Pilot Study Results

1. Table 1

<Cohort 1 graphs>

1. Included Paper Characteristics

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  | | | | | | |
| Included papers characteristics Grouped by EpochS | | | | | | | | |
|  |  | **Missing** | **Overall** | **2010-2013** | **2014-2016** | **2017** | **2018** | **2019** |
|  |  |  |  |  |  |  |  |  |
| n |  |  | 88 | 26 | 12 | 18 | 14 | 18 |
| Study\_Design\_Type,  n (%) | **retrospective cohort study** | 2 | 67 (77.9) | 21 (80.8) | 10 (90.9) | 12 (70.6) | 10 (71.4) | 14 (77.8) |
| **retrospective cross-sectional study** |  | 6 (7.0) | 3 (11.5) |  | 2 (11.8) |  | 1 (5.6) |
| **cluster randomized pragmatic clinical trials** |  | 1 (1.2) | 1 (3.8) |  |  |  |  |
| **longitudinal, before/after study design** |  | 1 (1.2) |  |  | 1 (5.9) |  |  |
| **prospective cohort study** |  | 6 (7.0) |  |  | 1 (5.9) | 2 (14.3) | 3 (16.7) |
| **quasi-experimental study** |  | 1 (1.2) |  |  | 1 (5.9) |  |  |
| **retrospective case–control study** |  | 2 (2.4) |  | 1 (9.1) |  | 1 (7.1) |  |
| **retrospective chart review** |  | 1 (1.2) | 1 (3.8) |  |  |  |  |
| **proof of Concept Study** |  | 1 (1.2) |  |  |  | 1 (7.1) |  |
| Country/district,  n (%) | **USA** | 0 | 52 (59.1) | 16 (61.5) | 6 (50.0) | 11 (61.1) | 7 (50.0) | 12 (66.7) |
| **UK** |  | 7 (8.0) | 2 (7.7) | 2 (16.7) | 3 (16.7) |  |  |
| **French** |  | 2 (2.3) |  |  |  | 1 (7.1) | 1 (5.6) |
| **Brazil** |  | 1 (1.1) |  |  | 1 (5.6) |  |  |
| **Germany** |  | 2 (2.3) |  | 1 (8.3) |  |  | 1 (5.6) |
| **Italy** |  | 1 (1.1) | 1 (3.8) |  |  |  |  |
| **Japan** |  | 2 (2.3) |  |  | 1 (5.6) |  | 1 (5.6) |
| **Korea** |  | 6 (6.8) |  | 1 (8.3) |  | 4 (28.6) | 1 (5.6) |
| **Netherland** |  | 4 (4.5) | 2 (7.7) | 1 (8.3) |  | 1 (7.1) |  |
| **Norway** |  | 1 (1.1) | 1 (3.8) |  |  |  |  |
| **Singapore** |  | 1 (1.1) |  |  |  |  | 1 (5.6) |
| **South Korea** |  | 1 (1.1) | 1 (3.8) |  |  |  |  |
| **Spain** |  | 2 (2.3) | 1 (3.8) |  | 1 (5.6) |  |  |
| **Sweden** |  | 1 (1.1) |  |  |  | 1 (7.1) |  |
| **Switzerland** |  | 1 (1.1) | 1 (3.8) |  |  |  |  |
| **Taiwan** |  | 1 (1.1) | 1 (3.8) |  |  |  |  |
| **Canada** |  | 2 (2.3) |  | 1 (8.3) |  |  | 1 (5.6) |
| **China** |  | 1 (1.1) |  |  | 1 (5.6) |  |  |
| Mentioned\_Mission\_Data, n (%) | **No** | 0 | 46 (52.3) | 17 (65.4) | 5 (41.7) | 6 (33.3) | 10 (71.4) | 8 (44.4) |
| **Yes Data Analytic** |  | 9 (10.2) | 1 (3.8) |  | 3 (16.7) | 2 (14.3) | 3 (16.7) |
| **Yes Data Cleaning** |  | 14 (15.9) |  | 3 (25.0) | 6 (33.3) | 2 (14.3) | 3 (16.7) |
| **Yes Limitation** |  | 19 (21.6) | 8 (30.8) | 4 (33.3) | 3 (16.7) |  | 4 (22.2) |
| Check\_List, n (%) | **Guidelines for good pharmacoepidemiology practices (GPP)** | 85 | 1 (33.3) |  |  |  |  | 1 (33.3) |
| **STROBE** |  | 2 (66.7) |  |  |  |  | 2 (66.7) |

1. Included papers by epoch

A screenshot of a cell phone

Description automatically generated

1. Proportion estimation and Confidence Interval

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Estimated Proportion and Confidence Interval of Methods used in EHRs Based Research** | | | | | |
|  | **2010-2013** | **2014-2016** | **2017** | **2018** | **2019** |
| **Addressed\_Missing\_Data** | 0.12 (0, 0.24) | 0.17(0, 0.38) | 0.17(0, 0.34) | 0.21(0, 0.43) | 0.22(0.03, 0.41) |
| **Real-World\_Method** | 0.04 (0, 0.11) | 0.08(0, 0.24) | 0.03(0, 0.1) | 0.21(0, 0.43) | 0.11(0, 0.26) |
| **Sensitivity\_Analysis** | 0.19(0.04,0.34) | 0.25(0.01, 0.5) | 0.28(0.07, 0.48) | 0.07(0, 0.21) | 0.22(0.03, 0.41) |

1. Proportion of Methods Used

A screenshot of a cell phone

Description automatically generated(Cohort 1)

Cohort 1

| Mixed-effects Meta-regressions for three methods | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | name | estimate | Se | z-score | p-value | ci\_0.025 | ci\_0.975 |
| 0 | intercept | -23.1124 | 47.2377 | 0.4892 | 0.6246 | 115.6968 | 69.4719 |
| 1 | Missing Data | 0.0115 | 0.02344 | 0.4927 | 0.6221 | -0.0343 | 0.0574 |
|  | name | estimate | Se | z-score | p-value | ci\_0.025 | ci\_0.975 |
| 0 | intercept | -0.0197 | 0.2301 | 0.0859 | 0.9314 | -0.4709 | 0.43134 |
| 1 | Real-World Methods | 0.0049 | 0.0148 | 0.3310 | 0.7406 | -0.0241 | 0.0340 |
|  | name | estimate | Se | z-score | p-value | ci\_0.025 | ci\_0.975 |
| 0 | intercept | 17.9639 | 49.1902 | 0.3651 | 0.7149 | -78.4473 | 114.3751 |
| 1 | Sensitivity Analysis | -0.0088 | 0.0243 | -0.3618 | 0.7174 | -0.0566 | 0.0389 |

Diagram

Description automatically generated

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Grouped by Epoch | | | | | | | | |
|  |  | **Missing** | **Overall** | **2010-2013** | **2014-2016** | **2017** | **2018** | **2019** |
| Total papers, n |  |  | **175** | **35** | **35** | **35** | **35** | **35** |
| Study Design Type,  n (%) | **retrospective chart review** | 0 | 1 (0.6) |  |  |  |  | 1 (2.9) |
| **cost-benefit analysis** |  | 1 (0.6) |  |  |  |  | 1 (2.9) |
| **prospective cohort study** |  | 12(6.9) | 4 (11.4) |  | 4 (11.6) | 1 (2.9) | 3 (8.6) |
| **prospective controlled study** |  | 1 (0.6) | 1 (2.9) |  |  |  |  |
| **retrospective case–control study** |  | 8 (4.6) |  | 3 (8.6) | 2 (5.7) |  | 3 (8.6) |
| **retrospective chart review** |  | 14 (8.0) | 2 (5.7) | 4 (11.4) | 2 (5.7) | 4 (11.4) | 2 (5.7) |
| **retrospective cohort study** |  | 120 (68.6) | 24 (68.6) | 25 (71.4) | 23 (65.7) | 26 (74.3) | 22 (62.9) |
| **retrospective cross-sectional study** |  | 14 (8.0) | 4 (11.4) |  | 4 (11.4) | 4 (11.4) | 2 (5.7) |
| **retrospective database study** |  | 1 (0.6) |  |  |  |  | 1 (2.9) |
| **retrospective review** |  | 3 (1.7) |  | 3 (8.6) |  |  |  |
| Country/district ,  n (%) | **Australia** | 0 | 3 (1.7) | 1 (2.9) |  |  |  | 2 (5.7) |
| **Brazil** |  | 1 (0.6) |  |  |  | 1 (2.9) |  |
| **Canada** |  | 3 (1.7) | 3 (8.6) |  |  |  |  |
| **China** |  | 7 (4.0) |  | 2 (5.7) |  | 3 (8.6) | 2 (5.7) |
| **Croatia** |  | 1 (0.6) |  |  |  |  | 1 (2.9) |
| **Denmark** |  | 1 (0.6) |  |  |  |  | 1 (2.9) |
| **France** |  | 5 (2.9) |  |  | 2 (5.7) | 2 (5.7) | 1 (2.9) |
| **Israel** |  | 6 (3.4) |  | 2 (5.7) | 1 (2.9) | 1 (2.9) | 2 (5.7) |
| **Italy** |  | 1 (0.6) |  | 1 (2.9) |  |  |  |
| **Japan** |  | 3 (1.7) |  |  |  |  | 3 (8.6) |
| **Japan** |  | 1 (0.6) |  |  |  | 1 (2.9) |  |
| **Korea** |  | 7 (4.0) | 2 (5.7) | 3 (8.6) | 2 (5.7) |  |  |
| **Malawi** |  | 1 (0.6) |  |  | 1 (2.9) |  |  |
| **Mexico** |  | 1 (0.6) |  | 1 (2.9) |  |  |  |
| **Netherlands** |  | 1 (0.6) |  | 1 (2.9) |  |  |  |
| **Oman** |  | 2 (1.1) |  | 1 (2.9) | 1 (2.9) |  |  |
| **Portugal** |  | 1 (0.6) |  | 1 (2.9) |  |  |  |
| **Singapore** |  | 4 (2.3) |  |  |  | 3 (8.6) | 1 (2.9) |
| **Spain** |  | 4 (2.3) | 1 (2.9) | 1 (2.9) |  | 1 (2.9) | 1 (2.9) |
| **Sweden** |  | 2 (1.1) | 1 (2.9) |  |  |  | 1 (2.9) |
| **Switzerland** |  | 1 (0.6) |  |  | 1 (2.9) |  |  |
| **Taiwan** |  | 1 (0.6) |  |  | 1 (2.9) |  |  |
| **Turkey** |  | 1 (0.6) |  |  |  |  | 1 (2.9) |
| **UK** |  | 20 (11.4) | 2 (5.7) | 3 (8.6) | 8 (22.9) | 4 (11.4) | 3 (8.6) |
| **USA** |  | 97 (55.4) | 25 (71.4) | 19 (54.3) | 18 (51.4) | 19 (54.3) | 16 (45.7) |
| Mention Missing Data,  n (%) | **No** | 0 | 94 (53.7) | 19 (54.3) | 23 (65.7) | 14 (40.0) | 20 (57.1) | 18 (51.4) |
| **Yes, data cleaning** |  | 34 (19.4) | 6 (17.1) | 6 (17.1) | 11 (31.4) | 6 (17.1) | 5 (14.3) |
| **Yes, data description** |  | 25 (14.3) | 5 (14.3) | 3 (8.6) | 6 (17.1) | 5 (14.3) | 6 (17.1) |
| **Yes, limitation** |  | 20 (11.4) | 5 (14.3) | 3 (8.6) | 4 (11.4) | 3 (8.6) | 5 (14.3) |
| **Yes, no missing** |  | 2 (1.1) |  |  |  | 1 (2.9) | 1 (2.9) |
| Addressed Missing Data  , n (%) | **No** | 0 | 136 (77.7) | 27 (77.1) | 28 (80.0) | 22 (62.9) | 29 (82.9) | 30 (85.7) |
| **Yes, Imputation** |  | 17 (9.7) | 3 (8.6) | 2 (5.7) | 5 (14.3) | 4 (11.4) | 3 (8.6) |
| **Yes, excluded** |  | 19 (10.9) | 4 (11.4) | 5 (14.3) | 6 (17.1) | 2 (5.7) | 2 (5.7) |
| **Yes, sensitivity analysis** |  | 3 (1.7) | 1 (2.9) |  | 2 (5.7) |  |  |
| Followed Check List,  n (%) | **No** | 0 | 171 (97.7) | 34 (97.1) | 34 (97.1) | 34 (97.1) | 35 (100.0) | 34 (97.1) |
| **STROBE** |  | 4 (2.3) | 1 (2.9) | 1 (2.9) | 1 (2.9) |  | 1 (2.9) |
| Analytic Tools Used ,  n (%) | **CART Salford Predictive Miner** | 0 | 1 (0.6) | 1 (2.9) |  |  |  |  |
| **Didn't mention** |  | 28 (16.0) | 6 (17.1) | 5 (14.3) | 8 (22.9) | 3 (8.6) | 6 (17.1) |
| **EZR** |  | 1 (0.6) |  |  |  |  | 1 (2.9) |
| **Excel** |  | 1 (0.6) |  |  |  |  | 1 (2.9) |
| **GraphPad Prism** |  | 1 (0.6) |  |  |  |  | 1 (2.9) |
| **JMP** |  | 1 (0.6) | 1 (2.9) |  |  |  |  |
| **Mplus** |  | 1 (0.6) | 1 (2.9) |  |  |  |  |
| **NCSS** |  | 1 (0.6) |  |  |  |  | 1 (2.9) |
| **MedCalc** |  | 1 (0.6) |  | 1 (2.9) |  |  |  |
| **Epidata** |  | 1 (0.6) |  |  |  |  | 1 (2.9) |
| **R** |  | 20 (11.4) |  | 2 (5.7) | 5 (14.3) | 9 (25.7) | 4 (11.4) |
| **SAS** |  | 41 (23.4) | 8 (22.9) | 8 (22.9) | 10 (28.6) | 10 (28.6) | 5 (14.3) |
| **SigmaPlot** |  | 1 (0.6) |  |  |  |  | 1 (2.9) |
| **SPSS ( & PASW Statistics)** |  | 50 (28.6) | 11 (31.4) | 13 (37.1) | 10 (28.6) | 10 (28.6) | 6 (17.1) |
| **Stata** |  | 37 (21.1) | 7 (20.0) | 10 (28.6) | 3 (8.6) | 8 (22.9) | 9 (25.7) |
| **Statistica** |  | 1 (0.6) | 1 (2.9) |  |  |  |  |
| **Statview** |  | 1 (0.6) | 1 (2.9) |  |  |  |  |

Table 7 Database Filed Definitions

|  |  |  |
| --- | --- | --- |
| Article |  | Source of truth for article entities; data taken from EndNote |
|  | EndNote\_ID | From EndNote |
|  | Article\_Name | From EndNote |
|  | Abstract | From EndNote |
|  | Author\_Institution | From EndNote |
|  | Year | From EndNote |
|  | Journal | From EndNote |
|  | PubMed\_ID | From EndNote |
|  | L\_Key\_Words | From EndNote |
|  | Language | From EndNote |
|  | DOI | From EndNote |
| Article\_Review |  | One row per review; allows multiple reviews per article |
|  | Recode\_Review\_ID | Primary Key |
|  | Reviewer\_ID | DD.Keyworks List |
|  | EndNote\_Index | Foreign key for Article table |
|  | Article\_Name | vlookup from Article table |
|  | Review\_Date | Manually enter timestamp |
|  | First\_Author | Manually enter |
|  | Key\_words | Manually enter |
|  | Research\_Design(Primary Objective) | Manually enter |
|  | Review/Original | Manually enter |
|  | Study\_Design\_Type | Select from DD.Keywords\_List Study Type |
|  | Database/Datasource | Manually enter |
|  | Analytic\_tool | Manually enter |
|  | Country/district | Manually enter |
|  | X | Manually enter |
|  | Y | Manually enter |
|  | Z | Manually enter |
|  | Association\_Type | Manually enter |
|  | Unit\_of\_Analysis | Manually enter |
|  | Check\_List | Manually enter |
|  | Mentioned\_Mission\_Data | Manually enter |
|  | Addressed\_Missing\_Data | Manually enter |
|  | Rate\_of\_Article | Manually enter |
|  | Include\_in\_Research | Manually enter |
|  | Exclusion Reason | Select from Exclusion Criteria(DD.Keywords\_List) |
|  | Real-World\_Method | TRUE/FALSE searched from Methods\_Used\_ In\_Literature table |
|  | Sensitivity\_Analysis | TRUE/FALSE searched from Methods\_Used\_ In\_Literature table |
|  | Other\_Notes |  |
| Methods\_Used\_in\_Literatures |  | One row per analytic method; enables multiple methods per review |
|  | ML\_ID | Methods records ID |
|  | Review\_ID | foreign key for Article\_Review table |
|  | EndNote\_ID | Foreign key for Article table |
|  | Analytic\_Method\_ID | foreign key for DD.Analytic\_Method table |
|  | Real\_World\_Evidence | vlookup from DD.Analytic\_Method table |
| Analytic\_Method |  |  |
|  | Analytic\_Method\_ID | Primary Key |
|  | Analytic\_Method\_Name | Manually enter |
|  | Method\_Category | Enter based on Guidelines |
|  | Domain | Manually enter |
|  | Definition | Manually enter |
|  | Definition\_Source | Manually enter |
|  | Reference\_Paper | Manually enter |
| DD.Keywords |  |  |
|  | Study\_Design\_Type | A list generated from reading process |
|  | Exclusion Reason | A list defined before reading |
|  | Reviewer | A list defined before reading |
|  | MeSH\_Term | A list extracted from EndNote |