DECIDE

Introduction to Health Interventions, Policy and Services

Real-world data studies

Luís Filipe Azevedo | Bernardo Sousa Pinto

lazevedo@med.up.pt | bernardo@med.up.pt

Summary

- Real-world data: Definitions
- Pragmatic trials
- Direct patient data
- New data sources: Infodemiology studies

Classical limitations of RCTs

Results: Three hundred eleven patients seen by 48 general practitioners were enrolled in this study. Only 7.4% (95% CI, 4.5% to 10.3%) of the patients would have been enrolled in the RCTs. The primary reasons for this difference were as follows: diagnosis of allergy based on skin test results, serum specific IgE levels, or both (20.4%); severity of allergic rhinitis (11.5%); other chronic diseases (11.4%); history of sinusitis (10.4%); and asthma comorbidity (10.1%). A sensitivity analysis excluding contraception and the diagnosis of allergy showed that the percentage of representative patients increased to 20.2% (95% CI, 15.8% to 24.7%).

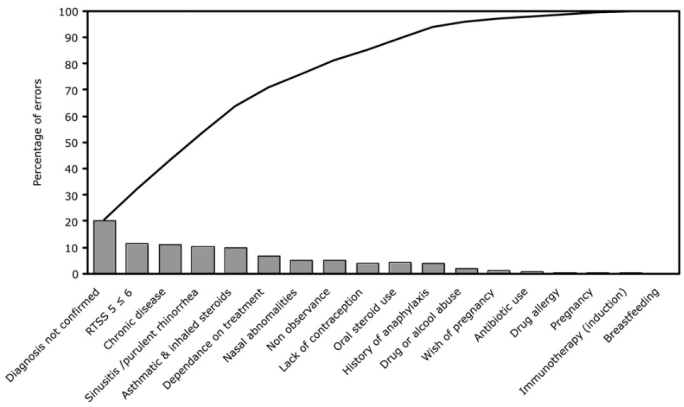

FIG 1. Pareto chart reporting the effect of inclusion/exclusion criteria of RCTs on patients seen in primary care daily practice. *RTSS 5*, Rhinitis total score of 5 symptoms (T5SS).

Costa DJ et al. J Allergy Clin Immunology. 2011

Real-world data

- **Real-world data studies**
  - No consensual definition. Typically understood as studies assessing the effectiveness of interventions in "real clinical practice";
  - Aim to overcome some of the limitations of classical clinical trials: Diverse populations, wider set of assessed clinical settings, wider range of assessed outcomes…
  - Can be observational/non-interventional or interventional/pragmatic

Real-world data

Table 1 Comparison of randomized controlled trials and real-world studies

	Randomized controlled trials	Real-world studies	
Type of study	Experimental/ interventional	Observational/non-interventional	Interventional/pragmatic
Design	Prospective	Retrospective/prospective	Prospective
Primary focus	Efficacy, safety, quality, cost-effectiveness	Efficacy, safety, quality, cost-effectiveness, natural history, compliance and adherence, service models, patient preferences, comparative	
Patient population	Narrow, restricted, motivated	Diverse, large, and unrestricted	
Monitoring	Intense (ICH-GCP compliant)	Not required (?)	Reflects usual care
Comparators	Gold standard/placebo	None/standard clinical practice/multiple iterations	Standard practice/ placebo/multiple iterations
Outcomes	Clear sequence	Wide range	
Data collection confounders	Standardized, controlled	Routine, recruitment bias (?), recall/interviewer bias	
Randomization	Yes	No	Yes
Blinding	Yes	No	Sometimes (participants or outcome assessment)
Follow-up	Generally short	Reflects usual care	Long

ICH-GCP International Conference on Harmonisation of Good Clinical Practice

Blonde L et al. Interpretation and Impact of Real-World Clinical Data for the Practicing Clinician. Adv Ther. 2008;35:1763-74.

Real-world data

Adv Ther (2018) 35:1763–1774 1765

Table 1 Comparison of randomized controlled trials and real-world studies

Common data sources: electronic health records, administrative datasets, patient registries…

Problems with unmeasured confounders and data quality or missing information (particularly in retrospective studies)

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Pragmatic trials

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Explanatory *versus* pragmatic trials

Assessing the nature of the trial based on a set of dichotomous questions:

Table 1
Proposed criteria to distinguish effectiveness from efficacy trials

Item 1	Populations in primary care
Item 2	Less stringent eligibility criteria
Item 3	Health outcomes
Item 4	Long study duration; clinically relevant treatment modalities
Item 5	Assessment of adverse events
Item 6	Adequate sample size to assess a minimally important difference from a patient perspective
Item 7	ITT analysis

Abbreviation: ITT, Intention-to-treat.

Gartlehneret G al. J Clin Epidemiol. 2006

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"For effectiveness trials, settings should reflect the initial care facilities available to a diverse population with the condition of interest."

"Efficacy studies are frequently conducted in large tertiary care, referral setting." → more specialized clinicians, better equipment, selection biases…

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"For effectiveness trials, eligibility criteria must allow the source population to reflect the heterogeneity of external populations: the full spectrum of the human population, their comorbidities, variable compliance rates, and use of other medications […].Comorbidities and other medications cannot be general exclusion criteria unless they contraindicate the use of the agent in ordinary practice."

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"Health outcomes [((e.g., functional capacity, quality of life, mortality)], relevant to the condition of interest, should be the principal outcome measures in effectiveness studies" instead of surrogate markers.

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"In effectiveness trials, study durations should mimic a minimum length of treatment in a clinical setting to allow the assessment of health outcomes."

"In effectiveness trials, […] investigators should define compliance as an outcome measure" (and not enforce it).

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"Effectiveness studies use objective scales with predefined symptoms [(e.g., World Health Organization scale of adverse reactions)] to determine adverse events rates." (and not enforce it).

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"The sample size of an effectiveness trial should be sufficient to detect at least a minimally important difference on a health-related quality of life scale. For conditions where rare but significant outcomes such as mortality or hospitalizations are of main interest, sample sizes must be greater and based on adequate power calculations."

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Table 4
Summary of diagnostic parameters for different cutoff points

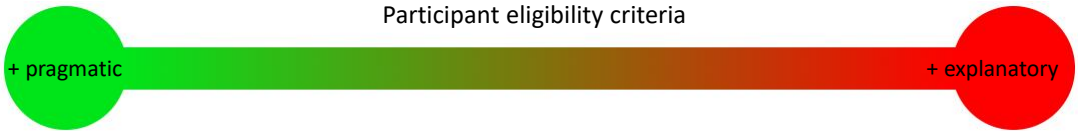
Diagnostic parameters	Estimate	95% Confidence interval
Cutoff: seven (all) criteria fulfilled		
Sensitivity (%)	0.28	0.10–0.53
Specificity (%)	0.83	0.36–1.00
+ Likelihood ratio	1.7	0.4–10.1
− Likelihood ratio	0.9	0.6–1.7
Cutoff: six criteria fulfilled		
Sensitivity (%)	0.72	0.46–0.90
Specificity (%)	0.83	0.36–1.00
+ Likelihood ratio	4.3	1.2–24.4
− Likelihood ratio	0.3	0.1–0.8
Cutoff: five criteria fulfilled		
Sensitivity (%)	0.89	0.65–0.99
Specificity (%)	0.67	0.22–0.96
+ Likelihood ratio	2.7	1.2–9.3
− Likelihood ratio	0.2	0.0–0.6

Compared with Evidence-based Practice Centers experts appraisal

Gartlehneret G al. J Clin Epidemiol. 2006

Explanatory *versus* pragmatic trials

Assessing the nature of the trial based on a pragmatic-explanatory continuum



All participants who have the condition of interest, regardless of their anticipated risk, responsiveness, co-morbidities, or past compliance.

Restrictions to individuals with highest risk of unfavourable outcomes

+ restrictions to individuals who are more likely to be responsive to the intervention

+ restrictions to individuals who are more likely to be compliant to the intervention

Thorpe KE al. J Clin Epidemiol. 2009

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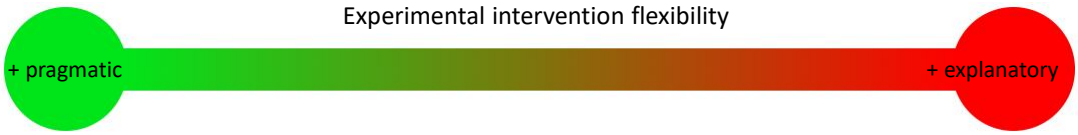

Highly flexible instructions on how to apply the experimental intervention (details left to the clinician)

Strict instructions on how to apply the experimental intervention (e.g., dosing schedule, delivery timing, allowed co-interventions)

Thorpe KE al. J Clin Epidemiol. 2009

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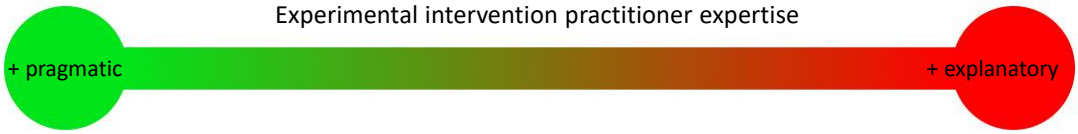

Experimental intervention applied by the full range of practitioners and in the full range of clinical settings, regardless of their expertise

Experimental intervention applied only by highly-experienced and well-succeeded practicioners

Thorpe KE al. J Clin Epidemiol. 2009

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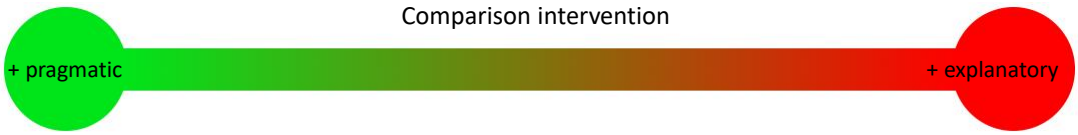

Comparator is “usual practice” or best available alternative strategy (details set by practitioners)

Strict definitions for application of comparator, which can be a placebo

Thorpe KE al. J Clin Epidemiol. 2009

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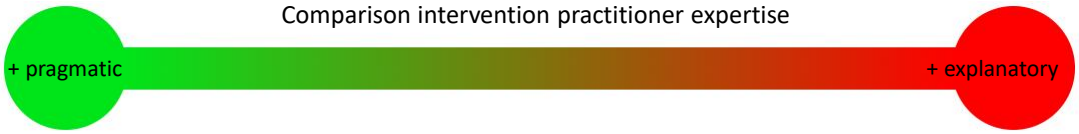

Comparison intervention applied by the full range of practitioners and in the full range of clinical settings, regardless of their expertise

Standardized practitioner expertise in applying the comparison intervention(s)

Thorpe KE al. J Clin Epidemiol. 2009

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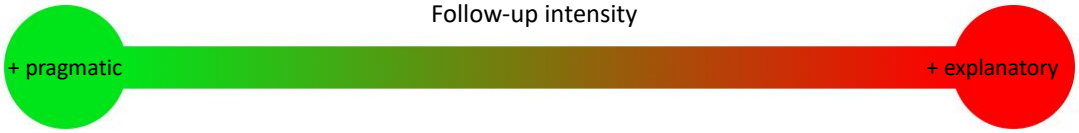

No formal follow-up visits of study individuals. Use of administrative databases for detecting outcomes

Follow-up visits as in usual care

Follow-up visits more frequent than in usual care

Unscheduled follow-up visits triggered by events. Contact if patients fail to keep trial appointments

Thorpe KE al. J Clin Epidemiol. 2009

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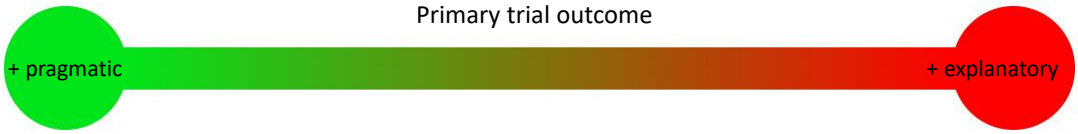

Meaningful non-surrogate outcome assessed at an adequate follow-up period

Surrogate outcome or outcome requiring specialized training to be assessed

Thorpe KE al. J Clin Epidemiol. 2009

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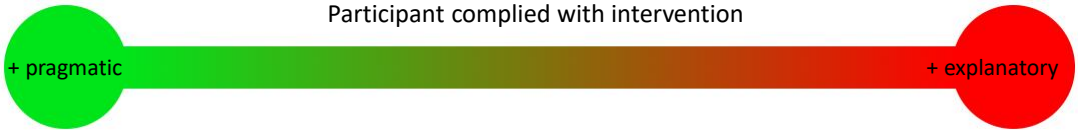

No special strategies to maintain or improve compliance

Compliance measured for descriptive purposes only

Uniform compliance-improving strategies applied to all participants

Compliance-improving strategies applied to participants with poor compliance.
Selection criteria excluding patients with poor compliance

Thorpe KE al. J Clin Epidemiol. 2009

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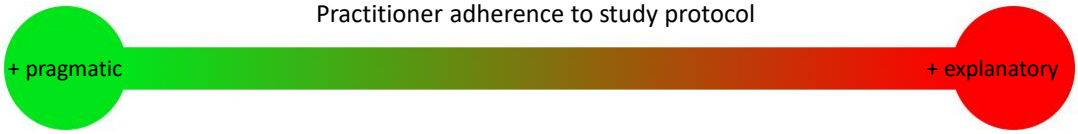

No measurement of practitioner adherence.

Adherence measured for descriptive purposes only. No strategies to maintain or improve it.

Uniform adherence-improving strategies applied to all practicioners

Adherence-improving strategies applied to practicioners with poor adherence

Thorpe KE al. J Clin Epidemiol. 2009

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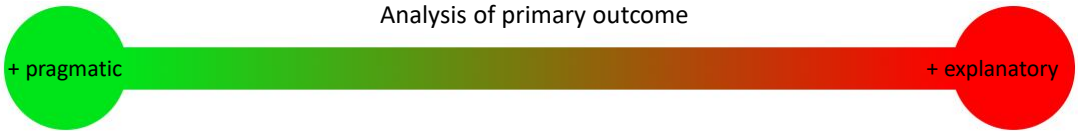

Analysis of all patients regarding of compliance, eligibility… (“intention-to-treat analysis”)

Exclusion of non-compliant participants, non-adherent practicioners, patients found to be ineligible postrandomization (“per protocol analysis”)

Thorpe KE al. J Clin Epidemiol. 2009

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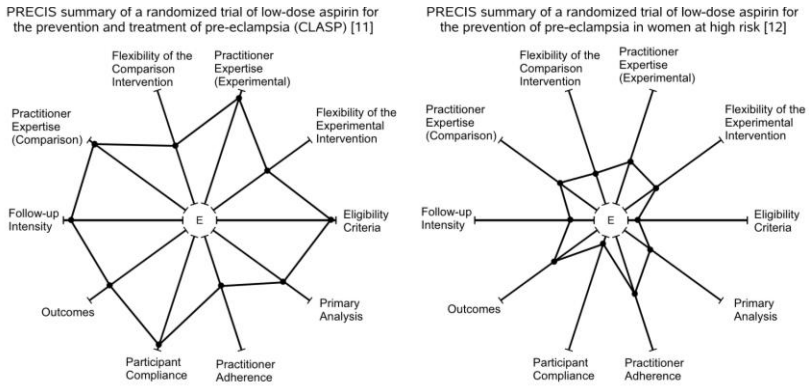

Thorpe KE al. J Clin Epidemiol. 2009

Direct patient data

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Direct patient data

- Correspond to data directly provided by patients about their health;
- Allow for an assessment of patients “in their natural state”;
- Often allow for the obtention of large data volumes or of frequent data by patient;
- Retrieval made easier by digital health tools (e.g., mHealth tools)

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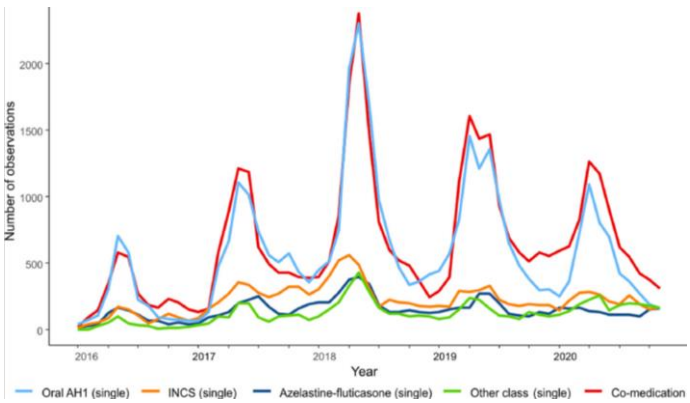

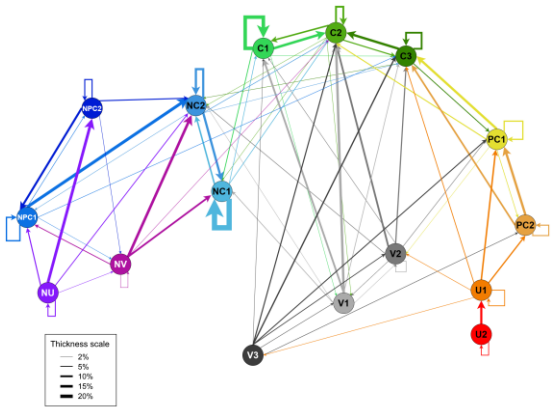

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Direct patient data in the context of infodemiology studies

- **Infodemiology studies**
  - Assessment of the distribution and determinants of the information in the electronic medium (namely the Internet) to inform health decision and policy.
  - Infodemiology studies – "supply" studies *vs* "demand-side" studies

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Eysenbach G. J Med Internet Res. 2009

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Infodemiology studies

- **Main subjects:**
  - Relative search volumes (e.g., Google Trends)
  - Prevalence, incidence and quality of available online information
  - Quantity and quality of health apps
  - Social media/microblogging posts: Quantity, content and sentiment
  - News coverage (e.g., MediaCloud): Quantity, content and sentiment

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Infodemiology studies

JMIR PUBLIC HEALTH AND SURVEILLANCE Mavragani & Ochoa

Tutorial

Google Trends in Infodemiology and Infoveillance: Methodology Framework

Amaryllis Mavragani, BSc, MSc; Gabriela Ochoa, BSc, MSc, PhD

Department of Computing Science and Mathematics, Faculty of Natural Sciences, University of Stirling, Stirling, United Kingdom

Corresponding Author:
Amaryllis Mavragani, BSc, MSc
Department of Computing Science and Mathematics
Faculty of Natural Sciences
University of Stirling
University Campus
Stirling, FK94LA
United Kingdom
Phone: 44 7523782711
Email: amaryllis.mavragani1@stir.ac.uk

Abstract

Internet data are being increasingly integrated into health informatics research and are becoming a useful tool for exploring human behavior. The most popular tool for examining online behavior is Google Trends, an open tool that provides information on trends and the variations of online interest in selected keywords and topics over time. Online search traffic data from Google have been shown to be useful in analyzing human behavior toward health topics and in predicting disease occurrence and outbreaks. Despite

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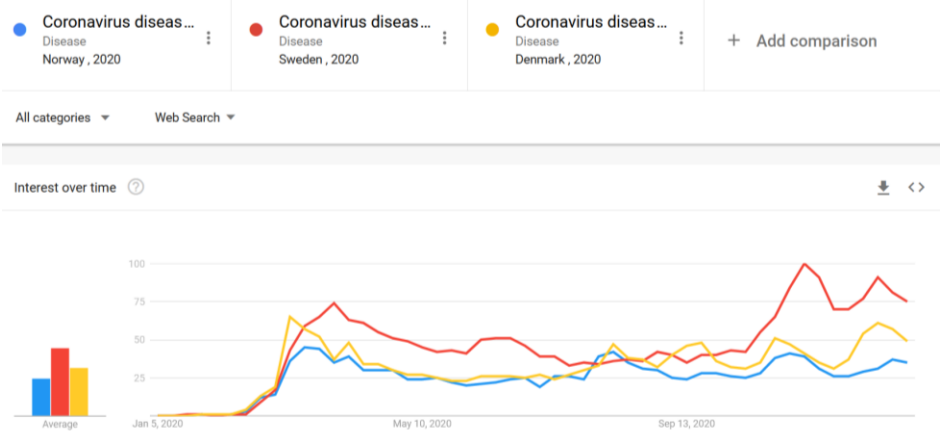
Infodemiology studies



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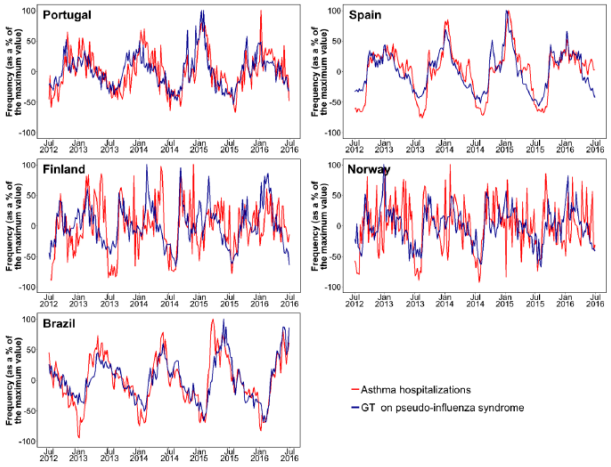
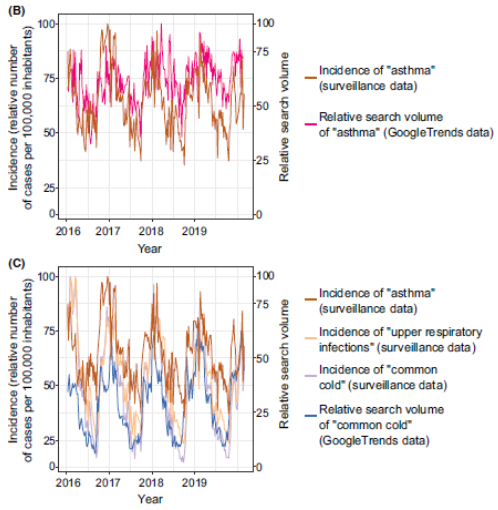
Infodemiology studies

Figure 3. Google Trends data on *pseudo-influenza syndrome* and asthma hospitalizations (2012-2016) in Portugal, Spain, Finland, Norway, and Brazil. The trend component of time series has been plotted after removal of the seasonal effects and random error components. GT: Google Trends.





Comparing News Articles and Tweets About COVID-19 in Brazil: Sentiment Analysis and Topic Modeling Approach

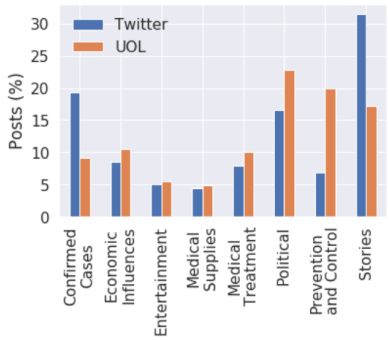


Table 5. Topics and themes for Twitter.

ID	Topic	Theme
1	president (*presidente*), bolsonaro (*bolsonaro*), minister (*ministro*), governors (*governadores*), sir (*senhor*), mayors (*prefeitos*), jairbolsonaro (*jairbolsonaro*), blame (*culpa*), mandetta (*mandetta*), meeting (*reunião*)	Political
2	instagram (*instagram*), igshid (*igshid*), covid (*covid*), twitter (*twitter*), mask (*máscara*), masks (*mascaras*), stay (*fique*), important (*importante*), prevention (*prevenção*), attention (*atenção*)	Medical Supplies
3	deaths (*mortes*), number (*número*), dead (*morte*), bigger (*maior*), covid (*covid*), numbers (*números*), countries (*países*), infected (*infectados*), weeks (*semanas*), months (*meses*)	Confirmed Cases
4	cases (*casos*), state (*estado*), confirmed (*confirmados*), tests (*testes*), city (*cidade*), twitter (*twitter*), deaths (*óbitos*), new (*novos*), coronavirus (*coronavirus*), total (*total*)	Confirmed Cases
5	health (*saúde*), hospitals (*hospitais*), combat (*combate*), professionals (*profissionais*), measures (*medidas*), public (*público*), actions (*ações*), beds (*leitos*), campaign (*campanha*), system (*sistema*)	Medical Supplies
6	twitter (*twitter*), pandemic (*pandemia*), covid (*covid*), lives (*vidas*), work (*trabalho*), moment (*momento*), video (*vídeo*), congratulations (*parabéns*), big (*grande*), save (*salvar*)	Stories
7	people (*gente*), quarantine (*quarentena*), doing (*fazendo*), do (*fazer*), stay (*ficar*), friends (*amigos*), really (*sério*), damn (*porra*), finish (*acabar*), seeing (*vendo*)	Stories
8	pandemic (*pandemia*), time (*tempo*), quarantine (*quarentena*), things (*coisas*), moment (*momento*), time (*tempos*), difficult (*difícil*), do (*fazer*), pass (*passar*), expect (*espero*)	Stories
9	pandemic (*pandemia*), world (*mundo*), economy (*economia*), worldwide (*mundial*), general (*geral*), war (*guerra*), finish (*acabar*), ended (*acabou*), history (*história*), can (*podem*)	Economic Influences
10	true (*verdade*), policy (*política*), press (*imprensa*), left (*esquerda*), tell (*dizer*), state (*estado*), political (*político*), said (*falou*), media (*mídia*), shame (*vergonha*)	Political
11	people (*pessoas*), risk (*risco*), lack (*falta*), covid (*covid*), group (*grupo*), dying (*morrendo*), cause (*causa*), can (*podem*), died (*morreram*), diseases (*doenças*)	Confirmed Cases
12	social isolation (*isolamento*), detachment (*distanciamento*), measures (*medidas*), keep (*manter*), governor (*governador*), required (*necessário*), need (*necessidade*), services (*serviços*), commerce (*comércio*)	Prevention and Control

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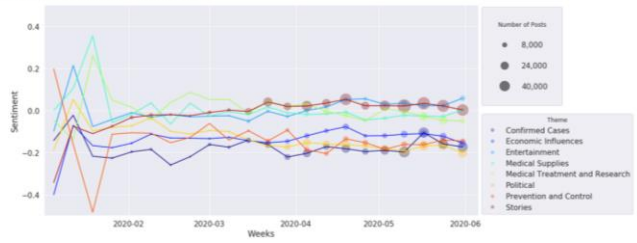
Comparing News Articles and Tweets About COVID-19 in Brazil: Sentiment Analysis and Topic Modeling Approach

Figure 15. Universo Online sentiment analysis over time.

Figure 16. Twitter sentiment analysis over time.



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Explore the NRC Word-Emotion Association Lexicon through this Interactive Visualization (version 0.2)

(Click on a treemap tile, legend item, or word to select and filter information. Click again to deselect. Undo, Redo, and Reset buttons are at the bottom left.)

Affect Categories: A treemap showing the number of words associated with each affect category

Sets of Categories: A treemap showing the number of words associated with *sets* of categories

Affect Categories to Include

(All)

Affect Categories Legend

negative · positive · anger · anticip · disgust

Note: 'anticip' is short for anticipation.

 # Records: Adjust filter to view only those affect sets with the desired number of records. (Lower threshold is set to 25 by default to show only larger affect sets.)

25 — 1,031

Word-Sentiment Associations	
abacus	
abandon	negative
abandoned	negative
abandonment	negative
abba	positive
abbot	
abduction	negative
aberrant	negative
aberration	negative
abhor	negative
abhorrent	negative
ability	positive
abject	negative
abnormal	negative
abolish	negative
abolition	negative
abominable	negative

Word-Emotion Associations	
abacus	trust
abandon	fear sadness
abandoned	anger fear sadness
abandonment	anger fear sadness surprise

+ableau https://saifmohammad.com/WebPages/NRC-Emotion-Lexicon.htm