciences, American finally, advocacy. We build on this analysis to develop policy options to ensure that health workers affected by the Syria conflict, and others elsewhere, receive the essential #2200mb.edu b attention needed to protect them, and to prevent threats to their neutrality and impartiality (panel).

#### Health workers under attack

In this paper, we propose the idea of weaponisation of health care to capture the phenomenon of large scale use of violence to restrict or deny access to care as a weapon of war. Weaponisation is multi-dimensional and includes practices such as attacking health-care facilities, targeting health workers, obliterating medical neutrality, and besieging medicine. Through large-scale violations of international humanitartan laws, wespontsation of health care amounts to what has been called a "war-crime strategy". Weaponisation of health care in the Syria conflict is manifested most notably in the targeting of health workers and facilities. The historical context is important to understand.

#### Global context: protection of health workers under international humanitarian law

The imperative for unobstructed humanitarian aid during armed conflicts is well established.5 The importance of allowing health workers to treat sick and wounded combatants led to the creation of the International Committee of the Red Cross (ICRC) in 1863 and drawe the development of the humanitarian principles of impartiality, independence, and neutrality underlying the first international humanitarian law in 1864.5 The four Geneva Conventions, codified in 1949, define the obligations of nation states engaged in armed conflict.4 The Fourth Geneva Convention, which requires warring parties to refrain from hostile actions against

www.thclances.com Vol 350 December 2, 2017

#### The Lancet Oncology's Commissions programme

#### Goal

Highlight and provide solutions for inequities in two domains:

- The patient journey from prevention through to end of life
- Global cancer control and regional variation

#### **Commissions**

Integration of oncology and palliative care: a Lancet Oncology Commission Kaasa S, et al

2018

Future Cancer Research Priorities in the USA

Jaffee E, Van Dang, C, et al November 2017

Progress and remaining challenges for cancer control in Latin America and the Caribbean

Strasser-Weipplet al October, 2015

The expanding role of primary care in cancer control

Rubin et al September, 2015

Global cancer surgery: delivering safe, affordable, and timely cancer surgery

Sullivan et al September, 2015

**Expanding global access to radiotherapy** 

Atun et al September, 2015

Challenges to effective cancer control in China, India, and Russia

Goss et al April, 2014

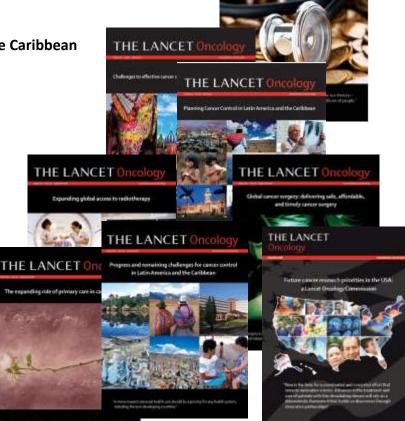
Planning cancer control in Latin America and the Caribbean

Goss et al April, 2013

Delivering affordable cancer care in high-income countries

Sullivan et al September, 2011

Four ongoing for launch 2019-21



THE LANCET Oncology

### The Lancet Oncology's Cancer Control Hub

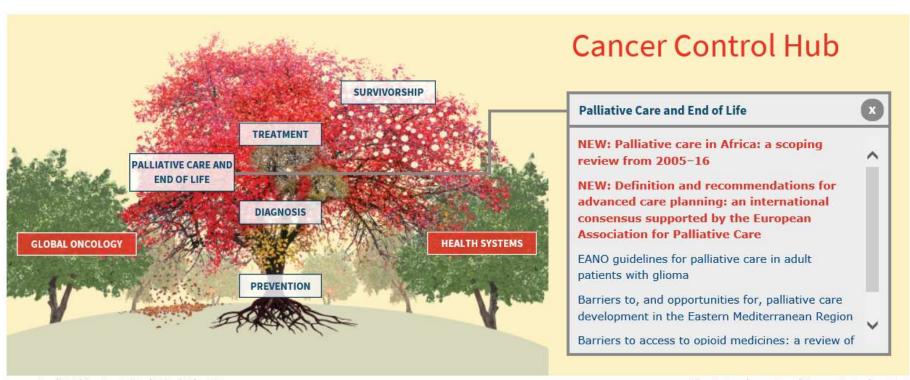


Image Credit: Adrian Roots/Paul Price/Debut Art

View text-only version of Cancer Control content

# Key developments shaping research and publishing

- Data reproducibility
- Open access
- Data-sharing
- Preprint servers

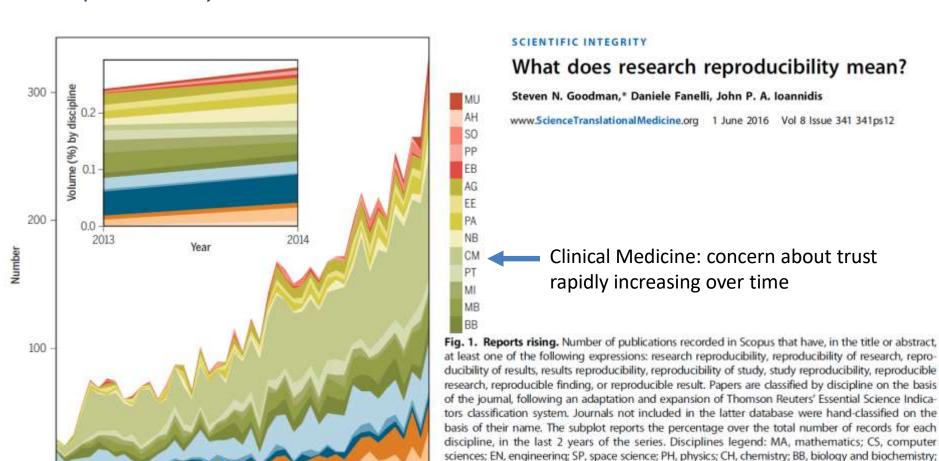


MB, molecular biology; MI, microbiology; PT, pharmacology and toxicology; CM, clinical medicine; NB, neurobiology and behavior; PA, plant and animal sciences; EE, environment and ecology; AG, agri-

cultural sciences; EB, economics and business; PP, psychology and psychiatry; SO, social sciences,

general; AH, arts and humanities; MU, multidisciplinary. The time series was truncated at 2014.

#### Data reproducibility and research waste



2000

1990

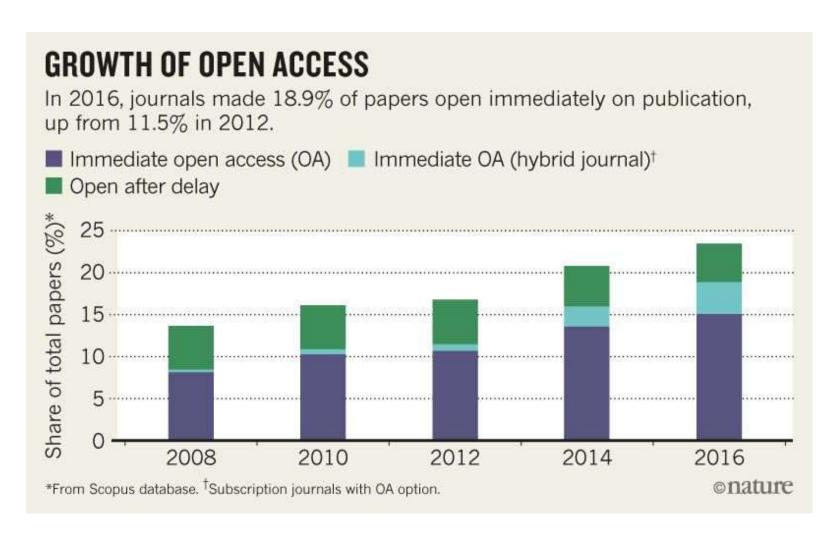
Year

1970

1980

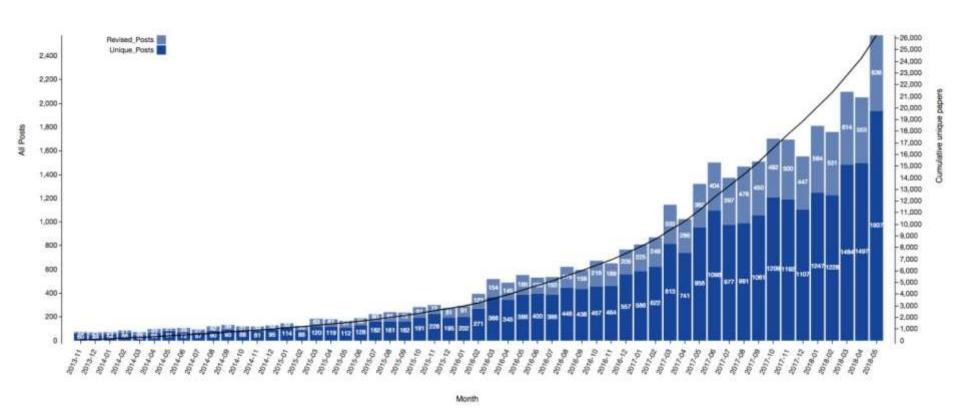
2010

### Growth in gold open access

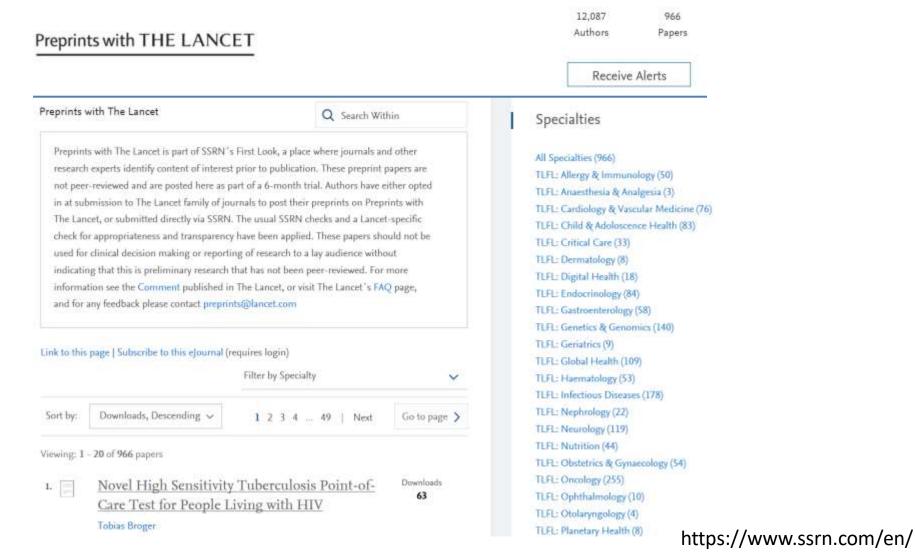


#### Preprint servers: another way of improving free access to the latest science

#### Growth in content in BioRxiv



### Preprint servers: another way of improving free access to the latest science



#### *Preprints: some facts*

- Preprints are scholarly manuscripts posted by the author in an open accessible platform, usually before, or in parallel with, the peer review process
- Increasing numbers of funders encourage preprints (Wellcome Trust, MRC, NIH)
- The Lancet family of journals are the first to launch medical preprints (research only)
  in partnership with SSRN
- As of the February 13, 2019: 1744 articles posted, 17,625 authors, 9,314 downloads
- <u>Caution:</u> preprints should not be used for clinical decision-making or reporting research findings to a lay audience without indicating they are preliminary research that has not been peer-reviewed

### Data-sharing: position of medical journals

- 1 As of July 1, 2018, manuscripts submitted to ICMJE journals that report the results of clinical trials must contain a data sharing statement as described below.
- 2 Clinical trials that begin enrolling participants on or after Jan 1, 2019, must include a data sharing plan in the trial's registration. The ICMJE's policy regarding trial registration is explained on the ICMJE website.

Comment

# Data sharing statements for clinical trials: a requirement of the International Committee of Medical Journal Editors



The International Committee of Medical Journal Editors (ICMJE) believes there is an ethical obligation to responsibly share data generated by interventional clinical trials because trial participants have put themselves at risk. In January, 2016, we published a proposal aimed at helping to create an environment in which the sharing of de-identified individual participant data becomes the norm.<sup>1</sup> In response to our request for feedback we received many comments from individuals and groups. Some applauded the

It is encouraging that data sharing is already occurring in some settings. Over the past year, however, we have learned that the challenges are substantial and the requisite mechanisms are not in place to mandate universal data sharing at this time. Although many issues must be addressed for data sharing to become the norm, we remain committed to this goal.

Therefore, the ICMJE will require the following as conditions of consideration for publication of a clinical trial report in our member journals: Published Online June 5, 2017 http://dx.doi.org/10.1016/ 50140-6736(17)31282-5

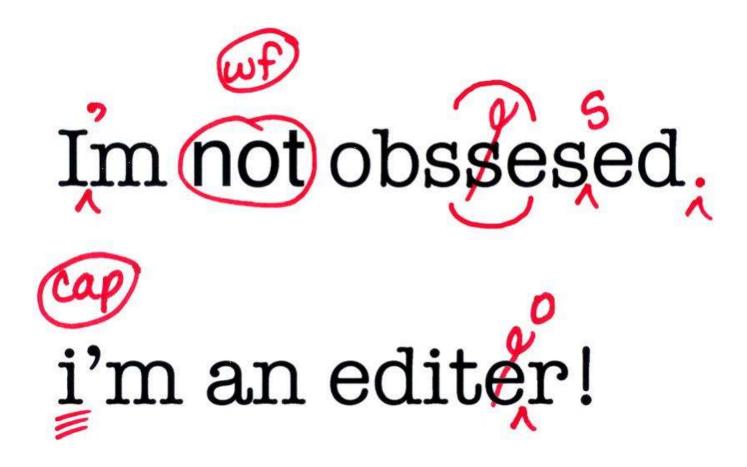
For ICMJE's website see www. icmie.org

For ICMJE's policy regarding trial registration see www. kmje.org/recommendations/ browse/publishing-andeditorial-issues/clinical-trialregistration.html

### Data-sharing: some reflections

- Ethical obligation for data-sharing as trial participants have placed themselves at risk
- Shared data might provide observations that would not have been seen
- Shared data will increase the confidence and trust in research conclusions by allowing independent validation
- Will hasten research speed and effectiveness while simultaneously reducing research waste
- Reduces risk for future patients (increased knowledge leading to better trial designs, and reduction in numbers of patients needed to be enrolled in trials)

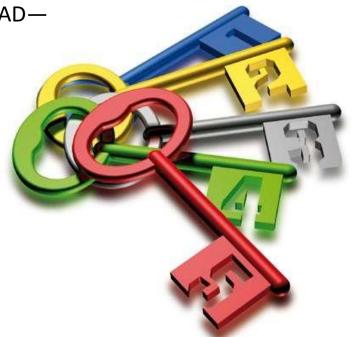
Getting published successfully (what Editors look for)



### Keys to a successful publication

- Answering the right question in the right way at the right time
- Making your submission as compelling as possible
- Writing in an accessible manner

 For research always following the basic rule: IMRAD— Introduction, Methods, Results, and Discussion



### Why publish?

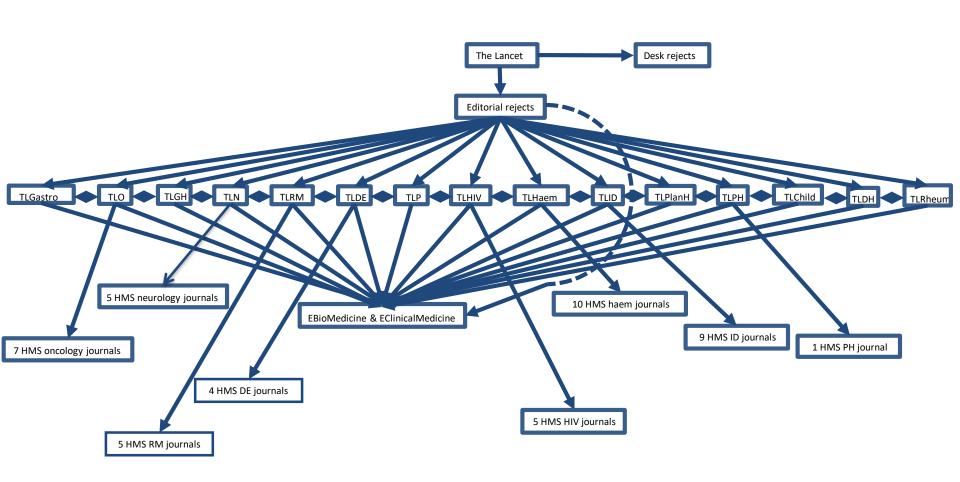
#### The positives:

- 1) To influence thinking and clinical practice
- 2) To improve patient outcomes
- 3) Personal recognition
- 4) To prove your work is a high calibre
- 5) As professional obligation to society
- 6) To access a privilege your work affords you
- 7) For personal challenge
- 8) Improve career prospects

#### The negatives:

- 1) Takes time away from core activities
- Opens yourself up to criticism and judgment by others
- 3) Can lead to rejection
- 4) Can be stressful

Journal collaborations and cascade workflows at The Lancet Group



### What do top-ranking journals publish?

- Novel work
- First and last
- Practice-changing
- Challenges convention or dogma
- Largest dataset to-date (with different or definitive results to all other papers)
- Robust methodology
- Not just positive results, some negatives are very important
- Clinical trials
- Large meta-analyses
- Topic relevant to a large demographic
- Messages that are not regionally or geographically limited

#### Common barriers to publication

#### Examples include...

Lack of novelty
Poorly defined objectives
Inappropriate analyses
Findings not validated, independently
Biased and illogical reporting
Poorly conceived arguments and discussion
'Me too' syndrome
Subject too specialised
Topic or article out of scope of chosen journal
Very poor presentation and use of language hindering understanding

#### Mathematical errors also affect success

#### Examples include...

Insufficient numbers to address objectives with confidence

Inappropriate analyses

Inconsistent reporting of data, or of facts and figures, throughout a paper

Over-emphasising interpretation of certain data or facts and figures

Lack of a prespecified statistical plan

Over-reliance on ad-hoc, exploratory analyses

Use of wrong statistical tests for comparisons

Use of outmoded analytics

Over-reliance on very rare, perhaps unvalidated, analytical tests

And sometimes...

Data that seem to be 'to good to be true'

#### What editors look for: general points

Does the topic or article type fall within the scope of the journal?

Is the topic important and timely?

Is the study interesting to our readers?

Does the study have potential to change clinical practice?

Does the study have a sound hypothesis and design?

Is it appropriately powered statistically?

Is the study analysed properly?

Are missing data handled appropriately?

Is the interpretation a fair reflection of the results?

For trials: does study have a protocol?

For trials: are main analyses presented protocol-defined?

For trials: are non-protocol (exploratory) analyses signposted?

For trials: is it registered?

#### What editors look for: general points

Has the paper been written according to Information for Authors?

For Lancet journals: does is contain a Research in Context panel (systematic review; interpretation)

For Lancet journals: does it contain Search Strategy and Selection Criteria panel

Is writing style concise and well ordered?

Have appropriate reporting standards been used?

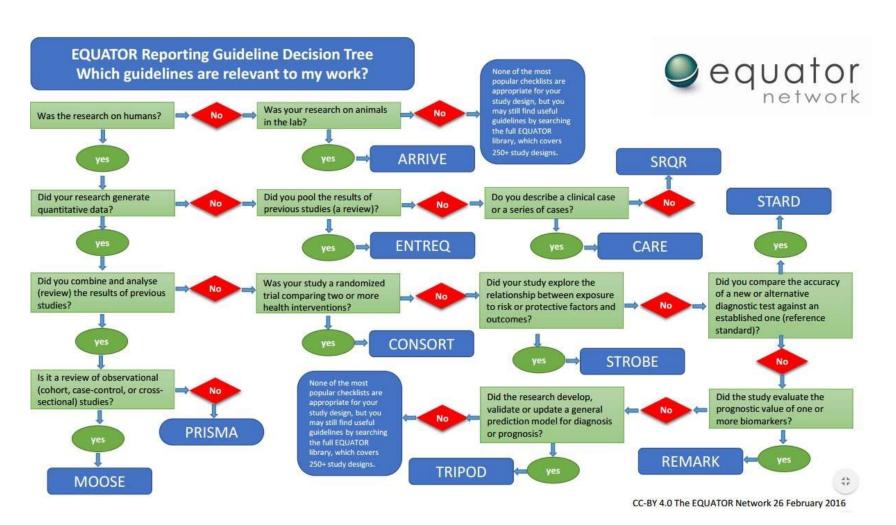
Have authors clearly stated the need for this study in context?

Is the paper a salami slice?

### What editors look for: Quality of life & patient-reported outcomes

Is QOL/PRO a valid endpoint in this study?
Is QOL/PRO protocol defined?
Is QOL/PRO measured with a validated instrument?
Do results represent an appropriate proportion of patients?
Should QOL/PRO data be presented with other endpoints?
Are data analysed and interpreted correctly?
Is result powered statistically, and if not, why not?
Is the result clinically relevant?

### What editors look for: use of reporting standards



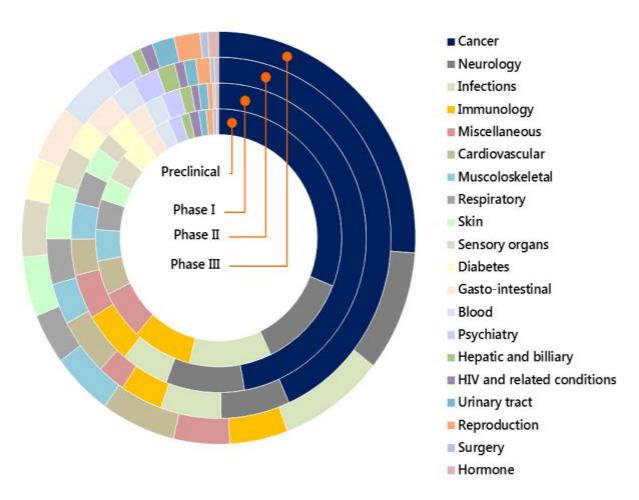
#### Clinical trial registration: why important?

Promotes transparency in reporting
Highlights those trials that might never report
Identifies whether there is a need for a trial
Allows any protocol amendments to be seen
Publicly available resource for patients and doctors

#### Clinical trial registration services, some examples...

WHO International Clinical Trials Registry (ICTRP) http://www.who.int/ictrp/en/ US NIH Clinical Trials http://www.clinicaltrials.gov Australia and New Zealand's (ANZCTR) http://www.anzctr.org.au Brazilian Clinical Trials Registry (ReBec) http://www.ensaiosclinicos.gov.br Chinese Clinical Trial Registry (ChiCTR) http://www.chictr.org Clinical Research Information Service (CRiS), Republic of Korea http://cris.cdc.go.kr Clinical Trials Registry - India (CTRI) http://ctri.nic.in Cuban Public Registry of Clinical Trials(RPCEC) http://registroclinico.sld.cu EU Clinical Trials Register (EU-CTR) https://www.clinicaltrialsregister.eu/ German Clinical Trials Register (DRKS) http://www.drks.de Iranian Registry of Clinical Trials (IRCT) http://www.irct.ir/ Japan's UMIN-CTR http://umin.ac.jp The Netherlands National Trial Register http://www.trialregister.nl The International ISRCTN http://isrctn.org/ Pan African Clinical Trial Registry (PACTR) http://www.pactr.org/ Sri Lanka Clinical Trials Registry (SLCTR) http://www.slctr.lk/

### Clinical trial registration: why important?



Distribution of pharmaceutical preclinical and clinical trials in 2016, by disease WHO Technical Report: Pricing of cancer medicines and its impacts, 2019

#### Research in Context panel

#### Research in context

#### Evidence before this study

To identify other studies of inhibitors of PD-1 or PD-L1 in advanced cancers, including melanoma, we did a detailed search of PubMed and congress abstracts from the annual meetings of the American Society of Clinical Oncology, European Society of Medical Oncology/European Cancer Congress, and Society for Melanoma Research, between Jan 1, 2010 and Jan 13, 2015. We used the search terms "PD-1", "PD-L1", "nivolumab", "MK-3475", "pembrolizumab", "lambrolizumab", "MPDL3280A", and "MEDI4736". Our search identified several non-randomised, non-controlled phase 1/2 studies with promising levels of antitumour response for PD-1 and PD-L1 inhibitors in patients with advanced solid tumours, including melanoma. Although these data suggest activity for PD-1 inhibition in patients with melanoma that have progressed after ipilimumab and BRAF inhibitors, the sample sizes were too small to allow firm conclusions to be drawn on the efficacy and safety of PD-1 inhibition. Our review identified only one randomised, controlled, phase 3 study comparing an

anti-PD-1 drug (nivolumab) with dacarbazine, but this study was done in treatment-naive patients who had BRAF wild-type tumours.

#### Added value of this study

For the patient population investigated in this study, treatment options are very restricted, and no prospective, randomised, controlled trial comparing an anti-PD-1 drug with any approved treatment has been done. Our data show that nivolumab led to clinically meaningful improvements in the proportion of patients achieving an objective response and provided a manageable safety profile when compared with chemotherapy.

#### Implications of all the available evidence

Nivolumab can now be deemed a new treatment option for patients that have progressed after ipilimumab, or a BRAF inhibitor and ipilimumab if their melanoma is BRAF<sup>v600</sup>-mutated. These data resulted in the accelerated approval of nivolumab by the US Food and Drug Administration for this indication in December, 2014.

### Search strategy for Reviews

#### Search strategy and selection criteria

We searched PubMed for early (phase 1 and 2) and randomised controlled (phase 3) clinical trials in advanced melanoma, published in English after 2000, with the terms "melanoma" and "treatment". These studies were reviewed for therapeutic approach, novelty, and clinical outcomes. We also searched PubMed with the terms "melanoma", "melanoma subtypes", "melanoma and BRAF V600E", "melanoma and KIT", "melanoma and bio-chemotherapy", "melanoma and CTLA-4", and "melanoma and survival". Relevant articles published after 1990 were selected as historical references and as a source of preclinical data to form the scientific rationale for current trial design in metastatic melanoma. Because of the novelty of the topic presented in this Review, several trials are ongoing; we therefore, searched for these clinical trials on the clinicaltrials.gov database and looked for "advanced melanoma" or "metastatic melanoma", or for specific novel agents being investigated.

### Conflicts of interest and disclosure

A conflict of interest exists when an author or the author's institution has financial or personal relationships with other people or organisations that inappropriately influence (bias) his or her actions

A conflict of interest can undermine the credibility of the journal, the authors, and of the science

Financial interests include employment, consultancies, stock ownership, honoraria, and paid expert testimony

Conflicts can occur for other reasons, such as personal relationships, academic competition, and intellectual passion

ICMJE common disclosure form: www.icmje.org/coi\_disclosure.pdf

For research articles: need full declaration. For reviews: might prevent submission

### Role of the funding source

All sources of funding should be declared

Authors must describe the role of any study sponsor(s) in study design; in the collection, analysis, and interpretation of data; in the writing of the report; and in the decision to submit the paper for publication

The corresponding author should confirm whether he or she had full access to all the data in the study and had final responsibility for the decision to submit for publication

### Role of medical writer or editor

If a medical writer or editor was involved, the name and information about funding of this person should be disclosed

Signed statements from any medical writers or editors declaring that they have given permission to be named as an author, as a contributor, or in the Acknowledgments section is important

### What editors look for: plagiarism

Plagiarism is becoming an increasingly prominent problem Editors expect all authors to submit original work and not be intellectually lazy Plagiarism covers the copying of others work, duplicate publication, and 'text recycling'

The Lancet's journals have been routinely checking reviews, opinions, and comments for plagiarism since 2010 using specialist software

Offenders can be reported to their institution

Institutions are taking allegations of plagiarism very seriously akin to professional misconduct

*The cover letter: important or not?* 

Be brief
Do not repeat abstract
Highlight the unique aspects of your paper vs current practice
Highlight why chosen journal is the best readership for your paper
Highlight upcoming events, or government or regulator decisions
Mention any people who would be inappropriate referees and why

