



Review of NLME articles published in clinical journals with a higher Impact Factor

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Background

Pharmacometrics aims to:

- Understand drug-patient-disease interaction
- Describe quantitative aspects of disease & pharmacology
- Connect multidisciplinary teams & convey results to clinicians, editors, reviewers, regulators & statisticians in a translational manner (Fig. I)



Figure I: Standard terminology commonly used in clinical pharmacological research. Figure modified based on S. Tannenbaum, WCoP 2016

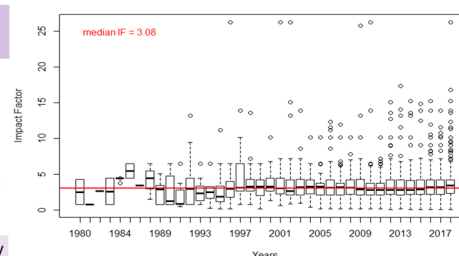


Figure IV: Journal Impact factor distribution per year; 391 unique IF were identified. Summary Statistics:

Median	3.1
Average	3.5
Max	26.3
25 th %ile	2.2
75 th %ile	4.3
90 th %ile	5.8
95 th %ile	6.5
99 th %ile	11.6

Aims

- Identify publications that have applied nonlinear mixed effects (NLME) modelling since its first appearance in 1979
- Identify NLME publications in high impact factor (IF)[#] clinical journals
- Review publication against standards for NLME articles [1,2]

[#]The tide is turning against the impact factor —one of publishing's most contentious metrics— and its outsized impact on science [3]

Methods

- Search terms: 'nonlinear mixed effect modeling', 'nonlinear mixed effect modelling', nonmem, monolix, pharmacometric*, NLME
- Databases: Pubmed [4], Web of Science [5] & Embase [6]
- Published in English between 1979 and 2018
- Journal IF identified via Web of Science or the journal's webpage
- Articles published in journals with an IF > 6.7 were read in full to examine the presentation of the NLME methods
- High IF cut-off was selected based on:
 - Clinical Pharmacology and Therapeutics (CPT): has highest IF of the 20 journals that publish most of the NLME articles
 - IF of CPT is 6.655 in 2018
 - CPT: Rank 7 among top 10 when all journals ordered

Results

- 4910 articles remained** after removing duplicates based on titles/abstracts
 - An increasing number of articles per year published since 1979 in 655 unique journals (Fig. II)
 - Majority (51%) of articles are published in only 13 journals (Fig. III)
 - Journal's IF range: 0.1 to 26.3 (Journal of Clinical Oncology) (Fig. IV)
 - Journal (CPT: Pharmacometrics & Systems Pharmacology) most commonly publishing NLME articles; currently without IF
 - Median IF: 3.08 (Figure IV)
 - 10.6% of articles published in journals without IF

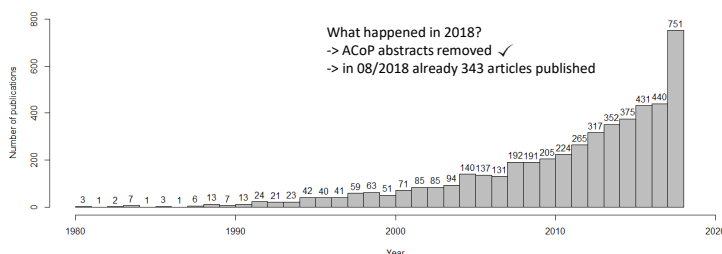


Figure II: Number of publications identified in the search per year

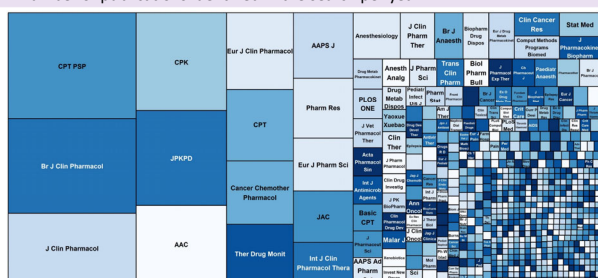


Figure III: Journals in which NLME articles were published, presented as treemap. Each rectangle has an area proportional to the number of articles published in the particular journal relative to the total number of NLME articles of 4910.

II.

- One-hundred (2.0%) articles published in journals with IF > 6.7** (Fig. V, VI)
- Over 64.9% had a first/corresponding author from academia, most common author teams were academics & clinicians (38.1%) followed by academics only & authors from industry (14.9%) (Fig. VII)
- When published in 'high' IF journals, presentation of data, methods used & description of results was seldom according to standards. Only 14% of 100 article reviewed were in line with recommendations [1,2]
- 19% of articles in higher IF journals had higher average number of citations per year compared to journal's IF, which is less compared to other fields (>25%) [3]

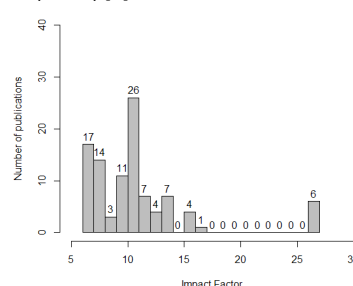


Figure V: Number of articles published in journals with a higher (>6.7) IF across the 'high' IF range

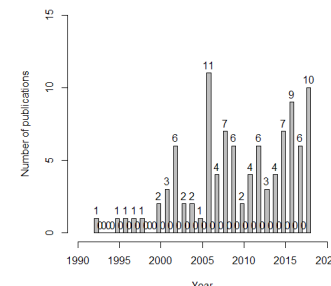


Figure VI: Number of articles published in journals with a higher (>6.7) IF across years

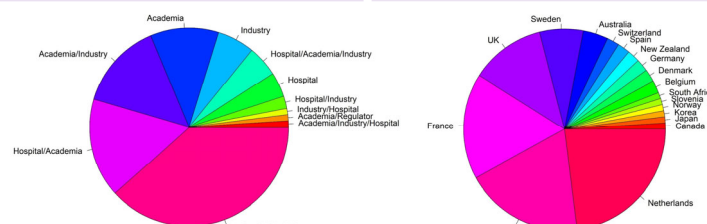


Figure VII: Pie charts illustrating the proportions of authorship teams background (left) and countries (right) across the 100 publication in 'high' IF journals

III.

- Methods were seldom completely reported, e.g. one third of articles displayed the methods only in Appendix, 3 articles did not report software used, only 29% displayed data (mainly as part of the VPC graphic)
- Models were insufficiently described: only 72% reported structural model equations, 71% mentioned stochastic model, 29% presented model figures, 38% displayed/described covariate relationships. Model evaluations were not reported (28%), 37% reported only a basic evaluation (e.g. GOF only), 14% used OFV, GOF & VPC & only 65% reported RSE or CI (with the methods used to obtain these rarely reported)

Conclusions

- While the number of NLME articles is increasing, representation in higher IF journals is not increasing over time. Initiatives to improve this could be to:
 - Improve the communication of the results arising from NLME studies
 - Increase peer-review within the area
 - Greater engagement with statistician, clinicians & stakeholders may increase the opportunity to improve impact (impact is defined by the journal's IF for the purpose of this presentation)

References

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