QUALITY ASSESSMENT OF PUBLISHED PHARMACOGENETIC ASSOCIATION IN RANDOMIZED CLINICAL TRIALS, A SYSTEMATIC REVIEW

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INTRODUCTION

These last few years, research in personalized medicine increased as the cost of genotyping decreased. Hence, the following of reporting guidelines may **enhance the quality and the harmonization of published studies**. Our aim was to **describe the quality of the reporting in published pharmacogenetics associations in randomized clinical trials**. This permits assessing the need for complementary specific reporting guidelines.

METHODS

From October 2015 to October 2018, we systematically searched for **Randomized, Controlled, Pharmacogenetics Clinical Studies, reporting a clinical outcome in Human**, in PubMed. References were screened based on Title/Abstract, then on the full text. The following flowchart shows the results of the study selection. We extracted the data for several items of

interest and provided a critical appraisal regarding the design of the study, the management of multiple testing the presence of a spin of conclusion and several items of the Strengthening the Reporting of Genetic Association studies (STREGA) guidelines¹.

RESULTS

38 Randomized Control Trials (RCT) were included. The sample sizes ranged from 22 to 3956. Medical area of the studies were:

Addiction	Neurology	Nephrology
Oncology	Psychiatry	Rheumatology
Cardiovascular system	Immune modulation/ internal medicine	Infectiology

The following table summarizes the reporting of the studies and our critical appraisal.

	Critical Appraisal of the reviewers		Clearly reported	Unclear or not reported
DESIGN				
Type of biomarker study design	Strategy design	26,3%	100,0%	0,0%
	Interaction design	0,0%	0,0%	0,0%
	Controlled sub-group analysis	50,0%	0,0%	100,0%
	Nested cohort in Clinical Trial	23,7%	11,1%	88,9%
Post Hoc or a priori hypothesis	A priori	60,5%	39,1%	60,9%
	Post hoc	23,7%	66,7%	33,3%
	Unclear	15,8%	0,0%	100,0%
Blinding	Double Blind	42,1%	100,0%	0,0%
	Single Blind	15,8%	100,0%	0,0%
	Open Label	15,8%	100,0%	0,0%
	Unclear	26,3%	0,0%	100,0%
STATISTICS				
Risk α managment	Only 23,7% controlled the risk α		55,3%	44,7%
GENETICS (STREGA Recommandations)				
Statement of the number of report	First report	73,7%	39,3%	60,7%
	Replication study	2,6%	100,0%	0,0%
	Unclear	23,7%	0,0%	100,0%
Hardy Weinberg equilibrium	On the 22 studies considering the HWE, only 5 studies reported the method used		57,9%	42,1%
Genotyping method	7,9% assessed one genetic variant 89,5% assessed several genetic variant 2,6% assessed the whole genom analysis		84,2%	15,8%
SPIN OF CONCLUSION	76,3%			

CONCLUSION

We observed a **low control of the alpha risk and frequent spin of conclusion**. It can bias the interpretation of the literature. We also showed a lack of reporting of crucial items in pharmacogenetics publications, despite the existing guidelines¹. This limits the comparability of studies and showed the need for specific reporting guidelines.