Journals on Ovid: Supporting Researchers, Supporting Open Science

Michael Fanning
Training Manager
Health Learning, Research & Practice

Wolters Kluwer

Agenda

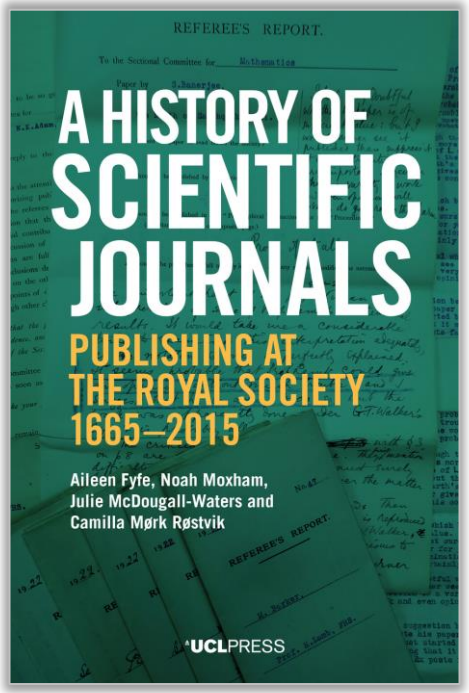
- Scientific Journals
- Journals on Ovid
- Open Access Publishing
- Open Data Sharing
- Society Journals on Ovid

Scientific Journals

Scientific Journals – Publishing Since 1665

"…it was in 1665 that the *Journal des Sçavans* and the *Philosophical Transactions* of the Royal Society of London were first published, in France and in England respectively. They were founded with the intent to advance scientific knowledge by building on colleagues' results and avoid duplication of results, and established both the principles of scientific priority and peer review."

(Note: Emphasis added)



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Larivière V, Haustein S, Mongeon P (2015) The Oligopoly of Academic Publishers in the Digital Era. PLoS ONE 10(6): e0127502. doi:10.1371/ journal.pone.0127502

Scientific Journals – Driving Search & Discovery

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Journals on Ovid

LWW High Impact Collection – Selection

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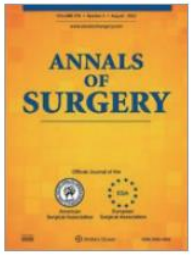
LWW High Impact Collection – By Impact Factor

TOP 10!

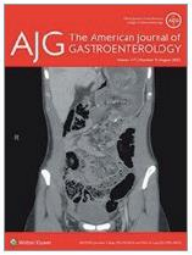
Top 10 Ranked Journals by Impact Factor

IMPACT FACTOR
50.717

IMPACT FACTOR
23.213



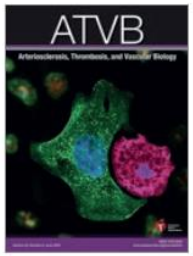
IMPACT FACTOR
13.787



IMPACT FACTOR
12.045

IMPACT FACTOR
11.800

IMPACT FACTOR
10.782



IMPACT FACTOR
10.514

IMPACT FACTOR
10.447

IMPACT FACTOR
10.170

IMPACT FACTOR
10.065

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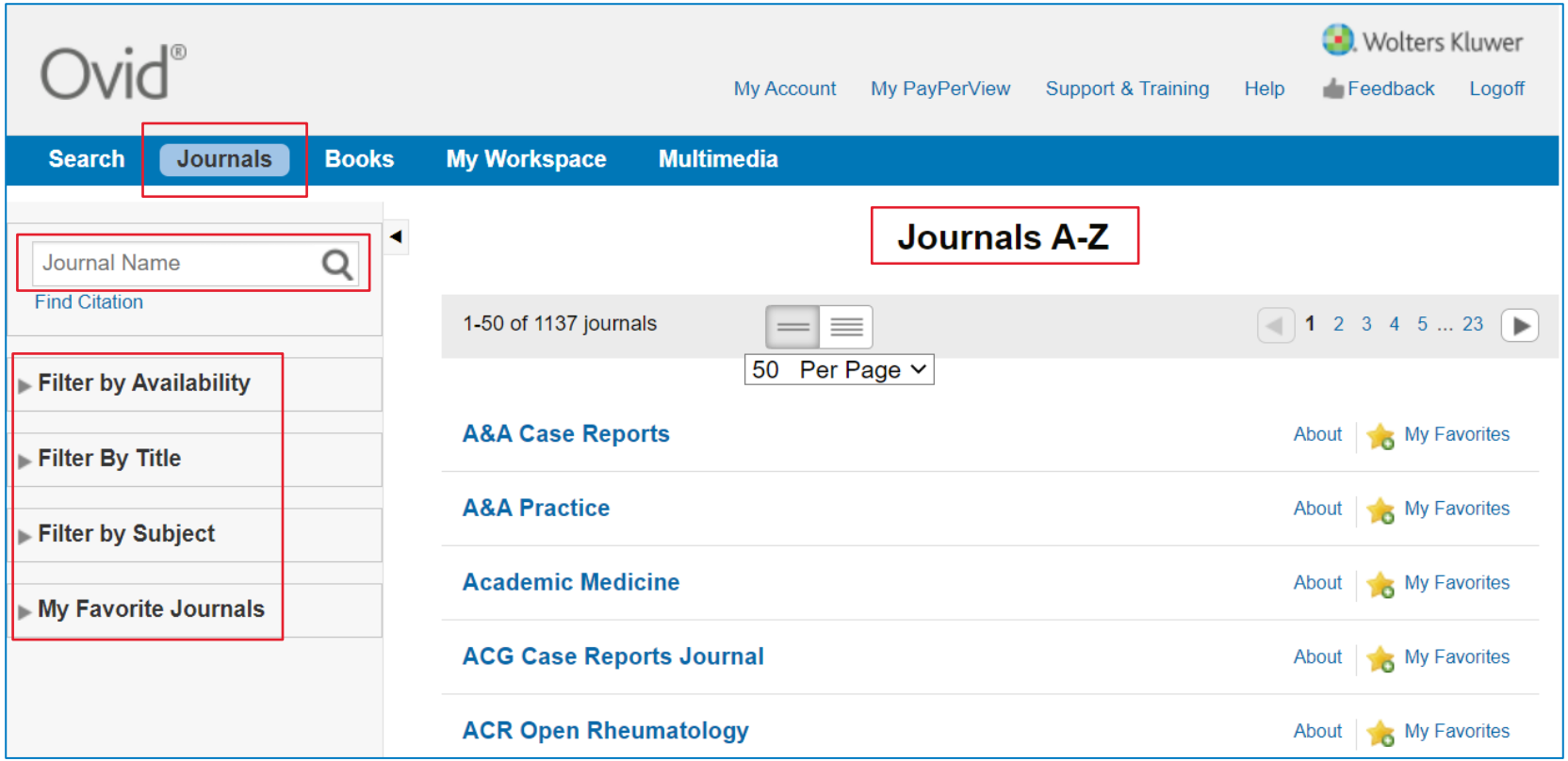
LWW High Impact Collection – On Ovid



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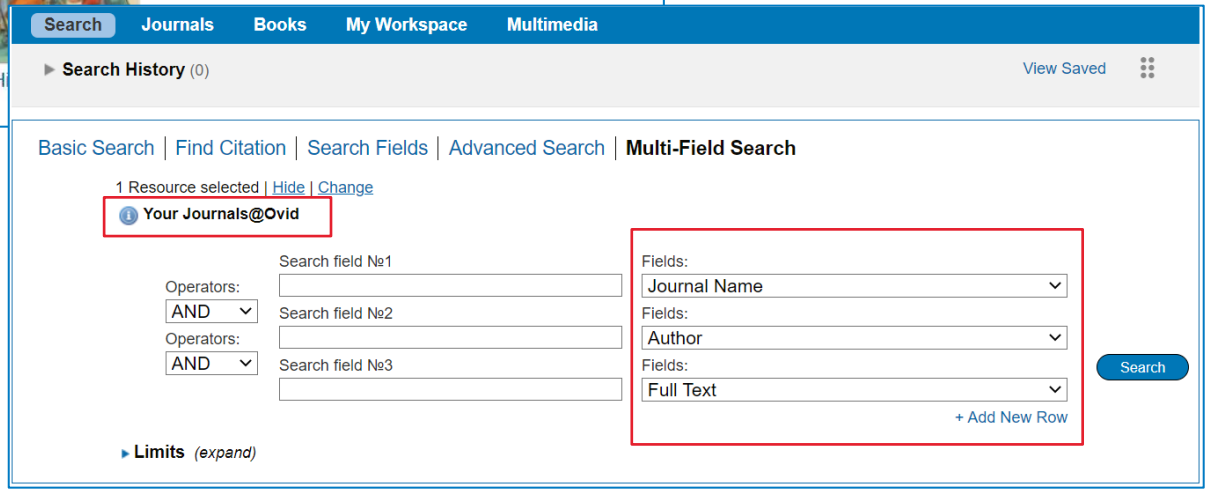
LWW High Impact Collection – Searchable

Individual journals



Individual journals and/or collection

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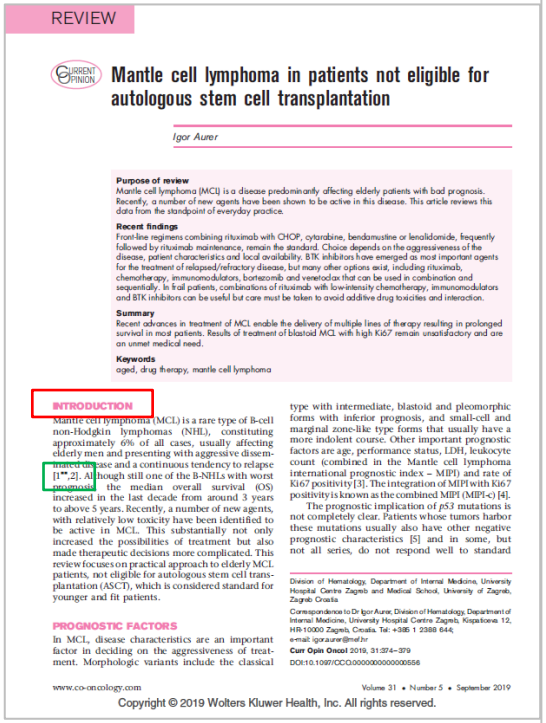
LWW High Impact Collection – Readable



REVIEW

Mantle cell lymphoma in patients not eligible for autologous stem cell transplantation

Igor Aurer

Purpose of review
Mantle cell lymphoma (MCL) is a disease predominantly affecting elderly patients with bad prognosis. Recently, a number of new agents have been shown to be active in this disease. This article reviews this data from the standpoint of everyday practice.

Recent findings
Front-line regimens combining rituximab with CHOP, cytarabine, bendamustine or lenalidomide, frequently followed by rituximab maintenance, remain the standard. Choice depends on the aggressiveness of the disease, patient characteristics and local availability. BTK inhibitors have emerged as most important agents for the treatment of relapsed/refractory disease, but many other options exist, including rituximab, chemotherapy, immunomodulators, bortezomib and venetoclax that can be used in combination and sequentially. In frail patients, combinations of rituximab with low-intensity chemotherapy, immunomodulators and BTK inhibitors can be useful but care must be taken to avoid additive drug toxicities and interaction.

Summary
Recent advances in treatment of MCL enable the delivery of multiple lines of therapy resulting in prolonged survival in most patients. Results of treatment of blastoid MCL with high Ki67 remain unsatisfactory and are an unmet medical need.

Keywords
aged, drug therapy, mantle cell lymphoma

INTRODUCTION

Mantle cell lymphoma (MCL) is a rare type of B-cell non-Hodgkin lymphomas (NHL), constituting approximately 6% of all cases, usually affecting elderly men and presenting with aggressive disseminated disease and a continuous tendency to relapse [1**,2]. Although still one of the B-NHLs with worst prognosis, the median overall survival (OS) increased in the last decade from around 3 years to above 5 years. Recently, a number of new agents, with relatively low toxicity have been identified to be active in MCL. This substantially not only increased the possibilities of treatment but also made therapeutic decisions more complicated. This review focuses on practical approach to elderly MCL patients, not eligible for autologous stem cell transplantation (ASCT), which is considered standard for younger and fit patients.

PROGNOSTIC FACTORS

In MCL, disease characteristics are an important factor in deciding on the aggressiveness of treatment. Morphologic variants include the classical type with intermediate, blastoid and pleomorphic forms with inferior prognosis, and small-cell and marginal zone-like type forms that usually have a more indolent course. Other important prognostic factors are age, performance status, LDH, leukocyte count (combined in the Mantle cell lymphoma international prognostic index – MIPI) and rate of Ki67 positivity [3]. The integration of MIPI with Ki67 positivity is known as the combined MIPI (MIPI-c) [4].

The prognostic implication of *p53* mutations is not completely clear. Patients whose tumors harbor these mutations usually also have other negative prognostic characteristics [5] and in some, but not all series, do not respond well to standard

Division of Hematology, Department of Internal Medicine, University Hospital Centre Zagreb and Medical School, University of Zagreb, Zagreb Croatia

Correspondence to Dr Igor Aurer, Division of Hematology, Department of Internal Medicine, University Hospital Centre Zagreb, Kispatićeva 12, HR-10000 Zagreb, Croatia. Tel: +385 1 2388 644; e-mail: igor.aurer@mef.hr

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KEY POINTS

- Indolent MCL exists and needs to be recognized in order to avoid unnecessary treatment.
- Rituximab, combined with standard cytotoxic agents (CHOP, bendamustine and cytarabine) or lenalidomide remains the preferred front-line therapy option.
- BTK inhibitors are the most important and effective agents for treatment of R/R/MCL, but multiple other options exist and should be exploited in the course of the disease.

immunochemotherapy [6**]. It seems possible that different agents (e.g. bendamustine) [7] are less sensitive to the effects of *p53* mutations than others (e.g. cytarabine).

STAGING

MCL is staged similar to other types of NHL. Lymph node biopsy should be performed whenever feasible because Ki67 positivity cannot be reliably determined from a bone marrow biopsy. Due to frequent marrow infiltration, bone marrow biopsy is strongly recommended except in cases with lymphoma cells in the blood. In patients with clinically localized MCL, PET scanning and colonoscopy are useful in excluding asymptomatic extranodal and colon involvement. Minimal residual disease (MRD) determination in blood or marrow, by PCR using individually sequenced primers spanning the IgH rearrangement region or flow cytometry, is not recommended outside of clinical studies.

INDOLENT MANTLE CELL LYMPHOMA

At least 10% of MCL cases are indolent and do not require therapy for a longer period of time [8**]. They typically present with leukemic disease and splenomegaly, without significant lymphadenopathy. Patients are usually women, and tumor cells are usually SOX11 negative. Rare findings of in-situ mantle cell neoplasia restricted to mantle zones of hyperplastic appearing lymphoid tissue have been described [9]. Occasionally, patients with typical nodal MCL (SOX11 positive) present with indolent features. Asymptomatic patients with low-tumor mass should first be observed without treatment in order to reliably determine their need for therapy. This is even more important in frail elderly.

FRONT-LINE THERAPY

European guidelines for front-line treatment of MCL recommend bendamustine with rituximab, R-CHOP (rituximab, cyclophosphamide, doxorubicine, vincristine, steroid), VR-CAP (bortezomib, rituximab, cyclophosphamide, doxorubicine, steroid) and R-BAC (rituximab, bendamustine, cytarabine, dexamethasone) [10**]. American (NCCN) recommendations also include Vcr-CVAD (rituximab, bortezomib, cyclophosphamide, vincristine, doxorubicin and dexamethasone) and lenalidomide with rituximab [11**]. A recently described regimen not included in these recommendations is R-CHOP alternating with intermediate doses of cytarabine and rituximab (R-CHOP/R-HD-AraC) [12*]. Published results of these regimens are presented in Table 1. All of them have excellent response rates, but the duration of response after less intensive regimens is suboptimal if maintenance is not used. Addition of bendamustine to lenalidomide with rituximab results in an increase in immune-mediated side-effects, without clear-cut improvement in efficacy, and should probably not be used outside of clinical trials [20].

Randomized studies compared R-CHOP to bendamustine with rituximab, and R-CHOP to VR-CAP [13,14]. R-CHOP had inferior PFS but not OS in both. In the former study, median PFS of patients treated with R-CHOP was 22 and 35 months with bendamustine with rituximab (hazard ratio 0.49, $P = 0.0044$). In the latter study, median PFS was 14 months with R-CHOP and 25 months with VR-CAP (hazard ratio 0.63, $P < 0.001$), 4-year OS was 54 vs. 64% ($P = 0.17$). None included rituximab maintenance making the interpretation of this difference for everyday practice difficult.

Rituximab maintenance is proven to be beneficial after R-CHOP induction [16]. Phase II studies and the extrapolation of data from a trial performed in younger patients, suggest that the same is true for HD-AraC containing regimens and Vcr-CVAD [12*,19,21**]. The role of rituximab maintenance for bendamustine containing regimens is debatable. The randomized study designed to address this question after bendamustine with rituximab has so far been presented only as an abstract with statistically insignificantly prolonged PFS (median 69 months with and 57 without maintenance) and no difference in OS (66% with vs. 70% without maintenance at 6 years) [17]. There are no data on rituximab maintenance after R-BAC [15**]. The seminal study [16] was designed using rituximab every 2 months until progression or unacceptable toxicity and a substantial number of patients continues with it for more than 5 years [22*]. Therefore, continuation of rituximab maintenance until progression or unacceptable toxicity, should be considered the standard of care in elderly MCL patients treated with R-CHOP or similar regimens.

In the lenalidomide plus rituximab regimen double maintenance with both agents was used

been no comparative studies to suggest its superiority over rituximab [47]. The efficacy of thalidomide in MCL has been known for years [48], but the drug was never directly compared with lenalidomide. Thalidomide is more toxic [49], causes more severe neuropathy, has a higher risk of thromboembolism, and is therefore nowadays rarely used except in countries where lenalidomide is not available and possibly in patients with severe renal failure. There are no data on the efficacy of pomalidomide in MCL. The combination of oral arsenic trioxide, chlorambucil and ascorbic acid in R/R MCL resulted in a response rate of 49% and 16 months median PFS [50]. A combination with the PI3K inhibitor idelalisib has been tested in MCL and found to be very toxic and not very effective [51*].

FOLLOW-UP

As with other types of lymphoma, routine performance of radiologic studies to detect asymptomatic relapse is not useful and should be avoided [52**].

FRAIL ELDERLY

It is paramount to balance treatment efficacy and toxicity. Rituximab is generally well tolerated, but not effective as monotherapy [53]. In patients with low Ki67 and nonblastoid morphology, it is reasonable to combine it with less aggressive chemotherapy, such as lower dosed bendamustine, mini-CHOP, CVP or even chlorambucil and steroids. Alternatives include combinations of rituximab with lenalidomide or thalidomide that can sometimes, if it does not cause neuropathy, be better tolerated than the former because of less systemic and hematologic side-effects. Ibrutinib (and other BTK inhibitors) are effective and usually reasonably well tolerated, but care must be taken to adjust comedications accordingly.

None of the available treatment options show reliable prolonged activity in very aggressive blastoid disease. In that case, best supportive care, after thorough discussions with the patient and his/her family, might be an appropriate option.

CONCLUSION

MCL remains an incurable lethal disease for most patients, but the sequential use of wisely chosen options enables the majority to receive multiple lines of therapy and enjoy prolonged survival with reasonable quality of life. Both older (i.e. cytotoxic agents, rituximab and radiotherapy) and newer agents (i.e. immunomodulators, BTK, proteasome and BCL2 inhibitors) should be used in sequence or combination adapted to patient characteristics and local circumstances. Due to the continuous propensity for relapse, continuous therapy or maintenance should be preferred. Current data suggest that BTK inhibitors, possibly in combination with rituximab, should be used as early in the course of R/R disease, as possible.

Prognosis of blastoid disease with high Ki67 is still grave. This remains an unmet need, together with the treatment of multiply relapsing patients.

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Conflicts of interest
The author received honoraria from Roche, Jansen, Abbvie, Celgene, Pfizer, Teva and Makpharm.

REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:
- * of special interest
- ** of outstanding interest

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Medicine

Open Access “Mega Journal”

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Medicine flips to an Open Access Mega Journal

- On March 31st, 2014 *Medicine* was transformed from a subscription journal to an open access multi-disciplinary “mega journal”.

- *Medicine*’s editorial mission is to “accept content that is scientifically, technically and ethically sound, and in compliance with standard reporting guidelines.”

2013 2014

Medicine and Decentralized Peer Review

- To achieve its editorial mission and address the increase in submissions, *Medicine* operates an inclusive, efficient, global peer review model.

Medicine's "Mega-Board"

- Comprised of over 800 members from 62 different nations.
- Board provides expertise in 43 therapeutic areas.

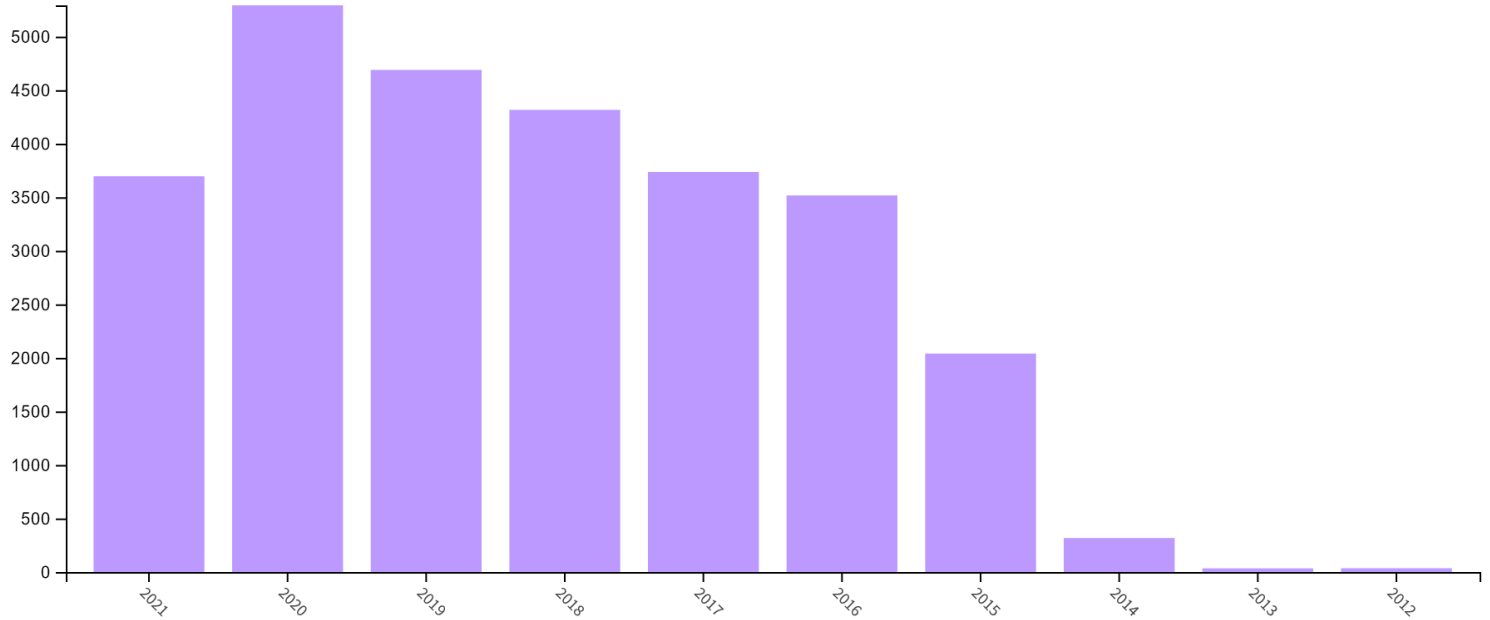
Efficient Peer-Review Process

- Efficiency is the result of closely matching editor, reviewer and manuscript interests.
- Automated matching of editors and reviewers to submitted manuscripts based on classifications.

Establishing Baseline Quality

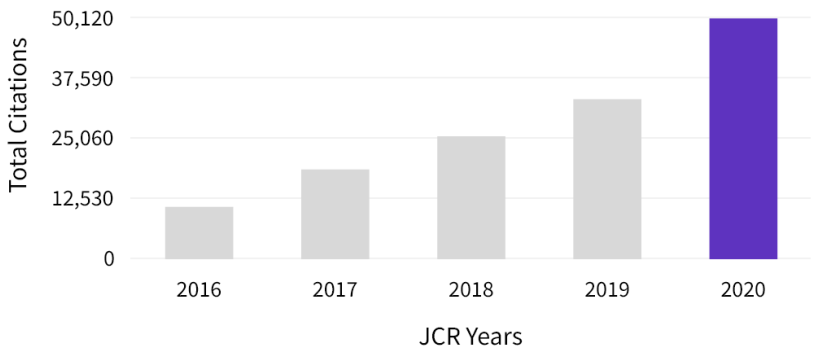
- Integrates reporting guidelines into article types and required submission items.
- All *Medicine* submissions require compliance with the corresponding reporting guideline.

Medicine Published Article Counts



Source: Web of Science

Medicine Citation Counts



Top 10 most cited journals in the MEDICINE, GENERAL & INTERNAL category 2020

Journal name	Total Citations
NEW ENGLAND JOURNAL OF MEDICINE	464,376
LANCET	369,614
JAMA-JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION	224,165
BMJ-British Medical Journal	158,758
Cochrane Database of Systematic Reviews	81,217
ANNALS OF INTERNAL MEDICINE	72,594
BMJ Open	55,070
MEDICINE	50,120
PLOS MEDICINE	42,447
AMERICAN JOURNAL OF MEDICINE	29,192

Source: Journal Citation Reports

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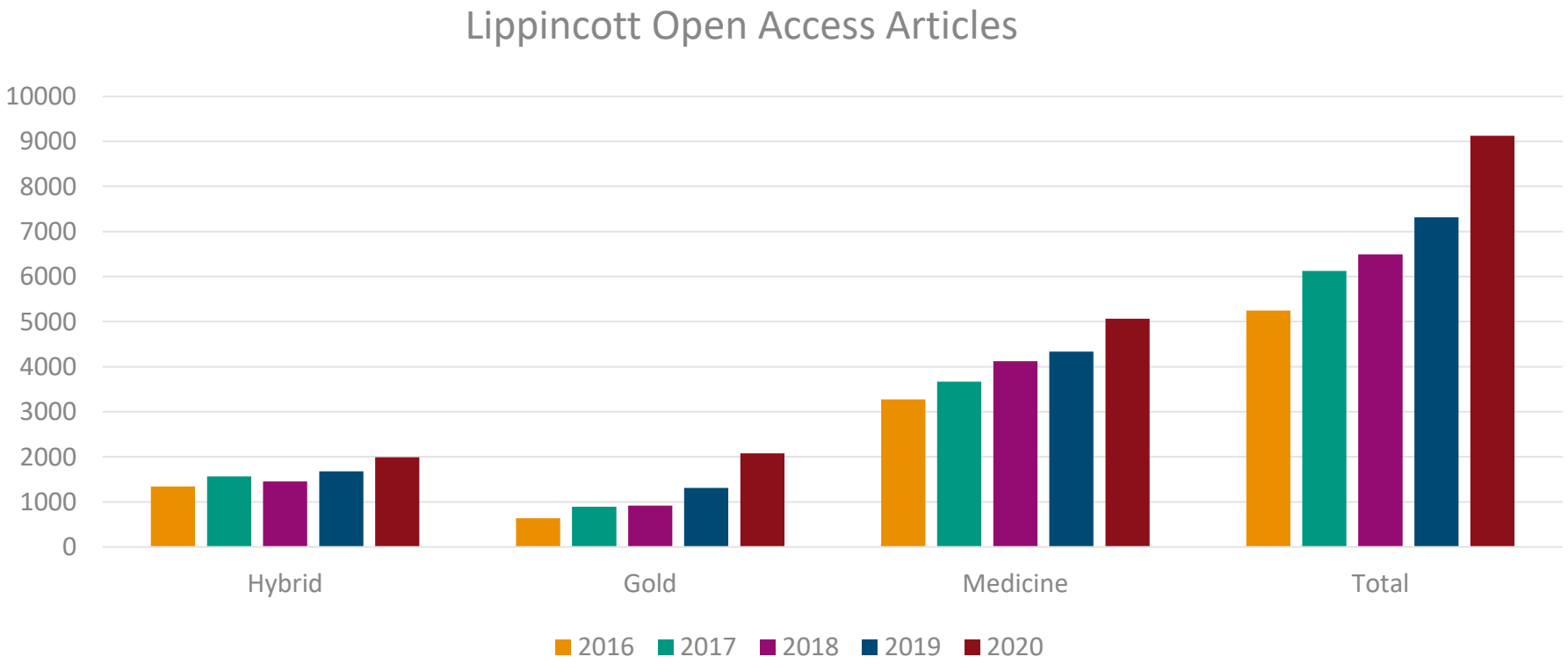

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What is a Preprint?

- A **preprint** is a version of a scholarly or scientific paper that precedes publication in a peer-reviewed scholarly or scientific journal.
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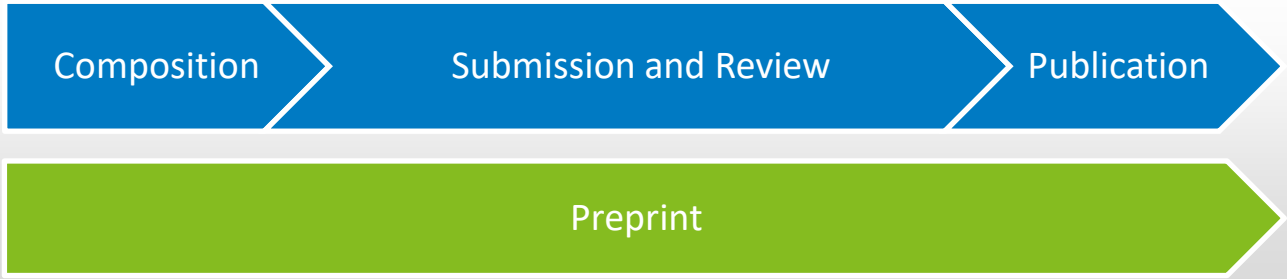


What is a Preprint?

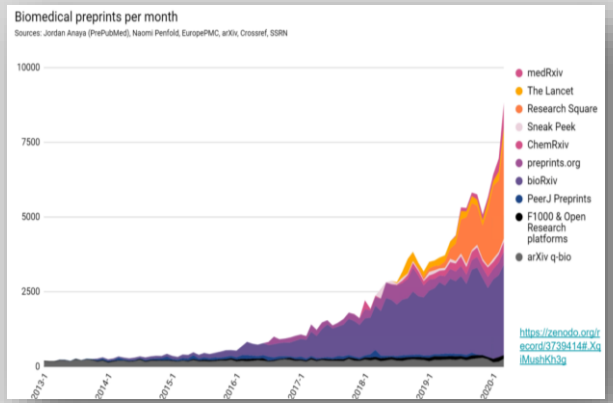
Research in real time, but without the quality stamp of peer review

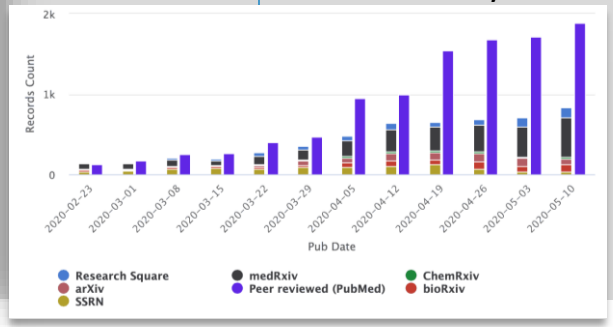
Arguments For

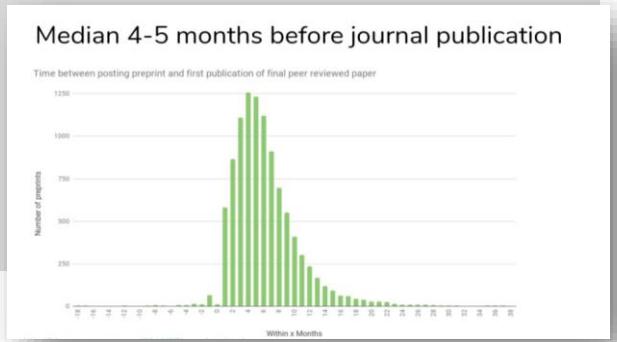
- Preprints are a rapid way to disseminate information.
- Journals review process can slow down the release of meaningful science.
- Free to access.

Arguments Against

- Preprint philosophy allows release of unvetted content.
- Instances of premature media coverage; concerns over the spread of misinformation and patient safety.
- Preprint servers host draft or rejected content; they don't clean up after themselves.
- No speed benefit; journals can accelerate when necessary.







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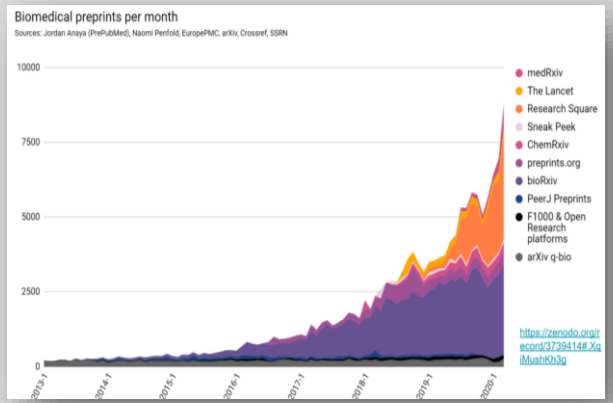

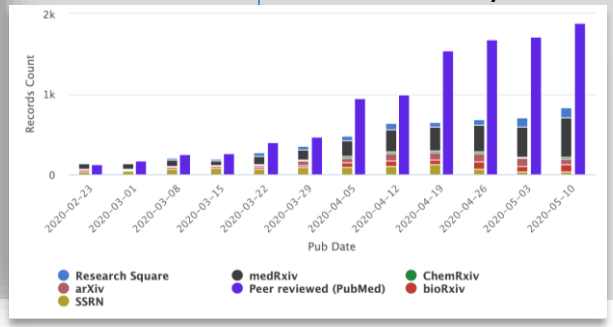

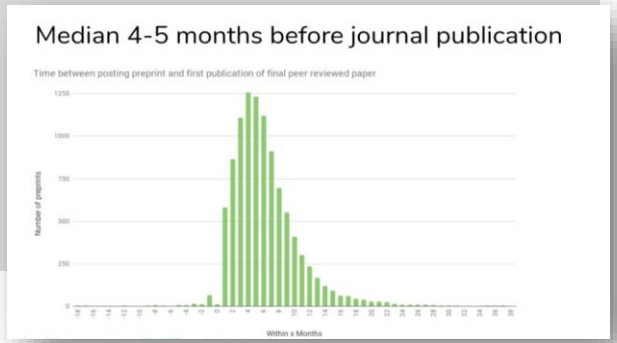

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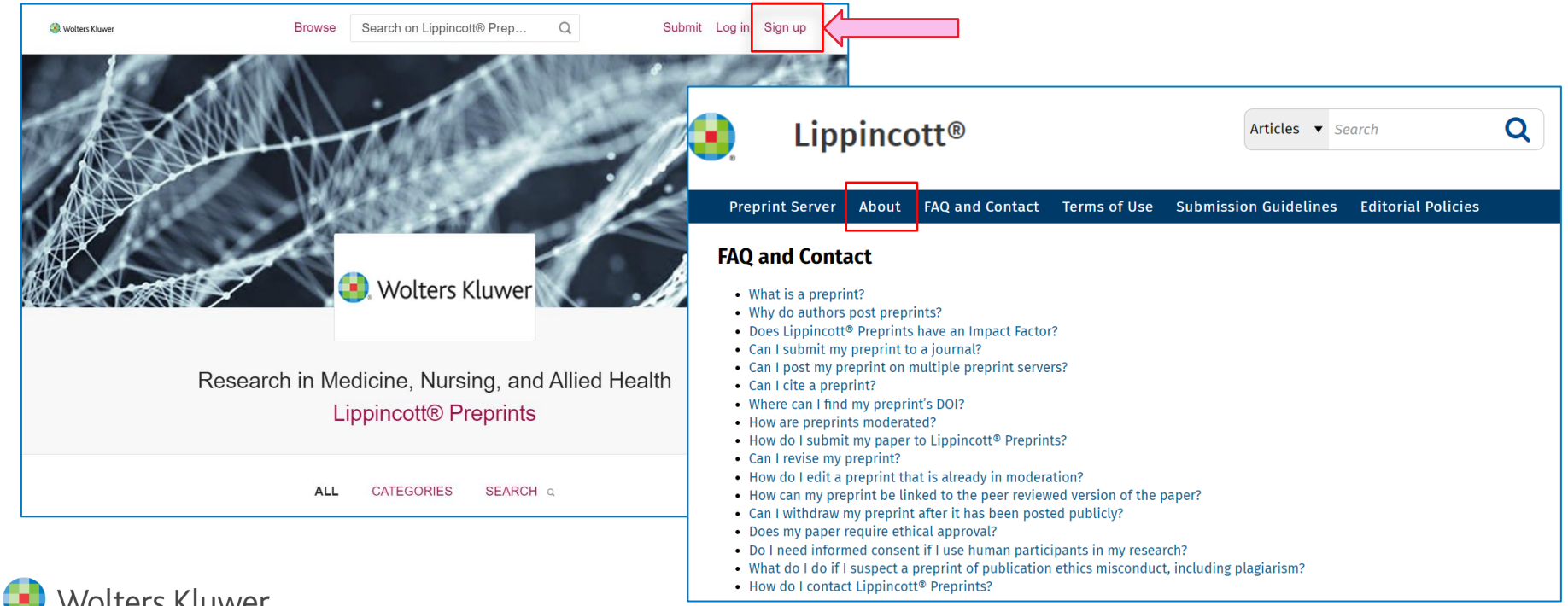

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Data Sharing

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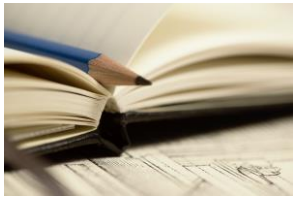

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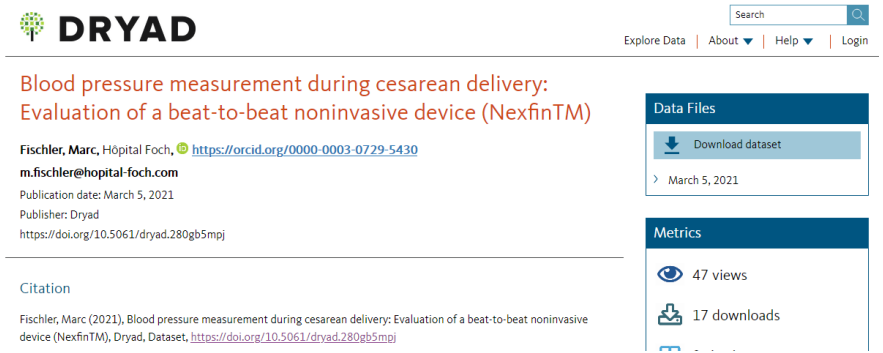
Example Article and Data

The data that support the findings of this study are openly available in the Dryad repository at https://datadryad.org/search [https://doi.org/10.5061/dryad.280gb5mpj].



	A	B	C
1	**Clinical data**		
2	**Age**	Mother's age	years
3	**Weight at Birth**	Mother's weight at Birth	kg
4	**Height**	Mother's height	cm
5	**ASA class**	Mother's ASA	class
6	**Spinal time**	Time of spinal anesthesia	hh:mm
7	**Incision Time**	Time of incision	hh:mm
8	**Hysterotomy time**	Time of hysterotomy anesthesia	hh:mm
9	**Time of bolus 1 of vasoactive drug**	Time of bolus 1 of vasoactive drug	hh:mm
10	**Bolus 1 - Vasoactive drug**	Drug of bolus 1	
11	**Bolus 1 - Dosage**	Dosage of bolus 1	

Sources: DOI: 10.1097/MD.0000000000026129 and https://datadryad.org/stash/dataset/doi:10.5061/dryad.280gb5mpj

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REVIEW ARTICLE

AI IN MEDICINE

Jeffrey M. Drazen, M.D., Editor, Isaac S. Kohane, M.D., Ph.D., Guest Editor, and Tze-Yun Leong, Ph.D., Guest Editor

The Current and Future State of AI Interpretation of Medical Images

Pranav Rajpurkar, Ph.D., and Matthew P. Lungren, M.D., M.P.H.

THE INTERPRETATION OF MEDICAL IMAGES — A TASK THAT LIES AT THE heart of the radiologist's work — has involved the growing adoption of artificial intelligence (AI) applications in recent years. This article reviews progress, challenges, and opportunities in the development of radiologic AI models and their adoption in clinical practice. We discuss the functions that AI-based algorithms serve in assisting radiologists, including detection, workflow triage, and quantification, as well as the emerging trend of the use of medical-imaging AI by clinicians who are not radiologists. We identify the central challenge of generalization in the use of AI algorithms in radiology and the need for validation safeguards that encompass clinician–AI collaboration, transparency, and post-deployment monitoring. Finally, we discuss the rapid progress in developing multimodal large language models in AI; this progress represents a major opportunity for the development of generalist medical AI models that can tackle the full spectrum of image-interpretation tasks and more. To aid readers who are unfamiliar with terms or ideas used for AI in general or AI in image interpretation, a Glossary is included with this article.

In recent years, AI models have been shown to be remarkably successful in interpretation of medical images.[1] Their use has been extended to various medical-imaging applications, including, but not limited to, the diagnosis of dermatologic conditions[2] and the interpretation of electrocardiograms,[3] pathological slides,[4] and ophthalmic images.[5] Among these applications, the use of AI in radiology has shown great promise in detecting and classifying abnormalities on plain radiographs,[6] computed tomographic (CT) scans,[7] and magnetic resonance imaging (MRI) scans,[8] leading to more accurate diagnoses and improved treatment decisions.

Even though the Food and Drug Administration (FDA) has approved more than 200 commercial radiology AI products, substantial obstacles must be overcome before we are likely to see widespread successful clinical use of these products. The incorporation of AI in radiology poses both potential benefits and challenges for the medical and AI communities. We expect that the eventual resolution of these issues and more comprehensive solutions, including the development of new foundation models, will lead to broader adoption of AI within this health care sector.

AI USE IN RADIOLOGY

Radiology as a specialty is well positioned for the application and adoption of AI because of several key factors. First, AI excels in analyzing images,[9] and unlike other specialties that use imaging, radiology has an established digital workflow and universal standards for image storage, so that it is easier to integrate AI.[10]

From the Department of Biomedical Informatics, Harvard Medical School, Boston (P.R.); the Center for Artificial Intelligence in Medicine and Imaging, Stanford University, Stanford, and the Department of Radiology and Biomedical Imaging, University of California, San Francisco, San Francisco — both in California (M.P.L.); and Microsoft, Redmond, Washington (M.P.L.). Dr. Rajpurkar can be contacted at pranav_rajpurkar@hms.harvard.edu.

Drs. Rajpurkar and Lungren contributed equally to this article.

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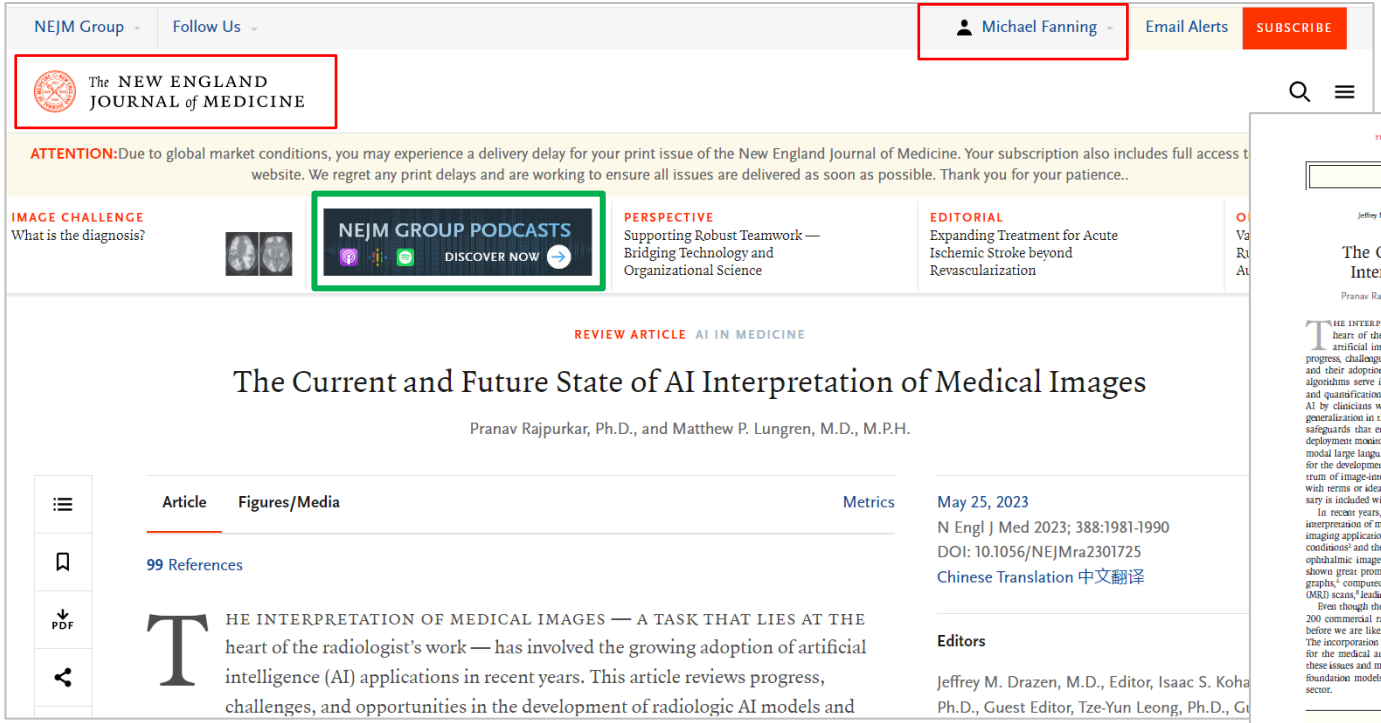

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Questions?

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